Pilot and Feasibility Studies

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Pilot trial of a new self-directed psychological intervention for infertility-related distress

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Abstract

Background Now affecting one in six couples in Canada, infertility is defined as a lack of conception after 12 or more months of regular, unprotected heterosexual intercourse. Infertility is associated with immense psychological burden, particularly for individuals assigned female at birth. Yet existing psychological interventions are not specialized to this population and have been shown to be only marginally effective at relieving distress related to infertility. Thus, a new online self-directed psychological intervention was co-created with a panel of women experiencing infertility, and ultimately consisted of six 10-min video modules addressing the cognitive, emotional, and interpersonal aspects of infertility-related distress.

Methods In the current study, 21 women experiencing reduced quality of life related to infertility were recruited to participate in a one-arm pre-post pilot testing the feasibility, acceptability, and preliminary efficacy of the program. Participant adherence and retention were monitored, and participants rated the credibility of the program and the helpfulness of each module as well as provided feedback on the content and format of the program. Pre-to-post changes in fertility quality of life, anxious symptoms, depressive symptoms, and relationship satisfaction were examined.

Results The program modules were highly rated by participants, with average helpfulness ratings ranging from 7.5 to 8.2/10. Two participants became pregnant and therefore stopped prematurely, 79% of the remaining participants completed all six modules, and participants reported completing 52.8 ($SD = 82.0$) min of homework per week. Participants perceived the intervention as highly credible and generally approved of the format, length, and speed; however, 68% of participants had recommendations for additional content to be included in the intervention. While relationship satisfaction did not change significantly over time, large pre-to-post improvements in fertility quality of life, depression, and anxiety were observed ($p < .001$; Cohen's $ds = 0.9–1.3$).

Conclusions This self-directed intervention was well received and has the potential to be highly effective in reducing infertility-related distress, informing future development and optimization.

Trial registration ClinicalTrials.gov, NCT05103982.

Keywords Infertility, Fertility, Distress, Quality of life, Depression, Anxiety, Relationship satisfaction, Psychological intervention, Self-help, Pilot

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Key messages regarding feasibility

- A new self-directed psychological intervention aimed at improving mental health symptoms among women experiencing infertility has been created. Its acceptability has yet to be tested.
- Participants perceived the intervention as highly credible and approved of the format, length, and speed. Retention and adherence were also acceptable. Large improvements in quality of life and mental health symptoms were observed. However, participants did also have some recommendations to improve the program as well as recommendations for additional content to be included in the intervention.
- The findings point to a few improvements/additions that can be made to the content of the program but largely suggest the program is ready to be submitted to a well-powered randomized controlled trial aimed at comparing the efficacy of our program relative to a treatment-as-usual control group.

Background

The experience of infertility is associated with significant negative psychological consequences [1], including increased stress, depression, and anxiety [2]. Sixteen percent of Canadian reproductive-aged couples are currently experiencing either primary (i.e., no prior live birth) or secondary infertility (i.e., at least one prior live birth) [3], with infertility being generally defined as the inability to achieve pregnancy despite 12 or more months of focused attempts to conceive through intercourse. Although male- and female-factor infertility are nearly equally prevalent [4], women bear the brunt of the infertility-related burden. Medical treatments for infertility, whether primary or secondary, require women to monitor their menstrual cycles, attend near-daily ultrasounds, self-inject gonadotropins, and undergo invasive and painful procedures [5]. If travel is required to obtain fertility treatments (known as cross-border reproductive care) [6, 7], women face additional psychosocial strain due to schedule disruptions, taking time off work, and coordinating care between multiple healthcare providers. Unsurprisingly, women also face additional psychological challenges associated with infertility. Women experiencing primary infertility consistently report lower self-esteem and satisfaction with life, and more depression and anxiety than their male partners [8, 9]. Likewise, in same-sex couples pursuing sperm donation, the individual who intends to become pregnant is also at higher risk for depression and anxiety relative to their partner [10]. Overall, 30% to 40% of women undergoing infertility evaluations report clinically significant depression or anxiety [11–14]. These levels of depression and anxiety are comparable to cancer survivors in active treatment and cardiac rehab patients following a myocardial infarction [15].

Infertility-related distress (i.e., depression, anxiety, reduced quality of life, general psychological distress, and detrimental impact on mental health) has increased in recent years, which may be partly attributable to suspensions and delays in receiving fertility treatment during the COVID-19 pandemic [16, 17]. This increase in psychological distress could have significant consequences for women experiencing infertility, as conflicting evidence suggests that untreated depression and anxiety may impact the outcome of ART and achieving pregnancy [18–21]. Similarly, psychological distress is the most cited reason for prematurely discontinuing fertility treatments [2, 22–25]. In one study of 450 couples offered three government-funded cycles of in vitro fertilization (IVF), 54% of couples suspended IVF due to psychological burden—despite not achieving pregnancy [26]. Emotional stress is also a key reason why couples choose not to pursue fertility treatments at all [27]. Therefore, it is critical that women experiencing infertility receive effective mental health treatment to reduce suffering and improve conception rates.

Psychological interventions for infertility

Despite the high level of psychological distress in women experiencing infertility, currently available psychological treatments are often ineffective or associated with relatively small benefits. Previous meta-analyses have produced conflicting results, often finding improvement in some domains but not others [28–31]. A more recent meta-analysis of psychological interventions for infertility-related distress sought to clarify these findings [32]. In this review, psychological interventions were associated with a small beneficial effect on anxiety but a non-significant effect on depressive mood, marital quality, and quality of life. This effect was moderated by region, with studies from the Middle East producing much larger effects than studies conducted in other regions, including North America. When controlling for region, neither intervention length, therapeutic approach, nor therapy format moderated the treatment effect [32]. Therefore, there is a scarcity of consistently helpful, specialized support available for those experiencing infertility, suggesting a new, more effective intervention is needed.

Developing a new infertility-specific intervention

To address the paucity of effective psychological interventions tailored to women experiencing infertility, our team aimed to develop a new intervention that would be more effective at improving mental health and well-being

than those currently available. The development of this intervention used a methodical and evidence-based approach guided by the Medical Research Council [33] and Obesity-Related Behavioral Intervention Trials [34] models for behavioral intervention development. Additionally, a panel of six patient advisors with relevant lived experience with infertility were closely involved as co-investigators. Specifically, the development of this intervention has involved a systematic review of available interventions [32], a needs-based assessment conducted using qualitative research methods [35], and an evaluation of potential intervention components (Balsom AA, Dube L, Bright K, Gordon JL: Exploring promising psychotherapies for the treatment of infertility related distress: a scoping review, submitted). Details of this intervention process are summarized in the " Methods" section below and described in further detail in Gordon et al. [36].

