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No Baby to Bring Home: Perinatal Loss, Infertility, and Mental Illness—Overview and Recommendations for Care

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Abstract

Purpose of Review Update readers on the state of the research on mental health, perinatal loss, and infertility with a focus on providing a comprehensive overview to empower clinicians in treating this population.

Recent Findings Rates of psychiatric illness are increased in people that experience perinatal loss and infertility. The research remains largely below the clear need for focused screening, prevention, and treatment.

Summary Clinicians and researchers need to remain attuned to the impact of perinatal loss and infertility on the mental health of patients and families. Screening, referral, and expanded therapeutic and psychiatric resources are imperative to improving the well-being of these patients and families.

Keywords Reproductive psychiatry · Grief · Postpartum depression · Postpartum anxiety · Pregnancy loss · Infertility

Introduction

Perinatal loss and infertility are common and debilitating for many individuals and families. One in five pregnancies will end in perinatal loss — miscarriage, stillbirth, or neonatal death [1]. Of married couples trying to conceive, one in five is unable to get pregnant after a year of trying, the standard definition of infertility [2]. In the USA in 2021, there were 3.66 million live births [3], which means, there are likely at least a million individuals that experienced perinatal loss or infertility — and many more if you consider partners and other family members.

In this review, we will discuss the psychological impact of pregnancy loss and infertility including miscarriage (loss < 20 weeks gestation), recurrent miscarriage (2 or more losses), stillbirth (loss ≥ 20 weeks gestation), and neonatal death (death within the first 28 days of life).

Our aim is to provide an overview of the experiences of perinatal loss and infertility for mothers and families to better inform and empower treating clinicians, provide tools to support this population, and demonstrate the need for more research in identification, prevention, and intervention of the psychological sequelae.

Perinatal Loss and Neonatal Death

The burden of perinatal loss has come to greater international attention with the series of articles in *The Lancet* in 2016 focused on stillbirths (a follow-up to a 2011 call to action) and in 2021 focused on miscarriage [4, 5••, 6–12]. In both series, the focus was on worldwide reforms on care, prevention of losses, particularly in stillbirth, and reduction of economic and psychosocial consequences. Unfortunately, the psychological burden remains clearly present and concerning but with suboptimal recognition, research, and without clear treatment guidelines.

Etiology in Loss

Perinatal loss has many causes, both fetal and maternal. Of clinically recognized pregnancies, about 10% end in miscarriage and 80% of these miscarriages happen in the

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first trimester [13, 14]. Many miscarriages occur without any clinical contact (i.e., without the first prenatal visit around 8–10 weeks of gestation). When considering these, combined with those that are reported, rates of loss may be as high as 30% and increase with age (≥ 35 years) [15]. Overall, about 50% of first trimester losses are due to chromosomal abnormalities; however, this rate varies with maternal age (with increased maternal age being associated with a higher rate of chromosomal abnormalities) [16]. Independent of maternal age, a history of prior pregnancy loss is a risk factor for recurrent loss [15]. Maternal medical conditions such as infection (particularly syphilis), obesity, thyroid disease, and diabetes are also associated with pregnancy loss [17–21]. Unlike maternal age and chromosomal abnormalities, however, some of the risk conferred by maternal medical conditions can be mitigated. While there are many known causes of pregnancy loss, and associated risk factors, nearly half of all miscarriages are without clear cause [22]. While early pregnancy losses are generally deemed part of normal reproduction, the lack of a clear "why" can have significant psychological implications for patients [23].

Stillbirth, or pregnancy loss from 20 weeks gestation to term, is much less common, occurring in fewer than 1% of pregnancies [24]. Comprehensive evaluation of stillbirths may reveal a probable cause; however, a definite cause is often elusive. There are many risk factors for stillbirth including maternal age, nulliparity, smoking, obesity, hypertensive disorders, diabetes, and autoimmune disease. In developed countries, disparities including being a member of a minority population, particularly Black women, low socio-economic status, rural locations, and low educational attainment, were all risk factors for stillbirth — in some cases leading to triple the rate of stillbirth [25, 26]. Common causes of stillbirth include fetal growth restriction, placental abruption, genetic and structural abnormalities, infection, and umbilical cord abnormalities, although, in many cases, no definitive cause is found.

Neonatal death, or death within 28 days of delivery, may be related to the aforementioned risk factors for stillbirth such as fetal growth restriction, placental abruption, genetic and structural abnormalities, infection, and umbilical cord abnormalities. Preterm birth (especially in the setting of extreme prematurity or low birth weight), intrapartum complications (including hypoxia), infection, and congenital malformations are the leading causes of neonatal death [27].

Consideration of Maternal Complications

Maternal medical issues can lead to perinatal loss and may also complicate the post loss experience. For women with pregnancy-related illnesses, such as preeclampsia with severe features, delivery may be required for maternal health. In rare cases of preeclampsia at a previable gestational age, termination of pregnancy may be recommended given the associated severe maternal morbidity and mortality with continuation of pregnancy. In many of these cases, mothers are critically ill, and the focus is on management of their medical illness. Mothers experiencing loss may not be medically stable enough to be emotionally and cognitively present at birth.

Role of Psychiatric Illness in Perinatal Loss

Research has been mixed on the role of untreated psychiatric illness in the etiology of miscarriage; however, a registry study out of Norway found that a wide range of psychiatric disorders were associated with an increased risk of miscarriage with adjusted odds ratios ranging from 1.07 to 1.27 for (in increasing order): eating disorders, unspecified mental illness, somatoform disorders, anxiety disorder, depressive disorders, schizophrenia spectrum disorders, attentional disorders, and bipolar disorders. Bipolar disorders had the highest aOR at 1.27 [28].

Standard Obstetric Care

Management of first trimester pregnancy loss depends on the clinical situation and may include medical management (with medications to expedite or facilitate passage of the pregnancy) or surgical management (with dilation and curettage). In some cases, a pregnancy passes spontaneously, and no intervention is required. For patients with recurrent pregnancy loss, evaluation may include a genetic evaluation of the products of conception, parental karyotype, uterine cavity evaluation, and serum labs for antiphospholipid antibodies.

Stillbirth encompasses a wide range of gestational ages, from 20 weeks to term. Depending on the gestational age at the time of stillbirth, either an induction with vaginal delivery or uterine evacuation with dilation and extraction is performed. In rare cases, a cesarean delivery may be required.

With induction and delivery for losses at more advanced gestational age, some studies have found that the opportunities to say goodbye, see (or not see) the fetus/baby (including an opportunity to have extended time with them in the postpartum room), have memories captured (i.e., photos together, birth blanket or cap, stuffed animal with recording of fetal heartbeat), and have a postmortem evaluation were perceived as contributing to healing, decreasing anxiety, and allowed for better coping with grief [29].

In addition to delivery management, a comprehensive evaluation for the cause of stillbirth should be offered to all patients [30]. This evaluation should include fetal autopsy and placental pathology which provides additional

information in up to 30% of cases. In addition, cytogenetic testing should be offered and can provide additional information in 8% of cases. Maternal evaluation should include testing for syphilis and antiphospholipid antibodies (lupus anticoagulant, anticardiolipin antibodies, and beta 2 glycoprotein). Routine testing for inherited thrombophilia is not recommended but may be considered in cases with a personal or family history of thromboembolism [31].

