

EMPIRICAL ARTICLE

A Randomized Controlled Trial of an iCBT Program to Reduce Infertility-Related Stress: A Novel Digital Approach

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ABSTRACT

The global burden of infertility and its associated psychological distress is substantial, yet many individuals face barriers to accessing psychological support. A scalable, low-cost online intervention presents a promising solution. A randomized controlled trial (RCT) was conducted (experimental vs. waitlist control group) to evaluate the efficacy of a fully automated cognitive behavioral therapy (CBT) program in reducing infertility-related stress among women attempting to conceive. Data were analyzed using linear mixed models on an intention-to-treat basis. The study enrolled 63 Icelandic women experiencing infertility-related stress. The intervention, *Overcome Fertility Stress*, is an online program designed to identify and modify maladaptive behaviors and thought patterns contributing to infertility-related distress. It delivers personalized treatment through prewritten text, audio, and video responses based on user input. Infertility-related stress was measured using the 46-item Fertility Problem Inventory (FPI), which assesses a global stress score and five domains of infertility-related stress. Participants in the experimental group demonstrated a significant reduction in infertility-related stress (mean reduction score = 22.85, $p < 0.05$), whereas the control group showed no significant changes ($p > 0.05$). The within-group effect was large, but controlled between-group effects and confidence intervals should be prioritized when interpreting treatment benefit. These findings provide preliminary controlled evidence that a fully automated CBT program may reduce infertility-related stress, although the underpowered sample and low adherence require cautious interpretation. This RCT, alongside prior feasibility studies, suggests that *Overcome Fertility Stress* may be a promising low-intensity intervention for infertility-related stress. No significant effects were observed on secondary outcomes measuring depression, anxiety, stress, or worry, suggesting the program is specific to infertility-related stress rather than a broader intervention for emotional disorder symptoms. Larger, adequately powered trials with stronger engagement strategies are needed. Future research should focus on expanding access and integrating digital psychological support into standard fertility care.

1 | Introduction

1.1 | Infertility

Annually, approximately 48.5 million couples worldwide struggle with infertility, which affects roughly one in six people (17.5) at some point in their lifetime (Mascarenhas et al. 2012; World Health Organization 2023). Infertility is a medical condition defined as the inability to achieve a clinical pregnancy after

engaging in regular, unprotected intercourse for twelve months or longer (World Health Organization 2019). This definition emphasizes the length and characteristics of the unsuccessful reproductive effort, which is used as a standardized criterion for diagnosis and research.

Infertility can profoundly affect emotional well-being, and the resulting stress affects many aspects of a person's life, including interpersonal relationships, social dynamics, economic stability, and

Key Points

- Infertility affects roughly 1 in 6 people and is linked to elevated anxiety and depression, yet access to evidence-based psychological interventions is limited, and randomized controlled evidence is sparse.
- In a randomized controlled trial, the Overcome Fertility Stress program, a fully automated, unguided internet-based CBT intervention, lowered infertility-related stress in women compared with a waitlist control.
- The program appears to target infertility-specific distress rather than acting as a broad mental-health intervention, as general depression, anxiety, and worry did not change.
- Larger, adequately powered trials with stronger adherence strategies are needed to confirm these preliminary effects.

psychological well-being (Luk and Loke 2015; Umesh et al. 2021). The term “infertility-related stress” refers to the combination of emotional, psychological, and societal challenges that individuals or couples grappling with fertility issues may routinely meet (Hazlina et al. 2022; Luk and Loke 2015; Newton et al. 1999).

Research indicates a markedly higher rates of depression (45%–57%) and anxiety (40%–76%) among people with infertility than in the general population (Lakatos et al. 2017; Pasch et al. 2016). Women tend to bear a greater share of this burden than men, often reporting elevated anxiety, depression and stress, along with lower self-worth (Dhaliwal et al. 2004; Wright et al. 1991). Miles et al. (2009) found that roughly 27% of women regard infertility as the most difficult be the most difficult experience of their lives.

Despite the risk of significant psychological distress stemming from infertility, only a small proportion (about 8.5%) of women experiencing infertility seek professional mental health counseling for their infertility-related stress symptoms (Boivin et al. 1999).

1.2 | Current Treatments for Infertility Stress

Recent literature has provided more evidence to support the effectiveness of Cognitive Behavioral Therapy (CBT) in lowering infertility-related stress, as well as reducing depressive and anxiety symptoms in infertile women (Faramarzi et al. 2008; Karaca et al. 2019; Zahra et al. 2019). The emergence of Internet-based Cognitive Behavioral Therapy (iCBT), a therapeutic modality that has been adapted for digital delivery, offers an opportunity for broader accessibility and engagement across varied demographics (Krämer et al. 2022; McCall et al. 2018; Pang et al. 2021). The growing popularity of iCBT is consistent with the trend in healthcare towards mental health solutions that are more accessible, cost-effective, and scalable (Pang et al. 2021). Despite the availability of numerous online programs for individuals dealing with infertility, there is a notable deficiency in empirical data to substantiate the effectiveness of these digital interventions (Meyers and Domar 2021). As a consequence, this study looks to contribute to bridging this gap by evaluating

the efficacy of an Internet-based Cognitive Behavioral Therapy (iCBT) program called “Overcome Fertility Stress” (OFS) in the context of infertility-related stress, focusing particularly on gathering and analyzing empirical data to measure its effectiveness.

The “Overcome Fertility Stress” (OFS) program is a tailored solution leveraging the principles of Internet-based Cognitive Behavioral Therapy (iCBT) to alleviate the psychological burden on individuals experiencing reproductive difficulties. The program sets up a patient-centered therapy regimen tailored to the unique cognitive, emotional, and behavioral patterns associated with infertility. A feasibility study of the OFS program, conducted in 2021 with 35 infertile women as participants, revealed a statistically significant decline in infertility-related stress. The effect sizes ranged from small to large across various metrics, underscoring the potential therapeutic efficacy of the intervention (Bjornsdottir et al. 2023).

iCBT programs targeting infertility-related stress are well positioned to address the cognitive and behavioral processes that maintain distress, including perseverative worry, avoidance of infertility-related social situations, and unhelpful interpretive patterns around fertility outcomes. The OFS program specifically targets these processes in Module 3 (Thoughts and Worries), where participants learn to identify and modify repetitive negative thinking associated with infertility.

1.3 | The Current Study

The current study is a randomized controlled trial (RCT), aiming to examine the efficacy of the Overcome Fertility Stress (OFS) program, a web-based iCBT intervention for women experiencing infertility. Participants were randomly assigned to either the treatment group or the waitlist control group. The main research question of this study is: *Is a web-based Cognitive Behavioral Therapy (CBT) treatment effective in reducing infertility-related stress in infertile women?* Building on this inquiry, the primary hypothesis was that subjects in the treatment condition would show a statistically significant reduction in infertility-related stress indices post-intervention compared to their counterparts in the waitlist condition.