The current study

The Coping with Infertility (CWI) program is the product of a comprehensive development process following best practice guidelines for behavioral intervention development and has been fully vetted in consultation with patient advisors. The next stage of development thus involves testing the feasibility and acceptability, as well as the preliminary efficacy of the program in a pilot study. The current one-arm pre-post trial was thus intended to examine a range of psychological outcomes, specifically fertility-related quality of life, anxiety, depression, and relationship satisfaction both prior to and following this new infertility-specific intervention. We recruited a population of individuals assigned female at birth and experiencing infertility, hereafter referred to based on their reproductive organ gender (i.e., female/woman); this distinction also matches the self-chosen gender identity of all participants. We expected participants to show improvements across all psychological outcomes that would be maintained one month post-intervention. We also expected that the program would be well accepted and perceived as highly credible.

Methods

Participants

Between October 2021 and November 2022, a total of 43 individuals were recruited to test a newly developed self-help program for individuals coping with the stresses of infertility. A target sample size of 20 participants was chosen in line with recent recommendations on sample size selection for pilot studies [37] and the primary goal of this pilot study being to conduct a preliminary assessment of the acceptability of the CWI program, as well as to gather feedback on how to improve it. A secondary goal was to examine whether there was any indication that the program might improve psychological outcomes, though the study was not specifically powered to detect a specific effect size. Twenty-one participants were ultimately recruited so as not to deny services to an additional interested individual.

Participants were recruited through Facebook advertisements and announcements in infertility support groups in Regina and Saskatoon, Canada. Of these 43 individuals, 39 completed the eligibility survey. To be considered eligible for this study, participants were required to have been assigned female at birth, reside in Saskatchewan, Canada, be of reproductive age (e.g., between 18 and 42 years of age), and be experiencing infertility. Infertility was defined as attempting to conceive through intercourse for 12 months or more or pursuing fertility treatments. Participants were also required to be experiencing a high level of infertility-related distress (defined as a score of ≤ 52 out of 100 on the Fertility Quality of Life Tool (FertiQoL)) [38] indicating that their quality of life was considerably impacted by infertility. A cutoff score of 52 was chosen based on the findings of one Dutch study identifying 52 as a clinical cutoff in relation to depressive symptoms [39].

Individuals were excluded from participation if they were receiving other psychological services, endorsed suicidal ideation or a history of suicide attempts, or if they were experiencing severe anxiety (defined as a score of ≥ 15 out of 21 on the Generalized Anxiety Disorder-7 (GAD-7)) [40] or depression (defined as a score of ≥ 20 out of 27 on the Patient Health Questionnaire-9 (PHQ-9)) [41]. Given the untested and self-help nature of the current intervention, it was reasoned that individuals with such severe anxiety, depression, or suicidal ideation would be better suited for in-person psychotherapy where more comprehensive, individualized support could be offered. Fourteen prospective participants were found to be ineligible due to current suicidal ideation ($n=5$), a history of attempted suicide ($n=2$), and currently receiving psychological treatment ($n=7$). The remaining 25 individuals were eligible and invited to participate; ultimately, 21 chose to enroll in the study.

Program

First, a systematic review and meta-analysis confirmed that currently available interventions were largely ineffective at improving mental health (e.g., depression, anxiety, and infertility stress) in North America but also that neither therapeutic approach nor therapy format modified treatment effects [32]. Second, a qualitative approach identified specific psychological challenges faced by women struggling with infertility, as well as which psychotherapeutic approaches are used to treat

infertility-related distress by mental health professionals specializing in infertility, illuminating targets for intervention [35]. Third, a scoping review identified evidence-based psychological interventions for anxiety, depression, or relationship distress that could be deconstructed into component techniques and applied to infertility-related distress (Balsom AA, Dube L, Bright K, Gordon JL: Exploring promising psychotherapies for the treatment of infertility related distress: a scoping review, submitted). Following this review, an online survey of 644 women experiencing infertility revealed how helpful each technique was perceived to be by this population, as well as the "most liked" and "most hated" techniques [42]. Eight of the top-rated techniques were incorporated into the CWI program in collaboration with patient advisors, following consideration of how the techniques could be combined to create a cohesive, logical intervention.

Ultimately, six core modules and one bonus module were created, each with accompanying homework assignments (Table 1). These modules were developed into 10-min videos consisting of PowerPoint slides with professional voiceover. A self-help, Internet-delivered intervention was chosen based on (a) recent findings that self-administered interventions were as effective at improving mental health in individuals experiencing infertility as other more costly formats [32], (b) the preference of the majority (72%) of participants from the qualitative needs assessment described above [35], and (c) previous research indicating that the Internet is increasingly being used by individuals experiencing infertility to seek fertility-related information and support [2, 43, 44], and online psychological interventions could reduce economic and accessibility barriers to treatment [45, 46]. Thus, it was determined that this format could be most effectively scaled up and made accessible to diverse populations of women throughout the world.

Procedure

Prospective participants contacted the research team via email and received a link to a brief eligibility survey assessing age, infertility status, fertility-related quality of life, anxious symptoms, and depressive symptoms (Fig. 1). If deemed eligible, participants were invited to undergo an enrollment session conducted via Zoom Video Communications software. During this session, a research assistant confirmed participants' eligibility, played a brief introductory video explaining the purpose of the study, and obtained informed consent. Participants were then asked to complete a baseline battery of questionnaires assessing demographic characteristics (e.g., age, race, ethnicity, education, income), reproductive health history (e.g., infertility diagnosis, past fertility treatments, living children), relationship satisfaction, and participants' first impressions of the intervention.

