

A systematic review of telemedicine solutions to provide psychological interventions for women receiving fertility treatments

Running title: ICT-based psychological programs in infertility

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Search terms: infertility, assisted reproduction treatments, technologies, telemedicine, treatment, prevention, psychological, emotional disorders.

Abstract:

Introduction: Infertility and Assisted Reproduction Treatments (ART) are frequently accompanied by the experience of emotional disorders. Psychological interventions are available for infertile populations, but the barriers of current face-to-face models of care difficult their dissemination. This systematic review (PROSPERO: *blinded*) aims to summarize how technologies are used in telemedicine psychological programs to manage emotional disorders in women undergoing fertility treatments. **Methods:** Searches were conducted in December 2023 in six different databases. Two independent researchers conducted the searches, extracted the information and assessed the quality of the studies (NIH tool). **Results:** Nineteen studies including 2520 participants met eligibility criteria. Interventions were provided mostly to women who were undergoing In Vitro Fertilization/Intracytoplasmic Sperm Injection (n=11). Emotional disorders most frequently addressed were anxiety and depression (n=11). The majority of the psychological programs were based on CBT (n=6), emotional writing (n=3), Acceptance and Commitment Therapy (n=3) or positive reappraisal (n=3). Many interventions were based on the use of Internet (n=5), diaries (n=3), self-administered manuals (n=2), SMS (n=1) or face-to-face sessions (n=5) supported by the inclusion of phone calls, e-mails or audios. There is a lack of preventive interventions (n=1). **Conclusions:** To the best of our knowledge, this is the first systematic review that explores the use of all kind of technologies to provide psychological interventions to manage emotional disorders during ART. Results derived from this work may guide the development of future telemedicine services to provide psychological interventions.

Keywords: Infertility, assisted reproduction treatments, technologies, telemedicine, prevention, treatment, psychological, emotional disorders.

Introduction

According to the World Health Organization (WHO), one in every six individuals of reproductive age experience fertility problems¹, understood as a chronic reproductive disease that impedes becoming pregnant after one year of regular sexual intercourse without contraception.² One of the most direct consequences of this alarming prevalence data is the increasing request for fertility treatments during recent years.³ In Europe, the number of clinics and fertility treatments provided has been constantly increasing over the past 20 years.^{4,5} Different fertility treatments are currently available, especially in high-income countries.¹ Solutions such as Intrauterine Insemination (IUI) and In Vitro Fertilization (IVF) offer a good chance for women to get pregnant. However, these treatments are also associated with both economic and personal costs. Global estimates indicated that one fertility cycle leading to a live birth may range from \$4,408 to \$13,216.⁶

In addition to these financial costs, the personal cost of fertility treatments includes psychological issues. It has been estimated that around 30% of women undergoing fertility treatment meet criteria for emotional disorders such as anxiety or depressive disorders⁷ before and during the treatments.⁸ Also importantly, it seems that one of the main reasons for fertility treatment discontinuation has to do with the emotional burden of such treatments.⁹ Drop-outs during fertility treatment may have important implications, both because women renounce an important vital desire and because it entails economic losses for the health system, the government and the women.¹⁰ Attending to these information, there is no doubt that access to psychological interventions during this vital period need to be urgently implemented.

Different systematic reviews have explored the use of psychosocial intervention to improve well-being in infertile couples.^{11,12} As reported in these studies, Cognitive-Behavioral Therapy (CBT) is one of the interventions most frequently used in the context of reproductive care¹³ with the strongest evidence.¹⁴ Moreover, other interventions and techniques such as mind-body interventions, coping skills, solving problem or relaxation are frequently integrated in these programs.^{11,12} These studies have shown promising efficacy results in the reduction of emotional suffering in women

undergoing fertility treatments.^{11,12} However, in a recent study, it was found that only 26.7% of women seeking fertility treatments were informed about mental health services, while only 21% received mental healthcare.¹⁵ Considering that women are indeed interested in receiving psychological care during the reproductive period¹⁴, there must be other factors for the inadequate access to these psychological treatments. One of the most salient factors is the limitations of the traditional face-to-face mental health systems. The access to mental health care is challenging in general populations¹⁶ and it can be even more difficult in the case of specific populations such as patients suffering chronic physical conditions^{14,16} because of the lack of well-trained, onsite professionals in medical settings.¹⁶ This is the case of most public Human Reproduction Units (HRU) which generally do not have mental health professionals who assess emotional disorders and refer women to the most convenient mental health service.

In this scenario, new models of care have been proposed with the aim to better disseminate evidence-based psychological interventions.¹⁷ It has been proposed that technologies used in telemedicine services could be a feasible tool to conduct real-time assessments and interventions in a remote way, allowing the patient to take an active role in the therapeutic process with less consumption of costs and time.^{18,19} Telemedicine has been successfully used in the context of mental disorders²⁰ and also in chronic health conditions.²¹ In the specific context of reproductive care, recent investigations have postulated that self-help resources and those based on the use of Information and Communication Technologies (ICTs) can be useful for infertile patients, especially for those with mild to moderate emotional symptoms.¹⁴

Recent systematic reviews about the use of telemedicine for infertile women have revealed positive efficacy and acceptability results in the management of emotional disorders during fertility treatments.²² However, some limitations of these systematic reviews should be highlighted. For instance, some reviews are focused exclusively on some mobile applications and Internet-based solutions²² and do not contemplate other telemedicine interventions (for example those using phone calls, video calls, e-mails, Short Message Service (SMS), or audiovisual materials such as audios and videos to support work between sessions). Others are not specific on technologies solutions²³ nor emotional disorders.^{24,25} Moreover, authors also noted the lack of scientific support of these mobile applications and claim the need to continue

exploring the efficacy of technology-supported programs.^{22,25} Thus, the main aim of this study was to explore how any kind of technologies have been used in telemedicine to address emotional disorders during fertility treatments. We expected to obtain information about current practices that are being implemented and identify needs that are not addressed or could be improved. Conclusions derived from this systematic review may help guide authors in the development of future psychological interventions for women undergoing fertility treatments supported by the use of telemedicine services.

Materials and Methods

This systematic review has been registered in PROSPERO (*blinded*) and has been conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA; Appendices A and B).²⁶ Authors did not publish a protocol for this systematic review.

