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Effect of Telecare Management on Pain and Depression in Patients with Cancer: A Randomized Trial

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Abstract

Context—Pain and depression are two of the most prevalent and treatable cancer-related symptoms, yet frequently go unrecognized and/or undertreated.

Objective—To determine whether centralized telephone-based care management coupled with automated symptom monitoring can improve depression and pain in cancer patients.

Design, Setting, and Patients—Randomized controlled trial conducted in 16 community-based urban and rural oncology practices across the state of Indiana. Recruitment occurred from March 2006 through August 2008 and follow-up concluded in August 2009. The 405 patients had depression (Patient Health Questionnaire-9 score ≥ 10), cancer-related pain (Brief Pain Inventory worst pain score ≥ 6), or both.

Intervention—Patients were randomly assigned to the intervention (n=202) or to usual care (n=203), stratified by symptom type. Intervention patients received centralized telecare management by a nurse-physician specialist team coupled with automated home-based symptom monitoring by interactive voice recording or internet.

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Main Outcome Measures—Blinded assessment at baseline, 1, 3, 6, and 12 months for depression (20-item Hopkins Symptom Checklist [HSCL-20]) and pain (Brief Pain Inventory [BPI]) severity.

Results—There were 131 patients enrolled with depression only, 96 with pain only, and 178 with both depression and pain. Of the 274 patients enrolled for pain, the 137 intervention patients had greater improvements than the 137 usual care patients in BPI pain severity over the 12 months of the trial whether measured as a continuous severity score or as a categorical pain responder ($P < .0001$ for both). Similarly, of the 309 patients enrolled for depression, the 154 intervention patients had greater improvements than the 155 usual care patients in HSCL-20 depression severity over the 12 months of the trial whether measured as a continuous severity score ($P < .0001$) or as a categorical depression responder ($P < .001$). The standardized effect size for between-group differences at 3 and 12 months was .67 and .39 for pain, and .42 and .44 for depression.

Conclusion—Centralized telecare management coupled with automated symptom monitoring resulted in improved pain and depression outcomes in cancer patients receiving care in geographically-dispersed urban and rural oncology practices.

Keywords

cancer; pain; depression; antidepressants; analgesics; telemedicine; care management

Pain and depression are the most common physical and psychological symptoms, respectively, in cancer patients.^{1–4} However, despite their prevalence and associated disability,^{5–10} cancer-related pain and depression are frequently undetected and undertreated.^{1,11–15}

Collaborative care is a team-based approach in which a care manager supervised by a physician specialist work together with the principal provider to optimize outcomes through educating patients, monitoring adherence and therapeutic response, and adjusting treatment. Various collaborative care models have well-established effectiveness for enhancing depression outcomes, with most trials conducted in primary care^{16,17}, though a few in specialty clinic settings have shown benefits in post-stroke¹⁸ and post-CABG depression.¹⁹ Two recent trials in primary care suggest collaborative interventions may enhance pain outcomes as well.^{20,21}

Therefore, we conducted the Indiana Cancer Pain and Depression (INCPAD) trial, a collaborative care approach to managing depression and pain in geographically-dispersed oncology practices. Centralized care management combined with automated disease monitoring facilitated coverage of multiple urban and rural oncology practices throughout an entire state. Our hypothesis was that this telecare management intervention would be superior to usual care in improving the co-primary study outcomes of pain and depression.

METHODS

Identifying and Enrolling Study Subjects

Details of the INCPAD trial design have been previously described.²² Study participants were enrolled from 16 urban and rural oncology practices in Indiana from March 2006 through August 2008. The practices included 10 that were staffed by Community Cancer Care which provides satellite oncology services to rural areas and mid-sized communities throughout Indiana, 4 large oncology clinics in Indianapolis, 1 oncology clinic providing care for underserved patients, and 1 VA oncology clinic. Patients presenting for oncology clinic visits who screened positive for either pain or depression underwent an eligibility

interview; all eligibility criteria relied on patient report. Eligible patients who were willing to participate provided audiotaped oral informed consent (with follow-up written consent forms obtained by mail) and completed a baseline interview after which they were randomized to the intervention or usual care group. Randomization was computer-generated in randomly varying block sizes of 4, 8 and 12 and stratified by symptom type (pain only, depression only, or both pain and depression). The study was approved by the institutional review boards.

