Pharmacoeconomic analysis of sertraline treatment of depression in patients with unstable angina or a recent myocardial infarction

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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 use of 24 weeks' sertraline, a selective serotonin reuptake inhibitor, for the treatment of depressive disorders in patients with unstable angina (UA) or a recent myocardial infarction (MI). Sertraline was initially given at a dosage of 50 mg/day and could be gradually increased to a maximum of 200 mg/day.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients who were hospitalised for acute coronary syndromes and who met the American Psychiatric Association's DSM-IV criteria for major depressive disorder (MDD).

Setting
The setting was secondary care and a hospital. The economic study was carried out in the USA.

Dates to which data relate
The clinical and resource use data were derived from a study published in 2002. The costs were estimated in 2001 and 2002. A unique price year was not reported.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was carried out prospectively on the same sample of patients as that used in the clinical trial.

Study sample
It was not stated whether power calculations were carried out to justify the sample size. Of the 11,546 patients initially screened, 8,191 failed to meet MI or UA criteria, or had other life-threatening diagnosis, 2,799 failed to meet modified MDD criteria, and 187 failed to meet full DSM-IV criteria or dropped out. Thus, the final study sample comprised 369 patients. There were 186 patients assigned to the sertraline group and 183 patients assigned to the placebo group. The mean age was 56.8 (+/-11) years in the sertraline group and 57.6 (+/- 10.4) years in the placebo group, and the proportions of men were 63% and 64%, respectively. About half of the patients in both groups had experienced at least
one episode of MDD, and more than 40% in both groups had experienced an MI.

**Study design**
This was a prospective, randomised, double-blind, clinical trial that was carried out at 40 outpatient cardiology centres and psychiatry clinics in the USA, Europe, Canada and Australia. Treatment was provided for 24 weeks. Details on randomisation and follow-up were not reported. The length of follow-up might have been 6 months. Researchers blinded to treatment allocation assessed the outcomes. Events occurring in the 30 days following the study duration were also recorded because they might have been treatment-related.

**Analysis of effectiveness**
The clinical outcomes appear to have been assessed among all treated patients (intention to treat, ITT). The outcome measure used in the analysis was the frequency of psychiatric or cardiovascular hospitalisations, emergency room visits, and cardiac catheterisation and revascularisation procedures. These were obtained from serious adverse events reports that were collected for all patients hospitalised during the study period. At study entry, the patients in the two groups were comparable in all clinical and demographic characteristics.

**Effectiveness results**
The number of psychiatric or cardiovascular hospitalisations was lower in the sertraline group than in the placebo group (55 versus 76). This difference did not achieve statistical significance, (p=0.054).

The majority of the hospitalisations were for cardiovascular events or procedures.

The number of emergency room visits was 26 in the sertraline group and 40 in the placebo group.

The total number of cardiac catheterisation and revascularisation procedures was 41 in the sertraline group and 48 in the placebo group.

**Clinical conclusions**
The effectiveness study showed that fewer adverse events were observed in the sertraline group than in the placebo group, although the difference was not statistically significant.

**Modelling**
The authors stated that a decision tree was constructed to describe treatment patterns on the basis of trial data, but no other details of the model were provided.

**Measure of benefits used in the economic analysis**
No summary benefit measure was used in the economic analysis. In effect, a cost-minimisation analysis was carried out since no statistically significant differences between the groups were found.

**Direct costs**
The analysis was carried out from the perspective of the third-party payer. Only costs strictly related to hospitalisations, emergency room visits, cardiac procedures and drug use were included in the economic analysis. Outpatient services and rehabilitation costs were excluded since they were not routinely included in discharge summaries. The unit costs were not presented, whereas the quantities of resources used were. The resource data came from the sample of patients that were included in the clinical data. The costs were estimated using Medicare fee schedule. The sertraline costs came from average wholesale prices, assuming perfect compliance. Discounting was not relevant since the costs were incurred during a short timeframe. The price year was not explicitly stated, but the costs were estimated in 2001 and 2002.
Statistical analysis of costs
The Wilcoxon non-parametric test was used to test the statistical significance of differences in costs between the groups.

