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A Prospective Study of Depression and Anxiety in Female Fertility Preservation and Infertility Patients

Angela K. Lawson, Ph.D.[1], **Susan C. Klock, Ph.D.**[1], **Mary Ellen Pavone, M.D.**[1], **Jennifer Hirshfeld-Cytron, M.D.**[2], **Kristin N. Smith, B.S.**[1], and **Ralph R. Kazer, M.D.**[1]

[1]Northwestern University, 675 North St. Clair Street, Suite 14-200, Chicago, Il, 60611

[2]Fertility Centers of Illinois, 8651 W 159th Street, Orland Park, IL, 60462

Abstract

Objective—To prospectively assess anxiety, depression, coping, and appraisal in female fertility preservation patients compared to infertile patients.

Design—Prospective pre- and post-treatment survey.

Setting—Academic medical center.

Patients—47 women with cancer (FP) and 91 age-matched infertile patients.

Interventions—None.

Main Outcome Measures—Depression, anxiety, coping, infertility–related stress, appraisal of treatment, and medical outcomes.

Results—FP patients reported more symptoms of anxiety and depression than infertile patients, but infertile patients' symptoms worsened over time. 44% of FP and 14% of infertile patients' scores exceeded the clinical cut-off for depression at pre-treatment. The interval between surveys and medical treatment data did not predict changes in mood symptoms. Coping strategies and infertility-related stress did not differ between groups and avoidant coping predicted higher depression and anxiety scores.

Conclusion—FP patients reported more anxiety and depression than infertile patients at enrollment in treatment, with more than one third of FP patients reporting clinically significant depressive symptoms. However, infertile patients' anxiety and depressive symptoms increased across treatment. This increase was not related to time between registration for IVF and oocyte retrieval or the medical aspects of treatment. FP and infertile patients should be provided psychological consultation prior to treatment to identify mood and anxiety symptoms and to refer patients for counseling as needed to prevent worsening of symptoms.

Reprint requests: Angela K. Lawson, Ph.D., Department of Obstetrics and Gynecology, Northwestern University Feinberg School of Medicine, 676 North St. Clair Street, Suite 1845, Chicago, IL 60611 (FAX: 312-695-4924; alawson@nmff.org).

Conflict of Interest: None

Keywords

Fertility preservation; IVF; psychological; counseling

INTRODUCTION

Young cancer patients are increasingly interested in preserving their fertility prior to undergoing gonadotoxic therapies (1–5). Female cancer patients can preserve their fertility by undergoing embryo or oocyte cryopreservation prior to beginning cancer treatment (6). Oocytes or embryos can be cryopreserved and stored until the cancer has been treated and the woman is ready to attempt pregnancy. Although the medical safety and treatment protocols for fertility preservation (FP) via controlled ovarian hyperstimulation (COH) have been well documented (1–4, 7), there is limited research addressing the psychological issues that arise in FP patients. Based on the research describing the emotional aspects of in vitro fertilization (IVF) for infertile couples (8), the psychosocial stressors associated with IVF or FP likely include the physical and emotional side effects of medications and procedures (9–12), treatment expense (13–17), relationship changes after embryo cryopreservation which may interfere with a patient's use of the embryos (18–21) and religious/ethical issues related to embryo disposition (14, 22–25).

IVF, while providing the hope of family building opportunities, has also been perceived by patients to be a stressful experience (26). Coping with IVF can be conceptualized from the stress and coping model of Lazarus and Folkman (27). This model has been used in previous studies of the stress of infertility but has not been applied to studies of the psychological adjustment to fertility preservation (28–30). In this model, psychological harm is mediated by an individual's appraisal of the event and the ways in which they cope with the event. If the individual appraises the event as harmful or threatening and their stress overwhelms their coping resources or results in problematic coping such as ignoring the problem, then depression and/or anxiety may result.

