A phamaco-economic analysis of patients with schizophrenia switching to generic risperidone involving a possible compliance loss
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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 compared the cost-effectiveness of branded versus generic risperidone, for patients with schizophrenia, assuming different losses in compliance after generic substitution. Assuming the price of the generic substitute was 40% below that of the branded drug, branded risperidone was cost-effective if the loss in compliance was greater than 5.2%. The focus was on the impact of compliance, but the modelling was not fully discussed. This was an exploratory analysis, which could inform discussion, but should not inform decisions.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to assess the impact on cost-effectiveness of switching from branded drugs to generic substitutes, which might lead to lower compliance, for patients with schizophrenia.

Interventions
The interventions were branded oral risperidone versus generic oral risperidone.

Location/setting
Germany/primary and secondary care.

Methods
Analytical approach:
A published discrete-event simulation, with a five-year time horizon, was used to assess the impact of switching patients from the branded oral risperidone to a generic substitute. A brief overview of the model was reported and full details were available in Heeg, et al. 2005, and 2008, (see ‘Other Publications of Related Interest’ below for bibliographic details). The perspective adopted was not explicitly stated.

Effectiveness data:
The effectiveness data appear to be those used in the original publication of the model. The focus of this analysis was compliance which was modelled as a dichotomous variable and shown to be linked directly to the Positive and Negative Syndrome Scale (PANSS) scores and relapse time. These links were based on published literature and expert opinion. The main clinical outcomes were the PANSS score and relapse time. A range of plausible compliance rates, based on authors' opinions, were evaluated, for the generic drug.

Monetary benefit and utility valuations:
The utility values were from published studies. The PANSS was used to assess the patients' symptom severity, which was considered to be the main influence on their quality of life.

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

Cost data:
The economic analysis included the costs of medications, treatment setting (out-patient clinics, sheltered living, day
care, hospitalisation, or long-term care institution), and psychiatric visits. The price of the generic drugs was based on authors’ assumptions. All costs were reported in Euros (EUR).

Analysis of uncertainty:
The parameter uncertainty was investigated using one-way sensitivity analysis, in which the price of the generic risperidone was varied. As compliance loss after generic substitution was based on authors’ assumptions, an analysis of the expected value of sample information was conducted to determine the impact of the size of a future trial, with different estimates of compliance loss due to generic substitution, on the probability of branded risperidone being cost-effective.

Results
The results were presented for various estimates of compliance loss due to generic substitution, compared with branded risperidone. For branded risperidone, the discounted expected QALYs were 3,622 and the total discounted costs were EUR 89,607. For generic risperidone, with no loss in compliance, the expected QALYs were the same at 3,622 and the total costs were EUR 88,378.

With a loss of 2.5%, the expected QALYs were 3,618 and the total costs were EUR 88,850. Comparing branded with generic risperidone resulted in an incremental cost-effectiveness ratio (ICER) of EUR 196,243 per QALY gained. With a loss of 5%, the expected QALYs were 3,615 and the total costs were EUR 89,265. Comparing branded with generic risperidone resulted in an ICER of EUR 46,032 per QALY gained. With a loss of 7.5% and 10%, the branded risperidone was dominant, as it was more effective and less costly than generic risperidone.

These results were sensitive to variation in the price of generic risperidone and in the compliance loss assumed after generic substitution. The expected value of sample information analysis demonstrated that larger numbers of patients included in a trial and increases in compliance loss after generic substitution, increased the probability of branded risperidone being cost-effective at a willingness-to-pay (WTP) threshold of EUR 40,000 per QALY gained.

Authors’ conclusions
The authors concluded that, at a WTP threshold of EUR 40,000 per QALY, it was more cost-effective to treat patients who have schizophrenia with branded risperidone than with generic risperidone if the probability of becoming non-compliant after generic substitution was more than 5.2%.

CRD commentary
Interventions:
The interventions were clearly described, but alternative treatments were not discussed. If there were any, which is likely, this was only a partial analysis.

Effectiveness/benefits:
No systematic review of the literature was reported and no details of the sources of effectiveness data were reported, such as their design, study population, and power calculations. The model inputs were not given, but the only elements that differed between the two interventions were the compliance rate and the costs, which were both based on assumptions. This lack of detail makes it impossible to objectively assess the validity of the data. Similarly, little information was reported on the utilities and an assessment of their validity is not possible.

Costs:
As with the other inputs, the cost data were not well reported. The focus was on the differences in compliance. The perspective adopted, the unit costs, quantities of resources, the sources of unit costs and resources, the discount rate, and the price year were not reported.

Analysis and results:
The model was published and was designed to evaluate long-acting injectable risperidone. Its details were not reported, but a well-conducted discrete-event simulation would be appropriate for evaluating these interventions. The focus of this analysis was to assess changes in compliance rates when switching to a generic drug. The compliance rates were based on assumptions and little evidence was given to support the idea that compliance rates were a major issue. The
authors did not discuss the limitations of their study, except that some assumptions were needed because data were not available.

**Concluding remarks:**
The focus was on evaluating the impact of compliance, but the modelling was not discussed in any depth. This should be considered to be an exploratory analysis, which could inform discussion, but is unlikely to directly inform decisions.

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