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CLINICAL TRIAL

A randomized trial of interpersonal psychotherapy, problem solving therapy, and supportive therapy for major depressive disorder in women with breast cancer

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Abstract

Purpose Breast cancer (BC) is a risk factor for major depressive disorder (MDD), yet little research has tested the efficacy of different psychotherapies for depressed women with BC. This study, the largest to date, compared outcomes of three evidence-based, 12-week therapies in treating major depressive disorder among women with breast cancer.

Methods This randomized trial compared interpersonal psychotherapy (IPT), problem solving therapy (PST), and brief supportive psychotherapy (BSP). Conducted at the outpatient clinic of the New York State Psychiatric Institute/Columbia University, the trial offered bilingual treatment by treatment-specific psychotherapists supervised by treatment experts. The primary outcome was change in the Hamilton Depression Rating Scale (HAM-D) at 12 weeks. Secondary outcomes included other validated patient-reported outcomes for depression and quality of life.

Results Of 179 women with breast cancer screening positive for depression at the Columbia Cancer Center, 134 eligible patients signed informed treatment consent. Half of patients were Hispanic and economically disadvantaged. Most women had stage I (35.2%) or II (36.9%) BC; 9% had stage IV. The three brief psychotherapies showed similar improvements on the HAM-D, with large pre-post effect sizes ($d \sim 1.0$); *a priori* defined response rates were 35% for IPT, 50% for PST and 31% for BSP, and remission rates 25%, 30% and 27%, respectively. The three treatments also showed similar improvements in the Quality of Life Enjoyment and Satisfaction Questionnaire. Dropout was high, ranging from 37 to 52% across treatments. Predictors of dropout included having < 16 years of education and annual family income < $20,000.

Conclusions Among patients who completed treatment, all three psychotherapies were associated with similar, meaningful improvements in depression. Physical distance between the oncology and psychiatric treatment sites might have contributed to high dropout. This study suggests various psychotherapy approaches may benefit patients with breast cancer and major depression.

Keywords Breast cancer · Major depressive disorder · Comorbidity · Randomized controlled trial · Psychotherapy · Interpersonal psychotherapy (IPT) · Problem solving therapy (PST) · Brief supportive psychotherapy (BSP)

Trial registration: Clinicaltrials.gov: NCT00742573.

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Introduction

Although the prevalence of depressive symptoms varies by cancer site and stage, cancer patients are significantly more likely to develop major depressive disorder (MDD) than the general population. Several factors likely explain this increased risk: the life-threatening nature of the diagnosis, associated feelings of vulnerability and uncertainty, physical and psychosocial limitations associated with the illness and its treatment, body image concerns; and in the case of breast cancer, menopause [1]. Biological factors, such as treatment with tamoxifen [2] or activated immune response including increased inflammatory cytokines in the blood and cerebrospinal fluid (CSF) and increased blood levels of acute phase proteins, chemokines, and adhesion molecules have also been associated with MDD [3–5]. Depressive disorders worsen over the course of cancer treatment, persist long after cancer therapy ends [6], recur when cancer recurs [7], and significantly impair the psychosocial functioning and quality of life of cancer patients [8]. Breast cancer patients carry an estimated risk for developing MDD of 10–33% [9–11], and major depressive disorder often persists months or years after the initial diagnosis [11–14].

Although numerous trials have established the general efficacy of medication and psychotherapy treatments for adults with MDD, these findings derive from highly selected patient samples [15]. Restrictive study eligibility criteria raise concerns that results may not generalize to other populations, including depressed cancer patients, especially those of minority or underserved backgrounds. Furthermore, some cancer patients may be reluctant to add antidepressant medications to their existing treatment regimens or to engage in psychotherapy. Although several interventions have been reported to decrease depressive *symptoms* among cancer patients, little is known about treatment efficacy in treating cancer patients with syndromal MDD. The paucity of data has provoked repeated calls to investigate the efficacy of psychosocial interventions in cancer patients with MDD [9, 16, 17].

Indeed, and surprisingly given the distress that many patients with cancer face, only one published study [18] has compared the efficacy of two empirically based psychotherapies for MDD in women with breast cancer ($N = 80$). Hopko and colleagues found 8 weeks of Behavioral Activation Treatment for Depression (BATD) and Problem Solving Therapy both associated with improved depressive symptoms and psychosocial functioning, without significant between-treatment differences in any of the assessed domains.

We conducted a randomized controlled trial of three distinct evidence-based treatments for MDD: Interpersonal Psychotherapy (IPT), Problem Solving Therapy (PST), and Brief Supportive Psychotherapy (BSP) for depressed adults with breast cancer. Recognizing the importance of quality of life and functional status among breast cancer patients, we included assessments of depressive symptoms, psychosocial functioning, and pain. Based on the efficacy differences between PST and BSP in a previous study of depressed cancer patients [19], between IPT and BSP in a large study of depressed HIV patients [20, 21], and on an open pilot study of IPT in depressed cancer patients [21], we hypothesized that IPT and PST would reduce depressive symptoms and improve quality of life more than BSP.

