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# Effect of Telecare Management on Pain and Depression in Patients With Cancer

## A Randomized Trial

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**P**AIN AND DEPRESSION ARE THE most common physical and psychological symptoms, respectively, in cancer patients.<sup>1-4</sup> However, despite their prevalence and associated disability,<sup>5-10</sup> cancer-related pain and depression are frequently undetected and undertreated.<sup>1,11-15</sup>

Collaborative care is a team-based approach in which a care manager supervised by a physician specialist work together with the principal clinician 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,<sup>16,17</sup> although a few in specialty clinic settings have shown benefits for patients with depression after experiencing a stroke<sup>18</sup> and after undergoing coronary artery by-pass graft surgery.<sup>19</sup> Two recent trials involving patients treated by their primary care physicians suggest collaborative interventions may enhance pain outcomes as well.<sup>20,21</sup>

**Context** Pain and depression are 2 of the most prevalent and treatable cancer-related symptoms, yet they frequently go unrecognized, undertreated, or both.

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

**Design, Setting, and Patients** Randomized controlled trial conducted in 16 community-based urban and rural oncology practices involved in the Indiana Cancer Pain and Depression (INCPAD) trial. Recruitment occurred from March 2006 through August 2008 and follow-up concluded in August 2009. The participating patients had depression (Patient Health Questionnaire-9 score  $\geq 10$ ), cancer-related pain (Brief Pain Inventory [BPI] worst pain score  $\geq 6$ ), or both.

**Intervention** The 202 patients randomly assigned to receive the intervention and 203 to receive usual care were stratified by symptom type. Patients in the intervention group received centralized telecare management by a nurse-physician specialist team coupled with automated home-based symptom monitoring by interactive voice recording or Internet.

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

**Results** Of the 405 participants enrolled in the study, 131 had depression only, 96 had pain only, and 178 had both depression and pain. Of the 274 patients with pain, 137 patients in the intervention group had greater improvements in BPI pain severity over the 12 months of the trial whether measured as a continuous severity score or as a categorical pain responder ( $\geq 30\%$  decrease in BPI) than the 137 patients in the usual-care group ( $P < .001$  for both). Similarly, of the 309 patients with depression, the 154 patients in the intervention group had greater improvements in HSCL-20 depression severity over the 12 months of the trial whether measured as a continuous severity score or as a categorical depression responder ( $\geq 50\%$  decrease in HSCL) than the 155 patients in the usual care group ( $P < .001$  for both). The standardized effect size for between-group differences at 3 and 12 months was 0.67 (95% confidence interval [CI], 0.33-1.02) and 0.39 (95% CI, 0.01-0.77) for pain, and 0.42 (95% CI, 0.16-0.69) and 0.41 (95% CI, 0.08-0.72) 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.

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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 outcomes of pain and depression.

## METHODS

### Identifying and Enrolling Study Subjects

Details of the INCPAD trial design have been previously described.<sup>22</sup> 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 Veterans Affairs 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 Indiana University and Community Hospitals' institutional review boards.

### Study Eligibility

Depression had to be at least moderately severe, defined as a Patient Health Questionnaire 9-item depression scale

(PHQ-9) score of 10 or higher and endorsement of either depressed mood, anhedonia; or both.<sup>23,24</sup> Pain had to be (1) definitely or possibly cancer related; (2) at least moderately severe, defined as a score of 6 or higher on the "worst pain in the past week" item of the Brief Pain Inventory<sup>14,25,26</sup>; and (3) persistent despite trying at least 1 pain medicine. Excluded were individuals who did not speak English, had moderately severe cognitive impairment as defined by a validated 6-item cognitive screener,<sup>27</sup> had schizophrenia or other psychosis, had a pending pain-related disability claim, were pregnant, or were in hospice care.