State Considerations

In the USA, each state has different legal considerations when it comes to medical management of perinatal loss. For example, some states regulate the management of fetal remains after a certain gestational age (i.e., patient or parents must decide on burial or cremation after 20 weeks gestation). Additionally, when maternal health is compromised, states have different regulations around when a pregnancy can be terminated for risk to maternal life. As a clinician, it is important to know the regulations of your state, as a patient's experience of perinatal loss management can be impacted by these regulatory differences.

Grief

Unsurprisingly, grief, or bereavement, is a common response to perinatal loss, occurring in up to 80% of all patients [32]. More concerning is the high rate of persistent complex grief (previously called complicated grief): 25–30% of parents that experience perinatal loss demonstrate persistent complex grief, three times higher than in other grief reactions [23]. Even with many studies demonstrating increased rates of grief in this population, there is minimal research into the trajectory of grief, whether complicated or uncomplicated. Some studies have found that grief declines significantly in the first six months but can persist for many years afterwards.

Davidson's model for perinatal bereavement is as follows as articulated by Rich in 2018 recommendations to obstetricians [33]:

1. Weeks 2–4: *Shock and numbness*—bereaved parents experience episodes of unreality alternating with emotional intensity. It is during this time when families are sharing news and potentially planning for handling of fetal/newborn remains.
2. Months 1–3: *Searching and yearning* — marked by profound longing for a relationship with the deceased child. Parents experience sleep disruption, decreased appetite, and difficulty with daily routines. There can be preoccupation with memorializing baby/pregnancy.
3. Months 4–6: *Disorientation* — a time of coming to terms with the new normal including forced adaptation and grappling with the reality of a lost baby.
4. Months 9–12: *Reintegration* – parents become more actively involved in life including normal activities and future planning. At this point, there is often also a subsequent pregnancy.

Grief can take on many permutations in both length and intensity, but often lessens with time, education, and social support. Complex grief, however, involves prolonged intense attachment to the lost child/pregnancy, feelings of guilt and blame, displaced anger, rejections of consolation, recurrent thoughts that life is meaningless, potential urges to join the deceased, ruminations, anger, bitterness, trouble trusting others, and avoidance or withdrawal from life. In these circumstances, reintegration can be viewed as a betrayal to the lost baby.

Beyond Grief: Psychiatric Illness

There are few studies that have used clinical evaluation of mental illness following perinatal loss in the USA. Instead, the majority of studies have relied on self-reported scales or, in a few cases, diagnostic codes in electronic medical records. A meta-analysis of 29 international studies following pregnancy loss in 2022 confirmed prior studies that perinatal loss increases the risk of depression ($RR = 2.14$) and anxiety disorders ($RR = 1.27$) when compared to controls. Interestingly, they found no increased rate of post-traumatic stress [34]. Gestational age was associated with increased rates of depression and anxiety.

Another expansive retrospective study out of Florida captured over a million singleton pregnancies from 2005–2014, of which 0.7% resulted in stillbirth ($n = 8812$) [35••]. After excluding women with pre-existing psychiatric morbidity, the primary outcomes were coding of psychiatric morbidity during an Emergency Department visit or inpatient hospitalization within a year of loss. Adjusted odds ratios for stillborn singletons versus liveborn singletons were as follows: 3.16 for suicide attempt, 2.75 of depression, 2.29 for anxiety, 2.27 for psychosis, 4.36 PTSD, 1.66 acute stress reaction, 4.15 adjustment disorders, 2.53 for drugs use/dependence, and 2.69 for alcohol use/dependence. There findings are further supported by another study following miscarriage and ectopic pregnancy that demonstrated cross-sectional rates of post-traumatic stress up to 34%, anxious symptoms up to 30%, and depressive symptoms up to 10% [36].

Black women suffer perinatal loss as disproportionate levels and, per one study, also have double the risk of depression compared to non-Black women as assessed by Center for Epidemiology Studies-Depression scale [37•].

Screening

While grief is a common and normal process following perinatal loss, screening for grief remains important for obstetric, primary, and psychiatric practitioners to assess severity, progress, and potential need for referral. A systematic review of instruments in 2020 found that The Perinatal Grief Scale (PGS) was the most commonly used [38]. The PGS is a 33-item 5-point Likert scale screener that groups results into subscales for active grief, difficulty coping, and despair [39].

While it is important to screen for grief severity, further screening for psychiatric conditions is also important as referral to counseling alone may not be sufficient for treatment. As with all perinatal patients, screening for both prior history of mental illness and screening for anxiety and depression with validated instruments (such as the Edinburgh Perinatal Depression Scale [40]) are also advised. Unfortunately, there is little research on validated scales for differentiating grief from depression following perinatal loss.

Treatment Options

Robust research into treatment remains lacking globally and particularly in the USA.

Immediate Treatment Considerations

There are various recommendations in obstetric literature for sharing a fetal loss diagnosis and of delivery management. While recommendations can be mixed, the overall considerations include patient-centered care to assist in shared decision making — This includes asking about seeing/holding a stillborn/fetus, taking photos, and providing mementos. As above, the early phase of grief includes shock and numbness, so providing patients with referrals, follow-up, and information that they can reference later is beneficial. This may include local loss groups, online resources such as Postpartum Support International (www.postpartum.net), and the national maternal mental health hotline (1–833-852–6262 (1–833-TLC-MAMA)) [40].

Therapy

A scoping review of therapeutic treatments for psychological trauma following perinatal loss in 2021 found only four studies targeting perinatal bereavement [41]. Overall, they found that psychosocial interventions are effective in reducing depression, anxiety, and grief, particularly when there is a component of early couples counseling. Four sessions of grief counseling were effective post-stillbirth in another study [42]. Overall, more research is needed but it remains clear that a space for processing loss is beneficial for the majority of mothers and families following loss.

In practice, therapy should include taking a thorough psychiatric and reproductive history as well as screening for mood, anxiety, stress, and suicidality.

Psychopharmacology

As noted in a review by Bhat and Byatt in 2016, there is a dearth of research into pharmacological treatment following perinatal loss [43••]. This has remained consistent over the last 7 years. In practice, a thorough psychiatric history can provide a roadmap for monitoring and treatment in the post-loss period. Because while grief can take many forms, treatment of depression, anxiety, PTSD, and other underlying conditions are necessary to allow patients to grieve. The aim is not to prevent grief, but rather to promote healthy grieving and reduce the risk of complex grief or psychiatric illness. More research is needed to understand how and if experiencing trauma during pregnancy differ biologically from other trauma.

Practice Recommendation Based on Our Experience

Given the overwhelming lack of specific evidence-based guidance, we recommend a few specific approaches to evaluation and treatment of psychiatric sequalae to loss based on our clinical experience and general evidence-based guidelines. First is a comprehensive initial intake including medical, reproductive, and psychiatric history to identify risk factors. Evaluation should include acute symptoms and a safety assessment of suicidal thoughts, basic self-maintenance, and ability to care for other children in the household. The presence of neurovegetative symptoms that last longer than a few days and/or active suicidal thoughts usually indicates depression superimposed on grief. In the first 4–6 months of loss, we also recommend frequent follow-up to assess changes in symptoms severity. In practice, it is this close follow-up that reveals whether grief is progressing as outlines above or whether depression, anxiety, or PTSD have developed.