Additionally, the secondary hypothesis was that the treatment group would show decreases in additional psychological distress factors, including symptoms of depression, anxiety, stress, and worry, as measured from baseline to the follow-up evaluation, compared to the waitlist control group. This study therefore looks to provide empirical evidence supporting the efficacy of digital therapeutic approaches in reproductive health.

2 | Method

2.1 | Participants

Participants were 63 Icelandic women who were experiencing infertility-related stress as a result of fertility difficulties. The mean age was 34.52 years (SD = 5.62; range 22–44). The recruitment process took place in the autumn of 2023–spring of 2024 and involved printed advertisements in clinics and other

locations that this demographic was likely to visit, as well as social media posts, social media advertisements, and media coverage. The requirements for inclusion were: (a) having a history of infertility lasting 12 months or longer; (b) the participant had to be a woman, 18 years of age or older; (c) the participant was not currently receiving cognitive behavioral therapy (CBT) for stress related to infertility; (d) the participant had to have access to a working email address and a computer with internet access; and (e) the participant had to be literate in Icelandic or English.

2.2 | Measures

2.2.1 | Fertility Problem Inventory (FPI) (Newton et al. 1999)

The 46-item FPI scale is a self-report tool used for evaluating infertility-related stress. A global infertility-related stress score (*Global Score*) is calculated from five domains: “*Social Concerns*” evaluates sensitivity to infertility-related remarks and feelings of isolation; “*Sexual Concerns*” measures issues like low sexual pleasure and difficulties with planned sexual activity due to infertility; “*Relationship Concerns*” assesses challenges in discussing infertility and its impact on relationships; “*Need for Parenthood*” measures identification with the parental role and the importance placed on parenthood; and “*Rejection of Childfree Lifestyle*” examines negative views towards a childfree life and the belief that happiness depends on having children (Newton et al. 1999). Psychometric properties of the FPI are believed to be sufficient (Bjornsdottir et al. 2023; Clifton et al. 2020; Sexton et al. 2010).

2.2.2 | Depression Anxiety and Stress Scale (DASS-21) (Lovibond and Lovibond 1995)

A 21-item measure with three subscales, each containing seven items: Depression, Anxiety, and Stress. Each item is rated on a 4-point scale, ranging from 0 (“never”) to 3 (“almost always”), meaning a higher score indicates more depression, anxiety, or stress. In studies using clinical samples, the DASS-21 has shown good internal consistency (Page et al. 2007).

2.2.3 | Penn State Worry Questionnaire (PSWQ) (Meyer et al. 1990)

A 16-item measure widely used as a self-assessment tool for measuring levels of worry experienced by people in various aspects of their lives. Each item is rated on a five-point scale, ranging from 1 (“not typical of me”) to 5 (“very typical of me”), with higher scores indicating more severe worry symptoms. Psychometric properties of the PSWQ are believed to be sufficient (Meyer et al. 1990).

2.3 | Design and Procedure

The study protocol was prospectively registered and received full approval from the Icelandic National Bioethics Committee (clinical study registration number: VSN-23-076). The goal of this randomized control trial was to investigate the efficacy of an online standalone intervention which targets infertility-related

stress among women aged 18–45 years. The allocation sequence was generated by the first author (S.H.) using a random number function in Microsoft Excel for Microsoft 365 MSO (Version 2403), independently of recruitment. Each participant received a randomly generated number between 0 and 1; participants were then ranked in ascending order and evenly split, with the lower half assigned to the control group and the upper half to the treatment group. All authors were blind to randomization, ensuring no researcher involved in recruitment could predict or influence assignment. Data were analyzed on an intention-to-treat basis using Linear mixed models.

Participants registered for the study through a customized QuestionPro intake webpage. They received an introductory letter detailing the research purpose, involved researchers, study processes, methodologies, and potential risks and benefits. Afterward, they completed an informed consent form, followed by baseline questionnaires and background information.

The participants who matched the inclusion criteria were randomly assigned to one of two groups: the treatment or the waitlist control group. Consequently, eligible treatment group members received an e-mail holding an access code for their 3-month OFS account. All communication with participants took place via e-mail during the research period. After three months of treatment, all study participants received an email with a link to an e-questionnaire for post-assessment measures.

Participants were assigned unique IDs linked to their personal information for confidentiality. Only the first author, who ensured strict confidentiality, had access to the raw data. These IDs anonymized the data, protected privacy, and enabled an unbiased review of the results.

The intervention, Overcome Fertility Stress (OFS) (Table 1; Bjornsdottir et al. 2023) is an iCBT program for those dealing with infertility-related stress. OFS is a customized internet-based intervention that does not involve the direct participation of a therapist (unguided iCBT). The OFS program comprises seven steps in total: a pre-assessment phase, five therapeutic modules, and a post-assessment phase. The pre-assessment includes the FPI, DASS-21, and PSWQ which help tailor the program for each individual.

Five modules are part of the program: 1: “*Getting Started*” with psycho-educational content; 2: “*Behaviors*” where participants receive guidance to recognize unhelpful behavior; 3: “*Thoughts and Worries*”, where participants learn to recognize negative thoughts associated with infertility; 4: “*Relationships*”, which covers interpersonal skills; and finally, 5: “*Redefine Your Life*”, where the individuals are encouraged to reinvent their lives and move forward, where the primary focus is not exclusively on having a child. The post-assessment phase comprises the FPI and DASS-21, completing the seven-step program structure. Table 1 provides a detailed description of each module's aims, core CBT techniques, and user tasks. Throughout the program, a clinical psychologist provides instructions via prepared audio or video clips, or text. Automated emails are sent to participants to promote program adherence. These emails include reminders after each module is finished, if the participants have not logged in for a set number of days, and a summary of each section of the program. Finally, at the end of the therapy, participants

TABLE 1 | Overview of the Overcome Fertility Stress (OFS) program modules.

