
Pharmacoeconomic evaluation of schizophrenia in Taiwan: model comparison of long-acting risperidone versus olanzapine versus depot haloperidol based on estimated costs

Yang Y K, Tarn Y H, Wang T Y, Liu C Y, Laio Y C, Chou Y H, Lee S M, Chen C C

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.

Health technology

The study compared three therapeutic strategies using the new generation of antipsychotics (or atypical antipsychotics) for the treatment of schizophrenia. Each strategy comprised a first-line treatment, followed by alternative therapies if the patient did not respond to treatment. The three strategies were as follows.

The risperidone strategy comprised initial treatment with long-acting risperidone, followed by a first alternative of olanzapine, a second alternative of clozapine, and a third alternative of depot haloperidol.

The depot haloperidol strategy comprised initial treatment with depot haloperidol, followed by a first alternative of long-acting risperidone, a second alternative of olanzapine, and a third alternative of clozapine.

The olanzapine strategy comprised initial treatment with olanzapine, followed by a first alternative of long-acting risperidone, a second alternative of clozapine, and a third alternative of depot haloperidol.

The study considered the long-acting form of the antipsychotic drug risperidone, administered as a water-based injection.

Type of intervention

Secondary prevention.

Economic study type

Cost-effectiveness analysis.

Study population

The model analysed data for a hypothetical cohort of 1,000 patients with schizophrenia. The inclusion criteria were patients younger than 35 years of age who had had the illness for less than 5 years, who had received treatment for at least 1 year, and had a score of less than 40 on the Brief Psychiatric Rating Scale (BSRS).

Setting

The setting was the community and primary and secondary care. The economic study was conducted in Taiwan.

Dates to which data relate

The effectiveness evidence data were gathered from studies published between 1991 and 2005. The cost data were taken from medical records and health service sources from 1996 to 2001. The price year appears to have been 2001.

Source of effectiveness data

The estimates for the final outcomes were derived from a synthesis of published studies. In addition, some of the

estimates of effectiveness were derived using expert opinion.

Modelling

A decision analysis model was used to estimate the costs and cost-effectiveness associated with each strategy. The time horizon for the model was 2 years, and this was divided into six 4-month periods. The three mental states considered in the model were response, clinical deterioration and inadequate response. A reduction in the BPRS score of at least 20%, or a marked improvement in clinical symptoms, was defined as a good response to treatment. Clinical deterioration and inadequate response were characterised by the appearance of positive symptoms, renewed delusions, suicidal ideation or behavioural problems. An initial period of non-response was classified as clinical deterioration. A further period was deemed to be an inadequate response, necessitating a change of treatment to an alternative drug as determined by the assigned strategy. The model assumed that patients were responsive to treatment when they responded to the initial treatment and had no more than 2 episodes of clinical deterioration or inadequate response without requiring a change of treatment over the 2 years of follow-up.

Outcomes assessed in the review

The following outcomes were assessed from an ad hoc review of the literature:

the improvement in efficacy attributable to long-acting risperidone compared with oral risperidone;

the incidence of extra-pyramidal side effects associated with each drug;

the average dosages of each drug given to a responding patient;

the average dosages of each drug given to a patient with clinical deterioration; and

the average dosages of each drug given to a patient with an inadequate response.

Study designs and other criteria for inclusion in the review

Not reported.

Sources searched to identify primary studies

Not reported.

Criteria used to ensure the validity of primary studies

Not reported.

Methods used to judge relevance and validity, and for extracting data

Not reported.

Number of primary studies included

The values for the parameters in the model were derived from 8 published studies.

Methods of combining primary studies

The outcomes from the literature were combined by the executive expert committee, with reference to their own clinical experience. This committee comprised six senior psychiatrists, two pharmaco-economists and a representative of Janssen Pharmaceutical Taiwan.

Investigation of differences between primary studies

No differences between the primary studies were investigated.

Results of the review

The following parameters were used in the model.

The improvement in efficacy attributable to long-acting risperidone compared with oral risperidone was 10%.

The incidence of extra-pyramidal side effects was 6% for long-acting risperidone, 30% for oral risperidone, 18% for olanzapine, 55% for depot haloperidol and 5% for clozapine.

The average dosages given to a responding patient were 25 mg/14 days for long-acting risperidone, 3 mg/day for oral risperidone, 15 mg/day for olanzapine, 100 mg/28 days for depot haloperidol and 350 mg/day for clozapine.

The average dosages given to a patient with clinical deterioration were 25 mg/14days for long-acting risperidone, 4 mg/day for oral risperidone, 17.5 mg/day for olanzapine, 150 mg/28 days for depot haloperidol and 425 mg/day for clozapine.

The average dosages given to a patient with an inadequate response were 37.5 mg/14 days for long-acting risperidone, 6 mg/day for oral risperidone, 20 mg/day for olanzapine, 200 mg/28 days for depot haloperidol and 450 mg/day for clozapine.