Research on infertile IVF patients has found that 20%–50% report mild to moderate symptoms of depression, 2% report severe symptoms of depression, 15% to 56% report clinically significant anxiety, and that these symptoms worsen after failed treatment cycles (31–33). Of the few studies that have been conducted with FP patients, it has been found that a considerable percentage of FP patients also experience emotional distress during treatment with as many as one third reporting significant anxiety or depression symptoms and 14% taking prescribed antidepressant medication (5, 14). These rates of anxiety and depression are comparable to those reported by Peate et al in which 32% of young breast cancer patients reported symptoms of anxiety and 10% reported symptoms of depression (34).

In addition to the similarities across infertile and FP patients' experiences, there are also unique stressors for both groups. Specifically, infertile patients are concerned about immediate chances of pregnancy whereas FP patients are in the early stages of coping with their cancer diagnosis. FP patients have cancer specific concerns about their mortality, future disease recurrence, implications of genetic testing (e.g. BRCA), body image concerns,

and are concerned about the effects of cancer treatment on their sexuality as well as on current and future relationships (14, 16, 35–39). FP patients are also likely to have fertility treatment specific concerns about the health consequences of delaying their cancer treatment in order to pursue FP, the potential impact of high doses of injectable gonadotropins on cancer recurrence (especially with hormonally sensitive cancer types), the need to make treatment decisions within days or weeks (17, 24, 35, 40), and the emotional consequences of posthumous reproduction should they ultimately succumb to their disease (7, 41–43).

The multiple differences in the emotional aspects of IVF for infertile patients and FP treatment via COH may result in differences in the psychological experiences of these two groups during treatment. However, there are no previous prospective assessments of the psychological status of FP patients as they undergo treatment and no direct comparison of the psychological experiences of FP and infertile patients. The purpose of the current study is to describe the occurrence of symptoms of depression and anxiety in FP and infertility patients at the onset of COH treatment and examine the change in depression and anxiety symptoms across patient's first treatment cycle. In addition, we hypothesize that negative appraisals of treatment and problematic coping (i.e., avoidance and internet use) will be related to higher scores on measures of depression and anxiety.

MATERIALS AND METHODS

Participants

The sample included 47 consecutive pre-menopausal female FP patients and 91 consecutive prospectively age-matched female infertile patients who were beginning their first cycle of COH between 2011 and 2013. Two additional FP patients are not included in the study as they consented to participate in the study but did not complete either questionnaire. 4 FP and 4 infertile patients declined study enrollment. Patients who were younger than 18 years or were non-English speaking were excluded from the study.

Procedures

All participants had a routine pre-treatment registration appointment that included physician, nurse, and psychologist consultations. The study participants completed two questionnaires. The pre-treatment survey (T1; 175 items) was administered upon registration for COH treatment and the post-COH survey was completed on the day of oocyte aspiration prior to sedation (T2; 104 items). The post-COH survey was administered at this time in order to assess the subject's emotional state after exposure to ovarian stimulation but prior to pregnancy. Thus, we could assess the relationship of a measure of mood unaffected by knowledge of pregnancy outcomes with later assessments of dependent variables. The surveys contained questions about the patients' demographics and medical history including age, marital status, reproductive history, racial/ethnic status, mental health history, insurance coverage, and previous cancer treatment. Treatment data included gonadotropin dosage, antimüllerian hormone (AMH) values, peak estradiol (E_2), oocyte quality and quantity, pregnancy data, and treatment expectations.

Measures

1. Depressive symptomatology was assessed at both time points with the Center for Epidemiologic Studies- Depression Scale (CES-D) (44) (a 20 item, Likert scaled questionnaire), with higher scores reflecting greater symptomatology. Scale scores between 16 and 21 indicate mild-moderate depressive symptomatology and scores > 21 indicate probable major depression.
2. The State-Trait Anxiety Inventory (STAI) (45) was used to assess both current (STAI-S; State) and general (STAI-T; Trait) levels of anxiety. The STAI contains 40 Likert-type items with higher scores reflecting greater symptomatology and a suggested cut-off of 39 for clinically significant anxiety (46). State anxiety was measured at both time points and trait anxiety was measured only at T1.
3. The Ways of Coping- Revised scale (WOC-R) contains 29 Likert scale items and was used at both time points to measure three dimensions of coping (SBA, Self-Blame and Avoidance; IES, Informational and Emotional Support Seeking; and CR, Cognitive Restructuring). Higher scores on the WOC-R subscales reflect more coping activity (47).
4. Appraisal of Life events Scale (ALE) (48) was used at both time points to assess three dimensions of the cognitive appraisal of treatment (Threat, Challenge, and Loss). The ALE has 16 Likert-type items with higher scores indicating greater appraisal.
5. Fertility Problems Inventory (FPI) (49) a 46 item measure was used at T1 to assess five dimensions of infertility-related stress (Social Concern, SOCON; Sexual Concern, SEXCON; Relationship Concern, RCON; Rejection of Childfree Lifestyle, RCL; and Need for Parenthood; NP).

