Evaluating the cost-effectiveness of reduced tardive dyskinesia with second-generation antipsychotics

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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 second-generation antipsychotic medication in the treatment of schizophrenia. The comparator was the first-generation class of antipsychotic medication.

Type of intervention
Treatment

Economic study type
Cost-utility analysis

Study population
The study population comprised patients with schizophrenia who were being treated with second-generation antipsychotics. No further details of the study population were given.

Setting
The setting was outpatient. The author did not state which country the analysis was intended for. However, the results were presented in US dollars and UK pounds sterling.

Dates to which data relate
The effectiveness data were derived from studies published between 1994 and 2006. No dates for resource use were explicitly reported. The price year was not reported.

Study designs and other criteria for inclusion in the review
The clinical parameters associated with the study included incidence of tardive dyskinesia, severity of tardive dyskinesia, the Heinrichs-Carpenter Quality of Life Interview scores, and recovery.

Sources searched to identify primary studies
The clinical effectiveness data were derived from published studies. The attributable risk of tardive dyskinesia complications with first-generation drugs was obtained from a literature review which included 4 randomised controlled trials (RCTs). The severity of tardive dyskinesia was also derived from an RCT.

Methods used to derive estimates of effectiveness
The author reported that a review of the literature was conducted, but the methods of the review were not reported in this paper. Where possible, the clinical data were derived from papers used in the review, but some unpublished data that addressed the expected ranges of severity and duration of tardive dyskinesia and its relationship to functional capacity and quality of life were also used.

Measure of benefits used in the economic analysis
The measure of benefits used was the quality-adjusted life-years (QALYs). Utility weights were obtained from the literature. They were elicited from 620 members of the general public using the standard gamble method.

Direct costs
The author did not state the perspective of the study. It appears that only the cost of antipsychotic medication was
included in the analysis, although this was not clear from the paper. The cost data used in this research were derived from a published study (Rosenheck et al. 2006, see 'Other Publications of Related Interest' below for bibliographic details). US cost estimates were used. No price year was stated. No discounting was required as the base-case time horizon was 1 year. No discounting was reported for the secondary 5-year analysis.

**Statistical analysis of costs**
The costs were treated deterministically.

**Indirect Costs**
No productivity losses were included.

**Currency**
UK pounds sterling (£) and US dollars ($). The currency conversion ($ to £) was not reported.

**Sensitivity analysis**
Best- and worst-case scenarios were developed in order to examine different values of incidence and severity of dyskinesia, recovery and cost. There was no other examination of uncertainty for the economic analysis.

**Estimated benefits used in the economic analysis**
The QALY decrement per case of tardive dyskinesia and the difference were reported, but no summary measure of benefit.

**Cost results**
Three annualised estimates for the incremental cost of second-generation antipsychotics were considered:

- a lower bound estimate of £1,200 ($2,400) per year based on a stable drug difference of £100 ($200) per month between perphenazine and second-generation antipsychotics;
- an intermediate cost of £1,700 ($3,500 per year), the annualised difference in monthly total health costs between perphenazine and olanzapine; and
- an upper bound cost-difference of £3,100 ($6,200), representing the annualised total health cost-difference between perphenazine and quetiapine.

**Synthesis of costs and benefits**
In the base-case analysis, using the best-case scenario for second-generation antipsychotics gave an incremental cost-effectiveness ratio of £26,000 ($52,000) per case of tardive dyskinesia avoided. This increased to £68,000 ($135,000) per case avoided with the higher cost estimates. The author suggested that, in the base-case, one case avoided was assumed to represent one QALY gained.

In the second analysis, the QALYs gained for a case avoided were 0.143. This produced a range of cost-effectiveness ratios from £186,335 to £482,609. Assuming a QALY gain of 0.093, the range of cost-effectiveness ratios was from $280,505 to £726,508.

It was also assumed that 15% of cases recovered and the estimated cost per QALY ranged from £330,000 ($660,000) to £855,000 ($1,700,000).

When considering a 5-year time horizon and assuming that cost-differences remained the same over the 5 years, the cost per QALY ratios ranged from of £75,000 ($149,000) to £193,000 ($386,000).

**Authors' conclusions**
The author concluded that second-generation antipsychotics for symptoms of extrapyramidal side-effects reduce the risk of tardive dyskinesia, but this does not appear likely to provide sufficient health benefit by itself to justify the predominant use of these agents in the treatment of schizophrenia.
CRD COMMENTARY - Selection of comparators
The author compared one class of drugs with another. Care must therefore be taken in applying the results to comparisons between two specific medications. The comparator of first-generation antipsychotic drugs appeared to be the class of drugs most commonly used.

Validity of estimate of measure of effectiveness
The sources of the clinical data were reported. The author stated that all relevant studies were reviewed, but no systematic search for clinical data was reported. Some of the data came from unpublished sources. Generally, there was limited information about the primary sources, which means that an objective assessment of the validity of the clinical estimates is not possible.

Validity of estimate of measure of benefit
QALYs were an appropriate measure because they capture the impact of the intervention on quality of life and survival, which are the most relevant dimensions of health. However, it was not clear whether all the relevant health outcomes were assessed. The author stated that there was evidence of no difference in extrapyramidal symptoms between first- and second-generation medication.

Validity of estimate of costs
The author did not explicitly state the perspective of the study. It was not clear what costs were actually included. If only drug costs were included this would have been inadequate. It is not possible to judge the validity of the costs given the information reported in this paper, and the reader of this abstract is referred to Rosenheck et al. 2006 for further details. The author acknowledged that it is not certain that US cost estimates would be generalisable to a UK setting. As stated in the 'Validity of estimate of measure of benefit' field (above), it was not clear if all the relevant outcomes were costed. In the secondary 5-year analysis, no discounting was reported even though it would have been appropriate.

Other issues
The author compared the findings with those of previous studies, and stated that this piece of research conformed to the previous trend of dyskinesia prevalence, severity and cost. The author acknowledged that cost data favoured the new drugs because they incorporated the cost of transfer of patients from first- to second-generation antipsychotics. The cost estimates did not apply to elderly people, in whom studies have shown greater risks of tardive dyskinesia. The issue of the generalisability of the results was not addressed. The author's conclusions adequately reflect the scope of the analysis.

Implications of the study
The author stated that, even for the best-case scenario, second-generation antipsychotics do not seem likely to meet conventional standards for cost-effectiveness treatments, and that this could be an argument for lowering payments for these products to a level at which tardive dyskinesia benefits would be worth the price.

Source of funding
Supported by AstraZeneca, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Janssen Pharmaceutica and Wyeth.

Bibliographic details

PubMedID
17766765

DOI
10.1192/bjp.bp.106.035063

Other publications of related interest
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abstract and their bibliographic details recorded here for information.


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Antipsychotic Agents /adverse effects /economics /therapeutic use; Cost-Benefit Analysis; Dyskinesia, Drug-Induced /economics; Humans; Psychotic Disorders /drug therapy /economics /psychology; Quality of Life /psychology; Quality-Adjusted Life Years

**AccessionNumber**
22007008221

**Date bibliographic record published**
29/08/2007

**Date abstract record published**
09/08/2008