Methods used to derive estimates of effectiveness

An expert panel of 10 psychiatrists, randomly selected from 158 candidates, provided estimates of treatment response rates. Each panel member was paid an incentive for participating (TWD 3,000), but was blinded to the purpose of the study and the sponsor. The treatment response rates from the expert panel were combined with estimates made by the executive expert committee. The authors did not specify the method used to combine these data. Kaplan-Meier graphs were used to estimate the relapse rate at given intervals of time.

Estimates of effectiveness and key assumptions

The 2-year treatment response rates used in the model were 0.55 for long-acting risperidone, 0.32 for depot haloperidol and 0.45 for olanzapine.

Measure of benefits used in the economic analysis

The measure of health benefit used was the responsiveness rate, This was obtained from expert opinion. The responsiveness rate was defined as the percentage of patients at the 2-year follow-up who had responded to the initial treatment and had no more than two episodes of clinical deterioration or inadequate response without needing a change of treatment in this time. Patients with three or more episodes of clinical deterioration or inadequate response were categorised as non-responsive.

Direct costs

Only the direct medical costs to the health service were considered in the analysis. These were the costs of the outpatient clinic, intensive care, home care, emergency service and drugs. The unit medical cost for treating schizophrenia was calculated from a data file of actual medical expenditure for 200,000 patients between 1996 and 2001. The drug costs were taken from the health service prices for 2001. However, the cost of long-acting risperidone was derived from the price in UK, Germany and Switzerland, for an unspecified year. The cost estimates were reported separately from the other model parameters. Discounting was not applied, which was appropriate as the costs were incurred during two years. No adjustment of the costs to a single price year was reported. However, the price year was likely to have been 2001.

In addition, two versions of the model were used to address the lack of data relating to the costs of the three mental states (response, clinical deterioration and inadequate response). Model I provided a high cost estimate and assumed that all patients received psychiatric intervention, such as outpatient clinics, day hospitals, sub-acute wards, home care services, and other community rehabilitation programmes during the 2-year follow-up. Model II provided a low cost estimate and assumed that only some patients received psychiatric intervention when it was needed during the 2-year follow-up.

The average 4-month costs and total costs were reported.

Statistical analysis of costs

No statistical analysis was conducted to compare the costs of the strategies.

Indirect Costs

The indirect costs were not included, which was appropriate given the study perspective.

Currency

Taiwan new dollars (TWD). The conversion rate to US dollars (\$) was \$1 = TWD 33.

Sensitivity analysis

A sensitivity analysis was conducted to investigate variability in the data. The methods used were not described. The sensitivity analysis investigated the effect of increasing the price of long-acting risperidone and the incremental rate of response to the drug, by 5, 10 and 15%. No justification was given for the chosen range over which the two variables were tested.

Estimated benefits used in the economic analysis

The treatment response rate at 2 years was 0.55 for long-acting risperidone, 0.32 for depot haloperidol and 0.45 for olanzapine. These values were not discounted. The extra-pyramidal side effects were considered in the model.

Cost results

For model I, the total costs associated with each drug were TWD 374,187 for long-acting risperidone, TWD 315,834 for depot haloperidol and TWD 381,285 for olanzapine.

For model II, the total costs associated with each drug were TWD 252,885 for long-acting risperidone, TWD 167,036 for depot haloperidol and TWD 244,055 for olanzapine.

The costs were incurred during 2 years and were not discounted.

Synthesis of costs and benefits

The costs and benefits were summarised in the form of average cost-effectiveness ratios for each drug, by dividing the costs by the benefits. The cost-effectiveness ratios were ranked, but an incremental analysis was not performed.

For model I, the average cost-effectiveness ratios were TWD 678,367 for long-acting risperidone, TWD 1,000,741 for depot haloperidol and TWD 841,875 for olanzapine.

For model II, the average cost-effectiveness ratios were TWD 458,457 for long-acting risperidone, TWD 529,265 for depot haloperidol and TWD 538,872 for olanzapine.

The sensitivity analysis showed that the ranking order of the average cost-effectiveness ratios was unchanged despite increases of up to 15% in the costs and the response rate of long-acting risperidone.

Authors' conclusions

From the perspective of the Taiwanese Bureau of National Health Insurance, long-acting risperidone is likely to be more effective and more cost-effective than either depot haloperidol or olanzapine in the treatment of schizophrenia among stable patients with 1 to 5 years- duration of illness.

CRD COMMENTARY - Selection of comparators

Although no explicit justification was given for the choice of depot haloperidol and olanzapine as comparators, they would appear to represent current practice in the authors' setting. However, the analysis included another drug, clozapine, and this was inconsistent with the objective of the study. In addition, no justification was given for the choice of the three strategies and, in particular, the drug order. You should decide if the comparators represent current practice for the treatment of schizophrenia in your own setting.