Finally, we recommend brief psychoeducation about trajectory of grief (that it is a normal and healthy response to loss) and traumatic responses, and safety planning should symptoms become more acute. Additionally, we provide local resources for groups or online education. If a patient demonstrates more acute psychiatric needs, several psychotherapies may be beneficial. Specifically, we have found Prolonged Exposure, a gold standard treatment of PTSD, to be beneficial for PTSD among women experiencing neonatal traumas, including stillbirth and traumatic loss [44]. Additionally, Acceptance and Commitment Therapy may be helpful for general grief, depression, and anxiety, as evidenced by its effectiveness in other loss populations (e.g., [45, 46]). Pharmacologically, once bipolar illness has been thoroughly ruled out, serotonin reuptake inhibitors often provide relief

for anxiety and depression. Because many patients go on to try to conceive again, it is important to have discussions about the risks of medications versus the risks of not pursuing treatment. The use of benzodiazepines during this period, particularly early on, remains understudied.

Future Pregnancies

Between 50 and 80% of women will conceive again following loss with 86% occurring within 18 months [47]. Prior studies have demonstrated increased rates of anxiety and depression in pregnancies following perinatal loss. In one study, out the UK that followed 112 women through a post-loss pregnancy, the authors found elevated levels of anxiety, depression, and cortisol levels from 15 weeks gestation to 6 weeks postpartum [48]. In another study of nearly 2 million Medicaid beneficiaries between 1999 and 2012, women with prior pregnancy loss were 35% more likely to require psychiatric treatment in the six months following a live birth. Additionally, 99% of women with a psychiatric history prior to their pregnancy loss required psychiatric treatment in the 6 months following a live birth [49].

Clinical Pearls

- While grief is very common, it is imperative to screen for other mental illnesses following loss.
- Frequent follow-up, particularly during the first 4–6 months following loss, can assist in differentiating grief from other mental illnesses.
- Early referral and brief therapy can be effective and should be pursued.
- Attention to mental health treatment and stress reduction in pregnancy following loss is critical.
- More research, clinical focus, and workforce training is needed.

Infertility

Causes

Infertility is a global health problem, defined by the failure to achieve a viable pregnancy after a year of regular unprotected intercourse if under age 35, or after 6 months of unprotected intercourse if over age 35 [50]. Causes of infertility are able to be identified in approximately 85% of cases, with the remaining 15% of cases having unknown etiology [51]. Infertility can be due to both male and female factors, underlying chronic disease or genetics, or lifestyle and environmental factors (e.g., smoking and obesity). The most common causes of infertility include ovulatory disorder, male factor infertility (e.g., low sperm count or poor sperm motility), and tubal disease; however, other common causes include endometriosis, diminished ovarian reserve, and uterine and cervical factors [51]. Psychological factors, such as depression and anxiety, are implicated in infertility struggles and infertility treatment outcomes; evidence is conflicting as to whether psychological factors are causes of infertility, effects, or some combination thereof [52••].

Preconception, Obstetrical Course, and Perinatal Risks

Approximately 50% of individuals diagnosed with infertility will engage in treatment to aid in conception [43••], resulting in medical burden prior to conception. Infertility treatment duration ranges from just over a year to more than 10 years, based on the cause, types of intervention needed, and recurrence of losses [43••, 53]. Therapeutic strategies depend on the cause of infertility and include pharmacological therapy (e.g., ovulation induction via clomiphene citrate or letrozole), surgery, and other types of assisted reproductive technology (ART; e.g., intrauterine insemination and in vitro fertilization with or without intracytoplasmic sperm injection) [50, 51]. Many individuals undergoing ART will face recurrent implantation failures and threatened or recurrent miscarriage [54, 55]. Such losses increase the risk of negative psychological outcomes.

Given the varied etiologies of infertility, there is no standard obstetrical course for individuals with infertility and many pregnancies will follow the typical standard of care. However, obstetrical course can be complicated by both the treatment of and causes for infertility. For example, ART and ovulation-inducing pharmacotherapy increase the risk for twin pregnancies, which enhances risk for perinatal morbidity and mortality. Adverse obstetric outcomes are more common in twin pregnancies conceived via ART than conceived naturally [56]. A systematic review and meta-analysis revealed that even among singleton pregnancies, IVF and ICSI are also associated with an increased relative risk for antepartum hemorrhage, congenital anomalies, preterm rupture of membranes, cesarean section, low birthweight, perinatal mortality, preterm delivery, gestational diabetes, induction of labor, and small for gestation age [57]. Relatedly, many of the underlying causes of infertility, such as polycystic ovarian syndrome and endometriosis, are associated with their own obstetrical risks irrespective route of conception, including risk of preterm delivery, placenta previa, and preeclampsia [58, 59]. As such, the cumulative effects of stress associated with prolonged lack of conception, potential for medical intervention with high side effect burden, possibility of multiple implantation failures and losses, and increased obstetric risks, converge to increase the risk for psychiatric sequelae.

Psychiatric Sequela

Infertility is associated with a variety of psychological struggles in both partners attempting to conceive, and evidence suggests that psychological impacts can persist across the lifespan [60]. Specifically, research demonstrates higher rates of overall stress [61], depression and associated guilt and self-blame [61, 62•, 63•, 64•, 65]. However, there is some evidence to suggest that a history of infertility can be protective against suicidal ideation and behavior among those who are able to conceive. High levels of distress or long duration of infertility are also associated with a higher risk of developing alcohol or other substance dependency in both partners [52••, 66••, 65]. During pregnancy, there is mixed evidence regarding increased risk for pregnancy-associated anxiety and depression following infertility [67, 68], with some research suggesting that pre-pregnancy infertility duration and history of treatment failures may explain the conflicting results [69]. Of the minimal evidence currently available, history of infertility does appear to confer slightly increased risk of postpartum mental health complications [70].

Infertility can also cause impairment in functioning. Specifically, psychiatric complications of infertility can be both a cause and effect of impaired sexual functioning in both genders [66••, 71], with many couples reporting that intimacy develops negative connotations (e.g., failure, chore-like). Furthermore, infertility is associated with relationship dissatisfaction [71], increased isolation [65], and general lower reported quality of life [64•].

Risk and Protective Factors for Psychological Complications

Factors that increase risk for psychological complications to infertility include:

Biological Among those trying to conceive, female sex confers greater risk than male sex for psychiatric complications of infertility [72]. Recent studies also suggest a shared genetic risk between infertility and depression [73]. Additionally, certain medications used to treat infertility via hormonal modulation can exacerbate affective dysregulation and risk for psychological disorders [61]. Poorer sleep quality was also predictive of anxiety and depression in individuals undergoing IVF [74]; however, the temporal nature of this relationship is unclear.

