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Citation for published version:

Fallon, M, Walker, J, Rodriguez Carbonell, A, Colvin, L, Murray, G & Sharpe, M 2018, 'Pain management in cancer center inpatients: a cluster randomised trial to evaluate a systematic integrated approach (the Edinburgh Pain Assessment and Management Tool, EPAT (c))' *Journal of Clinical Oncology*, vol 36, no. 13, pp. 1284-1290. DOI: 10.1200/JCO.2017.76.1825

Digital Object Identifier (DOI):

[10.1200/JCO.2017.76.1825](https://doi.org/10.1200/JCO.2017.76.1825)

Link:

[Link to publication record in Edinburgh Research Explorer](#)

Document Version:

Publisher's PDF, also known as Version of record

Published In:

Journal of Clinical Oncology

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Pain Management in Cancer Center Inpatients: A Cluster Randomized Trial to Evaluate a Systematic Integrated Approach—The Edinburgh Pain Assessment and Management Tool

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Published at jco.org on March 15, 2018.

Clinical trial information: NCT00595777.

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0732-183X/18/3699-1/\$20.00

A B S T R A C T

Purpose

Pain is suboptimally managed in patients with cancer. We aimed to compare the effect of a policy of adding a clinician-delivered bedside pain assessment and management tool (Edinburgh Pain Assessment and management Tool [EPAT]) to usual care (UC) versus UC alone on pain outcomes.

Patients and Methods

In a two-arm, parallel group, cluster randomized (1:1) trial, we observed pain outcomes in 19 cancer centers in the United Kingdom and then randomly assigned the centers to either implement EPAT or to continue UC. The primary outcome was change in the percentage of study participants in each center with a clinically significant (≥ 2 point) improvement in worst pain (using the Brief Pain Inventory Short Form) from admission to 3 to 5 days after admission. Secondary outcomes included quality of analgesic prescribing and opioid-related adverse effects.

Results

Ten centers were randomly assigned to EPAT, and nine were assigned to UC. We enrolled 1,921 patients and obtained outcome data from 93% ($n = 1,795$). Participants (mean age, 60 years; 49% women) had a variety of cancer types. For centers randomly assigned to EPAT, the percentage of participants with a clinically significant improvement in worst pain increased from 47.7% to 54.1%, and for those randomly assigned to continue UC, this percentage decreased from 50.6% to 46.4%. The absolute difference was 10.7% (95% CI, 0.2% to 21.1%; $P = .046$) and it increased to 15.4% (95% CI, 5.8% to 25.0%; $P = .004$) when two centers that failed to implement EPAT were excluded. EPAT centers had greater improvements in prescribing practice and in the Brief Pain Inventory Short Form pain subscale score. Other pain and distress outcomes and opioid adverse effects did not differ between EPAT and UC.

Conclusion

A systematic integrated approach improves pain outcomes for inpatients in cancer centers without increasing opioid adverse effects.

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ASSOCIATED CONTENT



See accompanying Editorial
DOI: <https://doi.org/10.1200/JCO.2018.78.2110>



Appendix
DOI: <https://doi.org/10.1200/JCO.2017.76.1825>



Data Supplements
DOI: <https://doi.org/10.1200/JCO.2017.76.1825>

DOI: <https://doi.org/10.1200/JCO.2017.76.1825>

INTRODUCTION

Half of patients with cancer suffer from pain.¹⁻³ Despite the availability of pain management guidelines, poor outcomes are common.⁴⁻¹⁰ Common shortcomings in pain management include unstructured assessment, use of treatment guidelines that lack explicit algorithms and do not address clinicians' concerns about prescribing opioids,

and lack of systematic monitoring of outcomes, including adverse effects.^{11,12}

