Routine screening for pain combined with a pain treatment protocol in head and neck cancer: a randomised controlled trial

J.E. Williams¹,*, J. Peacock²,3, A.N. Gubbay¹, P. Y. Kuo¹, R. Ellard¹, R. Gupta¹, J. Riley⁴, O. Sauzet⁵, J. Raftery⁶, G. Yao⁷ and J. Ross⁴,8

¹Department of Anaesthetics and Pain Management, Royal Marsden NHS Foundation Trust, London, UK, ²Division of Health and Social Care Research, King’s College, London, UK, ³NIHR Biomedical Research Centre at Guy’s and St Thomas’ NHS Foundation Trust, and King’s College, London, UK, ⁴Department of Palliative Medicine, Royal Marsden NHS Foundation Trust, London, UK, ⁵AG Epidemiologie & International Public Health, Universität Bielefeld, Bielefeld, Germany, ⁶Dept. of Health Economics, ⁷Department of Primary Care and Population Science, University of Southampton, UK, and ⁸National Heart and Lung Institute, Imperial College, London, UK

*Corresponding author. E-mail: john.williams@rmh.nhs.uk

Abstract

Background: We compared the effectiveness and cost of a pain screening and treatment program, with usual care in head and neck cancer patients with significant pain.

Methods: Patients were screened for the presence of pain and then randomly assigned to either an intervention group, consisting of a pain treatment protocol and an education program, or to usual care. Primary outcome was change in the Pain Severity Index (PSI) over three months.

Results: We screened 1074 patients of whom 156 were randomized to either intervention or usual care. Mean PSI was reduced over three months in both groups, with no significant difference between the two groups. The Pain Management Index (PMI) at three months, was significantly improved in the intervention group compared with usual care (P<0.001), as was Patient Satisfaction (mean difference in scores was statistically significant: −0.30 [−0.60 to −0.15]). All subjects reported clinically significant levels of anxiety and depression throughout the study. Treatment costs were significantly higher for intervention (mean=£400) compared with usual care (£200), with a low likelihood of being cost-effective.

Conclusions: There was no difference in the Pain Severity Index between the two groups. However there were significant improvements in the intervention group in patient satisfaction and PMI. The pain screening process itself was effective. Sufficient benefit was demonstrated as a result of the intervention to allow continued development of pain treatment pathways, rather than allowing pain treatment to be left to nonformalised ad hoc arrangements.

Key words: cancer; pain; screening
Editor’s key points

- Patients with head and neck cancer have a high level of pain that might be undertreated.
- The efficacy and cost-effectiveness of a combined pain screening, treatment and educational approach was compared prospectively to usual care over three months.
- Pain severity index was reduced in both groups, but pain management index and patient satisfaction were improved by the intervention.
- A formal pain screening process can be effective, but has a low likelihood of cost-effectiveness.

The adequacy of pain control in cancer patients is a subject of much debate amongst pain specialists. The overriding concern is that management of cancer pain has not improved since publication of World Health Organisation guidelines in 1986. Fisch and colleagues’ reported that one third of oncology outpatients receive inadequate pain treatment and that this proportion has not changed since publication of a similar study 20 years ago. Similarly, systematic reviews have reported pain and inadequately treated pain in over 50% of patients with cancer. There is a mismatch or ‘quality gap’ between the prevalence of pain reported in clinical observational studies (>50% patients in pain), and the reported effectiveness of cancer pain treatment when managed according to WHO guidelines, which should be effective in 70-90% of patients. In particular, previous studies have shown a high level of pain in patients with head and neck cancer. We had previously identified the problem of cancer pain in head and neck cancer patients, and therefore decided to determine whether there were any measures that we could implement in this patient population.

Numerous recommendations have been made by national and international bodies to overcome the problem of pain in cancer patients. They include screening for pain and use of analgesic treatment pathways integrated into routine oncological care. Widespread screening for pain isolation has not been as beneficial as was anticipated, and clinicians have recommended that screening needs to be combined with a pain treatment protocol.

Similarly, two randomized controlled trials have shown some benefit of pain treatment protocols, but have concluded that for best effect they need to be combined with routine screening for pain.

Our ‘usual care’ treatment is based on the Royal Marsden Hospital Pain and Palliative Care treatment guidelines. A previous study in patients with head and neck cancer showed a prevalence of ‘moderate-severe’ pain of 34% in patients treated with usual care guidelines. The purpose of this study was to determine whether we could improve pain scores by introducing a combined screening, treatment and educational approach (intervention group) to patients with head and neck cancer pain. Our aim was to compare the effectiveness and cost of the intervention with usual care. Our primary outcome measure was the difference in Pain Severity Index at three months between the usual care and intervention group.