Study Eligibility

Depression had to be at least moderately severe, defined as a Patient Health Questionnaire nine-item depression scale (PHQ-9) score ≥ 10 and endorsement of either depressed mood and/or anhedonia.^{23,24} *Pain* had to be: (a) definitely or possibly cancer-related; (b) at least moderately severe, defined as a score of ≥ 6 on the “worst pain in the past week” item of the Brief Pain Inventory;^{14,25,26} and (c) persistent despite trying one or more analgesics. Excluded were individuals who did not speak English; had moderately severe cognitive impairment as defined by a validated 6-item cognitive screener²⁷; had schizophrenia or other psychosis; had a pending pain-related disability claim; were pregnant; or were in hospice care.

Outcome Assessment

All five assessments (baseline, 1, 3, 6, and 12 months) were administered by telephone interview and conducted by research assistants blinded to treatment arm. These research assistants had no involvement in the study intervention and their call list included participant name and study number but not treatment arm. Depression and pain severity were the two co-primary study outcomes. Depression severity was assessed with the Hopkins Symptom Checklist twenty-item depression scale (HSCL-20)^{28–30} Pain severity was assessed with the Brief Pain Inventory (BPI) which rates the *severity* of pain on 4 items (current, worst, least, and average pain in past week).^{14,31} Scores range from 0 to 4 on the HSCL-20 and from 0 to 10 on the BPI, with higher scores representing greater severity.

Secondary depression-specific outcomes included the 3-item depression severity subscale of the SF-36 Mental Health Inventory³² and depression diagnostic status as assessed by the PHQ-9.²³ Secondary pain-specific outcomes included the SF-36 bodily pain scale,³³ the BPI interference scale,^{14,31} and global change in pain assessed with a 7-point scale with the options being worse, the same, or a little, somewhat, moderately, a lot, or completely better.³⁴

Secondary outcomes assessed in the full sample included health-related quality of life, disability, co-interventions, and self-reported health care use. The SF-12 was used to calculate Physical Component Summary (PCS) and Mental Component Summary (MCS) scores.³⁵ Overall quality of life was assessed with a single-item 0 to 10 scale.³⁶ Anxiety was assessed by the seven-item Generalized Anxiety Disorder (GAD-7) scale.^{37,38} Physical symptom burden was assessed with a 22-item somatic symptom scale.²² Fatigue was assessed with the SF-36 vitality scale.³³ Disability was assessed with the 3-item Sheehan Disability Scale³⁹ and the number of self-reported days in which activities were limited during the preceding 4 weeks.^{40,41} Because pain and depression treatment and outcomes may vary by race or ethnicity,^{42,43} race/ethnicity (identified by the patient from preselected options) was also included as a demographic characteristic.

A treatment survey inquired about treatments received for pain and depression as well as self-reported health care use. For intervention patients, the number of months on antidepressant and opioid medications and number of care manager contacts were abstracted

from care manager logs, and the number of automated symptom monitoring contacts was determined from computerized reports.

Intervention

Care Management—Telephonic care management was delivered by a nurse care manager (NCM) trained in assessing symptom response and medication adherence; in providing pain and depression-specific education; and in making treatment adjustments according to evidence-based guidelines. The NCM met weekly to review cases with the pain-psychiatrist specialist who was also available to discuss management issues that arose between case management meetings. Subjects received a baseline and 3 follow-up NCM calls (1, 4, and 12 weeks) during the first 3 months of treatment. In addition to these *scheduled* NCM phone contacts, *triggered* phone calls occurred when automated monitoring indicated inadequate symptom improvement, nonadherence to medication, side effects, suicidal ideation, or a patient request to be contacted.

Automated Symptom Monitoring—Automated symptom monitoring (ASM) was performed using either interactive voice recorded (IVR) telephone calls or web-based surveys based upon patient preference. The 21-item ASM survey included the PHQ-9 depression scale, 8 pain items from the BPI (3 severity and 5 interference), and a single item each on medication adherence, side effects, global improvement, and whether or not the patient would like a NCM call. ASM was administered twice a week for the first 3 weeks, then weekly during weeks 4 through 11, twice a month during months 3 through 6, and once a month during months 7 through 12. However, more frequent ASM could be reinstated for subjects who underwent treatment changes. Those not completing their scheduled assessment were contacted telephonically by the NCM.