Table 1 Description of the content included in the Coping with Infertility (CWI) program

Module	Focus
1. Cognitive restructuring	• Identifying and challenging the extreme negative thoughts that contribute to depressive and anxious mood • Example 1: "I didn't get pregnant because I went jogging" (targeting excessive guilt) • Example 2: "I'll never be pregnant" (targeting hopelessness) • Homework: Use a thought record to address negative thoughts and emotions
2. Challenging core beliefs	• Identifying and challenging unhelpful deep-seated beliefs about oneself, other people, and the world • Example: "Nothing ever works out for me" • Homework: Continue to use a thought record while identifying and challenging core beliefs
3. Behavioural activation	• Identifying activities that have been dropped because of an increased focus on infertility • Aiming to reintegrate previously enjoyed activities into day-to-day life • Incorporating diaphragmatic breathing to reduce stress • Homework: Schedule pleasure and mastery activities, rate mood before and after
4. Sharing your grief	• Learning about different coping styles and how clashes in coping style can lead to conflict within a couple • Homework: Communication exercise with partners or support persons about grieving style and how best to support one another when grieving
Bonus: Strengthening your relationship	• Providing evidence-based information about how to better connect with one's partner • Common relationship mistake #1: Being mindless • Common relationship mistake #2: Starting conversations with a harsh start-up • Common relationship mistake #3: Avoiding an important conversation
5. Living your values	• Reflecting on overarching life values and considering how daily actions align with those values • Encouraging consideration of ways to reduce avoidance without worsening distress • Example 1: How to deal with family members saying, "Just relax and you'll get pregnant" • Example 2: What to do when invited to a friend's baby shower • Homework: Write what you would like said in your "eulogy" to help identify your life values
6. Summary/wrap up	• Providing an overview of the program's content, encouraging reflection on accomplishments as well as areas for further development

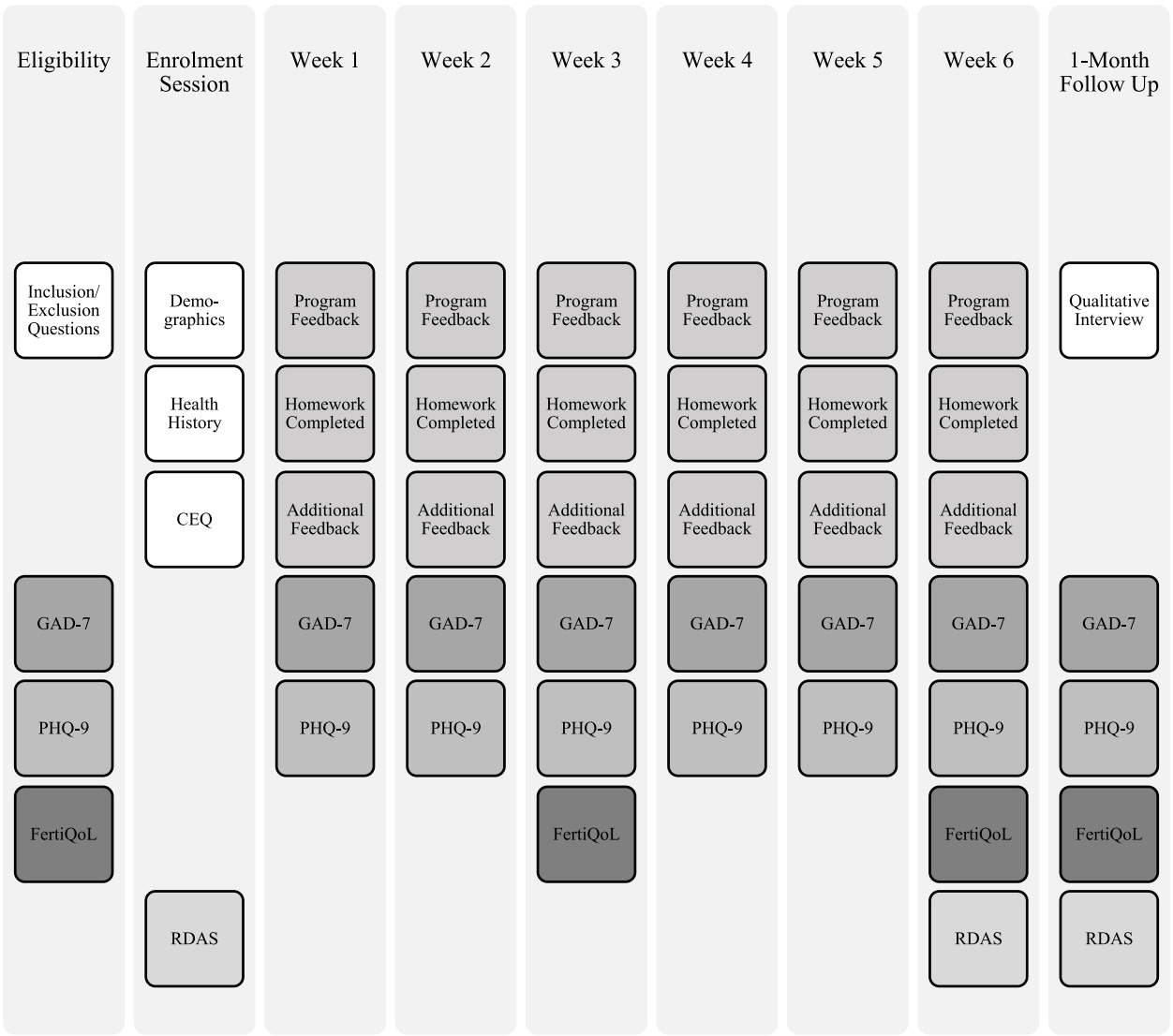

Fig. 1 Timeline of assessment. Note: FertiQoL = Fertility Quality of Life Tool; GAD-7 = Generalized Anxiety Disorder-7 Scale; PHQ-9 = Patient Health Questionnaire-9 Scale; RDAS = Revised Dyadic Adjustment Scale; CEQ = Credibility/Expectancy Questionnaire

Following the enrollment session, participants were emailed one 10-min video module every week for six weeks. These videos were sent in the morning on a day of the participant's choosing, and participants were asked to confirm via email that they had watched each video by the end of the day. Each video included a homework assignment aimed at integrating module content into participants' daily lives. Reminder emails about completing the homework assignments were sent three days after participants received the videos. At the end of each week, participants completed an outcome survey assessing fertility-related quality of life, depression, and anxiety, and received the next 10-min video module. They were also asked how they felt about the previous module, how much homework they had completed, and whether they had any recommendations for improving that week's content. One week after receiving the final video module, participants completed a post-treatment battery of questionnaires assessing fertility-related quality of life, anxious and depressive symptoms, and relationship satisfaction. At this time, participants were also invited to participate in a semi-structured qualitative interview lasting approximately 30 min and conducted via Zoom. Finally, one month post-intervention, participants completed the same battery of mental health questionnaires once more.

