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Psychiatric–Medical Comorbidity

The Psychiatric–Medical Comorbidity section will focus on the prevalence and impact of psychiatric disorders in patients with chronic medical illness as well as the prevalence and impact of medical disorders in patients with chronic psychiatric illness.

Cost effectiveness of telecare management for pain and depression in patients with cancer: results from a randomized trial☆,☆☆

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ABSTRACT

Objective: Pain and depression are prevalent and treatable symptoms among patients with cancer, yet they are often undetected and undertreated. The Indiana Cancer Pain and Depression (INCPAD) trial demonstrated that telecare management can improve pain and depression outcomes. This article investigates the incremental cost effectiveness of the INCPAD intervention.

Methods: The INCPAD trial was conducted in 16 community-based urban and rural oncology practices in Indiana. Of the 405 participants, 202 were randomized to the intervention group and 203 to the usual-care group. Intervention costs were determined, and effectiveness outcomes were depression-free days and quality-adjusted life years.

Results: The intervention group was associated with a yearly increase of 60.3 depression-free days (S.E.= 15.4; $P<0.01$) and an increase of between 0.033 and 0.066 quality-adjusted life years compared to the usual care group. Total cost of the intervention per patient was US$1189, which included physician, nurse care manager and automated monitoring set-up and maintenance costs. Incremental cost per depression-free day was US $19.72, which yields a range of US$18,018 to US$36,035 per quality-adjusted life year when converted to that metric. When measured directly, the incremental cost per quality-adjusted life year ranged from US$10,826 based on the modified EQ-5D to US$73,286.92 based on the SF-12.

Conclusion: Centralized telecare management, coupled with automated symptom monitoring, appears to be a cost effective intervention for managing pain and depression in cancer patients.

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1. Introduction

Pain and depression are two of the most prevalent and disabling symptoms among patients with cancer yet frequently are undetected and undertreated [1–6]. Telecare interventions have been shown to be effective at managing pain and depression among primary care patients, across a variety of health care settings, from large health systems to rural hospitals [7–9]. Extending telecare to management of pain and depression in patients with cancer is an emerging area of clinical and research interest spurred by a long-standing failure to adequately manage disabling symptoms among cancer populations [1–3,10].

The Indiana Cancer Pain and Depression (INCPAD) trial evaluated the effectiveness of centralized telecare management coupled with automated symptom monitoring for patients with cancer. The INCPAD trial was conducted in 16 community-based geographically dispersed urban and rural oncology practices in Indiana and showed that telecare management improved both cancer-related pain and depression over the 12 months of the trial [11].

In the present paper, we investigate the cost effectiveness of the INCPAD telecare intervention. New contributions made by this paper include mapping of information from outcome assessment questionnaires into depression-free days (DFDs) and quality-adjusted life years (QALYs), accounting for intervention costs and a regression analysis of the effectiveness measures to allow comparisons with other pain and depression management interventions.

2. Methods

2.1. Experimental design and sample

The INCPAD trial design [12] and its effectiveness in reducing pain and depression [21] have been previously described. Patients presenting for oncology clinic visits were screened for depression and pain. Patients

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who screened positive for depression or pain were contacted for a telephone eligibility interview to determine if they had clinically significant depression or pain. Depression had to be at least moderately severe, defined as a Patient Health Questionnaire nine-item depression scale score ≥10 and endorsement of either depressed mood and/or anhedonia. 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 (BPI). Excluded were individuals who did not speak English; had moderately severe cognitive impairment, schizophrenia or other psychosis; had a pending pain-related disability claim; were pregnant; or were in hospice care. Informed consent and Health Insurance Portability and Accountability Act authorization were obtained from eligible patients who desired to participate.

Of the 405 eligible participants who consented to enroll in the study, 202 patients were randomized to the intervention group and 203 to the usual-care group. Randomization was stratified by symptom type: 131 patients had depression only, 96 had pain only and 178 had both depression and pain. Patient mean age was 58.8 years, and 68% were women. The type of cancer was breast (29%), lung (20%), gastrointestinal (17%), lymphoma or hematological (13%), genitourinary (10%) and other (10%). The phase of cancer was newly-diagnosed (37%), disease-free or maintenance therapy (42%) and recurrent or progressive (20%).

2.2. Outcomes

Outcomes were assessed by blinded telephone interviews over 12 months (baseline and at Months 1, 3, 6 and 12, with some of the outcomes assessed less frequently). Depression, pain, mental health and disability outcomes were used to estimate the DFDs and QALYs associated with the intervention.

