A one year health economic model comparing transdermal fentanyl with sustained-release morphine in the treatment of chronic noncancer pain

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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
The study examined two treatments for chronic non-cancer pain. One was the fentanyl transdermal therapeutic system (fentanyl-TTS) and the other was oral sustained-release (SR) morphine. Monthly medication use was reported for patients with well-controlled pain (20,000 microg for fentanyl-TTS and 2,000 mg for SR morphine) and for patients with badly-controlled pain (30,000 microg for fentanyl-TTS and 3,000 mg for SR morphine).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of patients with non-malignant pain disorders for whom opioid titration and stabilisation has already been achieved.

Setting
The setting was an outpatient setting. The economic study was carried out in Denmark.

Dates to which data relate
Most of the clinical and economic data were derived from studies published in 2001. The price year was 1999.

Source of effectiveness data
The clinical data used in the decision model were the transition rates across health states (percentage of patients staying in well-controlled pain, moving to badly-controlled pain or switching treatment, both for fentanyl-TTS and for SR morphine) and the rates of adverse events.

Modelling
A Markov model was constructed to simulate the treatment of a hypothetical cohort of patients with chronic non-cancer pain. The model comprised 12 treatment cycles, each of 30 days. The health states and transition patterns were reported and accurately described. Basically, patients could take one of the two medications under analysis and move to well-controlled pain or badly-controlled pain. Patients could switch between treatments in the case of badly-controlled pain or adverse events (11 possible adverse events were considered). The time horizon of the model was 1 year and a half-cycle correction was made. The basic structure of the tree was represented graphically.
Sources searched to identify primary studies
Treatment effect and toxicity for fentanyl-TTS were derived from a long-term (12 months), non-randomised, single-arm study of 532 patients with chronic moderate to severe non-cancer pain and from an open-label, 8-week, crossover study comparing fentanyl-TTS and SR-morphine in 256 patients. Some data for SR-morphine were also taken from this open-label study, but the majority of clinical and toxicity (probability of adverse events) estimates were obtained from expert opinion.

Methods used to judge relevance and validity, and for extracting data
The authors stated that no long-term, double-blind, randomised controlled trials were available for the comparison between the two drugs under analysis. Thus, the authors selectively chose two studies, probably because of their large sample size and relatively long follow-up. No systematic search for data was reported. Other clinical inputs were estimated using a Delphi panel, the details of which were reported in detail.

Measure of benefits used in the economic analysis
The summary benefit measure that was combined with the costs was the number of days of good pain control. This was estimated using the decision model framework. Another relevant model output, which was not used as a further benefit measure, was the number of days on initial treatment.

Direct costs
The viewpoint of the analysis was that of the health care system. It included the costs of baseline treatment, breakthrough medication, co-medication and the treatment of adverse events. Specifically, medication costs and physician costs (visit and telephone consultation) were considered. The co-medications included tricyclic antidepressants, non-steroidal anti-inflammatory drugs, codeine, laxatives and antiemetics. The unit costs and the quantities of resources used were presented separately.

Patterns of resource consumption were derived from the two fentanyl-TTS studies previously described and from the Delphi panel. The costs of the drugs were derived from the Danish Medical Association's Drug Register. The costs of the doctor's time were obtained from the National Board of Health in Denmark, the Health Care Reimbursement Negotiating Committee and the Praktiserende Laegers Organisation (a general practitioners' organisation). The percentage of patients treated with fentanyl-TTS or SR-morphine who received co-medication was estimated from the UK General Practice Research Database (UK-GPRD). Discounting was not relevant given that the costs were incurred during 1 year. The price year was 1999.

Statistical analysis of costs
The costs were treated deterministically in the base-case.

Indirect Costs
Productivity costs were not considered.

Currency
Denmark kroner (DKK). The costs were converted into euros (EUR) and US dollars ($) at the following rate: DKK 1 = EUR 0.1346 = $0.1433.