Measures

Demographic and medical history questionnaire

General demographic information (e.g., age, race, ethnicity, education, income), reproductive health history (e.g., infertility diagnosis, past fertility treatments, living children), and past conception strategies (e.g., timing intercourse, IVF, intrauterine insemination) were assessed at baseline using a survey created by the authors.

Intervention credibility and expectancy

Participants' beliefs regarding the credibility of the intervention and their expectations regarding the efficacy of the intervention were assessed at baseline. Intervention credibility and expectancy were measured via the six items contained within the Credibility/Expectancy Questionnaire (CEQ) [47]. For all but two items, participants indicated how much they believed the program would help to reduce their distress, using a 9-point Likert scale ranging from 1 ("*Not at all*") to 9 ("*Very*"). For the remaining items, participants indicated how much improvement in distress symptoms they thought would occur, in 10-percent increments from 0% to 100%. Sample items include: "At this point, how logical does the program seem to you?" and "At this point, how much do you really feel that the program will help to reduce distress?" Items were summed to create two subscales reflecting credibility and expectancy; higher scores indicate greater program credibility and participant expectancy. Internal consistency for the CEQ in the current sample was good, with a Cronbach's alpha of 0.84.

Fertility-related quality of life

Fertility-related quality of life was considered the primary outcome and assessed at baseline, midway through the intervention, and at the end of the intervention. Fertility-related quality of life was measured via the 26 items contained within the core FertiQoL scale [48]. This primary outcome was chosen in collaboration with patient advisors as it provides an integrated measure of the emotional, physical, and interpersonal impacts of infertility. Following Koert et al. [38], participants were considered to exhibit significantly poorer quality of life if their FertiQoL score was less than or equal to 52. Consistent with prior research [48, 49], the FertiQoL demonstrated high internal consistency reliability, with a Cronbach's alpha of 0.88.

Anxious symptoms

Past-week anxious symptoms were assessed at baseline, weekly during the intervention, and at the end of the intervention. Anxious symptoms were measured via the seven items contained within the GAD-7, modified to ask about symptoms over the last week instead of two [40, 50]. The GAD-7 has been shown to be superior to other questionnaires in detecting change in anxious mood following treatment [51]. For each item, participants indicated how often they have been bothered by a specific symptom over the past two weeks, using a 4-point Likert scale ranging from 0 ("*Not at all*") to 3 ("*Nearly every day*"). Based on guidelines from Spitzer et al. [40], individuals scoring ≥ 5 are categorized as experiencing mild anxiety, those scoring ≥ 10 are considered to have moderate anxiety, and those scoring ≥ 15 are considered to have severe anxiety. Internal consistency for the GAD-7 in the current sample was good, with a Cronbach's alpha of 0.90.

Depressive symptoms

Past-week depressive symptoms were assessed at baseline, weekly during the intervention, and at the end of the intervention. Depressive symptoms were measured via the nine items contained within the PHQ-9, modified to ask about symptoms over the last week instead of two [41, 52]. The PHQ-9 has been shown to be superior to other questionnaires in detecting change in depressive mood following treatment [53]. For each item, participants indicated how often they had been bothered by a specific symptom over the past two weeks, using a 4-point Likert scale ranging from 0 ("*Not at all*") to 3 ("*Nearly every day*"). Items were summed to create one total score of depression severity. Following Kroenke et al. [41], participants were grouped into five categories, with individuals scoring ≤ 4 being categorized as experiencing no depressive symptoms, those between five and nine experiencing mild depressive symptoms, those between 10 and 14 experiencing moderate depressive symptoms, those between 15 and 19 experiencing moderately severe depressive symptoms, and those ≥ 20 experiencing severe depressive symptoms. Internal consistency for the PHQ-9 in the current sample was good, with a Cronbach's alpha of 0.86.

Relationship satisfaction

Relationship satisfaction was assessed at baseline and at the end of the intervention. Relationship satisfaction was measured via the 14 items contained within the Revised Dyadic Adjustment Scale (RDAS) [54]. For each item, participants rated certain aspects of their relationship on a 5- or 6-point Likert scale (e.g., ranging from 0 ["*Always disagree*"] to 5 ["*Always agree*"]). Higher scores indicate greater relationship stability, satisfaction, and quality; lower scores indicate greater relationship distress. Following Crane et al. [55], participants were considered to exhibit relationship distress

if their RDAS score was less than 48. The RDAS demonstrates strong internal consistency reliability, with Cronbach's alphas ranging between 0.81 and 0.90 [54]. Internal consistency for the RDAS in the current sample was good, with a Cronbach's alpha of 0.83.

Homework completion and weekly feedback

Each week, participants were asked to report the total number of minutes spent engaged in homework related to the program. They were also asked to rate how effective each module and homework assignment was in helping them cope with the emotional challenges of infertility using an 11-point Likert scale ranging from 0 ("*Extremely unhelpful*") to 10 ("*Extremely helpful*"). Space was also provided for participants to enter any additional feedback on any aspect of the past week's module (e.g., aspects they liked/should be kept, aspects they did not like/should be changed).

One week following the end of the intervention, participants were invited to participate in a semi-structured interview to provide detailed feedback on the program. The interview consisted of seven questions designed to capture participants' thoughts and experiences of the program to identify areas for further improvement. The interview guide was developed in collaboration with patient advisors. Sample questions include "What aspects did you like about the program? Were there any modules in particular that you found helpful?" and "How did you find the pace and length of the program (i.e., one module per week for six weeks)? What about the length of the videos themselves?" The interviews were conducted, audio-recorded, and transcribed via Zoom for the purpose of content analysis.

Data analysis

Statistical analyses were performed using SAS software (version 9.4) [56]. Descriptive statistics were used to examine the baseline characteristics of the sample, as well as treatment acceptability and adherence. A mixed model design (PROC MIXED) was used to examine the effect of time on all distress outcomes (i.e., scores on the FertiQoL, GAD-7, and PHQ-9 by intervention week). Continuous score on the FertiQoL, as assessed at the end of the intervention, was identified as the primary outcome; continuous scores on the PHQ-9 and GAD-7, also assessed at the end of the intervention, were identified as secondary outcomes. Each outcome was examined in a separate model where subject was treated as a random effect and time as a fixed effect. Assessment week was identified as a repeated measures factor using a repeated statement.