Social and Economic Stigmatization of infertility confers greater risk for adverse psychological outcomes and is more likely in pronatalist societies [75]. Cohabitation and divorce in infertile couples are associated with worse psychological outcomes [76]. Finally, economic burden of fertility treatments is associated with stress, anxiety, and depression in both genders [77].

Experiences of Infertility Extended duration of infertility, such as three to five years or more, is linked to higher risk of adverse psychological outcomes [76]. Relatedly, previous failures of ART treatment [78] and delay in receiving treatment for infertility are also independent risk factors [79]. Finally, lack of resolution of infertility [80], lack of living children [76], and loss after ART-based treatments [65] also increase risk.

Psychological Personality traits such as negative affectivity and social inhibition confer risk for depression in infertility [81]. Additionally, characteristics such as intolerance of uncertainty [82] and somatization [74] increase risk for both depression and anxiety. Finally, cognitive appraisals related to self-blame [83], negative consequences of infertility, lack of perceived control, illness coherence [84], and beliefs about the centrality of motherhood [85] were all related to adverse psychological outcomes in individuals coping with infertility.

Protective Factors of Psychological Outcomes Higher levels of self-compassion [86], self-esteem [72, 87], and resilience [88] are inversely related to psychological distress. Additionally, emotional expression and emotional self-disclosures provided protective effects [86, 89]. Marital and family functioning, perception of support from the marital partner, and higher levels of social support were also inversely related to adverse outcomes [90, 91]. Finally, religious based coping strategies, especially in pronatalist societies, helped protect against depression [92, 93], lending support for the benefit of culturally adapted treatments.

Treatment Guidelines

Despite the high rates of mental health symptoms among men and women seeking fertility treatment, there are low rates of education about mental health symptoms and services, and correspondingly low mental health service utilization [94]. As such, best practices highlight the importance of all medical providers involved in infertility assessment and treatment to provide education on common psychological, sexual, and relational outcomes associated with infertility and its treatments, alongside warning signs and guidelines for accessing care [66••, 71].

There are a number of interventions well poised to support the psychological and relational health of people with infertility, including psychotherapies, pharmacotherapies, alternative treatments, and adjustments to medical care delivery. Psychotherapeutic approaches are the most well-studied and meta-analysis suggests that when compiled, psychological interventions are associated with small effects on distress and moderate effects on conception rates [95]. Cognitive behavioral therapy (CBT) and mind–body therapies

(e.g., Mindfulness Based Stress Reduction) demonstrate the strongest evidence for treatment of depression and anxiety in men, women, and couples with infertility [96, 97, 98••, 99•, 100], to different cultures [101•], demonstrated prophylactic utility in a single session intervention [102], and has been successfully modified to be administered over the internet with noninferior results to standard face-to-face CBT [88]. Mind–body interventions have similarly been successfully adapted to group settings [103], self-guided programs [104], and mobile applications and internet-based programs [105]. A meta-analysis suggests that CBT is particularly beneficial for depression and infertility, whereas mind–body therapies are particularly beneficial for anxiety in infertility; both approaches demonstrate improvements in conception rates [97]. Other group and individual therapies with preliminary evidence include Acceptance and Commitment therapy (ACT), positive psychotherapy [100], and self-compassion training [106]. Among couples, in addition to CBT and mind–body therapies, behavioral couple therapy [107] and ACT [108] show promise in mental health symptom reduction. For women experiencing infertility and sexual dysfunction, psychosexual therapy, a combination of mindfulness-based cognitive therapy, behavioral sex therapy, and relaxation training, resulted in significant improvement in sexual functioning and was superior to medication [109].

There is also evidence for the role of pharmacotherapy in the treatment of mental health symptoms and sexual functioning during infertility. A variety of selective serotonin reuptake inhibitors (SSRIs) are used in the treatment of mental health symptoms during infertility, with recent studies using sertraline, fluoxetine, and escitalopram. In a triple-arm randomized control trial (RCT) for women with infertility and recurrent pregnancy loss, there was a comparison between CBT, sertraline, and treatment as usual (TAU) on depression and anxiety symptoms [110]. For anxiety, sertraline was the only intervention that produced clinically significant reductions in anxiety, though these results were not maintained at follow-up. For depression, CBT outperformed sertraline, and both were superior to TAU; results replicated previous research demonstrating that CBT was superior to fluoxetine in the treatment of depression during infertility [111]. Another RCT examined the prophylactic use of escitalopram in women meeting criteria for adjustment disorder and undergoing IVF. Results indicated that short-term SSRI treatment was protective against worsening depression and anxiety symptoms [112]. Finally, bupropion-extended release, a norepinephrine and dopamine reuptake inhibitor, has been used in the treatment of sexual dysfunction in women experiencing infertility [109]. Of note, in this RCT, bupropion was superior to the control group but inferior to psychosexual therapy, so psychotherapy should be considered the frontline treatment for sexual dysfunction unless there are issues with treatment accessibility or acceptability.

Alternative treatments, including yoga, meditation, acupuncture, and adjustments to the delivery of medical care, have all shown promise in psychological symptom reduction among people with infertility. Yoga, both alone and in combination with meditation, demonstrates significant and consistent reductions in anxiety [113], as well as depression and stress, and improvement in pregnancy outcomes [113]. Both needle and laser acupuncture demonstrated improvement to ART outcomes, anxiety, and depressive symptoms; needle acupuncture results in superior outcomes over laser [114, 115]. Finally, a few medical care adaptations show promise for supporting mental health during infertility. For example, emphasis on education [116], use of an online healthcare platforms emphasizing education and communication [117], and case management [118] are all associated with decreased psychological symptoms and increased patient satisfaction.

Clinical Pearls

- The stress of infertility can be compounded by the physical and psychological effects of treatment, possibility of recurrent loss and implantation failure, and increased obstetrical and neonatal risks.
- Infertility most commonly results in anxiety, depression, and grief, along with impacting relationships and sexual functioning.
- Education on the possible psychological impacts and availability of treatment is a vital step to increasing treatment engagement among women, men, and couples.
- A variety of treatment approaches show strong evidence for improving psychological distress, including psychotherapy, pharmacology, and alternative treatments.
- There is a small evidence base for prophylactic treatment, including a single session of CBT or prescription of escitalopram.

Conclusions

Perinatal loss and infertility are complex experiences for patients and their treatment teams. While much more research and training in necessary, it is clear from our clinical experience that patients and families demonstrate incredible resilience when faced with these obstacles. A continued focus on collaborative efforts between obstetrics, family medicine, and psychiatry will be vital in mitigating poor outcomes.

Data Availability This is a review of existing literature. No separate data was analyzed for the purposes of this manuscript.

Declarations

Conflict of Interest Julia N. Riddle receives funding from the Foundation of Hope for pilot research and serves on the advisory board for cercle.ai for which she received stock options. Tiffany Hopkins declares no conflicts. Amanda Yeaton-Massey chairs the NIMH-funded MInD study data safety monitoring board, serves on the clinical advisory board for the Policy Center for Maternal Mental Health, and was a consultant for Seven Starling from July 2022 to May 2023 for which she received financial compensation. Samantha Hellberg received funding from International OCD Foundation (IOCDF) Michael Jenike Young Investigator Award and the National Science Foundation Graduate Research Fellowship (NSF GRFP; #DGE-1650116).