Methods

Patients

Eligible patients were at least 18 years old, had breast cancer of any stage and a current diagnosis of DSM-IV nonpsychotic unipolar MDD based on the Structured Clinical Interview for DSM-IV (SCID) [22], and lived in or could travel regularly to New York City. Patients were recruited through clinician referral across the Greater New York area, advertisement, and patient advocacy organizations. Although both sexes were eligible, all patients recruited were women. All patients signed informed consent prior to study participation. The study, conducted between July 1, 2010 and April 4, 2016, was approved by the IRB of New York State Psychiatric Institute and registered in Clinicaltrials.gov: NCT00742573.

Treatments

The three manualized psychotherapies differ markedly from one another. Interpersonal Psychotherapy (IPT) was selected because it is an evidence-based, life event- and affect-focused treatment based on the premise that depression does not occur in a social vacuum, but is influenced by and itself affects the patient's psychosocial environment. Changes in relationships or other life events—including the role transition of the diagnosis of breast cancer—may precipitate depressive episodes; conversely, depressive episodes strain relationships and often generate negative life events. The goal of IPT is to help patients solve a crisis in her or his role functioning or social environment, which leads to improvement in depressive symptoms. Research has established its efficacy as an acute and chronic treatment for patients with MDD, leading to its inclusion in treatment guidelines and its adaptation and testing for other mood and non-mood disorders [21, 23]. IPT has been used successfully without need for adaptation in treating MDD in patients with comorbid

medical illnesses, including those like HIV having high historical mortality and morbidity [20, 24], and in patients whose decline in physical health has led to more dependent and strained relationships [25]. Two small pilot studies have suggested the promise of IPT for treating MDD in patients with breast cancer [21, 26].

Problem Solving Therapy (PST) is an evidence-based, cognitive-behavioral intervention based on research demonstrating a strong link between social problem-solving and psychopathology [27]. The overarching treatment goal of PST is to foster adoption and implementation of adaptive problem-solving attitudes and behaviors as a means of decreasing emotional distress and improving one's overall quality of life. PST is geared toward increasing optimism, improving emotional regulation, and fostering successful resolution of stressful problems. Several studies have shown the efficacy of PST for MDD in breast cancer patients [19, 28–30].

Brief Supportive Psychotherapy (BSP) is considered the most frequently used psychotherapeutic modality in clinical practice [31]. Current models [32, 33] define BSP as an active treatment that uses techniques such as clarification, suggestions, praise, reassurance, normalization, and rehearsal and anticipation to promote a supportive patient-therapist relationship, enhance the patient's strengths and ability to use environmental supports, reduce distress and behavioral dysfunction, and maximize autonomy for the patient's treatment decisions. It is often used a comparator in depression trials, and has frequently matched other therapies in outcome. It is thus a very active control condition, far from a sham or placebo treatment [34–36]. Several studies have found BSP efficacious in decreasing anxious and depressive *symptoms* and improving the quality of life in individuals with breast cancer or cancer in other sites [37–39], but its efficacy in cancer patients with a full diagnosis of MDD has never been investigated.

Treatment occurred weekly for 12 sessions. Each session lasted 45 min and took place in English or Spanish at patient preference. All treatments were delivered in the New York State Psychiatric Institute, located two blocks from the Breast Cancer Clinic. Patients who missed sessions were contacted by the study coordinator, who offered to reschedule the session.

Therapists

Psychologist, psychiatrist, or social worker study therapists treated at least two pilot cases prior to subject assignment to ensure expertise. Therapists were audiotaped, and supervised weekly by experts to ensure adherence and competence. Because the study was conceived more as an effectiveness than a pure efficacy trial, we did not have independent raters use formal adherence ratings. JM supervised IPT therapists, AN supervised PST therapists, and DH supervised BSP therapists.

Assessments

Assessments occurred at baseline, before sessions 4 and 8, and at week 12. Measures administered by independent evaluators blinded to treatment condition included: (1) the 17-item Hamilton Depression Scale [40], a standard measure of depressive symptom severity and the primary outcome instrument; and (2) the Clinical Global Impression Severity scale [41]. Patients were reminded not to identify their therapy or therapist during study evaluations.

Patient-administered measures included: (1) Beck Depression Inventory-II, a widely used self-report rating scale for depressive symptoms; (2) Quality of Life Enjoyment and Satisfaction Questionnaire [42], a self-report measure assessing quality of life with sensitivity to symptom severity and treatment response; and (3) the Medical Outcomes Study Short Form, version 2 (SF-12): a measure of psychosocial functioning frequently used in clinical and population-based studies that includes a Mental Component Summary (MCS) and a Physical Component Summary (PCS). Scores range from 0 to 100 and are normed to have a mean of 50 and a standard deviation of 10 in the general population. (4) The Client Satisfaction Questionnaire [43] contains eight items querying patient satisfaction with services received. The SCID assessed psychiatric comorbidity at baseline [17]. We also collected patients' general medical history and the course and stage of breast cancer, including age at diagnosis, type of treatment received, and family history of breast cancer, pain level (scored 0 to 10 on a Likert scale), and Eastern Cooperative Oncology Group performance status (ECOG; scored 0 to 4, where 0 is fully active and 4 completely disabled) [44].