Qualitative participant feedback from the post-program Zoom interview was analyzed using quantitative content analysis. Specifically, the main data analysis was conducted independently by one of the authors, MMLP, and another research assistant. JLG acted as an auditor of the data. Interview transcripts were reviewed for similar words, themes, or concepts, which were then developed into coding guidelines. Interview data were coded using the Statistical Package for the Social Sciences (version 28.0.0.0) [57] based on these guidelines. Disagreements

Table 2 Baseline demographic, medical, and psychological characteristics

Variable	Mean (*SD*) or %
Age	34.8 (4.5)
White (%)	100%
Marital status	
Married	67%
Common-law	29%
Single	1%
Sexual orientation	
Heterosexual	95%
Other sexual orientation	5%
Education level	
High school diploma	10%
Trade school degree	29%
Some college	24%
Undergraduate university degree	29%
Post-graduate degree	10%
Years of education	15.9 (3.3)
Family income	
$20,000–49,999 CAD	10%
$50,000–89,999 CAD	14%
$90,000+ CAD	68%
No response	8%
Cause of infertility[a]	
Polycystic ovarian syndrome	19%
Low ovary reserve	14%
Blood clot disorder	5%
Repeat pregnancy loss	10%
Pelvic inflammatory disease	1%
Uterine abnormalities	15%
Tubal abnormalities	15%
Unexplained	57%
Baseline Fertility Quality of Life score	43.1 (11.5)
Baseline Generalized Anxiety Disorder-7 score	9.7 (4.4)
Baseline Patient Health Questionnaire-9 score	9.9 (4.6)
Baseline Revised Dyadic Adjustment Scale score	52.5 (6.2)

N = 21

[a] Multiple causes could be endorsed

in the analysis process were discussed and resolved by consensus.

Results

Participant characteristics

Participant demographic characteristics are shown in Table 2. This sample had a mean age in the mid-thirties and all identified as White. Nearly all participants were married or living common-law and identified as heterosexual. Many were well-educated (39% had a Bachelor's degree or higher), with 16 years of education on average. Most participants reported that their experience with infertility was due to unexplained causes. At baseline, participants reported mild to moderate anxiety and depression, with 13 scoring in the clinical range of both the GAD-7 and PHQ-9 (i.e., score $\geq$ 10). Fertility-related quality of life was approximately nine points below the clinical cutoff, indicating poorer than average fertility-related quality of life. Relationship satisfaction was also nearing the cutoff for relationship distress prior to the start of the program.

Study retention and adherence

Of the 21 women enrolled in the study, two became pregnant and were removed from the program prematurely (after program weeks 1 and 4, respectively). Of the remaining 19 women, 15 completed all six modules, two completed two modules before dropping out, and two completed only the first module before dropping out. All outcome data collected prior to the point of pregnancy or withdrawal were included in our final statistical analyses. Participants reported completing an average of 52.8 (SD = 82.0) minutes of homework per week.

Intervention credibility and expectancy

Participant responses to the CEQ are reported in Table 3. Results indicated that prior to starting the program, participants considered the program description and rationale to be logical. They also predicted a 60% to 70% improvement in symptoms following participation in the program, which approaches the actual improvements found in the current study.

Table 3 Pre-intervention responses to the Credibility and Expectancy Questionnaire (CEQ)

	Mean (*SD*)
How logical does the Coping with Infertility program seem? (1–10)	7.2 (1.5)
How successful do you think the program will be in reducing your symptoms? (1–10)	6.5 (1.1)
How confident would you be in recommending it to a friend? (1–10)	6.6 (1.7)
How much improvement in your symptoms do you think will occur? (1–100)	67.6 (19.5)
How much do you really feel that the program will help you to reduce your symptoms? (1–10)	5.6 (1.6)
How much improvements in your symptom do you really feel will occur? (1–100)	63.3 (21.1)

N = 21

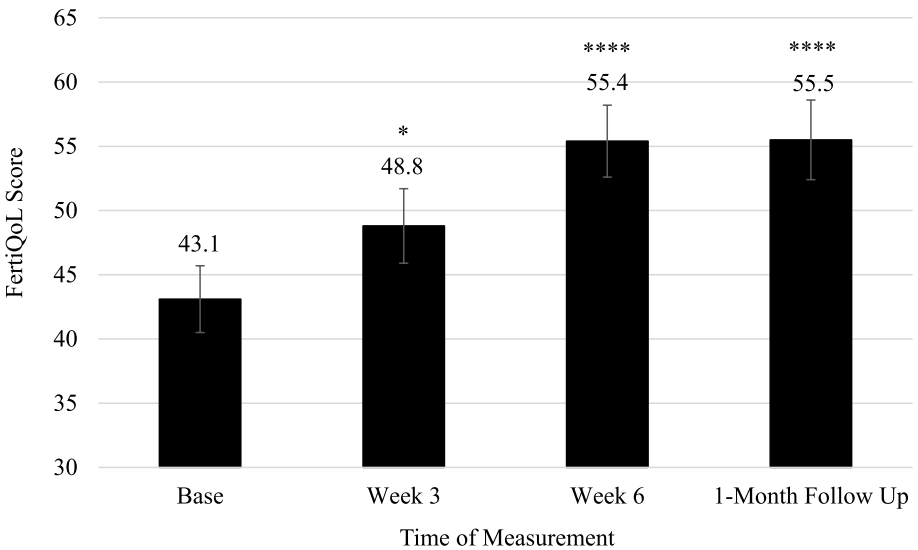

Fig. 2 Mean (*SE*) scores on the FertiQoL throughout the intervention. Note: N = 15–21. *p < .05, compared to baseline. ****p < .0001, compared to baseline