### Outcome Assessment

All 5 assessments (baseline and at months 1, 3, 6, and 12) were administered by telephone interview and conducted by research assistants who had no involvement in the study intervention and whose call list included only the participant's name and study number but not his/her treatment group. Depression and pain severity were the copri-mary study outcomes. Depression severity was assessed with the Hopkins Symptom Checklist 20-item depression scale (HSCL-20).<sup>28-30</sup> 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).<sup>14,31</sup> 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 36-Item Short Form Health Survey (SF-36) Mental Health Inventory<sup>32</sup> and depression diagnostic status as assessed by the PHQ-9.<sup>23</sup> Secondary pain-specific outcomes included the SF-36 bodily pain scale,<sup>33</sup> the BPI interference scale,<sup>14,31</sup> 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.<sup>34</sup>

Secondary outcomes assessed in the full sample included health-related quality of life, disability, cointerventions, and

self-reported health care use. The SF-12 was used to calculate physical component summary and mental component summary scores.<sup>35</sup> Overall quality of life was assessed with a single-item 0 to 10 scale.<sup>36</sup> Anxiety was assessed by the 7-item Generalized Anxiety Disorder scale.<sup>37,38</sup> Physical symptom burden was assessed with a 22-item somatic symptom scale.<sup>22</sup> Fatigue was assessed with the SF-36 vitality scale.<sup>33</sup> Disability was assessed with the 3-item Sheehan Disability Scale<sup>39</sup> and by the number of self-reported days in which activities were limited during the preceding 4 weeks.<sup>40,41</sup> Because pain and depression treatment and outcomes may vary by race or ethnicity,<sup>42,43</sup> 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 taking 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 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 nurse care manager met weekly to review cases with the pain-psychiatrist specialist who was also available to discuss management issues that arose between case management meetings. Participants received a baseline and 3 follow-up calls (1, 4, and 12 weeks) during the first 3 months of treatment. In addition to these scheduled telephone contacts, triggered telephone calls occurred when automated monitoring indicated inadequate symptom improvement, non-adherence to medication, adverse ef-

fects, suicidal ideation, or a patient request to be contacted.

**Automated Symptom Monitoring.** Automated symptom monitoring was performed using either interactive voice-recorded telephone calls or Web-based surveys based on patient preference. The 21-item survey included the PHQ-9 depression scale, 8 pain items from the BPI (3 severity and 5 interference), and a single question for each of the following: medication adherence, adverse effects, global improvement, and whether the patient wanted a nurse care manager call. The monitoring survey 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 administration could be reinstated for participants who underwent treatment changes. Those not completing their scheduled assessment were contacted telephonically by the nurse care manager.

**Medication Management.** Details of the INCPAD treatment protocol including the antidepressant and analgesic algorithms have been previously published.<sup>22</sup> Treatment recommendations were provided to the study participant's oncologist who was responsible for prescribing all medications. The antidepressant algorithm was informed by the multicenter Sequenced Treatment Alternatives to Relieve Depression (STAR\*D) trial and our primary care-based Stepped Care for Affective disorders and Musculoskeletal Pain (SCAMP) trial.<sup>34,44</sup> The analgesic algorithm used in INCPAD was adapted from the National Comprehensive Cancer Network Cancer Pain Guidelines,<sup>45</sup> with some simplification based on other guidelines.<sup>46-48</sup> For depression, the goal was remission (PHQ-9 score <5) or, failing this, a PHQ-9 score of less than 10 with a decline of at least 50% from the baseline score. Participants who preferred not to take antidepressants were encouraged to consider a referral for psychotherapy. For pain, the goal was to obtain a reduction of at least 30% in the BPI pain score

and, ideally, a score of 3 or less. For 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  $\geq 15$ ).<sup>23,24</sup> If depression persisted despite this initial treatment period for pain, antidepressant therapy was recommended.

**Usual-Care Group.** Patients randomized to the usual-care group 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 (eg, suicidal ideation was detected on baseline or follow-up outcome assessment).

### Statistical Analysis

The study was powered to detect clinically significant improvement in the 2 primary outcomes of depression (HSCL-20) and pain (BPI). A reduction of at least 50% in depression severity and at least 30% in pain severity are accepted thresholds for clinically significant improvement in depression and pain trials, respectively.<sup>49,50</sup> It was determined that 97 participants per symptom group would provide 80% power to detect a 20% absolute difference in response rates with a 2-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 between 40% and 45% had both depression and pain. Thus, to enroll at least 240 patients with pain and 240 patients with depression, INCPAD required an overall estimated sample size of 380 because patients with pain and depression were counted in each category.