Following completion of the treatment cycle, the subjects' IVF medical data were obtained via chart review. Treatment data included gonadotropin dosage, antimüllerian hormone (AMH) values, peak estradiol, oocyte quality and quantity, embryo quality and quantity, pregnancy data, and treatment expectations. The study was approved by the Institutional Review Board at Northwestern University.

Statistical Analysis

Statistical analyses using SPSS (IBM, Armonk, New York) were performed employing parametric tests for normally distributed data and non-parametric tests for non-normally distributed data, unequal sample variances, categorical data, and/or comparisons with small sample sizes. Logistic multiple regression analyses were used to test the model for appraisal and coping as predictors of depression and anxiety. Analyses are based on available data, sample sizes are provided, and $p < .05$ (two-tailed) was considered significant.

RESULTS

The average age of women undergoing FP was 31.84 years old (*range* = 19–39; *SD* = 2.39) and the average age of the age –matched infertile comparison group was 31.49 (range = 26–36; SD = 4.76) *ns*. The majority of women in both groups was white, nulligravid, and had

completed at least a college degree. Although the majority of women in both groups had a spouse or heterosexual partner, fewer of the FP women (46.8%) were married compared to the women in the infertile comparison group (95.6%) ($p < .001$). Further, despite treatment occurring in a state with an insurance mandate for fertility treatment coverage, only 23.4% of FP patients had most of their treatment expenses covered by their insurance compared to 56% of those in the infertile comparison group ($p <.001$). The demographic characteristics of the two groups are presented in Table 1.

The majority of FP patients had been diagnosed with breast cancer (63.8%) and an additional 12.8% of patients had been diagnosed with a hematological cancer (i.e. leukemia or lymphoma), 12.8% with a gynecologic cancer, and 10.6% with brain or colon cancer. Three FP patients (2 with a hematologic cancer and 1 with brain cancer) presented with a previous history of chemotherapy treatment. The median time interval between registration for treatment and oocyte retrieval was significantly shorter ($p <.05$) for fertility preservation patients (14.0 days, *range* = 10–62) than the infertile comparison group (38.5 days, *range* = 11–200).

Median scores and significant group differences for the FP patients and the infertile comparison group on all psychological measures are listed in Table 2. Overall, fertility preservation patients reported more symptoms of depression and anxiety than infertile controls. Group differences were also found in measures of appraisal and coping but not specific fertility problem stress. Forty-four percent (17/39) of FP women compared to 14% (10/74) of the infertile comparison group had a score >16 on the CES-D at T1. Sixty-two percent of FP women compared to 27% of the infertile comparison group had STAI-S scores ≥ 39. At the time of the pre-treatment psychological consultation, in terms of self-reported anxiety and depression disorders, 13% (6/46) of FP patients reported a current depressive disorder and 13% (6/46) reported a current anxiety disorder. Of the infertile comparison group, 9% (8/87) reported a current depressive disorder and 14% (12/87) reported a current anxiety disorder.

At T2, 32% (9/28) of FP patients had a score >16 on the CES-D at T2 compared to 23% (15/66) of the infertile comparison group. 50% of FP patients and 51% of the infertile comparison group had STAI-S scores >39 at T2. Scores on the CES-D and STAI-S were unchanged for FP patients and increased across survey periods for the infertile comparison group. Almost half (47%) of FP patients and only 18% of the infertile comparison group reported unrealistic treatment expectations indicating that they believed they had a greater than a 60% chance of pregnancy with each embryo transfer in IVF ($p < .05$). National data from the Society for Assisted Reproductive Technology indicates a pregnancy rate of approximately 50% for women under 35 years old (50).

