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Depressive Symptoms among Young Breast Cancer Survivors: The Importance of Reproductive Concerns

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Abstract

Purpose—Breast cancer diagnosis and treatment can negatively impact fertility in premenopausal women and influence reproductive planning. This study investigates whether concerns about reproduction after breast cancer treatment were associated with long-term depressive symptoms.

Patients and Methods—Participants include 131 women diagnosed with early-stage breast cancer at age 40 or younger participating in the Women's Healthy Eating and Living (WHEL) Survivorship Study. Participants were enrolled an average of 1.5 years post-diagnosis and depressive symptoms were monitored 6 times throughout the average additional 10 year follow-up period. Detailed recall of reproductive concerns after treatment was collected an average of 12 years post-diagnosis. Multilevel regression was used to evaluate whether mean long-term depressive symptoms differed as a function of reproductive concerns and significant covariates.

Results—Multilevel regression identified greater recalled reproductive concerns as an independent predictor of consistent depressive symptoms after controlling for both social support and physical health ($B = 0.02$, $SE = 0.01$, $p = 0.04$). In bivariate analyses, being nulliparous at diagnosis and reporting treatment-related ovarian damage were both strongly associated with higher reproductive concerns and with depressive symptoms.

Conclusion—Reported reproductive concerns after breast cancer treatment were a significant contributor to consistent depressive symptoms. Younger survivors would benefit from additional information and support related to reproductive issues.

Keywords

breast cancer; young; depression; fertility; reproduction

INTRODUCTION

In the United States, premenopausal women account for 25% of breast cancer diagnoses [1]. Women younger than 40 years account for 5% of diagnoses [2], and have a 5-year survival rate of 82%, slightly lower than the 89% survival rate for women diagnosed at 40–74 years [3]. While adjuvant therapy has improved survival, it can lead to amenorrhea, early menopause, and fertility difficulties [4–7].

Young breast cancer survivors have unique concerns, including anxiety about their ability to have children, raising children as a cancer survivor, premature menopause, loss of fertility, early ovarian decline and related symptoms, and how pregnancy may affect recurrence risk [8-11]. They also have greater psychosocial needs, especially dealing with the physical effects of treatment and associated gynecological and reproductive consequences [12,13]. Psychological concerns can last for years after treatment and negatively influence quality of life (QOL) [13-18]. Several studies have identified the need for support related to fertility and early menopause [8,12,13,15,19].

Young women diagnosed with breast cancer are more likely to experience anxiety and distress and to need greater social support [8,20-23]. Among young women recently diagnosed with breast cancer, those with greater pain and lower emotional support are at greater risk of depressive symptoms [20]. Some studies have found that symptoms diminish several months after diagnosis, indicating that young women adapt over time [24,25]. However, a recent study suggests that younger age is a risk factor for depression and anxiety 2-5 years after diagnosis [23]. After the first year, personal and psychosocial characteristics, rather than disease or treatment characteristics, predict elevated depressive symptoms and anxiety [23,26,27]. Depression may influence cancer progression and mortality [28-30] and symptoms can lower QOL, including family life [31-33], and prevent women from attaining their previous level of functioning [12,34].

A number of researcher studies have predicted levels of distress and depression among breast cancer survivors [20,23,26,35] using a biopsychosocial approach [36,37], which provides a framework for understanding how multiple factors contribute to depressive symptoms. Among breast cancer survivors in general, risk factors include cancer treatment characteristics [38-41], health behaviors [42], physical functioning [38,41], and psychosocial functioning [20,23,26]. Depressive symptoms are strongly associated with physical health symptoms of pain and fatigue [38,43,44] and lack of social support and/or an intimate confiding relationship [23,45-47]. However, research evaluating distress and depression in young women is sparse and most studies are cross-sectional. Although younger women represent a minority of breast cancer patients, their reproductive concerns are a potentially important risk factor for depression that has not been evaluated.