Medication Management—Details of the INCPAD treatment protocol including the antidepressant and analgesic algorithms have been previously published.²² Treatment recommendations were provided to the study participant's oncologist who was responsible for prescribing all medications. The antidepressant algorithm was informed by the multi-center STAR*D trial and our primary care based SCAMP trial.^{34,44} The analgesic algorithm used in INCPAD was adapted from the National Comprehensive Cancer Network Cancer Pain Guidelines,⁴⁵ with some simplification based upon other guidelines.^{46–48} For depression, the goal was remission (PHQ-9 score < 5) or, failing this, a PHQ-9 score < 10 with a ≥50% decline from the baseline score. Subjects who preferred not to take antidepressants were encouraged to consider a referral to mental health referral for psychotherapy. For pain, the goal was to obtain a ≥30% reduction in the BPI pain score and, ideally, a score of ≤3. In participants with both pain and depression, the protocol focused on pain treatment for the first 4 weeks, unless depression was more severe (PHQ-9 scores ≥ 15)^{23,24} If depression persisted despite this initial treatment period for pain, antidepressant therapy was recommended.

Usual Care Group—Patients randomized to usual care were informed of their depressive and pain symptoms and their screening results were provided to their oncologist. There were no further attempts by study personnel to influence depression or pain management unless a psychiatric emergency arose (e.g., suicidal ideation was detected on baseline or follow-up outcome assessment).

Statistical Analysis

The study was powered to detect clinically significant improvement in the two primary outcomes of depression (HSCL-20) and pain (BPI). A reduction of ≥ 50% in depression severity and ≥ 30% in pain severity are accepted thresholds for clinically significant

improvement in depression and pain trials, respectively.^{49,50} It was determined that 97 subjects per symptom group would provide 80% power to detect a 20% absolute difference in response rates with two-tailed $\alpha < .05$. This sample size also provided 80% power to detect a moderate treatment effect size of 0.4 when analyzing depression and pain as continuous outcomes. Enrollment of 120 patients per group with pain (240 total) and 120 patients per group with depression (240 total) allowed for up to a 20% attrition rate. Preliminary work demonstrated that approximately a quarter of patients had pain only, a third had depression only and 40–45% had both depression and pain. Thus, to enroll at least 240 patients with pain and 240 patients with depression, INCPAD required an estimated sample size of 380.

Analyses were based on intention-to-treat in all randomized participants. Group differences over the 12 months of the trial were compared using mixed effects model repeated measures (MMRM) analysis, adjusting for baseline value of the outcome variable and time.⁵¹ To accommodate the large variability of the health care use data, negative binomial distribution regression analysis was used to model count data.

Analyses were not adjusted for multiple comparisons. This does not affect interpretation of our primary outcomes (HSCL-20 and BPI severity), but findings for secondary outcomes should be interpreted cautiously unless they are highly significant ($P < .001$). Analyses were performed using SAS Version 9.1 (SAS Institute, Cary, North Carolina).

As a sensitivity analysis, we also compared group differences using two imputation strategies: last-observation carried forward (LOCF) imputation for all outcomes and multiple regression imputation for our primary outcomes. There was no difference in the magnitude of missing data between the treatment groups. Further, logistic regression models showed that intervention and control participants for which 12-month data was missing did not differ in terms of baseline depression or pain severity, age, gender, cancer type, or phase of cancer. For participants who died during the 12-month period following their study enrollment, imputation was right censored, i.e., no data was imputed beyond the date of death.

Depression-specific outcomes were compared in participants enrolled with depression, pain-specific outcomes in those enrolled with pain, and secondary outcomes (health-related quality of life, disability, health care use, and co-interventions) in the full sample. Stratifying randomization by symptom type assured that the proportion of patients with depression only, pain only, and comorbid pain and depression was balanced among intervention and control groups. For the primary outcomes, standardized effect sizes were calculated as the mean group difference divided by the pooled standard deviation at baseline. For patients who died, time to death was compared between treatment groups using survival analysis.

RESULTS

Participant Enrollment and Baseline Characteristics

Figure 1 summarizes the participant flow in INCPAD. Of the 616 subjects in which eligibility could be ascertained, about two-thirds consented to enroll in the study and were randomized to either the intervention or the usual care control group. The intervention and control groups were similar in terms of overall mortality (42 [20.8%] vs. 43 [21.2%] as well as time to death [$P = .94$ by log-rank test]). Among participants still alive at each follow-up point, assessment rates were similar in both groups and uniformly high, including 88.1% (354/402) at 1 month, 86.1% [335/389] at 3 months, 83.7% [304/363] at 6 months, and 84.1% [269/320] at 12 months

Of the 405 participants enrolled, randomization resulted in intervention ($n = 202$) and control ($n = 203$) groups balanced in terms of baseline characteristics (Table 1). The sample included 131 (32%) participants with depression only, 96 (24%) with pain only, and 178 (44%) with both depression and pain. The average SCL-20 depression score in the 309 depressed participants was 1.64 (on a 0–4 scale), and the average BPI severity score (i.e., mean of the 4 severity items) in the 274 participants with pain was 5.2 (on a 0–10 scale), representing at least moderate levels of symptom severity. Also, 283 (92%) of the 309 patients enrolled for depression had major depression, dysthymia, or both.