Statistical analyses

Subjects were randomized in 1:1:1 ratio to IPT, PST, or BSP, stratified by breast cancer stage (< III versus III–IV). Efficacy of the three treatments with respect to symptom severity was estimated based on longitudinal mixed effects models (LMM). All outcomes were modeled as a function of categorical time (baseline, weeks 4, 8, and 12), treatment, and the treatment × time interaction with a random intercept to control for repeated measures within individuals. Within treatment group changes in outcomes from baseline, and differences in those changes between treatment groups, were estimated and tested at each time point using contrasts formed from the LMM. An *a priori* power analysis, based on previous studies of MDD in individuals with cancer and other medical conditions, estimated that the study could detect a difference of Cohen's $d \geq 0.5$ (equivalent to 3–4

points in the HAM-D, depending on the expected standard deviation) between IPT and BSP or PST and BSP. Because we did not hypothesize differences in efficacy between IPT and PST, no power analysis was conducted for that potential comparison.

Response and remission rates were calculated among study completers at 12 weeks and compared between groups using Chi square tests of independence. Based on widely accepted criteria [45], response was defined as HAM-D improvement of $\geq 50\%$ from baseline. Remission from MDD was defined as HAM-D score ≤ 8. Differences in treatment retention, specifically time until study drop-out, were examined with Kaplan–Meier and tested by log-rank test. Predictors of treatment retention were examined using Cox proportional hazards survival functions. Effect sizes were calculated by dividing the mean difference by the baseline standard deviation. All tests were considered significant at $\alpha = 0.05$, 2-tailed. All analyses were based on the intention-to-treat sample and conducted in SAS (Version 9.4, SAS Institute, Cary, North Carolina) and IBM SPSS Statistics (Version 23). Because 13 patients were taking antidepressants at the beginning of the study, we repeated our analyses excluding those 13 patients; the results remained unchanged. We present the analyses of the full sample in this paper. Results of the sensitivity analyses are available on request.

Results

Sample characteristics

Figure 1 illustrates the flow of the 179 subjects assessed for study participation. Table 1 presents the baseline demographic and clinical characteristics of patients

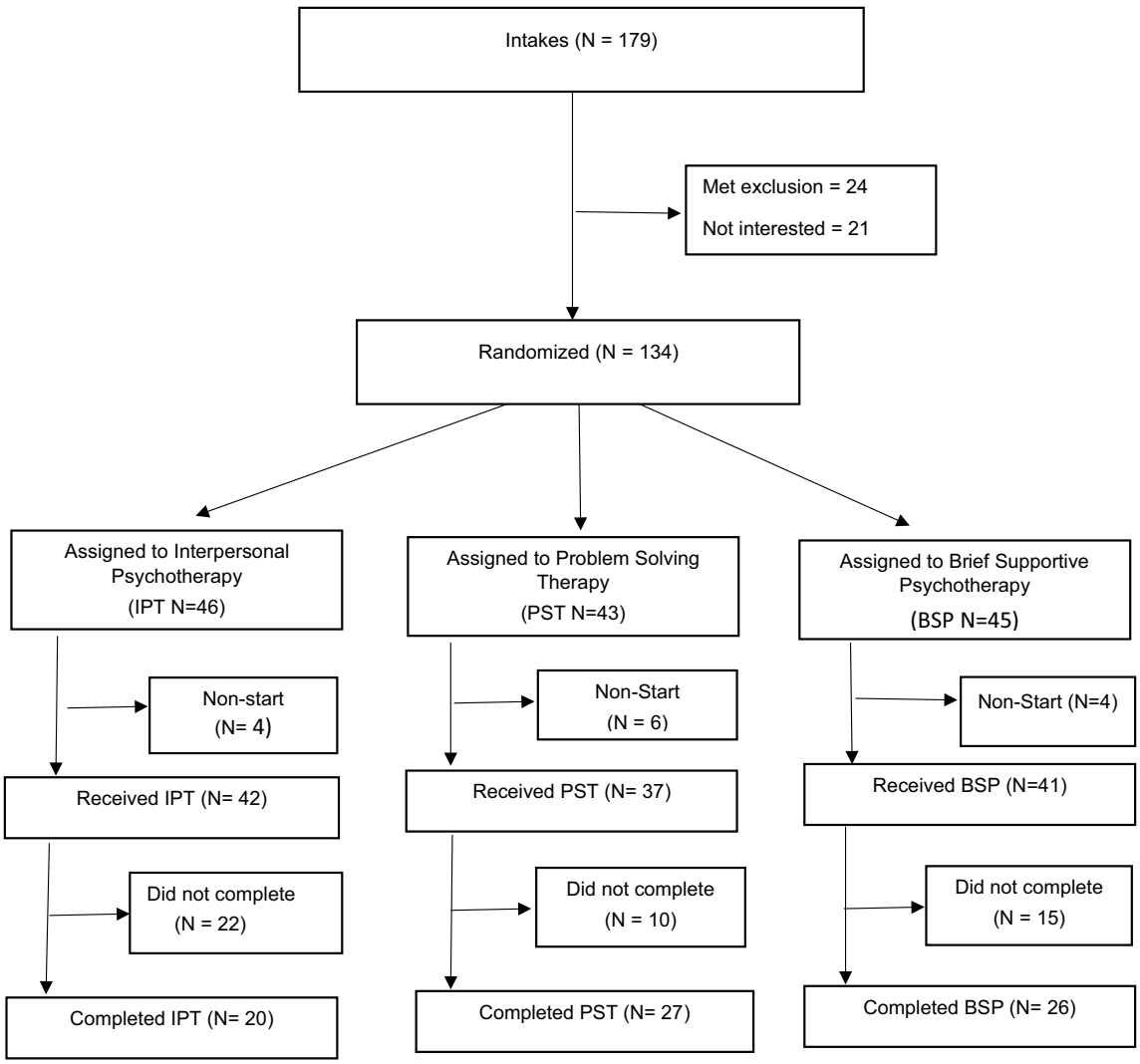

Fig. 1 CONSORT flow diagram

Table 1 Demographic characteristics of breast cancer survivors with major depressive disorder treated with problem-solving therapy (PST), interpersonal psychotherapy (IPT), and brief supportive therapy (BSP)