DFDs during the 12-month follow-up period were calculated from the HSCL-20 scores [13,14]. At each assessment, patients received a portion of a DFD for that day according to the following algorithm: if patients had an HSCL-20 score of 0.50 or less, they were coded as having one DFD; if patients had HSCL-20 score of 2.00 or greater, zero DFDs; and if patients scored between 0.50 and 2.00, they were assigned a DFD value between zero and one by linear interpolation (e.g., a HSCL-20 score of 1.25 was coded as 0.5 DFD). DFDs between assessments (intervals of baseline to Month 1, Month 1 to Month 3, etc.) were calculated by averaging the DFDs between the two assessments and multiplying by the number of days between assessments. DFDs between assessments were summed for all assessment intervals to yield the number of DFDs during the 12 month follow-up.

DFDs were calculated two ways, depending on how the missing follow-up assessments were coded. The first measure excluded patients who had missing follow-up assessments or died during the trial. The second imputed DFDs by: (a) carrying the last observation forward to impute the missing follow-up assessment and (b) including patients who died up to their last assessment prior to death. Patients who died before their Month 1 assessment were excluded from imputation. DFDs represent an estimate of the number of days out of the year a patient is depression free by summarizing the HSCL-20 scores measured at each follow-up period into a single measure. Twelve-month follow-up period yields one measure of DFD for a given patient. Because DFD is not repeatedly measured for a given patient but summative over the 12-months, last observation carried forward (LOCF) was considered preferable to mixed models repeated measures (MMRM) analysis. Moreover, LOCF and MMRM produced similar results for outcomes in the INCPAD trial [11].

QALYs were calculated using four methods. First, QALYs were derived from DFDs [13,15,16]. Previous literature estimated that depression corresponds to a 0.2 to 0.4 decrement in quality-of-life weights, so 1 year of depression would reduce QALYs by the same decrement. The number of DFDs out of the year would correspond to a proportional reduction in QALYs. For example, a reduction of 30 DFDs is equivalent to a 0.016 to 0.033 reduction in QALYs, depending on whether 0.2 or 0.4 was used. Second, patient responses to the SF-12 were used to generate preference-based quality-of-life weights known as the SF-6D [17]. Third, a modified EQ-5D survey was constructed from the responses to a combination of depression, pain, mental health and disability items from various questionnaires and used to generate quality-of-life weights [18] (Appendix 1). Fourth, a visual analog scale on a 0–10 scale was used to measure quality of life during the past month at each assessment. Several methods for calculating QALYs were used because DFDs only applied to the subgroup of 309 depressed patients and because the SF-6D and EQ-5D may produce divergent results [19–25]. Thus, derivation of QALYs from several methods provides a possible range of QALYs and in effect a type of sensitivity analysis. Quality-of-life weights at each assessment were rescaled to 0 to 1, and QALYs were calculated by area under the time curves.

2.3. Costs

Costs were calculated from a payer's perspective. Intervention cost per patient was determined using provider payroll data and capital expenditure associated with the intervention. The nurse care manager time devoted to each study patient was maintained in a detailed log, and physician time spent in weekly care management conferences and staffing outside of these weekly meetings was determined. Using annual salaries including fringe rates of the physician supervisor and nurse care manager combined with the hours they devoted to the study over the course of the INCPAD trial allowed us to calculate physician and nurse costs. Further details regarding cost determinations are provided in Appendix 2.

Capital expenditures for startup and maintenance of the automated symptom monitoring were included as an intervention cost. Automated symptom monitoring costs can be spread over a number of patients hence intervention cost per patient will decrease with increasing number of patients. In addition, after paying these startup costs, subsequent maintenance costs are fairly low. However, the cost of purchasing the automated symptom monitoring may vary depending on the purchasing power of the buyer.

Since INCPAD involved multiple community-based practices across the state of Indiana, it was not possible to obtain prescription or other medical cost data. However, neither patient-reported health care use nor co-interventions differed significantly between the intervention and the usual care group [11].

2.4. Analysis

Incremental intervention costs and effectiveness were calculated separately for (a) all 202 patients in the intervention group, including those who had only pain, only depression or both pain and depression and (b) the subset of 154 patients in the intervention group with depression, including those with only depression and those with both pain and depression. This is because the cost-effectiveness analyses based upon the SF-12 and EQ-5D used the full sample of 405 patients (202 intervention and 203 control), while the analysis based upon DFDs used the 309 patients with depression (154 intervention and 155 control). Physician and nurse time cost was calculated based on administrative data on annual salary plus fringe and hours spent on the intervention during the year (Appendix 2).

