Relationship Between Modelling Approaches and Reported Outcomes: Case Studies of Models for the Treatment of Schizophrenia

Birgitta Von Scheele,[1] Josephine A Mauskopf,[2] Thor-Henrik Brodtkorb,[1] Claire Ainsworth,[3] Carmen Galani Berardo,[4] Anita Patel[5]

[1]RTI Health Solutions, Lund, Sweden; [2]RTI Health Solutions, Research Triangle Park, NC, United States; [3]RTI Health Solutions, Manchester, United Kingdom; [4]F. Hoffmann-La Roche Ltd, Basel, Switzerland; [5]Institute of Psychiatry, King's College, London, United Kingdom

BACKGROUND

- Different modelling approaches (i.e. modelling techniques, structural assumptions, and input parameter values) have been used to estimate the cost-effectiveness of antipsychotics used to reduce psychotic symptoms of schizophrenia.
- The International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Modeling Good Research Practice Task Force has developed best practices for conceptualising and developing economic models (Caro et al., 2012) (see Table 1).
- ISPOR recommendations include cross-validation of models to assess how the modelling technique influences the results.
- Studies are needed to evaluate the impact of modelling technique as well as structural assumptions and input parameter values on cost-effectiveness estimates for new health care interventions, including those for the treatment of schizophrenia.
- The objective of this study was to evaluate the relationship between the modelling approaches and the resulting estimates of the cost-effectiveness for various antipsychotic treatments for schizophrenia.

Table 1. Overview of Four Cost-effectiveness Modelling Techniques Used to Estimate the Cost-effectiveness of Schizophrenia Treatments

Modelling Technique	Characteristics	Trade-offs
Decision tree	• Uses tree-like structure to model the consequences of using different therapies • Applies probabilities, costs, and utilities for efficacy and safety outcomes	• Transparent • Computationally efficient • Short time horizon • Limited number of outcomes • Minimal software requirements
Markov model	• Represents disease as a series of mutually exclusive, collectively exhaustive health states • Transition probabilities determine movements of a disease cohort between health states in each fixed cycle • Applies costs and utilities for each health state	• Simple to develop • Transparent • Transitions between health states do not account for disease history of individual patients • Long time horizon possible • May require a large number of health states to capture disease history
Discrete event simulation	• Simulates disease progression for a large number of patients	• Increased complexity
	• Patient pathways strongly influenced by disease history	• Flexibility to match simulated patient experiences to reality
	• Driven by events or time-steps	• Reduced transparency and efficiency
	• Can allow more than 1 event to occur at once	• Advanced software requirements
Micro-simulation	• Individual patients tracked through fixed health states	• Increased complexity
	• Transitions occur in fixed cycle periods	• Reduced transparency and efficiency
	• Only 1 event can occur during each cycle	• Advanced software requirements

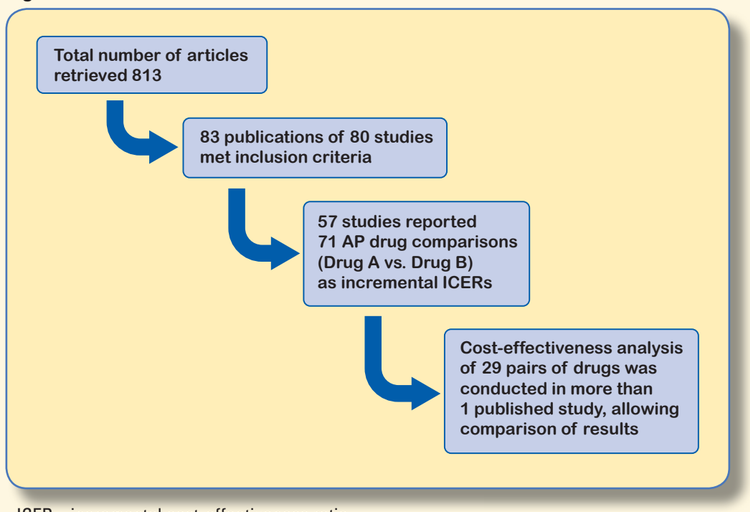
Source: Reproduced from Caro et al., 2012.

METHODS

- A systematic literature review of Medline, EconLit, Embase, and the Cochrane Library from 2000 to 2011 and an Internet search identified published results of schizophrenia cost-effectiveness modelling studies (see Figure 1).
- Two independent reviewers performed searches according to a prespecified protocol limited to English-language articles focusing on schizophrenia and its economics from any country.
- A detailed analysis was performed of sets of studies that compared the same two drugs to assess the relationship between the model technique, structural assumptions, and input parameter values and the cost-effectiveness results (see Figure 2).

