Cost-effectiveness of fluoxetine plus pindolol in patients with major depressive disorder: results from a randomized, double-blind clinical trial

Sacristan J A, Gilaberte I, Boto B, Buesching D P, Obenchain R L, Demitrack M, Sola V P, Alvarez E, Artigas F

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

Fluoxetine plus pindolol for patients with depressive disorder.

Type of intervention

Treatment.

Economic study type

Cost-effectiveness analysis.

Study population

Patients over the age of 18 years suffering from unipolar major depression (DSM-IV criteria) with moderately severe symptoms, scoring at least 18 on the Hamilton Depression Rating Scale (HAMD). Exclusion criteria included pregnancy, organic brain disease/history of seizures, delusions or hallucinations, a recent history of substance abuse, or recent heart attack.

Setting

The practice setting was primary care centres. The economic analysis was carried out by the Spanish Ministries of Health and Industry, Spain.

Dates to which data relate

It was not clear when the effectiveness and resource data were obtained. 1996 prices were used.

Source of effectiveness data

The evidence for the cost-effectiveness of fluoxetine plus pindolol versus fluoxetine plus placebo for patients with depressive disorder was obtained from a single study.

Link between effectiveness and cost data

Prospective resource data were collected from the effectiveness study sample.

Study sample

A total of 111 patients were selected for inclusion in the study: 55 were allocated to the control group and 56 to the comparator group. Baseline control characteristics were: 61.8% female, mean age 44.1 years, median HAMD score 21, and mean previous depressive episodes 0.6. Baseline comparator group characteristics were: 80.4% female, mean age 42.6 years, median HAMD score 22, and mean previous depressive episodes 0.9. No power calculations were stated in the determination of the required study sample size. Exclusions and refusals to participate were not reported.

Study design
This was a single centre, double-blind, randomised controlled trial. The method of randomisation was not explicitly stated. No loss to follow-up was reported.

Analysis of effectiveness
The basis for the analysis of the clinical study (intention to treat or treatment completers) was not stated. The primary health outcomes were response rate and remission rate, expressed as percentages. The proportion of women and patients with at least one previous episode of depression were lower in the fluoxetine plus placebo group, ($p < 0.05$).

Effectiveness results
A significantly greater number of patients in the fluoxetine plus pindolol group experienced a therapeutic response at 6 weeks than in the fluoxetine plus placebo group: 74.5% +/- 0.4% versus 58.9% +/-0.5%, ($p<0.05$). This represents an incremental effectiveness of +15.6%. The remission rate in the fluoxetine plus pindolol group was 60% +/- 0.5% versus 44.6% +/- 0.5% in the fluoxetine plus placebo group, ($p<0.05$), an incremental effectiveness of +15.9%.

Clinical conclusions
In terms of response and remission rates, fluoxetine plus pindolol offers improved outcomes at statistically significant levels.

Measure of benefits used in the economic analysis
The health benefits used in the economic analysis were response rate and admission rate, directly derived from the effectiveness measures reported above.

Direct costs
Direct cost estimations, derived from governmental and hospital data, included healthcare professional visits, healthcare facilities, procedures related to the treatment of depression, hospitalisations, and concomitant medication. Costs appear to have been calculated from the perspective of the health service. Quantities and costs were not reported separately. The price year was 1996.

Statistical analysis of costs
Direct medical cost distributions were analysed using a Kolmogorov-Smirnov test, and found to be non-normal. The Mann-Whitney U test was therefore used to analyse the cost results. Bootstrapping techniques were used to calculate confidence intervals for the incremental cost-effectiveness ratios.

Currency
Spanish pesetas (Pta), with an estimation that $1 = 145 Pta.

Sensitivity analysis
No sensitivity analysis was performed.

Estimated benefits used in the economic analysis
A significantly greater number of patients in the fluoxetine plus pindolol group experienced a therapeutic response at 6 weeks: 74.5% +/- 0.4% versus 58.9% +/-0.5% in the fluoxetine plus placebo group, ($p<0.05$). The incremental effectiveness was +15.6%. The remission rate in the fluoxetine plus pindolol group was 60% (+/- 0.5%) versus 44.6% (+/- 0.5%) in the fluoxetine plus placebo group, ($p<0.05$). The incremental effectiveness was +15.9%.