We were interested in examining the relationship between the role of coping and cognitive appraisal in the prediction of depression and anxiety. First, Spearman correlations between the psychological measures, demographics, and medical variables were conducted (see Table 3). Only those variables with significant correlation coefficients were included in subsequent regression analyses (see Table 3). We conducted hierarchical logistic regression to examine the ability of our measures to predict scores ≥ 16 on the CES-D and ≥ 39 on the

STAI-S. Significant individual variables were entered into the first block. ALE Threat and Loss scores and FPI subscales were entered into the second block as both the ALE and FPI measure perceived stress. The FPI was only measured at T1 but was included in models predicting T2 depression and anxiety as it was hypothesized to predict anxiety and depression at both time points. The relevant WOC subscales were entered into the final block as individuals do not engage in coping strategies unless they perceive an event as distressing. Group (i.e., FP or infertile comparison group) was excluded from the model as it was expected to account for major variance in depression or anxiety scores and would mask the importance of other predictors. A summary of regression results are listed below. Complete regression results may be obtained from the first author.

At T1, evaluation of the log-likelihood test of the overall model for Depression (CES-D ≥ 16) including the insurance and AMH variables in the first block, T1 ALE Loss and Threat subscales and T1 FPI Sexual, Social, and Relationship Concerns subscales in the second block, and T1 WOC avoidant coping subscale in the third block was significant [χ^2 (N =64) = 42.28, *df* = 8, $p < .001$]. The Hosmer-Lemeshow (H-L) goodness-of-fit statistic was not significant ($p = .781$) suggesting a good model fit. The log odds of being diagnosed with depression was related to higher elevations on T1 WOC avoidant coping subscale [OR = 1.90, (95% CI = 1.08, 3.34)]. Nagelkerke's R^2, a measure of strength of association between the predictors and the dependent variable was .781 for the entire model (96.9% correctly classified). This demonstrates that depression at T1 is largely driven by engagement in a problematic coping strategy, namely avoidant coping.

An evaluation of the log-likelihood test of the overall model for T1 Anxiety (STAI-S ≥ 39) including the insurance variable in the first block, the T1 ALE Loss and Threat subscales and T1 FPI Sexual, Social, and Relationship Concerns subscales in the second block, and T1 WOC avoidant coping and information seeking subscales in the third block the model was significant [χ^2 (N =76) = 38.34, *df* = 8, $p < .001$]. The Hosmer-Lemeshow (H-L) goodness-of-fit statistic was not significant ($p = .561$) suggesting a good model fit.. The log odds of having a score ≥39 was related to poorer insurance coverage [OR = 2.49, (95% CI = 1.30, 4.77)], higher elevations on T1 FPI Sexual Concerns subscale [OR = 1.16, (95% CI = 1.01, 1.32)], and higher elevations on T1 WOC avoidant coping subscale [OR = 1.13, (95% CI = 1.01, 1.28)]. Nagelkerke's R^2 was .561 for the entire model (80.3% correctly classified). This demonstrates that anxiety at T1 is driven by financial and sexual problems as well as engagement in avoidant coping.

At T2, evaluation of the log-likelihood test of the overall model for Depression (CES-D ≥ 16) including the T2 ALE Loss and Threat subscales, and T2 WOC avoidant coping subscale, and T1 FPI Sexual, Social, and Relationship Concerns subscales in the model was significant [χ^2 (N =58) = 24.457, *df* = 6, $p < .001$]. The Hosmer-Lemeshow (H-L) goodness-of-fit statistic was not significant ($p = .883$) suggesting a good model fit. The log odds of being diagnosed with depression was related to higher elevations on the T2 WOC avoidant coping subscale [OR = 1.21, (95% CI = 1.00, 1.45)]. Nagelkerke's R^2, a measure of strength of association between the predictors and the dependent variable was .525 for the entire model (81.0% correctly classified). As with depression at T1, this demonstrates that depression at T2 is driven by engagement in avoidant coping.