Search strategy

Searches were conducted in six different bibliographic databases: Web of Science, PubMed, Scopus, PsycINFO, Cochrane and CINAHL. Two independent investigators (*blinded*) conducted the search for scientific articles on February 28, 2023. An update of the searches was conducted on December 05, 2023. All the results are presented according to the latest searches from December. As showed in table 1, combinations of keywords related to infertility, psychological interventions, emotional disorders and technologies were made. Investigators conducted additional searches from reference lists of review articles in order to identify potential articles to be included in the systematic review. Rayyan software²⁷ was used to store and combine the results from the different databases and to conduct an automatic search for duplicates.

Once the search was conducted, two independent researchers (*blinded*) conducted the screening of scientific articles in two phases. First, authors checked the articles by title and abstract. If articles were selected, then researchers read the complete article to determine if they met eligibility criteria. Authors discussed the results and a third researcher (*blinded*) was consulted in case of disagreement.

-Table 1-

Eligibility criteria

Scientific articles were included according to some inclusion criteria: (a) any kind of psychological intervention was provided; (b) at least some type of technology was used; (c) participants were undergoing fertility treatment; (d) changes in emotional disorders were reported; (e) interventions were focused on women with and without the inclusion of their partner. Pre-specified exclusion criteria were: (a) the main intervention was not a psychological program; (b) no technologies were included (i.e., exclusively face-to-face interventions); (c) participants were not receiving fertility treatment; (d) no changes in emotional disorders were provided; (e) participants presented severe mental disorders (i.e., psychotic disorders); (f) intervention was focused exclusively on relatives or professionals.

Data extraction

One author performed data extraction according to a pre-specified list of outcomes. A second researcher checked the data extraction and all authors approved the final version of the data extraction. All studies included in the review were eligible for data extraction and synthesis. Based on Cochrane recommendations²⁸, author and year, location, sample characteristics, intervention characteristics, outcomes and results were extracted. Due to the objective of this systematic review, we also extracted information about infertility characteristics. We have reported the effect measure indicated in the study (i.e., means comparisons, effect sizes, reliable change index). Data presentation is supported by tables and was based on the direct information obtained from the article without converting the data. No additional statistical analyses were calculated.

Quality assessment

Two independent researchers (*blinded*) assessed the quality of the studies included in the systematic review. The Study Quality Assessment Tool developed by the National Heart, Lung and Blood Institute²⁹ was used for this purpose. The tool is composed of different items with “yes”/“no”/“CD” (cannot determine)/“NA” (not applicable)/“NR” (not reported) answers. According to the total number of “yes” answers, each study can be rated as “good”, “fair” or “poor quality”.

Results

Study selection

As shown in Figure 1, a total of 641 records were identified from electronic searches on databases and additional searches on citation searching. Of those, 523 were kept after eliminating duplicated records and were screened using abstract and title. In this first phase of screening, 458 studies were excluded. In the second phase, a total of 65 full-text articles were assessed for eligibility and, finally, 19 were included in this review for synthesis. Agreement on the final selection of studies between the two independent researchers was 97.59% (Cohen's $k=0.61$, substantial agreement).

-Figure 1-

Study characteristics

As shown in table 2, the vast majority of studies had been conducted in United States ($n=4$)^{30,33,34,38} followed by Denmark ($n=2$),^{35,41} Netherlands ($n=2$),^{32,43} and Iran ($n=2$).^{36,37} The remaining countries were represented by isolated studies: United Kingdom,³⁹ Germany,⁹ Portugal,⁴⁰ Switzerland,⁴² China,³¹ Japan,⁴⁴ Greece,⁴⁵ and Spain.⁴⁶ One study recruited the sample both in United States and United Kingdom.⁴⁷

With regards to sample characteristics, a total of 2,520 participants were included in this systematic review (sample size from different studies ranged from 8 to 377 participants). Most studies included participants aged between 32-34 while other researches included younger (around 28-29 years old)^{36,37} and older (around 35-36 years old)^{9,33,47} women. One study recruited male partners who were around 38 years old.⁹

In general terms, interventions were focused exclusively on infertile women ($n=13$)^{30,21,33,34,36-39,43-47} but one study focused on infertile women allowed the participation of the partner in 3 specific sessions (the first, the sixth and the eighth session) out of the ten proposed sessions.⁴⁰ Other interventions offered the choice to participate as a couple or individually ($n=3$),^{9,41,42} and the minority of interventions were provided only to couples ($n=2$).^{32,35} Duration of infertility ranged from 1 to 6.3 years. Type of fertility treatment provided was IVF or Intracytoplasmic Sperm Injection (ICSI) ($n=11$),^{9,31-33,35,37,39-41,43,45} IUI or IVF ($n=4$),^{30,34,36,47} or exclusively IUI ($n=2$).^{44,46} Half of the studies ($n=9$) recruited participants who were receiving the first fertility treatment cycle.^{31-33,35,36,39,41,43,47} Two studies did not provide information about infertility characteristics.^{38,42}

-Table 2-

Emotional disorders and assessment instruments

Table 3 summarizes the main outcomes of studies included with regards to the emotional disorders addressed, measures employed to conduct the assessments, the main characteristics of the psychological interventions and their efficacy outcomes.