Pain-Specific Outcomes

Table 2 summarizes the pain-specific outcomes among the 274 patients enrolled for pain. For the primary outcome (BPI pain severity), the 137 intervention patients had significantly greater improvement than the 137 usual care patients by MMRM analysis ($P < .0001$) over the 12 months of the trial whether measured as a continuous severity score or as a categorical pain responder (Table 2 and Figure 2). Between-group differences for BPI pain severity as both a continuous variable and a categorical response variable were also significant at all time points for assessed cases (Table 2) and for assessed and imputed cases using LOCF and multiple regression imputation analyses (not shown). The standardized effect size for the between-group differences at 1, 3, 6 and 12 months was .36, .67, .46, and .39, respectively. Effect sizes of 0.2 and 0.5 represent modest and moderate differences, respectively.⁵²

Intervention patients also had greater improvement in the secondary pain-specific outcomes of BPI pain interference and SF-36 bodily pain scores (Table 2). Additionally, global ratings of change showed there were significant between-group differences at 1, 3, 6, and 12 months (eFigure 1 [<http://www.jama.com>]).

Depression-Specific Outcomes

Table 3 summarizes the depression-specific outcomes among the 309 depressed patients enrolled in INCPAD. For the primary outcome (HSCL-20 depression severity), the 154 depressed intervention patients had significantly greater improvement than the 155 depressed usual care patients by MMRM analysis ($P < .0001$) over the 12 months of the trial whether measured as a continuous severity score or as a categorical depression responder (Table 3 and Figure 2). Between-group differences for HSCL-20 as a continuous variable were also significant at all time points for available cases (Table 3) and for assessed and imputed cases using LOCF and multiple regression imputation analyses (not shown); a categorical depression response was significantly more likely in the intervention group at 1, 3, and 6 months but not at 12 months. The standardized effect size for these between-group differences at 1, 3, 6 and 12 months was .31, .42, .45, and .44, respectively.

Intervention patients also had greater improvement in the secondary depression-specific outcomes of MHI depression severity and depression diagnostic status. While a similar proportion of intervention and usual care patients met criteria for major depressive disorder at baseline, significantly fewer intervention patients had major depressive disorder at 3 months and 12 months.

Health-Related Quality of Life (HRQL), Health Care Use, and Co-Interventions

Between-group differences in secondary outcomes that were not pain- or depression-specific were assessed in all 405 participants. The intervention group had better outcomes by MMRM analysis for several HRQL domains, including mental health, vitality, anxiety, and physical symptom burden (eTable 1 [<http://www.jama.com>]). The intervention group also had greater improvement on the Sheehan Disability Scale but did not differ from the usual

care group in self-reported disability days, physical health, or overall quality of life. In contrast to MMRM, LOCF analyses were not significant for any of the HRQL outcomes.

Compared to controls, intervention patients showed a trend towards fewer hospital days (mean of 3.6 vs. 5.8) and emergency department visits (mean of 1.0 vs. 1.4), but there was large variability in all 5 measures of health care use and none of the between-group differences were statistically significant (eTable 2 [<http://www.jama.com>]). The groups were also similar in self-reported use of 11 of 12 potential co-interventions (eTable 2), differing only in use of “other pain treatments” ($p = .03$).