	Full sample $n=134$	By treatment			
		IPT $n=46$	PST $n=43$	Supportive $n=45$	*P*
Age, y					
Mean	52.7	51.9	50.9	55.2	0.119
SD	10.3	10.6	8.8	11.0	
Range	56.8	43.2	38.5	56.8	
Min–max	28.1–84.9	30.9–74.1	29.8–68.3	28.1–84.9	
Marital status, *N* (%)					
Married	43 (32.1)	16 (34.8)	11 (25.6)	16 (35.6)	0.850
Single, never married	37 (27.6)	12 (26.1)	15 (34.9)	10 (22.2)	
Divorced	50 (37.3)	17 (37.0)	16 (37.2)	17 (37.8)	
Widowed	4 (3.0)	1 (2.2)	1(2.2)	2 (4.4)	
Ethnicity/race, *N* (%)					
White	30 (22.4)	11 (23.9)	6 (14.0)	13(28.9)	0.237
Black	14 (10.4)	3 (6.5)	7 (16.3)	4 (8.9)	
Hispanic	84 (62.7)	30(65.2)	28 (65.1)	26 (57.8)	
Other	6 (3.5)	2 (4.4)	2 (4.6)	2 (4.4)	
Employment, *N* (%)					
Full-time employment	23 (17.2)	5 (10.9)	9 (20.9)	9 (20.9)	0.347
Full-time student	1 (0.7)	1 (2.2)	0	0	
Part-time/homemaker/retired	41 (30.6)	15 (32.6)	14 (32.6)	12(26.7)	
Unemployed/disabled/public Assistance	66 (49.3)	24 (52.1)	20 (46.5)	22 (48.9)	
Failed to report	3 (2.2)	1 (2.2)	0	2 (4.4)	
Yearly family income, *N* (%)					
< $9,999 or public assistance	34 (25.4)	10 (21.7)	11 (25.6)	13 (28.9)	0.421
$10,000–$19,999	21 (15.7)	8 (17.4)	9 (20.9)	4 (8.9)	
$20,000–$39,999	21 (15.7)	8 (17.4)	8 (18.6)	5 (11.1)	
More than $40,000	29 (21.6)	12 (26.1)	6 (14.0)	11 (24.4)	
Failed to report	29 (21.6)	8 (17.4)	9 (20.9)	12 (26.7)	
Education, year					
Mean	12.9	12.7	13.4	12.6	0.586
SD	4	4.2	3.9	4	
Range	20	17	20	16	
Min–max	0–20	3–20	0–20	4–20	
Missing or failed to report	2	0	0	2	

randomized into the study ($N=134$). Mean patient age (standard deviation) was 52.7 (10.3) years. Most women had never married or were divorced. More than half were Hispanic. The mean educational level was 12.9 years, or slightly beyond high school completion. Almost half of the sample was unemployed, disabled, or on public assistance. Annual family income for about one quarter of the sample fell below $10,000, and for another 35% ranged between $10,000 and $40,000. There were no differences in baseline sociodemographic characteristics across treatments. Mean age at diagnosis of breast cancer was 50.7 (10.4) years of age. Most women had stage < III (91%) disease; 9% had stage IV. Hormone therapy (72.4%) and chemotherapy (51.5%) were common across groups during the study period. Most women were postmenopausal (60.7%) and had no family history of breast cancer (58.2%). Average pain score was 0.36 (1.49) on a scale of 0–10, and mean ECOG Performance score was 0.15 (0.36) on a scale of 0–4, indicating low pain and high functioning. Breast cancer recurrence was rare across groups (20.1%) but significantly more common among women randomized to PST (37.8%) than those randomized to IPT (14.6%) or BSP (16.7%). There were no other group differences in baseline clinical characteristics (Table 2).

Table 2 Baseline clinical characteristics of breast cancer survivors with MDD treated with PST, IPT and BSP

