A clinical decision and economic analysis model of cancer pain management
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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Three different strategies of cancer pain management were investigated. These were guideline-based care (GBC), oncology-based care (OBC) and usual care (UC). In the GBC strategy, the authors assumed that clinicians recognised, assessed and treated cancer pain in a manner consistent with the 1994 US Agency for Health Care Policy and Research.

Type of intervention
Palliative care.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of 100,000 American patients with the age, gender and racial distribution of the US population, based on the May 1999 US census estimate.

Setting
The setting was secondary care. The economic study was carried out in Duke University Medical Centre, Durham, USA.

Dates to which data relate
The studies used to derive effectiveness dated from 1982 to 1999. The dates to which the prices related were not explicitly reported, but year 2000 prices appear to have been used.

Source of effectiveness data
The effectiveness and resource data were obtained from a review and synthesis of published studies, and from expert opinion and authors' assumptions.

Modelling
A decision analytic model was constructed in two parts. The first part facilitated estimates of cancer pain prevalence. The second part evaluated the impact of cancer pain and its management in a health care population. The results were modelled over a one-month period with a steady state assumption. The complete spreadsheet for the model can be found on the Duke Center's website http://diseasemodels.duhs.duke.edu

Outcomes assessed in the review
The outcomes assessed in the review were:
the prevalence of cancer;
the prevalence of cancer pain in different cancer types;
the probability of a cancer pain patient requiring an intervention, and receiving an intervention if it is required; and
the probability that a patient will both require and receive an intervention. Examples of such interventions were short- and long-acting opioids, non-steroidal anti-inflammatory drugs, medication for side effects, surgery and radiation.

**Study designs and other criteria for inclusion in the review**
Not reported.

**Sources searched to identify primary studies**
MEDLINE was searched for primary studies and the bibliographies of selected articles were reviewed. The search for English-language articles on cancer pain prevalence used the MeSH keywords "neoplasms", "pain", "probability", "prevalence" and "epidemiology". The search for English-language articles on cancer pain management used the MeSH keywords "neoplasms", "pain", "therapy", "analgesics", "practice guidelines", "algorithms", "longitudinal studies", "treatment outcome" and "decision-making".

**Criteria used to ensure the validity of primary studies**
All the studies were graded according to the evidence-based medicine guidelines developed by Sackett et al. (see Other Publications of Related Interest). Because the highest quality studies reporting pain cancer prevalence separated patients into two groups, locoregional (Stages I-III) versus advanced disease (Stage IV or metastatic), only patients in these staging groups were considered to have pain. Patients with in situ diseases were assumed not to have pain.

**Methods used to judge relevance and validity, and for extracting data**
Not reported.

**Number of primary studies included**
At least 8 studies were included in the review. The probability of cancer was derived using the 1999 estimated US prevalence counts published by the National Cancer institute. Estimates of cancer pain prevalence were derived from 4 studies. The efficacy of cancer pain strategies was mainly derived from a study by Du Pen et al. (see Other Publications of Related Interest), which randomised 81 patients to care according to a cancer pain management algorithm versus standard care according to the treating oncologist. The efficacy of usual care on cancer pain management was based on 3 studies reporting the suboptimal care that many cancer patients receive.

**Methods of combining primary studies**
Not reported. For the burden of cancer and cancer pain, data from the multiple studies provided the ranges for the probabilities used in the sensitivity analysis.

**Investigation of differences between primary studies**
Not reported.

**Results of the review**
The probabilities of cancer pain were derived for over 20 different cancer types. The probability of cancer pain ranged from 0.20 (range: 0.14 - 0.60) for cancer of the uterus (locoregional) to 0.79 (range: 0.72 - 1.00) for cancer of the pancreas (distant).
Under the GBC strategy, neuropathic pain was identified in two thirds of the cases. Round-the-clock long-acting opioids were standard and all of the patients received non-steroidal or acetaminophen co-analgesics. Opioid side effects were recognised and treated. Under the OBC strategy, long-acting opioids were prescribed half as often, non-opioid analgesics were prescribed two thirds as often, and neuropathic pain was recognised one third as often. Patterns of usage for nonpharmaceutical interventions were similar for GBC and OBC.

**Methods used to derive estimates of effectiveness**
The authors made several assumptions and also used expert opinion to determine the outcome probabilities. The main assumptions are reported below.