Admission to a cancer center provides an important opportunity to improve pain outcomes. We developed a simple clinician-administered bedside tool—the Edinburgh Pain Assessment and management Tool (EPAT)—that builds on the concept of pain as the fifth vital sign.¹³⁻¹⁶ EPAT aims to change routine practice by directing a systematic assessment of cancer-related pain, guiding treatment

pain BPI-SF score < 4); the mean changes in BPI-SF scores (worst pain, pain subscale, pain interference subscale, and total score); the mean change in global distress in the past 24 hours using the National Comprehensive Cancer Network thermometer (0 to 10 thermometer, where 0 is no distress and 10 is extreme distress)²¹; the mean change in opioid adverse effects (using the mean of 0 to 10 scales for drowsiness, confusion, disorientation, shadows, vivid dreams, hallucinations, and muscle twitching; a modification of a previously used scale)²²; the percentage of participants receiving good practice prescribing (rated based on the appropriateness of the medication[s] prescribed, along with how they were prescribed, compared with guidelines; Data Supplement); the percentage of participants readmitted to the cancer center with uncontrolled pain within 14 days of discharge; and in EPAT centers, satisfaction with the attention given to pain and the ease of use of EPAT rated on a 0 to 10 scale by patients and nurses, respectively.

Outcome data were collected from participants, medical records, and relevant staff, and as appropriate, by the research nurses. If participants had been discharged from the cancer center before the time of the follow-up assessment, the research nurse collected the outcome data by telephone.

Statistical Analysis

We estimated that two treatment groups of nine cancer centers each, with 100 participants per cancer center (50 recruited in the first phase before random assignment of the cancer center, and 50 recruited in the second phase after random assignment) would give 80% power at the 5% significance level to detect a difference of at least 15% between the trial arms in the primary outcome. The main analysis was conducted (using SAS version 9.2 software; SAS Institute, Cary, NC) at the end of the trial, using an intent-to-treat principle that included all participants who provided usable outcome data.

Because there were, as planned, relatively few clusters (cancer centers) and little variability in the cluster size, we performed the analyses using summary measures.²³ For each analysis, we calculated a single summary measure for each cancer center and compared the UC centers with the EPAT centers using a two-sample *t* test. Hence, the summary statistic for the primary outcome was the difference between the percentage of participants who achieved a clinically significant reduction in pain before random assignment (phase 1) and the percentage who achieved a clinically significant reduction in pain after random assignment (phase 2). For continuous outcome measures, the summary statistic was the difference in the mean score before and after random assignment.

In a prespecified sensitivity analysis, hierarchical patient-level analyses were performed using random-effects models. The results for the primary end point (achieving a reduction of ≥ 2 points in the severity of worst pain reported over the previous 24 hours) and a secondary end point (the magnitude of the reduction in the severity of worst pain reported over the previous 24 hours) are reported. In addition to the main analysis, we performed a post hoc sensitivity analysis of the primary outcome and of good practice prescribing excluding cancer centers that had been randomly assigned to EPAT but were unable to implement it.

RESULTS

The United Kingdom has 40 cancer centers. We selected 20 centers from those eligible to participate, aiming for geographical spread and a range of center sizes. Each center took part in the trial for approximately 1 year (including both pre- and post-random assignment phases). Center participation was staggered and occurred between December 2007 and January 2013. One center dropped out before random assignment. Ten cancer centers were randomly assigned to implement EPAT, and nine were assigned to continue providing UC (Fig 2).

Of the 42,000 patients admitted to the cancer centers during the trial, 8,400 were assessed as having moderate or severe pain

(worst pain in the past 24 hours of ≥ 4 on a 0 to 10 scale), and 1,921 patients were enrolled (985 before center random assignment and 936 after assignment; Data Supplement). The most common reason for excluding patients was that their admission was for planned chemotherapy and too brief to allow completion of the protocol. Only 2.7% of eligible patients (53 of 1,974 patients) declined to participate. Participants had a mean age of 60 years (range, 20 to 90 years), and 49% were female (Table 1). Patients had a variety of cancers, the most common of which were genitourinary (272 of 1,921 patients; 14.2%), GI (260 of 1,921 patients; 13.5%), breast (234 of 1,921 patients; 12%), and lung (220 of 1,921 patients; 11.5%). These characteristics were well balanced between EPAT and UC centers. We obtained outcome data from 93% of participants (1,795 of 1,921 patients). These data included 150 telephone follow-up assessments for patients who had been discharged from hospital (the number of telephone assessments was similar in both trial arms). The mean number of days from admission to the primary outcome assessment was 4 and was similar between trial arms.

