An economic evaluation of short-acting opioids for treatment of breakthrough pain in patients with cancer

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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.

CRD summary
This study examined the cost-effectiveness of treatments for breakthrough cancer pain, including intranasal fentanyl spray, oral transmucosal fentanyl citrate, and fentanyl buccal tablets. The authors concluded that intranasal fentanyl spray was the most cost-effective strategy, in Sweden. The study used valid and transparent methods, which ensured that the authors’ conclusions are robust.

Type of economic evaluation
Cost-utility analysis

Study objective
This study examined the cost-effectiveness of treatments for breakthrough cancer pain, including intranasal fentanyl spray, oral transmucosal fentanyl citrate, and fentanyl buccal tablets.

Interventions
The three treatments were intranasal fentanyl spray, oral transmucosal fentanyl citrate, and fentanyl buccal tablets. These were compared with placebo or no intervention.

Location/setting
Sweden/primary care.

Methods
Analytical approach:
This economic evaluation was based on a decision model, with a time horizon of 180 days. The authors stated that it was carried out from the perspective of the health care payer.

Effectiveness data:
A literature review was performed to identify the clinical inputs for the model. The key parameter was the clinical efficacy of the treatments, which was defined as a reduction in pain intensity. This was estimated using a mixed-treatment comparison meta-analysis and data from six published randomised controlled trials. None of the trials directly compared all three treatments and placebo was used as the common comparator. The patients’ characteristics were based on these trials. Some assumptions were made.

Monetary benefit and utility valuations:
The utility of breakthrough cancer pain episodes was directly measured by 99 members of the UK general public, using the time trade-off approach.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure.

Cost data:
The economic analysis included the costs of drugs and other health care resources, such as general practitioner visits, home care, and hospital stay. The drug costs were based on Swedish pharmacy selling prices. Assumptions were made for drugs not available in Sweden. The costs of other medical items were from official Swedish sources. The patterns of
resource consumption were from a published US telephone survey, identified by the literature review. The economic data were validated to the Swedish setting by a panel of four independent specialist physicians. They were presented in Euros (EUR) and the price year was 2008.

Analysis of uncertainty:
Alternative scenarios were considered by changing the assumptions for the background pain intensity and by including only the drug costs. A probabilistic sensitivity analysis was carried out, with conventional probability distributions for sets of parameters, based on published confidence intervals or expert opinion.

Results
The total QALYs were 0.167 with placebo, 0.266 with intranasal fentanyl spray, 0.220 with oral transmucosal fentanyl citrate, and 0.223 with fentanyl buccal tablets. The drug costs were zero with placebo, EUR 5,034 for the spray, EUR 5,034 for the oral citrate, and EUR 4,348 for the tablets. The total costs were EUR 877 with placebo, EUR 5,534 for the spray, EUR 5,708 for the citrate, and EUR 5,011 for the tablets.

The spray dominated the citrate, as it was less expensive and more effective. The incremental cost per QALY gained with the spray over the tablets was EUR 12,203. At a willingness-to-pay threshold of EUR 45,000 per QALY, the spray was cost-effective over the tablets in more than 99% of simulations.

The dominance and cost-effectiveness of intranasal fentanyl spray were confirmed in the scenario analyses.

Authors’ conclusions
The authors concluded that intranasal fentanyl spray was the most cost-effective strategy for the management of breakthrough cancer pain in Sweden.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear as three of the four available fentanyl formulations were used. The authors reported that sublingual fentanyl was excluded because there were insufficient clinical trial data.

Effectiveness/benefits:
The clinical part of the analysis was satisfactorily carried out. A literature review was performed to identify the relevant sources of data, but the methods and conduct of the review were not reported. The selection of randomised controlled trials should have ensured the validity of the clinical inputs. All the trials were randomised, double-blind, cross-over trials, except one, which was open label. The mixed-treatment comparison was appropriate for pooling the evidence because of the lack of published head-to-head trials. The methods of pain intensity assessment and utility valuation were extensively reported. QALYs were a valid benefit measure given the impact of pain on the patients’ health. An appropriate validated instrument (time trade-off) and the UK general public were used to elicit the preferences and utility weights.

Costs:
The cost categories reflected the viewpoint of the health care payer. The drug costs were from Swedish sources for the citrate and the spray, which were assumed to be equal, and the price of the tablets was assumed to be 14% less, based on the UK market, as they were not available in Sweden. Other health care resource use was from a US source and validated by Swedish clinical experts. This was acknowledged as a limitation of the analysis, but no Swedish estimates were found. The authors stated that indirect costs of productivity lost were not analysed because the patients were unlikely to be in employment due to the advanced stage of cancer. Other costs, such as travel to hospital, were not relevant from the perspective of the health care payer. The costs were varied in the probabilistic sensitivity analysis and the price year was reported.

Analysis and results:
The results were clearly reported. An incremental approach was used to synthesise the costs and benefits of the strategies. The uncertainty was satisfactorily investigated, using a probabilistic approach, and the results were extensively discussed. The authors acknowledged some limitations of their analysis, which mainly related to the economic information, which was from one US source, and the need for assumptions for some drug costs. The results
might be transferable to settings with similar drug costs.

Concluding remarks:
The study used valid and transparent methods, which ensured that the authors’ conclusions are robust.

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