	Full sample $n=134$	By treatment			
		IPT $n=46$	PST $n=43$	BSP $n=45$	p
Age at diagnosis of breast cancer					
Mean	50.7	50	49.2	52.7	0.305
SD	10.4	10.8	9.3	11	
Range	27–85	31–72	28–67	27–85	
Unknown	18	8	6	4	
Menopausal status, *n* (%)					
Premenopausal	41 (33.6)	15 (36.6)	13 (33.3)	13 (31.0)	0.811
Postmenopausal	74 (60.7)	23 (56.1)	24 (61.5)	27 (64.3)	
Unknown	19 (5.7)	8 (17.4)	6 (14.0)	5 (11.1)	
Breast cancer stage, *n* (%)					
Stage < III	122 (91.0)	42 (91.3)	39 (90.7)	41 (91.1)	0.995
Stage III–IV	12 (9.0)	4 (8.7)	4 (16.3)	4 (11.1)	
Breast surgery, *n* (%)					
Lumpectomy	55 (41.0)	18 (43.9)	16 (41.1)	21 (50.0)	0.692
Mastectomy	54 (40.3)	19 (46.3)	17 (43.6)	18 (42.9)	
No surgery	5 (3.7)	1 (2.4)	3 (7.7)	1 (2.4)	
Unknown	20 (14.9)	8 (17.4)	7 (16.3)	5 (11.1)	
Chemotherapy, *n* (%)					
Yes	69 (51.5)	25 (61.0)	20 (51.3)	24 (57.1)	0.639
No	43 (32.1)	12 (29.3)	15 (38.5)	16 (38.1)	
Unknown	22 (16.4)	9 (19.6)	8 (18.6)	5 (11.1)	
Hormone therapy, *n* (%)					
Yes	97 (72.4)	34 (82.9)	30 (76.9)	33 (78.6)	0.724
No	16 (11.9)	4 (9.8)	6 (15.4)	6 (14.3)	
Unknown	21 (15.7)	8 (17.4)	7 (16.3)	6 (13.3)	
Disease relapse, *n* (%)					
Yes	27 (20.1)	6 (14.6)	14 (37.8)	7 (16.7)	0.043
No	88 (65.7)	32 (78.1)	23 (62.2)	33 (78.6)	
Unknown	19 (14.2)	8 (17.4)	6 (14.0)	5 (11.1)	
Family history of breast cancer, *n* (%)					
Yes	36 (26.9)	11 (26.8)	10 (25.6)	15 (35.7)	0.679
No	78 (58.2)	26 (63.4)	26 (66.7)	26 (61.9)	
Unknown	20 (14.9)	9 (19.6)	7 (16.3)	4 (8.9)	
Number of medical comorbidities					
Mean	1.8	1.5	1.9	2.1	0.151
SD	1.5	1.2	1.6	1.6	
Range	0–7	0–5	0–7	0–5	
Unknown	18	7	6	5	
Pain score					
Mean	0.4	0.03	0.5	0.6	0.305
SD	1.5	0.2	2	1.6	
Range	0–10	0–1	0–10	0–7	
Unknown	36	13	11	12	
ECOG performance status					
Mean	0.2	0.2	0.1	0.1	0.261
SD	0.4	0.4	0.3	0.3	
Range	0–1	0–1	0–1	0–1	
Unknown	36	12	8	16	

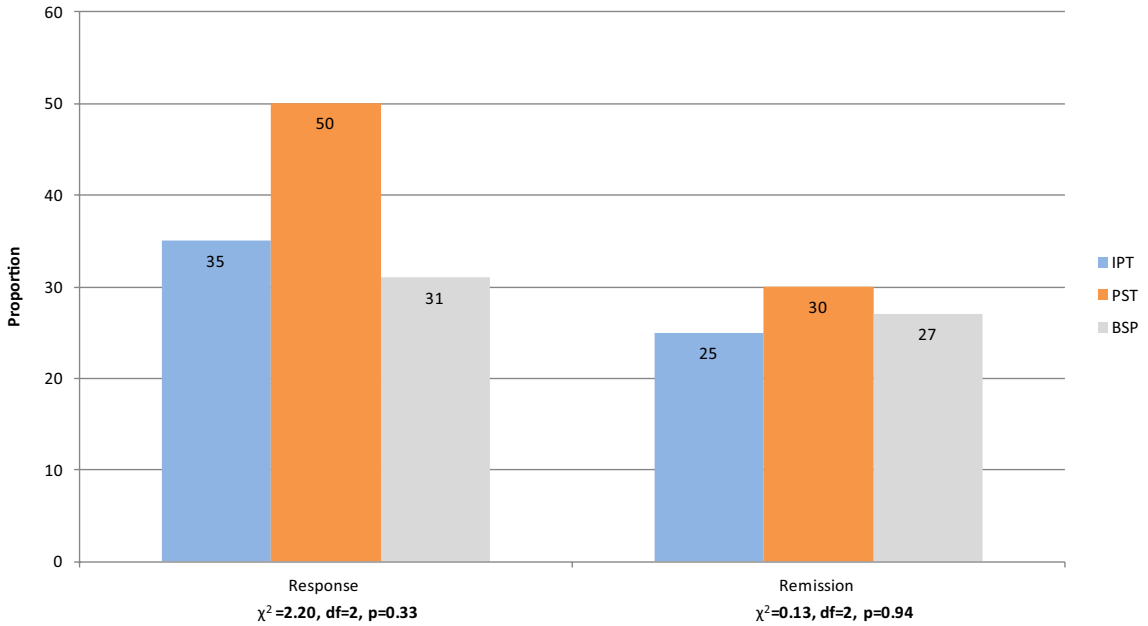

Fig. 2 Proportion of response and remission by treatment

Outcome evaluation

Most psychiatric outcome measures showed large effect sizes for pre- to post-treatment improvement for all three treatments: the effect size for HAM-D was $d = 1.07$ for IPT, 0.98 for PST and 0.91 for BSP at week 12 (Table 3). Response rates were 35% for IPT, 50% for PST and 31% for BSP ($\chi^2 = 2.20$, $df = 2$, $p = 0.33$); corresponding remission rates were 25%, 30% and 27% ($\chi^2 = 0.13$, $df = 2$, $p = 0.94$) (Fig. 2).