Regarding the main emotional disorders that were addressed, almost all studies were focused on anxiety symptoms combined with depression (n=11)^{9,30,32,35,36,39,40,42-44,46} or stress (n=3).^{33,34,45} Other studies combined the assessment of depression and stress (n=2).^{41,47} The remaining three studies were focused solely on stress symptoms (n=2)^{37,38} and emotion dysregulation (n=1).³¹ Most studies employed non-infertility specific instruments to assess anxiety, depressive and stress symptoms, for example, HADS (n=4),^{32,39,43,44} BAI (n=1),³⁰ STAI (n=7),^{34,35,40-42,45,47} BDI (n=7),^{30,35,36,38,40,41,47} ODSIS/OASIS (n=1),⁴⁶ SCL-90 (n=1),³⁸ SF-36 (n=1),⁴⁴ GHQ (n=1),³⁶ CES-D (n=1)⁴² and Perceived Stress Scale.³³ Infertility-specific measures were used to a lesser extent, only 7 measures specifically developed to be used on infertile populations were used in the articles: SCREENIVF,^{9,43} FPI,^{34,37,38} FertiQol,^{31,46,47} Infertility distress scale,⁴² COMPI,⁴¹ Infertility and Strain Scale,⁴⁵ and Physical stress reactions scale.⁴⁵

Psychological interventions characteristics

Regarding time of provision of the psychological interventions, some studies provided the intervention before starting fertility treatments³¹ or before the ovarian stimulation.^{32,35,41} Others continued with the intervention during the stimulation and up to the pregnancy test.⁴⁷ Five studies focused on specific moments during the fertility treatments, namely from oocyte retrieval to pregnancy test⁹, from embryo transfer to pregnancy test^{32,39,45} or before and after embryo transfers.³⁷ Three studies^{43,44,46} provided the intervention during the entire fertility treatment cycle (Table 3).

In terms of type of technology employed (delivery format), five programs were Internet-based that added e-mails to send online questionnaires,³⁴ reminders,³⁸ or to contact the therapist.^{30,42} One intervention integrated contact with the therapist through the online platform itself.⁴³ Three interventions were based on the use of diaries both online (n=1) and paper-based (n=2) combined with phone contact with therapist.^{34,41,45} Two interventions were based on the use of a self-administered intervention through a

manual combined with online questionnaires⁴⁷ or e-mail therapist contact.⁴⁴ Five blended interventions were found; in these programs, face-to-face sessions individually (n=2) and in group format (n=3) were supported by the use of book and CD/mp3 audios to practice muscle relaxation and meditation at home^{31,36,37,40} or the use of e-mail to send online questionnaires.³² The remaining studies were based on video calls to provide group sessions,⁴⁶ daily SMS or cards to promote positive reappraisal^{9,39} or phone calls to conduct emotional follow-up.³³

Different psychological approaches were provided to manage the aforementioned emotional disorders. The most common were CBT (n=6)^{36,38,42-44,46} and emotional writing (n=3).^{35,41,45} Third wave psychological approaches included mind/body programs alone³⁰ or combined with Acceptance and Commitment Therapy (ACT)^{31,40} positive reappraisal alone^{9,39} or combined with mind/body interventions.⁴⁷ Other interventions included active coping + self-efficacy,³⁴ emotional follow-up,³³ interpersonal therapy,³² or relaxation techniques.³⁷ Length of interventions varied across the studies, CBT programs ranged from 3-5 modules, or 6-13 sessions, usually provided on a weekly basis. Emotional writing interventions were generally shorter, daily sessions (from 3-4 days^{35,41} to 7 days⁴⁵) and lasted 20 minutes. While number of sessions in third wave interventions seemed to be around 10 modules/sessions,^{30,93,40} high heterogeneity was found in the length of these interventions (13 days-6 weeks).^{9,31} The vast majority of studies were focused on the treatment of emotional disorders and only one study⁴⁶ provided a preventive intervention.

Changes in psychological variables

Different efficacy results have been found across studies (Table 3). Below we describe the changes in psychological variables according to the type of psychological approach provided. In general terms, interventions with a CBT approach showed a reduction in stress,³⁸ anxiety and depression.^{36,43} While other CBT-based programs showed no decrease in anxiety and depression levels⁴⁴ or showed an improvement only on more depressed participants.⁴² One transdiagnostic CBT-intervention of a preventive nature showed positive results on non-clinical anxiety and depression symptoms over the course of fertility treatments.⁴⁶

Inconsistent results were found when emotional writing interventions were provided. Some authors found a reduction in depression³⁵ or stress⁴¹ but others found no reduction in stress levels.⁴⁵ Results in third-wave psychological programs showed that mind/body interventions achieved an improvement in depression, anxiety, stress, quality of life and emotion dysregulation^{30,31,40} even when combined with positive reappraisal interventions.⁴⁷ On the other hand, positive reappraisal intervention itself did not improve depression nor anxiety.^{9,39}

Regarding the remaining psychological interventions, active coping intervention showed improvements in stress associated with social concerns³⁴ and relaxation technique showed a reduction in stress.³⁷ Conversely, a brief emotional follow-up and interpersonal therapies did not improve anxiety, depressive symptoms³² nor stress.³³

Satisfaction and adherence

Satisfaction outcomes can be seen in table 3. Satisfaction rates were around 80% in three studies.^{30,42,46} Some interventions had been found to be useful and informative.^{34,39,43,46} In fact, some participants would like to use the intervention in future and would recommend its use to peers in similar situations.^{39,46} Sometimes the intervention group (i.e., emotional writing) show increased satisfaction rates compared with control ones (i.e., fact writing).³⁵ However, other CBT-based interventions found that satisfaction decreased over time in both groups.⁴⁴ Ten studies did not provide information about satisfaction outcomes.

As shown in table 3, the lowest adherence rates across the interventions was 37.8%-48%^{32,43} and the highest were 81%-95.7%.^{34,39}

-Table 3-

Quality of studies included

Appendices C-E show the results for the assessment of the quality of studies included. According to their design, studies were classified as pre-post studies with no control group (Appendix C), Controlled Intervention Studies (Appendix D) or Non-Randomized Controlled Studies (Appendix E). Controlled Interventions (both randomized and non-randomized) were assessed with the same tools, but they are presented in separate tables to facilitate the understanding of the results.

The pre-post study was of “good” quality as it only failed in two criteria related to the sample characteristics (i.e., enrollment and sample size).⁴⁶ As shown in appendix D, according to the scores obtained in controlled intervention studies, 6 investigations were rated to be of “fair” quality with total scores between 7-8 points out of 14 points.^{9,35,41,43-45} The remaining RCT studies (n=9) were rated as “good” quality, total scores ranged from 9 to 14 points out a total of 14 points.^{30,32-34,36,38,39,42,47} In general terms, the criteria that need to be improved in RCT are related with blinding, drop-out rates, lack of information about protocol adherence, control of other undesired interventions, sample size justification and statistical analyses conducted according to pre-specified hypothesis. Finally, the rest of the studies (n=3) were classified as non-randomized studies. Overall, non-randomized controlled studies did not meet most criteria required in controlled researches (criteria 2-5). Consequently, low scores have been found in the studies presented in appendix E.^{31,37,40} Apart from this non-applicable criteria, the main concern in these studies had to do with lack of information about participants’ adherence, sample size and lack of intention-to-treat analysis.