Module	Title	Content
	Pre-questionnaires	Automatic administration of the DASS-21 and FPI to create an individualized participant profile
A	Getting started	Introduction to basic CBT concepts, psychoeducation about infertility-related stress, coping strategies, and cognitive biases that may contribute to myths about conception
B	Behaviors	Introduction to the behavioral component of CBT, including how behavior impacts emotions and contributes to long-term difficulties. Participants identify their own patterns of behavioral avoidance from a list of common responses to infertility-related stress, then complete behavioral experiments tailored to their individual avoidance patterns
C	Thoughts and worries	Exploration of the role of thoughts on mood, identification and re-evaluation of unhelpful thoughts, a directed worry experiment, and coping strategies for stress, uncertainty, grief, and loss. Superstitions about conception are also addressed. Participants identify their own unhelpful thoughts and worries from a list of common infertility-related concerns, and receive cognitive exercises tailored to their specific selections, including sample therapist responses that model how to challenge and reframe those particular thoughts
D	Relationships	Focus on social pressure and relationships, including strategies for disclosing infertility to others, handling unhelpful comments, preparing for challenging social situations, and improving relationship and sexual wellbeing with a partner
E	Redefine your life	Encouragement to focus on the future independent of parenthood outcomes, including goal-setting exercises and discussion of a childfree lifestyle
	Post-questionnaires	Re-administration of the DASS-21 and FPI, presentation of pre- and post-treatment scores, and provision of a downloadable PDF of all program materials

Abbreviations: CBT = Cognitive Behavioral Therapy, DASS-21 = Depression Anxiety Stress Scale, FPI = Fertility Problem Inventory.

can download an e-book with program content. In this study, complete treatment is defined as the completion of four or more modules, with a threshold reflecting the average completion rate for such programs (Bjornsdottir et al. 2023; Clifton et al. 2020). This level of engagement is considered sufficient for participants to potentially benefit from the therapy, although completing all modules is encouraged.

2.4 | Statistical Analysis

A priori power analysis was conducted to determine the required sample size for detecting statistically significant difference between the groups, with significance level of 0.05 and power set at 0.80. The analysis indicated a minimum sample size of 51 per group was needed to detect a clinically relevant difference on the FPI.

Demographic characteristics and adherence to treatment were summarized using descriptive statistics. To compare baseline demographic and adherence characteristics between groups (e.g., treatment vs. control), we used the *tableone* package in R. Furthermore, *tableone* package was used to analyze differences among non-users, dropouts, and completers of the trial.

To account for repeated measurements within subjects and variability across participants, Linear mixed models (LMM) were implemented in SPSS to analyze repeated measures, incorporating both fixed effects of time and group, their interaction, and random effects with random intercepts for subjects over time. The missing data was not imputed. An intent-to-treat approach

included all randomized participants in the analysis, with missing data addressed through Maximum Likelihood, using all available data points and acknowledging within-subject correlation. Of the 32 treatment and 31 control participants randomized, 9 and 19, respectively, contributed post-treatment data on the FPI Global Score; counts for secondary outcomes are reported in Table 2 in the results section.

The linear mixed model assumes that data are missing at random (MAR), meaning that missingness can be accounted for by observed variables in the model. Given that some participants did not activate the program and thus did not provide post-treatment data, the plausibility of this assumption should be noted when interpreting results.

The effect sizes of between-group comparisons were quantified using Cohen's *d*. Effect sizes were classified as small ($d > 0.2$), medium ($d > 0.5$), and large ($d > 0.8$) (Cohen 1988). The threshold for statistical significance in all analyses was set at $p < 0.05$ (Cohen 1988). Statistical analyses were conducted in R and SPSS version 28.

3 | Results

3.1 | Retention of Participants

A total of 86 women expressed interest in the study (see Figure 1 for participant flow). One applicant was excluded for not meeting inclusion criteria, and 22 did not complete the pre-assessments. The remaining 63 were randomized into two groups: 32 in the

TABLE 2 | Effects of treatment over time: Linear mixed-model analysis of control and treatment group simple effects and group $\times$ time interaction effects.

Groups		Waitlist-control group			Treatment group		Treatment versus waitlist control group × time						
Outcome	Pre M (SE)	Post M (SE)	p	Pre M (SE)	Post M (SE)	p	B	df	F	t	p	w-d	b-d
FPI													
Global score	164.07 (4.66)	168.88 (5.05)	0.176	165.68 (4.44)	142.85 (6.03) ^{*,**}	<0.001	−27.64	27.85	20.43	−4.52	<0.001	1.70	2.0
Social	39.68 (1.78)	40.39 (1.83)	0.592	36.80 (1.74)	30.96 (2.24) ^{*,**}	0.005	−6.56	28.41	7.82	−2.80	0.009	1.82	1.27
Sexual	26.34 (1.18)	27.24 (1.32)	0.472	25.70 (1.13)	22.22 (1.72) ^{*,**}	0.044	−4.39	27.57	5.97	−2.12	0.043	0.63	1.06
Relationship	25.97 (1.54)	26.95 (1.73)	0.481	29.03 (1.47)	27.05 (2.12)	0.284	−2.96	27.11	1.70	−1.30	0.204	0.53	0.71
Child	30.77 (1.15)	30.41 (1.35)	0.770	30.34 (1.11)	24.91 (1.77) ^{*,**}	0.003	−5.07	38.03	5.96	−2.44	0.019	0.66	0.83
Parenthood	42.39 (1.47)	43.63 (1.30)	0.274	43.03 (1.43)	40.22 (1.94)	0.081	−4.05	29.60	4.47	−2.12	0.043	0.44	0.77
DASS-21													
Depression	16.07 (1.65)	15.43 (2.03)	0.747	14.12 (1.60)	11.09 (2.71)	0.259	−2.40	39.14	0.532	−0.73	0.470	0.39	0.45
Anxiety	9.48 (1.35)	9.87 (1.59)	0.779	6.3 (1.31)	6.94 (2.05)	0.737	0.25	33.76	0.012	−0.11	0.915	−0.10	−0.07
Stress	16.45 (1.40)	18.21 (1.70)	0.278	17.00 (1.38)	15.36 (2.426)	0.456	−3.40	39.52	1.58	−1.26	0.216	0.48	0.50
PSWQ worry	55.36 (2.01)	58.82 (2.28) [*]	0.043	51.59 (1.96)	52.28 (2.74)	0.767	−2.77	29.50	0.961	−0.98	0.335	0.06	0.48

Abbreviations: b-d = between groups effect size after intervention, Beta (B) = The estimated coefficient for the group $\times$ time interaction effect, DASS = Depression Anxiety Stress Scale, df = denominator df, F = F statistic for the group $\times$ time interaction effect, FPI = Fertility Problem Inventory (Subscales = Social Concern, Sexual Concern, Relationship Concerns, Rejection of Childfree Lifestyle, Need for Parenthood), M = estimated marginal means, PSWQ = Penn State Worry Questionnaire, SE = standard error, w-d = treatment group within-subject effect size.

^{*}*p* < 0.05.