This study uses data from a large cohort of breast cancer survivors who participated in a randomized trial to investigate whether level of reproductive concerns after treatment is associated with long-term depressive symptoms among women diagnosed at age 40 or younger.

PARTICIPANTS AND METHODS

Women's Healthy Eating and Living (WHEL) Survivorship Study

Participants were originally enrolled between 1995 and 2000 in the Women's Healthy Eating and Living (WHEL) Study, a multi-site randomized controlled trial evaluating the influence of diet on breast cancer recurrence in women diagnosed with Stage I (≥ 1 cm) (39%), II, (45%), or IIIA (16%) breast cancer within the previous 4 years [48]. The average age at enrollment was 53.3 and 376 (12.2%) participants were 40 or younger at diagnosis. Women pregnant at enrollment were excluded. Other eligibility criteria for WHEL are described elsewhere [49].

After the WHEL Study concluded, researchers re-enrolled participants from all 7 WHEL study sites into the WHEL Survivorship Study. Of the original 3088 participants, 2364 were eligible for the Survivorship Study. Reasons for ineligibility were 582 breast cancer recurrences or deaths, 68 non-breast cancer deaths, 24 lost to follow up and 50 withdrawals.

Of 1495 participants enrolled by April 1 2009 (63% of eligible) and a total possible sample size of 144 diagnosed with breast cancer at age 40 or younger, the present study sample includes 131 women. No eligible participants refused, but 12 who consented to participate had not completed the survey by the time of this analysis and 1 was excluded due to missing data.

Measurement

Depressive symptoms were assessed using the 8-item Center for Epidemiologic Studies Depression Scale (CES-Dsf) [50] at WHEL Study timepoints (baseline, 1 year, 2 or 3 years, 4 years, 6 years), and at time of Survivorship Study enrollment. The raw score is log transformed and a higher score indicates a higher level of depressive symptoms. While originally developed to identify people who may have a mood disorder (cut point of 0.06 has high sensitivity/specificity for major depression/dysthymia [50]), we use the score to indicate a spectrum of symptoms. Acceptable reliability of the scale with WHEL participants has been reported ($\alpha=0.73$) [26] and was similar at Survivorship Study enrollment ($\alpha=0.71$).

Recalled reproductive concerns were assessed at Survivorship Study enrollment with an instrument specific to cancer survivors, the Reproductive Concerns Scale (RCS) ($\alpha=0.91$) [51]. RCS score is the sum of responses to 14 questions (range=0-56), with a higher score indicating reproductive concerns ($\alpha=0.81$ in the present study). The RCS assesses: Loss of control over reproductive future, discontent with number of children, inability to talk openly about fertility, illness affected ability to have children, sadness about inability to have children, frustration that ability to have children was affected, anger that ability to have children was affected, mourning over the loss of ability to have children, concerns related to having children, guilt about reproductive problems, lower satisfaction w/life because of this problem, feeling like less of a woman, blaming self for reproductive problems, and blaming others for reproductive problems. The RCS does not have established cut points.

Potential covariates were identified based on a review of the literature and, following the broad approach of the biopsychosocial model [37], include cancer-related characteristics, health behavior/physical health, and psychosocial characteristics.

Demographics, cancer characteristics/treatment, lifestyle, physical/mental health and family cancer history were obtained at WHEL Study baseline [49]. Lifestyle variables included smoking history, Body Mass Index (BMI), a validated 9-item physical activity questionnaire, and four 24-hour dietary recalls [48]. This study evaluated diet quality by adherence to national dietary guidelines (1 point each for $\leq 30\%$ energy from fat, ≥ 20 g fiber, and ≥ 5 servings of fruit/vegetables for a score that ranged from 0 to 3).