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References

Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance

1. Dugas C, Slane VH. Miscarriage. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 [cited 2023 Mar 1]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK532992/.
2. NSFG - listing I - key statistics from the National Survey of Family Growth [Internet]. 2022 [cited 2023 Sep 6]. Available from: https://www.cdc.gov/nchs/nsfg/key_statistics/i-keystat.htm.
3. Hamilton BE. Births: provisional data for 202. 2021.
4. Lancet T. Miscarriage: worldwide reform of care is needed. The Lancet. 2021;397(10285):1597.
5. •• Quenby S, Gallos ID, Dhillon-Smith RK, Podesek M, Stephenson MD, Fisher J, et al. Miscarriage matters: the epidemiological, physical, psychological, and economic costs of early pregnancy loss. Lancet. 2021;397(10285):1658–67. **Important overview of the global impact of stillbirths.**
6. Coomarasamy A, Gallos ID, Papadopoulou A, Dhillon-Smith RK, Al-Memar M, Brewin J, et al. Sporadic miscarriage: evidence to provide effective care. The Lancet. 2021;397(10285):1668–74.
7. Coomarasamy A, Dhillon-Smith RK, Papadopoulou A, Al-Memar M, Brewin J, Abrahams VM, et al. Recurrent miscarriage: evidence to accelerate action. Lancet. 2021;397(10285):1675–82.
8. Heazell AEP, Siassakos D, Blencowe H, Burden C, Bhutta ZA, Cacciatore J, et al. Stillbirths: economic and psychosocial consequences. Lancet. 2016;387(10018):604–16.
9. Lawn JE, Blencowe H, Waiswa P, Amouzou A, Mathers C, Hogan D, et al. Stillbirths: rates, risk factors, and acceleration towards 2030. Lancet. 2016;387(10018):587–603.
10. Flenady V, Wojcieszek AM, Middleton P, Ellwood D, Erwich JJ, Coory M, et al. Stillbirths: recall to action in high-income countries. Lancet. 2016;387(10019):691–702.
11. de Bernis L, Kinney MV, Stones W, ten Hoope-Bender P, Vivio D, Leisher SH, et al. Stillbirths: ending preventable deaths by 2030. Lancet. 2016;387(10019):703–16.
12. Frøen JF, Friberg IK, Lawn JE, Bhutta ZA, Pattinson RC, Allanson ER, et al. Stillbirths: progress and unfinished business. Lancet. 2016;387(10018):574–86.
13. Wilcox AJ, Weinberg CR, O'Connor JF, Baird DD, Schlatterer JP, Canfield RE, et al. Incidence of early loss of pregnancy. N Engl J Med. 1988;319(4):189–94.
14. Wang X, Chen C, Wang L, Chen D, Guang W, French J. Conception, early pregnancy loss, and time to clinical pregnancy: a population-based prospective study. Fertil Steril. 2003;79(3):577–84.
15. Magnus MC, Wilcox AJ, Morken NH, Weinberg CR, Håberg SE. Role of maternal age and pregnancy history in risk of miscarriage: prospective register based study. BMJ. 2019;20(364):l869.
16. American College of Obstetricians and Gynecologists. Early pregnancy loss. ACOG Practice Bulletin No. 200. Obstet Gynecol 2018;132:e197–207.
17. Giakoumelou S, Wheelhouse N, Cuschieri K, Entrican G, Howie SEM, Horne AW. The role of infection in miscarriage. Hum Reprod Update. 2016;22(1):116–33.
18. Metwally M, Ong KJ, Ledger WL, Li TC. Does high body mass index increase the risk of miscarriage after spontaneous and assisted conception? A meta-analysis of the evidence. Fertil Steril. 2008;90(3):714–26.
19. Maraka S, Ospina NMS, O'Keeffe DT, Espinosa De Ycaza AE, Gionfriddo MR, Erwin PJ, et al. Subclinical hypothyroidism in pregnancy: a systematic review and meta-analysis. Thyroid. 2016;26(4):580–90.
20. Evers IM, de Valk HW, Visser GHA. Risk of complications of pregnancy in women with type 1 diabetes: nationwide prospective study in the Netherlands. BMJ. 2004;328(7445):915.
21. Kitzmiller JL, Wallerstein R, Correa A, Kwan S. Preconception care for women with diabetes and prevention of major congenital malformations. Birth Defects Res A Clin Mol Teratol. 2010;88(10):791–803.
22. Practice Committee of the American Society for Reproductive Medicine. Evaluation and treatment of recurrent pregnancy loss: a committee opinion. Fertil Steril. 2012;98(5):1103–11.
23. Kokou-Kpolou K, Megalakaki O, Nieuviarts N. Persistent depressive and grief symptoms for up to 10 years following perinatal loss: involvement of negative cognitions. J Affect Disord. 2018;1(241):360–6.
24. Gregory ECW, Valenzuela CP, Hoyert DL. Fetal mortality: United States, 2020. National Vital Statistics Reports; vol 71 no 4. Hyattsville, MD: National Center for Health Statistics. 2022.
25. Stillbirth Collaborative Research Network Writing Group. Causes of death among stillbirths. JAMA. 2011;306(22):2459–68.
26. Flenady V, Middleton P, Smith GC, Duke W, Erwich JJ, Khong TY, et al. Stillbirths: the way forward in high-income countries. Lancet. 2011;377(9778):1703–17.
27. Heron M. Deaths: leading causes for 2015. Natl Vital Stat Rep. 2017;66(5):1–76.
28. Magnus MC, Havdahl A, Morken NH, Wensaas KA, Wilcox AJ, Håberg SE. Risk of miscarriage in women with psychiatric disorders. Br J Psychiatry. 2021;219(3):501–6.
29. Burden C, Bradley S, Storey C, Ellis A, Heazell AEP, Downe S, et al. From grief, guilt pain and stigma to hope and pride – a systematic review and meta-analysis of mixed-method research of the psychosocial impact of stillbirth. BMC Pregnancy Childbirth. 2016;16(1):9.
30. Page JM, Christiansen-Lindquist L, Thorsten V, Parker CB, Reddy UM, Dudley DJ, et al. Diagnostic tests for evaluation of stillbirth: results from the stillbirth collaborative research network. Obstet Gynecol. 2017;129(4):699–706.
31. ACOG Practice Bulletin No. 102: management of stillbirth. Obstet Gynecol. 2009;113(3):748–61.
32. Mergl R, Quaatz SM, Edeler LM, Allgaier AK. Grief in women with previous miscarriage or stillbirth: a systematic review of cross-sectional and longitudinal prospective studies. Eur J Psychotraumatol. 2022;13(2):2108578.