^{***}*p* < 0.05 between groups.

treatment group and 31 in the wait-list control group. Of these, 17 in the treatment group activated their access to the OFS program. After a three-month wait, control participants were reassessed and offered the treatment. Two participants withdrew from each group post-activation. No significant baseline or demographic differences were found between program users and completers (all $p > 0.05$).

Figure 2 depicts the amount of engagement among individuals who activated their access to the OFS program. On average, participants completed 3.32 (SD = 2.48) modules out of seven (including pre- and post-measurements). Treatment

completion (four or more modules) was achieved by 32% (8 of 25) participants. Overall, adherence to the treatment (as defined above) was low. Of the 32 participants randomized to treatment, 17 (53%) activated their account, and of the 25 who activated the program, only 8 (32%) reached the completion threshold of four or more modules, representing just 25% of all those randomized to treatment. It is important to note that the intention-to-treat analysis includes all 32 randomized participants regardless of whether they activated or engaged with the program; the observed effects therefore reflect the program as offered to all eligible participants, not only those who chose to engage.

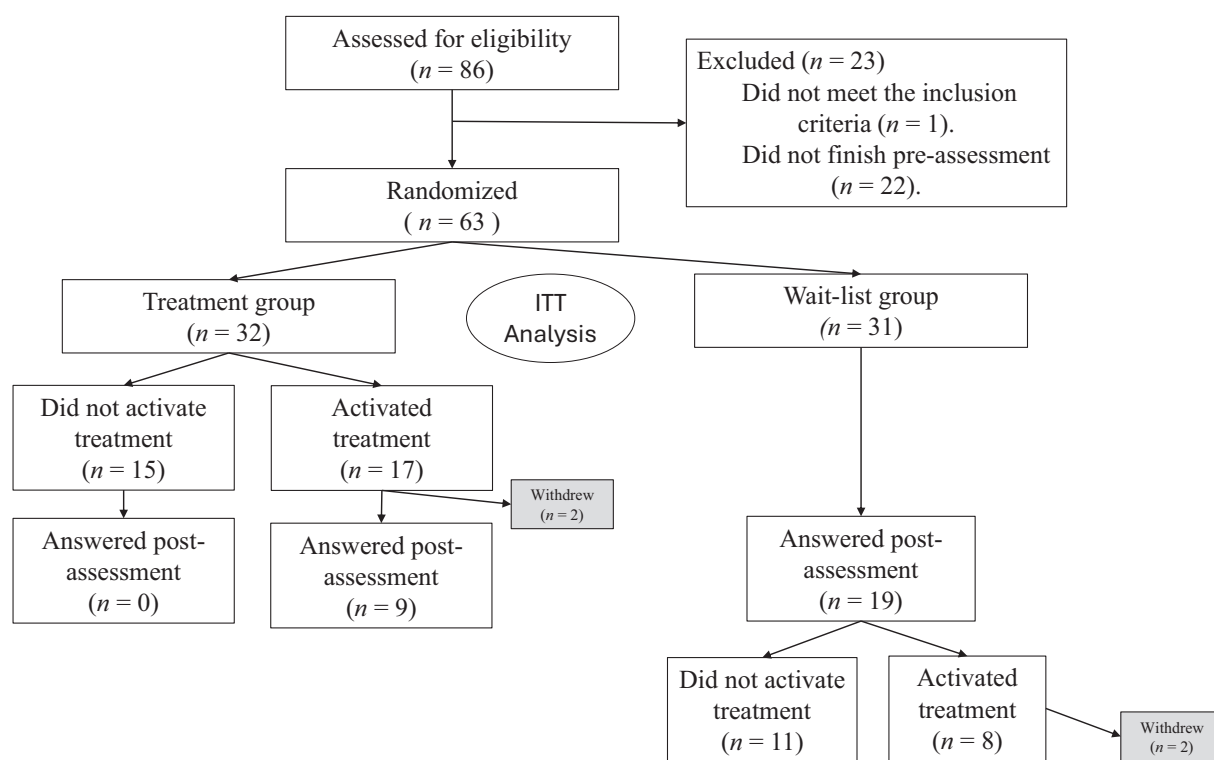


FIGURE 1 | Participants flow through the study. ITT Analysis = shows which participants were included in the Intention to Treat analysis.

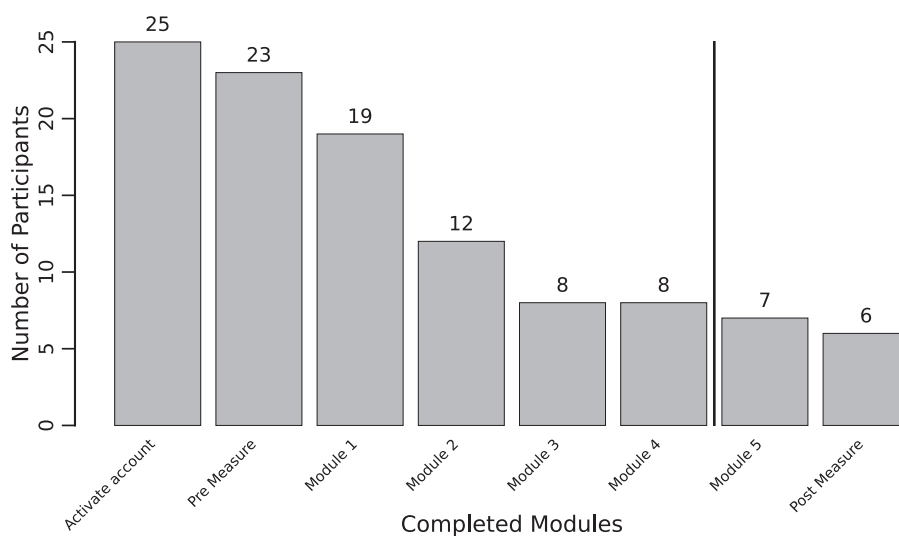


FIGURE 2 | Treatment completion was defined as completion of four or more of the five therapeutic modules, consistent with Bjornsdottir et al. (2023). The vertical black line marks the point at which treatment is considered completed, occurring when a participant finishes module 4.

TABLE 3 | Sociodemographic characteristics of participants at baseline.