Methods

We conducted a randomized controlled trial between February 2011 and January 2013 in the head and neck outpatient oncology clinics at the Royal Marsden Hospital, London. Ethics Committee Approval was granted.

Study subjects were patients attending the routine head and neck oncology outpatient clinics. The clinics were a mix of oncological clinics (four per week) and surgical clinics (two per week). All patients were more than 18 years old and had a diagnosis of head and neck cancer. All patients were informed about the study and gave written consent. All patients were under the care of a clinical oncologist.

The study comprised an initial pain screening process to identify patients with moderate-severe pain, and then randomization to either an intervention or usual care group. Eligible patients were able to comprehend English and were not already seeing a pain specialist. We systematically attended one head and neck oncology clinic each week until we had recruited 156 subjects.

Patients were screened using the single pain question, ‘Please rate your pain by circling the one number that best describes your pain at its worst in the last seven days’, which was answered using a 0–10 numerical rating scale. Patients scoring 4/10 or more were randomized to intervention or control, stratified by cancer treatment status. Randomization was conducted by the Institute of Cancer Research Randomization Service, accessed by the research nurse calling a centralized phone number. The randomization was performed in blocks to give balance in numbers but disguise the sequence, to prevent the recruiting clinician from guessing the next allocation. To ensure a balanced allocation, patients who were either still receiving anticancer treatments or who had completed such treatments were stratified by two subgroups: stratification group 1, patients still undergoing anticancer treatments such as radiotherapy and chemotherapy, and stratification group 2, patients who had completed anticancer treatments. The research nurse notified the patient of group allocation when the baseline assessment had been completed. The oncologists/surgeons were neither informed nor formally blinded to patient assignment.

Baseline assessment

Patient characteristics and clinical characteristics were measured at study entry by the study pain physician. Health-related variables included: cancer diagnosis, tumour status, anti-tumour therapy, pathophysiology and aetiology of pain, and presence of neuropathic pain using the Leeds assessment of neuropathic symptoms and signs scale (S-LANSS self-complete). Formal pain and other symptom assessments (primary and secondary outcome measures) took place at baseline, 1 month, 2 months and 3 months.

It was not possible to ‘blind’ patients or clinicians to group assignment because of the nature of the interventions. However, there was a clear distinction between the research team (nurse and doctor) who performed the assessments and the clinical team (pain control therapy team consisting of doctors and nurses) who delivered pain management to both intervention and control group as per protocol.

Description of the intervention

Pain assessment and treatment was conducted by two pain clinic doctors and two nurses who were independent of the research team. Treatment took place immediately after allocation to the intervention group, and continued throughout the three month study period. Treatment was individualized according to analgesic needs and requirements according to the Royal Marsden Hospital Palliative Care & Pain Control guidelines, which are based on the WHO and British Pain Society guidelines. The initial consultation took on average 35 min. Further follow-up sessions took place weekly either by telephone or in a pain clinic...
consultation, and lasted on average 15 min. All consultations were recorded using a template in the electronic medical patient record. Patients in this group received the following:

- Initial pain assessment (history and examination) of pain severity, aetiology (nociceptive/neuropathic), presence of breakthrough pain, assessment of associated problems (physical, anxiety, depression).
- Formulation of an individual Pain Treatment Plan using the guidelines tailored to individual requirements.
- Treatment of pain and associated symptoms such as nausea and constipation.
- Reassessment according to individual assessment of the patient for analgesic response and side-effects performed on a weekly basis for three months by telephone (or in person) by the pain specialist doctor.
- Referral to palliative care, physiotherapy, psychological medicine as required.
- Coordinated care. Routine contact with oncologist or clinical nurse specialist for head and neck cancer and primary care doctor or nurse.

Each subject was also given an educational brochure about cancer pain and its treatment. A pain control doctor discussed the brochure with each subject at the baseline time point of the study. This brochure contained information on the cause of pain and potential treatment modalities including medication, physical, psychological, alternative therapy and palliative care. Subjects were asked proactively about their suitability for these additional pain control treatments. Different analgesics drugs and their expected benefit and side-effects were discussed.

Description of the usual care group

Subjects were allowed to use all oncology and support services without restrictions including referral to the pain control team, but were not proactively scheduled to meet with the pain team, unless a meeting was specifically requested by either the subject or their oncologist.

Difference between intervention and control group

Subjects in the usual care group were not proactively assessed at baseline, nor did they receive a timetabled weekly pain assessment conducted by the pain physician. The usual care group also did not receive the pain education brochure.