Physical health was measured using the physical health summary score (PHSS), a subscale of the RAND- 36 Item Health Survey, composed of physical functioning, general health perceptions, bodily pain, and role limitations due to physical health problems [52,53] ($\alpha=0.93$ with WHEL data) [54]. Social support was assessed with the 9-item Medical Outcomes Study Social Support measure, covering emotional/informational/tangible support, affection, and positive interaction($\alpha=.93$) [55]. Life events were assessed using nine items from the Alameda County Study [56]. Participants were interviewed about reproductive characteristics retrospectively during the Survivorship Study. In addition to the RCS, questions included live births before and after their cancer diagnosis, whether they wanted to have (more) children before and after their breast cancer diagnosis, pregnancy attempt/avoidance after treatment, whether they based cancer treatment decisions on the desire to preserve fertility, whether they were told their ovaries were damaged after treatment, and their experience with irregular periods either during or after treatment.

Menopausal status was assessed at WHEL Study baseline (women were enrolled up to 4 years post-diagnosis).

Statistical analysis

Univariate analysis of RCS scores revealed a significantly skewed distribution toward lower scores. We log-transformed this score to approximate a normal distribution. After characterizing the sample using descriptive statistics, we compared the mean and standard deviation of CES-Dsf scores across reproductive characteristics. We calculated the bivariate association between CES-Dsf scores across study timepoints and potential covariates (correlations for continuous variables and ANOVA for categorical variables).

We developed an intercept-only (unconditional) model to calculate the intraclass correlation coefficient (ICC), which identifies the percent of variability in the scores between individuals (level-2) and across timepoints (level-1). We then developed an unconditional growth model to evaluate the association between depressive symptoms and time and a conditional growth model with reproductive concerns as the primary predictor. We evaluated the slope to determine whether scores of depressive symptoms reflected an increase, decrease, or stable pattern. After determining that depressive symptoms did not change over time in the unconditional or conditional models, we developed a multilevel regression model to predict mean depressive symptoms. We first evaluated whether level of reproductive concerns predicted mean depressive symptoms (continuous level-2 predictor). We added potential covariates in the following order: demographics, cancer characteristics and treatment, health behavior/physical health, reproductive characteristics, WHEL Study randomized assignment, and psychosocial characteristics. Continuous level-2 covariates were grand mean centered to provide an average score across participants. We used a step-up approach to model building. Covariates were added to the initial model based on preliminary analyses of an association with the criterion variable ($p < 0.25$). The primary predictor variable and covariates that were significantly associated with the criterion variable ($p \leq 0.05$) were retained in the final model. We evaluated potential interactions between RCS and covariates in the final model and assessed how much the variance component for each model was reduced as covariates were added to develop the final model. In exploratory analyses, we developed a multilevel regression model with having children (ever and post-diagnosis) as the primary predictor of depressive symptoms. Finally, we explored the construct measured by the RCS by conducting chi-square tests to evaluate whether several reproductive characteristics were associated with high vs. low RCS scores.

RESULTS

Sample characteristics

We compared WHEL participants who re-enrolled in the Survivorship Study with those who did not (Table 1). There was little difference across socio-demographic characteristics with the exception of race/ethnicity; enrollment in the WHEL Survivorship Study was higher in non-Hispanic White compared to other populations ($p \leq 0.05$). The average age at diagnosis for young survivorship participants was 36.7 years, with a quarter diagnosed at younger than 35 years. On average, participants enrolled in the WHEL study 1.5 years after diagnosis and completed the Survivorship Study survey 11.9 years post-diagnosis at 49.1 years of age. Most participants were married (76%), White (88%) and had a college degree or higher (62%). Both groups showed clinically elevated levels of depressive symptoms in one fifth of the sample, a proportion similar to that reported for the entire WHEL Study cohort (17%) [26]. WHEL participants with higher grade disease and chemotherapy treatment were less likely to be eligible for the Survivorship Study. Both cancer stage and chemotherapy treatment were somewhat higher ($p \leq 0.10$) among those not enrolled.