Cost results
Average total costs were Pta 2,508 (+/- 4,707) for the pindolol group, and Pta 31,870 (+/- 115,431) for the placebo group, producing an incremental cost of Pta -29,362.

Synthesis of costs and benefits
Although the intervention was demonstrated to be the dominant strategy (less costly and more effective) the authors reported both average and incremental cost-effectiveness ratios, using cost per percentage response and cost per percentage remission. The average C/E response was Pta 3,366 in the fluoxetine plus pindolol group and Pta 54,042 in the fluoxetine plus placebo group. Incremental cost-effectiveness response analysis found that the pindolol group versus placebo group point estimate was Pta -187,764 (CI: -3,746,062 to 12,403). Similarly, the incremental cost-effectiveness remission analysis found that the pindolol group versus placebo group point estimate was Pta -190,940 (CI: -7,600,979 to 2,119).

Authors' conclusions
The results show that fluoxetine plus pindolol, over a course of 6 weeks of treatment, incurs lower direct medical costs than treatment with fluoxetine plus placebo, whilst increasing therapeutic response, increasing remission and reducing admission to hospital.

CRD COMMENTARY - Selection of comparators
The selection of fluoxetine plus placebo was justified in order to assess the influence of additional medication in the form of pindolol.

Validity of estimate of measure of benefit
The two principal benefit measures were derived from a randomised trial and are therefore likely to have high validity. The economic data were collected prospectively alongside the trial, which reduces the likelihood, inherent in retrospective economic evaluations, of various biases being present. Some limitations were that no medication consumption relating to side-effects was mentioned, and no power calculations were stated in the determination of an adequate study sample size. Moreover, the analysis was conducted over a period of only 6 weeks, when antidepressants are required to be prescribed for at least 6 months (WHO guidelines, cited by the authors) to have their fullest effect, and this may explain why no side-effects were reported in the paper. The two groups were not comparable in all respects at baseline, which may have influenced the results.

Validity of estimate of costs
The authors took into account the non-normal distribution of cost data in their statistical analyses and used appropriate tests. No sensitivity analysis of prices was conducted. Since all costs were incurred in less than 1 year, discounting was unnecessary. The price year was reported. The major limitation of the reporting of costs was that only totals for each category were reported.

Other issues
The study has a number of merits as the economic evaluation was undertaken alongside the clinical trial, and issues around sample size requirements for clinical and economic analyses were addressed. However, it is rather surprising that the authors utilised some analyses that were either nugatory or misleading. Their results demonstrated that the intervention was both more effective and less costly, which is sufficient information for a decision-maker to make an optimal choice. The reporting of average cost-effectiveness ratios is of limited value and is mostly misleading, and incremental ratios are not required in situations of extended dominance (the CIs did, however, change direction and were extremely wide). As such, the analysis was overly complicated. The issue of generalisability was well addressed and the authors conclude that the results have limited validity outside the Spanish setting. This was an early study of the use of fluoxetine plus pindolol for this patient population and therefore comparisons with other studies were not made.

The sample appears to have been representative of the population to which it relates.

Implications of the study
Further long-term studies are required with more adequate clinical and cost-effectiveness methodologies in order to confirm the findings of this and similar studies.

Source of funding
Supported by Lilly Laboratories. Work conducted under the R & D Spanish Plan for the Pharmaceutical Industry (Farma II) from the Spanish Ministries of Health and Industry.

Bibliographic details
Sacristan J A, Gilaberte I, Boto B, Buesching D P, Obenchain R L, Demitrack M, Sola V P, Alvarez E, Artigas F. Cost-effectiveness of fluoxetine plus pindolol in patients with major depressive disorder: results from a randomized, double-blind clinical trial. International Clinical Psychopharmacology 2000; 15(2): 107-113

PubMedID
10759342

Indexing Status
Subject indexing assigned by NLM

MeSH
Adult; Antidepressive Agents, Second-Generation /economics /therapeutic use; Cost-Benefit Analysis; Depressive Disorder /drug therapy /economics; Double-Blind Method; Drug Therapy, Combination; Female; Fluoxetine /economics /therapeutic use; Health Care Costs /statistics & numerical data; Humans; Male; Middle Aged; Pindolol /economics /therapeutic use; Serotonin Antagonists /economics /therapeutic use

AccessionNumber
22000000602

Date bibliographic record published
30/04/2001

Date abstract record published
30/04/2001