RESULTS

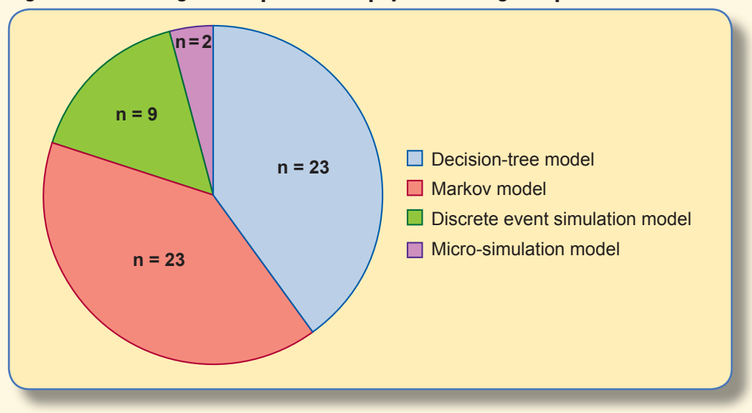
Figure 1. Literature Searches



ICER = incremental cost-effectiveness ratio.

- The most common drug comparisons included:
  - Risperidone long-acting injection (LAI) versus typical depot injections
  - Oral risperidone versus
    - Paliperidone extended release (ER) or LAI
    - Oral haloperidol
    - Ziprasidone
  - Oral olanzapine versus
    - Haloperidol or haloperidol LAI
    - Paliperidone or paliperidone ER or LAI
    - Quetiapine or quetiapine prolonged release (XL)
    - Oral or risperidone LAI
    - Ziprasidone
    - Aripiprazole
  - Clozapine versus oral haloperidol

Figure 2. Modelling Technique for Antipsychotic Drug Comparisons



Consistency of Results

- In 18 of the 29 drug comparisons for which there were multiple studies, the cost-effectiveness results agreed (e.g., Drug A was consistently dominant or cost-effective [defined as ICER ≤$50,000/QALY] versus Drug B or vice versa) regardless of the modelling technique (see Figure 3).
- For the remaining 11 drug comparisons for which there were multiple studies, the results were contradictory (see Figure 4).
- In the 29 drug comparisons for which there were multiple studies:
  - A variety of modelling techniques were used, and no clear relationship was found between modeling technique and the result: contradictory results were found when the same or a different modelling technique was used, and similarly, consistent results were found when the same or a different modelling technique was used.
  - Differences in model structural assumptions that affected consistency of results included whether some or all of the following events were tracked in the model: response rate, relapse rate, discontinuation rate, and adverse events.
  - Differences in the model input values that affected consistency of results included different data sources for response, relapse, and discontinuation rates and for utility weights.

Figure 3. Cost-effectiveness Modelling Techniques for Schizophrenia Treatment and Relationship to Results— Consistent Cost-effectiveness Results