Of the two physical health measures, the PCS showed no improvement over the 12-week trial for any of the treatments, whereas the BPI only improved among patients treated with PST. In contrast to within-treatment effects, there were no between-treatment differences on any outcomes, dimensional, categorical, self-reported, or evaluator-administered. Attrition rates were high across treatments: 52% for IPT, 37% for PST and 42% for BSP, with no statistically significant difference across treatments (log-rank Chi square = 3.9, $df = 2$, $p = 0.14$) (Fig. 3). Having less than 16 years of education or having an annual family income below $20,000 predicted dropout (Supplemental Table 1).

Discussion

This is the largest randomized trial to date of psychotherapies treating major depressive disorder in women with breast cancer. IPT, PST, and BSP were all associated with significant improvements across a broad range of depression and quality of life assessments. No statistically significant differences were observed between treatment groups. While treatment across groups fell by some seven points on the HAM-D, differences in HAM-D scores among the three groups were less than half the 3-point threshold that is often considered clinically significant [46, 47], suggesting that a larger sample size would have been unlikely to yield substantially different results. That the three treatments did not differ from one another on the primary study outcome measure raises the important question of whether the improvements reflect specific treatment effects, non-specific effects (e.g., increased contact and support), or the natural course of patients' symptoms. Two factors suggest that the study treatments had real efficacy. First, despite generalized improvements in psychological symptoms and functioning across treatments, neither pain nor the PCS, the two measures of physical functioning, improved. The discrepancy between the improvement in the SF-12 MCS and the PCS suggests mental health-specific improvement. This response pattern suggests that the efficacy of IPT, PST and BSP, while comparable, targets psychological rather than physical functioning domains.

Second, a longitudinal study of a large, nationally representative epidemiological study of US adults found that individuals who remitted from major depressive disorder over a three year period showed an average improvement of 4.25 points on the SF-12 MCS (and a worsening of 1 point for non-remitters) [48]. By contrast, the mean acute improvement in our full sample was 11.3 points for IPT, 7.8 for PST and 12.7 for BSP. Remitters improved still more: 22.9 points for IPT, 12.7 for PST and 16.4 for BSP. The present results converge with prior studies, including the