33. Rich D. Psychological impact of pregnancy loss: best practice for obstetric providers. Clin Obstet Gynecol. 2018;61(3):628–36.
34. Herbert D, Young K, Pietrusińska M, MacBeth A. The mental health impact of perinatal loss: a systematic review and meta-analysis. J Affect Disord. 2022;15(297):118–29.
35.•• Lewkowitz AK, Rosenbloom JI, Keller M, López JD, Macones GA, Olsen MA, et al. Association between stillbirth ≥23 weeks gestation and acute psychiatric illness within 1 year of delivery. Am J Obstet Gynecol. 2019;221(5):491.e1-491.e22. **Comprehensive claims data in Florida (n = 8812) demonstrates high aOR was suicide attempts and psychiatric illness as collected from inpatient and ED admission.**
36. Farren J, Jalmbrant M, Falconieri N, Mitchell-Jones N, Bobdiwala S, Al-Memar M, et al. Differences in post-traumatic stress, anxiety and depression following miscarriage or ectopic pregnancy between women and their partners: multicenter prospective cohort study. Ultrasound Obstet Gynecol. 2021;57(1):141–8.
37.• Shorter JM, Koelper N, Sonalkar S, Oquendo MA, Sammel MD, Schreiber CA. Racial disparities in mental health outcomes among women with early pregnancy loss. Obstet Gynecol. 2021;137(1):156–63. **Study on the racial disparities of loss and mental illness.**
38. Setubal MS, Bolibio R, Jesus RC, Benute GG, Gibelli MA, Bertolassi N, et al. A systematic review of instruments measuring grief after perinatal loss and factors associated with grief reactions. Palliat Support Care. 2021;19(2):246–56.
39. Toedter LJ, Lasker JN, Alhadeff JM. The Perinatal Grief Scale: development and initial validation. Am J Orthopsychiatry. 1988;58(3):435–49.
40. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression: development of the 10-item Edinburgh Postnatal Depression Scale. Br J Psychiatry. 1987;150(6):782–6.
41. Human Resources and Services Administration, Maternal & Child Health. National Maternal Mental Health Hotlines. Last reviewed June 2023. https://mchb.hrsa.gov/national-maternal-mental-health-hotline.
42. Hollins Martin CJ, Reid K. A scoping review of therapies used to treat psychological trauma post perinatal bereavement. J Reprod Infant Psychol. 2022:1–17.
43.•• Shaohua L, Shorey S. Psychosocial interventions on psychological outcomes of parents with perinatal loss: a systematic review and meta-analysis. Int J Nurs Stud. 2021;1(117):103871. **Global meta-analysis of psychosocial interventions following loss. Demonstrates both the dearth of data and the necessity of early intervention.**
44. Bhat A, Byatt N. Infertility and perinatal loss: when the bough breaks. Curr Psychiatry Rep. 2016;18(3):31.
45. Hopkins T, Hellberg S. Assessing and treating PTSD from obstetrical and neonatal traumas: a case series. J Prenat Perinat Psychol Health. 2022;36(2):28–41.
46. Jones K, Methley A, Boyle G, Garcia R, Vseteckova J. A systematic review of the effectiveness of acceptance and commitment therapy for managing grief experienced by bereaved spouses or partners of adults who had received palliative care. Illn Crisis Loss. 2022;30(4):596–613.
47. Malmir T, Jafari H, Ramezanalzadeh Z, Heydari J. Determining the effectiveness of acceptance and commitment therapy (ACT) on life expectancy and anxiety among bereaved patients. Mater Sociomed. 2017;29(4):242.
48. Charrois EM, Mughal MK, Arshad M, Wajid A, Bright KS, Giallo R, et al. Patterns and predictors of depressive and anxiety symptoms in mothers affected by previous prenatal loss in the ALSPAC birth cohort. J Affect Disord. 2022;15(307):244–53.
49. Thomas S, Stephens L, Mills TA, Hughes C, Kerby A, Smith DM, et al. Measures of anxiety, depression and stress in the antenatal and perinatal period following a stillbirth or neonatal death: a multicentre cohort study. BMC Pregnancy Childbirth. 2021;10(21):818.
50. Reardon DC, Craver C. Effects of pregnancy loss on subsequent postpartum mental health: a prospective longitudinal cohort study. Int J Environ Res Public Health. 2021;18(4):2179.
51. Tavousi SA, Behjati M, Milajerdi A, Mohammadi AH. Psychological assessment in infertility: a systematic review and meta-analysis. Front Psychol. 2022;28(13):961722.
52.•• Carson SA, Kallen AN. Diagnosis and management of infertility: a review. JAMA. 2021;326(1):65. **Article provides a recent comprehensive review of the causes of and treatment for infertility.**
53. Hegyi BE, Kocsis K, Király A, Kazinczi C, Ando B, Kovács I, et al. Clustering infertile couples with dyadic approach: WHO-5-WBI as a promising tool for assessing psychological state. Psychol Belg. 2020;60(1):152–63.
54. Allow AK. The relationship between duration of infertility and intrauterine insemination: a multi-centers study. J Clin Dev Biol [Internet]. 2016 [cited 2023 Jun 29];1(3). Available from: http://clinical-developmental-biology.imedpub.com/the-relationship-between-duration-of-infertility-and-intrauterine-insemination-a-multicenters-study.php?aid=11105.
55. Szamatowicz M. Assisted reproductive technology in reproductive medicine — possibilities and limitations. Ginekol Pol. 2016;87(12):820–3.
56. Bashiri A, Halper KI, Orvieto R. Recurrent implantation failure-update overview on etiology, diagnosis, treatment and future directions. Reprod Biol Endocrinol. 2018;16(1):121.
57. Wang Y, Shi H, Chen L, Zheng D, Long X, Zhang Y, et al. Absolute risk of adverse obstetric outcomes among twin pregnancies after in vitro fertilization by maternal age. JAMA Netw Open. 2021;4(9):e2123634.
58. Pandey S, Shetty A, Hamilton M, Bhattacharya S, Maheshwari A. Obstetric and perinatal outcomes in singleton pregnancies resulting from IVF/ICSI: a systematic review and meta-analysis. Hum Reprod Update. 2012;18(5):485–503.
59. Kobayashi H, Kawahara N, Ogawa K, Yoshimoto C. A relationship between endometriosis and obstetric complications. Reprod Sci. 2020;27(3):771–8.
60. Berlanda N, Alio W, Angioni S, Bergamini V, Bonin C, Boracchi P, et al. Impact of endometriosis on obstetric outcome after natural conception: a multicenter Italian study. Arch Gynecol Obstet. 2022;305(1):149–57.
61. Vikström J, Josefsson A, Bladh M, Sydsjö G. Mental health in women 20–23 years after IVF treatment: a Swedish cross-sectional study. BMJ Open. 2015;5(10):e009426.
62.• Sharma A, Shrivastava D. Psychological problems related to infertility. Cureus [Internet]. 2022 [cited 2023 Jun 29]; Available from: https://www.cureus.com/articles/115993-psychological-problems-related-to-infertility. **Article provides a comprehensive review of common psychological sequelae to infertility.**
63.• Kiani Z, Simbar M, Hajian S, Zayeri F, Shahidi M, Saei Ghare Naz M, et al. The prevalence of anxiety symptoms in infertile women: a systematic review and meta-analysis. Fertil Res Pract. 2020;6(1):7. **Article completes a systematic review and meta-analysis of anxiety symptoms during infertility.**
64.• Kiani Z, Simbar M, Hajian S, Zayeri F. The prevalence of depression symptoms among infertile women: a systematic review and meta-analysis. Fertil Res and Pract. 2021;7(1):6. **Article completes a systematic review and meta-analysis of depression symptoms during infertility.**
65. Dadhwal V, Choudhary V, Perumal V, Bhattacharya D. Depression, anxiety, quality of life and coping in women with infertility: a cross-sectional study from India. Intl J Gynecol Obstet. 2022;158(3):671–8.
66.•• De Castro MHM, Mendonça CR, Noll M, De Abreu Tacon FS, Do Amaral WN. Psychosocial aspects of gestational

grief in women undergoing infertility treatment: a systematic review of qualitative and quantitative evidence. IJERPH. 2021;18(24):13143. **Article fills a gap in the literature examining the overlap between recurrent loss and infertility, as well as unique psychological presentations associated with its' co-occurrence.**