Reproductive characteristics and depressive symptoms

Sixty eight percent of this cohort had at least one live birth before their breast cancer diagnosis and 12% had at least one afterward (Table 2). At Survivorship Study baseline, participants had a median of 2 children. Forty-eight percent reported possibly wanting a(another) child pre-diagnosis compared to only 28% post-diagnosis. Twenty three participants (18%) reported wanting a child before or after breast cancer, but were nulliparous at the time of the Survivorship Study. More than half of participants reported not avoiding pregnancy after treatment, but 22% of those (n=15) were postmenopausal at WHEL Study entry, which may have influenced their reports. Only 9 participants (7%) reported trying to become pregnant after treatment.

Higher RCS scores were associated with higher depressive symptoms ($p=0.0002$) as were not having children, being nulliparous at diagnosis, not avoiding pregnancy after diagnosis, treatment-related ovarian damage, and menopausal status (all with $p<0.01$) (Table 2).

Reproductive concerns scale and reproductive characteristics

Table 3 shows associations between RCS scores and reproductive characteristics. By convention, we defined the low concerns group as those at or below the sample mean of the log-transformed score (n=58 participants, 24% of which reported no concerns). Seventy three participants (56%) were the high concerns group. Those in the high concerns group had untransformed scores ranging from 7-45, with a median score of 16. Women in the high concerns group were more likely to choose treatment based on fertility preservation and report treatment-related ovarian damage. While those in the high concerns group were three times more likely to report that fertility was a factor in choosing treatment, only 16% mentioned this concern. A larger proportion of those in the high concerns group had no children at diagnosis (45% vs. 15%), wanted children pre-diagnosis (66% vs. 26%), wanted children post-diagnosis (37% vs. 15%), and wanted children but were nulliparous at Survivorship Study follow-up (23% vs. 10%). Finally, 18% of those in the high concerns group had a child post-diagnosis, compared to 4% of those in the low concerns group. Being diagnosed at younger than age 35 and reporting irregular periods during or after treatment did not vary by RCS group.

Models predicting depressive symptoms

In preliminary bivariate analyses, marital status was the only demographic characteristic significantly associated with depressive symptoms ($p<0.001$), with those who were married at study enrollment having lower scores. Three lifestyle variables (adherence to dietary recommendations, higher physical activity level and lower BMI) were significantly associated with lower depressive symptoms ($p \leq 0.05$). Later cancer stage at diagnosis ($p=0.001$) and ER positive receptor status ($p<0.01$) were significantly associated with higher depressive symptoms. WHEL Study randomization group ($p=0.07$) and time between diagnosis and study entry ($p=0.21$) were not significantly associated. Greater social support and fewer life events were significantly associated with lower depressive symptoms ($p<0.0001$). Women who were nulliparous at the time of the Survivorship Study but who reported wanting children before and/or after their diagnosis also had significantly higher scores ($p=0.03$).

Without controlling for other variables, the mean CES-Dsf score across all timepoints was 0.056 (SE=0.01), just under the established cut point for clinically elevated depressive symptoms. The ICC indicated that 41% of the variance in depressive symptoms scores was between individuals. After adding the primary predictor to the model, the regression coefficient relating RCS to depressive symptoms was positive and statistically significant ($B=0.02$, $p=0.01$). After adding significant covariates ($p \leq 0.10$) to the model, CES-Dsf was

significantly higher in those with a higher RCS score ($B = 0.02$, $p = 0.04$) and lower in those with higher scores of physical health ($B = -0.002$, $p < 0.0001$) and those with higher scores of social support ($B = -0.01$, $p < 0.0001$). We observed no significant interaction between RCS and social support or RCS and time. However, we identified a significant interaction between RCS and physical health, in which physical health moderated the relationship between RCS and depressive symptoms. This relationship was minimally changed with the interaction term in the model, and the slopes of the RCS-depression association were very similar across physical health levels, indicating no clinically meaningful effect. Evaluation of random effects provided information about the proportion of variance explained [57] by adding each covariate to the final model: 5% of the explainable variation in individual depressive symptoms was explained by RCS, 40% by social support, and 12% by physical health (Table 4).

