The long-term cost-effectiveness of improving alcohol abstinence with adjuvant acamprosate


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 acamprosate as an adjuvant therapy for improving alcohol abstinence.

Type of intervention
Adjuvant therapy.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised detoxified alcoholic male patients with an average age of 41 years. There were 80% with fatty liver, 15% with cirrhosis, 22% with pancreatitis, and 1% with alcoholic cardiomyopathy.

Setting
The setting of the study was unclear. The economic study was carried out in Germany.

Dates to which data relate
The effectiveness and resource use data were derived from studies published between 1961 and 1999. The price year was 1996.

Source of effectiveness data
The effectiveness evidence was derived from published studies, supported by the authors’ assumptions.

Modelling
A decision model based on Markov cycles was constructed to assess the long-term costs and benefits of using adjuvant acamprosate. In addition, a set of submodels simulating the progression of important complications of alcoholism (abstinence, liver disease, gastrointestinal disease, alcoholic cardiomyopathy, and other complications) was constructed in parallel. This allowed for the patients to develop more than one complication concurrently.

Outcomes assessed in the review
The outcomes assessed from the literature and used as model inputs were numerous. Thus, only some probabilities are reported in this abstract:

the development of fatty liver,

cirrhosis in the presence of fatty liver,
the resolution of fatty liver,
acute alcoholic hepatitis,
death from an acute hepatitis episode,
ascites in the presence of cirrhosis,
ascites becoming infected,
death from infected ascites,
hepatic encephalopathy in the presence of cirrhosis,
death from an episode of encephalopathy,
oesophageal varices in the presence of cirrhosis,
death following liver transplant,
primary bleed from oesophageal varices with cirrhosis,
death or recurrence following variceal bleed,
primary hepatic carcinoma in the presence of cirrhosis,
death if hepatic carcinoma, and
liver transplant if alcohol-induced end-stage liver failure.

Study designs and other criteria for inclusion in the review
The study designs were not reported. The authors stated that more recent German studies were preferred over older studies published abroad.

Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
Not stated.

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

Number of primary studies included
The effective evidence was derived from 28 primary studies.

Methods of combining primary studies
The primary studies were not combined.
Investigation of differences between primary studies
Not reported.

Results of the review
In patients who relapse, the estimated probability values were:

- 0.167 for the development of fatty liver,
- 0.020 for cirrhosis in the presence of fatty liver,
- 0 for resolution of fatty liver,
- 0.1 for acute alcoholic hepatitis,
- 0.130 for death from an acute hepatitis episode,
- 0.05 for ascites in the presence of cirrhosis,
- 0.15 for ascites becoming infected,
- 0.62 for death from infected ascites,
- 0.5 for hepatic encephalopathy in the presence of cirrhosis,
- 0.5 for death from an episode of encephalopathy,
- 0.17 for oesophageal varices in the presence of cirrhosis,
- 0.18 in the first year for death following liver transplant, and 0.025 in the subsequent years,
- 0.163 for primary bleed from oesophageal varices with cirrhosis,
- 0.22 for death following variceal bleeding,
- 0.7 for recurrent variceal bleed,
- 0.0462 for primary hepatic carcinoma in the presence of cirrhosis,
- 0.668 for death if hepatic carcinoma, and
- 0.03 for liver transplant if alcohol-induced end-stage liver failure.

Methods used to derive estimates of effectiveness
The authors made some assumptions due to the lack of data derived from the literature.

Estimates of effectiveness and key assumptions
When the data were unavailable, the authors made conservative assumptions, assuming that the same probability values applied to both abstinent and relapsed patients. In other cases, a probability value of zero was used for abstinent patients.

Measure of benefits used in the economic analysis
The benefit measure used in the economic analysis was the number of life-years gained with adjuvant acamprosate over standard therapy. It was modelled, and a 5% discount rate was used.
Direct costs
A 5% discount rate was used for future costs. The unit costs and the quantities of resources were not reported separately. The cost/resource boundary adopted was that of the third-party payer. The analysis of the costs included the costs for drug acquisition and treating complications. The costs and the quantities of resources used were estimated, first, from published data, and then, using German sources. The price year was 1996.

Statistical analysis of costs
No statistical analysis of the costs was carried out.

Indirect Costs
The indirect costs were not included.

Currency
German marks (DM).

