Eur J Health Econ 2006 · 7:173–175
DOI 10.1007/s10198-006-0348-z
Published online: 22. July 2006


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# Decision models in the evaluation of psychotropic drugs

## Useful tool or useless toy?

In their contribution to the *European Journal of Health Economics* Beard and colleagues [1] use a decision model to compare health care costs of olanzapine and risperidone treatment for schizophrenia. The model suggested that a treatment strategy of first-line olanzapine is cost-saving over a 1-year period, with additional clinical benefits in the form of avoided relapses in the long-term. From a clinical perspective this finding is undoubtedly relevant, but can physicians and policy makers believe it? The study is presented in a balanced way, assumptions are based on data extracted from clinical trials published in major psychiatric journals, and the theoretical underpinnings of the model are reasonable. Despite these positive aspects we believe that the method used in this study – the decision model approach – is an unsuitable and potentially misleading tool for evaluating psychotropic drugs. Taking the olanzapine vs. risperidone model as an example, this commentary provides arguments to support this statement.

### Model structure

Decision models should reproduce everyday clinical practice. In reality at best they simplify what happens under real-world circumstances. Intriguingly, in the field on mental health what happens under real-world circumstances is very complex, and there is wide heterogeneity both between and within countries [2]. In Italy, for example, mental health services usually comprise one psychiatric ward located in the general hospital and a network of outpatient community mental health centers, each serving a population of 25,000–150,000. Multidisciplinary teams assure continuity of care through inpatient and outpatient treatment, providing domiciliary and rehabilitative care in close conjunction with the general hospital and its district. The local mental health service may in addition have day-care centers and community residential facilities where patients with housing problems are admitted for the medium term. The system works in such a way that patients are expected to have a first contact with the community mental health center of their catchment area and then, depending on symptoms, diagnosis, social needs, and patient preferences, they are usually followed as outpatients by the community team and referred to the local psychiatric ward for acute phases, or to the local community residential facilities for psychosocial problems and residential needs. In this system of care psychiatric hospitals are no longer used. In other countries, however, psychiatric hospitals represent the mainstay of treatment, community facilities are rarely available, and residential facilities are never used [3].

Does the model structure developed in the olanzapine vs. risperidone study take into account this complexity? Is the role of hospital admission developed in the model similar to the role that it plays in the Italian system of psychiatric care or does it resemble the German system of psychiatric care? It seems impossible to answer these questions. It also seems impossible to predict whether the impact of competing pharmacological drugs on resource use and costs would vary according to different conceptualization of psychiatric care. Inevitably, decision models oversimplify clinical practice to such an extent that they cannot be considered a simplification of what happens under real-world circumstances, they just can be considered a distortion of reality.

Additionally, oversimplification occurs not only in the conceptual development of the model framework but also in the possible consequences of prescribing different pharmacological agents. In the field of mental health there is a huge gap between treatment recommendations and prescribing practices, and a conceptual model which presumes the use of olanzapine and risperidone only, without other psychotropic and nonpsychotropic

## Abstract

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# Decision models in the evaluation of psychotropic drugs. Useful tool or useless toy?

### Abstract

A current contribution in the *European Journal of Health Economics* employs a decision model to compare health care costs of olanzapine and risperidone treatment for schizophrenia. The model suggests that a treatment strategy of first-line olanzapine is cost-saving over a 1-year period, with additional clinical benefits in the form of avoided relapses in the long-term. From a clinical perspective this finding is indubitably relevant, but can physicians and policy makers believe it? The study is presented in a balanced way, assumptions are based on data extracted from clinical trials published in major psychiatric journals, and the theoretical underpinnings of the model are reasonable. Despite these positive aspects, we believe that the methodology used in this study-the decision model approach-is an unsuitable and potentially misleading tool for evaluating psychotropic drugs. In this commentary, taking the olanzapine vs. risperidone model as an example, arguments are provided to support this statement.