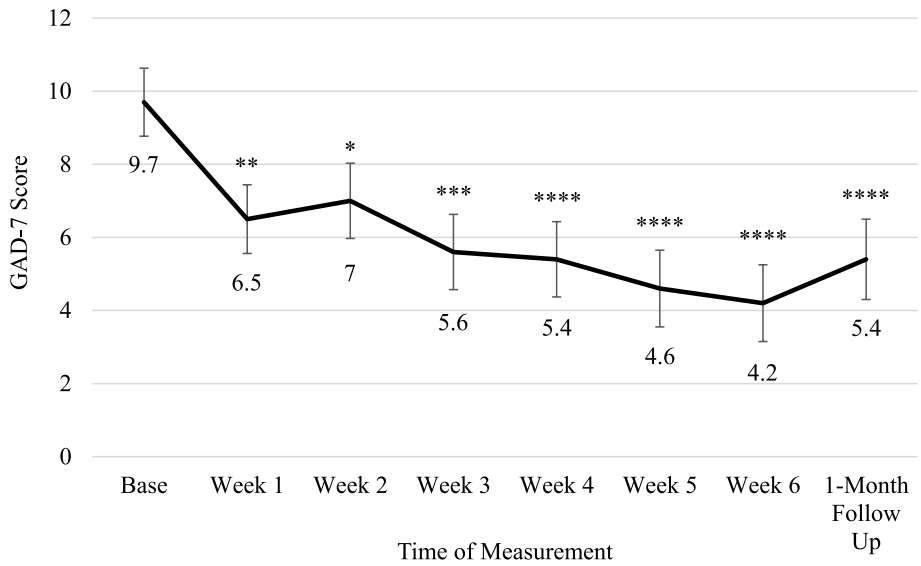

Fig. 3 Mean (*SE*) GAD-7 scores throughout the intervention. Note: $N = 15–21$. $^{*}p < .05$, compared to baseline. $^{**}p < .01$, compared to baseline. $^{***}p < .001$, compared to baseline. $^{****}p < .0001$, compared to baseline

Mental health outcomes

Fertility-related quality of life improved significantly over time ($F(6, 84) = 4.4$, $p = .0007$) as seen in Fig. 2. This effect translates to a Cohen's *d* of 1.05 from baseline to the end of the intervention, and a Cohen's *d* of 0.93 from baseline to the one-month follow-up. Similarly, as seen in Fig. 3, anxious symptoms improved significantly over time ($F(7, 107) = 6.3$, $p < .0001$) such that mean anxiety scores for each week of the intervention were significantly lower than baseline. This effect was large at both the end of the intervention and after a one-month follow-up, translating to Cohen's *d*s of −1.36 and −1.34 relative to baseline, respectively. In participants who reported clinical levels of psychopathology at baseline, this effect was even more pronounced. Specifically, in nine women who reported clinical levels of anxiety at baseline (defined as a score of ≥ 10 out of 21 on the GAD-7) and completed post-intervention outcomes, a Cohen's *d* of −1.9 was obtained

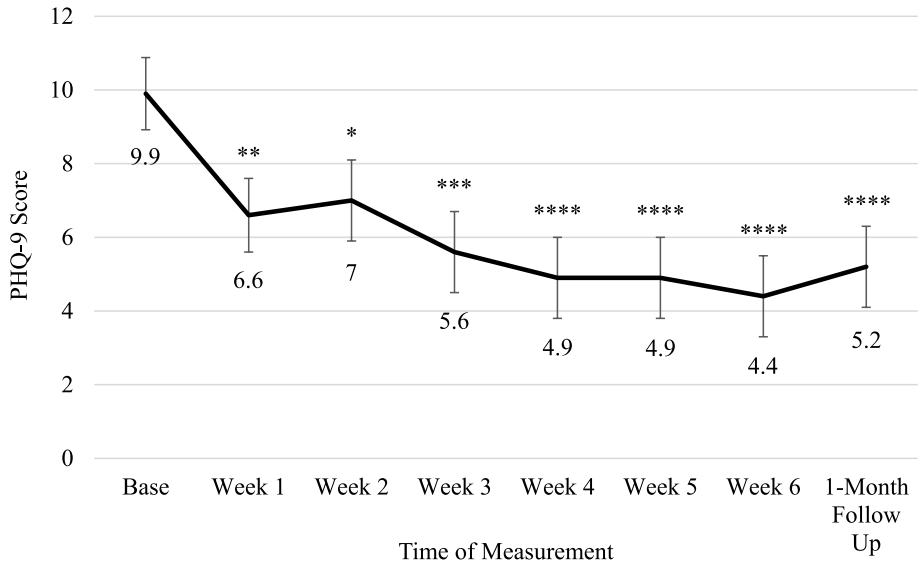

Fig. 4 Mean (*SE*) PHQ-9 scores throughout the intervention. Note: $N = 15–21$. $^{*}p < .05$, compared to baseline. $^{**}p < .01$, compared to baseline. $^{***}p < .001$, compared to baseline. $^{****}p < .0001$, compared to baseline

at the end of the intervention relative to baseline. Finally, as seen in Fig. 4, depressive symptoms also improved significantly over time ($F(7, 109) = 5.3$, $p < .0001$) such that mean depression scores for each week of the intervention were significantly lower than baseline. This effect was large at both the end of the intervention and after a one-month follow-up, translating to Cohen's *d*s of −1.22 and −0.97 relative to baseline, respectively. As with anxious symptoms, this effect was even more pronounced in participants who reported clinical levels of psychopathology at baseline. Specifically, in nine women who reported clinical levels of depression at baseline (defined as a score of ≥ 10 out of 27 on the PHQ-9) and completed post-intervention outcomes, a Cohen's *d* of −2.9 was obtained at the end of the intervention relative to baseline.

In contrast to the mental health effects observed above, relationship satisfaction did not change significantly over time ($F(2, 28) = 0.22$, $p = .80$), with the average post-intervention score being 53.1 ($SD = 1.5$) and the one-month follow-up score being 53.2 ($SD = 1.5$).

Program feedback

When asked about the helpfulness of the homework, each assignment was highly rated by participants, with average ratings of 7.1 or higher (ranging from 7.1 to 8.1) on a scale from 0 ("*Extremely unhelpful*") to 10 ("*Extremely helpful*"). Table 4 further outlines the individual module and homework assignment ratings.

After completing the program, participants were interviewed via Zoom to gather further feedback about the program. Participant feedback is summarized in Table 5, generally reflecting an overall appreciation for the length and format of the program. Cognitive restructuring and challenging core beliefs were the top-rated modules. While 40% of participants indicated that they would make no changes to the program, four participants suggested modifying the homework assignment tied to the Living Your Values module and three participants recommended removing this module altogether. Otherwise, the general pace, length, and order of the program were largely approved.