An evaluation of the log-likelihood test of the overall model for T2 Anxiety (STAI-S ≥ 39) including the T2 ALE Loss and Threat subscales and T1 FPI Sexual and Social Concerns subscales in the first block and T2 WOC avoidant coping subscale in the second block the model was significant [χ^2 (N =62) = 20.76, *df* = 5, *p* = .001]. The Hosmer-Lemeshow (H-L) goodness-of-fit statistic was not significant (*p* = .955) suggesting a good model fit. The log odds of having a score ≥39 was related to higher elevations on T2 ALE Threat subscale [OR = 1.24, (95% CI = 1.02, 1.52)]. Nagelkerke's R^2 was.380 for the entire model (74.2% correctly classified). This demonstrates that at T2, patients with the most anxiety are those who anticipate that treatment will have a negative physical or emotional outcome.

Last, in terms of medical treatment data, median scores and significant group differences for the FP patients and the infertile comparison group are listed in Table 4. Thirty-one FP patients had embryos cryopreserved and 15 cryopreserved oocytes. One patient was unable to have either oocytes or embryos cryopreserved. Regarding the disposition of unused frozen embryos, 60% of FP and 30% of the infertile comparison group directed the embryos to be donated for research, 15% of FP and 26% of the infertile comparison group would donate them to another couple and 22% of FP and 11% of the infertile comparison group designated their unused embryos to be discarded (χ^2 = 22.7, p < .000). At the time of this writing, one FP woman returned approximately one year after her embryos were created to use her embryos via a gestational carrier and has an ongoing pregnancy. There was no relationship between clinical pregnancy and CES-D or STAI-S scores at either time point nor was there a relationship between clinical pregnancy and change in CES-D or STAI-S score from T1 to T2 in the infertile comparison group.

DISCUSSION

Fertility treatment is associated with emotional distress for both cancer patients and the infertile comparison group and this distress worsens during the treatment cycle for the infertile comparison group. Using a CES-D score of ≥ 16 and a STAI-S score ≥ 39, the majority of FP patients and a substantial minority of the infertile comparison group could be classified as having a clinically significant level of depressive and/or anxiety symptoms at enrollment for fertility treatment. This is in contrast to the lower level of patient self-reported symptoms of depression or anxiety at T1 during the psychological consultation. The discrepancy between self-reported depressive symptoms during consultation and classification of depression based on the CES-D scores in FP and infertile women is somewhat unexpected. Research finds that many patients underreport mental health symptoms and treatment histories to their medical providers (51, 52). The discrepancy between self-reported history and mood scale scores may therefore be a function of the social desirability to underreport such symptoms during the psychological consultation.

In the current study, women beginning FP treatment reported higher levels of depression and anxiety symptoms compared to infertile patients. However, the relatively high levels of depression and anxiety among FP women at T1 did not worsen as the women went through treatment. In contrast, levels of depression and anxiety in the infertile comparison group increased over the course of treatment and matched the high levels seen in the FP group with at least half of women reporting significant symptoms of depression and/or anxiety. It is

unclear why the infertile patients' symptoms worsened over time. It is possible that differences in the medical aspects of IVF or longer time intervals between T1 and T2 for the infertile comparison group provided greater opportunity for symptoms of depression and anxiety to develop. However, this does not appear to be the case in our study as neither the medical aspects of IVF nor time between surveys predicted increased scores on the measures of depression or anxiety. Another hypothesis would be that mood symptoms worsened for the infertile comparison group as they got closer to learning whether or not IVF would result in a pregnancy. The significant increase in anxiety for the infertile comparison group has been previously reported (53, 54) in longitudinal IVF studies and others have noted that the time of retrieval (55) or following embryo transfer (56) are times of high anxiety for women undergoing IVF. Recent research however found no change in anxiety at multiple time points during stimulation, retrieval, and awaiting pregnancy results although elevations in scores on measures of anxiety were noted at all time points (57). It is also possible that less social desirability existed in the FP patients as it is generally accepted that a cancer diagnosis will result in distress whereas the infertile comparison group may have worried that acknowledging symptoms of depression or anxiety would negatively affect their ability to proceed with IVF. Alternately, FP patients' high initial scores on the depression and anxiety measures may reflect patient's distress by the recent diagnosis of cancer and the stress of future cancer treatment (e.g., chemotherapy and radiation). FP patients are also not concerned about immediate pregnancy results as FP treatment helps them delay family building until their cancer treatment is complete. Therefore, anxiety and depression levels in FP patients may be elevated and stay elevated because completing FP treatment does not represent the end of their medical ordeal, just the end of a part of it. Additional assessment at a more distal time point could clarify this finding.