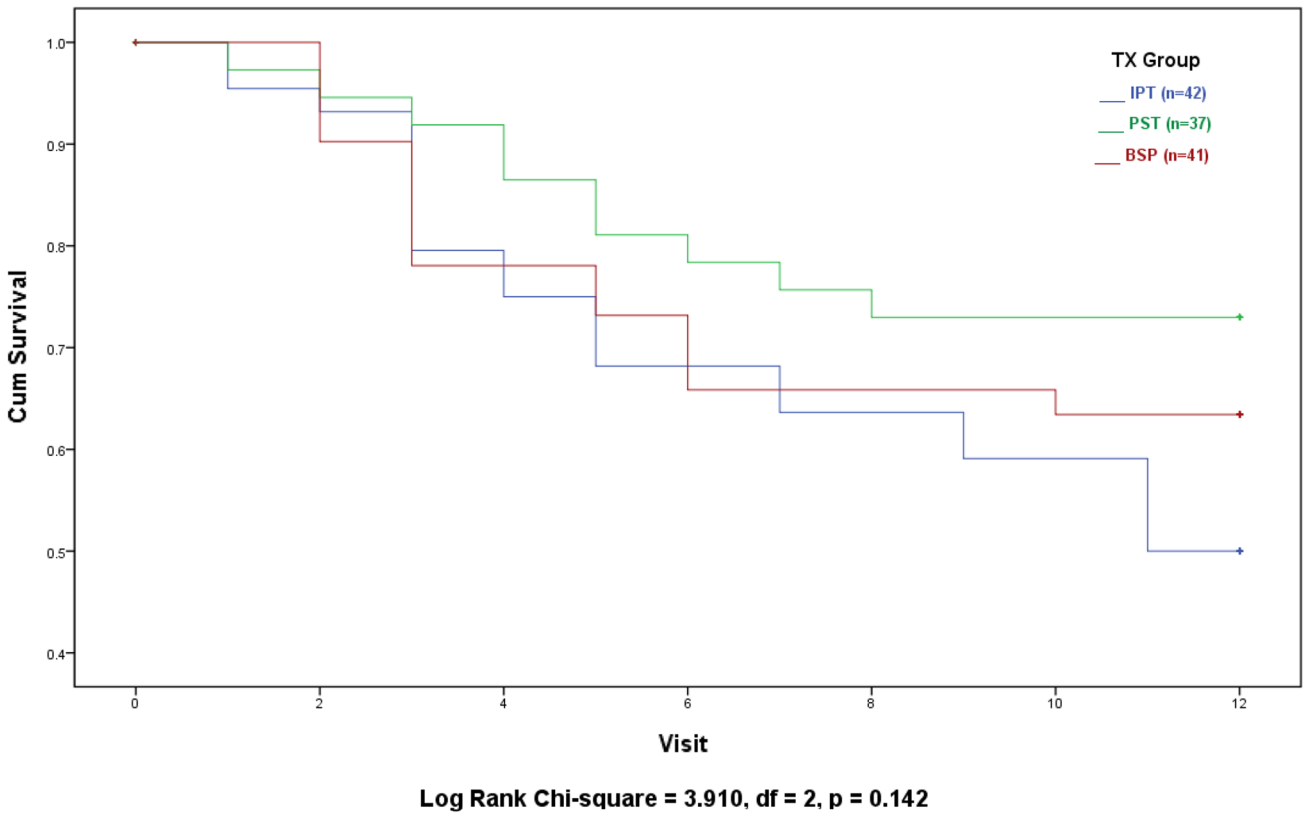

Fig. 3 Kaplan–Meier survival curves for dropout by treatment (TX) groups

previous PST trial for depression in women with breast cancer that found improvements in both PST and BADT but no between-treatment differences [49]; and with the broader literature, which has shown it is difficult to find statistical differences between active psychotherapies [50–52]. More than one psychotherapeutic approach may have efficacy in treating depression associated with breast cancer; or the shared non-specific aspects of the treatments may have greater efficacy than their unique aspects on the outcome measures.

The average improvement across treatments was lower than in the prior BATD versus PST study for depressed women with breast cancer, but similar to symptom reduction in our pilot IPT study targeting a depressed breast cancer patient sample similar to the current study [21]. Differences in baseline characteristics may partially account for outcome differences between studies. For example, patients in the Hopko et al. [49]. and Nezu et al. [19]. studies had higher average educational achievement, were more likely to be married, and were less likely to belong to ethnic minority groups, all of which might have influenced dropout rates as well as access to interpersonal and community resources.

Contrasting with the substantial clinical psychiatric improvement observed in the trial, the dropout rate was high across all treatments. Lower income and educational achievement predicted premature dropout. Consistent with prior studies of psychotherapy and of antidepressant medications, Hispanic participants had low rates of treatment adherence and completion [53–55]. The burden of multiple medical appointments, low economic resources, and competing demands on time such as family obligations often interferes with consistent attendance at psychotherapy visits in this patient population. Moreover, the weekly study psychotherapy sessions required far more frequent visits than many oncology patients may have been used to. That psychotherapy took place in the New York State Psychiatric Institute, a building at a distance from the Breast Cancer Clinic, may have also lowered patient appointment attendance or made them perceive their antidepressant treatment as distinct from and possibly alien to their cancer treatment. Beyond topographic distance, the stigma attached to entering a psychiatric hospital might partially explain dropout. Collaborative care models or other approaches that emphasize co-location of cancer care and mental health care, facilitate combined provision of medication and psychotherapy, and offer treatment for more than one psychiatric disorder may improve retention in care [56, 57]. Alternatively, remote interventions (telepsychiatry) might facilitate greater treatment access

Table 3 Means and SDs for the outcome measures in MDD among breast cancer survivors ($n = 134$)[a]

	IPT					PST					BSP					p-value of test of differences among IPT, PST and BSP
	Mean	SD	Effect Size	*N*	*P*	Mean	SD	Effect Size	*N*	*P*	Mean	SD	Effect Size	*N*	*P*	
HAM-D17																
Baseline	19.56	4.48	N/A	43	N/A	19.22	5.09	N/A	36	N/A	18.68	4.85	N/A	41	N/A	N/A
Week 4	17.58	5.65	0.39	33	0.031	16.65	5.32	0.44	34	0.018	14.00	4.93	0.94	32	0.000	0.105
Week 8	14.00	5.85	0.94	25	0.000	14.58	6.56	0.93	26	0.000	11.76	6.61	0.88	25	0.000	0.534
Week 12	12.00	6.93	1.08	21	0.000	12.04	7.22	0.98	27	0.000	12.69	7.55	0.91	26	0.000	0.695
CGI-S																
Baseline	4.00	1.13	N/A	43	N/A	3.86	1.33	N/A	36	N/A	4.15	1.00	N/A	40	N/A	N/A
Week 4	3.55	1.2	0.48	33	0.010	3.41	1.1	0.43	34	0.022	2.94	1.11	1.00	32	0.000	0.075
Week 8	3.20	1.26	0.71	25	0.002	2.89	1.25	0.85	27	0.000	2.60	1.35	1.28	25	0.000	0.153
Week 12	2.62	1.32	1.29	21	0.000	2.48	1.42	0.84	27	0.000	2.38	1.13	2.23	26	0.000	0.309
BDI																
Baseline	25.72	9.73	N/A	43	N/A	25.34	11.55	N/A	38	N/A	25.28	9.03	N/A	40	N/A	N/A
Week 4	20.76	9.05	0.85	33	0.000	19.75	8.79	0.66	32	0.001	17.66	8.97	0.89	32	0.000	0.237
Week 8	17.96	8.23	0.75	27	0.001	16.32	9.42	0.80	28	0.000	14.85	9.35	1.19	26	0.000	0.509
Week 12	13.41	8.94	1.11	22	0.000	14.38	10.95	1.11	26	0.000	14.84	8.39	1.50	25	0.000	0.792
Q-LES-Q																
Baseline	44.7	11.37	N/A	43	N/A	43.32	15.57	N/A	38	N/A	46.71	14.94	N/A	38	N/A	N/A
Week 4	46.24	12.8	−0.09	33	0.600	49.66	17.91	−0.41	32	0.029	52.35	15.42	−0.46	31	0.017	0.301
Week 8	51.59	12.73	−0.58	27	0.006	56.61	17.8	−0.82	28	0.000	55.62	17.46	−0.65	26	0.004	0.306
Week 12	57.36	16.02	−0.89	22	0.000	59.58	20.21	−0.84	26	0.000	52.16	15.55	−0.44	25	0.044	0.136
CSQ																
Baseline	23.18	7.6	N/A	39	N/A	24.03	7.45	N/A	35	N/A	24.71	6.72	N/A	35	N/A	N/A
Week 4	27.39	2.55	−0.67	33	0.001	26.34	4.2	−0.45	32	0.017	28.03	4.11	−0.53	31	0.009	0.245
Week 8	28.33	3.84	−0.72	27	0.002	27.46	3.21	−0.50	28	0.016	28.46	3.31	−0.59	26	0.009	0.241
Week 12	28.55	2.42	−0.94	22	0.001	28.85	2.66	−0.67	26	0.003	28.96	2.91	−0.68	25	0.004	0.275
SF-12 SF																
Baseline	40.48	27.02	N/A	42	N/A	43.92	34.56	N/A	37	N/A	41.67	31.59	N/A	39	N/A	N/A
Week 4	43.18	28.14	−0.13	33	0.465	41.94	26.13	−0.03	31	0.884	67.97	30.61	−0.60	32	0.002	0.019
Week 8	49.07	28.15	−0.25	27	0.214	52.88	29.43	−0.29	26	0.161	65.00	32.27	−0.69	25	0.003	0.615
Week 12	67.05	28.23	−0.91	22	0.000	65.38	30.06	−0.47	26	0.026	66.00	25.9	−0.56	25	0.009	0.484
SF-12 MCS																
Baseline	32.57	8.12	N/A	37	N/A	34.68	9.53	N/A	32	N/A	33.24	8.72	N/A	34	N/A	N/A