Intensity of Intervention in Terms of Contacts and Medication

Intervention intensity could only be assessed in the intervention group because this data was abstracted from care manager and automated symptom monitoring logs. Participants in the intervention group had a mean of 11.2 ± 8.1 care manager telephone contacts and 20.5 ± 10.6 automated symptom monitoring (ASM) contacts. The care manager spent a mean of 157 ± 104 minutes of direct telephone time per intervention subject. At least 1 care manager and 1 ASM contact occurred in 196 and 185 of the intervention subjects, respectively, and ≥ 5 care manager and ≥ 10 ASM contacts each occurred in 165 subjects. The inter-subject variability in nurse and ASM contacts was due to death early drop-out by some intervention patients and extra contacts required for others. The 154 intervention patients enrolled for depression were on antidepressants a mean of 5.4 ± 5.2 months, with 89 (58%) on an antidepressant ≥ 3 months. The 137 intervention patients enrolled for pain were on opioid medication a mean of 4.0 ± 5.1 months, with 66 (48%) on ≥ 1 month. The care manager coordinated a pain-specific referral for 12 patients and a mental health referral for 11 patients.

DISCUSSION

Our INCPAD trial has several important findings. First, the telecare management intervention resulted in significant improvements in both pain and depression. Second, the trial demonstrated that it is feasible to provide telephone-based centralized symptom management across multiple geographically dispersed community-based practices in both urban and rural areas by coupling human with technology-augmented patient interactions. Third, the findings did not appear to be confounded by differential rates of co-interventions or health care use.

The moderate effect sizes and improvement rates for pain in INCPAD were comparable to those found in recent collaborative care interventions for pain²⁰ as well as pain with comorbid depression.²¹ Although several recent trials demonstrated somewhat greater improvements in depression at 12 months than those produced by our INCPAD intervention,^{53–55} these trials enrolled fewer patients with advanced cancer and delivered more intensive depression treatment including in-person visits and psychotherapy. Telephone-based psychotherapy can be effectively delivered⁵⁶ and might augment the optimized medication intervention provided in INCPAD.

Our study has several limitations. First, our sample included a wide range of cancer types and phases. This increases the generalizability of our findings to real-world practice but precludes more precise estimates of treatment effective in specific types or stages of cancer. Second, the lack of electronic medical records in most of the community-based practices resulted in a less complete assessment of pain- and depression-specific treatments in the control group. Third, an economic analysis might further strengthen the case for dissemination. To this end, we are currently integrating self-report measures of health care

use and work productivity with hospital data to better clarify the cost-effectiveness of the INCPAD intervention.

The fact that INCPAD was beneficial for the most common physical and psychological symptoms in cancer patients demonstrates that a collaborative care intervention can cover several conditions, both physical and psychological. In 3 trials involving 796 cancer patients undergoing chemotherapy Givens et al showed that a nurse-administered cognitive-behavioral therapy (CBT) intervention improved physical symptom burden.^{57–59} The model was more disease management rather than collaborative care in that the nurse worked with the patient independent of the oncology practice. Such interventions may be strengthened by closer integration with practices.⁶⁰ Combining the collaborative care approach and physician-nurse team that facilitated optimized medication management in INCPAD with the nurse-administered CBT and symptom self-management approach tested by Givens might provide an even more effective way to manage multiple cancer-related symptoms.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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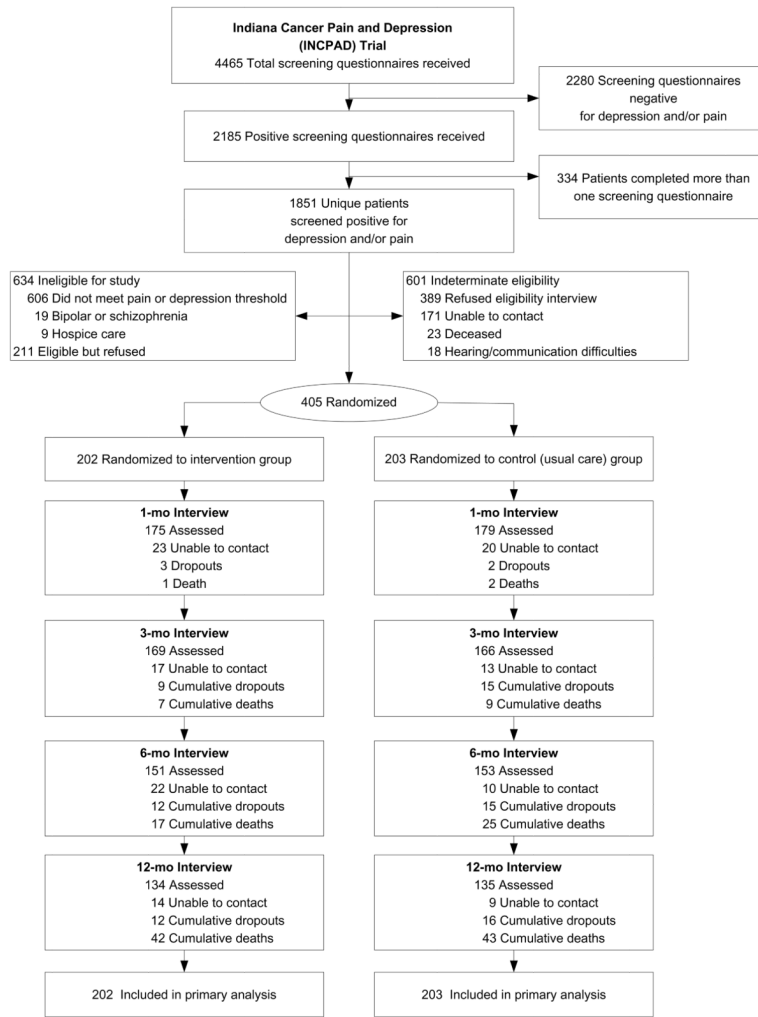