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.<sup>51</sup> 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 Inc, Cary, North Carolina).

As a sensitivity analysis, we also compared group differences using 2 imputation strategies: last observation carried forward for all outcomes and multiple regression for our primary outcomes. There was no difference in the magnitude of missing data between treatment groups. Furthermore, logistic regression models showed that intervention and control participants for which 12-month data were missing did not differ in terms of baseline depression or pain severity, age, sex, cancer type, or phase of cancer. For participants who died during the 12-month period following their study enrollment, imputation was right censored, ie, no data were imputed beyond the date of death.

Depression-specific outcomes were compared among participants with depression, pain-specific outcomes in those with pain, and secondary outcomes (health-related quality of life, disability, health care use, and cointerventions) for the full sample. Stratifying randomization by symptom type ensured 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 participants in which eligibility could be ascertained, 405 consented to enroll in the study. Two hundred two patients were randomized to the intervention group and 203 to the usual-care group. Forty-two participants (20.8%) in the intervention group died vs 43 (21.2%) in the usual-care group died. Time to death was similar in each group ( $P=.94$  by log-rank test). Among participants still

alive at each follow-up point, assessment rates were similar in both groups and uniformly high, with 88.1% (354 of 402) participation at 1 month, 86.1% (335 of 389) at month 3, 83.7% (304 of 363) at month 6, and 84.1% (269 of 320) at month 12.

Baseline characteristics between groups were balanced (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 mean HSCL-20 depression score among the 309 participants with depression

was 1.64 (on a 0-4 scale), and the mean BPI severity score (ie, mean of the 4 severity items) among 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 with depression had major depression, dysthymia, or both, according to their PHQ-9 assessments.

### Pain-Specific Outcomes

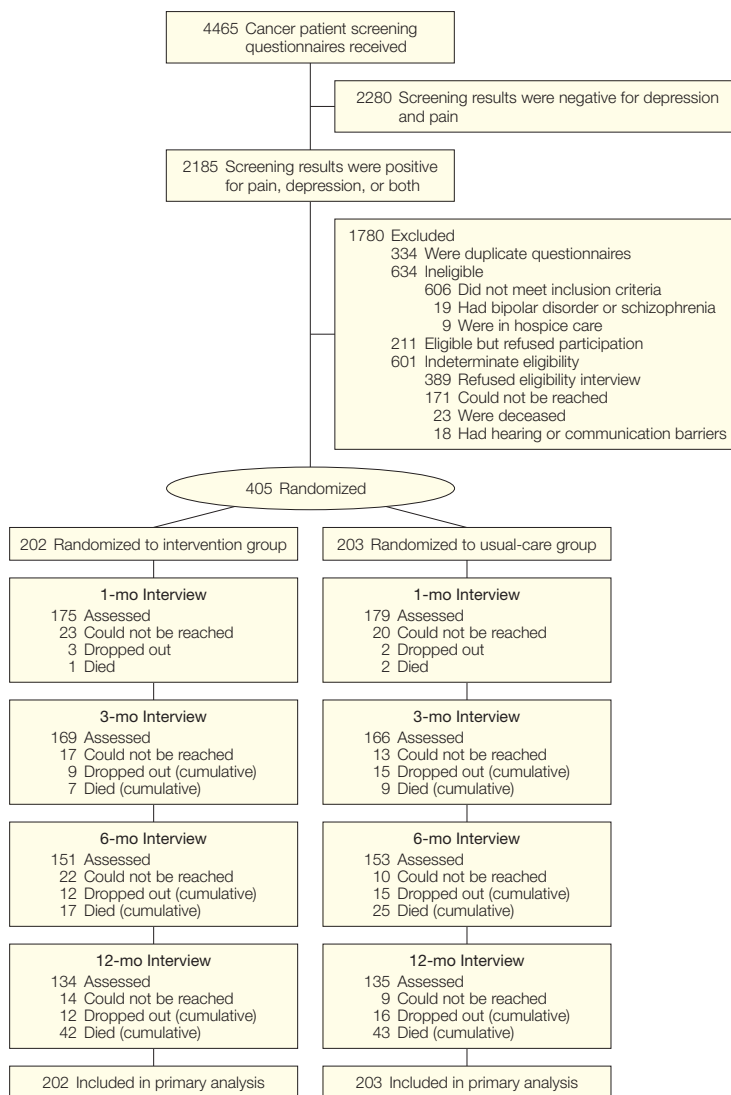
TABLE 2 summarizes the pain-specific outcomes among 274 patients with pain. For the primary outcome (BPI pain severity), the intervention group had significantly greater improvement than the usual-care group by MMRM analysis ( $P<.001$ ) over the 12 months of the trial whether measured as a continuous 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 and imputed cases using the last observation carried forward and multiple regression imputation analyses (not shown). The standardized effect sizes for the between-group differences were 0.36 (95% confidence interval [CI], 0.05-0.68) at 1 month and 0.67 (95% CI, 0.33-1.02) at 3, 0.46 (95% CI, 0.11-0.81) at 6, and 0.39 (95% CI, 0.01-0.77) at 12 months. An effect size of 0.2 represents a modest difference and 0.5 represents a moderate difference.<sup>52</sup>