Discussion

In recent years there has been an increased interest in developing telemedicine solutions to address women’s needs during the reproductive period. The aim of this study was to review current practices in the use of telemedicine to address emotional disorders during fertility treatments. Below we discuss the main results of this systematic review.

Congruent with previous studies⁴⁸, results derived from our work indicate that psychological interventions are usually focused exclusively on infertile women, with fewer studies including couples or significant relatives in the interventions. It has been suggested that the inclusion of partners could be beneficial regardless of the infertility cause.⁴⁸ For instance, it was found that the inclusion of the partner could encourage men to take an active role during fertility treatments⁹, which may in turn facilitate women’s adjustment during the fertility treatment process. Therefore, future efforts should be made to include the partner (or a relative or other supportive person) in interventions provided during fertility treatments.

Regarding infertility characteristics, the vast majority of programs are designed for women undergoing IVF/ICSI. Recent investigations indicated that the presence of

anxiety and depressive symptoms during IUI is frequent.⁴⁹ In this sense, it could be useful to provide information and emotion regulation skills to women who are undergoing IUI and may feel concerns, fears and doubts related to these procedures.⁴⁹ Also importantly, in our context, IUI is usually the first step for most women who are diagnosed with infertility and start fertility treatments. Providing interventions at this early stage may result in a reduction of emotional disorders onset and chronification. Yet only 9 studies in our systematic review recruited women who were undergoing the first cycle of their fertility treatment. Repeated failed cycles are a risk factor for the development or aggravation of emotional symptoms⁵⁰ so patients who are undergoing fertility treatments for a long also need to be included in these psychological interventions.

Our systematic review also outlined an increased interest in providing psychological interventions during specific fertility treatment phases (i.e., embryo implantation and pregnancy test waiting period). While these are two of the most critical and emotionally hard periods for many women⁷, as suggested by international clinical guidelines⁵¹, future interventions should be developed to be longitudinally implemented including regular assessments and interventions before and after each cycle of the fertility treatments. Ideally we suggest a patient-centered approach focused on women's needs and preferences.⁵² Thus, we should facilitate longitudinal interventions being available and women being able to use the program according to their needs (i.e., emotional needs and according to fertility treatment stage) and preferences.

In our systematic review, most interventions addressed anxiety symptoms combined with depressive symptoms or stress. However, as evidenced by our results, there is a lack of transdiagnostic interventions that allow to address comorbidity. In fact, in our systematic review, only one intervention⁴⁶ had a transdiagnostic approach. The use of transdiagnostic psychological interventions has several benefits. From an economic perspective, it has been proposed that the use of a transdiagnostic approach, such as the Unified Protocol⁵³, could be a cost-effective solution in public mental health systems.⁵⁴ Moreover, in our work we found that some non-transdiagnostic interventions reduced both anxiety and depressive symptoms, but others found a reduction only in depressive or anxiety symptoms. Additional research is required to explore whether

transdiagnostic interventions could serve to provide a cost-effective solution in the context of fertility treatments.

In terms of measures employed to assess the aforementioned changes in psychological outcomes, we found that studies rely mostly on non-specific infertility measures. Different professional organizations have recognized the relevance of conducting regular assessments during fertility treatments.⁵¹ According to our systematic review and previous researches⁵⁵, different non-specific fertility measures could be employed for this purpose (i.e., BDI, STAI, etc.). However, it has also been postulated that infertility-specific measures could provide a more precise picture of the cognitive, behavioral and emotional state of infertility populations.⁵¹ Therefore, we should focus on developing and validating fertility-specific measures. Also importantly, given the burden of applying diverse and long psychological assessments, we should consider the validation of short measures in this population.

An additional outcome derived from our work worthy of mention is the lack of psychological preventive interventions in the context of fertility treatments. This is worrisome because psychological issues that are not properly addressed may result in worse physical health and less effective medical treatment with increased use of mental health services.¹⁶ Preventive interventions have been delivered in the context of fertility treatments⁵⁶ with promising results in the prevention of anxiety and depressive symptoms. Consequently, new developments should consider the implementation of preventive interventions for infertile populations through technology-based solutions.

Regarding the use of telemedicine to address emotional disorders during fertility treatments, some studies employed the technology as the main tool to provide the intervention, while others used technologies to support face-to-face interventions (i.e., by sending questionnaires). Whatever the technological tool employed was, it seems that some contact with therapists could be useful in telemedicine solutions. The efficacy of these blended interventions has been previously described in the context of emotional disorders^{57,58} but more research in the specific context of fertility treatments is needed to demonstrate the feasibility and effectiveness of such interventions. According to the results obtained in this systematic review regarding satisfaction and adherence rates in technology-based interventions, and considering the positive attitudes of psychologist

towards blended care⁵⁹ we expect the feasibility of implementing blended programs in healthcare systems to be high.

The present study certainly has limitations. First, some studies included in this review failed to provide important information about the intervention that could help understand their results. We recommend that these methodological issues are improved in future research efforts. Second, although a comprehensive search was conducted, other combinations and searches could also be proposed (i.e., summary of studies registered in clinicaltrials.org or searches for apps in app and play store). Reasons for not including these additional searches were that the main interest of authors was to review practices already developed (as opposed to planned interventions registered in clinicaltrials.org) and focusing on psychological interventions with efficacy results (contrary to available applications without research support). Finally, meta-analysis, sub-group analysis and meta-regression and sensitivity analyses that could help to better interpret our results were not conducted.

While we acknowledge these limitations, the present systematic review provides important contributions in the field of telemedicine for women undergoing fertility treatments. To the best of our knowledge, this is the first study that explored the role of diverse ICTs (i.e., phone calls, video calls, e-mails, SMS, audios and videos) as opposed to previous systematic reviews focused on isolated mobile applications or Internet-based programs.^{24,25} Additionally, it is focused on emotional disorders, which are the most frequent psychological issues in this population. Second, we conducted the research according to the recommended guidelines to conduct systematic reviews (PRISMA).²⁶ Third, we propose some future lines that may guide the development of new telemedicine services to address emotional symptoms and disorders during fertility treatments.