Twelve participants had at least one recommendation for additional content. Specific recommendations included the following: (1) Navigating fertility treatment (including communicating with healthcare professionals, advocating for specialized fertility treatment, or dealing with the mental strain of appointments, as endorsed by five participants); (2) coping with pregnancy loss and pregnancy announcements (including strategies for seeking social support, managing grief related to the loss, or handling online and in-person announcements, as endorsed by six participants); and (3) mindfulness (including skills to reduce stress or meditation practice, as endorsed by three participants). It was also recommended that the bonus module, Strengthening Your Relationship, be made part of the core program, with many participants highlighting the applicability of the module to all interpersonal relationships, not only romantic relationships. Lastly, three participants recommended increasing the inclusivity and applicability of the program to all causes (e.g., male-factor infertility) and experiences of infertility (e.g., secondary infertility, wherein women already have at least one child).

Table 4 Mean (*SD*) weekly module and homework helpfulness scores (0–10)

Module title	Average module helpfulness (*SD*)	Average homework Helpfulness (*SD*)
Module 1: Cognitive restructuring	7.5 (1.1)	7.1 (1.2)
Module 2: Challenging core beliefs	7.8 (1.4)	7.3 (1.4)
Module 3: Behavioral activation	8.2 (1.0)	8.1 (1.6)
Module 4: Sharing your grief	8.1 (1.4)	7.3 (1.8)
Module 5: Living your values	7.7 (1.9)	7.5 (2.0)
Module 6: Summary/wrap up	7.9 (1.5)	7.6 (1.5)
Bonus: Strengthening your relationship	7.6 (1.4)	N/A

$N = 21$

Discussion

The purpose of this pilot study was to test the feasibility, acceptability, and preliminary efficacy of a new self-directed psychological intervention for infertility-related distress. In line with expectations, participants showed significant improvements in fertility-related quality of life, anxiety, and depression over the course of the CWI program; those individuals who were experiencing clinical levels of psychopathology prior to starting the program experienced the greatest improvement in symptoms relative to baseline. The program was also very well-received by women experiencing infertility.

Women experiencing infertility reported mild to moderate anxiety and depression, and poorer than average fertility-related quality of life, prior to starting the CWI program. Over the course of the program, participants improved significantly across all distress outcomes. The capacity for the CWI program to increase fertility-related quality of life is an improvement on existing psychological interventions, which have previously been shown to be ineffective in this domain [30, 58]. Those few interventions that have successfully increased fertility-related quality of life have employed mindfulness-based [59, 60] and cognitive coping and relaxation strategies [61]. Mindfulness skills were one of the techniques explored during

Table 5 Post-program interview results

Question	*n* endorsing given options (%)							
	Questionnaires	**Homework assignments**	**Module content**		**Videos**	**Length of program**		**No**
What aspects did you like about the program?	1 (6.7%)	11 (73.3%)	11 (73.3%)		5 (33.3%)	3 (20.0%)		N/A
Were there any aspects that you suggest we change?	3 (20.0%)	5 (33.3%)	4 (26.7%)		2 (13.3%)	0 (0.0%)		6 (40.0%)
	Cognitive restructuring	**Challenging core beliefs**	**Behavioral activation**	**Sharing your grief**	**Strengthening your relationship**	**Living your values**	**Summary/wrap up**	**No**
Were there any modules that you found helpful or that stood out to you?	13 (86.7%)	10 (66.7%)	6 (40.0%)	2 (13.3%)	4 (26.7%)	2 (13.3%)	1 (6.7%)	0 (0.0%)
Were there any modules that you could do without?	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (20.0%)	0 (0.0%)	11 (73.3%)

	Yes	**No**
Did the order of the modules seem logical to you?	12 (80.0%)	3 (20.0%)
Do you think there are any other bonus modules that should be created?	12 (80.0%)	3 (20.0%)
Was there any content missing, any topics or difficulties that you experienced that were not covered?	10 (66.7%)	5 (33.3%)
Should the relationship module be a standalone module that everyone should go through?	13 (86.7%)	2 (13.3%)

	Too fast/too much	**Too slow/too little**	**Just right**
How did you find the pace and the length of the program?	1 (6.7%)	0 (0.0%)	14 (93.3%)
What about the length of the videos, was that okay or was that too little or too much?	1 (6.7%)	0 (0.0%)	14 (93.3%)

	Like	**Did not like**	**Neutral**
What do you think about ordering the modules based on needs?	9 (60.0%)	2 (13.3%)	4 (26.7%)
What about skipping one module altogether?	4 (26.7%)	5 (33.3%)	4 (26.7%)
What do you think of the questionnaires that we included?	6 (40.0%)	4 (26.7%)	4 (26.7%)

	Keep as is	**Keep but revise summary**	**Replace with new content**	**Replace but keep summary**
What do you think of the summary module?	4 (26.7%)	3 (20.0%)	1 (6.7%)	7 (46.7%)

n = 15. For the first four questions, multiple responses are possible

the development process for the CWI program [42] and were further recommended by participants in the current pilot study as an option for additional content. Thus, combining the cognitive-behavioral coping strategies of the current program with mindfulness-based approaches could be explored to optimize the impact of the CWI program on fertility-related quality of life.

Similarly, anxiety and depression are core features of infertility-related distress [35] that were effectively addressed by the CWI program. On average, participants experienced improvements in anxious and depressive symptoms within the 50% to 60% range between baseline and the end of the intervention, with 85% of participants experiencing a clinically significant decline in symptoms. Previous research has been mixed on the effect of psychological interventions for anxiety and depression in women experiencing infertility, as well as potential moderators of these effects [28–32]. One reason that the CWI program may have produced larger effects than those previously observed for existing psychological interventions is its unique tailoring to infertility-related distress. To date, mental health interventions targeting infertility have primarily consisted of existing psychotherapy approaches (e.g., CBT, mindfulness-based interventions) with only surface-level tailoring to infertility (e.g., use of infertility-specific examples). By comparison, tailored psychological interventions have produced greater improvement in health outcomes and behaviors related to infertility compared to both generic interventions and waitlist control conditions [62–65]. Tailored interventions may also be more beneficial than standard interventions when addressing comorbidity in online [66] and self-help formats [67], such as that of the CWI program.