Statistics

The primary outcome measure was the difference in Pain Severity Index CPST, average of the four BPI pain scales, over three months. The PSI has previously been used in other chronic pain studies and provides a comprehensive assessment of pain as it is based on all four BPI subscales, rather than just ‘average’ pain.

Secondary outcome measures were: brief Pain Inventory (BPI), Pain Management Index, (PMI), EQ-5D, Health State Thermometer, Patient Satisfaction, Hospital Anxiety and Depression Scale.

Costs included: resource use such as analgesic drug costs, pain clinic visits, use of physiotherapy, psychological and other resources.

Sample size of 70 subjects per group enables a mean difference of 1.0 on the PSI to be detected assuming a common SD of 1.8. Power was set at 90% with two-sided significance level 5%. This size of difference is considered to be clinically important.

The primary analysis compared mean PSI in the two groups using a random intercept mixed model to control for repeated measures and allow subjects to be included in the analysis, as long as they had baseline and at least one follow-up assessment. Stratification group was included as a covariate in the model together with randomized group. Control for baseline values was derived from the residual change method. The PMI at 3 months was compared using a t-test.

Statistical analyses were conducted using Stata 11 (StataCorp. 2009. Stata Statistical Software: Release 11. College Station, TX, USA).

Results

A total of 2212 out-patient appointments were scheduled over the 23 months of the study. This represented 1074 individual patients, as some patients attended more than once. Of the 1074 patients, 505 (47%) gave their consent and were screened. Of these, 156 (31%) scored 4/10 or more, and were randomized to intervention or usual care. Please see Consort Flow Chart, Fig. 1. Table 1 outlines the Baseline Characteristics of both groups.

Primary outcome

There was no significant difference in PSI between the groups over the three month study period (Fig. 2). The difference in mean PSI (usual care-intervention) was 0.36 with 95% CI, −0.29 to 1.01. There were no significant differences between the two groups for any of the four sub-components of the BPI.

Changes in adequacy of analgesic treatment

There was a significantly improved ‘adequacy of the analgesic prescription’ as measured using the PMI at three months in the intervention group compared with usual care (adequate analgesia score increasing from 49% to 85% in the intervention group compared with 45–58% for usual care, P<0.001). These improved PMI scores were associated with an increase in mean daily morphine equivalent dosages in both groups, by 37 mg day−1 for intervention and by 20 mg day−1 for usual care. Percentages of subjects prescribed adjuvant analgesic medications were similar in both groups.

Quality of life

Mean EQ-SD scores did not change during the course of the study (difference [95% CI] 0.015[−0.83 to 0.113]), and there were no significant differences between groups in any of the analgesic subset categories. Impact of health related issues on lifestyle (health state thermometer) showed improved scores in both groups but was not statistically significant (2.15 [−3.21 to 7.52]).

All subjects in both groups scored positive for clinically significant levels of anxiety and depression at all times throughout the study with no significant differences between groups (anxiety: −0.1 [−0.8 to 0.7], depression: −0.0 [−0.5 to 0.4]. Patient satisfaction (satisfied/very satisfied) improved from 54% to 80% in the intervention group, compared with 60% rising to 61% in the usual care group. Mean differences in scores was statistically significant: (−0.30 [−0.60 to −0.15]).

Cost-effectiveness

The mean cost of pain treatment (drugs and staff costs) over three months was significantly higher in the intervention group at £430 (£460) per subject, compared with £230 (£450) in the usual care group, a statistically significant difference of £200 (26 to 380). EQSD scores were multiplied by population weights to generate quality adjusted life days (QALD’s). The mean QALD per
subject for intervention and usual care was 49 in both groups. A Scatter Plot of results is in Supplementary Appendix 3.

The Cost Effectiveness Acceptability Curve (CEAC, Fig. 3) shows a low probability of the intervention being cost-effective at levels of willingness to pay below around £2000 but rising to between 0.5 and 0.6 for levels above that.

**Discussion**

This study showed that it was possible to systematically identify patients with moderate-severe pain in a busy oncology outpatient centre. However, once these patients had been identified, we were not able to show a significant benefit of intervention over usual care in the primary outcome measure. Despite this, there was some indication of superiority of the intervention, with significantly improved adequacy of pain treatment compared with usual care, as measured by the pain management index (PMI). This also provided an indication that the pain protocol was adhered to by the subjects in the intervention group. In addition, the level of patient satisfaction was significantly higher in the intervention group compared with usual care.
The prevalence of pain was universally high, with 31% of subjects reporting moderate-severe pain at baseline, and 55% with ‘inadequate’ pain prescribing. These prevalence rates are consistent with other published reports of moderate-severe pain in 31–45% of cancer patients, and ‘inadequate’ pain prescribing in 43%. These figures alone justify the conduct of further trials in this population, in an attempt to determine effective management strategies.