Sensitivity analysis
One-way sensitivity analyses were carried out on the life expectancy and estimated costs, in order to assess the factors that had the greatest impact on the results. Each parameter used in the decision model was varied by +/- 10%. In addition, a break-even analysis was performed, by varying the cost of adjuvant acamprosate until the total lifetime costs of acamprosate were equal to the total costs of the standard therapy.

Estimated benefits used in the economic analysis
The life expectancy from age 41 years increased from 14.60 to 15.90 years with adjuvant acamprosate over standard therapy. The resulting incremental, discounted life-years gained of adjuvant acamprosate over standard therapy were 0.52 (1.20 when undiscounted).

Cost results
The undiscounted costs estimated in the analysis with standard therapy were DM 16,962 for relapse (alcohol dependence), DM 23,042 for liver disease, DM 15,610 for gastrointestinal disease, DM 150 for cardiomyopathy, and DM 21,178 for alcohol psychosis and peripheral neuropathy. The corresponding undiscounted costs for adjuvant acamprosate were DM 16,243 (relapse), DM 21,947 (liver disease), DM 14,727 (gastrointestinal disease), DM 149 (cardiomyopathy), and DM 19,845 (alcohol psychosis and peripheral neuropathy).

The cost of 48 weeks of acamprosate therapy was DM 2,177.

The discounted (and undiscounted) lifetime costs were DM 48,245 (DM 75,081) with adjuvant therapy and DM 49,907 (DM 76,942) with standard therapy.

Synthesis of costs and benefits
An incremental cost-effectiveness analysis was carried out to combine the costs and the benefits. However, adjuvant acamprosate therapy represented the dominant strategy, as it was more effective and cheaper than standard therapy. The sensitivity analyses suggested that, on the life expectancy side, the probabilities of hepatic disease, suicide and relapse rate had the greatest impact on the study results. On the cost side, the probability of relapse in the first year, suicide at age 45, various liver complications, alcohol psychosis, and the costs of treatment of chronic pancreatitis and alcohol dependence, had the greatest impact on the study results. The break-even point of the acquisition cost of adjuvant acamprosate was DM 4,000. This means that, below this figure, acamprosate was always cost-saving in comparison with standard therapy.
Authors’ conclusions
The use of adjuvant acamprosate for the improvement of alcohol abstinence was cost-effective, despite the high acquisition costs of acamprosate.

CRD COMMENTARY - Selection of comparators
The rationale for the comparator was clear. Standard therapy was selected as it represented the routine intervention for the patients included in the study. You should assess whether it represents a current intervention in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence was derived from several published studies. However, a formal review of the literature was not undertaken. In addition, the data were not combined as the authors used data from the available studies selectively. The design of the primary studies was not reported. More recent German data were used when available. The authors did not report whether the impact of differences among the primary studies was taken into account when estimating the effectiveness.

Validity of estimate of measure of benefit
The benefit measure was the number of discounted life-years gained with adjuvant acamprosate therapy over standard therapy. This was modelled using what appears to have been an appropriate decision model. Valuations in terms of the quality of life would have been useful.

Validity of estimate of costs
The analysis of the costs was carried out from the perspective of the German third-party payer. However, the cost items included in the analysis were not reported in detail. The price year was reported. The quantities were assessed from published sources, and the costs were derived from actual German data. The unit costs and the quantities of resources were not reported separately. No statistical analyses were conducted on the quantities. However, sensitivity analyses were carried out on all of the cost parameters. The authors stated that the inclusion of the indirect costs would have increased the cost-savings of adjuvant acamprosate.

Other issues
The authors made some comparisons of their findings with those from other studies. The issue of the generalisability of the study results to other settings was not explicitly addressed. However, numerous sensitivity analyses were carried out on all input parameters within reasonable ranges of values, thus increasing the external validity of the study. The unit costs and the quantities of resources were not reported though. The authors considered a specific population of detoxified alcoholic male patients and this was reflected in the study conclusions.

The authors highlighted some limitations of their analysis. First, the limited validity of the data derived from the literature. Second, measures of dispersions were not calculated, although there was wide use of sensitivity analyses. Third, there was no assessment of the patients’ quality of life. Finally, there was no modelling of alcohol-related complications, such as autonomic neuropathies and nonfatal accidents. In addition, the side effects of acamprosate were not considered as it is generally well tolerated.

Implications of the study
The authors pointed out that interventions that improve abstinence rates, such as acamprosate, should be implemented since they both improve life expectancy and reduce lifetime costs from the health insurance perspective.

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