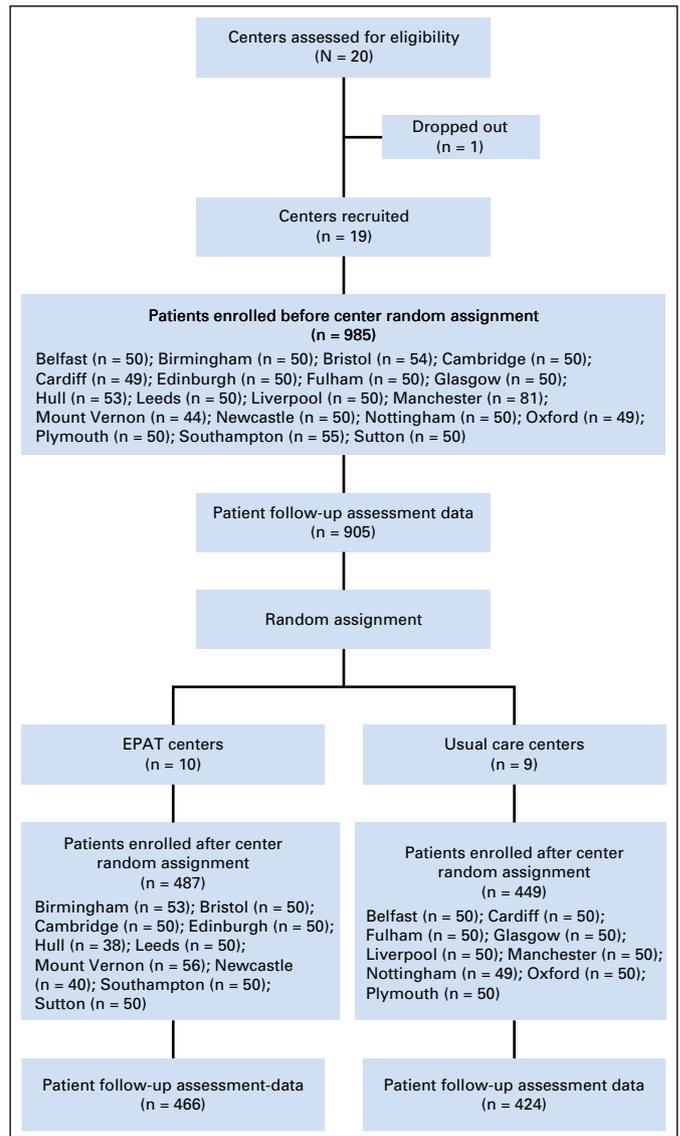


Fig 2. CONSORT diagram. EPAT, Edinburgh Pain Assessment and management Tool.