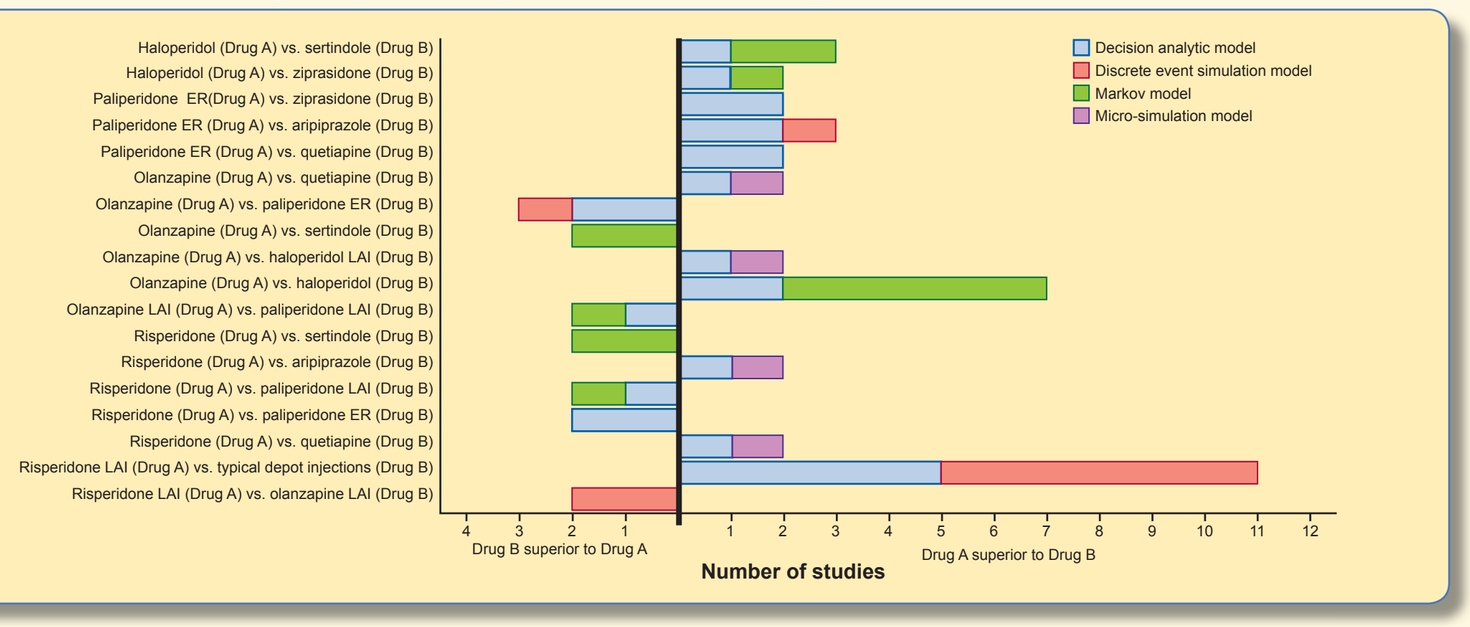
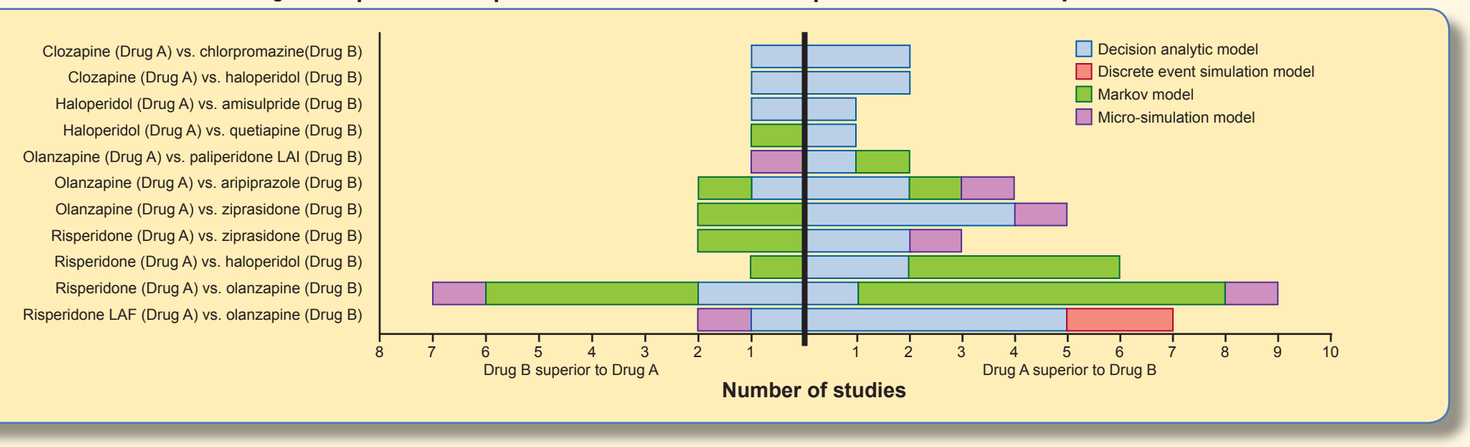


Figure 4. Cost-effectiveness Modelling Techniques for Schizophrenia Treatment and Relationship to Results—Contradictory Cost-effectiveness Results



CONCLUSIONS

- Particular model structural assumptions and input parameter values are more important sources of variability in cost-effectiveness estimates for alternative treatments for schizophrenia than the modelling technique used.
- Nevertheless, the cost-effectiveness results of the majority of modelling studies were in agreement, regardless of the modelling technique; structural assumptions or input parameter values.
- For models in which the results were contradictory, most differences could be explained by one or more of the following:
  - Differences in whether the model included response, relapse, discontinuation, or adverse-event rates
  - Choice of data sources or expert opinion to estimate the probabilities of different treatment outcomes
  - Methodology used to derive the utility weights

REFERENCE

Caro JJ, Briggs AH, Siebert U, Kuntz KM. Modeling good research practices—overview: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force—1. Value Health. 2012 Sep-Oct;15(6):796-803.

For a full list of references from the literature review please contact Josephine Mauskopf at jmauskopf@rti.org.

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CONTACT INFORMATION

Carmen Galani Berardo MD, PhD
Sr. International Payer Strategy Leader
Global Pricing & Market Access

F. Hoffmann-La Roche Ltd.
Grenzacherstrasse 124
4070 Basel Switzerland 4O.Z05.60

Phone + 41 61 688 84 30
Fax + 41 61 688 23 21
E-mail: carmen.berardo@roche.com

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