Sensitivity analysis
One-way sensitivity analyses were performed to test the robustness of the cost-effectiveness results to variations in clinical and economic inputs. These inputs were varied by +/- 20% of their baseline values (authors' assumption).
Estimated benefits used in the economic analysis
The expected number of days of good pain control over a 1-year time period was 99 with fentanyl-TTS and 63.9 with SR-morphine.

Patients treated with fentanyl-TTS remained considerably longer on initial treatment compared with those treated with SR-morphine (166 days versus 117 days).

Cost results
The expected per patient costs over the 1-year time period were DKK 6,284 (EUR 845; $900) with fentanyl-TTS and DKK 3,772 (EUR 508; $540) with SR-morphine.

A breakdown of the costs showed that the main cost driver was the baseline treatment cost. This represented the predominant cause of the difference between the two treatments, accounting for 76% of the total cost of treatment with fentanyl-TTS and 50% of the cost of treatment with SR-morphine. However, the costs of treatment for adverse events were twice as high with SR-morphine compared with fentanyl-TTS, accounting for 31% of the baseline cost of treatment with SR-morphine.

Synthesis of costs and benefits
Average and incremental cost-effectiveness ratios (ACERs and ICERs, respectively; the average and incremental cost per day of good pain control) were calculated in order to combine the costs and benefits of the alternative strategies.

The ACERs were DKK 63.49 (EUR 8.54; $9.10) with fentanyl-TTS and DKK 59.05 (EUR 7.94; $8.46) with SR-morphine.

The ICER with fentanyl-TTS in comparison with SR-morphine was DKK 71.60 (EUR 9.63; $10.26).

The results of the sensitivity analysis showed that the most sensitive variable was the unit cost of fentanyl-TTS. A 20% reduction in this variable led to an ICER of DKK 53.42 ($7.65).

Variations in other model inputs did not substantially alter the results of the base-case analysis.

Authors’ conclusions
The fentanyl transdermal therapeutic system (fentanyl-TSS) was a cost-effectiveness alternative to the conventional treatment of chronic non-cancer pain.

CRD COMMENTARY - Selection of comparators
The authors justified the choice of the comparators, which were appropriately selected in their context and given the availability of published head-to-head studies. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The clinical data used in the model were derived from two multinational clinical trials, which were identified selectively in order to consider the most valid source of data. However, both studies were open-label, thus open to potential investigator and/or patient bias. The authors selected these studies given the lack of randomised clinical trials. Thus, a Delphi panel was used in order to integrate the published information with data from experts in the field of pain control. The procedure of the Delphi panel was reported extensively.

Validity of estimate of measure of benefit
The authors justified their choice of the summary benefit measure. However, it represents an intermediate end point of the impact of treatment on patient health and cannot be compared with other outcome measures.
Validity of estimate of costs
The analysis of the costs was consistent with the authors’ stated perspective. Extensive details of the economic analysis were reported, which enhances the possibility of replicating the analysis in other settings and time periods. Sources of the costs, patterns of resource consumption, price year and unit costs were reported. Currency conversions were also performed. Statistical analyses of the costs were not carried out. The costs reflected the Danish setting and the impact of variations in the cost estimates was only partially investigated in the sensitivity analysis.

Other issues
The authors stated that their findings corroborated those from other economic evaluations carried out in other countries. The issue of the generalisability of the study results to other settings was not explicitly addressed, but the use of a sensitivity analysis enhanced to some extent the external validity of the analysis. Overall, the authors reported many details of the study and presented the results of the analysis clearly and extensively. They also noted some limitations of their analysis, mainly related to the fact that it proved impossible to obtain sufficient data from prospective and randomised clinical trials to use in their analysis. It was also acknowledged that the costs associated with the initiation and stabilisation of treatment were not taken into account in this model. However, in a recently reported study, the expected costs during the titration phase were lower for fentanyl-TTS.

Implications of the study
The study results suggest that fentanyl-TTS can be recommended for use in the treatment of non-cancer pain.

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Other publications of related interest
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