**Estimates of effectiveness and key assumptions**
As pain management practices in the UC setting had not been systematically studied, the authors assumed that pain was sporadically assessed. They also assumed that round-the-clock dosing with long-acting opioids, the prescription of short-acting opioids, and the treatment of neuropathic pain problems were infrequent.

The authors estimated that the probability that a cancer patient would both require and receive an intervention was smaller for patients receiving UC.

The authors assumed UC providers prescribed nonpharmaceutical interventions at least 20% less often because of inadequate assessment and knowledge.

As several studies found that standard therapy was approximately less effective than the algorithm in the Du Pen et al. study, the effectiveness of UC was assumed to be 25% less than OBC.

**Measure of benefits used in the economic analysis**
The measure of benefit used was the number of patients successfully relieved from pain, as demonstrated by a reduction in the usual pain level to less than or equal to 3 on a 0-10 visual analogue scale. The effectiveness of GBC and OBC were derived directly from the dataset of Du Pen et al.

**Direct costs**
The resource quantities and the costs were reported separately. The direct costs of the health service were included in the analysis. The costs were calculated from direct medical resource use and unit costs. Pharmaceutical use was divided into medications for pain and medications for side effects. Year 2000 Red Book values for average wholesale price were used for unit drug costs, while generic costs were used if a generic product was available. For parenteral opioids, Medicare fee schedules were used for medical services and durable medical equipment. Nonpharmaceutical utilisation was divided into anaesthesiology procedures, radiotherapy, psychosocial modalities and physical therapy.

Each procedure was built into a scenario based on the required components and the typical period of effectiveness, with the total cost of the scenario being determined using 2000 Medicare Current Procedural Terminology or diagnosis-related group reimbursement for each component. A weighted per patient cost was generated for each procedural scenario by multiplying the scenario cost by the relative frequency of the scenario. The scenario costs were then summed to generate the total per patient cost within each intervention group. Discounting was not relevant, as all the costs were incurred during one month, hence it was not performed. The price year used appears to have been 2000.

**Statistical analysis of costs**
The total costs per cancer pain patient were treated as point estimates (i.e. the data were deterministic).

**Indirect Costs**
The indirect costs were not included.
Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were conducted to evaluate the effect of variations in clinical probabilities and cost estimates on the results. For both the prevalence of cancer and cancer pain, the variations reflected the probability ranges reported in the literature. For pharmaceutical and nonpharmaceutical utilisation, the variations reflected the likely probability ranges and costs according to clinical experts in these areas. One to two inputs were varied at a time. Worst- and best-case scenarios were examined by using cumulative changes in the likelihood that an intervention would be used and in the intervention cost. The influences of these parameters on model outputs were compared with each other by normalising the results to a standard unit (influence of input). The influence of input was calculated by dividing the percentage change in model output by the percentage change from the baseline model input. The model was also tested with other populations to ensure that all outputs responded to user-defined changes in the model inputs.

Estimated benefits used in the economic analysis
Of the 205 patients suffering from cancer-related pain, 164 (80%) patients in the GBC group, 113 (55%) patients in the OBC group and 61 (30%) patients in the UC group, would be relieved of cancer pain.

Cost results
The estimated total cost per cancer pain patient was $578.59 in GBC patients, $465.56 in OBC patients and $315.29 in UC patients.

The population costs were $118,436 with GBC, $95,300 with OBC and $64,540 with UC.

The costs per member per month were $1.18 with GBC, $0.95 with OBC and $0.65 with UC.

Synthesis of costs and benefits
The costs and benefits were combined by calculating an incremental cost-effectiveness ratio (ICER). This reflected the additional expense required to effectively treat an extra patient when changing from one cancer pain management strategy to another. Compared with OBC, GBC had an ICER of $452.11 per additional patient relieved of cancer pain. Compared with UC, OBC had an ICER of $601.07 per additional patient relieved of cancer pain. Compared with UC, GBC had an ICER of $526.59 per additional patient relieved of cancer pain.

From the sensitivity analysis of the Veterans Administration population, the per member per month cost of cancer pain management was 2.6 times higher for each of the strategies. This was due to fact that the relative risk of having cancer in this population was 2.5 times higher than that in the baseline population.

An examination of the clinical and cost inputs showed that the cost of each of the strategies was most sensitive to the prevalence of cancer pain in locoregional disease, the probability that surgical interventions would be required, and the cost of surgical interventions. When the prevalence of cancer pain in patients with locoregional disease was increased to 75%, the population cost in the GBC group increased 40% from baseline. When the probability that surgery would be performed for a cancer patient was increased to 3%, the population cost in the GBC group increased by 33% from baseline.