According to Lazarus and Folkman's (27) model of stress, appraisal, and coping, individuals who experience an event they perceive to be stressful and then are unable to adequately cope with that event are at risk for depression and/or anxiety. For example, if a woman experienced a traumatic event which she perceived as upsetting and subsequently engaged in avoidant coping rather than active coping strategies; she would be at increased risk of for depression and/or anxiety. In the context of our study, we hypothesized that patients who developed significant depressive or anxiety symptoms likely appraised fertility treatment as distressing. Although we did not see an increase in the appraisal of Threat or Loss in the infertile comparison group over time, higher scores on the Threat and Loss subscales were positively related to higher scores on the CES-D and STAI-S. Consistent with previous research, three subscales of the FPI (sexual, social, and relationship concerns), a measure of perceived stress (49), also correlated with higher depressive and anxious symptomatology thus supporting our hypothesis. We also hypothesized that maladaptive coping strategies would be related to depression and anxiety and indeed avoidant based coping (WOC SBA) and information and emotional support seeking (WOC IES) were associated with greater psychological distress. It is not surprising that the (WOC IES) correlated with anxiety at T1 as this subscale assesses use of the internet for information gathering and research has found that such coping strategies may result in increased distress (58). The WOC IES subscale includes both positive (emotional support seeking) and potentially negative (use of the internet) coping strategies which likely contributed to its limited contribution to explained

variance in the logistic regression model of anxiety. WOC (SBA) however, accounted for the greatest unique amount of overall explained model variance in T1 depression and anxiety and also contributed (along with fertility-related sexual concerns and limited insurance coverage for treatment) to the prediction of T1 anxiety. From the coping perspective, there were no significant differences in coping across time for the infertile comparison group and a significant decrease in information and emotional support seeking coping for the FP group. It may be that compared to FP patients, the infertile comparison groups' prolonged engagement in the perceived threatening experience (IVF) and continued inability to actively cope with the experience (avoidant coping) resulted in increased symptomatology over time. Regardless of the explanation for initial psychological distress or change in distress over time, early patient screening for avoidant coping and/or negative appraisals of IVF could be used to identify and treat patients at risk for increased depression or anxiety at time of oocyte retrieval.

This study is limited by the description of the experiences at a single fertility center with a demographically homogenous sample. However, this study was a preliminary study to highlight areas of future multi-center studies of this patient population. Future research may also be limited by a homogeneous subject group as only patients who have access to medical care and can afford fertility preservation or IVF will likely present for treatment and be available for clinical study. Our sample of FP patients is also limited to those women who self-select for treatment. In our clinic, since 2005, we have found that approximately 1/3 of referred cancer patients opt to undergo FP. This is consistent or somewhat lower than rates found in other clinics (16, 34, 59, 60); albeit, definitions of enrollment greatly differ across studies. It is unclear if patients who pursue FP do so because they are less distressed than non-FP cancer patients or if they pursue FP because they are more distressed (albeit about their fertility) than non-FP cancer patients. Regardless, the FP patients in this study reported significant symptoms of depression and anxiety. Finally, this study is also limited by the administration of questionnaires at only two time points prior to pregnancy results. However, the study is ongoing with additional data collection scheduled for participants.