Before controlling for covariates, women without children (pre- or post-diagnosis) had mean depressive symptoms scores 0.04 points greater than those with children ($SE = 0.02$, $p = 0.01$). However, this variable became insignificant after adding other variables to the model. No significant difference was observed between women who had a child after breast cancer compared to those who did not ($B = -0.01$, $SE = 0.03$, $p = 0.80$, without controlling for covariates).

DISCUSSION

This investigation of young breast cancer survivors suggests that concern about reproduction after treatment contributed to long-term depressive symptoms. At WHEL Study entry, almost 20% of young cancer survivors reported clinically elevated depressive symptoms [50]. In the multilevel regression model, depressive symptoms scores averaged 0.057 and did not change significantly over time, suggesting that many young breast cancer survivors experience long-term depressive symptoms post-diagnosis. This is consistent with other research suggesting that young breast cancer survivors are at higher risk for long-term psychological distress [13,16,58]. In our sample, higher levels of recalled reproductive concerns predicted higher levels of depressive symptoms, even after controlling for social support and physical health.

Greater reproductive concerns, less social support, and poorer physical functioning were associated with higher depressive symptoms. Compared to their older counterparts, younger breast cancer survivors have a greater need for social support, which is critical to long-term physical and mental well-being [21]. As in previous research, social support significantly predicted depressive symptoms in our sample [8,20-23], and described the greatest percentage of explainable variation in CES-Dsf scores (40%). The lack of an interaction between social support and RCS suggests that reproductive concerns are uniquely associated with depression, regardless of support from a spouse or significant other.

Our findings are consistent with other research suggesting that many young breast cancer survivors need information and support related to reproductive issues [8,12,15,19]. One way to help address this need is through improved patient-provider communication. Young cancer survivors' concerns about fertility issues may not be fully addressed by their health care providers [59,60], and these women would benefit from additional information and support [11,61]. The development of patient education materials to facilitate these discussions would help providers to fill this gap in the narrow window of time prior to treatment. Physicians, nurses, psychologist, and social workers can continue to play an important role in addressing reproductive concerns after initial treatment ends and well into survivorship.

Our multivariate analysis found no significant difference in depressive symptoms among those who had children compared to those who did not, similar to another study [20]. Depressive symptoms were also not significantly associated with having a child after breast cancer. Another small study found no significant differences in QOL or psychosocial characteristics among those who became pregnant after breast cancer compared with those who did not [62]. However, in that study women who had children after breast cancer reported that their families provided the greatest satisfaction and were important to quality of life. Further studies with larger sample sizes are needed to adequately address these questions.

A significant strength of this study is the longitudinal depressive symptoms data collected multiple times over approximately 10 years. We incorporated a broad range of potential covariates, although our sample size required that we limit inclusion of covariates to those of primary interest and important predictors of depression in previous studies. For example, while we controlled for overall physical health, we did not have sufficient statistical power to evaluate more specific physical symptoms, such as those related to menopause or comorbidities, which could be associated with depressive symptoms. We also did not have data on some predictors of depression, including previous history of mental illness or substance abuse. The generalizability of these findings is limited to long-term breast cancer survivors diagnosed with lower grade, early stage breast cancer at age 40 or younger. While not significant in the final model, preliminary analyses suggested the importance of exploring the association between depressive symptoms and other reproductive characteristics, such as having children before and after diagnosis, with larger sample sizes. While sample size limited our power to detect significant effects, our statistical approach allowed us to include data across multiple timepoints, including participants with missing data.