Baseline characteristic	Treatment group (<i>n</i> = 32)		Wait-list group (<i>n</i> = 31)		<i>p</i>
Age ^b	35.88	(5.82)	33.13	(5.14)	0.052
Female ^a	32	(100%)	31	(100%)	1.00
Partnered (%)	30	(93.8%)	28	(90.3%)	0.970
Primary fertility ^a	18	(56.2%)	23	(74.2%)	0.186
CBT due to infertility ^a	0	(0%)	0	(0%)	1.00
Infertility in years ^b	4.39	(4.12)	4.90	(3.41)	0.599
Fertility treatment ^a	28	(87.5%)	22	(77%)	0.190
FPI—total score ^b	164.40	(24.62)	164.00	(27.66)	0.954
Social concern ^b	36.30	(10.01)	30.42	(4.77)	0.246
Sexual concern ^b	25.34	(5.64)	26.43	(7.01)	0.501
Relationship concern ^b	28.78	(8.64)	25.45	(9.00)	0.218
Rejection of childfree lifestyle ^b	30.39	(6.21)	30.77	(5.83)	0.807
Need for parenthood ^b	42.97	(8.23)	42.39	(8.89)	0.788
DASS-21 depression ^b	13.38	(8.37)	16.06	(9.65)	0.242
DASS-21 anxiety ^b	5.94	(6.97)	9.48	(7.57)	0.058
DASS-21 stress ^b	16.65	(7.42)	16.45	(7.74)	0.920
PSWQ-16 worrying ^b	51.09	(11.46)	55.35	(10.55)	0.133

Abbreviations: DASS-21 = Depression Anxiety Stress Scale, FPI = Fertility Problem Inventory, PSWQ 16 = Penn State Worry Questionnaire.

^aReflects the number and percentage (%) of participants answering “yes” to this question or falling into this category.

^bReflects the mean and standard deviation (SD) for this variable.

3.2 | Participants Characteristics

Table 3 shows sociodemographic characteristics of participants at baseline for each group. There were no significant baseline differences between the treatment and waitlist groups in demographics or levels of stress, depression, anxiety, and worry (all *p* values > 0.05).

Figure 3 shows that many participants had symptoms above normal at baseline across all psychological categories as measured by the FPI, DASS-21, and PSWQ. The FPI Global scores of study participants were all classified above the normal threshold (see Figure 3).

3.3 | Treatment Effect

Using an intent-to-treat (ITT) approach, treatment effects were evaluated at pre- and post-intervention time points with a linear mixed-effects model including all randomized participants (*N* = 63); details of results for each measure are displayed in Table 2. The experimental group demonstrated a statistically significant reduction in infertility-related stress symptoms over the course of the intervention (mean reduction score = 22.85, *p* < 0.05), whereas the control group showed no significant change (*p* > 0.05). Specifically, participants in the experimental group reported improvements in emotional and psychological well-being, with reduction in mean scores for four FPI

subscales Social Concern, Sexual Concern, Rejection of child-free lifestyle, and Need for parenthood (*p* < 0.05). In contrast, no notable changes were observed in the control group for any of these subscales (*p* > 0.05). The group × time interaction was statistically significant (*F* = 20.43, *t* = −4.52, *p* < 0.001), with a between-group effect size of *d* = 2.0 (95% CI [1.40, 2.61]). The within-group effect size for the treatment group was *d* = 1.70 (95% CI [1.06, 2.34]), retained here for comparability with prior uncontrolled studies.

4 | Discussion

The main goal of the study was to evaluate the effectiveness of a web-based intervention ‘Overcome Fertility Stress’ (OFS) that is designed to lower infertility-related stress symptoms among individuals facing infertility. The primary hypothesis of the study was supported by the results: participants in the treatment group had a statistically significant reduction in infertility-related stress post-intervention, with effect sizes ranging from small to large across various FPI subscales. In contrast, during the same period, the control group showed no significant changes in infertility-related stress levels. This finding underscores the effectiveness of the Overcome Fertility Stress (OFS) program in addressing the core aspect of infertility-related stress, further confirming the targeted approach of the treatment protocol utilizing unguided internet intervention.

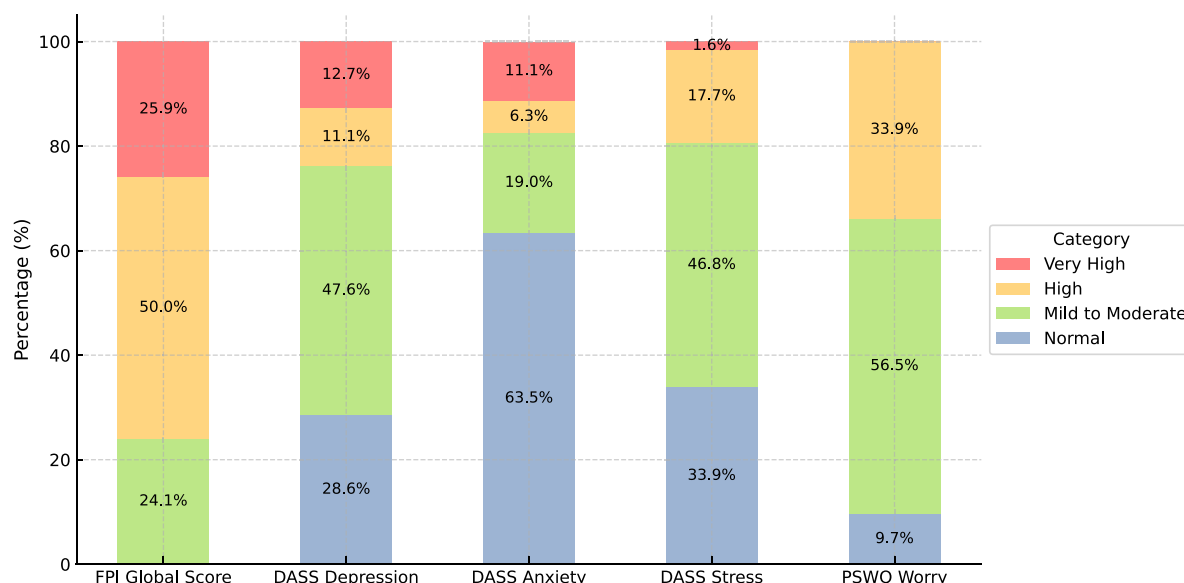


FIGURE 3 | Baseline participant profiles by severity of measurement properties. DASS-21=Depression Anxiety Stress Scale (Subscales: Depression, Anxiety, Stress), FPI=Fertility Problem Inventory (Subscales: Social Concern, Sexual Concern, Relationship Concerns, Rejection of Childfree Lifestyle, Need for Parenthood), PSWQ 16= Penn State Worry Questionnaire. Ranges: FPI Global Score (normal: 46–86, mild to moderate: 87–146, high: 147–181, very high: 182+); DASS Depression (normal: 0–9, mild to moderate: 10–20, high: 21–27, very high: 28+); DASS Anxiety (normal: 0–7, mild to moderate: 8–14, high: 15–19, very high: 20+); DASS Stress (normal: 0–14, mild to moderate: 14–25, high: 26–33, very high: 34+); PSWQ Worry (normal: 16–39, mild to moderate: 40–59, high: 60–80).

