A modeled economic evaluation comparing atomoxetine with stimulant therapy in the treatment of children with attention-deficit/hyperactivity disorder in the United Kingdom

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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 atomoxetine for the treatment of children with attention deficit hyperactivity disorder (ADHD) in comparison with the current alternatives, in patient groups with varying treatment histories and existence of co-morbidities, which ruled out stimulant medication. Atomoxetine offered value for money in the treatment of ADHD from the perspective of the National Health Service. The study considered different patient populations and was based on valid methodology, which makes the authors’ conclusions more valid and robust.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to examine the cost-effectiveness of atomoxetine for the treatment of children with attention deficit hyperactivity disorder (ADHD) in comparison with the current alternatives, in different patient groups, according to their treatment history and the existence of co-morbidities, which rule out stimulant medication.

Interventions
Oral atomoxetine at an average 1.1 capsule per day dose was compared with methylphenidate hydrochloride (MPH), either as an immediate release (IR) 25.46mg per day or an extended release (XR) 32.75mg per day formulation, and to dexamphetamine sulphate (DEX) IR at 13.11mg per day. Different comparisons were made on the basis of the patient characteristics and a background strategy of no medication was also considered.

Location/setting
UK/secondary care.

Methods
Analytical approach:
This economic evaluation was based on a Markov model with a time horizon of one year. The authors stated that the analysis was carried out from the perspective of the National Health Service (NHS) in England and Wales.

Effectiveness data:
The clinical data appear to have been derived from a selection of known, relevant studies. Multiple sources were used, including randomised controlled trials (RCTs), a meta-analysis of RCTs, and manufacturers’ information. The data on the treatment effect and adverse events generally came from head-to-head trials. Treatment response was the key clinical input.

Monetary benefit and utility valuations:
The utility values were derived from a survey of 83 parents of children with ADHD, using the standard gamble approach.

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

Cost data:
The economic evaluation included only the drug costs. Those costs associated with the side effects related to drug therapies were not considered. The unit costs and quantities of resources used were presented. The resource use data were based on a study of patients in the primary care setting. All costs were derived from the UK edition of the Monthly Index of Medical Specialties. The price year was not explicitly reported and all costs were in UK pounds sterling (£).

Analysis of uncertainty:
The issue of uncertainty was addressed by means of extensive one- and multi-way sensitivity analyses on all the model inputs.

Results
The costs and QALYs were reported for all patient groups.

The incremental cost-effectiveness ratio (ICER) or additional cost per QALY gained with atomoxetine, for stimulant naive patients (those with no previous drug use and no contraindications for stimulants), was £15,224 over IR MPH, and £13,241 over XR MPH.

For stimulant failed patients (those who had previously received MPH, but had stopped because of a lack of efficacy or intolerable side effects) the ICER was £14,945 over IR DEX.

For stimulant averse patients (those who had received a stimulant medication and who had responded successfully, but who wanted to stop their medication if a non-stimulant medication was available) the ICER was £15,878 over IR MPH and £14,169 over XR MPH.

For stimulant contraindicated naive patients (those who had no history of drug use, but who were unable to use stimulant therapies because of a pre-existing contraindicated condition) the ICER was £11,523 over no treatment and for stimulant contraindicated exposed patients (those who were previously treated with a stimulant therapy, but stopped because of one or more conditions which may have developed while receiving stimulant therapy) the ICER was £12,370 over no treatment.

The sensitivity analysis confirmed that these findings were robust and the utility valuations were the key drivers for the model. When the differences in the utility values, between corresponding health states for the different treatments, were reduced to 75% of the base-case value, the ICERs ranged from £17,000 to £24,000 per QALY, but they ranged from £42,000 to £62,000 per QALY when the utility differences were reduced to 25% of their original values.

Authors’ conclusions
The authors concluded that atomoxetine offered value for money in the treatment of ADHD in comparison with the current alternatives, from the perspective of the NHS, in different patient populations.

CRD commentary
Interventions:
The authors provided a justification for their selection of the relevant comparators. MPH was the most widely used medication for ADHD in both formulations and DEX was prescribed less frequently and mainly as a second-line therapy, but was included to cover all the available drugs. The option of no treatment was included to assess the active value of all the treatments. The treatment algorithms for all patient populations were reported in detail.

Effectiveness/benefits:
The primary studies were selected, and the authors did not report the methods and conduct of a systematic literature review. Thus, such studies may have been known to the authors, and it is not possible to determine whether other relevant sources were excluded. Most of the studies were RCTs, which are usually considered to be a valid source of data given the strengths of their design. Furthermore, these RCTs were based on head-to-head comparisons of the alternative therapeutic strategies. These factors enhance the validity of the clinical analysis. The details of the method used to elicit the utility valuations were provided. QALYs are a validated benefit measure, which are relevant for this specific patient population given the impact of the disease on quality of life.
Costs:
The categories of costs appear to have been consistent with the perspective. The authors justified the exclusion of non-drug costs on the assumption that all the other costs were equal. This, as the authors pointed out, biased the findings against the active therapies, which could reduce symptoms and, consequently, the use of health care resources. The cost calculations were explicitly reported, which enhances the transparency of the economic analysis. The sources of data were reported, but the price year was not, which makes it difficult to repeat the analysis for other time periods.

Analysis and results:
The synthesis of the costs and benefits was carried out using an incremental approach, which was appropriate given the higher costs and benefits of one treatment over the comparator. The findings were clearly reported, but few details of the sensitivity analyses were given. The authors provided a clear description of the decision model and its pathways. Some potential limitations were discussed, such as the relatively short time horizon and the derivation of health utilities from proxies rather than patients.

Concluding remarks:
The study considered different patient populations and was based on valid methodology, which makes the authors’ conclusions more valid and robust.

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