Figure 1.
Flowchart of participants in the INCPAD trial

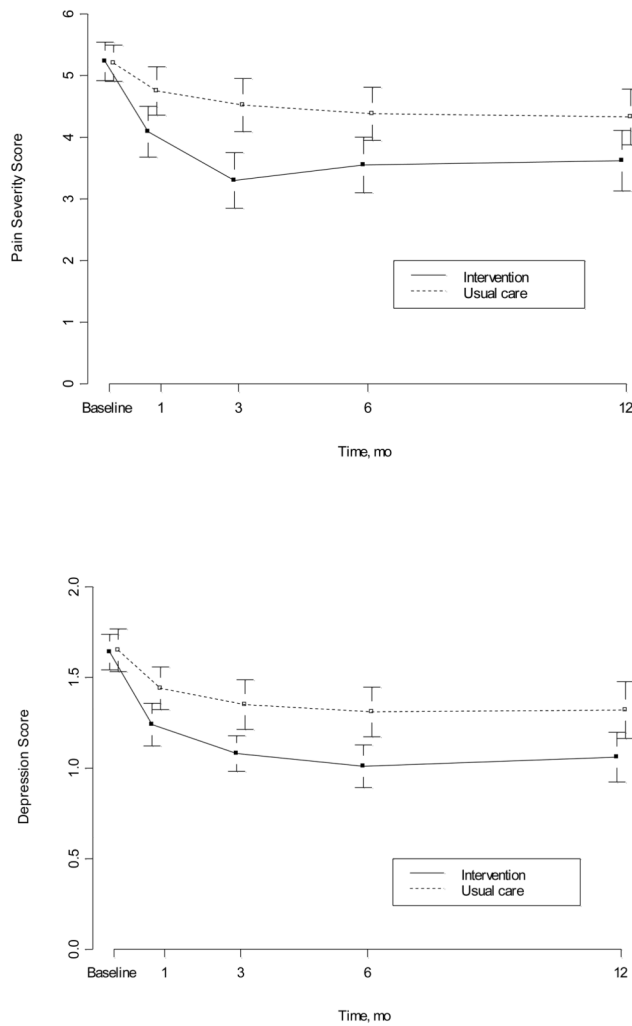


Figure 2.

Co-primary outcomes. Error bars indicate 95% confidence intervals. Top graph represents mean Brief Pain Inventory Severity scores, which can range from 0 to 10. There were 137 intervention and 137 control patients with pain assessed at baseline, 117 and 120 at 1 month, 117 and 113 at 3 months, 103 and 103 at 6 months, and 91 and 89 at 12 months. Bottom graph represents mean 20-item Hopkins Symptoms Checklist depression scores, which can range from 0 to 4. There were 154 intervention and 155 control patients with depression assessed at baseline, 131 and 136 at 1 month, 124 and 122 at 3 months, 110 and 113 at 6 months, and 98 and 104 at 12 months. Intervention patients had significantly lower pain ($P < .0001$) and depression ($P < .0001$) severity scores over the 12 months of the trial by mixed effects model repeated measures (MMRM) analysis.