Those in the intervention group 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 available at <http://www.jama.com>).

### Depression-Specific Outcomes

TABLE 3 summarizes the depression-specific outcomes among the 309 pa-

**Figure 1.** Patient Flowchart



tients with depression. For HSCL-20 depression severity, the 154 patients in the intervention group had significantly greater improvement than the 155 patients in the usual-care group by MMRM analysis ( $P < .001$ ) over the 12-month 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 (Table 3) and for assessed and imputed cases using last observation carried forward and multiple regression imputation analyses (not shown); a categorical depression response was significantly more likely in the intervention group at all follow-up points except at 12 months. The standardized effect sizes for these between-group differences were 0.31 (95% CI, 0.06-0.55) at 1 month and 0.42 (95% CI, 0.16-0.69) at 3, 0.45 (95% CI, 0.19-0.73) at 6, and 0.41 (95% CI, 0.08-0.72) at 12 months.

Patients receiving the intervention also had greater improvement in the secondary depression-specific outcomes of Mental Health Inventory depression severity and depression diagnostic status. Although a similar proportion of intervention and usual-care patients met PHQ-9 criteria for major depressive disorder at baseline, significantly fewer patients receiving the intervention had major depressive disorder at months 3 and 12.

### Health-Related Quality of Life, Health Care Use, and Cointerventions

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 health-related quality of life domains, including mental health, vitality, anxiety, and physical symptom burden (eTable 1 available at <http://www.jama.com>). The intervention group also had greater improvement on the Sheehan Disability Scale but did not dif-