These findings align with the results reported by Bjornsdottir et al. (2023). Their study similarly reported that the OFS program had positive effects across four FPI subscales among participants. However, these findings are somewhat inconsistent with prior research in the field, which has generally not reported a reduction in overall infertility-related stress (Clifton et al. 2020; Sexton et al. 2010). In a recent RCT by Shafierizi et al. (2023), the efficacy of iCBT versus conventional CBT for infertile women was explored. While the study found reductions in anxiety and depressive symptoms, it did not reduce infertility-related stress, possibly because the iCBT program targeted anxiety and depression rather than stress specific to infertility, unlike the OFS program.

All participants had high levels of infertility-related stress at baseline and had not previously received CBT for infertility-related psychological symptoms, highlighting the need for targeted interventions for this group. This aligns with the findings of Boivin et al. (1999), who found that only a small portion of women sought professional mental health services for infertility-related stress symptoms. This highlights a gap in care, as participants experienced infertility for an average of five years without adequate support, underscoring the need for interventions like the OFS program to provide relief.

The pattern of findings across FPI subscales is clinically interpretable. Social Concern, Sexual Concern, Rejection of Childfree Lifestyle, and need for Parenthood showed significant improvement in the treatment group, and these domains map closely onto the core targets of the OFS program. These shifts are in line with reductions in repetitive negative thinking and behavioral avoidance. Module 2 (Behaviors) addresses unhelpful avoidance of social situations; Module 3 (Thoughts and Worries) targets negative cognitions including distress around planned sexual

activity; and Module 5 (Redefine Your Life) directly engages identity-level beliefs about parenthood and life meaning. In contrast, Relationship Concerns did not show significant change. Relationship Concerns may be less responsive to a self-directed, individual format, as Module 4 (Relationships) covers interpersonal skills but cannot replicate the depth of a dyadic or couples-focused approach.

The secondary hypothesis was not supported: no significant reductions were observed on the DASS-21 Depression, Anxiety, or Stress subscales, or on the PSWQ. This finding warrants careful consideration. The most clinically coherent interpretation is that OFS is a targeted, infertility-specific intervention rather than a general psychological distress program, and the pattern of results is consistent with this. The subscales on which improvement was observed map directly onto the infertility-specific content of the program, while broader emotional disorder symptoms did not change. Alternative explanations include floor effects on the DASS-21, as many participants scored within the normal range at baseline, insufficient statistical power given the underpowered sample, and the relatively short duration of the intervention compared to programs designed to treat depression or anxiety directly.

This lack of reduction on depression and stress is at odds with earlier findings by Bjornsdottir et al. (2023), who observed reductions in depressive and stress symptoms with the OFS program. This discrepancy may be due to low adherence, small sample size, and a possible floor effect, as many participants scored within the normal range on the DASS subscales at baseline. Additionally, the treatment was focused on infertility-related stress and is shorter in duration than typical treatments for depression and anxiety, which might explain the limited impact on broader psychological symptoms.

Previous literature suggests that iCBT can be comparable to face-to-face CBT for some conditions; however, the present study did not compare OFS with face-to-face therapy (Carlbring et al. 2018; Kiropoulos et al. 2008; Wagner et al. 2014). This study supports these findings, showing a significant impact of the OFS program on global FPI scores. iCBT reduces costs by eliminating the need for physical visits and offers flexible, timely support, making it a versatile option for extending mental health care and easing the burden on the healthcare system (Boivin et al. 1999; Krämer et al. 2022; Pang et al. 2021; Stjerneklar et al. 2019).

4.1 | Limitations and Strengths

This study has several strengths, including a robust randomized controlled design for comparing two active conditions and the use of mixed effects models to account for intra-individual variability and inter-group differences, enhancing accuracy and generalizability. It examines the efficacy of internet-based CBT (iCBT) for reducing infertility-related stress in women, addressing a gap in care and the research landscape, especially given the lack of studies on women's health issues. Our research highlights the need for targeted health interventions.

A primary limitation of this study is that the trial was underpowered: the *a priori* power analysis indicated a minimum of 51 participants per group, yet only 32 were randomized to treatment and 31 to waitlist control (approximately 60% of the required sample). Accordingly, all findings should be treated as preliminary and interpreted with caution, pending replication in an adequately powered trial. Additionally, participant recruitment and retention were challenging, possibly due to an earlier related study in Iceland and the chronic nature of infertility, which may have limited the availability of new participants. Furthermore, a distinctive barrier to treatment retention in fertility-related distress is the phenomenon of pregnancy-contingent dropout, whereby participants discontinue therapy upon achieving pregnancy, often before completing the full course of treatment.

Engagement was also limited: only 17 of 32 randomized participants (53%) activated the program, and only 8 of those 25 who activated (32%), representing just 25% of all those randomized to treatment, reached the completion threshold. The clinical implications of these engagement figures are worth noting. Low activation and completion rates are a recognized challenge in unguided iCBT (Fleming et al. 2018; Kelders et al. 2012; Melville et al. 2010), and when fewer than half of randomized participants activate the program and fewer than one in four complete a meaningful dose, the ITT result reflects the effect of being offered access to the program rather than the effect of the program among those who engage with it. Any signal of benefit observed here should therefore be interpreted with this in mind. Future research could explore whether guided or blended delivery formats in which some therapist contact or other supplements to the online content might improve activation and completion rates, as has been shown to be effective in other iCBT contexts (Sigurðardóttir et al. 2022).

All outcomes relied on self-report measures (FPI, DASS-21, PSWQ), with no objective or clinician-rated outcomes included. The waitlist control design does not control for attention,

expectation, or self-monitoring effects, meaning that some improvement in the treatment group may reflect non-specific factors rather than the intervention itself. No follow-up assessment was conducted beyond the 3-month post-treatment point, so the durability of any treatment gains is unknown. The linear mixed model assumes data are missing at random (MAR); however, given that non-activators are unlikely to have provided post-treatment data for reasons related to their non-engagement, a missing not at random (MNAR) pattern cannot be excluded. Finally, recruitment was restricted to Icelandic women, which limits the generalizability of findings to other cultural, linguistic, and healthcare contexts.

4.2 | Future Research

Future research should investigate the specific barriers that prevent participation in online treatment programs, especially those faced by women dealing with infertility-related stress. A deeper understanding of these obstacles will enable researchers to tailor recruitment and retention strategies more effectively. Furthermore, studying the long-term impacts of iCBT programs like OFS on mental health and fertility outcomes is also necessary, which could give insights critical for refining clinical practices and developing effective treatments.