### Keywords

Decision support techniques · Atypical antipsychotics · Schizophrenia · Health care costs

drugs, is not realistic. In recent years, for example, data have shown that the switch from first to second-generation antipsychotic drugs has been producing a progressive rise in the concurrent prescription of two or more antipsychotic drugs [4]. Given that in clinical practice there are some "classical" antipsychotic combinations, it can be hypothesized that the probability of antipsychotic polypharmacy differs between different compounds, with economic consequences that cannot be ignored. However, the olanzapine vs. risperidone model considered the concomitant use of anticholinergic drugs as a proxy indicator of the development of extrapyramidal symptoms. Although this is a positive aspect, since a substantial proportion of patients suffers from neurological reactions and differences between antipsychotics are thought to exist, it is not clear why other adverse reactions, including, for example, weight gain and metabolic dysregulations, glucose and lipid abnormalities, were not considered. These dysregulations cause the so-called metabolic syndrome, a well-known risk factor for cardiovascular problems [5, 6]. Excluding metabolic dysregulations from the model is particularly problematic in general and specifically in the olanzapine vs. risperidone comparison because their frequency seems higher in olanzapine users in comparison with users of other agents.

## Technical aspects

Decision models are usually based on a set of predefined assumptions. If assumptions are extrapolated from published studies, they are considered "proven assumptions." Unfortunately, in comparison with other fields of medicine, the field of psychotropic drug evaluation is characterized by the following three elements: (a) there are many clinical trials; (b) most trials are financially supported by manufacturers, and data have consistently shown a relationship between sponsor and outcome [7, 8]; and (c) there is a wide variability in response rates. Consequently a key technical aspect is the choice of clinical trials, because different "'proven assumptions" may produce different results with the same model.

In the olanzapine vs. risperidone model, for example, definition of clinical response strongly favored olanzapine over risperidone, according to a clinical trial carried out by the olanzapine manufacturer. However, according to a recently published Cochrane systematic review the two drugs were similarly effective in the short-term, with some differences only in terms of adverse reactions [9]. In terms of risk of relapse the olanzapine vs. risperidone model assumed an annual relapse rate of 19.7% for olanzapine and 23.4% for risperidone. The olanzapine figure was derived from a pooled analysis comparing olanzapine with haloperidol, carried out by the olanzapine manufacturer, where the annual risk of relapse for haloperidol was 28%. Conversely, the risperidone figure was derived from an economic model of schizophrenia developed by the olanzapine manufacturer.

What if the model had assumed an annual risk of relapse for risperidone derived from another study? Csernansky and colleagues [10] carried out a double-blind prospective study randomly assigning outpatients to either risperidone or haloperidol for a minimum of 1 year and found an annual risk of relapse of 25.4% for risperidone and 39.9% for haloperidol. This difference yields an absolute risk reduction of 14.5% and a relative risk reduction of 36%, favoring risperidone over haloperidol. The absolute risk reduction for olanzapine vs. haloperidol, derived from the pooled analysis mentioned above, was 8.3% and the relative risk reduction 29.6%, favoring olanzapine over haloperidol. Comparing these absolute and relative risks it seems problematic to assume a difference in favor of olanzapine over risperidone. Clearly, if the Csernansky et al. data had been used, different findings would have emerged.

Ideally, models should not be based on data from single studies because this inevitably creates a problem of subjective choice. Possibly models should be based on data extracted from systematic reviews, which are unbiased reanalyses of data extracted from clinical trials selected on the basis of predefined inclusion and exclusion criteria. However, in the field of mental health there are many systematic reviews addressing similar clinical ques-

tions with different methods. It is therefore difficult to avoid the problem of subjective selection.

## Conclusion

The decision model approach is an unsuitable and potentially misleading tool for evaluating psychotropic drugs. Physicians and policy makers should be very cautious in basing decisions on economic models. Instead of developing newer, more sophisticated and expensive models researchers should make an effort to generate cost-effectiveness data in everyday patients enrolled in typical settings of care. As health care providers in different settings are those who ultimately pay for new innovations, it seems appropriate that they commission research on cost-effectiveness.

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**Conflict of interest.** No information supplied.

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