We collected data on fertility and reproduction, including the RCS, an average of 12 years after breast cancer diagnosis. Retrospective reports introduce potential for biases based on recall and memory, including the negative recall bias associated with depression [63]. It is possible that women did not accurately recall feelings experienced after their cancer treatment or that their life experiences influenced their answers. Research suggests that young survivors' feelings about fertility change over time [64] and concerns may increase as they move farther away from diagnosis [65]. However, no longitudinal studies have evaluated how fertility concerns evolve over the long-term. Chi-square analysis (Table 3) provided additional details about this study's measurement of reproductive concerns. A valid assessment tool should show a relationship between reproductive concerns and several key variables. We found the expected associations across the key variables, including greater likelihood of being nulliparous at diagnosis, wanting children before and after diagnosis, reporting that fertility was a factor in treatment decisions, and attempting pregnancy after diagnosis.

Breast cancer treatment can affect fertility, which is a major issue affecting young breast cancer survivors who have not finished growing their families. While research is limited, infertility and concerns about reproductive issues after cancer treatment can negatively influence QOL [51,66]. Our multilevel regression model showed that participants had CES-Dsf scores just under the threshold for high depressive symptoms. Women with greater recalled reproductive concerns experienced higher levels of depressive symptoms over time, even after controlling for other significant variables. While fertility may not be the primary concern during diagnosis and treatment, it may become more important afterward [64,65]. Longitudinal studies would provide valuable information about how reproductive concerns change over time, the influence of experiences with infertility and pregnancy, and how these factors are related to survivors' overall well-being. This information will help identify

groups at risk for depressive symptoms and develop effective interventions to address their needs.

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Table 1

Comparison of baseline sample characteristics and enrollment

	No. (%) enrolled	No. (%) not enrolled
Total enrollment (diagnosed $\leq$ 40 years)	131	245
Depressive symptoms		
Clinically elevated depressive symptoms ^I	24 (18.3)	50 (20.4)
Demographic characteristics		
Age at diagnosis		
Younger than 35	33 (25.2)	68 (27.8)
35 or older	98 (74.8)	177 (72.2)
Marital status		
Married	99 (75.6)	177 (72.2)
Single / Other	32 (24.4)	68 (27.8)
Race/ethnicity		
White	115 (87.8)	190 (77.6)*
Other	16 (12.2)	55 (22.4)
Education		
Some college or less	50 (38.2)	107 (43.7)
College graduate	81 (61.8)	138 (56.3)
Cancer and treatment characteristics		
Stage at diagnosis		
I	43 (32.8)	74 (30.2) [†]
IIA	54 (41.2)	76 (31.0)
IIB	17 (13.0)	36 (14.7)
IIIA	13 (9.9)	40 (16.4)
IIIC	4 (3.1)	19 (7.8)
Breast conserving surgery	55 (42.0)	99 (40.4)
Radiation	73 (55.7)	146 (59.6)
Chemotherapy	116 (88.6)	229 (93.5) [†]
Receptor status		
ER+/PR+ and ER+/PR-	92 (70.2)	168 (66.6)
ER-/PR-	39 (29.8)	77 (31.4)

^I CES-Dsf $\geq$ 0.06 at study entry* Difference between groups based on χ^2 . $p \leq 0.05$ [†] Difference between groups based on χ^2 . $p \leq 0.10$

Table 2

Mean depressive symptoms across reproductive characteristics (N=131)