Table 1. Participant Baseline Characteristics

Characteristic	Centers Randomly Assigned to Implement EPAT		Centers Randomly Assigned to Continue UC		All Participants (N = 1,921)
	Participants Recruited Before Random Assignment (n = 506)	Participants Recruited After Random Assignment (n = 487)	Participants Recruited Before Random Assignment (n = 479)	Participants Recruited After Random Assignment (n = 449)	
Sex					
Female	258 (51.0)	240 (49.3)	229 (47.8)	218 (48.6)	945 (49.2)
Male	248 (49.0)	247 (50.7)	250 (52.2)	231 (51.4)	976 (50.8)
Age, years					
Mean (SD)	60.0 (14.0)	59.4 (13.1)	60.0 (12.8)	59.7 (13.2)	59.8 (13.3)
Range	20-90	20-90	20-88	21-88	20-90
Marital status					
Spouse/partner	340 (67.2)	317 (65.1)	317 (66.2)	304 (67.7)	1,278 (66.5)
No spouse/partner	154 (30.4)	156 (32.0)	153 (31.9)	134 (29.8)	597 (31.1)
Unknown	12 (2.4)	14 (2.9)	9 (1.9)	11 (2.4)	46 (2.4)
Living arrangements					
Living with others	398 (78.7)	371 (76.2)	366 (76.4)	364 (81.0)	1,499 (78.0)
Living alone	108 (21.3)	116 (23.8)	112 (23.4)	85 (18.9)	421 (21.9)
Unknown	0 (0)	0 (0)	1 (0.2)	0 (0)	1 (0.1)
Primary cancer					
Breast	72 (14.2)	64 (13.1)	56 (11.7)	42 (9.4)	234 (12.2)
Genitourinary	64 (12.6)	69 (14.2)	66 (13.8)	73 (16.3)	272 (14.2)
Gynecologic	34 (6.7)	35 (7.2)	35 (7.3)	37 (8.2)	141 (7.3)
GI	74 (14.6)	69 (14.2)	61 (12.7)	56 (12.5)	260 (13.5)
Lung	63 (12.5)	49 (10.1)	60 (12.5)	48 (10.7)	220 (11.5)
Head and neck	35 (6.9)	38 (7.8)	56 (11.7)	45 (10.0)	174 (9.1)
Hematologic	37 (7.3)	41 (8.4)	15 (3.1)	21 (4.7)	114 (5.9)
Other	120 (23.7)	115 (23.6)	116 (24.2)	113 (25.2)	466 (24.3)
Unknown	7 (1.4)	5 (1.0)	14 (2.9)	14 (3.1)	40 (2.1)
Cancer status					
No active disease	9 (1.8)	9 (1.8)	3 (0.6)	10 (2.2)	31 (1.6)
Local disease	107 (21.1)	126 (25.9)	89 (18.6)	92 (20.5)	414 (21.6)
Locally advanced	62 (12.3)	63 (12.9)	59 (12.3)	76 (16.9)	260 (13.5)
Metastatic	327 (64.6)	287 (58.9)	326 (68.1)	270 (60.1)	1,210 (63.0)
Unknown	1 (0.2)	2 (0.4)	2 (0.4)	1 (0.2)	6 (0.3)
Cancer treatment*					
No active treatment	126 (24.9)	119 (24.4)	98 (20.5)	127 (28.3)	470 (24.5)
Chemotherapy	194 (38.3)	161 (33.1)	142 (29.6)	113 (25.2)	610 (31.8)
Radiotherapy	85 (16.8)	75 (15.4)	108 (22.5)	125 (27.8)	393 (20.5)
Hormone therapy	13 (2.6)	9 (1.8)	18 (3.8)	11 (2.4)	51 (2.7)
Other	13 (2.6)	14 (2.9)	15 (3.1)	6 (1.3)	48 (2.5)
Multiple	75 (14.8)	108 (22.2)	97 (20.3)	66 (14.7)	346 (18.0)
Unknown	0 (0)	1 (0.2)	1 (0.2)	1 (0.2)	3 (0.2)
Performance status					
Mean (SD)	2.2 (0.9)	2.2 (1.0)	2.3 (1.0)	2.3 (1.0)	2.2 (1.0)
Range	0-4	0-4	0-4	0-4	0-4
Baseline scores					
Worst pain					
Mean (SD)	7.5 (1.8)	7.8 (1.8)	7.6 (1.8)	7.8 (1.9)	7.7 (1.8)
Range	4-10	4-10	4-10	4-10	4-10
Total BPI-SF score					
Mean (SD)	5.6 (1.8)	5.7 (1.8)	5.5 (1.8)	5.6 (1.9)	5.6 (1.8)
Range	1-10	1-10	1-10	1-10	1-10
Global distress					
Mean (SD)	6.5 (2.9)	6.4 (3.0)	6.6 (3.0)	6.0 (3.2)	6.4 (3.0)
Range	0-10	0-10	0-10	0-10	0-10

NOTE. Data presented as No. (%) unless otherwise indicated

Abbreviations: BPI-SF, Brief Pain Inventory Short Form; EPAT, Edinburgh Pain Assessment and management Tool; GI, gastrointestinal; SD, standard deviation; UC, usual care.

*Current anticancer treatment at the time of trial enrollment.