The effect of the intervention on each outcome measure (DFDs, SF-12 quality-of-life weights, visual analog scale and modified EQ-5D quality-of-life weights) at each assessment timepoint (Month 1, 3, 6 and 12 for visual analog scale, DFDs and the modified EQ-5D; Months 3 and 12 for the SF-12) was estimated using ordinary least squares (OLS) regression, controlling for baseline value of the outcome measure and standard sociodemographic variables (age, gender, education, race, marital status, employment and income). Because patients were recruited from a large number (i.e., 14) of different clinics which in turn contributed a wide range (9 to 78) of enrolled

patients, parameter estimates were not adjusted for clustering of patients within clinics [26]. Each outcome at a given assessment month was modeled separately in cross-sectional regressions. Coefficients of the intervention dummy variable were used to test for significance of the intervention effect. Since the intervention was centralized and telephone-administered to patients throughout the entire state of Indiana, we did not expect an unobserved hospital or clinic-level effect in these randomized data. Accordingly, those variables were omitted from the regression.

Based on the regression coefficients, average outcomes (DFD, SF-12 quality-of-life weights, modified EQ-5D quality-of-life weights) for the intervention group and the intervention group were predicted holding the covariates at observed values [15,27]. The area under the curve that captured the predicted quality-of-life weights over time was used to calculate QALYs. As mentioned earlier, the analysis for DFD was done with and without imputation. Analyses for SF-12 and EQ-5D were done only without imputation. Quality-of-life weights derived from the visual analog scale were not significantly different between the intervention and usual care group, and therefore, no further cost-effectiveness calculations were performed.

3. Results

3.1. Costs

Table 1 summarizes the costs attributable to the intervention. Total physician time cost to treat all intervention patients was US$43,226, and the resulting physician cost per patient was US$214. Total physician time cost to treat the patients with depression was US $43,226, and the resulting physician cost per patient was US$281.

Total nurse care manager time cost to treat all intervention patients was US$71,224, and the resulting total nurse care manager cost per patient was US$353. Total nurse care manager time cost to treat the patients with depression was US$61,906, and the resulting total nurse care manager cost per patient was US$402.

The cost of the automated monitoring system and its maintenance during the trial was US$78,000. Spread out over all intervention patients, monitoring cost per patient was US$386. Spread out over the patients with depression, monitoring cost per patient was US$506. The sum of the physician, nurse care manager and monitoring cost was US$953 per patient for all intervention patients and US$1189 per patient for the patients with depression.

Projected costs of the intervention for new patients enrolled after the trial should decrease because the automated monitoring system is already set up and only maintenance costs of the system would be required. Post start up, automated monitoring maintenance cost was estimated to be about US$20,000 over the 3 years of the trial, which would reduce the incremental cost per new intervention patient treated to about US$666 and cost per new depressed patient treated to about US$813.

Table 1
Costs of INCPAD intervention for entire trial and 12-month per patient costs*

Intervention component (202 out of 405 total sample)	Total trial costs (US$)	Per patient 12-month costs (US$)
Physician time	43,226	213.99
Nurse care manager time	71,224	352.59
Automated monitoring start-up/maintenance	78,000	386.14
Total	192,450	952.72
Intervention component (154 out of 309 depressed subgroup)	**Total trial costs (US$)**	**Per patient 12-month costs (US$)**
Physician time	43,226	280.69
Nurse care manager time	61,906	401.99
Automated monitoring start-up/maintenance	78,000	506.49
Total	183,132	1189.17

* For details regarding cost calculations, see Appendix 2. First column includes total intervention costs for all patients during the 42 months of the trial. Second column is the per patient cost for the 12 months each patient was in the trial.

3.2. Effectiveness

OLS regression estimated the effect of the intervention on DFDs controlling for baseline characteristics. Table 2 summarizes the incremental cost-effectiveness ratios (ICERs). As previously noted, the regression model for DFD only included the subset of patients who had depression. From the subset of 309 depressed patients, 187 patients had complete follow-up, with 90 in the intervention group and 97 in usual care group. For these patients, predicted average DFD during the 12-month follow-up for the intervention group was 227.38 days and, for the usual care group, was 167.08 days. Thus, the intervention group was associated with an increase of 60.30 DFDs (S.E.= 15.38; $P<0.01$) compared to the usual-care group. Based on the existing estimates of the increase in quality of life of from 0.2 to 0.4 per additional DFD, the intervention was associated with gain of between 0.033 and 0.066 QALYs.