67. Patel A, Sharma PSVN, Kumar P. Role of mental health practitioner in infertility clinics: a review on past, present and future directions. J Hum Reprod Sci. 2018;11(3):219.
68. Salih Joelsson L, Tydén T, Wanggren K, Georgakis MK, Stern J, Berglund A, et al. Anxiety and depression symptoms among sub-fertile women, women pregnant after infertility treatment, and naturally pregnant women. Eur psychiatr. 2017;45:212–9.
69. Simoni MK, Gilstad-Hayden K, Naqvi SH, Pal L, Yonkers KA. Progression of depression and anxiety symptoms in pregnancies conceived by assisted reproductive technology in the United States. J Psychosom Obstet Gynecol. 2022;43(2):214–23.
70. Hashemieh C, Neisani L, Taghinejad H. Assessment of anxiety in pregnancy following assisted reproductive technology (ART) and associated infertility factors in women commencing treatment. Iran Red Crescent Med J [Internet]. 2013 [cited 2023 Jun 30];15(12). Available from: https://archive.ircmj.com/article/15/12/71476-pdf.pdf.
71. Dayan N, Velez MP, Vigod S, Pudwell J, Djerboua M, Fell DB, et al. Infertility treatment and postpartum mental illness: a population-based cohort study. CMAJ Open. 2022;10(2):E430–8.
72. Quinlivan JA, Lambregtse van Den Berg M. More than a number – time to implement agreed psychological outcomes for infertility clinics. J Psychosom Obstet Gynecol. 2022;43(1):1–1.
73. Fang M, Li G, Kang X, Hou F, Lv G, Xu X, et al. The role of gender and self-esteem as moderators of the relationship between stigma and psychological distress among infertile couples. Psychol Health Med. 2021;26(10):1181–94.
74. Ma M, Guo L, Liu X, Zheng Y, Gu C, Li B. Genetic correlation between female infertility and mental health and lifestyle factors: a linkage disequilibrium score regression study. Health Sci Rep [Internet]. 2022 [cited 2023 Jun 29];5(5). Available from: https://onlinelibrary.wiley.com/doi/10.1002/hsr2.797.
75. Wang L, Tang Y, Wang Y. Predictors and incidence of depression and anxiety in women undergoing infertility treatment: a cross-sectional study. Di Giuseppe J, editor. PLoS ONE. 2023;18(4):e0284414.
76. Yokota R, Okuhara T, Okada H, Goto E, Sakakibara K, Kiuchi T. Association between stigma and anxiety, depression, and psychological distress among Japanese women undergoing infertility treatment. Healthcare. 2022;10(7):1300.
77. Teklemicheal AG, Kassa EM, Weldetensaye EK. Prevalence and correlates of infertility related psychological stress in women with infertility: a cross-sectional hospital based survey. BMC Psychol. 2022;10(1):91.
78. Abdishahshahani M, Torabi M, Kazemi A. Investigating related factors to psychological symptoms of infertile couples undergoing assisted reproductive treatment. J Educ Health Promot. 2020;9:21.
79. Sohbati F, Hasanpoor-Azghady SB, Jafarabadi M, Amiri-Farahani L, Mohebbi M. Psychological well-being of infertile women and its relationship with demographic factors and fertility history: a cross-sectional study. BMC Womens Health. 2021;21(1):22.
80. Jaiswal P, Mahey R, Singh S, Vanamail P, Gupta M, Cheluvaraju R, et al. Psychological impact of suspension/postponement of fertility treatments on infertile women waiting during COVID pandemic. Obstet Gynecol Sci. 2022;65(2):197–206.
81. Shreffler KM, Greil AL, Tiemeyer SM, McQuillan J. Is infertility resolution associated with a change in women's well-being? Hum Reprod. 2020;35(3):605–16.
82. Tola EN, Eris Yalcin S, Dugan N, Oral B. The association of type D personality and depression with infertility in women. J Psychosom Obstet Gynecol. 2020;41(2):98–105.
83. Mitrović M, Kostić JO, Ristić M. Intolerance of uncertainty and distress in women with delayed IVF treatment due to the COVID-19 pandemic: the mediating role of situation appraisal and coping strategies. J Health Psychol. 2022;27(11):2515–28.
84. Guštin K, Globevnik Velikonja V, Vrtačnik-Bokal E, Lep Ž, Svetina M. Self-blame predicts anxiety and depression in infertile couples who opt for in vitro fertilisation (IVF) treatment. Psychol Health Med. 2023;28(6):1562–71.
85. Moutzouri M, Sarantaki A, Gourounti K. The association of cognitive representations with psychological adjustment in experience of infertility and fertility treatment: a systematic review. Eur J Midwifery. 2021;5:33.
86. Foti FL, Karner-Huţuleac A, Maftei A. The value of motherhood and psychological distress among infertile women: the mediating role of coping strategies. Front Public Health. 2023;2(11):1024438.
87. Hoyle RH, Davisson EK, Novice ML. Relations between protective traits and psychological distress among women experiencing infertility. J Health Psychol. 2022;27(2):397–407.
88. Cui C, Wang L, Wang X. Effects of self-esteem on the associations between infertility-related stress and psychological distress among infertile Chinese women: a cross-sectional study. Psychol Res Behav Manag. 2021;14:1245–55.
89. Shafierizi S, Faramarzi M, Nasiri-Amiri F, Chehrazi M, Basirat Z, Kheirkhah F, et al. Therapist-guided internet-based cognitive behavioral therapy versus face-to-face CBT for depression/anxiety symptoms in infertile women with adjustment disorders: a randomized controlled trial. Psychother Res. 2023;33(6):803–19.
90. Kim M, Hong JE, Ban M. Mediating effects of emotional self-disclosure on the relationship between depression and quality of life for women undergoing in-vitro fertilization. Int J Environ Res Public Health. 2021;18(12):6247.
91. Li X, Wang K, Huo Y, Zhou M. The effect of infertility-related stress on Chinese infertile females' mental health: the moderating role of marital adjustment. Psych J. 2019;8(2):232–9.
92. Adelosoye AA, Fasipe OJ, Medunoye EI, Adelosoye OC, Sunday EO. Assessment of family function impact on depression severity among infertile women attending a teaching hospital in South-South Nigeria. Future Sci OA. 2020;6(8):FSO595.
93. Nouman H, Benyamini Y. Religious women's coping with infertility: do culturally adapted religious coping strategies contribute to well-being and health? IntJ Behav Med. 2019;26(2):154–64.
94. Honarvar N, Taghavi M. Relation of religious coping and depression levels in infertile women. Iran J Psychiatry. 2020;15(2):134–42.
95. Pasch LA, Holley SR, Bleil ME, Shehab D, Katz PP, Adler NE. Addressing the needs of fertility treatment patients and their partners: are they informed of and do they receive mental health services? Fertil Steril. 2016;106(1):209-215.e2.
96. Dube L, Bright K, Hayden KA, Gordon JL. Efficacy of psychological interventions for mental health and pregnancy rates among individuals with infertility: a systematic review and meta-analysis. Hum Reprod Update. 2023;29(1):71–94.
97. Masoumi SZ, Parsa P, Kalhori F, Mohagheghi H, Mohammadi Y. What psychiatric interventions are used for anxiety disorders in infertile couples? A systematic review study. IJPS [Internet]. 2019 [cited 2023 Jun 27]; Available from: https://publish.knepublishing.com/index.php/IJPS/article/view/996.
98.•• Zhou R, Cao YM, Liu D, Xiao JS. Pregnancy or psychological outcomes of psychotherapy interventions for infertility: a meta-analysis. Front Psychol. 2021;31(12):643395. **Article conducts a meta-analysis examining effects of various psychological interventions on common psychological problems and conception rates in people experiencing infertility.**
99.• Abdollahpour S, Taghipour A, Mousavi Vahed SH, Latifnejad RR. The efficacy of cognitive behavioural therapy on stress, anxiety