Table 3 (continued)

	IPT					PST					BSP					p-value of test of differences among IPT, PST and BSP
	Mean	SD	Effect Size	*N*	*P*	Mean	SD	Effect Size	*N*	*P*	Mean	SD	Effect Size	*N*	*P*	
Week 4	35.22	8.95	−0.30	32	0.114	35.82	10.21	−0.23	28	0.246	42.64	7.81	−0.89	28	0.000	0.047
Week 8	38.08	10.13	−0.56	26	0.011	41.08	11.4	−0.48	25	0.030	44.47	8.19	−1.09	23	0.000	0.649
Week 12	43.62	11.69	−0.88	22	0.001	42.85	10.72	−0.57	25	0.017	46.28	5.77	−1.27	24	0.000	0.390
SF-12 PCS																
Baseline	38.97	8.65	N/A	37	N/A	40.26	10.33	N/A	32	N/A	40.4	11.86	N/A	34	N/A	N/A
Week 4	36.87	9.01	0.34	32	0.074	39.64	11.25	0.31	28	0.114	39.59	10.99	0.24	28	0.233	0.867
Week 8	37.3	9.79	0.48	26	0.028	39.6	11.44	0.07	25	0.742	38.9	8.21	0.28	23	0.221	0.351
Week 12	37.5	8.56	0.18	22	0.410	41.98	13.67	−0.18	25	0.429	40.38	9.3	0.17	24	0.432	0.425
BPI-severity																
Baseline	4.33	2.53	N/A	43	N/A	4.17	3.1	N/A	36	N/A	3.51	2.62	N/A	39	N/A	N/A
Week 12	4.03	2.75	0.11	22	0.611	3.67	2.85	0.09	25	0.653	3.44	2.58	0.00	25	1.000	0.916
BPI-interference																
Baseline	4.34	2.89	N/A	43	N/A	4.64	3.35	N/A	36	N/A	3.12	2.82	N/A	39	N/A	N/A
Week 12	4.06	3.02	0.10	22	0.656	3.00	3.29	0.58	25	0.007	3.05	2.66	0.22	25	0.285	0.229

Ham-D17 hamilton depression 17 Items, *CGI-S* CGI severity, *QLESQ* quality of life satisfaction questionnaire, *BPI* brief pain inventory, *CSQ* the client satisfaction questionnaire, *BDI* beck depression inventory, *SF-12 PCS* SF-12 physical component summary, *SF-12 MCS* SF-12 mental component summary, *SF-12 SF* SF-12 social functioning

[a]$n = 134$ subjects randomized Note, due to non-starting (see Consort) and missing data, baseline variables (at least one) are available on $n = 122$ subjects

for cancer patients who may have difficulty traveling to the clinic [58].

This study has several limitations. As the study recruited patients by referral, this precluded estimation of depression prevalence in our screening sample. Although all three treatments were associated with significant statistical and clinical improvements from baseline to endpoint, the lack of significant differences and high attrition across treatments suggest caution in interpreting the results. Regression to the mean cannot be excluded as an explanation for the results. Results from the study sample of mostly low income, ethnic minority women might not generalize to other women with breast cancer. The study was limited to psychotherapy and did not examine the effect of medication or combined medication and psychotherapy treatment.

Despite these limitations, the current study, which is the largest trial for patients with depression and breast cancer to date, suggests that IPT, PST and BSP are each associated with improvements in depressive symptoms and quality of life among depressed women with breast cancer. Patients who stayed in treatment improved. The study results contribute to the evidence base of effective treatments for this highly prevalent and impairing condition, and suggest avenues for future additional research.

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