	No. (%)	Mean CES-Dsf (SD) ¹	p-value ²
Reproductive characteristics			
Reproductive concerns after treatment ³	---	---	0.0002
Total live births			
0	34 (26.0)	0.09 (0.19)	0.0007
1 or more	97 (74.0)	0.04 (0.12)	
Live births prior to breast cancer diagnosis			
0	42 (32.1)	0.08 (0.18)	0.004
1 or more	89 (67.9)	0.04 (0.12)	
Live births after breast cancer diagnosis			
0	116 (88.5)	0.06 (0.15)	0.79
1 or more	15 (11.5)	0.05 (0.12)	
Wanted (more) children before breast cancer diagnosis			
Definitely / Maybe	63 (48.1)	0.06 (0.15)	0.29
No	68 (51.9)	0.05 (0.13)	
Wanted (more) children after breast cancer diagnosis			
Definitely / Maybe	36 (27.5)	0.05 (0.14)	0.59
No	95 (75.5)	0.06 (0.14)	
Nulliparous at follow-up but wanted children before or after diagnosis			
Definitely/ Maybe	23 (17.6)	0.08 (0.20)	0.03
No	108 (82.4)	0.05 (0.13)	
Attempted pregnancy			
Attempted/ Did not avoid	69 (52.7)	0.07 (0.16)	0.004
Avoided	62 (47.3)	0.04 (0.11)	
Treatment decision-making			
Fertility a factor	15 (11.5)	0.08 (0.18)	0.13
Fertility not a factor	116 (88.5)	0.05 (0.14)	
Treatment related ovarian damage			
Reported by doctor	22 (16.8)	0.16 (0.24)	<0.0001
None reported	109 (83.2)	0.04 (0.10)	
Treatment-related amenorrhea			
Irregular periods during or after treatment	95 (72.5)	0.06 (0.15)	0.27
None	36 (27.5)	0.05 (0.10)	
Menopausal status at WHEL Study entry			
Postmenopausal	26 (19.9)	0.13 (0.21)	<0.0001
Premenopausal	105 (80.2)	0.04 (0.11)	

¹ Unadjusted mean score for categorical variables.² Based on correlation for continuous variables and ANOVA for categorical variables.³ Natural log plus one of reproductive concerns scale summary score.

Table 3Characteristics associated with reproductive concerns scale (RCS) score¹

Characteristic	High RCS score No. (%) (N=73)	Low RCS score No. (%) (N=58)	p-value ²
Younger than 35 at time of diagnosis	19 (26.0)	14 (24.1)	0.80
Irregular periods during or after treatment	55 (75.3)	40 (69.0)	0.42
Treatment-related ovarian damage	17 (23.3)	5 (8.6)	0.03
Treatment decision based on fertility preservation	12 (16.4)	3 (5.2)	0.05
Did not prevent pregnancy after diagnosis	44 (60.3)	25 (43.1)	0.05
Wanted children before breast cancer diagnosis	48 (65.8)	15 (25.9)	<0.0001
Wanted children after breast cancer diagnosis	27 (37.0)	9 (15.0)	0.01
Nulliparous at follow-up but wanted children before or after diagnosis	17 (23.3)	6 (10.3)	0.07
Nulliparous at time of diagnosis	33 (45.2)	9 (15.5)	0.0003
Child born after diagnosis	13 (17.8)	2 (3.5)	0.01
No children	26 (35.6)	8 (13.8)	0.005

¹Grand mean centered and log transformed RCS score, higher score greater than mean.²Based on X².

Table 4

Results of fitting models to depressive symptoms data (N=131)

Variable	Unconditional Means Model	p-value	Conditional Univariate Model	p-value	Conditional Multivariate Model [†]	p-value	PRE [‡]
	Estimate (SE)		Estimate (SE)		Estimate (SE)		
Intercept	0.056 (0.0093)	<0.0001	0.056 (0.0091)	<0.0001	0.057 (0.007)	<0.0001	
Reproductive concerns ¹			0.023 (0.0094)	0.016	0.015 (0.0074)	0.037	5%
Social support ²					-0.0076 (0.0012)	<0.0001	40%
Physical health ³					-0.0019 (0.00041)	<0.0001	12%

[†] Level-2 covariates are grand mean centered. The intercept represents a participant with an average value of reproductive concerns, physical health and social support.

[‡] Proportion of reduction in error [57].

¹ Natural log plus one of reproductive concerns scale summary score.

² Medical Outcomes Study Social Support measure. Includes nine items covering emotional and informational support, affection, tangible support and positive interaction.

³ Physical health summary score from RAND-36 item health survey. Includes physical functioning, general health perceptions, bodily pain, and role limitations due to physical health problems.