Introducing EPAT into cancer centers had an effect on pain outcomes. The percentage of participants with a clinically significant improvement in pain increased after random assignment in eight of the 10 EPAT centers and in three of the nine UC centers (Fig 3). In EPAT centers, the mean percentage of participants with a clinically significant improvement in pain increased from 47.7%

(before random assignment) to 54.1% (after random assignment), an absolute increase of 6.4%. In UC centers, the mean percentage of participants with a clinically significant improvement in pain decreased from 50.6% (before random assignment) to 46.4% (after random assignment), an absolute decrease of 4.2%. Thus, the absolute difference between trial arms was 10.7% (95% CI, 0.2% to

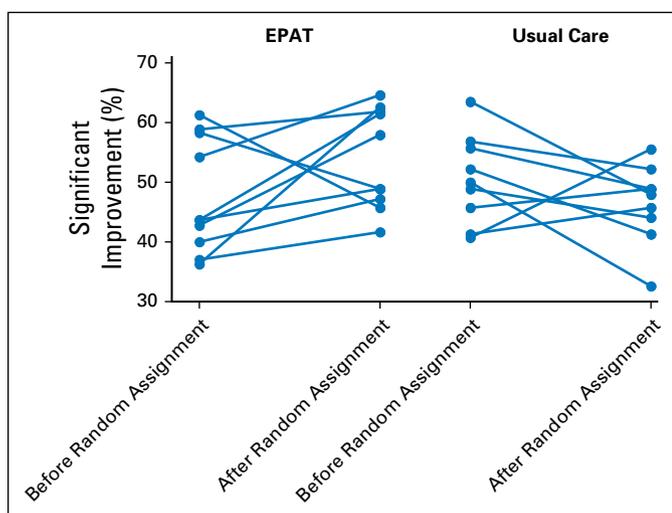


Fig 3. Plot of primary outcome by center. EPAT, Edinburgh Pain Assessment and management Tool.

21.1%; $P = .046$). There was no difference in outcomes between participants assessed by telephone after discharge and those who were assessed as inpatients.

Two of the centers randomly assigned to implement EPAT were unable to do so because of unanticipated organizational changes. In these centers, the percentage of participants with a clinically significant improvement in pain actually decreased after random assignment (Fig 3). A post hoc sensitivity analysis that excluded these two centers found a larger difference between EPAT and UC (absolute difference, 15.4%; 95% CI, 5.8% to 25.0%; $P = .004$). The remaining eight centers that implemented EPAT used it in at least 90% of patient assessments as indicated by entries on the participants' charts.

Regarding the trial's secondary outcomes, EPAT centers had greater improvements in good practice prescribing (a difference that was larger when the two centers unable to implement EPAT were excluded) and greater changes in the mean worst pain item and in mean pain subscale scores. However, there were no statistically significant differences between EPAT and UC centers in the percentage of participants with controlled pain, the mean pain interference score, the mean total pain score, or the mean severity of global distress. There was also no difference between EPAT and UC centers in the percentage of patients who had received strong opioids (80%), in the mean total 24-hour oral morphine equivalent (10 mg), or importantly, in opioid-related adverse effects (Table 2). We were unable to analyze readmissions to hospital because the available data were inadequate. Participants who received EPAT reported (on a 0 to 10 scale) high satisfaction with the attention given to their pain (mean score, 8.6; standard deviation, 1.8), and nurses reported (on a 0 to 10 scale) moderate satisfaction with the ease of using EPAT (mean score, 6.4; standard deviation, 2.5).

From the prespecified patient-level sensitivity analysis of the primary end point, the estimated intraclass correlation coefficient was 0.004, and the estimated treatment effect was 11.6% (95% CI, 2.4% to 20.9%; $P = .014$). For the corresponding analysis of the magnitude of the reduction in the patients' worst pain scores, the estimated intraclass correlation coefficient was 0. The estimated treatment effect was 0.82 (95% CI, 0.31 to 1.32; $P = .002$).