Indirect Costs
No indirect costs were reported.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were not carried out.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
Excluding medication costs, the mean cost per patient was $2,733 (+/- 6,764) in the sertraline group and $3,326 (+/- 7,195) in the control group, (p=0.32).

After including the cost of sertraline, the costs in the sertraline group increased to $3,093.

Synthesis of costs and benefits
A synthesis of the costs and benefits was not relevant since it appears that a cost-minimisation analysis has been carried out.

Authors' conclusions
The use of 24-week sertraline for the treatment of depression in a population with acute coronary syndromes led to a trend towards fewer cardiac or depressive events, without increasing the costs from the perspective of a third-party payer.

CRD COMMENTARY - Selection of comparators
The selection of the comparator was appropriate because no intervention was likely to represent usual care in the authors' setting and it was the basic comparator in the primary clinical trial. You should decide whether this is a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The evidence came from a clinical trial, which was appropriate for the study question and limited the impact of confounding factors and selection bias. Since the study had been published before, only key characteristics of the patient sample and study design were reported in the current publication. Thus, it was difficult to assess the validity of the study. However, some details of the study, such as the randomised design, the blindness of the study investigators and the baseline comparability of the study groups, ensure the robustness of the clinical information used in the analysis. The evidence came from several centres, thus the study sample appears to have been representative of the patient population. The authors stated that the study was powered to detect statistically significant differences in clinical outcomes (i.e. depressive symptoms), which were not used in this study. In fact, the main outcome measure, the number
of hospitalisations, represents an intermediate proxy for the impact of the interventions on patient health.

**Validity of estimate of measure of benefit**
No summary benefit measure was used in the analysis because a cost-minimisation analysis was conducted. Please refer to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

**Validity of estimate of costs**
The inclusion of costs was consistent with the perspective adopted in the study. Thus, indirect costs, the inclusion of which might have been interesting, were not taken into consideration. The source of the data was reported and the choice of Medicare reimbursement rates was justified. The authors stated that Medicare data were preferred because they are usually generalisable across the USA. However, the use of resource consumption data from international countries might have introduced some heterogeneity in service utilisation. Statistical analyses of the costs were carried out, but the cost estimates were specific to the study setting. A great variability in cost data was observed, as the high values for standard deviations suggested. The price year was not explicitly stated, but the years to which the cost data referred were reported. The authors noted that their results were likely to have underestimated real cost-differences because some potential cost-savings associated with sertraline, such as reduced rehabilitation costs, were not considered.

**Other issues**
The authors did not make extensive comparisons of their study results with those from other pharmacoeconomic studies. They noted that their economic results should be generalisable to other third-party payers, including managed care organisations. Further, since the patients were recruited at multiple centres, the transferability of the clinical results to other settings is ensured. The study referred to the management of depression in patients with acute coronary syndromes and this was reflected in the authors' conclusions.

**Implications of the study**
The preliminary results of the current study suggested that antidepressant treatment with sertraline among patients with acute coronary syndromes might be cost-effective and provide a strong rationale for the routine identification and treatment of depression in this at-risk population. The authors suggested that a large study, powered to detect significant differences in the total costs, should be undertaken.

**Source of funding**
Supported by Pfizer Inc., NY.

**Bibliographic details**

**PubMedID**
15766301

**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM

MeSH
Angina, Unstable /economics /psychology /therapy; Cardiac Catheterization /economics /utilization; Cost-Benefit Analysis; Depressive Disorder /drug therapy /economics /psychology; Diagnosis-Related Groups /economics; Double-Blind Method; Drug Costs; Emergency Service, Hospital /economics /utilization; Fee Schedules; Female; Health Care Costs; Hospital Costs; Hospitalization /economics; Humans; Male; Medicare /economics; Middle Aged; Myocardial Infarction /economics /psychology /therapy; Outcome Assessment (Health Care); Placebos; Psychiatric Status Rating Scales; Serotonin Uptake Inhibitors /economics /therapeutic use; Sertraline /economics /therapeutic use

AccessionNumber
22005000688

Date bibliographic record published
31/12/2005

Date abstract record published
31/12/2005