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Prevalence and Predictors of Major Depressive Disorder for Fertility Treatment Patients and their Partners

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Structured Abstract

Objective—To examine the prevalence and predictors of major depressive disorder (MDD) for women and their partners during the course of fertility treatment.

Design—Prospective cohort study over an 18-month period. Participants completed interviews and questionnaires at baseline and at 4, 10, and 18 months follow-up.

Setting—Five community and academic fertility practices.

Patients—174 women and 144 of their male partners who did not have a successful child-related outcome during the timeframe of the study.

Interventions—No interventions administered.

Main Outcome Measures—MDD was assessed using the Composite International Diagnostic Interview (CIDI) Major Depression module, a structured diagnostic interview. Additional variables were assessed with self-report questionnaire measures.

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Results—39.1% of the women and 15.3% of the men met the criteria for MDD during the 18-month course of the study. A binary logistic covariate-adjusted model including showed that, for both women and men, past MDD was a significant predictor of MDD during treatment. Past MDD further predicted significant risk for MDD during treatment after controlling for other well-established risk factors (i.e., baseline levels of depression, anxiety, and partner support).

Conclusions—MDD was highly prevalent for fertility treatment patients and their partners. Past MDD predicted risk for MDD during treatment, and it contributed to MDD risk over and above other commonly-assessed risk factors. This suggests patients and their partners would benefit from being routinely assessed for a history of MDD prior to the start of treatment in order to best direct psychosocial support and interventions to those most in need.

Keywords

fertility treatment; depression

The psychological distress associated with infertility is comparable to that associated with heart disease, cancer, or HIV, and fertility treatment patients often characterize infertility as the most upsetting experience in their lives (1, 2). In most studies specifically examining the association between depression and infertility, fertility treatment patients show a higher prevalence of depressive symptoms as compared to a range of control groups (3).

Importantly, very few studies have assessed the rates of major depressive disorder (MDD) associated with fertility treatment, instead employing self-report questionnaires (see reviews in 3, 4-6). While self-report measures are efficient and can provide an index of a patient's current level of depression symptomatology, they do not confirm or disconfirm whether someone actually meets the criteria for a MDD diagnosis (7, 8). Such a distinction is important for guiding mental health treatment decisions; while some level of depressive symptomatology may be relatively normative for fertility patients, MDD represents a more serious condition. Episodes are associated with impaired psychosocial functioning, are recurrent, tend to remit slowly without treatment, may spill over into pregnancy or postpartum stages, or may lead to treatment discontinuation (9-11). Thus, identifying patients who are suffering from MDD, or are at high risk for the disorder, is crucial in order to be able to direct care to those most in need (12).

Only a handful of studies have employed structured interviews to determine psychiatric diagnoses. Chen and colleagues conducted an assessment of 112 fertility patients in Taiwan who were initiating a new round of in vitro fertilization (IVF) treatment (some had undergone previous treatment cycles). They found that 17% of the women met the criteria for MDD (8). Volgsten and colleagues evaluated psychiatric diagnoses in Swedish women and men three weeks after an IVF cycle. Among those who did not have a successful cycle, they found that 19.5% of women and 8.4% of their male partners met the criteria for MDD (13). When these rates are compared to the global point prevalence rate for MDD of 5.9% for women and 3.8% for men, it is clear that fertility treatment patients and their partners are experiencing relatively high rates of MDD (14). Both of these studies, however, were cross-sectional in design. Given that distress appears to increase as the duration of infertility continues (2, 15, 16), the rate of MDD as treatment progresses unsuccessfully over time

needs to be explored. Further, it is not known how rates of MDD compare for patients in the United States where several factors may compound the burden of treatment (e.g., fertility treatment is expensive and rarely covered by medical insurance).

Beyond characterizing rates of MDD, it is important to identify those most at risk for developing this debilitating disorder during fertility treatment. Prospective treatment studies assessing risk factors for depression during fertility treatment are relatively rare, tend to focus exclusively on women, and have also commonly relied only on self-report questionnaire outcome measures. Of the prospective studies that exist, a few categories of risk factors have received empirical validation from multiple researchers and represent domains that are commonly assessed by fertility treatment providers. The first relates to pre-treatment psychological state. Prospective studies have demonstrated that pre-treatment levels of depression and anxiety symptoms are predictive of depressive symptomatology after failed treatments (17-19). The second relates to level of support, with studies showing that low levels of social support and high levels of relational strain are predictive of depression during fertility treatment (18-20).