Conclusions

According to our results, it seems that telemedicine-based services could be a good solution to provide psychological interventions for women undergoing fertility treatments. Specially those based on CBT approaches (we found positive results in three good quality studies). The expected clinical impact of this systematic review is to provide recommendations that facilitate the development of telemedicine solutions that

allow to better disseminate evidence-based psychological interventions (both preventive and treatment) to all women and couples (or families) who are undergoing fertility treatments and are not receiving appropriate psychological care.

Concrete actions recommended in this work are: including an additional support person in the interventions (i.e., partner, relative or a significant person), provide longitudinal and earlier psychological interventions to all women who are undergoing fertility treatments (including preventive and treatment approaches), cover all types of fertility treatments (from IUI to more complex treatments such as IVF/ICSI), include some therapist contact in telemedicine interventions, validate fertility-specific short questionnaires to be applied during fertility treatments and, through ICTs, explore the cost-effectiveness of these programs, specifically, those from a transdiagnostic and blended approach.

Declarations

Funding: this study was supported by the Department of Psychology and Sociology, University of Zaragoza, and by Gobierno de Aragón (Department of Science, University and Society knowledge) [Grant Number Research team S31_23R].

Conflict of interest: the authors declare they have no conflict of interest.

Ethics approval and patients consent: not required.

Data availability statement: The data underlying this article are available in the article and in its online supplementary material.

Registration: this systematic review was registered on PROSPERO (CRD42023401795)

Author contributions: All authors contributed to the study conception and design. Literature search and analysis were performed by VM-B, and BL-D. The first draft of the manuscript was written by VM-B, and BL-D. The manuscript was supervised and critically revised by JO. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Table 1. Detailed keywords selected for databases searches.

Domain	Keywords
Infertility	“fertility problem” OR infertility OR “fertility treatment” OR childlessness OR “assisted conception” OR reproductive OR “Assisted Reproductive Techniques” OR “Assisted Reproductive Treatment” OR “assisted reproductive technology” OR “assisted reproduction” OR “in vitro fertilization” OR IVF OR “fertilisation in vitro” OR “embryo implantation” OR in-vitro OR “artificial inseminations” OR IUI OR ICSI OR “intracytoplasmic sperm injections” OR “intrauterine insemination” OR “intra-uterine insemination”
	AND
Psychological intervention	“psychological intervention” OR “psychological treatment” OR “preventive intervention” OR “preventive treatment” OR “preventive program” OR “psychological program” OR psychotherapy
	AND
Emotional disorders	“affective disorders” OR “mood disorder” OR “emotional disorder” OR anxiety OR depressive OR depression OR PTSD OR “posttraumatic stress” OR OCD OR obsessive-compulsive OR phobia OR panic OR agoraphobia OR dysthymia OR dysthymic OR hypochondria OR “social anxiety”
	AND
Technologies	Internet OR smartphone OR virtual OR web-based OR website OR online OR mobile OR application OR apps OR self-administered OR telemedicine OR mhealth OR m-health OR e-health OR ehealth OR computer OR e-mental OR telehealth OR telemental OR teletherapy OR cyber OR tablet OR phone OR “phone app” OR ICT OR “information and communication technologies” OR ICT OR telephone

Note: no restriction with regards data or language were applied within the searches.

Table 2. Descriptive characteristics of studies included (n=19).

Author, year, location	Sample, age (SD) ^a	Infertility characteristics
Ockhuijsen, 2014 ³⁹ UK	N=377 (PRCI=127; control=126, TAS=124), 34.6-34.9 years old (4.7-5). Only women	Infertility duration: 3.1-3.4 years. ART type: IVF, ICSI. First cycle.
Bernd, 2020 ⁹ Germany	N=141 (women=81; men=60), women=36.62 years old (4.02); men=38.04 years old (5.62). Couple/individually	Infertility duration: 4.88 years. Time undergoing ART: 2.6 years. ART type: IVF, ICSI.
Clifton, 2020 ³⁰ US	N=71 (intervention=36; control=35), 32.83-33.49 (3.56-3.97). Only women	Time undergoing ART: 2.38-2.87 years. ART type: drugs, IUI, IVF.
Frederiksen, 2017 ³⁵ Denmark	N=295 (intervention=153; control=142), women=31.9-32.9 (4.4-4.8), partner=33.9-34.7 (5.-6.2). Only couples	Infertility duration: 2.6-2.7 years. ART type: IVF, ICSI. 46.9-55% first cycle.
Sexton, 2010 ³⁸ US	N=43 (intervention=21; control=22), 32.6 (4.8). Only women	Infertility duration, type of ART and duration of ART not specified.
Domar, 2015 ⁴⁷ US, UK	N=166 (intervention=89; control=77), 34.67-35.03 (4.18-4.26). Only women	Time undergoing ART: 2.22-2.3 years. ART type: IVF, IUI. First cycle.
Galhardo, 2013 ⁴⁰ Portugal	N=92 (intervention=55; control=37), 33.14-34.87 (3.94-4.2). Only women (men included in 3 sessions).	Infertility duration: 3.05-3.35 years. ART type: IVF, ICSI, drugs.
Skiadas, 2011 ³³ US	N=131 (intervention=65; control=66), 34.1-35 (4.2-4.9). Only women	Infertility duration: 1-2.5 years. ART type: IVF. First cycle.
Van Dongen, 2016 ⁴³ Netherlands	N=120 (intervention=61, control=59), 32-32.4 (4.1-4.8). Only women	Infertility duration: 3.04-3.18 years. ART type: IVF. First cycle.
Cousineau, 2008 ³⁴ US	N=190 (intervention=98; control 90), 33.93-34.53 (4.29-4.58). Only women	ART Type: IUI, IVF. 2.62-3.41 cycles.
De Klerk, 2005 ³² Netherlands	N=84 couples (intervention=43; control=41), women's age=33.3-33.4 (4.7-5.2). Only couples	Infertility duration: 4-4.3 years. ART type: IVF. First cycle.
Faramarzi, 2008 ³⁶ Iran	N=124 (CBT=42; pharmacotherapy=42; control=40), 28.3-29.8 (3.8-5.3) Only women	Infertility duration: 5.4-6.3 years. ART type: IFV, ICSI, IUI. 75% first cycle.
Haemmerli, 2010 ⁴² Switzerland	N=124 (intervention=60; control=64), 32.81-34. Couples/individual	Infertility duration, type of ART and duration of ART not specified.