To our knowledge, this is the first study to prospectively report on the psychological status of FP patients during FP treatment and to compare FP patients with an infertile comparison group. Although our sample size precluded our ability to conduct logistic regressions for each treatment group, the results of our regression analyses would not be expected to differ between groups as the theory of stress, appraisal, and coping is theorized to function similarly across all types of stressors (e.g., medical conditions). It is evident from the current study that anxiety and depression in FP and infertile patients is clinically significant and warrants early intervention from the IVF team and mental health professionals. Early assessment of avoidant coping in patients is also warranted as patients who engage in such problematic coping are at increased risk of depression and/or anxiety. It is encouraging that medical aspects of IVF (e.g., gonadotropin dose, ovarian reserve markers) do not appear to be associated with increased depression or anxiety. However, IVF programs should routinely assess levels of depression and anxiety among FP and infertile patients and have appropriate support services for these women as some face the dual challenges of cancer and fertility preservation and/or worry about their ability to complete their reproductive dreams.

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Table 1

Demographic characteristics of (n = 47) fertility preservation and (n = 91) infertile participants who began a cycle of COH.

Variable	Fertility Preservation N (%)	Infertile Controls N (%)
Ethnicity		
Caucasian	36 (76.6)	68 (74.7)
African American	1 (2.1)	2 (2.2)
Asian	3 (6.4)	11 (12.1)
Hispanic	5 (10.7)	4 (4.4)
Other	2 (4.3)	1 (1.1)
Unknown	0 (0)	5 (5.5)
Marital Status[a]		
Single	13 (27.7)	0 (0)
Married	22 (46.8)	87 (95.6)
Partnered	11 (23.4)	2 (2.2)
Unknown	1 (2.1)	2 (2.2)
Gravidity		
Never pregnant	32 (68.1)	65 (71.4)
1 pregnancy	11 (23.4)	15 (16.5)
2+ pregnancies	4 (8.6)	8 (8.8)
Unknown	0 (0)	3 (3.3)
Parity		
No children	38 (80.9)	79 (86.8)
1 child	7 (14.9)	7 (7.7)
2+ children	2 (4.3)	2 (2.2)
Unknown	0 (0)	3 (3.3)
Elective abortions		
None	40 (85.1)	80 (87.9)
1 elective abortions	7 (14.9)	4 (4.4)
2+ elective abortions	0 (0)	1 (1.1)
Unknown	0 (0)	6 (6.6)
Miscarriage		
None	44 (93.6)	73 (80.2)
1 miscarriage	3 (6.4)	9 (9.9)
2+ miscarriages	0 (0)	2 (2.2)
Unknown		7 (7.7)
Education		
High school diploma	1 (2.1)	1 (1.1)
Some college	4 (8.5)	0 (0.0)
College graduate	19 (40.4)	33 (36.3)
Some graduate school	2 (4.3)	6 (6.6)

Variable	Fertility Preservation N (%)	Infertile Controls N (%)
Graduate school degree	18 (38.3)	45 (49.5)
Unknown	3 (6.4)	6 (6.6)
Insurance coverage for IVF[a]		
Most expenses covered	11 (23.4)	51 (56.0)
50% of expenses covered	3 (6.4)	13 (14.3)
<50% expenses covered	0 (0)	2 (2.2)
No coverage	19 (40.4)	7 (7.7)
Unknown	14 (29.8)	18 (19.8)

[a] $p < .001$

Table 2

Psychological characteristics of fertility preservation (FP) and infertile participants who began a cycle of COH.