Previous studies have shown the benefit of stand-alone measures in the management of cancer pain such as education, screening, and pathway development. However, our study shows that it is difficult to demonstrate a clinically meaningful benefit of these interventions when formally assessed in a research project. There are a number of possible reasons why we were not able to demonstrate a benefit of intervention over usual care. In practice, effective treatment is dependent on a number of additional influences such as institutional factors (e.g., the relative ease of making pain clinic appointments, availability of staff), individual patient related factors (e.g., co-morbidities, patient focus on anti-cancer treatments etc.), and staff factors (e.g., development of analgesic educational strategies amongst the oncological and surgical teams), which may not have been fully addressed in our study.

Treatment of other symptoms might also be important in making a difference to pain scores. Our study showed that all subjects recorded significant levels of anxiety and depression; and it may be that focusing mainly on analgesic treatments might not be enough to yield a measurable effect of the intervention. For example, Temel and colleagues showed benefit of early palliative care, where there was an emphasis on treatment of all symptoms, not just pain.

In our study, pain scores were significantly reduced in both groups, and it is possible that usual care subjects benefited from being managed at close quarters to the intervention.

The prevalence of pain was universally high, with 31% of subjects reporting moderate-severe pain at baseline, and 55% with ‘inadequate’ pain prescribing. These prevalence rates are consistent with other published reports of moderate-severe pain in 31–45% of cancer patients, and ‘inadequate’ pain prescribing in 43%. These figures alone justify the conduct of further trials in this population, in an attempt to determine effective management strategies.

Previous studies have shown the benefit of stand-alone measures in the management of cancer pain such as education, screening, and pathway development. However, our study shows that it is difficult to demonstrate a clinically meaningful benefit of these interventions when formally assessed in a research project. There are a number of possible reasons why we were not able to demonstrate a benefit of intervention over usual care. In practice, effective treatment is dependent on a number of additional influences such as institutional factors (e.g., the relative ease of making pain clinic appointments, availability of staff), individual patient related factors (e.g., co-morbidities, patient focus on anti-cancer treatments etc.), and staff factors (e.g., development of analgesic educational strategies amongst the oncological and surgical teams), which may not have been fully addressed in our study.

Treatment of other symptoms might also be important in making a difference to pain scores. Our study showed that all subjects, recorded significant levels of anxiety and depression; and it may be that focusing mainly on analgesic treatments might not be enough to yield a measurable effect of the intervention. For example, Temel and colleagues showed benefit of early palliative care, where there was an emphasis on treatment of all symptoms, not just pain.

In our study, pain scores were significantly reduced in both groups, and it is possible that usual care subjects benefited from being managed at close quarters to the intervention.