Table 1

Baseline Characteristics of the 405 Subjects Enrolled in INCPAD Trial*

Baseline Characteristic	Intervention Group (N=202)	Usual Care Group (N=203)	P Value
Mean (SD) age, yr	58.7 (11.0)	59.0 (10.6)	.81
Female sex, n (%)	128 (63)	147 (72)	.051
Race, n (%)			.32
White	159 (79)	163 (80)	
Black	40 (20)	33 (16)	
Other	3 (2)	7 (3)	
Education, n (%)			.36
Less than High school	45 (22)	42 (21)	
High school	83 (41)	77 (38)	
Some college or trade school	55 (27)	53 (26)	
College graduate	19 (9)	31 (15)	
Married, n (%)	109 (54)	90 (44)	.053
Employment status, n (%)			.57
Employed	36 (18)	45 (22)	
Unable to work due to poor health or disability	90 (45)	86 (42)	
Retired	62 (31)	55 (27)	
Other	13 (6)	17 (8)	
Patient-perceived level of income, n (%)			.67
Comfortable	46 (23)	54 (27)	
Just enough to make ends meet	99 (49)	95 (47)	
Not enough to make ends meet	57 (28)	54 (27)	
Mean (SD) no. of medical diseases	2.0 (1.6)	2.2 (1.6)	.23
Symptom group, n (%)			1.00
Depression only	65 (32)	66 (33)	
Pain only	48 (24)	48 (24)	
Depression and pain	89 (44)	89 (44)	
Phase of cancer, n (%)			.082
Newly-diagnosed	74 (36.6)	76 (37.4)	

Baseline Characteristic	Intervention Group (N=202)	Usual Care Group (N=203)	P Value
Maintenance or disease-free	78 (38.6)	94 (46.3)	
Recurrent or progressive	50 (24.8)	33 (16.3)	
Type of cancer, n (%)			.21
Breast	55 (27)	63 (31)	
Lung	42 (21)	39 (19)	
Gastrointestinal	40 (20)	30 (15)	
Lymphoma and hematological	22 (11)	31 (15)	
Genitourinary	17 (8)	24 (12)	
Other	26 (13)	16 (8)	
Mean (SD) scores			
BPI pain severity (score range, 0–10)	4.30 (2.36)	4.23 (2.35)	.74
SCL-20 depression (score range, 0–4)	1.43 (0.71)	1.46 (0.71)	.62
Sheehan Disability Index (score range, 0 to 10)	5.44 (2.84)	5.44 (2.88)	.99
Overall quality of life (score range, 0 to 10)	5.74 (2.28)	5.51 (2.27)	.30
Bed days in past 4 weeks			
Median (interquartile range)	2 (0–10)	1 (0–10)	
Mean (SD)	5.6 (7.3)	5.7 (8.1)	.91
Days in which activities reduced by ≥ 50% in past 4 weeks (excluding bed days)			
Median (interquartile range)	10 (4–16)	10 (3–18)	
Mean (SD)	11.3 (8.9)	11.1 (9.1)	.84
Baseline medication use, n (%) ^b			
Antidepressants (excluding tricyclics)	71 (36)	80 (41)	.24
Tricyclic antidepressants	13 (7)	22 (11)	.09
Psychotropics (excluding antidepressants)	52 (26)	64 (33)	.13
Opioid analgesics	107 (54)	107 (55)	.75
Nonopioid analgesics	87 (44)	91 (46)	.50
Currently being seen by a mental health professional, n (%)	18 (9)	26 (13)	.21
Currently being seen in a pain clinic, n (%)	12 (6)	9 (4)	.49

^b Baseline medication data was available from the oncology medical records for 396 (97.8%) of the 405 participants, including 200 in the intervention group and 196 in the usual care group

Table 2
Pain-Specific Outcomes in the 274 Participants Enrolled in the INCPAD Trial for Pain