Variable	Fertility Preservation Median (Range)	Infertile Controls Median (Range)
CES-D T1 [ac]	13.0 (1–41)	6.0 (0–29)
CES-D T2	11.0 (1–37)	9.0 (0–41)
STAI-State T1 [ac]	41.0 (20–74)	32.5 (20–66)
STAI-State T2	38.5 (20–64)	40.0 (22–62)
STAI-Trait T1 [a]	35.0 (24–59)	31.0 (23–62)
ALE T1		
Loss[c]	3.0 (0–10)	4.0 (0–15)
Threat	5.5 (0–19)	5.0 (0–24)
Challenge [a]	9.0 (1–24)	12.0 (1–28)
ALE T2		
Loss [b]	2.0 (0–16)	3.0 (0–12)
Threat	3.5 (0–20)	5.0 (0–19)
Challenge	8.0 (3–22)	10.0 (2–25)
FPI T1		
Social Concern	22.0 (10–54)	26.0 (10–43)
Sexual Concern	14.0 (8–33)	16.0 (8–36)
Relationship concern	16.0 (10–35)	17.0 (10–39)
Reject child-free lifestyle	25.0 (9–36)	29.0 (14–42)
Need for parenthood	38.5 (12–48)	38.5 (11–54)
WOC T1		
Self-Blame/avoidance	12.0 (0–30)	10.0 (0–31)
Support Seeking[d]	11.0 (4–19)	11.0 (1–20)
Cognitive Restructuring	7.0 (2–13)	6.0 (0–14)
WOC T2		
Self-Blame/avoidance	10.0 (2–32)	12.0 (1–29)
Support Seeking	9.0 (2–17)	10.0 (2–19)
Cognitive Restructuring	7.0 (0–15)	6.0 (1–15)

Note. Mann-Whitney U tests.

[a] $p < .05$ at Time 1.

[b] $p < .05$ at Time 2.

[c] Wilcoxon Signed Ranks test $p < .05$ change from T1 to T2 in infertile controls.

[d] Wilcoxon Signed Ranks test $p < .05$ change from T1 to T2 in FP patients.

Table 3

Correlation Coefficients for variables significantly related to the CES-D or STAI-S

Variable	CES-D T1	STAI-S T1	CES-D T2	STAI-S T2
CES-D T1	--			
STAIS-S T1	.80**	--		
CES-D T2	.70**	.55**	--	
STAI-S T2	.48**	.40**	.58**	--
ALE- Threat T1	.30**	.32**	.30**	.41**
ALE-Loss T1	.33**	.32**	.43**	.48**
WOC-SBA T1	.69**	.61**	.51**	.37**
WOC-IES T1	.19	.20*	.05	.13
FPI-SOCON T1	.40**	.36**	.47**	.27*
FPI-SEXCON T1	.33**	.37**	.33**	.28*
FPI-RCON T1	.27**	.21*	.32**	.04
Threat T2	.18	.12	.36**	.59**
Loss T2	.20	.17	.38**	.43**
WOC-SBA T2	.47**	.44**	.59**	.51**
AMH	−.25*	−.17	−.07	.05
Insurance	−.31**	−.29*	−.16	−.03

Note. T1 = Time 1 survey, T2 = Time 2 survey, CES-D = Center for Epidemiologic Studies- Depression Scale, STAI-S = State-Trait Anxiety Inventory State Scale, ALE = Appraisal of Life Events Scale, WOC = Ways of Coping-Revised Scale, SBA = Self-Blame and Avoidance, IES = Informational and Emotional support Seeking, FPI = Fertility Problem Inventory, SOCON = Social Concern subscale, SEXCON = Sexual Concern subscale, RCON = Relationship Concern subscale, and Insurance = coverage for treatment.

* $p < .05$ level, two-tailed.

** $p < .01$, two-tailed.

Table 4

Medical data for non-chemo exposed fertility preservation (FP) and infertile participants who completed a cycle of COH.

Variable	Fertility Preservation Median (Range)	Infertile Controls Median (Range)
AMH[a]	1.34 (.2 – 10.70)	2.05 (.10 – 17.26)
Total FSH/LH dose	4,312.5 (2,250.0 – 10,500.0)	4,125.0 (825.0 – 9,750.0)
Days Stimulated	11.0 (8–15)	11.0 (8–14)
Peak E_2[a]	1709.0 (351–3,013.0)	2,424.0 (681.0 – 6,852.0)
Oocytes retrieved	14.0 (0–41)	11.0 (1–37)

Note. Data for infertile controls (n = 7) and FP patients (n = 2) who had their cycle canceled or did not begin a cycle of COH are excluded from all but AMH and No oocyte retrieval data points.

[a] $p <$ .05 group difference. Independent samples Kruskal-Wallis tests followed by Mann Whitney U tests were conducted.