One potential risk factor that has not been assessed is the presence of past episodes of major depression. MDD is a recurring disorder, and in the general population, past episodes appear to increase the likelihood of future episodes (21, 22). Given that infertility and its treatment are a major source of stress, and that stress can trigger major depressive episodes, those with a history of MDD may be particularly vulnerable (23). No known study has specifically assessed whether a history of MDD predicts MDD during fertility treatment. Volgsten and colleagues did report retrospectively that 60.5% of women and 53.3% of men who met the full criteria for a DSM-IV diagnosis (of any disorder) during treatment reported a previous history of depression (13). This suggests that the presence of past MDD may play an important role in understanding who is at risk for MDD during treatment.

The present study used a prospective design and structured diagnostic interviews for MDD to assess the prevalence of and risk factors for MDD during fertility treatment. First, we characterized levels of MDD in women and their male partners in the United States who did not have a successful fertility treatment outcome. Second, we examined whether a past history of MDD predicted a greater likelihood of MDD over the course of treatment. We further compared the predictive power of a history of MDD to previously validated risk factors for depression, including pre-treatment levels of depressive symptoms, anxiety symptoms, and partner support. Finally, we assessed whether a history of MDD predicted MDD during treatment after controlling for the effects of these well-established risk factors.

Materials and Methods

Study Population and Protocol

The participants in this study were a part of the Fertility Experiences Project, a large-scale investigation involving women and their male partners as they sought treatment for infertility. The participants were recruited between 2000-2004; they were drawn from five reproductive endocrinology practices (over eight locations) in the San Francisco Bay Area. All participants met the following eligibility criteria: a) it was their first visit to the fertility

clinic; b) they had not previously received in vitro fertilization (IVF) treatment; c) they had not previously received a hysterectomy or sterilization; d) they did not have a history of recurrent miscarriage; e) they were currently attempting pregnancy with a male partner; f) they were fluent in English. The study protocol was approved by the University of California, San Francisco Internal Review Board, and informed consent was obtained from each participant. A detailed description of the recruitment procedures and cohort statistics is available in previously published studies using this sample (e.g., 24, 25-28). Briefly, a total of 448 women enrolled in the study. Of the women who participated, 386 (86.2%) of their partners also participated in the study.

Baseline in-person interviews were scheduled within 3 months of the first clinic visit and before the start of fertility treatment. Participants were additionally sent a paper-and-pencil questionnaire in the mail, which they returned at the baseline interview. Demographic information collected at the baseline assessment included age, ethnicity, educational level, and the length of time the couple had been attempting conception (i.e., the length of infertility). Baseline in the context of this study is represented by the point at which couples met with a doctor with the intention of pursing IVF treatment; they may have had prior treatments in the form of intrauterine insemination.

Three additional waves of data collection occurred at 4, 10, and 18 months, respectively, after the baseline assessment. Each involved the completion of questionnaires and telephone interviews. Participants remained in the study regardless of the treatments they received or the outcomes that occurred. Retention rates were high—participation rates at the 4, 10, and 18-month assessments was 96%, 93%, and 89% of the original sample, respectively.

The present study focuses on the participants (N = 174 women and 144 men) who a) had complete data for all predictor variables, and b) did not achieve a successful child-related outcome by the end of the study (i.e., couples who had conceived a child, either as a result of treatment or naturally (N = 154), were currently pregnant (N = 51), or had adopted a child (N = 11) were not included). The reason for selecting this subsample was twofold. First, we did want to confound predictors of depression for those requiring fertility treatment with experiences related to pregnancy or new parenthood. The predictors of MDD for people in the latter categories may be different and were not taken into consideration when measures were selected for the present study. Second, a primary goal of the study was to help inform fertility treatment clinics on how best to address the needs of their patients. It was therefore important to focus on those who remained within the purview of this system (i.e., those who were still without child), versus those who would be falling under the care of other service providers (e.g., obstetrician, pediatrician, adoption agency).