**Table 1.** Baseline Characteristics of the 405 Subjects Enrolled in INCPAD Trial<sup>a</sup>

Baseline Characteristic	Intervention Group (n = 202)	Usual-Care Group (n = 203)	P Value
Age, mean (SD) age, y	58.7 (11.0)	59.0 (10.6)	.81
Female sex, No. (%)	128 (63)	147 (72)	.05
Race, No. (%)			
White	159 (79)	163 (80)	.32
Black	40 (20)	33 (16)	
Other	3 (2)	7 (3)	
Education achievement, No. (%)			
<High school	45 (22)	42 (21)	.36
High school	83 (41)	77 (38)	
Some college or trade school	55 (27)	53 (26)	
College graduate	19 (9)	31 (15)	
Married, No. (%)	109 (54)	90 (44)	.05
Employment status, No. (%)			
Employed	36 (18)	45 (22)	.57
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, No. (%)			
Comfortable	46 (23)	54 (27)	.67
Just enough to make ends meet	99 (49)	95 (47)	
Not enough to make ends meet	57 (28)	54 (27)	
Medical diseases, mean (SD), No.	2.0 (1.6)	2.2 (1.6)	.23
Symptom group, No. (%)			
Depression only	65 (32)	66 (33)	>.99
Pain only	48 (24)	48 (24)	
Depression and pain	89 (44)	89 (44)	
Phase of cancer, No. (%)			
Newly diagnosed	74 (37)	76 (37)	.08
Maintenance or disease free	78 (39)	94 (46)	
Recurrent or progressive	50 (25)	33 (16)	
Type of cancer, No. (%)			
Breast	55 (27)	63 (31)	.21
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)	
Scale scores, mean (SD)			
BPI pain severity, range, 0-10	4.30 (2.36)	4.23 (2.35)	.74
HSCL-20 depression, range, 0-4	1.43 (0.71)	1.46 (0.71)	.62
Sheehan Disability Index, range, 0 to 10	5.44 (2.84)	5.44 (2.88)	.99
Overall quality of life, range, 0 to 10	5.74 (2.28)	5.51 (2.27)	.30
Bed days in past 4 wk			
Median (IQR)	2 (0-10)	1 (0-10)	.91
Mean (SD)	5.6 (7.3)	5.7 (8.1)	
Days in which activities reduced by $\geq 50\%$ in past 4 wk, excluding bed days			
Median (IQR)	10 (4-16)	10 (3-18)	.84
Mean (SD)	11.3 (8.9)	11.1 (9.1)	
Baseline medication use, No. (%) <sup>b</sup>			
Antidepressants, excluding tricyclics	71 (36)	80 (41)	.24
Tricyclic antidepressants	13 (7)	22 (11)	.09
Psychotropic agents, excluding antidepressants	52 (26)	64 (33)	.13
Opioid analgesics	107 (54)	107 (55)	.75
Nonopioid analgesics	87 (44)	91 (46)	.50
Currently seeing a mental health professional, No. (%)	18 (9)	26 (13)	.21
Currently receiving treatment in a pain clinic, No. (%)	12 (6)	9 (4)	.49

Abbreviations: BPI, Brief Pain Inventory; IQR, interquartile range; HSCL-20, 20-item Hopkins Symptom Checklist.

<sup>a</sup>Percentages may not sum to 100 due to rounding.

<sup>b</sup>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.

fer from the usual care group in self-reported disability days, physical health, or overall quality of life. However, health-related quality of life improvements were not statistically significant when analyzed by the last observation carried forward.

Patients in the intervention group had a mean 3.6 hospital days vs 5.8 in the usual care group and a mean 1.0

emergency department visits 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 available at <http://www.jama.com>). The groups were also similar in self-reported use of 11 of 12 potential cointerventions (eTable 2), differing only in use of "other pain treatments" ( $P=.03$ ).

**Intensity of Intervention in Terms of Contacts and Medication**

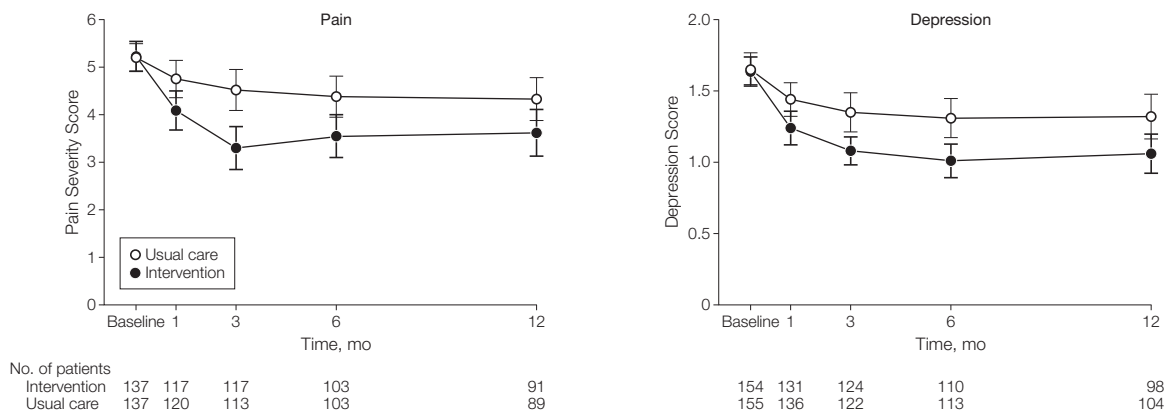
Intervention intensity could only be assessed in the intervention group because these data were abstracted from care manager and automated symptom monitoring logs. Participants in the intervention group had a mean (SD) of 11.2(8.1) care manager telephone contacts and 20.5(10.6) automated symp-