Clinical Outcome	Intervention (137) ^a	Usual Care (137) ^a	Time-Specific Between-Group Difference or Relative Risk (95% CI)	Overall P value by MMRM ^b
Primary pain outcome (n = assessed cases)				
BPI pain severity, mean (SD) (range, 0–10)				<.0001
Baseline (n = 274)	5.23 (1.85)	5.20 (1.78)	0.03 (–0.40 to 0.46)	
3-mo follow-up (n = 230)	3.30 (2.45)	4.52 (2.33)	–1.22 (–1.85 to –0.60)	
6-mo follow-up (n = 206)	3.55 (2.36)	4.38 (2.21)	–0.83 (–1.46 to –0.20)	
12-mo follow-up (n = 180)	3.62 (2.42)	4.33 (2.21)	–0.70 (–1.39 to –0.02)	
BPI pain severity responder, N (%)^c				
3-mo follow-up (n = 230)	67 (57.3)	34 (30.1)	1.90 (1.38 to 2.63)	<.0001
6-mo follow-up (n = 206)	51 (49.5)	27 (26.2)	1.89 (1.29 to 2.76)	
12-mo follow-up (n = 180)	46 (50.6)	31 (34.8)	1.45 (1.02 to 2.06)	
Secondary pain outcomes (n = assessed cases)				
BPI pain interference, mean (SD) (range, 0–10)				
Baseline (n = 274)	5.35 (2.62)	5.96 (2.48)	–0.61 (–1.22 to 0.00)	<.0001
12-mo follow-up (n = 168)	3.86 (2.45)	5.08 (2.88)	–1.22 (–2.04 to –0.40)	
SF-36 bodily pain scale, mean (SD) (range, 0–100)				
Baseline (n = 272)	32.8 (18.1)	30.7 (17.5)	2.1 (–2.1 to 6.4)	.004
12-mo follow-up (n = 179)	48.4 (24.7)	39.0 (22.6)	9.4 (2.4 to 16.4)	

^aThe number of subjects with pain who were assessed for pain outcomes was 230 (117 intervention and 113 controls) at 3 months, 206 (103 intervention and 103 controls) at 6 months, and 180 (91 intervention and 89 controls) at 12 months.

^bMixed effects model repeated measures (MMRM) analysis was used to compare group differences over 12 months, adjusting for time effect and for baseline value of outcome variable. Assessments were conducted at baseline, 1, 3, 6 and 12 months for BPI severity and interference and at baseline, 3 and 12 months for SF-36 bodily pain.

^cDefined as 30% or greater decrease in BPI severity from baseline

Table 3
Depression-Specific Outcomes in the 309 Participants Enrolled in the INCPAD Trial for Depression

Clinical Outcome	Intervention (154) ^d	Usual Care (155) ^d	Time-Specific Between-Group Difference or Relative Risk (95% CI)	Overall P value by MMRM ^b
Primary depression outcome (n = assessed cases)				
HSCL-20 depression severity, mean (SD) (range, 0–4)				
Baseline (n = 309)	1.64 (0.63)	1.64 (0.65)	0.00 (–0.15 to 0.14)	<.0001
3-mo follow-up (n = 246)	1.08 (0.61)	1.35 (0.73)	–0.27 (–0.44 to –0.10)	
6-mo follow-up (n = 223)	1.01 (0.59)	1.31 (0.73)	–0.29 (–0.47 to –0.12)	
12-mo follow-up (n = 202)	1.06 (0.65)	1.32 (0.83)	–0.26 (–0.46 to –0.05)	
HSCL-20 depression severity responder, N (%) ^c				
3-mo follow-up (n = 246)	45 (36.3)	25 (20.5)	1.77 (1.16 to 2.70)	<.001
6-mo follow-up (n = 223)	42 (38.2)	27 (23.9)	1.60 (1.06 to 2.40)	
12-mo follow-up (n = 202)	33 (33.7)	29 (27.9)	1.21 (0.80 to 1.83)	
Secondary depression outcomes (n = assessed cases)				
Major depressive disorder, N (%)				
Baseline (n = 309)	94 (61.0)	96 (61.9)	0.99 (0.83 to 1.18)	.002
3-mo follow-up (n = 247)	30 (24.2)	47 (38.2)	0.63 (0.43 to 0.93)	
12-mo follow-up (n = 203)	21 (21.4)	37 (35.2)	0.61 (0.38 to 0.96)	
Mental Health Inventory depression severity subscale, mean (SD), range (3–15)				
Baseline (n = 309)	8.61 (2.82)	8.99 (2.59)	–0.38 (–0.98 to 0.23)	.009
12-mo follow-up (n = 202)	7.01 (2.58)	7.91 (3.00)	–0.90 (–1.68 to –0.12)	

^aThe number of depressed subjects who were assessed for depression outcomes was 246–247 (124 intervention and 122–123 controls) at 3 months, 223 (110 intervention and 113 controls) at 6 months, and 202–203 (98 intervention and 104–105 controls) at 12 months.

^bMixed effects model repeated measures (MMRM) analysis was used to compare group differences over 12 months, adjusting for time effect and for baseline value of outcome variable. Assessments were conducted at baseline, 1, 3, 6 and 12 months for HSCL-20 and at baseline, 3 and 12 months for secondary depression outcomes.

^cDefined as 50% or greater decrease in HSCL-20 from baseline