Cost effectiveness of quetiapine in patients with acute bipolar depression and in maintenance treatment after an acute depressive episode

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 study examined the cost-effectiveness of pharmacological treatments in all phases of bipolar disorder, comparing quetiapine with olanzapine and olanzapine plus lithium as well as with other available drugs. The authors concluded that compared with olanzapine, quetiapine was a cost-effective treatment and maintenance therapy for patients with bipolar depression. The study used transparent and well-reported cost-effectiveness methods, so the authors’ conclusions should be robust.

Type of economic evaluation
Cost-utility analysis

Study objective
The study examined the cost-effectiveness of pharmacological treatments in all phases of bipolar disorder, comparing quetiapine with olanzapine and olanzapine plus lithium as well as with other available drugs.

Interventions
Quetiapine 300mg per day was compared with olanzapine 15mg per day as well as other available pharmacological treatments including olanzapine plus lithium, aripiprazole, risperidone, venlafaxine plus lithium, lamotrigine, paroxetine plus lithium, or valproate. Both patients in an initial state of acute depression and in initial state of remission (maintenance) were considered.

Location/setting
UK/secondary and tertiary care.

Methods
Analytical approach:
The analysis was based on a discrete-event simulation with a five-year time horizon. The authors stated that the analysis took the perspective of the UK health care payer.

Effectiveness data:
The sources included various double-blind, randomised, placebo-controlled trials, published meta-analyses, and other studies. In particular, baseline risk was based on the placebo arms of various quetiapine clinical trials, while relative risk was taken from two published meta-analyses. Given the lack of head-to-head comparisons for some drugs, indirect comparisons were made using lithium as common comparator. Side-effects were from published trials. The primary end point was the efficacy of treatment, which was modelled based on the relative risk of events with active pharmacological therapy compared with placebo.

Monetary benefit and utility valuations:
The utility values were from published studies that were identified through a literature review. One of the key sources elicited the utility estimates from patients using the standard gamble method. Another source used the European Quality of life (EQ-5D) instrument and UK tariffs.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and were discounted at an annual rate of
Cost data:
The economic analysis included the costs of drugs and the direct medical costs associated with the treatment of mood events (mania, depression, and remission) and the management of selected adverse events (weight gain and extrapyramidal symptoms). The quantities of resources used were based on clinical trials and a National Institute for Health and Clinical Excellence (NICE) guideline on bipolar disorder. This latter source was used to derive some of the unit costs. Drug costs were taken from the UK NHS Electronic Drug Tariff. Costs were in UK £. The price year was 2011. A 3.5% annual discount rate was applied.

Analysis of uncertainty:
One-way sensitivity analyses were carried out to see how robust the model outcomes were to variations in selected inputs such as costs, start age, time horizon, treatment duration, disutilities and costs of discontinuation and adverse events, dosage of quetiapine and quetiapine as additional therapy. Indirect costs associated with sick leave were included in a sensitivity analysis, using data from a published study. A probabilistic sensitivity analysis was carried out by assigning distributions to the model inputs, excluding unit costs, which were generally based on fixed estimates from price lists.

Results
In acute depression, compared with olanzapine, quetiapine led to a gain of 0.038 QALYs at an additional cost of £323, resulting in an incremental cost per QALY gained of £8,591. The cost-effectiveness of quetiapine varied slightly depending on the comparators used in the different phases (mania, depression and maintenance), but quetiapine remained dominant, as it was more effective and less expensive than the comparator, or cost-effective in most scenarios.

In depression in remission, the costs of maintenance treatment were £18,928 with quetiapine and £18,209 with olanzapine in all phases. The QALYs were and 3.551 with quetiapine and 3.525 with olanzapine in all phases, resulting in an incremental cost per QALY with quetiapine over olanzapine of £27,437. Quetiapine remained dominant or cost-effective in all cases except when it was compared with a strategy of risperidone for manic episodes, venlafaxine plus lithium for depressive episodes, and olanzapine for maintenance.

These findings were robust in most deterministic sensitivity analyses. The most influential inputs were the time horizon, duration and dosage of treatment, and the inclusion of indirect costs.

In the probabilistic sensitivity analysis that used olanzapine as the comparator for acute depression, the likelihood of quetiapine being cost-effective was 21% at a willingness-to-pay threshold of zero and 90% at a threshold of £30,000 per QALY gained. For depression in remission, the likelihood was 29% at zero threshold and 92% at £30,000 per QALY gained.

Authors' conclusions
The authors concluded that compared with olanzapine, quetiapine was a cost-effective treatment and maintenance therapy for patients with bipolar depression.

CRD commentary
Interventions:
The selection of the comparators was clear as the authors stated that olanzapine and olanzapine plus lithium were the two main alternatives to quetiapine used at the time of the study in the UK. Alternative drugs were used in the sensitivity analyses to reflect the less common available treatments.

Effectiveness/benefits:
The clinical data were mainly from clinical trials or meta-analyses of clinical trials which usually have high internal validity. The authors stated that no head-to-head comparisons were available for some treatments and that indirect comparisons were needed. Lithium was chosen as the common comparator and relative risks were calculated. Extensive sensitivity analysis was conducted on all model parameters. QALYs were an appropriate benefit measure to capture the relevant health outcomes of bipolar disorder. Both survival and quality of life were relevant dimensions of health for
patients with bipolar disorder. Other health outcomes were appropriately reported and might be useful for other decision makers.

Costs:
The economic analysis was consistent with the perspective of the public payer. Appropriate cost categories were included in the analysis and a broader perspective was taken in a scenario that included the indirect costs. The unit costs were reported separately from quantities of resources, which enhanced the transparency of the analysis. Clinical management was based on NICE guidelines, which were based on expert opinions. Other quantities of resources used were from clinical trials. Unit costs were from standard UK sources. The price year was explicitly reported, allowing reflation exercises. The cost estimates were varied in the deterministic sensitivity analyses.

Analysis and results:
The study results were clearly presented for a variety of scenarios. Incremental and total outcomes were appropriately reported for all the comparators. The uncertainty was satisfactorily investigated using various approaches, and the methods and results were clearly reported and discussed. The authors highlighted the advantages of using a discrete-event simulation compared with standard Markov models, used in other publications. The findings appear to be specific to the UK and can be difficult to directly transfer to other settings.

Concluding remarks:
The study used transparent and well-reported cost-effectiveness methods, so the authors' conclusions should be robust.

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