From the subset of 309 depressed patients, 298 patients had either complete or imputed follow-up data on DFDs, with 148 in the intervention group and 150 in usual care group. The intervention group was associated with an increase of 44.12 DFDs (S.E.= 12.86; $P<0.01$) compared to the usual care group. The predicted average DFD during the 12-month follow-up for the intervention group was 185.81 days and for the usual care group was 141.70 days. Based on the existing estimate of the increase in quality of life in DFDs, the intervention was associated with gain of between 0.024 and 0.048 QALYs.

Quality-of-life weights from SF-12 and modified EQ-5D were also modeled using OLS regression. The regression model for quality-of-life weights included all patients. However, patients included in the regression model decreased over time, due to death or nonresponse, and those with missing data were not imputed. For the SF-12, 405 patients were included at baseline but diminished to 267 patients at month 12. For EQ-5D, 362 patients were included at baseline but fell to 211 patients at month 12.

The effect of the intervention on SF-12-based quality-of-life weight was not significant at Month 3 but significant at month 12 with intervention group associated with 0.03 point (S.E.= 0.02; $P<0.05$) higher quality-of-life weight. The gain in SF-12 quality of life based on the area under the weight curve over 12 months was 0.013 QALYs.

The intervention group was associated with significantly higher quality-of-life weights from the modified EQ-5D at Month 1, 3, 6 and 12. Specifically, at Month 1, the weights were 0.06 points (S.E.= 0.02; $P<0.01$) higher; at Month 3, 0.08 points (S.E.= 0.03; $P<0.05$) higher; at Month 6, 0.08 points (S.E.= 0.03; $P<0.05$) higher; at Month 12, 0.14 points (S.E.= 0.04; $P<0.01$) higher. The area under the quality-of-life weight curve showed a gain of 0.088 QALYs.

3.3. Cost effectiveness

The reference case ICERs were calculated including the automated monitoring as a startup cost. For patients with depression who completed the trial without missing follow-ups, incremental cost per DFD gained was US$19.72 per DFD, and US$18,018 to US$36,035 per QALY gained.

For patients with depression who either completed follow-ups or whose follow-up scores were imputed, incremental cost per DFD gained was US$26.95, which corresponds to a cost per QALY gained of between US$24,774 and US$49,549, when evaluated by the range in quality-of-life gains found in the literature. For the modified EQ-5D, the incremental cost for all patients was US$10,826 per QALY gained. Cost per QALY gained from the SF-12 was US$73,286.

As a sensitivity analysis, poststart cost-effectiveness ratios were projected for new patients who might receive the 12-month intervention after the trial. This assumed similar physician and nurse care manager costs in providing care for a similar number of

Table 2
INCPAD incremental cost effectiveness ratios

Effectiveness metric [a]	Δ Cost per patient	Δ Effectiveness	ICER
DFD (Complete follow-ups)	1189.17 (US$)	60.30 (DFD)	19.72 (US$/DFD)
DFD (Complete and imputed follow-ups)	1189.17 (US$)	44.12 (DFD)	26.95 (US$/DFD)
QALY (derived from DFD complete follow-ups)	1189.17 (US$)	.066 QALY to .033 QALY	18,017.73 (US$/QALY) to 36,035.45 (US$/QALY)
QALY (derived from DFD complete and imputed follow-ups)	1189.17 (US$)	.048 QALY to .024 QALY	24,774.38 (US$/QALY) to 49,548.75 (US$/QALY)
QALY from EQ-5D	952.72 (US$)	.088 (QALY)	10,826.48 (US$/QALY)
QALY from SF-12 (SF-6D)	952.72 (US$)	.013 (QALY)	73,286.92 (US$/QALY)

[a] DFD = depression-free days; QALY = quality-adjusted life years.

patients but lower automated monitoring costs due to the fact that the system had already been set up and only maintenance costs would be required (Table 3). For patients with depression who completed the trial without missing follow-ups, poststartup incremental cost per DFD gained was US$13.48, which corresponds to US$12,311 to US $24,623 per QALY gained.

For patients with depression who either completed follow-ups or whose responses were imputed, poststartup incremental cost per DFD gained was US$18.42, which corresponds to US$16,928.13 to US $33,856.25 per QALY gained.

Post start-up incremental cost per QALY gained was US$7,564 for all patients using the modified EQ-5D weights and US$51,199 using the SF-12 quality-of-life weights.

4. Discussion

Centralized telecare management coupled with automated symptom monitoring for cancer patients with pain and depression significantly increased DFDs and associated QALYs compared to usual care. Intervention cost of telecare management was greater than usual care. The range of point estimates for the ICER calculated from various outcome measures was within the range of other disease management interventions and generally below US$50,000 per QALY [13–16,27,28].