Study Measures

Diagnoses of Major Depressive Disorder were assessed using the Composite International Diagnostic Interview (CIDI), Depression Module (29). The CIDI is a structured interview used by trained interviewers to assess depression according to DSM-IV-TR criteria (30). The CIDI is a well-established diagnostic tool, and a number of studies have demonstrated its reliability and validity (see review in 31). At baseline, the interview assessed any previous major depressive episodes in the individual's lifetime. At each follow up, the time

frame covered the previous time point to the current interview. Two dichotomous variables were created from these interviews: *past MDD*, indicating whether or not the individual had met the criteria for MDD at some point in her or his life before the baseline interview, and *treatment MDD*, indicating whether or not the individual met the criteria for MDD at some point during the course of the 18-month study period.

Depression symptomatology at baseline (*baseline depression*) was measured with the Center for Epidemiologic Study of Depression Scale (32). This 20-item measure assesses how frequently symptoms associated with depression were experienced within the past week. The measure uses a 4-point ordered response set ranging from 0 (“rarely or none of the time”) to 3 (“most or all of the time”). Item responses were summed; the possible range of the measure was 0 – 60, with higher scores indicating more current depressive symptoms. Scores of 16 or greater are considered indicative of clinically significant symptoms of depression (33).

Anxiety symptomatology at the start of treatment (*baseline anxiety*) was assessed with the State-Trait Anxiety Inventory, State Anxiety subscale (34). This 20-item measure assessed how frequently symptoms associated with anxiety (e.g., feelings of tension, anxiety, and apprehension) were experienced within the past week. The measure uses a 4-point ordered response set ranging from 1 (“not at all”) to 4 (“most or all of the time”). Item responses were summed; the possible range of the measure was 20 – 80, with higher scores indicating more current anxiety-related symptoms. Scores of 39 or greater are considered indicative of clinically significant symptoms of state anxiety (35).

Partner support was assessed with a 15-item measure assessing the extent to which partners were perceived as unsupportive (e.g., uncaring, judgmental) or supportive (e.g., warm, empathic)(36). A difference score was computed; the resulting *baseline support* variable indicated the extent to which partners were overall perceived as supportive (positive scores) or unsupportive (negative scores).

Participant demographic characteristics (e.g., age, ethnicity, education, duration of infertility) were assessed with a general questionnaire. Finally, the number of treatment cycles (e.g., medication only, intrauterine insemination, in vitro fertilization) each couple engaged in was assessed at each of the follow up assessment points.

Results

All analyses were conducted using SPSS Statistics, version 22.0. The characteristics of the study sample are summarized in Table 1. The average age of the women and men at baseline was 36.4 years and 37.8 years, respectively. A majority of the sample was Caucasian and highly educated. Participants had been attempting conception for an average of 2.4 years, with a range of less than a year to 11 years. During the course of the study, the couples experienced an average number of 2.5 failed treatment cycles, with a range of zero to 11 failed cycles.

Prevalence of MDD during Treatment

Descriptive analyses were conducted to assess prevalence rates of MDD during the study. For women, 68 (39.1%) of the sample met the criteria for MDD at some point during the 18-month study period. Of those, 43 (24.7%) met the criteria at one assessment point, 18 (10.3%) met the criteria at two assessment points, and 7 (4.0%) met the criteria at all three assessment points. For men, 22 (15.3%) of the sample met the criteria for MDD at some point during the 18-month study period. Of those, 16 (11.1%) met the criteria at one assessment point, 5 (3.5%) met the criteria at two assessment points, and 1 (0.7%) met the criteria at all three assessment points.

Predicting MDD: Individual Variables

To examine the effect of each of the risk factors individually on MDD during treatment, four separate multiple logistic regression models were tested. Model construction and interpretation followed the guidelines presented by Field (37). Each model examined treatment MDD (ever present or absent during treatment) as the binary outcome variable. In step 1 of the model, covariates of age, ethnicity (Caucasian vs. other), education (college graduate or above vs. other), duration of infertility, and number of failed treatment cycles were entered. In step 2, each risk factor (baseline depression, baseline anxiety, partner support, past MDD) was individually entered. While past MDD was the primary variable of interest, we wanted to additionally assess the effect of the other three risk factors to ensure that our data was consistent with findings from past research (reviewed above). In all models, all continuous variables were standardized prior to analyses, and all categorical variables were specified in the model. Table 2 summarizes these findings. The table presents the parameter estimates for each variable in model (beta coefficients (i.e., log odds) with standard error estimates, odds ratio, 95 percent confidence interval, and p values), as well as goodness-of-fit indicators (the Nagelkerke pseudo R squared statistic and the Chi squared statistic) for each model step.

