Cost-effectiveness of different clinical interventions for reducing the burden of schizophrenia in Spain


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 aimed to compare different clinical interventions for the treatment of schizophrenia at the population level. In particular:

- older antipsychotic drugs alone (haloperidol);
- new antipsychotic drugs alone (risperidone);
- older antipsychotic drugs in combination with psychological treatment;
- new antipsychotics in combination with psychological treatment;
- older antipsychotics in combination with case management and psychological treatment;
- new antipsychotics in combination with case management and psychological treatment; and
- current situation in the authors’ settings regarding the use of antipsychotics (39% use of conventional oral antipsychotics such as haloperidol, 29% use of risperidone, 15% use of olanzapine and 16% use of depot antipsychotics).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised the general population in Spain. Therefore, no inclusion or exclusion criteria were applied.

Setting
Although the setting was not explicitly stated, it appears to have been the community. The economic study was carried out in Spain.

Dates to which data relate
The demographic data were based on official sources published in 2000 (Spanish National Statistics Institute). The effectiveness and epidemiological data were derived from sources published between 1995 and 2005. Resource use was derived from sources published in 2003. The cost data were obtained from sources published in 1999 and 2005. The price year was 2000.
Source of effectiveness data
The effectiveness data were derived from a review and synthesis of published data, augmented by authors’ assumptions.

Modelling
The authors constructed a state-transition population model (PopMod). Although a lifetime analytic horizon was applied, the duration of treatment was 10 years. Based on population epidemiological data, the prevalence of schizophrenia was estimated using DisMod II. DisMod II is a disease model designed by the WHO that allows the burden of and projection of the disease to be modelled.

Outcomes assessed in the review
The following input parameters were used in the models:

- the annual population incidence of schizophrenia according to gender;
- the case-fatality rate;
- the remission rate;
- the efficacy of treatment options and rate of extra-pyramidal side effects of treatment options (change in Brief Psychiatric Rating Scale (BPRS) and use of anti-Parkinson medication); and
- the effectiveness of additional psychological intervention.

Study designs and other criteria for inclusion in the review
Prospective follow-up studies, official sources (Spanish Psychiatric Case Registers) and published meta-analyses were included in the review. However, specific criteria for inclusion in the review were not reported.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
It appears that no criteria were applied to ensure the validity of the primary studies.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
Overall, 7 primary studies were used as sources of effectiveness evidence.

Methods of combining primary studies
The prevalence of disease was estimated using the DisMod II model, whilst most effectiveness estimates were based on published meta-analyses. However, no further methods of combining the results of the primary studies were reported.

Investigation of differences between primary studies
The authors do not appear to have investigated differences between the primary studies.
Results of the review
The annual population incidence of schizophrenia was 3.0 per 1,000 inhabitants per year for men and 2.86 per 1,000 inhabitants per year for women.

The standardised mortality ratio was 1.4.

The efficacy of treatment option and rate of extra-pyramidal side effects was estimated as the effect size.

The estimated Cohen's coefficient (d) was 0.465 for haloperidol and 0.495 for risperidone.

Methods used to derive estimates of effectiveness
The authors appear to have made assumptions when deriving some estimates of effectiveness.

Estimates of effectiveness and key assumptions
The Cohen's coefficient of the additional effect size of combined pharmo/psychosocial treatment was assumed to be 0.05.

The instantaneous remission rate per person was assumed to be 0.01 (1 per 100).

These assumptions were based on data in the literature.

Measure of benefits used in the economic analysis
Disability measures (i.e. disability-adjusted life-years, DALYs, averted) were used as the measure of benefit in the economic analysis. DALYs averted were derived from the model and were estimated as the difference between the total number of healthy years lived by the population with and without intervention. Social preferences were also represented by applying non-uniform age weights (less weight to years lived at younger and older ages). A unique disability value was applied for schizophrenia disease, regardless of the course of the disease and related symptoms.

Direct costs
The health service costs used in economic analysis were for hospital inpatient days, outpatient visits, drugs and laboratory tests. The costs of the programme covered central planning of the intervention, policy and administration functions, the training of health providers, and preventive programmes. The costs and the quantities were not reported separately. As the time horizon for the intervention implementation was 10 years, the costs were appropriately discounted at an annual rate of 3%. Resources used at patient level and programme-level resources were based on existing guidelines and published sources. The unit costs were derived from published sources. All costs were reported for the price year 2000.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs were not included in the analysis.

Currency
Euros (EUR). The costs were converted to US dollars ($) using the exchange rate for 31 December 2000, $1 = EUR 1.062. The costs were also reported in International Dollars ($) using appropriate Purchasing Power Parity (PPP) exchange rates.
Sensitivity analysis
A one-way sensitivity analysis was conducted to investigate the robustness of the cost-effectiveness results to variability in the data. The parameters investigated were the impact of analytical social preferences (i.e. discounting and age weighting), the disability weight effect size associated with every treatment option (+/-10%), and the cost per dose of risperidone (brand and generic). Further sensitivity analyses were conducted using McLeaf software, which reports the results in stochastic league tables as well as in graphs that plot the probability of inclusion of independent sets of mutually exclusive interventions in the optimal mix of interventions at different levels of resources availability.