Effectiveness of the INCPAD intervention may persist beyond conclusion of the intervention. The Improving Mood: Promoting Access to Collaborative Treatment trial conducted a 12-month collaborative care management program for depressed older primary care patients and found that effectiveness benefits were sustained at 2-year follow-up and the intervention group had lower healthcare costs during the 4-year follow-up period [29,30]. If the improved depression outcomes generated by the INCPAD intervention were to persist beyond the 12-month trial, the ICERs would be even lower.

Regarding DFDs, our study in patients with cancer compares favorably to nine previous studies conducted in primary care populations (Table 4). The latter have shown that a variety of interventions yield annualized gains in DFDs of 25.2 to 58 DFDs (compared to 60.2 DFDs in INCPAD) and a cost per DFD of US$2.76 to US$35.15 (compared to US$19.72 in INCPAD).

The cost effectiveness of telecare management also compares favorably with many other cancer treatments. Some new anticancer drugs have costs per QALY exceeding US$100,000 to US$200,000 [31–33]. Moreover, drivers of increased costs include not only new drugs but also advances in therapeutic radiology, imaging and other treatment [34,35]. In contrast, the estimated cost of the INCPAD intervention ranged from US$7500 to US$75,000 per QALY, with most CEA methods yielding an estimate under US$50,000.

The wide range in ICERs produced by different QALY methods may be due to several factors. Numerous studies have shown that the EQ-5D and SF-12 (SF-6D) — two of the most commonly used measures in cost-effectiveness analyses — can produce substantially divergent ICERs [19–25], depending upon type of disease studied, severity of disease and fundamental differences between the measures (score distributions, floor and ceiling effects, responsiveness to interventions and other factors). Second, we used a modified version of the EQ-5D in INCPAD. Third, the DFD method of calculating QALYs could only be applied to the subgroup of depressed patients, although the latter did constitute 76% (309/405) of our study sample. Because ICERs may vary by type of QALY method, the calculation of QALYS by several methods provides a type of sensitivity analysis for estimating the range in which the true ICER is likely situated.

Our cost-effectiveness analysis has three limitations. First, because the INCPAD trial intervention focused on community-based rural and urban oncology practices (many of which lacked electronic medical records and integrated health care systems), our analysis was limited to intervention costs rather than total health care costs. However, self-reported health care use as well as co-interventions did not differ significantly between intervention and control groups, and indeed, there was a trend for lower rates of hospitalization and emergency department use (two of the more expensive health care use indicators) in the intervention group [11]. Thus, it is unlikely that health care costs were higher in the intervention group. Cost-effectiveness acceptability curves are desirable in CEAs but require patient-level data on both cost and effectiveness. Like many trials facing the additional cost of the large number of additional participants required to power a cost analysis, ours focused on the effectiveness side and provided patient-level results only for measures of DFD and QALYs. Thus, there were neither patient-specific cost observations nor information on the distribution of total costs on which to base a bootstrapping analysis. However, costs included the cost of the intervention alone and not any potential cost savings from less medical care (e.g., fewer hospital days or emergency department visits). Thus, the ICERs we have calculated are most likely conservative, which is desirable when trying to evaluate the cost-effectiveness of a new intervention. Second, our study found significant improvements in only three of the four measures investigated. Third,

Table 3
INCPAD postStartup Projected Incremental Cost Effectiveness Ratios for New Patients Receiving the Intervention*

Effectiveness Metric[a]	Δ Cost per patient	Δ Effectiveness	ICER
DFD (complete follow-ups)	812.55 (US$)	60.30 (DFD)	13.48 (US$/DFD)
DFD (complete and imputed follow-ups)	812.55 (US$)	44.12 (DFD)	18.42 (US$/DFD)
QALY (derived from DFD complete follow-ups)	812.55 (US$)	.066 to .033 (QALY)	12,311.36 (US$/QALY) to 24,622.73 (US$/QALY)
QALY (derived from DFD complete and imputed follow-ups)	812.55 (US$)	.048 to .024 (QALY)	16,622.13 (US$/QALY) to 33,856.25 (US$/QALY)
QALY from EQ-5D	665.59 (US$)	.088 (QALY)	7,563.52 (US$/QALY)
QALY from SF-12 (SF-6D)	665.59 (US$)	.013 (QALY)	51,199.23 (US$/QALY)

* Poststart-up costs are projected to be US$134,450 for 202 new patients receiving the INCPAD intervention and US$125,132 for the subset of 154 new depressed patients receiving the intervention. This is based upon the assumption that physician and nurse care manager times would be the same for treating the same number of new patients for 12 months as in the trial, but that only automated symptom monitoring (ASM) costs would be needed since the ASM system would already be set up.

[a] DFD = depression-free days; QALY = quality-adjusted life years.