For women, in the separate covariate-adjusted models, each of the risk factors was a significant predictor of MDD during treatment. Specifically, consistent with past research, baseline depression (OR 2.67, 95% CI 1.76-4.09, $p < .001$) and baseline anxiety (OR 2.48, 95% CI 1.69-3.64, $p < .001$) significantly increased the odds of experiencing MDD during treatment, whereas baseline support (OR 0.69, 95% CI 0.51-0.95, $p < .05$) significantly decreased the odds of MDD during treatment. Supporting our hypothesis, past MDD (OR 6.94, 95% CI 3.42-14.13, $p < .001$) was also a significant predictor of MDD during treatment, with results indicating that the odds of women experiencing MDD during treatment were almost seven times greater if they had a past history of MDD.

For men, in the separate covariate-adjusted models, most but not all of the risk factors were significant predictors of MDD during treatment. For the baseline variables, baseline depression (OR 2.27, 95% CI 1.40-3.70, $p < .01$) and baseline anxiety (OR 2.02, 95% CI 1.23-3.31, $p < .01$) predicted a significantly greater likelihood of MDD during treatment. Baseline support, however, was not a significant predictor of MDD during treatment. Supporting our hypothesis, the variable of past MDD (OR 10.10, 95% CI 3.21-31.74, $p < .001$) was a significant predictor of MDD during treatment, with results indicating that the

odds of men experiencing MDD during treatment were more than ten times greater if they had a past history of MDD.

Predicting MDD: Relative Contribution of Risk

To examine the relative contribution of past MDD in comparison to the other risk variables, two models were tested. The first model used a stepwise analysis (Table 3). In step 1, the same covariates noted above were entered. In step two, all baseline variables (depression, anxiety, support) were entered. In step 3, past MDD was entered.

The results showed that past MDD significantly improved model fit and was a significant predictor of MDD during treatment for both women ($\chi^2(1) = 14.82$; OR 4.36, 95% CI 2.03-9.36, $p < .001$) and men ($\chi^2(1) = 11.58$; OR 7.24, 95% CI 2.20-23.77, $p < .01$). This indicates that, after controlling for the effect of all the other risk factors, the odds of women experiencing MDD during treatment were more than four times greater if they had a past history of MDD; the odds of men experiencing MDD during treatment were more than seven times greater if they had a past history of MDD.

A second model was examined that accounted for the shared variance between all the predictor variables. This model was set up the same as the previous model, except that all predictor variables were entered in Step 2 (Table 4). For both women and men, results showed that when the relative contribution of all variables are considered simultaneously, past MDD emerged as the only significant predictor of MDD during treatment. None of the other variables (i.e., baseline depression, anxiety, and partner support) accounted for a significant proportion of the model fit.

Addressing the Possibility of Reverse Causality

As noted above, the present study focused on couples who did not have a successful child-related outcome by the end of the 18-month study period. There remained the possibility, however, that depression itself differentiated between those with a “successful” outcome and those with an “unsuccessful” outcome. That is, perhaps individuals who either had a history of MDD or were depressed at baseline were less likely to conceive a child or complete an adoption. To address this possibility, we compared rates of past MDD and baseline depression for the women and men who were included in the study versus those who were excluded. For women, results showed no differences between the two groups in past MDD, $\chi^2(1, N = 390) = 1.53$, $p = .22$, or baseline depression, $t(385) = .16$, $p = .87$. The same was true for men, with no differences between the two groups in past MDD, $\chi^2(1, N = 335) = 1.84$, $p = .18$, or baseline depression, $t(333) = .40$, $p = .69$. These results suggest that pre-treatment depression (i.e., a history of MDD or baseline levels of depressive symptomatology) did not impact whether a couple will experience a successful versus unsuccessful child-related outcome.

Discussion

This prospective study is one of the only known studies to examine rates of MDD in women and men over the course of unsuccessful fertility treatment, and the only known study to assess the extent to which a history of MDD predicts risk for MDD during treatment.

