Modeling the economic and health consequences of managing chronic osteoarthritis pain with opioids in Germany: comparison of extended-release oxycodone and OROS hydromorphone

Ward A, Bozkaya D, Fleischmann J, Dubois D, Sabatowski R, Caro J J

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
The objective was to assess the cost-effectiveness of the Osmotic controlled-Release Oral delivery System hydromorphone compared with an equally analgesic dose of extended-release oxycodone, administered two or three times a day, in patients with chronic osteoarthritis and severe pain. The hydromorphone was a cost-effective alternative to oxycodone from the perspective of the German health insurance system. The study used validated methodology, with a clear presentation of data sources. The authors' conclusions are likely to be valid and robust.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to assess the cost-effectiveness of the Osmotic controlled-Release Oral delivery System (OROS) hydromorphone in comparison with an equally analgesic dose of extended release (ER) oxycodone taken two or three times a day, for patients with chronic osteoarthritis and severe pain.

Interventions
The OROS strategy, where hydromorphone was released at a continuous rate over 24 hours, was compared with the ER strategy, where oxycodone was given two or three times a day. The conversion to morphine dose was one to five for OROS hydromorphone and one to two for ER oxycodone. The initial dosage and dose titration depended on whether or not patients had previously received opioids.

Location/setting
Germany/primary and secondary care.

Methods
Analytical approach:
This economic evaluation was based on a discrete event simulation model which predicted the costs and benefits of the alternative treatments based on efficacy, discontinuation rate and adverse events. The time horizon of the analysis was one year and the authors stated that the perspective of the German health insurance system was adopted.

Effectiveness data:
The clinical data appear to have been derived from a selection of known, relevant studies. For example, key clinical data on the efficacy of the two treatments were derived from a recent head-to-head phase III, open-label, randomised controlled trial (RCT) of 138 patients with chronic, moderate-to-severe osteoarthritis pain. The demographic and clinical characteristics of the eligible patient population were obtained from German sources. Adverse event data were taken from a systematic review of 15 placebo controlled trials. The clinical experience of one of the study authors and a Delphi panel of experts were also used to determine some clinical aspects of the model. The key clinical outcome was improvement in the Sleep Problems Index-II (SPI) score with the two treatments.

Monetary benefit and utility valuations:
The utility valuations were derived using the Short Form 6D questionnaire from a previously published study. SPI values found in the clinical trials were translated into utility weights using a regression.
**Measure of benefit:**
Quality-adjusted life-years (QALYs) were used as the summary benefit measure.

**Cost data:**
The health services were medications, doctor visits (both specialists and general practitioners), and treatment options for dissatisfied patients (including other drugs, steroid injections, and surgical procedures). The unit costs and quantities of resources used were presented separately. The resource use was based on guidelines and German legislation. The drug costs were derived from the Rote Liste, while other costs came from official prices. All costs were in Euros (EUR) and the price year was 2005.

**Analysis of uncertainty:**
Univariate sensitivity analyses were carried out on all model inputs using published or author-chosen ranges. Scenarios were also run for the proportion of opioid naive patients and prior users of an opiate. In addition, a probabilistic sensitivity analysis was carried out by varying multiple parameters simultaneously. The types of parameters investigated and the types of probabilistic distributions used were reported.

**Results**
The expected costs at one year were EUR 2,101 with OROS hydromorphone and EUR 1,959 with ER oxycodone (difference: EUR 141). Medications were the largest component of both costs and the difference between them.

The QALYs at one year were 0.698 with OROS hydromorphone and 0.681 with ER oxycodone (difference: 0.017).

The incremental cost per QALY gained with OROS hydromorphone over ER oxycodone was EUR 8,343.

The sensitivity analysis confirmed that these base-case findings were robust. The most influential model inputs were conversion factors and utility values. Different combinations of initial and final drug dosages, and the proportion of opioid naive patients also had an impact on the study findings. However, OROS hydromorphone always remained cost-effective compared with ER oxycodone.

The probabilistic sensitivity analysis suggested that 10% of all simulations had an incremental cost per QALY below the threshold of EUR 5,000 and 72% were below the threshold of EUR 10,000.

**Authors' conclusions**
The authors concluded that OROS hydromorphone was a cost-effective alternative to ER oxycodone for the management of severe pain associated with chronic osteoarthritis in Germany.

**CRD commentary**

**Interventions:**
The two drugs were appropriately selected, given their wide use among opioids.

**Effectiveness/benefits:**
The approach used to derive the clinical data was not explicitly stated, but it appears that the authors selected the most relevant evidence with which to populate their decision model. Some inputs relating to the patient population reflected the German setting. The use of a head-to-head RCT to derive the drug treatment effects represents a valid strategy given its robust design. Some information on the process of dose titration in the RCT was provided. In general, the use of multiple sources augmented with expert opinions introduces some uncertainty, but this was extensively investigated in the sensitivity analysis. The details of the methodology used to derive the utility valuations and to calculate QALYs were given. QALYs are not only a validated benefit measure but permit cross-disease comparisons which enhances the generalisability of the study findings.

**Costs:**
The categories of costs were consistent with the economic viewpoint. A breakdown of cost items was provided, and detailed information on resource consumption and unit costs was reported, thus improving the transparency of the economic analysis. The sources of costs were reported and the price year was reported, which enhances the possibility
of making refation exercises in other time periods. Alternative assumptions on economic inputs were analysed.

**Analysis and results:**
The synthesis of costs and benefits was appropriately performed and presented. The issue of uncertainty was satisfactorily addressed in the sensitivity analyses. Germany was selected for this economic evaluation because it was the country where OROS hydromorphone was first made available in 2006. A schematic representation of the model structure was given and the use of a discrete event simulation is a strength of the analysis.

**Concluding remarks:**
On the whole, the study was based on validated methodology, with a clear presentation of data sources. The authors’ conclusions are likely to be valid and robust.

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