The cost effectiveness of acamprosate in the treatment of alcoholism in Germany: economic evaluation of the Prevention of Relapse with Acamprosate in the Management of Alcoholism (PRAMA) study

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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
Using adjuvant acamprosate therapy versus standard (placebo) treatment (in addition to counselling or psychotherapy according to routine practices) in the treatment of alcoholism.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients fulfilling at least five Diagnostic and Statistical Manual (DSM-III-R) criteria for alcohol dependence, diagnosed as being alcohol-dependent according to the Munich Alcoholism Test, and being completely abstinent from any alcohol consumption for a minimum period of 14 days and maximum period of 28 days.

Setting
Hospital. The economic study was carried out in Hamburg, Germany.

Dates to which data relate
The effectiveness data were derived from a double-blind randomised controlled study the results of which were published in 1996. The data related to the duration of hospitalisation and rehabilitation were extracted from the reports published by the National Association of Local Sickness Funds and the Federal Association of Pension Funds in 1992 and 1993, respectively. Treatment costs were valued in terms of 1995 acquisition costs for acamprosate, 1993 prices for treatment-day in hospital while rehabilitation costs were valued in terms of 1992 prices.

Source of effectiveness data
The evidence for the final outcomes was derived from a single study.

Link between effectiveness and cost data
Costing was performed retrospectively and not on the same patient sample as that used in the effectiveness analysis.

Study sample
There were 136 alcohol-dependent patients randomised to each study group. No power calculations were reported.
Study design
The study was a double-blind randomised controlled trial, carried out in 12 centres. The duration of follow-up was 48 medication-free weeks in addition to 48 with-medication weeks.

Analysis of effectiveness
The analysis of the clinical data was based on intention to treat. The main health outcome measures were the percentage of patients remaining abstinent at the end of the 48-week medication-free follow-up period and adverse effects.

Effectiveness results
The percentage of patients who remained abstinent at the end of 48-week medication-free follow-up period was 39.9% in the acamprosate group versus 17.3% in the placebo group (P=0.003). It was reported that the adverse effects of acamprosate therapy were mild, transient, and had a low frequency of occurrence.

Clinical conclusions
The study revealed the significant effect of acamprosate therapy in reducing the relapse rate in previously weaned alcoholics.

Modelling
A decision analytic model was constructed to estimate the cost-effectiveness ratio combining the clinical, resource use, cost data, and expert opinion.

Methods used to derive estimates of effectiveness
An interview with two experts was conducted to establish transition probabilities and latent periods of the target events, alcoholic psychoses (ICD 291) and alcohol-dependent syndrome (ICD 303).

Estimates of effectiveness and key assumptions
A long list of transition probabilities was reported in the study. The estimates of other parameters assessed by the experts were not reported systematically.

Measure of benefits used in the economic analysis
The main benefit measures were cases of target events avoided including cases of alcoholic psychoses (ICD 291) avoided, cases of alcohol dependence syndrome (ICD 303) avoided, cases of acute alcoholic hepatitis (ICD 571.1) avoided, and cases of alcoholic liver cirrhosis (ICD 571.2) avoided, from a hypothetical 1000 patients in each study group.

Direct costs
Costs were discounted. Quantities were not reported separately. The costs of hospital treatment, acamprosate acquisition, and rehabilitation costs for the cases of target events were reported separately. The upper and lower boundaries of the hospital treatment were derived from the costs for hospitals with fewer than 50 beds, and costs in university clinics. The cost analysis was performed both from the perspective of the German healthcare system (direct medical costs) and the statutory health insurance expenses. The sources of cost data related to hospital and rehabilitation treatments were the Federal Statistical Office and the Federal Association of Pension Funds. The date to which the price data referred was 1995.

Indirect Costs
Not considered.
Currency
German Marks (DM). No conversion was carried out. The exchange rate was reported to be DM1=$US0.6931 (1995 values).

Sensitivity analysis
A Monte Carlo simulation was used to assess the impact of the rates of abstinence and the duration of hospitalisation, treated as random variables, on the target variables. The method of the total differential (deterministic model) was employed to quantify the impact of exogenous variables on the target variables.

Estimated benefits used in the economic analysis
From a hypothetical 1,000 patients in each study group the estimated benefits were:

- 34 cases of alcoholic psychosis (ICD 291) avoided;
- 226 cases of alcohol dependence syndrome (ICD 303) avoided;
- 57 cases of acute alcoholic hepatitis (ICD 571.1) avoided;
- 28 cases of alcoholic liver cirrhosis (ICD 571.2) avoided.

The duration of the benefits estimated in the model was lifetime.

Cost results
The discount rate was 5%. The average treatment cost for target events in the acamprosate group was DM7,333,131 (range:DM6,013,362 - DM11,076,534) versus DM10,090,681 (range:DM8,274,626 - DM15,241,754) in the standard-care group on the basis of 1,000 hypothetical patients in each group. The acquisition cost of acamprosate was DM2,169,600.

Synthesis of costs and benefits
Incremental analysis was performed. An incremental cost-effectiveness ratio (additional cost per additional abstinent alcoholic) was calculated as the measure of synthesis of costs and benefits. The incremental cost-effectiveness ratio of acamprosate was -DM2,602 (net saving) (range: -DM406 to -DM8,830) per additional abstinent alcoholic using the perspective of the German healthcare system (direct medical costs). The authors reported that when the cost-effectiveness ratio was calculated from the perspective of Statutory Health Insurance the result was -DM 530 (net saving) per additional abstinent alcoholic. The Monte Carlo simulation revealed a range of between -DM10,000 and DM4,000 for the variance of adjuvant acamprosate therapy. The sensitive parameters in the total differential analysis were the rate of abstinence, transition probability to ICD 303, medication cost of acamprosate, and cost of treatment-day in hospital.

Authors' conclusions
From the perspective of both the German healthcare system (i.e. direct medical costs) and the Statutory Health Insurance expenses, adjuvant acamprosate therapy led to net savings, while at the same time improving the patient's state of health. Based on the naturalistic design of the underlying clinical trial and on this economic evaluation, it can be concluded that adjuvant acamprosate therapy leads to net savings under "real world" conditions.

CRD COMMENTARY - Selection of comparators
The reason for the choice of the comparator is clear.
Validity of estimate of measure of benefit
Since the main benefit of the intervention was estimated based on a randomised controlled trial, the internal validity of the results is likely to be assured.

Validity of estimate of costs
The resource quantities were not reported separately from the costs. Since the costing was performed retrospectively and not on the same patient sample as that used in the effectiveness analysis (i.e. it was not based on a randomised controlled trial), the internal validity of cost calculations is not assured. The costs of any adverse effects of adjuvant acamprosate therapy were not included.

Other issues
Performing a set of comprehensive sensitivity analyses enabled the study to deal with the issue of generalisability.

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