DISCUSSION

The findings of this multicenter, cluster randomized trial indicate that a policy of integrating systematic pain assessment and management into routine cancer center care using a simple tool (EPAT) improves pain outcomes for patients with moderate or severe cancer-related pain. The difference between EPAT and UC centers in the percentage of patients with a clinically significant reduction in their worst pain was 10.7%. This difference increased to 15.4% when the two centers that had been unable to implement EPAT were excluded. It should be noted, however, that the 95% CI for the 10.7% difference is wide (0.2% to 21.1%).

Inspection of the results by cancer center revealed that the difference in the primary outcome between centers delivering EPAT and centers continuing UC reflected not only an improvement in pain management with EPAT (except in the two centers that failed to implement EPAT), but also a deterioration in pain management in most of the centers that continued UC. We did not find any differences in patient or cancer characteristics in the samples studied in each phase that could account for this. Therefore, we suggest that a likely explanation for the deterioration in outcome in some, but not all, of the UC centers in the post-random assignment period reflects a return to pretrial standards of pain management after improvement during the pre-random assignment phase of the trial. This short-term effect on clinicians' behavior might be expected as a result of awareness that their center was participating in a study that monitored their patients' pain scores.²⁴ This effect would also be expected to decline over the many months of study in centers continuing with UC. The effect was not seen in centers implementing EPAT, which overall had better outcomes.

EPAT centers prescribed analgesics more appropriately (as defined in the Data Supplement) and not in higher doses. Although the concept of pain as the fifth vital sign has been criticized as a potential cause of increased opioid-related adverse effects, the use of EPAT did not increase opioid adverse effects.^{25,26} This absence of increased adverse effects despite better pain management may be because EPAT alerts clinicians to monitor adverse effects of pain treatment, as well as efficacy.

EPAT did not improve all of the secondary trial outcomes. The percentage of participants with controlled pain, the severity of general distress, and the degree to which pain interfered with activities did not differ between trial arms. The short duration of this study and inpatient setting arguably made it difficult to change these outcomes.

An additional and notable finding is that implementation of EPAT was hampered by organizational and leadership changes in two trial centers, which also subsequently had worse patient outcomes. This observation highlights the importance of organizational factors and leadership, as well as clinician education, in achieving positive changes in patient care.²⁷ As expected, the patient-level sensitivity analyses yielded parameter estimates and CIs that were broadly similar to those obtained in the primary cluster-level analyses and with levels of statistical significance that were more extreme.

Previously published smaller studies have evaluated the effects of systematic management for cancer pain. Two randomized trials compared algorithm-based pain management by pain specialists, rather than oncology teams, with variable

Table 2. Trial Outcomes

Outcome	Centers Randomly Assigned to EPAT (n = 10)			Centers Randomly Assigned to Continue Usual Care (n = 9)			Difference Between Trial Arms (95% CI)	P
	Before Random Assignment (n = 464)	After Random Assignment (n = 466)	Difference Between Before and After Random Assignment	Before Random Assignment (n = 441)	After Random Assignment (n = 424)	Difference Between Before and After Random Assignment		
Primary outcome								
Patients with clinically significant improvement in pain, mean %	47.7	54.1	6.4	50.6	46.4	-4.2	10.7 (0.2 to 21.1)	.046
Secondary outcomes								
Patients with controlled pain, %	20.9	20.0	-1.0	25.6	18.3	-7.3	6.3 (-0.7 to 13.3)	.074
Mean change in worst pain score (SD)	-1.62 (0.43)	-2.00 (0.35)	0.38 (0.53)	-2.00 (0.40)	-1.62 (0.40)	-0.37 (0.61)	0.75 (0.20 to 1.30)	.011
Mean change in BPI-SF pain subscale score (SD)	-0.93 (0.27)	-1.25 (0.24)	0.32 (0.47)	-1.05 (0.36)	-0.81 (0.37)	-0.25 (0.48)	0.57 (0.10 to 1.03)	.019
Mean change in BPI-SF interference subscale (SD)*	-1.91 (0.45)	-2.10 (0.55)	0.19 (0.61)	21.73 (0.34)	-1.64 (0.56)	-0.09 (0.80)	0.29 (-0.40 to 0.97)	.391
Mean change in total BPI-SF score (SD)	-1.58 (0.35)	-1.78 (0.38)	0.20 (0.56)	-1.46 (0.23)	-1.27 (0.25)	-0.20 (0.41)	0.40 (-0.09 to 0.88)	.101
Mean change in global distress score (SD)	-1.80 (0.52)	-1.98 (0.60)	0.17 (0.90)	-1.92 (0.56)	-1.68 (0.84)	-0.24 (1.06)	0.41 (-0.54 to 1.36)	.372
Mean opioid toxicity score (SD)	1.45 (0.32)	1.32 (0.26)	0.13 (0.45)	1.41 (0.40)	1.28 (0.24)	0.13 (0.43)	0.00 (-0.42 to 0.43)	.993
Patients who received good practice prescribing, %	46.8	54.8	8.0	50.8	46.5	-4.3	12.2 (1.4 to 23.1)	.030
Sensitivity analysis excluding two EPAT centers								
Patients with clinically significant improvement in pain, %†	44.6	55.8	11.2	50.6	46.4	-4.2	15.4 (5.8 to 25.0)	.004
Patients who received good practice prescribing, %†	45.8	55.4	9.6	50.8	46.5	-4.3	13.9 (4.1 to 23.6)	.008