Findings suggest that 1) MDD is highly prevalent in this population of patients, and 2) above and beyond a set of other commonly-assessed pre-treatment risk factors, a history of MDD is a significant risk factor for predicting who will be vulnerable to episodes of major depression during treatment.

In terms of the prevalence rates of MDD, findings showed that the degree to which women and men experienced MDD over the course of treatment was quite high. To put the numbers into perspective, the annual prevalence rate of MDD in the United States is 8.4% for women and 5.2% for men (38). Therefore, even accounting for the fact that this study covered an 18-month period, the fertility patients and their male partners had notably higher rates of MDD as compared to the general population. That the women suffered higher levels of MDD than their male partners was not surprising. Women in general experience a higher rate of MDD than men (22, 38). Women also have higher levels of distress during treatment than men and undergo treatment for infertility problems more often than men (e.g., 7, 16, 39, 40, 41). Thus, it makes sense that the rates of MDD were observably higher for the women in this sample as compared to their male partners.

In terms of assessing individual risk factors for MDD during treatment, for both women and men, we replicated past findings showing that pre-treatment depression and anxiety symptoms are predictive of depression during treatment. The findings further suggest that partner support may offer somewhat stronger protective effects against depression for women than for men, though this should be interpreted with caution as the effects of partner support were reduced to non-significant levels when considered alongside the other predictor variables.

Most importantly, results indicate that a history of MDD is a significant risk factor for MDD during treatment, both when considered individually and when considered in multivariate models adjusted for other predictor variables. Critically, when the models accounted for shared variance between each of the predictor variables, a history of MDD was the single most robust predictor of MDD during treatment, rendering each of the other variables non-significant in comparison. These results therefore suggest that for both women and men, a history of MDD functions as the strongest predictor of MDD during treatment.

While in some ways the finding that past MDD is predictive of MDD during treatment is intuitive (i.e., it has been long established that MDD is a recurring disorder), it is important because of the major implications it has for pre-treatment patient assessments and the provision of mental health care. Specifically, clinician assessments and risk screening tools tend to focus on the state of the patient at treatment entry (e.g., baseline levels of depression, anxiety, and/or support); typically, mental health history is not closely attended to (if assessed at all). But these findings suggest that a) past MDD is predictive of MDD during treatment regardless of how the person is doing in these commonly-assessed baseline domains, and b) given the predictive strength of past MDD relative to these other risk factors, it might be the single most important piece of patient data to assess. Thus, the results suggest it would be beneficial to routinely screen both women and their partners for a history of MDD at the start of fertility treatment. Those meeting the criteria for this potent

risk factor could then be offered counseling resources, as well as psychoeducation around warning signs that a major depressive episode may be starting.

This study had several notable strengths, including the prospective design and a period of data collection that included four waves of data collection spanning 18 months. This study also benefitted from the use of a structured clinical interview that enabled an assessment of past and present MDD. Further, this is one of the few studies that included men. This is particularly important as men are often excluded from fertility treatment research. The results highlight the fact that men are also suffering from high levels of depression during the course of treatment, and their mental health needs should be addressed alongside those of their female partners.

Despite the many study strengths, we acknowledge certain limitations. The present study examined a risk factor model that focused on variables that a) had replicated empirical support from prospective studies, and b) represented risk factors commonly assessed by fertility treatment providers and/or fertility counselors. Other studies (most cross-sectional) have suggested a number of other factors that appear to be associated with depression symptoms in fertility patients, including gender roles, social pressure for motherhood, shame, self-judgment, acceptance, helplessness, and coping strategies (e.g., 18, 19, 42, 43-45). Future research could test a more comprehensive model of risk factors to further delineate the unique contribution of each variable to risk for MDD, as well as more directly explore the specific mechanisms by which a history of MDD increases the risk of MDD during treatment.