Li, 2016 ³¹ China	N=108 (intervention=58; control=50), 30.66-30.7 (4.29-4.77). Only women	Infertility duration: 4.66-5.2 years. Time undergoing ART: 2.34-2.68 years. ART type: IVF. First cycle.
Matthiesen, 2012 ⁴¹ Denmark	N=82 (intervention=42; control=40), 33.17 (4.15). Couples/individual	Infertility duration: 1.2 years. ART type: IVF, ICSI. First cycle.
Mori, 2009 ⁴⁴ Japan	N=140 (intervention=96; control=44), 30.4-31.3 (2.49-2.87). Only women	Infertility duration: 2.2-2.3 years. Time undergoing ART: 2 years maximum. ART type: drugs, IUI.
Panagopoulou, 2009 ⁴⁵ Greece	N=148 (emotional writing; fact writing; control), 33.8 (4.6). Only women	Infertility duration: 1.5 years. ART type: IVF. 2.5 cycles.
Valiani, 2010 ³⁷ Iran	N=76 (intervention=36; control=36), 29.4 (4.1). Only women	Infertility duration: 5.6 years. Time undergoing ART: 5 years. ART type: IVF, ICSI.
Martínez, 2022 ⁴⁶ Spain	N=8, 32.88 (3.56). Only women	Infertility duration: 1.65 years. Type of ART: IUI. 1-3 cycles.

Note: UK: United Kingdom; US: United States; SD: Standard Deviation PRCI: Positive Reappraisal Coping Intervention; TAS: Treatment As Usual; CBT: Cognitive-Behavioral Therapy; ART: Assisted Reproductive Treatment; IVF: In Vitro Fertilization; ICSI: Intracytoplasmic Sperm Injection; IUI: Intrauterine Insemination.

^a Age and standard deviation range is reported when the study includes two or more comparison groups.

Table 3. Characteristics of psychological interventions of studies included (n=19).

Author, year	Emotional disorder	Psychological intervention	Measures	Results
Ockhuijsen, 2014 ³⁹	Anxiety, depression Subclinical symptoms at BL.	Positive Reappraisal Coping Intervention (PRCI) (10 positive sentences, twice daily). Format: Card, SMS reminders to fill questionnaires. Timing: embryo transfer-pregnancy test.	HADS	Time effect in anxiety [F (2,670)=47.37, $p<.001$] and depression [F (2,673)=7.04, $p=.001$] was found. No group effect in anxiety [F (4,670)=1.79, $p=.129$] and depression was found [F (2,376)=0.32, $p=.728$]. At time 2, higher anxiety and depression was found. Satisfaction: intervention was considered useful, they would use it in future and would recommend it. Adherence: 72-81%.
Bernd, 2020 ⁹	Anxiety, depression Subclinical symptoms at BL.	Positive adjustment technique (PACI) (positive reappraisal “today I am going to do something good for me”), 13 days. Format: daily SMS. Timing: oocyte retrieval-pregnancy test.	SCREENIVF	In women there was a non-significant trend of worsening of depression and anxiety. In men, non-significant trend of improvement of anxiety and trend of worsening of depression was found. Adherence: 63-83%
Clifton, 2020 ³⁰	Anxiety, depression At BL some participants had clinical diagnosis.	Mind/body intervention, 10 modules of 1h (psychoeducation, relaxation emotion awareness, cognitive restructuring, stress reduction, communication, emotional expression). Format: Internet-based, e-mail contact with therapist.	BAI BDI	Compared with control group, the intervention group obtained significant improvements in depression ($p=.007$), anxiety ($p=.003$) and stress ($p=.041$). Satisfaction: 82% are satisfied with the intervention. Adherence: 61%.
Frederiksen, 2017 ³⁵	Anxiety, depression At BL patients presented clinical symptoms.	Emotional writing intervention (EWI), 3 sessions of 20 minutes during 3 consecutive days (intervention: infertility writing; control: daily tasks writing). Format: online diary and phone calls (schedule the writing and solve doubts). E-mail to answer questionnaires. Timing: previous starting ART/ovarian stimulation.	BDI STAI	Depressive symptoms in the experimental group had a slightly increase compared with the control group ($t=-2.0$, $p=.049$, $d=-0.27$). There were no significant changes in anxiety symptoms. Satisfaction: participants in experimental group showed increased satisfaction with the intervention.
Sexton, 2010 ³⁸	General and specific stress Subclinical symptoms at BL.	Coping With Infertility (CWI). CBT, 5 modules (psychoeducation, cognitive restructuring, relaxation, behavioral activation, social support). Format: web page, e-mail reminders.	BDI SCL-90 FPI	In comparison with the control group, the intervention group showed a higher reduction in general stress ($F(1,28)=6.04$, $p=.02$, $\eta^2_p=1.78$). There was a non-significant reduction of infertility-specific stress. Adherence: 72%