NOTE. Each analysis is based on a single summary statistic per center. Outcomes at 3 to 5 days after admission to the cancer center. Abbreviations: BPI-SF, Brief Pain Inventory Short Form; EPAT, Edinburgh Pain Assessment and management Tool; SD, standard deviation. *Subscale is as follows: worst, average, least, and pain now combined. †Analysis excluding two centers unable to implement EPAT.

results.^{28,29} Two preliminary studies evaluated the integration of systematic pain management into the usual clinical care delivered by oncology teams with more promising findings.^{30,31} Finally, it is notable that published studies of integrated and systematic approaches to the management of other symptoms in patients with cancer, in particular depression, have also found these to be effective.³²⁻³⁴

The strengths of this trial include the participation of many cancer centers in the United Kingdom and negligible missing outcome data. However, the trial has limitations. First, the trial was carried out within one particular health care system (the United Kingdom National Health Service), although the issues associated with cancer pain assessment and management are similar in most developed countries. Second, we do not have information on participants' longer term outcomes. Third, oncology teams and those collecting the outcome data from patients could not be masked to the treatment allocation.

In conclusion, this study is, to our knowledge, the first large randomized evaluation of the integration of systematic pain assessment and management into routine care of patients with cancer. The implementation of EPAT improved both prescribing practice and pain outcomes. Furthermore, it did not increase opioid-related adverse effects. This latter finding is important given concerns that the measurement of pain as a vital sign and linked opioid prescribing can be harmful.^{14,15} The findings of this trial add to the accumulating evidence for the efficacy of more integrated and systematic approaches to symptom management in patients with cancer.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at jco.org.

AUTHOR CONTRIBUTIONS

Conception and design: Marie Fallon, Lesley Colvin, Gordon Murray, Michael Sharpe

Collection and assembly of data: Marie Fallon, Gordon Murray

Data analysis and interpretation: All authors

Manuscript writing: All authors

Final approval of manuscript: All authors

Accountable for all aspects of the work: All authors

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Support

Supported by Cancer Research UK Grant No. C17958/A6823. J.W. is supported by Sir Michael Sobell House Hospice, Oxford, and the National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care Oxford at Oxford Health NHS Foundation Trust. M.S. is supported by the NIHR Senior Investigator program. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Pain Management in Cancer Center Inpatients: A Cluster Randomized Trial to Evaluate a Systematic Integrated Approach—The Edinburgh Pain Assessment and Management Tool

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/jco/site/ifc.

Marie Fallon

Research Funding: Pfizer (Inst)

Jane Walker

No relationship to disclose

Lesley Colvin

No relationship to disclose

Aryelly Rodriguez

No relationship to disclose

Gordon Murray

No relationship to disclose

Michael Sharpe

No relationship to disclose

Acknowledgment

We thank the trial participants, their families and caregivers, and the staff of the participating cancer centers.

Appendix

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†Deceased September 2015.