Estimated benefits used in the economic analysis
The total discounted DALYs averted annually in Spain were:

2,558 in the current situation arm;
2,808 in the conventional antipsychotic at 90% coverage;
3,416 in the risperidone (patented or generic) at 90% coverage;
5,532 when using conventional antipsychotics in combination with psychosocial treatment at 90% coverage;
6,489 when using risperidone (patented or generic) in combination with psychosocial treatment at 90% coverage;
7,027 when using conventional antipsychotics in combination with psychosocial treatment and case management at 90% coverage; and
7,259 when using risperidone (patented or generic) in combination with psychosocial treatment and case management at 90% coverage.

Cost results
The total annual intervention costs for the whole Spanish population were:

$198 million in the current situation arm;
$152 million when using conventional antipsychotics at 90% coverage arm;
$274 million when using risperidone (patented) at 90% coverage; and
$182 million when using generic risperidone at 90% coverage.

The cost of using conventional antipsychotics in combination with psychological treatment at 90% coverage was $161 million.

The costs of using risperidone patented or generic in combination with psychosocial treatment at 90% coverage were $289 million (patented) and $196 million (generic), respectively.

The cost of using conventional antipsychotics in combination with psychosocial treatment and case management at 90% coverage was $208 million.

The costs of using risperidone patented and generic in combination with psychosocial treatment and case management at 90% coverage were $304 million (patented) and $211 million (generic), respectively.

Synthesis of costs and benefits
Undiscounted results were as follows:
the current situation resulted in a cost of $65,774 per DALY averted;
conventional antipsychotics at 90% coverage resulted in a cost of $46,011 per DALY averted;
risperidone patented or generic at 90% coverage resulted in costs of $68,351 and $45,197 per DALY averted, respectively;
use of conventional antipsychotics in combination with psychosocial treatment at 90% coverage resulted in a cost of $24,818 per DALY averted;
risperidone patented or generic in combination with psychosocial treatment at 90% coverage resulted in costs of $37,859 and $25,670 per DALY averted, respectively;
use of conventional antipsychotics in combination with psychosocial treatment and case management at 90% coverage resulted in a cost of $25,166 per DALY averted;
risperidone patented or generic in combination with psychosocial treatment and case management at 90% coverage resulted in costs of $35,663 and $24,767 per DALY averted, respectively.
The sensitivity analyses demonstrated that the results were most sensitive to changes in social preferences and the substitution of a generic version for a branded version of risperidone.

**Authors' conclusions**
The use of generic risperidone in combination with psychosocial treatment and case management seems to be the most cost-effective options. "The addition of a psychosocial treatment to pharmacotherapy increases both the efficacy and the cost-effectiveness of interventions in reducing the burden of schizophrenia."

**CRD COMMENTARY - Selection of comparators**
The selection of the comparators was explicitly justified. The study compared treatment strategies at the population level. You should decide if this represents a widely used technology in your own setting.

**Validity of estimate of measure of effectiveness**
Although some effectiveness estimates were taken from published meta-analyses, a systematic review was not undertaken. This does not ensure that the best available data are used in the model. In addition, the data from available studies were used selectively. The impact of differences between the studies identified was not taken into account when estimating effectiveness. However, the authors did apply age weights to health gains to represent social preferences. The weights applied and the extrapolation methods used were not reported. This may hinder the reworking of the analysis for other settings. Some estimates of effectiveness were based on authors' assumptions, which were justified with reference to the medical literature.

**Validity of estimate of measure of benefit**
The authors used DALYs as the measure of benefit in the economic analysis. However, the valuation tool employed and the time of valuation were not reported. In addition, the values were not tested in sensitivity analyses, thereby introducing some uncertainty into the results.

**Validity of estimate of costs**
Although the perspective adopted in the economic analysis was not reported, it was not societal as the indirect costs were not included. The costs and the quantities were not reported separately, which will prevent the analysis from being easily revised for different settings. The resource use and cost data were taken from published sources, but the costs were treated deterministically and no sensitivity analyses were conducted to assess the robustness of the estimates used. This may limit the interpretation of the study findings. Appropriate currency conversions were conducted, discounting
was carried out and the price year was reported, which will aid any future inflation exercises.

**Other issues**  
The authors compared their results with the findings of other studies of schizophrenia and found them generally to be in agreement. However, comparisons with studies referring to different mental disorders (bipolar disorder or depression) were not possible because of differences in the methodology used. The issue of the generalisability of the results was not directly addressed. The authors do not appear to have presented their results selectively, although results from the sensitivity analyses were not reported in detail. The study was conducted at the general population level and this was reflected in the authors’ conclusions. The lack of Spanish studies at the population level constituted one of the main limitations to the study. In addition, due to the lack of available data, productivity losses and the family burden of disease (e.g. informal care giving) were not accounted for in the analysis.

**Implications of the study**  
The authors did not make explicit recommendations for changes in policy or practice. In light of the study findings, the authors recommended that future research should focus on the development of new pharmacological and psychosocial strategies that will improve the long-term care of patients with schizophrenia. The discussion highlighted areas where more research-based information is necessary.

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**Bibliographic details**  

**Other publications of related interest**  
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**Indexing Status**  
Subject indexing assigned by NLM

**MeSH**  
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