Domar, 2015 ⁴⁷	Anxiety, depression, stress At BL participants presented emotional symptoms.	Cognitive Coping and Relaxation Intervention (CCRI). Positive reappraisal + mind/body. Format: mailed book and CD. Online platform to answer questionnaires. Timing: before stimulation-pregnancy test.	FertiQol STAI BDI	A significant reduction was found in the intervention group in anxiety (B=-2.80, IC=-5.42—0.17) and quality of life (B=4.07, IC=2.07-6.06). No improvement was found in the control group. Satisfaction: 43% considered the intervention effect lasted 1h or less.
Galhardo, 2013 ⁴⁰	Anxiety, depression At BL participants presented some emotional symptoms.	Mindfulness-Based Program for Infertility (MBPI). Mindfulness-based + ACT, 10 group sessions (15 participants each), 2h + 1-day session. Format: face-to-face group sessions + manual +CD for meditation.	BDI STAI	Intervention group showed a significant improvement in depression ($t=5.46, p<.001$) and anxiety ($t=2.13, p=.009$). The control group did not show significant improvement in depression ($t=1.28, p=.209$) and anxiety ($t=0.01, p=1.00$).
Skiadas, 2011 ³³	Anxiety, stress At BL participants presented emotional symptoms.	Brief Intervention. Emotional follow-up, 2 phone calls (5-15 minutes). Format: Phone calls. Timing: embryo transfer-pregnancy test.	PSS	At the time of the pregnancy test, both groups presented higher stress symptoms ($p<.010$). There were no significant differences between both groups ($p=.320$). Adherence: 64.1%
Van Dongen, 2016 ⁴³	Anxiety, depression Women at risk at BL.	Digicoach. CBT, 3 modules (5 weeks each module=15 weeks) (relaxation + psychoeducation, cognitive restructuring, social support + communication). Format: Online program + weekly feedback by the e-therapist. Timing: all ART cycle and up to pregnancy test.	SCREENIVF HADS	Pre-protocol analyses indicated a reduction in the percentage of women with clinical symptoms 3 months after ART in the intervention group compared with the control group (risk difference=24%, $p=.030$). However, intention-to-treat analysis showed no significant differences in the risk for anxiety and depression 3 months after ART (intervention=19% - control 40%, $p=.060$). Satisfaction: the program was rated 6.6 (out of 10) Adherence: 48% Digicoach.
Cousineau, 2008 ³⁴	Anxiety, stress At BL women presented emotional symptoms.	Infertility Source: Interactive Support Tool When Trying to Conceive. Active coping and self-efficacy, length: 90 minutes (2 sessions or 4 weeks). Format: web page. E-mail to send online questionnaires.	FPI STAI	The intervention group obtained improvement only in social concerns ($F(1,86)=4.45, p=.038, d=0.45$). No significant improvements were found in the remaining FPI subscales. Satisfaction: the program was found informative 6/7; useful: 5/7. Adherence: 95.7%
De Klerk, 2005 ³²	Anxiety, depression At BL women presented some emotional symptoms.	Interpersonal therapy (thoughts about infertility and ART), 3 sessions of 1 hour. Format: face-to-face couple sessions and email to answer questionnaires. Timing: before ovarian stimulation-pregnancy test.	HADS	There were no significant improvements in anxiety ($d=0.29$) and depression ($d=0.46$). Adherence: 48%

Faramarzi, 2008 ³⁶	Anxiety, depression At BL women reported clinical scores at BDI.	CBT (psychoeducation, relaxation, cognitive restructuring), 10 group sessions (8-10 participants each) of 2h. Format: face-to-face group sessions + book + CD to conduct muscle relaxation.	BDI (scores 10-47) GHQ	There was a significant improvement in the CBT group in anxiety and depression ($p<.001$). Pharmacotherapy group also improved in anxiety ($p=.020$), and depression ($p=.030$). Better results were found in the CBT group than in pharmacotherapy. The control group did not show improvements ($p>.050$). Adherence: 71%
Haemmerli, 2010 ⁴²	Anxiety, depression At BL women reported emotional symptoms.	Child Wish Online Coaching Program. CBT (expectations, psychoeducation, coping with stress, relaxation, communication, behavioral activation, doubts and fears), 13 sessions (8 weeks). Format: web page and forums, e-mail to contact therapists and solve doubts. Weekly messages to adhere to the intervention. Timing: before starting ART.	CES-D STAI IDS	The intervention group improved in comparison with the control group. However, differences in depression ($F(1,117)=1.99$; $P=0.16$), state anxiety ($F(1,117)=0.01$; $P=0.93$), trait anxiety ($F(1/117) =0.01$; $P=0.92$) and distress ($F(1,116)=2.75$; $P=0.10$) were not significant. A significant reduction of depressive symptoms was found in those participants who were clinically depressed ($F(1,47)=8.82$, $P\leq 0.01$). Satisfaction: 80% considered the intervention was positive or very positive. Adherence: 79%
Li, 2015 ³¹	Emotion dysregulation At BL participants showed high emotion dysregulation.	Mindfulness-Based Intervention (MBII). Mindfulness + ACT (emotion awareness, acceptance, yoga), 6 weeks, 2-2.5h, groups of 15 women. Format: face-to-face group sessions, book, meditation audio mp3s to practise meditation.	FertiQol DERS	The intervention group showed significant improvement in emotion dysregulation ($p<.001$, $h^2_p=.108$) and quality of life ($p<.001$, $h^2_p=.188$). No significant improvements were found in the control group. Adherence: 67.45% (control), 62.5% (intervention).
Matthiesen, 2012 ⁴¹	Anxiety, depression, stress At BL participants showed emotional symptoms.	Expressive Writing Intervention (EWI). Emotional writing (about thoughts, infertility and ART), 3 tasks of 20 minutes over 3-4 days. Format: diary booklet + phone calls to give instructions about the writing tasks. Timing: previous ovarian stimulation	COMPI BDI STAI	The intervention group showed significant reduction in stress compared with the control group [$F(2,28)=2.92$, $p=.007$, $d=.91$]. Anxiety and depressive symptoms were only analyzed to explore differences in drop-outs. Adherence: 37.8%
Mori, 2009 ⁴⁴	Anxiety, depression At BL some participants showed emotional symptoms.	CBT (stress registers, coping with stress techniques), 3 months. Format: book + therapist contact by e-mail or telephone to know about the participants' situation and solve doubts. Timing: during all ART.	HADS SF-36	There were no significant differences between groups in anxiety and depression ($p>.050$). Satisfaction: satisfaction decreased over time in both groups. Adherence: 71%.