<table>
<thead>
<tr>
<th>Table 1 Baseline characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention n=75</td>
</tr>
<tr>
<td>Female: (%)</td>
</tr>
<tr>
<td>Age: mean (range)</td>
</tr>
<tr>
<td>Type of outpatient clinic</td>
</tr>
<tr>
<td>Oncology</td>
</tr>
<tr>
<td>Radiotherapy</td>
</tr>
<tr>
<td>Thyroid</td>
</tr>
<tr>
<td>Surgical</td>
</tr>
<tr>
<td>Type of head and neck cancer</td>
</tr>
<tr>
<td>Larynx/Pharynx</td>
</tr>
<tr>
<td>Tongue</td>
</tr>
<tr>
<td>Tonsil</td>
</tr>
<tr>
<td>Neck</td>
</tr>
<tr>
<td>Maxilla</td>
</tr>
<tr>
<td>Other head and neck cancer</td>
</tr>
<tr>
<td>Cause of worst pain</td>
</tr>
<tr>
<td>Tumour related</td>
</tr>
<tr>
<td>Post surgery</td>
</tr>
<tr>
<td>Post chemotherapy</td>
</tr>
<tr>
<td>Post radiotherapy</td>
</tr>
<tr>
<td>Oral mucositis</td>
</tr>
<tr>
<td>Non-cancer pain</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td>Pathophysiology of worst pain</td>
</tr>
<tr>
<td>Neuropathic</td>
</tr>
<tr>
<td>Nociceptive</td>
</tr>
<tr>
<td>Mixed</td>
</tr>
<tr>
<td>Baseline characteristics for outcome measures</td>
</tr>
<tr>
<td>Pain and other symptom scores</td>
</tr>
<tr>
<td>Pain Severity Index</td>
</tr>
<tr>
<td>Neuropathic pain (S-LANSS)</td>
</tr>
<tr>
<td>Pain Management Index</td>
</tr>
<tr>
<td>% inadequate analgesia</td>
</tr>
<tr>
<td>Quality of Life score, EQ5D [mean (SD) range]</td>
</tr>
<tr>
<td>Anxiety score,[mean (SD) range]</td>
</tr>
<tr>
<td>Depression score</td>
</tr>
<tr>
<td>Analgesic use</td>
</tr>
<tr>
<td>Paracetamol + NSAID</td>
</tr>
<tr>
<td>Weak opioids (e.g. tramadol, co-codamol)</td>
</tr>
<tr>
<td>Strong opioids (e.g. morphine, oxycodone, fentanyl)</td>
</tr>
<tr>
<td>Antineuropathic drugs (e.g. amitriptyline, gabapentin, pregabalin)</td>
</tr>
<tr>
<td>Lidocaine patch</td>
</tr>
<tr>
<td>Morphine mean equivalent daily dosage at baseline(range)</td>
</tr>
</tbody>
</table>
group, thereby deriving benefit from the increased exposure to the study interventions. Also both groups could have received a sufficiently high standard of care, and that this high standard of ‘usual care,’ when linked to an effective pain screening process, was enough to reduce pain scores, without the need for more intensive pain control measures. We also excluded patients who were already seeing pain/palliative care teams, and it is possible that we excluded the very group that could have most benefited from the intervention. Furthermore, we did not formally assess the impact of the patient education component of the intervention. It is possible that the educational intervention was not effective in improving overall levels of pain care. It might have been useful to formally assess the impact of this intervention using an assessment tool such as the Ferrell pain questionnaire as used in other similar trials.

We identified five other studies\textsuperscript{14 18 19 26 27} that performed similar evaluations in a cancer pain population. Only two of the five previous studies\textsuperscript{14 18} showed a significant benefit of

![Fig 2 Change in Pain Severity Index.](image)

![Fig 3 Cost-effectiveness acceptability curve.](image)
intervention over control, which could be a result of the use of a much tighter algorithm and a more intensive pain treatment approach.

Our study differed from all of the other studies in two main ways:

(i) **Recruitment into the study was via a screening process**, rather than as a result of a referral to the pain control team. The intention was that the screening process itself would be easy to perform, could be incorporated into routine oncological care, would trigger pain treatment for patients at any point in their cancer treatment trajectory, and could be performed relatively inexpensively. We considered that the screening process was successful in that one person (pain research nurse) was able to screen nearly all patients at each outpatient clinic being studied. In addition the screening process was well received by patients and staff and easily incorporated into routine oncological practice.

(ii) **We formally assessed cost-effectiveness**, and demonstrated that treating a patient in the intervention group was twice the cost of usual care. It was unlikely that this additional cost would produce an improved quality of life at usual levels of cost acceptability.

In conclusion, we were not able to demonstrate an additional benefit of the intervention over usual care using our primary outcome measure, partly because both groups experienced substantial improvements in pain scores. We demonstrated significant improvements in adequacy of pain management and patient satisfaction in the intervention group compared with usual care, but these improvements came at a substantially increased cost, that was unlikely to be cost-effective. The pain screening process itself was easily implemented and could be combined with good ‘usual care’ to provide an effective and cost-effective treatment strategy for patients with cancer pain. Despite our inability to show superiority of our intervention in all outcome measures, we consider that enough positive patient benefit was demonstrated as a result of the intervention to allow continued development of pain treatment pathways, rather than allowing pain treatment to be left to non-formalized ad hoc arrangements.

**Authors’ contributions**


Data analysis: J.P., R.E., O.S., J.Raftery, G.Y.


Revising paper: all authors

**Supplementary material**

Supplementary material is available at British Journal of Anaesthesia online.

**Declaration of interest**

None declared.

**Funding**

This study was funded by the UK National Institute for Health Research (NIHR), Research for Patient Benefit Programme (RfPB), Grant number PB-PG-0808-16260. JLP was additionally supported by the NIHR Biomedical Research Centre based at Guy’s and St Thomas’ NHS Foundation Trust and King’s College London. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

**References**

11. IASP/EFIC. Unrelieved pain is a major global healthcare problem. [http://www.efic.org/eap.htm](http://www.efic.org/eap.htm)


24. Twisk JWR, de Vente W. The analysis of randomised controlled trial data with more than one follow-up measurement. A Comparison Between Different Approaches. European J of Epidemiology 2008; 23: 655–60


Handling editor: H. C. Hemmings