Future trials should also consider couples-adapted or guided delivery formats, which may better address relationship concerns that appear less responsive to the current unguided individual format.

4.3 | Conclusion

This study evaluated the efficacy of a web-based Cognitive Behavioral Therapy (iCBT) program among 63 Icelandic women experiencing infertility, divided into a treatment group ($n = 32$) and a wait-list control group ($n = 31$). Despite most participants having had reproductive treatments, none had previously received CBT for their infertility-related stress. The study's results revealed significant reductions in infertility-related stress and concerns among participants. These findings suggest that the low cost, accessible web-based CBT intervention can positively impact infertility-related stress symptoms.

Author Contributions

Sigurbirna Haflídadóttir: conceptualization, writing – original draft, review and editing, methodology, statistical analysis. **Fjola Dogg Helgadóttir:** conceptualization, writing – original draft, review and editing, methodology, resources, statistical analysis, supervision. **Magnus Blondahl Sighvatsson:** conceptualization, review and editing, supervision.

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The authors have nothing to report.

Ethics Statement

The study's protocol was approved in full by the Icelandic National Bioethics Committee (clinical study registration number: VSN-23-076).

Consent

All participants provided informed consent before participation began.

Conflicts of Interest

F. D. Helgadottir is an owner of AICBT/AI-Therapy and OFS. F.D.H. provided no funding for the study. F.D.H. had no access to the data and did not conduct any data analyses. The other authors declare no conflicts of interest.

Data Availability Statement

Data will be made available upon request.

References

- Bjornsdottir, R. R., F. D. Helgadottir, and M. B. Sighvatsson. 2023. "Evaluating the Efficacy of an Internet-Based Cognitive Behavioural Therapy Intervention for Fertility Stress in Women: A Feasibility Study." *Behavioural and Cognitive Psychotherapy* 51, no. 2: 180–185. <https://doi.org/10.1017/s1352465822000534>.
- Boivin, J., L. C. Scanlan, and S. Walker. 1999. "Why Are Infertile Patients Not Using Psychosocial Counselling?" *Human Reproduction* 14, no. 5: 1384–1391. <https://doi.org/10.1093/humrep/14.5.1384>.
- Carlbring, P., G. Andersson, P. Cuijpers, H. Riper, and E. Hedman-Lagerlöf. 2018. "Internet-Based vs. Face-To-Face Cognitive Behavior Therapy for Psychiatric and Somatic Disorders: An Updated Systematic Review and Meta-Analysis." *Cognitive Behaviour Therapy* 47, no. 1: 1–18. <https://doi.org/10.1080/16506073.2017.1401115>.
- Clifton, J., J. Parent, M. Seehuus, G. Worrall, R. Forehand, and A. Domar. 2020. "An Internet-Based Mind/Body Intervention to Mitigate Distress in Women Experiencing Infertility: A Randomized Pilot Trial." *PLoS One* 15, no. 3: 1–13. <https://doi.org/10.1371/journal.pone.0229379>.
- Cohen, J. 1988. *Statistical Power Analysis for the Behavioral Sciences*. 2nd ed. Routledge.
- Dhaliwal, L. K., K. R. Gupta, S. Gopalan, and P. Kulhara. 2004. "Psychological Aspects of Infertility due to Various Causes—Prospective Study." *International Journal of Fertility and Women's Medicine* 49, no. 1: 44–48.
- Faramarzi, M., A. Alipor, S. Esmaelzadeh, F. Kheirkhah, K. Poladi, and H. Pash. 2008. "Treatment of Depression and Anxiety in Infertile Women: Cognitive Behavioral Therapy Versus Fluoxetine." *Journal of Affective Disorders* 108, no. 1–2: 159–164. <https://doi.org/10.1016/j.jad.2007.09.002>.
- Fleming, T., L. Bavin, M. Lucassen, K. Stasiak, S. Hopkins, and S. Merry. 2018. "Beyond the Trial: Systematic Review of Real-World Uptake and Engagement With Digital Self-Help Interventions for Depression, Low Mood, or Anxiety." *Journal of Medical Internet Research* 20, no. 6: e199. <https://doi.org/10.2196/jmir.9275>.
- Hazlina, N. H. N., M. N. Norhayati, I. S. Bahari, and N. A. N. M. Arif. 2022. "Worldwide Prevalence, Risk Factors and Psychological Impact of Infertility Among Women: A Systematic Review and Meta-Analysis." *BMJ Open* 12, no. 3: e057132. <https://doi.org/10.1136/bmjopen-2021-057132>.
- Karaca, A., A. Yavuzcan, S. Batmaz, Ş. Cangür, and A. Çalışkan. 2019. "The Effect of Cognitive Behavioral Group Therapy on Infertility Stress, General Health, and Negative Cognitions: A Randomized Controlled Trial." *Journal of Rational-Emotive & Cognitive-Behavior Therapy* 37, no. 4: 375–394. <https://doi.org/10.1007/s10942-019-00317-3>.
- Kelders, S. M., R. N. Kok, H. C. Ossebaard, and J. E. Van Gemert-Pijnen. 2012. "Persuasive System Design Does Matter: A Systematic Review of Adherence to Web-Based Interventions." *Journal of Medical Internet Research* 14, no. 6: e152. <https://doi.org/10.2196/jmir.2104>.
- Kiropoulos, L. A., B. Klein, D. W. Austin, et al. 2008. "Is Internet-Based CBT for Panic Disorder and Agoraphobia as Effective as Face-To-Face CBT?" *Journal of Anxiety Disorders* 22, no. 8: 1273–1284. <https://doi.org/10.1016/j.janxdis.2008.01.008>.
- Krämer, R., L. Köhne-Volland, A. Schumacher, and S. Köhler. 2022. "Efficacy of a Web-Based Intervention for Depressive Disorders: Three-Arm Randomized Controlled Trial Comparing Guided and Unguided Self-Help With Waitlist Control." *JMIR Formative Research* 6, no. 4: e34330. <https://doi.org/10.2196/34330>.
- Lakatos, E., J. F. Szigeti, P. P. Ujma, R. Sexty, and P. Balog. 2017. "Anxiety and Depression Among Infertile Women: A Cross-Sectional Survey From Hungary." *BMC Women's Health* 17, no. 1: 1–9. <https://doi.org/10.1186/s12905-017-0410-2>.
- Lovibond, P. F., and S. H. Lovibond. 1995. "The Structure of Negative Emotional States: Comparison of the Depression Anxiety Stress Scales (DASS) With the Beck Depression and Anxiety Inventories." *Behaviour Research and Therapy* 33, no. 3: 335–343. [https://doi.org/10.1016/0005-7967\(94\)00075-U](https://doi.org/10.1016/0005-7967(94)00075-U).
- Luk, B. H.-K., and A. Y. Loke. 2015. "The Impact of Infertility on the Psychological Well-Being, Marital Relationships, Sexual Relationships, and Quality of Life of Couples: A Systematic Review." *Journal of Sex & Marital Therapy* 41, no. 6: 610–625. <https://doi.org/10.1080/0092623X.2014.958789>.
- Mascarenhas, M. N., S. R. Flaxman, T. Boerma, S. Vanderpoel, and G. A. Stevens. 2012. "National, Regional, and Global Trends in Infertility Prevalence Since 1990: A Systematic Analysis of 277 Health Surveys." *PLoS Medicine* 9, no. 12: e1001356. <https://doi.org/10.1371/journal.pmed.1001356>.
- McCall, H. C., C. G. Richardson, F. D. Helgadottir, and F. S. Chen. 2018. "Evaluating a Web-Based Social Anxiety Intervention Among University Students: Randomized Controlled Trial." *Journal of Medical Internet Research* 20, no. 3: e91. <https://doi.org/10.2196/jmir.8630>.
- Melville, K. M., L. M. Casey, and D. J. Kavanagh. 2010. "Dropout From Internet-Based Treatment for Psychological Disorders." *British Journal of Clinical Psychology* 49, no. 4: 455–471. <https://doi.org/10.1348/014466509X472138>.
- Meyer, T. J., M. L. Miller, R. L. Metzger, and T. D. Borkovec. 1990. "Development and Validation of the Penn State Worry Questionnaire." *Behaviour Research and Therapy* 28, no. 6: 487–495. [https://doi.org/10.1016/0005-7967\(90\)90135-6](https://doi.org/10.1016/0005-7967(90)90135-6).
- Meyers, A. J., and A. D. Domar. 2021. "Supported Mobile Applications and Internet-Based Technologies to Mediate the Psychological Effects of Infertility: A Review." *Reproductive Biomedicine Online* 42, no. 3: 679–685. <https://doi.org/10.1016/j.rbmo.2020.12.004>.
- Miles, L. M., M. Keitel, M. Jackson, A. Harris, and F. Licciardi. 2009. "Predictors of Distress in Women Being Treated for Infertility." *Journal of Reproductive and Infant Psychology* 27, no. 3: 238–257. <https://doi.org/10.1080/02646830802350880>.
- Newton, C. R., W. Sherrard, and I. Glavac. 1999. "The Fertility Problem Inventory: Measuring Perceived Infertility-Related Stress." *Fertility and Sterility* 72, no. 1: 54–62. [https://doi.org/10.1016/S0015-0282\(99\)00164-8](https://doi.org/10.1016/S0015-0282(99)00164-8).
- Page, A. C., G. R. Hooke, and D. L. Morrison. 2007. "Psychometric Properties of the Depression Anxiety Stress Scales (DASS) in Depressed Clinical Samples." *British Journal of Clinical Psychology* 46, no. 3: 283–297.
- Pang, Y., X. Zhang, R. Gao, et al. 2021. "Efficacy of Web-Based Self-Management Interventions for Depressive Symptoms: A Meta-Analysis of Randomized Controlled Trials." *BMC Psychiatry* 21, no. 1: 1–13. <https://doi.org/10.1186/s12888-021-03396-8>.
- Pasch, L. A., S. R. Holley, M. E. Bleil, D. Shehab, P. P. Katz, and N. E. Adler. 2016. "Addressing the Needs of Fertility Treatment Patients and