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

Clinical Outcome	No. of Assessed Cases	Intervention (n = 137) <sup>a</sup>	Usual Care (n = 137) <sup>a</sup>	Time-Specific Between-Group Difference or Relative Risk (95% CI)	Overall P Value <sup>b</sup>
<b>Primary pain outcome</b>					
BPI pain severity, mean (SD) range, 0-10					
Baseline	274	5.23 (1.85)	5.20 (1.78)	0.03 (-0.40 to 0.46)	<.001
3 mo	230	3.30 (2.45)	4.52 (2.33)	-1.22 (-1.85 to -0.60)	
6 mo	206	3.55 (2.36)	4.38 (2.21)	-0.83 (-1.46 to -0.20)	
12 mo	180	3.62 (2.42)	4.33 (2.21)	-0.70 (-1.39 to -0.02)	
BPI pain severity responder, No. (%) <sup>c</sup>					
3 mo	230	67 (57.3)	34 (30.1)	1.90 (1.38 to 2.63)	<.001
6 mo	206	51 (49.5)	27 (26.2)	1.89 (1.29 to 2.76)	
12 mo	180	46 (50.6)	31 (34.8)	1.45 (1.02 to 2.06)	
<b>Secondary pain outcomes</b>					
BPI pain interference, mean (SD), range, 0-10					
Baseline	274	5.35 (2.62)	5.96 (2.48)	-0.61 (-1.22 to 0.00)	<.001
12 mo	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	272	32.8 (18.1)	30.7 (17.5)	2.1 (-2.1 to 6.4)	.004
12 mo	179	48.4 (24.7)	39.0 (22.6)	9.4 (2.4 to 16.4)	

Abbreviations: BPI, Brief Pain Inventory; CI, confidence interval; SF-36, 36-Item Short Form Health Survey.  
<sup>a</sup>The number of participants with pain who were assessed for pain outcomes was 230 (117 intervention; 113 usual care) at 3 months, 206 (103 intervention; 103 usual care) at 6 months, and 180 (91 intervention; 89 usual care) at 12 months.  
<sup>b</sup>Mixed-effects model repeated-measures 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; month 1; and months 3, 6, and 12 for BPI severity and interference and at baseline and at months 3 and 12 for SF-36 bodily pain.  
<sup>c</sup>Defined as 30% or greater decrease in BPI severity from baseline.

**Figure 2.** Pain and Depression Outcomes



The Brief Pain Inventory Severity scores range from 0 to 10. The 20-item Hopkins Symptoms Checklist depression scores range from 0 to 4. Patients in the intervention group had significantly lower pain ( $P<.001$ ) and depression ( $P<.001$ ) severity scores over the 12 months of the trial by mixed-effects model repeated-measures (MMRM) analysis. Error bars indicate 95% confidence intervals.

tom monitoring contacts. The care manager spent a mean (SD) of 157 (104) minutes of direct telephone time per patient in the intervention group. One hundred ninety-six patients had received at least 1 care manager contact and 185 patients received at least 1 automated symptom monitoring contact with 165 patients receiving 5 or more care manager contacts and an equal number receiving 10 or more automated symptom monitoring contacts. The variability in contacts was due to death and early drop-out by some patients and extra contacts required for others. The 154 patients with depression in the intervention group were taking antidepressants a mean (SD) of 5.4 (5.2) months, with 89 (58%) taking an antidepressant for 3 or more months. The 137 patients with pain in the intervention group were taking opioid medication a mean (SD) of 4.0 (5.1) months, with 66 (48%) taking it for 1 month or more. The care manager coordinated a pain-specific referral for 12 patients and a mental health referral for 11 patients.

## COMMENT

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 cointerventions or health care use.

The moderate effect sizes and improvement rates for pain in INCPAD were comparable with those found in recent collaborative care interventions for pain<sup>20</sup> as well as for pain with comorbid depression.<sup>21</sup> Although several recent trials demonstrated somewhat greater improvements in depression at 12 months than those produced by our INCPAD intervention,<sup>53-55</sup> these trials enrolled fewer patients with ad-

vanced cancer and delivered more intensive depression treatment including in-person visits and psychotherapy. Telephone-based psychotherapy can be effectively delivered<sup>56</sup> 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 effect 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.