Table 4
Incremental per patient costs and effectiveness of depression care interventions compared to usual care

Study [a]	Year	Intervention	Duration (months)	Costs captured [b]			DFDs per patient		Incremental outpatient costs per patient (dollars)		QALY method[c]
				Int	Dir	Ind	In trial	Annualized	Total	Per DFD	
Katon et al [d] [41,42]	1995,1998	Psychiatrist collaborative care	6	✓	✓		15.8	31.6	383	24.24	None
Katon et al [d] [42,43]	1996,1998	Psychologist collaborative care	6	✓	✓		13.4	26.8	471	35.15	None
Schulberg et al [13,44]	1996,1998	Pharmacotherapy or Interpersonal psychotherapy	12	✓	✓	✓	49–58	49–58	-	13.14–17.56	DFD US$11,270–US$19 510
Katzelnick et al [45,46]	2000,2001	Depression care management	12	✓	✓		47.4	47.4	675	14.24	None
Simon et al [d] [47]	2000	Telephone care management	6	✓	✓		12.6	25.2	130	10.32	None
Simon et al [14]	2001	Stepped collaborative care	6	✓	✓		16.7	33.4	242	14.49	None
Schoenbaum et al [15]	2001	Quality improvement	24	✓	✓		36.5	36.5	-	-	DFD, SF12 US$9.478–US $36,467
Katon et al [16]	2005	Collaborative care (late life)	12	✓	✓		52.6	52.6	-	2.76	DFD US$2,519–US$5,037
Rost et al [48]	2005	Depression care management	24	✓	✓	✓	59.4	29.7	470–701	7.91–11.80	DFD US$9,592 to US$14,306
Choi-Yoo et al	2014	Telecare management (cancer)	12	✓			60.3	60.3	1189	19.72	DFD, SF-12, EQ5D, Global QoL US$10,829–US$73,287

[a] All studies except that by Choi-Yoo were conducted in primary care populations. An additional primary care study by Pyne et al. [33] showed no significant incremental effect of the intervention on DFDs.
[b] Int = intervention costs; Dir = other direct health care costs not related to intervention; Ind = indirect costs.
[c] If QALYs calculated in article, the method (metric) used to calculate QALYs. SF-12 = Medical Outcome Study 12-item Short-Form. EQ5D = 5-item EuroQoL. Global QoL = single item overall quality of life.
[d] Some of DFD data and/or cost per DFD not in original article(s) but in the summary table in Simon et al. 2001 article [14].

our study used a novel but untested approach that modeled the items and responses for the EQ-5D from the responses to questions from other survey instruments. That this method translated into quality-of-life weight improvements that were consistent with the improvements found using two of the other effectiveness measures gave us a level of confidence in the validity of this measure.

Although INCPAD focused on depression and pain, telephone-based management has also proven effective for multiple cancer-related symptoms [36,37]. Cancer symptoms frequently cluster so that many patients often have more than one type of symptom [10,38,39]. Thus, providing centralized telecare management for a range of cancer-related symptoms might further enhance its cost-effectiveness. In addition, increasing the number of patients who can have their symptom management optimized at home without the time and travel costs of coming to the clinic makes the care more convenient and less costly from the perspective of the patient. This was reflected by the high patient adherence to and satisfaction with the telecare intervention in the INCPAD trial [40]. Given the high symptom burden associated with cancer in all its stages, the responsiveness of symptoms to a cost-effective telecare management approach makes this a promising avenue for improving quality of life in cancer patients.

Appendix 1. Effectiveness metrics

1.A. Converting DFD to QALY

−0.2 to −0.4 QALY = 1 year of depression

$$X/(DFD/365)\ year\ of\ depression = -0.2\ to -0.4\ QALY/1\ year\ of\ depression$$

Solve for X
Where:

