Metabolic effects and cost-effectiveness of aripiprazole versus olanzapine in schizophrenia and bipolar disorder
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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
The objective was to assess the cost-effectiveness of aripiprazole versus olanzapine for schizophrenia or bipolar disorder, focusing on the risk of developing treatment-related metabolic syndrome, leading to type 2 diabetes or coronary heart disease. The lower risk of metabolic syndrome with aripiprazole resulted in lower treatment costs and improved quality of life. Some of the methods were not fully reported, but the results were sufficient. Given the assumptions required, the conclusions appear to be appropriate.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The objective was to assess the cost-effectiveness of treatment for schizophrenia or bipolar disorder, focusing on the risk of developing metabolic syndrome, which can lead to type 2 diabetes or coronary heart disease, as an adverse effect of treatment.

Interventions
Aripiprazole 15mg per day was compared with olanzapine 10mg per day, for patients with schizophrenia or bipolar disorder.

Location/setting
Sweden/out-patient secondary care.

Methods
Analytical approach:
A Markov model was used to combine published evidence to assess the costs and outcomes for the two interventions. The time horizon was the lifetime of the patient. The authors reported that a societal perspective was adopted.

Effectiveness data:
The effectiveness data were from published studies. Based on those comparing aripiprazole with olanzapine, in patients with schizophrenia, their efficacy was found to be equivalent. The same was assumed for patients with bipolar disorder, as there were no head-to-head trials for these patients and studies had shown that the risk of metabolic syndrome was comparable for patients with either schizophrenia or bipolar disorder. Published risk prediction models were used to estimate the risk of developing coronary heart disease or diabetes. The main effectiveness estimate was the risk of developing metabolic syndrome after one year of treatment. This risk was from a pooled analysis of three randomised controlled trials.

Monetary benefit and utility valuations:
The literature was reviewed to identify the health utility data. Studies that used the European Quality of life (EQ-5D) questionnaire were selected.

Measure of benefit:
The measures of benefit were life-years and quality-adjusted life-years (QALYs) gained. Future benefits were discounted at an annual rate of 3%.
Cost data:
The direct costs were those of the drugs and the monitoring and treatment of metabolic syndrome, diabetes, and coronary heart disease. This included office visits to the doctor, nurse or dietician, tests, medications, and in-patient care. A clinical expert estimated the resource use for the monitoring and treatment of metabolic risk factors, and this was valued using Swedish unit costs. The drug costs were from national pharmaceutical price lists. A literature review was undertaken to identify the costs of treating diabetes and coronary heart disease. Productivity lost due to metabolic syndrome, diabetes, and coronary heart disease was included. The number of sick days was from published studies, and was valued using average national gross income. All costs were updated to 2009 prices, using Swedish health care consumer price indices, and presented in Swedish kronor (SEK). Future costs were discounted at an annual rate of 3%.

Analysis of uncertainty:
One-way sensitivity analyses were undertaken to determine which parameters had the most impact on the results. A probabilistic sensitivity analysis was performed to analyse the overall uncertainty in the model; every parameter was assigned a statistical distribution and the results were presented in cost-effectiveness scatter plots.

Results
The average cost per patient with schizophrenia was SEK 115,178 with aripiprazole and SEK 145,751 with olanzapine. The average life-years gained were 22.32 with aripiprazole and 22.28 with olanzapine. The average QALYs gained were 15.61 with aripiprazole and 15.53 with olanzapine.

The average cost per patient with bipolar disorder was SEK 130,442 with aripiprazole and SEK 158,889 with olanzapine. The average life-years gained were 22.10 with aripiprazole and 22.06 with olanzapine. The average QALYs gained were 17.17 with aripiprazole and 17.09 with olanzapine.

Aripiprazole was dominant over olanzapine, as it was more effective and less costly, for patients with schizophrenia or bipolar disorder.

The probabilistic sensitivity analysis showed that aripiprazole was dominant in 84% of simulations for schizophrenia and in 77% of simulations for bipolar disorder.

Authors' conclusions
The authors concluded that the lower risk of metabolic syndrome with aripiprazole resulted in lower treatment costs and improved quality of life.

CRD commentary
Interventions:
The interventions were briefly described. Clozapine and ziprasidone were mentioned as alternative antipsychotics and it was unclear why they were not included as comparators.

Effectiveness/benefits:
The effectiveness data were from published studies, and these sources were well reported, but it was unclear if a systematic review of the literature was undertaken, making it impossible to determine if all the relevant information was included. The methods used to pool the results of the three trials for the main clinical effectiveness estimates were not reported, and it is unclear if they were appropriately synthesised. The benefit measure appears to have been appropriate and the details of its derivation were provided.

Costs:
The perspective was explicitly reported and it appears that all the direct and indirect costs relevant to this societal perspective were analysed. The price year, time horizon, discount rate, currency, and the sources for the resource use and costs were reported.

Analysis and results:
The costs and outcomes were appropriately synthesised in a Markov model. The model structure was well reported and a diagram was given. The results were sufficiently presented and the uncertainty in these results was assessed in one-way and probabilistic sensitivity analyses. As the main limitation to their study, the authors reported that the
efficacy of aripiprazole and olanzapine in patients with bipolar disorder had to be assumed due to a lack of head-to-head trials.

**Concluding remarks:**
The methods were good, but some, such as the selection of the effectiveness data, were not fully reported. The results were adequately reported. Given the assumptions required, the authors' conclusions appear to be appropriate.

**Funding**
Funded by Bristol-Myers Squibb, a manufacturer of aripiprazole.

**Bibliographic details**

**PubMedID**
21609324

**DOI**
10.1111/j.1600-0447.2011.01716.x

**Original Paper URL**

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Adult; Antipsychotic Agents /administration & dosage /adverse effects /economics /metabolism; Aripiprazole; Benzodiazepines /administration & dosage /adverse effects /economics /metabolism; Bipolar Disorder /diagnosis /drug therapy /metabolism; Coronary Disease /chemically induced /epidemiology /metabolism; Costs and Cost Analysis /statistics & numerical data; Female; Humans; Male; Metabolic Diseases /chemically induced /epidemiology; Metabolic Phenomena /drug effects; Middle Aged; Piperazines /administration & dosage /adverse effects /economics /metabolism; Quality-Adjusted Life Years; Quinolones /administration & dosage /adverse effects /economics /metabolism; Risk Assessment /statistics & numerical data; Schizophrenia /diagnosis /drug therapy /metabolism; Sweden /epidemiology

**AccessionNumber**
22011001494

**Date bibliographic record published**
16/11/2011

**Date abstract record published**
04/04/2012