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

Clinical Outcome	No. of Assessed Cases	Intervention (n = 154) <sup>a</sup>	Usual Care (n = 155) <sup>a</sup>	Time-Specific Between-Group Difference or Relative Risk (95% CI)	Overall P Value <sup>b</sup>
Primary depression outcome					
HSCL-20 depression severity, mean (SD), range, 0-4					
Baseline	309	1.64 (0.63)	1.64 (0.65)	0.00 (-0.15 to 0.14)	<.001
3 mo	246	1.08 (0.61)	1.35 (0.73)	-0.27 (-0.44 to -0.10)	
6 mo	223	1.01 (0.59)	1.31 (0.73)	-0.29 (-0.47 to -0.12)	
12 mo	202	1.06 (0.65)	1.32 (0.83)	-0.26 (-0.46 to -0.05)	
HSCL-20 depression severity responder, No. (%) <sup>c</sup>					
3 mo	246	45 (36.3)	25 (20.5)	1.77 (1.16 to 2.70)	<.001
6 mo	223	42 (38.2)	27 (23.9)	1.60 (1.06 to 2.40)	
12 mo	202	33 (33.7)	29 (27.9)	1.21 (0.80 to 1.83)	
Secondary depression outcomes					
Major depressive disorder, No. (%)					
Baseline	309	94 (61.0)	96 (61.9)	0.99 (0.83 to 1.18)	.002
3 mo	247	30 (24.2)	47 (38.2)	0.63 (0.43 to 0.93)	
12 mo	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	309	8.61 (2.82)	8.99 (2.59)	-0.38 (-0.98 to 0.23)	.009
12 mo	202	7.01 (2.58)	7.91 (3.00)	-0.90 (-1.68 to -0.12)	

Abbreviations: Confidence interval, CI; HSCL-20, 20-item Hopkins Symptom Checklist.

<sup>a</sup>The number of depressed participants who were assessed for depression outcomes was 246 to 247 (124 intervention; 122-123 usual care) at 3 mo, 223 (110 intervention; 113 usual care) at 6 mo, and 202 to 203 (98 intervention; and 104-105 usual care) at 12 mo.

<sup>b</sup>Mixed-effects model repeated-measures 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; at month 1; and at months 3, 6, and 12 months for HSCL-20 and at baseline, 3 and 12 mo for secondary depression outcomes.

<sup>c</sup>Defined as 50% or greater decrease in HSCL-20 from baseline.

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, Given et al showed that a nurse-administered cognitive behavioral therapy intervention improved physical symptom burden.<sup>57-59</sup> Their model involved more disease management than collaborative care in that the nurse worked with the patient independently of the oncology practice. Such interventions may be strengthened by closer integration with practices.<sup>60</sup> Combining the collaborative care approach and physician-nurse team that facilitated optimized medication management in INCPAD with the nurse-administered cognitive behavioral therapy and symptom self-management approach tested by Given et al might provide an even more effective way to manage multiple cancer-related symptoms.

**Author Contributions:** Dr Kroenke had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Kroenke, Theobald, Carpenter, Morrison

**Acquisition of data:** Kroenke, Theobald, Norton  
**Analysis and interpretation of data:** Kroenke, Wu, Tu, Theobald, Carpenter, Morrison,

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**Statistical analysis:** Kroenke, Wu, Tu.

**Obtained funding:** Kroenke.

**Administrative, technical, or material support:** Kroenke, Theobald, Norton

**Study supervision:** Kroenke, Theobald, Norton

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**Online-Only Material:** eTables 1 and 2 and the eFigure are available at <http://www.jama.com>.

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The province of the instructor should be . . . awakening, invigorating, directing, rather than the forcing of the child's faculties upon prescribed and exclusive courses of thought. He should look to the child to see what is to be done, rather than to his book or his system. The Child is the Book. The operations of his mind are the true system.

—Bronson Alcott (1799-1888)