Panagopoulou, 2009 ⁴⁵	Anxiety, stress At BL some participants showed emotional symptoms.	Emotional writing (writing about infertility thoughts and feeling vs writing about infertility facts), 7 days (once daily), 20 minutes. Format: diary, phone calls to remember to complete the task. Timing: embryo transfer-pregnancy test.	STAI ISS PSRS	There were no significant differences in specific infertility-related stress [$F(3,193)=0.51, p=.670$] and general stress [$F(3,193)=1.39, p=.250$].
Valiani, 2010 ³⁷	Stress At BL some participants showed emotional symptoms.	Jacobson relaxation technique, 12 sessions. Format: face-to-face + CD to practise muscle relaxation at home. Participants who could not travel to the clinic answered the questionnaire by phone. Timing: before and after the embryo transfer.	FPI	At post-intervention stress, scores were significantly higher in the control group compared with the intervention group ($t=9.56, p<.001$).
Martínez-Borba, 2022 ⁴⁶	Anxiety, depression Prevention: At BL women did not have any emotional disorders.	Unified Protocol Prevention Program (UP-PP). CBT (psychoeducation, emotion awareness, cognitive flexibility, emotion-driven behaviors, pleasant activities, assertive communication skills), 6 sessions (1 individual + 5 group) of 2h. Format: video call, e-mail. Timing: during the entire IUI process.	OASIS ODSIS PANAS FertiQol DERS	All study variables remained under the clinical cut-off. Satisfaction: 80% were satisfied with the format, participants considered the program was useful and would recommend it. Adherence: 62.5%

Note: UK: United Kingdom; US: United States; BL: baseline; SMS: Short Message Service; CD: Compact Disc; ACT: Acceptance and Commitment Therapy; ART: Assisted Reproductive Treatment; CBT: Cognitive-Behavioral Therapy; IUI: Intrauterine Insemination; HADS: Hospital Anxiety and Depression Scale; BAI: Beck Anxiety Inventory; BDI: Beck Depression Inventory; STAI: State-Trait Anxiety Inventory; SCL-90: Symptoms Checklist 90; FPI: Fertility Problem Inventory; FertiQol: Fertility Quality of Life; PSS: Perceived Stress Scale; GHQ: General Health Questionnaire; CES-D: Center for Epidemiologic Studies Depression Scale; IDS: Infertility Distress Scale; DERS: Difficulties in Emotion Regulation Scale; COMPI: Copenhagen Multicentre Psychosocial Infertility; SF-36: Short Form 36 items; ISS: Infertility and Strain Scale; PSRS: Physical Stress Reactions Scale; OASIS: Overall Anxiety Severity and Interference Scale; ODSIS: Overall Depression Severity and Interference Scale; PANAS: Positive and Negative Affect Schedule.

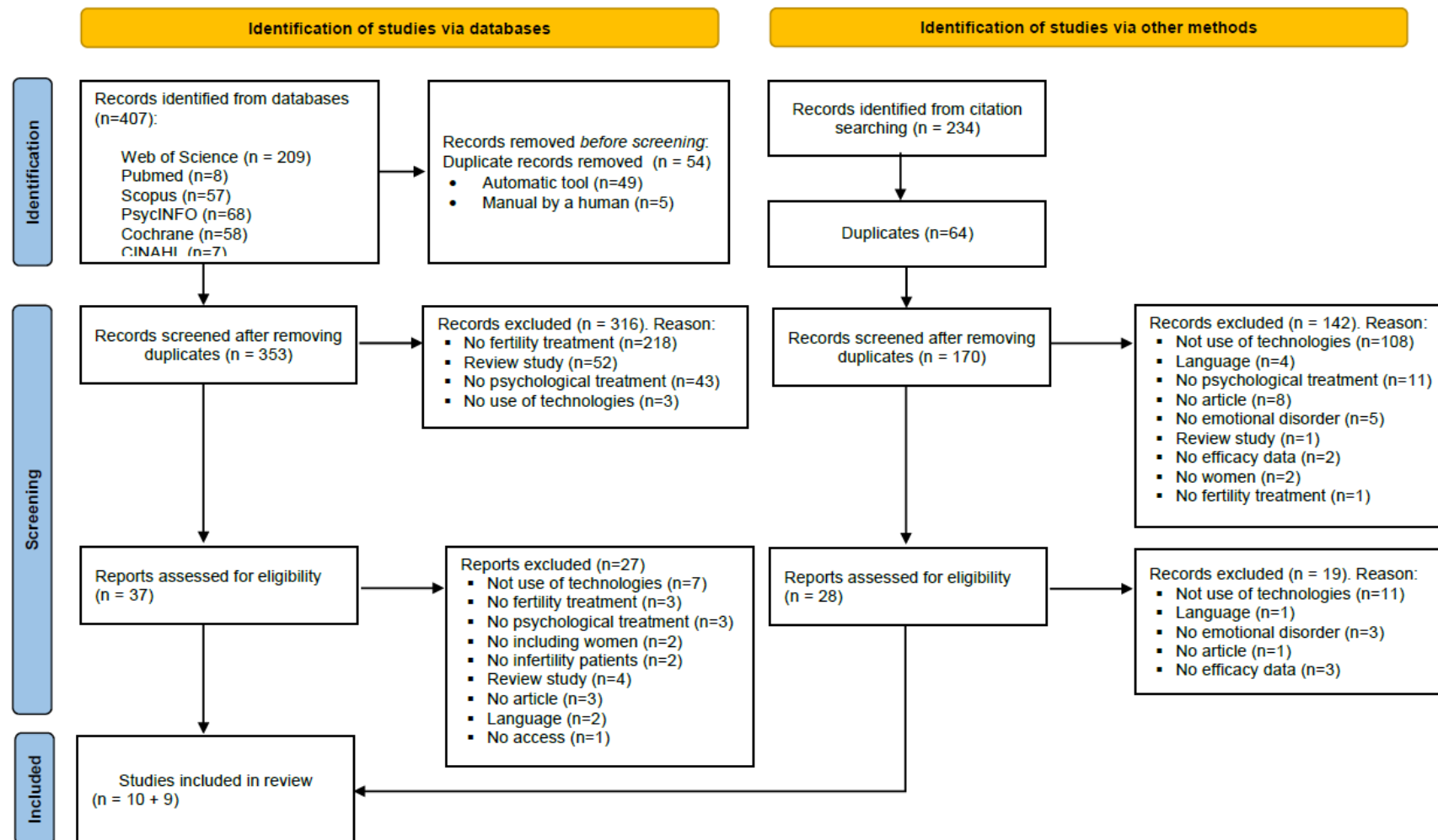


Figure 1. PRISMA flow diagram for systematic reviews which included searches of databases and other sources.