The added benefits of tailoring may also explain why the CWI program's effects on anxious and depressive symptoms were particularly amplified in participants who initially reported clinical levels of psychopathology. By tailoring the program to infertility-related distress, the CWI program frequently focused on experiences of shame, self-criticism, and negative automatic thoughts in its content, examples, and homework assignments. Self-criticism has been found to mediate the link between shame and psychological distress (i.e., depression and anxiety) [68], and automatic associations often contribute to the maintenance of anxious and depressive symptoms [69–71]. Thus, these participants had the most potential to improve prior to the program (in reporting a greater number of symptoms), and the program then addressed the very mechanisms maintaining their symptoms (shame, self-criticism, and automatic thoughts).

Surprisingly, the CWI program did not improve relationship satisfaction. One potential explanation for these unexpected findings is our use of the RDAS as a measure of relationship satisfaction. The RDAS assesses seven dimensions of couple relationships (e.g., decision making, values, affection, stability, conflict regulation, activities, and discussion) within three overarching categories (e.g., consensus, satisfaction, and cohesion). While it is common practice to infer relationship satisfaction based on total RDAS score, previous research has challenged this method of interpretation [72]. Thus, our results may have been different if we used dedicated, total score measures of relationship satisfaction. There are numerous scales assessing relationship satisfaction that could be used in place of the RDAS, including the Couples Satisfaction Index [73] or the Relationship Assessment Scale [74]. These scales assess more immediate relationship issues, including how many problems there are in the relationship and how well each partner's needs are met, and both have been validated for use with individuals experiencing infertility [75, 76]. Utilizing an alternative means of measuring relationship satisfaction may more clearly illustrate differences that occur as a result of the CWI program.

Ultimately, the CWI program was viewed as both credible and beneficial, with the module content and homework assignments considered to be quite helpful. Specifically, helpfulness scores ranged from 7.5 to 8.2 for the module content and from 7.1 to 8.1 for the homework, on a scale from 0 ("*Extremely unhelpful*") to 10 ("*Extremely helpful*"). Many participants indicated that they would make no changes to the program; others suggested changes to the content and homework of the Living Your Values module, specifically. Only 20% of participants supported removing a module entirely, and most supported the addition of even more content, including themes of mindfulness and tips for talking to healthcare professionals. Overall, these results suggest a high rate of satisfaction with the program, as well as the continued need for such an intervention in this population.

Implications and future directions

The results of the current study should be viewed in light of some limitations, including its small sample size, homogeneous demographic characteristics (e.g., White, upper middle class, heterosexual), and restriction to self-selection and self-report data. Specifically, as participants were recruited from infertility support groups, they were already seeking additional help with their experience with infertility when they opted to participate in the study. Our sample was thus an exclusively treatment-seeking sample, which was reflected in their poor baseline mental health and could have resulted in larger effect sizes at post-intervention relevant to other recruitment methods. Further, participants' responses may not have accurately reflected their level of symptomology or engagement in

the program. Participants' responses could have been subject to practice effects due to repeated outcome measurement or to social desirability bias, with participants potentially over- or under-reporting their level of depressive or anxious symptoms based on the time of measurement out of a desire for continued support for the program and this field of research.

These findings are encouraging overall and suggest that the CWI program is worthy of further development and testing. In particular, an adequately powered randomized controlled trial would allow for a comparison of the CWI program to women's ordinary coping strategies or other generic psychological interventions. Incorporating objective measures of program engagement and adherence, such as metrics on the program modules (e.g., number of views), would further account for the limitations of self-report data noted above. A larger trial could also adopt an intent-to-treat approach to address the constraints imposed by the inclusion and exclusion criteria of the current study. Namely, given the substantial improvements observed in quality of life, anxiety, and depression following the CWI program, a trial could aim to include individuals with varying degrees of mental health concerns to determine the magnitude of benefit across symptom severity. For example, it is probable that individuals whose quality of life was above the cutoff used in the current study could still experience improvements in other psychological outcomes (e.g., anxiety and depression) following the program or vice versa. A larger trial could also examine the potential effects of the CWI program on perinatal anxiety and depression by retaining participants who become pregnant during the course of the study.

Following a successful trial, research focus could turn to optimizing the CWI program such that women who participate in future iterations of the program experience even greater improvements in areas that are demonstrably important to those living with infertility. Optimizing the program could involve identifying particularly influential components, including any effects of tailoring the order of the modules or adding additional content. A factorial design could be employed to systematically vary these components and assess their impact on distress outcomes similar to those explored in the current study. Once the program is optimally effective, it could be made widely available online or through a mobile app to increase accessibility.

Conclusion

Infertility is associated with severe psychological consequences [77], yet current psychological interventions are neither specialized nor largely effective in this population. The six-week CWI program was developed to address this need. The program was well accepted and considered helpful in addressing the various facets of infertility-related distress, establishing the feasibility of the intervention and its procedures. Participants demonstrated large, significant improvements in fertility-related quality of life, anxiety, and depression in a one-arm pre-post trial of women experiencing distress related to infertility. These results suggest that the CWI program is ready to be tested in a randomized trial. Future program development and optimization should also be pursued, including looking at the influence of additional module content or module order on treatment outcomes, or the effects of the program against or in combination with other forms of psychotherapy.

Abbreviations

CBT	Cognitive behavioral therapy
CEQ	Credibility/Expectancy Questionnaire
CWI	Coping with Infertility
FertiQoL	Fertility Quality of Life Tool
GAD-7	Generalized Anxiety Disorder-7
IVF	In vitro fertilization
PHQ-9	Patient Health Questionnaire-9
RDAS	Revised Dyadic Adjustment Scale

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Authors' contributions

JLG and AAB formulated the study question, developed the study design, and collected the data. JLG and MMLP analyzed the data and drafted the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets generated and analyzed in the current study are not publicly available to protect participant confidentiality but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study obtained ethical approval through the University of Regina's Research Ethics Board (REB 2021–108). Informed consent to participate was obtained during the initial enrolment session. Consent was obtained by trained research assistants who completed the Tri-Council Policy Statement Course on Research Ethics. Participants received $75.00 CAD for full participation in the study or were compensated based on their partial participation.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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