and depression of infertile couples: a systematic review and meta-analysis. J Obstet Gynaecol. 2022;42(2):188–97. **Article completes a systematic review and meta-analysis regarding the effects of CBT on common psychological sequelae in infertile couples.**

100. Patel A, Sharma PSVN, Kumar P. Application of mindfulness-based psychological interventions in infertility. J Hum Reprod Sci. 2020;13(1):3.
101.• Warne E, Oxlad M, Best T. Evaluating group psychological interventions for mental health in women with infertility undertaking fertility treatment: a systematic review and meta-Analysis. Health Psychol Rev. 2022;11:1–25. **Article completes a systematic review and meta-analysis regarding the effects group psychotherapy interventions on common psychological sequelae during infertility.**
102. Naab F, Brown R, Ward EC. Culturally adapted depression intervention to manage depression among women with infertility in Ghana. J Health Psychol. 2021;26(7):949–61.
103. Heredia A, Padilla F, Castilla JA, Garcia-Retamero R. Effectiveness of a psychological intervention focused on stress management for women prior to IVF. J Reprod Infant Psychol. 2020;38(2):113–26.
104. Kalhori F, Masoumi SZ, Shamsaei F, Mohammadi Y, Yavangi M. Effect of mindfulness-based group counseling on depression in infertile women: randomized clinical trial study. Int J fertil Steril [Internet]. 2020 [cited 2023 Jun 27];14(1). Available from: https://doi.org/10.22074/ijfs.2020.5785.
105. Bai CF, Cui NX, Xu X, Mi GL, Sun JW, Shao D, et al. Effectiveness of two guided self-administered interventions for psychological distress among women with infertility: a three-armed, randomized controlled trial. Human Reprod. 2019;34(7):1235–48.
106. Meyers AJ, Domar AD. Research-supported mobile applications and internet-based technologies to mediate the psychological effects of infertility: a review. Reprod Biomed Online. 2021;42(3):679–85.
107. Alireza Afshani S, Abooei A, Mohamad Abdoli A. Self-compassion training and psychological well-being of infertile female. IJRM [Internet]. 2019 [cited 2023 Jun 27]; Available from: https://knepublishing.com/index.php/ijrm/article/view/5300.
108. Ahmadi SM, Shahverdi J, Rezaei M, Bakhtiari M, Sadeghi K, Veisy F, et al. The effect of behavioral couple therapy on the improvement of mental health and reduction of marital conflict in infertile couples in Kermanshah: a randomized controlled trial (RCT). J Reprod Infertil. 2019;20(1):16.
109. Hosseinpanahi M, Mirghafourvand M, Farshbaf-Khalili A, Esmaeilpour K, Rezaei M, Malakouti J. The effect of counseling based on acceptance and commitment therapy on mental health and quality of life among infertile couples: a randomized controlled trial. J Edu Health Promot. 2020;9(1):251.
110. Pasha H, Basirat Z, Faramarzi M, Kheirkhah F. Is psychosexual therapy a reliable alternative to bupropion extended-release to promote the sexual function in infertile women? An RCT. Int J Reprod Biomed [Internet]. 2020 [cited 2023 Jun 28]; Available from: https://knepublishing.com/index.php/ijrm/article/view/6714.
111. Basirat Z, Kheirkhah F, Faramarzi M, Esmaeilzadeh S, Khafri S, Tajali Z. Treatment of depression in infertile women with recurrent pregnancy loss: a triple-arm randomized controlled trial of pharmacotherapy vs psychotherapy. Int J fertil Steril [Internet]. 2021 [cited 2023 Jun 27];(Online First). Available from: https://doi.org/10.22074/ijfs.2021.529258.1124.
112. Faramarzi M, Kheirkhah F, Esmaelzadeh S, Alipour A, Hjiahmadi M, Rahnama J. Is psychotherapy a reliable alternative to pharmacotherapy to promote the mental health of infertile women? A randomized clinical trial. Eur J Obstet Gynecol Reprod Biol. 2008;141(1):49–53.
113. Aisenberg Romano G, Fried Zaig I, Halevy A, Azem F, Amit A, Bloch M. Prophylactic SSRI treatment for women suffering from mood and anxiety symptoms undergoing in vitro fertilization—a prospective placebo-controlled study. Arch Womens Ment Health. 2019;22(4):503–10.
114. Demir Yıldırım A, Güngör Sİ. The effects of yoga on pregnancy, stress, and anxiety in infertile individuals: a systematic review. Holist Nurs Pract. 2022;36(5):275–83.
115. Taguchi R, Sato K, Adomi S, Tanaka N, Tamura H, Tamura T. Acupuncture and laser acupuncture as treatments for emotional distress in infertile women in Japan. Med Acupunct. 2019;31(6):372–8.
116. Hullender Rubin LE, Smith CA, Schnyer RN, Tahir P, Pasch LA. Effect of acupuncture on IVF-related anxiety: a systematic review and meta-analysis. Reprod Biomed Online. 2022;45(1):69–80.
117. Farnia F, Aflatoonian A, Kalantari A. Comparing the effects of nursing versus peer-based education methods on the preoperative anxiety in infertile women: an RCT. Int J Reprod Biomed [Internet]. 2019 [cited 2023 Jun 27]; Available from: https://knepublishing.com/index.php/ijrm/article/view/5795.
118. Ye L, Chen J, Qi Q, Zhou J, Zhu C, Jiang Y, et al. A physician-nurse partnership *via* online healthcare platforms protects infertile women from anxiety and depression: a multi-center prospective study from Shanghai, China. Glob Health Med. 2022;4(5):273–7.