The present study identified the individuals who suffered from MDD during the course of the study, though it did not isolate when those depressive episodes occurred in relation to treatment. For example, we did not have the specific timeline data needed to pinpoint whether depressive episodes were more likely to occur immediately following failed treatment cycles or during waiting periods. Future studies would benefit from capturing the timing of major depressive episodes, which would in turn help to direct clinical intervention efforts. Of note, the total number of failed treatment cycles (included as a covariate in all models) was not a significant predictor of MDD during treatment, which may seem surprising. This null result likely stems from multiple reasons. First, because this study focused exclusively on the couples who did who did not have a successful child-related outcome, cycle failure was a common thread amongst most in the sample. Such a lack of variance may account for why this variable doesn't contribute significantly to model fit for this specific study sample. Second, what the result suggests is that the overall number of failures doesn't significantly predict MDD; thus, some people experience multiple failed cycles and don't become depressed, whereas others become depressed after only one. Failure of specific types of treatment cycles, on the other hand, might be associated with higher risk of MDD. For example, we examined specifically the number of failed IVF cycles and found that it was a significant predictor of MDD. We felt, however, that it was better to include the total number of any type of failed cycle in the model since it more fully represented treatment use over the course of the study period (note: the risk factor regression model findings remained the same regardless of whether failed IVF cycles or total failed cycles was used as the control variable).

Generalizability was limited by inclusion of predominantly Caucasian, well-educated individuals from Northern California. Further, the study sample consisted exclusively of partnered, heterosexual couples, thereby limiting the generalizability to other patient populations such as single parents by choice or same-sex couples. Future research that encompasses these groups would be important. For example, while lesbian and gay couples are increasingly utilizing fertility treatment services, very little is known about the prevalence rates of or risk factors for depression during treatment (46).

In sum, the present study indicates that women and men are at high risk for MDD during the course of unsuccessful fertility treatment. Importantly, it appears that a past history of MDD serves as a significant risk factor for MDD during treatment, and it contributes to MDD risk over and above other risk factors that are commonly assessed at treatment entry. Therefore, it seems that patients and their partners would benefit from being routinely screened for a history of MDD prior to the start of treatment in order to be able to direct psychosocial support and interventions to those most in need.

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Table 1

Participant Characteristics

Baseline Characteristics	Women (N = 174)	Men (N = 144)
Mean age (SD) (range)	36.4 (5.2) (23 – 52)	37.8 (5.8) (24 – 60)
Ethnicity		
Caucasian	69.5%	75.0%
Asian/Pacific Islander	11.5%	11.1%
Hispanic/Latino	5.7%	4.2%
Black	4.6%	2.1%
Other	8.7%	7.6%
Education		
High school graduate	39.3%	36.1%
College graduate or above	70.7%	63.9%
Mean duration of infertility (SD) (range)	2.4 (2.3) (0 – 11 years)	2.4 (2.2) (0 – 11 years)
Mean number of failed treatment cycles (SD) (range)	2.5 (2.5) (0 – 11 cycles)	2.5 (2.5) (0 – 11 cycles)
Baseline depression score (CESD)	11.3 (9.0) (0 – 49); 24% in clinical range	7.3 (9.0) (0 – 38); 11% in clinical range
Baseline anxiety score (STAI)	39.6 (11.2) (20 – 75); 49% in clinical range	34.1 (9.1) (20 – 63); 29% in clinical range
Past MDD Diagnosis	66 (37.9%)	36 (25.0%)

Table 2

Models of Individual Risk Factors for MDD during Treatment

Women	**β(SE)**	**Odds Ratio**	**95% CI**	***p***	**R^2 Change**	**χ^2 Change**
Step 1: Control variables					.03	4.44
Age	-0.10 (.16)	0.90	0.66 – 1.24	.53		
Ethnicity	0.20 (.36)	1.23	0.61 – 2.47	.57		
Education	-0.43 (.36)	0.65	0.32 – 1.33	.24		
Duration of infertility	0.09 (.16)	1.09	0.79 – 1.50	.59		
Number of failed cycles	0.25 (.17)	1.28	0.93 – 1.77	.14		
Individual Models						
Step 2: Baseline depression	0.99 (.22)	2.68	1.76 – 4.09	<.001	.20	27.60***
Step 2: Baseline anxiety	0.91 (.20)	2.48	1.69 – 3.64	<.001	.19	26.57***
Step 2: Baseline support	-0.37 (.16)	0.69	0.51 – 0.95	.02	.04	5.34*
Step 2: Past MDD	1.94 (.36)	6.95	3.42 – 14.13	<.001	.22	32.18***
Men	β(SE)	Odds Ratio	95% CI	*p*	R^2 Change	χ^2 Change
Step 1: Control variables					.08	6.41
Age	0.07 (.24)	1.07	0.66 – 1.72	.79		
Ethnicity	0.08 (.60)	1.08	0.33 – 3.50	.90		
Education	0.90 (.59)	2.46	0.78 – 7.74	.13		
Duration of infertility	0.53 (.24)	1.71	1.06 – 2.74	.03		
Number of failed cycles	-0.09 (.27)	0.92	0.54 – 1.55	.74		
Individual Models						
Step 2: Baseline depression	0.82 (.25)	2.27	1.40 – 3.70	.001	.13	11.98**
Step 2: Baseline anxiety	0.70 (.25)	2.02	1.23 – 3.31	.006	.09	8.00**
Step 2: Baseline support	-0.22 (.23)	0.80	0.51 – 1.25	.33	.01	0.92
Step 2: Past MDD	2.31 (.58)	10.10	3.21 – 31.74	<.001	.20	17.79***

