Clinical and economic outcomes of olanzapine compared with haloperidol for schizophrenia: results from a randomised clinical trial


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
Olanzapine compared with haloperidol for treatment of schizophrenia.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
US-residing patients with schizophrenia who were at least 18 years old and who either had a baseline Brief Psychiatric Rating Scale score (BPRS) higher than 18 and/or were no longer tolerating current antipsychotic therapy.

Setting
Hospital. The study was carried out in the USA.

Dates to which data relate
Effectiveness and resource use data were collected from a single study published in 1997. Cost data were derived from 1995 sources. The price year was 1995.

Source of effectiveness data
Effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was undertaken on the same patient sample as that used in the effectiveness study and was carried out prospectively alongside the effectiveness study.

Study sample
817 US-residing patients were included in the trial. 551 patients were randomised to olanzapine and 266 patients to haloperidol. Of these patients, 344 continued on to the maintenance phase (270 patients treated with olanzapine and 74 patients treated with haloperidol). No power calculations were reported. Reasons for exclusion included: documented treatment resistance to antipsychotic agents; DSM-III-R organic mental disorder or substance-use disorder; and/or a serious, unstable medical illness.
Study design
This was a multi-centre, randomised, double-blind clinical trial involving 66 clinical centres in the USA. Patients were followed-up for 52 weeks. Of the 817 original patients, 344 continued on to the maintenance phase.

Analysis of effectiveness
The analysis was based on the intention to treat principle. The primary health outcomes studied included acute and maintenance phase completion rates. At analysis, groups were shown to be comparable in terms of demographic characteristics.

Effectiveness results
The acute phase completion rate was significantly greater for patients treated with olanzapine, (p<0.001). A significantly greater proportion of patients treated with haloperidol discontinued the acute phase because of a lack of efficacy (p<0.001) and patient decision (p=0.006). A significantly greater proportion of patients treated with haloperidol discontinued the maintenance phase as the result of sponsor decision, (p=0.007).

Clinical conclusions
Patients treated with haloperidol were more likely to discontinue both the acute phase and the maintenance phase.

Modelling
For all patients, those who completed the study and those who discontinued after the acute phase, total costs per day were calculated by dividing each patient's total health care costs by the number of days the patient was in the trial, the result of which was multiplied by the total number of days for the phase in which costs were being compared. ANOVA models were used in which the dependent variable was the logarithm of costs per exposure rate and the independent variables were baseline demographics, clinical variables, previous psychiatric hospitalisations, geographical region, and treatment group.

Measure of benefits used in the economic analysis
The primary measures of benefit were the BPRS extracted from the Positive and Negative Syndrome Scale (PANSS) and quality of life (QOL). QOL outcomes were evaluated using the Quality of Life Scale (QLS).

Direct costs
Direct costs were not discounted given the time frame of the study (1 year). The quantities and costs were reported separately. Direct costs included inpatient and outpatient medical costs and medication costs incurred in both the acute and maintenance phases. The quantity/cost boundary adopted was that of the health service. The estimation of quantities and costs was based on actual data. The prices for outpatient and inpatient physician services were based on Healthcare Financing Administration Data. Costs for days in hospital were estimated based on cost data for inpatient psychiatric and medical stays from the Monroe-Livingston Mental Health Capitation Program and were inflated to 1995 prices using the medical care component of the consumer price index. Costs per day for concomitant medications were estimated using the Physicians GenRx and the Red Book. The price year was 1995.

Statistical analysis of costs
Not reported.

Indirect Costs
Not reported.
Currency
US dollars ($).

Sensitivity analysis
Not reported.

Estimated benefits used in the economic analysis
After 6 weeks of treatment, 38.5% of patients treated with olanzapine and 26.8% of patients treated with haloperidol demonstrated clinically important improvements in BPRS total scores, (p=0.002). Patients treated with olanzapine had a trend towards greater improvements in QLS total scores compared with patients treated with haloperidol (32.7% versus 24.8%, p=0.094). During the maintenance phase, no significant differences in the proportion of patients with clinical improvements based on the BPRS or QLS were observed at the time points examined.

Cost results
Mean total medical costs during the acute phase were $388 more for patients treated with haloperidol, (p=0.033). Acute phase mean olanzapine medication costs were significantly greater than haloperidol medication costs, (p<0.001). Patients treated with olanzapine had significantly lower inpatient (p=0.038) and outpatient (p=0.001) costs than patients treated with haloperidol. Mean total medication costs for patients treated with olanzapine in the maintenance phase were found to be $636 less than for patients treated with haloperidol, (p=0.128). During the maintenance phase, patients treated with haloperidol had significantly lower mean medication costs, (p<0.001). Patients treated with olanzapine had significantly lower mean inpatient (p=0.044) and outpatient (p=0.038) costs than patients treated with haloperidol.

Synthesis of costs and benefits
Cost and benefit measures were not combined into a cost-effectiveness ratio.

Authors’ conclusions
Olanzapine treatment was more effective than haloperidol in producing clinical response in the acute phase. In addition, olanzapine treatment led to reductions in inpatient and outpatient costs which more than offset olanzapine’s higher medication costs relative to haloperidol.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. You, as a user of this database, should verify whether these health technologies are relevant to your setting.

Validity of estimate of measure of benefit
Relevant measures of benefit were used. The degree to which these results are generalisable to community practice is unclear. Clinical trials impose standardised treatment regimens which may not reflect the actual treatment of patients in community settings. In addition, the patient inclusion and exclusion criteria, while broad, in some instances, excluded patients with comorbidities which would commonly be seen in practice. Another limitation is the lack of data after patient withdrawal.

Validity of estimate of costs
Only direct costs were included. Indirect costs were not considered. Costs were estimated by assigning prices from a standard list and, hence, do not reflect actual accounting costs. No sensitivity analysis was performed on costs. Efforts to address incomplete data collection may have led to an underestimation of the total cost difference between the olanzapine and haloperidol treatment groups. Cost distributions were highly skewed.
Other issues
The sample size and associated statistical power may explain the lack of difference in statistical significance in maintenance phase QOL findings. The generalisability of the results to other settings or countries was discussed and appropriate comparisons with other relevant studies were made. The authors did not present their results selectively. The study enrolled US-residing patients with schizophrenia and this was reflected in the authors’ conclusions.

Implications of the study
Olanzapine resulted in greater improvements in clinical symptoms and reductions in inpatient and outpatient costs offset olanzapine's greater medication costs.

Source of funding
Funded by Eli Lilly and Company, Indianapolis, Indiana, USA.

Bibliographic details

PubMedID
10537964

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Adult; Antipsychotic Agents /economics /therapeutic use; Benzodiazepines; Double-Blind Method; Haloperidol /economics /therapeutic use; Humans; Pirenzepine /anals & derivatives /economics /therapeutic use; Schizophrenia /drug therapy /economics; Treatment Outcome; United States

AccessionNumber
22000008077

Date bibliographic record published
31/05/2000
Date abstract record published
31/05/2000