Y = incremental DFD/365

60.30/365=0.1652
44.12/365=0.1209

0.1652 * −0.2=−0.0330 QALY
0.1652*−0.4=−0.0661 QALY

0.1209 * −0.2=−0.0242 QALY
0.1209 * −0.4=−0.0484 QALY

1.B. ICER = ΔCOST/ΔDFD

DFD
DFD ICER = 1249.68/60.30 = 20.72
DFD imputed
DFD imputed ICER = 1249.68/47.25 = 26.45
SF-12
ΔQALY = area between the curves
Area under intervention curve from Month 3 to Month 12 − Area under control curve from month 3 to month 12
ΔQALY = area inside big triangle − area inside small triangle
ΔQALY = (QOL_intervention *0.75year)/2 – (QOL_control*0.75year)/2
(.647 * 0.75)/2 - (.613*0.75)/2 = .013
SF6 ICER = 952.72/.013 = 73286.92
EQ-5D
ΔQALY = area between the curves
ΔQALY = (area under intervention curve from Month 0 to Month 1 – area under control curve from Month 0 to Month 1) + (area under intervention curve from Month 1 to Month 3 – area under control curve from Month 1 to Month 3) + (Area under intervention curve from Month 3 to Month 6 – Area under control curve from Month 3 to Month 6) + (Area under intervention curve from Month 6 to Month 12 – Area under control curve from Month 6 to Month 12)
ΔQALY = (area inside big trapezoid – area inside small trapezoid) + (area inside big trapezoid – area inside small trapezoid) + (area inside big trapezoid – area inside small trapezoid) + (area inside big trapezoid – area inside small trapezoid).

ΔQALY = [(.404+.49) *(1/12)/2 – (.411+.427)*(1/12)/2] + [(.49+.534) *(2/12)/2 – (.427+.458)*(2/12)/2] + [(.534+.558) *(3/12)/2 – (.458+.477)*(3/12)/2] + [(.558+.574) *(6/12)/2 – (.477+.437)*(6/12)/2] = .088

EQ-5D ICER = 952.72/.088 = 10826.48

1.C. Imputed EQ-5D responses

EQ-5D mobility

Two SF-12 items used were limitations in moderate activities and in climbing. "Does your health now limit you in moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf; and in climbing several flights of stairs?" SF-12 response choices were "1. Yes, limited a lot; 2. Yes, limited a little; 3. No, not limited at all."

If the moderate activities response was 2 or 3 and the climbing response was 2 or 3, this was mapped to modified EQ-5D mobility of: 1. "I have no problems in walking about."

If moderate activities response was 1 and climbing response was 2 or 3, this was mapped to modified EQ-5D mobility of: 2. "I have moderate problems in walking about."

If moderate activities response was 2 or 3 and climbing response was 1, then the response was mapped to modified EQ-5D mobility of: 2. "I have moderate problems in walking about."

If moderate activities response was 1 and climbing response was 1, then the response was mapped to modified EQ-5D mobility of: 3. "I am unable to walk about."

EQ-5D Self-care

The response from survey item (bed days) "During the past 4 weeks, how many days did your physical health or emotional problems keep you in bed all or most of the day? Your answer may range from 0 to 28 days." was mapped to EQ-5D self-care response.

If bed days response was 0 to 6 days, this was mapped to modified EQ-5D self-care of:

1. "I have no problems washing or dressing myself."

If bed days response was 7 to 13 days, this was mapped to modified EQ-5D self-care of:

2. "I have moderate problems washing or dressing myself."

If bed days response was 14 to 28 days, this was mapped to modified EQ-5D self-care of:

3. "I am unable to wash or dress myself."

EQ-5D Usual activities

The response from Sheehan Disability Index (SDI) was mapped to EQ-5D usual activities response. The SDI asks to what extent health has interfered with the respondent's work, family life and social life in the past month, each on a scale of 0, *not at all* to 10, *unable to carry on any activities*. Responses were averaged to construct the SDI score.

If SDI score was 0 to 3.49, then the response was mapped to modified EQ-5D.

1. "I have no problems doing my usual activities."

If SDI score was 3.50 to 6.99, then the response was mapped to modified EQ-5D.

2. "I have moderate problems doing my usual activities."

If SDI score was 7.0 to 10, then the response was mapped to modified EQ-5D.

3. "I am unable to do my usual activities."

EQ-5D pain and discomfort

Two BPI items used were average pain in the past week and current pain, each rated on a 0 to 10 scale where 0 is *no pain* and 10 is *pain as bad as you could imagine*. The responses to these two items were averaged to construct the BPI score.

If BPI score was 0 to 3.49, then the response was mapped to modified EQ-5D.

1. "I have no pain or discomfort."

If BPI score was 3.50 to 6.49, then the response was mapped to modified EQ-5D.

2. "I have moderate pain or discomfort."

If BPI score was 6.50 to 10, then the response was mapped to modified EQ-5D.

3. "I have extreme pain or discomfort."

EQ-5D mood (anxiety and depression)

Responses to one Generalized Anxiety Disorder (GAD-7) scale item and four Hopkins Symptom Checklist (SCL-20) depression items were used.

The GAD-7 item used was: "Over the last 2 weeks have you been bothered by feeling nervous, anxious or on edge?" Responses were: 0 (*not at all*), 1 (*several days*), 2 (*more than half the days*) or 3 (*nearly every day*). These were then recoded as 1 (if 0), 2 (if 1 or 2) or 3 (if 3).