Note: DV: Treatment MDD. R^2 Change refers to the Nagelkerke pseudo R2 value associated with each step of the model; this value is often employed as an analogue for approximating model variance, but it more accurately represents the degree to which each step improves the model fit. χ^2 Change is a goodness-of-fit index for each step of the model; statistically significant values indicate that the addition of the variables in a given step significantly improved the model's predictive power as compared to the previous model step.(37)

* p < .05,
** p<.01,
*** p<.001

Table 3

Models of Stepwise Effects of Risk Factors for MDD During Treatment

Women	**β (SE)**	**Odds Ratio**	**95% CI**	***p***	**R^2 Change**	**χ^2 Change**
Step 1: Control variables					.03	4.44
Step 2:						
Baseline depression	0.62 (.32)	1.86	1.00 – 3.48	.05	.22	30.60***
Baseline anxiety	0.49 (.30)	1.64	0.92 – 2.92	.10		
Baseline support	0.07 (.20)	1.07	0.73 – 1.58	.73		
Step 3: Past MDD	1.47 (.39)	4.36	2.03 – 9.36	<.001	.09	14.82***
Total:					**.34**	**49.86*** **
Men	β (SE)	Odds Ratio	95% CI	*p*	R^2 Change	χ^2 Change
Step 1: Control variables					.08	6.41
Step 2:						
Baseline depression	0.70 (.35)	2.01	1.01 – 4.00	.05	.13	12.32**
Baseline anxiety	0.21 (.37)	1.23	0.59 – 2.55	.58		
Baseline support	0.08 (.27)	1.08	0.64 – 1.83	.77		
Step 3: Past MDD	1.98 (.61)	7.24	2.20 – 23.77	.001	.12	11.58**
Total:					**.33**	**30.31*** **

Note: DV: Treatment MDD. R^2 Change is the Nagelkerke pseudo R2 value for each model step; χ^2 Change is a goodness-of-fit index for each model step (see Table 2 note for more information on these values)

** p<.01,

*** p<.001

Table 4

Models of Effects of Risk Factors on MDD During Treatment When Accounting for Shared Variance

Women	**β (SE)**	**Odds Ratio**	**95% CI**	***p***	**R^2 Change**	**χ^2 Change**
Step 1: Control variables					.03	4.44
Step 2:						
Baseline depression	0.50 (.34)	1.65	0.85 – 3.20	.14	.31	45.42***
Baseline anxiety	0.37 (.31)	1.45	0.79 – 2.66	.23		
Baseline support	0.12 (.21)	1.12	0.74 – 1.70	.59		
Past MDD	1.47 (.39)	4.36	2.03 – 9.36	<.001		
Total:					**.34**	**49.86*** **
Men	β (SE)	Odds Ratio	95% CI	*p*	R^2 Change	χ^2 Change
Step 1: Control variables					.08	6.41
Step 2:						
Baseline depression	0.66 (.40)	1.93	0.87 – 4.27	.10	.25	23.90***
Baseline anxiety	0.08 (.41)	1.08	0.48 – 2.44	.85		
Baseline support	0.09 (.33)	1.09	0.58 – 2.07	.79		
Past MDD	1.98 (.61)	7.24	2.20 – 23.77	.001		
Total:					**.33**	**30.31*** **

Note: DV: Treatment MDD. R^2 Change is the Nagelkerke pseudo R2 value for each model step; χ^2 Change is a goodness-of-fit index for each model step (see Table 2 note for more information on these values).

*** p<.001