Cost-effectiveness of olanzapine long-acting injection in the treatment of patients with schizophrenia in the United States: a micro-simulation economic decision model
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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 olanzapine long-acting injection (LAI). The authors concluded that olanzapine-LAI was cost-effective compared with oral olanzapine and other LAI formulations. The methods were appropriate, but the lack of detail surrounding the derivation of the clinical inputs means that the results may not be robust.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to assess the cost-effectiveness of olanzapine long-acting injection (LAI) compared with alternative antipsychotic agents in the treatment of patients with schizophrenia who had been non-adherent or partially adherent with oral antipsychotics.

Interventions
The study compared olanzapine LAI to oral olanzapine, risperidone-LAI, paliperidone-LAI and haloperidol-LAI.

Location/setting
USA/out-patient secondary care.

Methods
Analytical approach:
A fixed-time advanced Monte Carlo microsimulation with quarterly cycles was used to assess the cost-effectiveness of the interventions under study. The authors reported that the model was developed in consultation with experts in the field and by an academic health economist. The time horizon was one year. The authors reported that the perspective adopted in the economic analysis was that of a third-party health care system payer.

Effectiveness data:
Most of the clinical and effectiveness parameters were derived from published literature. Expert opinion was used where no estimates were identified from the literature. All input parameters were reported. The main effectiveness estimate used in the model was level of adherence to therapy derived from published trials.

Monetary benefit and utility valuations:
Utility data were derived from an expert panel who used published disease-specific utility values and assigned these to each of the nine health state combinations. The authors reported that further details of this analysis were published elsewhere (Furiak, et al. 2009, see 'Other Publications of Related Interest' below for bibliographic details).

Measure of benefit:
The measure of benefit was quality-adjusted life-years (QALYs).

Cost data:
The direct costs included medications (acquisition and administration) and the treatment of patients with schizophrenia and treatment-emergent adverse events. The treatment of schizophrenia included in-patient treatment, day hospital
treatment, emergency room services, physician visits, mental health clinic visits, home care, group interventions, nutritionist visits, nurse visits, and ambulance transport. The costs of treatment-emergent adverse events included treatment for diabetes, hyperlipidaemia, extrapyramidal symptoms, and dyskinesia, and metabolic monitoring. These costs were derived mostly from published literature; expert opinion was used where information was not identified. Details of resource use were presented. All costs were reported in 2009 prices. The currency was US dollars ($).

Analysis of uncertainty:
A series of one-way sensitivity analyses was used to assess the impact of varying the model parameters. A probabilistic sensitivity analyses was undertaken by placing distributions around three key drivers of the model results: adherence levels, rates of relapse and persistence rates. Further probabilistic analyses were performed by sampling two of the three key parameters and then modifying the third.

Results
Mean direct medical costs per patient were $13,151 for oral olanzapine, $14,063 for olanzapine-LAI, $15,207 for risperidone-LAI, $16,190 for paliperidone-LAI and $16,675 for haloperidol-LAI.

Mean QALYs gained per patient were 0.677 for oral olanzapine, 0.711 for olanzapine-LAI, 0.667 for risperidone-LAI, 0.667 for paliperidone-LAI and 0.648 for haloperidol-LAI.

When olanzapine-LAI was compared with oral olanzapine, the additional cost per QALY gained was $26,824. Paliperidone-LAI, risperidone-LAI, and haloperidol-LAI were all dominated (more costly and less effective) by oral olanzapine and olanzapine-LAI.

Probabilistic simulations of 1,000 cohorts of 100 patients, varying the three key parameters, showed that olanzapine-LAI was dominant over oral olanzapine in 12% of simulations and olanzapine-LAI was cost-effective at a $50,000 per QALY threshold in 92% simulations.

Authors' conclusions
The authors concluded that olanzapine-LAI was cost-effective compared with oral olanzapine and other LAI formulations.

CRD commentary
Interventions:
The interventions under study were reported adequately.

Effectiveness/benefits:
The authors reported that clinical and effectiveness estimates were mostly derived from previously published studies. No details were presented on how studies were identified or whether a systematic review of the literature was performed and this made it impossible to determine whether all relevant evidence was included in the model. Methods used to elicit information from the expert panel were not reported. It appeared that network meta-analytic methods were not used even though a lack of head-to-head trials meant that such methods could have been used to derive relative treatment effects. All the information on treatment switching was based on expert opinion. Without more details of the derivation of these clinical estimates, it was unclear how appropriate or uncertain the clinical estimates used in the model were.

Costs:
The authors explicitly reported that the perspective was that of a third-party payer. It appeared that all cost categories were included for this perspective and no major cost was omitted from the analysis. The sources from which unit costs and resource use were derived were reported adequately. All costs used in the model, along with some resource use details, were reported adequately in the study. The price year, time horizon, and currency were all reported.

Analysis and results:
All available evidence on costs and outcomes obtained by the authors was synthesised using a decision analytic model. Appropriate details of the model were given with a diagram. A probabilistic sensitivity analysis was undertaken to
evaluate uncertainty in the main parameters of the model. However, in order to evaluate overall model uncertainty, the authors should have varied all the parameters included in their model. The main limitation reported by the authors was that sparse head-to-head comparative data on the studied depot antipsychotics required assumptions to be made about the therapies. The lack of reporting on methods used to derive clinical inputs made the findings more uncertain than the authors conveyed.

**Concluding remarks:**
The methods were appropriate, but uncertainty surrounding the derivation of the clinical inputs might limit the robustness of the conclusions.

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