Their Partners: Are They Informed of and Do They Receive Mental Health Services?" *Fertility and Sterility* 106, no. 1: 209–215. <https://doi.org/10.1016/j.fertnstert.2016.03.006>.

Sexton, M. B., M. R. Byrd, W. T. O'Donohue, and N. N. Jacobs. 2010. "Web-Based Treatment for Infertility-Related Psychological Distress." *Archives of Women's Mental Health* 13, no. 4: 347–358. <https://doi.org/10.1007/s00737-009-0142-x>.

Shafierizi, S., M. Faramarzi, F. Nasiri-Amiri, et al. 2023. "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." *Psychotherapy Research* 33, no. 6: 803–819. <https://doi.org/10.1080/10503307.2022.2158763>.

Sigurðardóttir, S., F. D. Helgadóttir, R. E. Menzies, M. B. Sighvatsson, and R. G. Menzies. 2022. "Improving Adherence to a Web-Based Cognitive-Behavioural Therapy Program for Social Anxiety With Group Sessions: A Randomised Control Trial." *Internet Interventions* 28: 100535. <https://doi.org/10.1016/j.invent.2022.100535>.

Stjerneklar, S., E. Hougaard, L. F. McLellan, and M. Thastum. 2019. "A Randomized Controlled Trial Examining the Efficacy of an Internet-Based Cognitive Behavioral Therapy Program for Adolescents With Anxiety Disorders." *PLoS One* 14, no. 9: e0222485. <https://doi.org/10.1371/journal.pone.0222485>.

Umesh, S., S. Bose, and B. Roy. 2021. "Marital Duration, and Fertility-Related Stress as Predictors of Quality of Life: Gender Differences Among Primary Infertile Couples." *Journal of Human Reproductive Sciences* 14, no. 2: 184–190. https://doi.org/10.4103/jhrs.jhrs_233_20.

Wagner, B., A. B. Horn, and A. Maercker. 2014. "Internet-Based Versus Face-To-Face Cognitive-Behavioral Intervention for Depression: A Randomized Controlled Non-Inferiority Trial." *Journal of Affective Disorders* 152: 113–121. <https://doi.org/10.1016/j.jad.2013.06.032>.

World Health Organization. 2019. "ICD-11. International Classification of Diseases 11th Revision." <https://icd.who.int/en>.

World Health Organization. 2023. "Infertility Prevalence Estimates: 1990–2021." <https://www.who.int/publications/i/item/978920068315>.

Wright, J., C. Duchesne, S. Sabourin, F. Bissonnette, J. Benoit, and Y. Girard. 1991. "Psychosocial Distress and Infertility: Men and Women Respond Differently." *Fertility and Sterility* 55, no. 1: 100–108. [https://doi.org/10.1016/s0015-0282\(16\)54067-9](https://doi.org/10.1016/s0015-0282(16)54067-9).

Zahra, O. A., R. Soheila, B. Tahereh, A. Marzieh, and Y. Atefeh. 2019. "The Effectiveness of Counseling With a Cognitive-Behavioral Approach on Infertile Women's Stress." *Maedica* 14, no. 4: 363–370. <https://doi.org/10.26574/maedica.2019.14.4.363>.