The four SCL-20 items used were: "Overall, in the past 4 weeks how much were you distressed by a) feeling lonely or blue… b) feeling no interest in things… c) inability to take pleasure in things… d) feeling hopeless about the future." Responses for each item were 0 (*not at all*), 1 (*a little bit*), 2 (*moderately*), 3 (*quite a bit*) or 4 (*extremely*). The responses to these four items were averaged to construct the SCL-20 depression score, which was then recoded as 1 (if 0 to 0.99), 2 (if 1.0 to 2.49) or 3 (if 2.50 to 4.0).

If both the GAD-7 and the SCL-20 were 1, this was mapped to modified EQ-5D mood of:

1. "I am not anxious or depressed."

If either the GAD-7 or the SCL-20 was 3, this was mapped to a modified EQ-5D mood of:

3. "I am extremely anxious or depressed."

All other GAD-7 and SCL-20 combinations were mapped to a modified EQ-5D mood of:

2. "I am moderately anxious or depressed."

Appendix 2. Detailed INCPAD cost determination

Aggregate actual study costs — 202 intervention patients

Intervention component (202 intervention)	Costs (US$)
Physician time	43,226
Nurse care manager time	71,224
Automated monitoring start-up/maintenance	78,000
Total	192,450

Aggregate actual study costs — 154 depressed patients.

Intervention component (154 depressed)	Costs (US$)
Physician time	43,226
Nurse care manager time	61,906
Automated monitoring start-up/maintenance	78,000
Total	183,132

Aggregate projected poststartup costs — 202 theoretical new intervention patients.*

Intervention component (202 intervention)	Costs (US$)
Physician time	43,226
Nurse care manager time	71,224
Automated monitoring maintenance	20,000
Total	134,450

Aggregate projected poststartup costs — 154 theoretical new depressed patients.*

Intervention component (154 depressed)	Costs (US$)
Physician time	43,226
Nurse care manager time	61,906
Automated monitoring maintenance	20,000
Total	125,132

* Projected poststartup costs would be the costs for all new patients receiving the intervention after the study. Physician and nurse time is estimated to be the same for the same number of patients, but automated monitoring costs are only maintenance since system is already setup.

Physician costs: US$43,226.

- Weekly care management conferences: 456 h
- Staffing outside care management conferences: 590+585 min = 1175 min ~ 20 h
- Training nurse manager: 8 h
- Total hours: 484 h
- Physician hourly costs: US$89.31, calculated as follows:
  - US$214,354 annually with 22% fringe, US$175,700 without fringe
  - Hours per year: 50 per week × 48 weeks = 2400 h
  - Hourly costs: 214,354/2400 = US$89.31
- Total physician costs: 484 × US$89.31 = US$43226.04

Nurse care manager costs: US$71,224 all patients; [US$61,906 depressed only]

- Total time outside of care manager conference: 1401 h
- Total time outside care manager conference (depressed only): 1157 h
- Weekly care management conferences: 456 h
- Training time: 8 h
- Total hours: 1865 h
- Total hours (depressed only): 1621 h
- Nurse hourly costs: US$38.19, calculated as follows:
  - US$73,322 annually with 22% fringe, US$60,100 without fringe
  - Hours per year: 40 per week × 48 weeks × 40 = 1920 h
  - Hourly costs: 73,322/1920 = US$38.19
- Total nurse costs (all patients): 1865 × US$38.19 = US$71,224
- Total nurse costs (depressed only): 1621 × US$38.19 = US$61,906

Automated symptom monitoring costs: US$78,000

- Possibly an overestimate since most of cost (US$50,000) is start-up, and once in place this could continue to provide care for thousands of patients at low maintenance costs. Thus, a sensitivity analysis is to estimate poststart-up incremental costs as well.

Calculating weekly care management conference hours: 456 h

- 336 h → 42 months
  - 30-month enrollment & 12-month follow-up (March 2006 through August 2009)
  - 2 h per week for 12 months (first 4 months and last 8 months of study period) and 3 h per week for 30 months.
  - 48 work weeks/12 month → (48 weeks × 2 h) + (120 weeks × 3 h) = 96 h + 360 h = 456 h

Nurse care manager time outside weekly staffing conference

- All 202 intervention patients = 1401 h
  - [Nurse B: 57,946 min/60 = 965.8 h] + [Nurse S: 26,128 min/60 = 435.5 h]
- 154 depressed patients only = 1157 h
  - [Nurse B: 47,199 min/60 = 786.7 h] + [Nurse S: 22,211 min/60 = 370.2 h]

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