Another major influence on population cost was the cost of the surgical interventions. Increasing the cost of surgery by 20% increased the total population cost by 7% from baseline. Other influential interventions included short- and long-acting opioids and radiotherapy.

Authors’ conclusions
More cancer patients were free from pain when a guideline-based strategy was used. This was achieved at a small increase in costs.

**CRD COMMENTARY - Selection of comparators**
The authors compared GBC with OBC and UC. The use of these comparators was justified because they both represented usual practice in the management of cancer pain. You should decide if they are widely used technologies in your own setting.

**Validity of estimate of measure of effectiveness**
The authors did not state that a systematic review of the literature had been undertaken to identify relevant research and minimise bias. The authors only used one database, MEDLINE, to identify primary studies. However, they did check the bibliographies of the identified studies for further evidence. The methodology and conduct of the review could have been better reported, as it was sometimes unclear which estimates were actually derived from the review of the literature and which were estimated from assumptions or opinion. Even though the authors graded the evidence according to medical guidelines, the results of such assessments were not reported. In addition, it was unclear whether those studies of lower grades were excluded from the review. The authors did not discuss how the estimates of effectiveness from the primary studies were combined, or how any possible differences between the studies were conducted. However, much of the information for the effectiveness of both GBC and OBC came from what would seem to have been a well-conducted randomised controlled trial of both of these strategies (Du Pen et al.).

The authors also used their own assumptions and expert opinion to determine the probability of receiving and needing particular interventions. As already mentioned, it was sometimes unclear whether some estimates were derived from the literature, from authors’ assumptions, or from expert opinion. There were no details on how many experts gave their opinion. Despite these limitations, uncertainty was properly investigated in a sensitivity analysis.

**Validity of estimate of measure of benefit**
The estimation of health benefit was modelled. Successful cancer pain relief was demonstrated by the usual pain level on a 0-10 visual analogue scale being reduced to less than or equal to 3. This was appropriate.

**Validity of estimate of costs**
All the categories of cost relevant to the perspective adopted were included in the analysis, although some relevant costs were omitted. For example, the cost of untreated pain such as hospitalisation was not included, which may understate the costs. However, even if such relevant costs were omitted from the analysis, these were unlikely to have affected the authors' conclusions, as they appeared to be common to all strategies. The costs and the quantities were reported separately, which will enhance the generalisability to other settings. Resource use was derived from published sources and opinions. The sensitivity analyses performed and the ranges used appear to have been appropriate. The unit costs were also derived from published sources and appropriate sensitivity analyses were conducted. Discounting was unnecessary since all the costs were incurred during one month. Medicare charges were used to proxy prices. The price year was not explicitly reported, which will make any possible reflation exercises look dubious.

**Other issues**
As this was the first evidence-based clinical decision and economic analysis model on cancer pain and its management, the authors did not make any comparisons with other similar studies. However, the results from the Du Pen et al. study found that patients in the GBC strategy achieved significant reductions in pain intensity when compared with OBC patients. The issue of generalisability to other settings was addressed in the sensitivity analysis and the nature of the model, which could be customised for user-defined populations. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis.

The authors reported some limitations of their study. First, for some tumour types, the prevalence of pain had to be estimated from other similar tumours. However, the estimated composite pain prevalence rates for all cancer patients
derived from a large cohort study corresponded well to a summation of the model estimate by tumour type and extent of the disease. Second, many of the estimates were based on the reanalysis of a single study (Du Pen et al.) which, even if properly conducted, only consisted of 81 patients. A third limitation was the scope of the model, which was designed to estimate the costs and cost-effectiveness of three different practice patterns from trial data and extrapolation. Limitations in the background data and the assumptions made will make it impractical to use this model to test the exact result of a particular organisational decision. A further limitation of the model was the use of charges to derive the costs, as different organisations will have individualised costs based on contractual agreements, utilisation volumes and policies.

**Implications of the study**
The authors suggested that controlled trials examining GBC in the UC environment should be conducted, especially as more primary care providers are asked to participate in the routine care of cancer patients. Robust evaluation of new cancer pain management guidelines should also be undertaken, especially for those including both pharmaceutical and nonpharmaceutical interventions.

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**Other publications of related interest**


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