Validity of estimate of measure of effectiveness

A systematic review of the literature was not undertaken. Although this is common practice with models, it does not always ensure that the best data available are used in the model. Details of the primary studies and the methods used to combine the primary estimates were not provided. In addition, expert opinion was used for some estimates, such as the efficacy of long-acting versus oral risperidone and the incidence of extra-pyramidal side effects. Therefore, it was not possible to evaluate the validity of the effectiveness model input parameters. A sensitivity analysis was conducted on the response rate of long-acting risperidone, but it was unclear how the range was derived and whether it was appropriate. The principal input parameters for the model were derived from an ad hoc review and relied heavily on expert opinion, which might have biased the results of the health benefit measures obtained. Therefore, the quality of the input parameters is a limiting feature of the study.

Validity of estimate of measure of benefit

The summary measure of benefit was the response rate to drug therapy. This was derived from expert opinion. The commentaries reported earlier are also applicable here. It would have been useful to have taken the quality of life associated with each treatment into consideration, since this might represent an important issue for patients with schizophrenia.

Validity of estimate of costs

The analysis of costs was performed from the perspective of the Taiwanese Bureau of National Health Insurance. It appears that all the relevant categories of costs have been included. Although the costs were reported separately to other model parameters, they were presented in an aggregated manner. Details of the unit costs and the quantities of resources used were not given, and this limits the transferability of the study results to other settings. Kaplan Meier techniques were used to estimate time-to-relapse for the two years of treatment. The costs were treated deterministically and no statistical tests were conducted. Only the cost of long-acting risperidone was explored in the sensitivity analysis. No justification was given for the range over which it was varied, and it was not possible to determine whether it was appropriate. The source of the cost data was reported for each item. The cost of long-acting risperidone was based on European prices for the drug because a local price was not available. Discounting was not applied, which was appropriate given the two-year study horizon. However, no adjustments appear to have been made to a single price year, and this decreases the generalisability of the results.

Other issues

The authors made limited comparisons of their findings with those from other studies, and reported similar findings to one previous Taiwanese study. Although studies in other settings found that olanzapine was the most cost-effective therapy, the authors stated that the results were not directly comparable as different treatment modalities were used. Presumably, this would also limit the generalisability of the current findings to other settings, as few sensitivity analyses were carried out. The authors do not appear to have presented their results selectively. The inclusion criteria resulted in a highly selected sample population which represented those patients expected to be most responsive to treatment. This

would result in an overestimation of the benefits of long-acting risperidone if the results were applied to patients with a chronic condition.

The authors noted that the main limitation of the study was the reliance on expert opinion to form estimates and the consequent risk of bias. Specifically, there was uncertainty surrounding the response rates to the different drug therapies. In addition, the authors acknowledged that the cost figures were underestimates of the actual cost of side effects for each agent as costs for several side effects were omitted (such as weight gain, sexual dysfunction, endocrine dysfunctions and cardiovascular problems). An incremental cost-effectiveness ratio would have been a better measure of the relative value of the three drug interventions instead of simply ranking the cost-effectiveness ratios. It was not possible to recalculate the same cost-effectiveness ratios from the data presented.

The authors acknowledged the financial support of Janssen Pharmaceutical Taiwan, manufacturers of long-acting risperidone.

Implications of the study

The authors stated that long-acting risperidone is more cost-effective than either olanzapine or depot haloperidol for treating stable schizophrenic patients with a short illness duration, in Taiwan. They recommended that a prospective study be undertaken to confirm their findings.

Source of funding

Supported in part by Janssen Cilag Taiwan.

Bibliographic details

Yang Y K, Tarn Y H, Wang T Y, Liu C Y, Laio Y C, Chou Y H, Lee S M, Chen C C. Pharmacoeconomic evaluation of schizophrenia in Taiwan: model comparison of long-acting risperidone versus olanzapine versus depot haloperidol based on estimated costs. *Psychiatry and Clinical Neurosciences* 2005; 59(4): 385-394

PubMedID

16048443

DOI

10.1111/j.1440-1819.2005.01390.x

Indexing Status

Subject indexing assigned by NLM

MeSH

Adult; Antipsychotic Agents /adverse effects /economics /therapeutic use; Benzodiazepines /adverse effects /economics /therapeutic use; Cohort Studies; Cost Savings; Costs and Cost Analysis; Decision Trees; Delayed-Action Preparations; Dyskinesia, Drug-Induced /economics /epidemiology; Female; Hospitalization /economics; Humans; Long-Term Care /economics; Male; Mental Health; Models, Economic; Patient Compliance; Public Health; Risperidone /adverse effects /economics /therapeutic use; Schizophrenia /drug therapy /economics; Schizophrenic Psychology; Taiwan; Treatment Outcome

AccessionNumber

22005006456

Date bibliographic record published

30/06/2006

Date abstract record published

30/06/2006

