Cost and cost-effectiveness of the COMBINE study in alcohol-dependent patients
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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.

CRD summary
This study compared the cost-effectiveness of nine treatment strategies for alcohol dependence that combined medical management, medications, and a combined behavioural intervention. The authors concluded that medical management plus naltrexone and acamprosate was the most effective strategy, but had a low probability of being the most cost-effective. Despite some limitations with data transparency, the methods appear to have been appropriate. The conclusions reached by the authors reflect the scope of their analysis.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The objective was to compare the cost-effectiveness of nine strategies for the treatment of alcohol dependence.

Interventions
The interventions were different combinations of medical management, pharmacotherapy using naltrexone 100mg per day or acamprosate 3g per day, and a combined behavioural intervention. Four strategies combined medical management with placebo, acamprosate, naltrexone, or both, four strategies added a combined behavioural intervention to the previous combinations, and one strategy was the combined behavioural intervention alone.

Location/setting
USA/primary care.

Methods
Analytical approach:
The analysis was based on a single study with a 16-week time horizon. The authors stated that the perspective was that of the provider of the interventions.

Effectiveness data:
The clinical data came from a multi-centre, randomised controlled trial (RCT), namely the Combined Pharmacotherapies and Behavioral Intervention (COMBINE) trial (Anton, et al. 2006, see ‘Other Publications of Related Interest’ below for bibliographic details). This trial was performed in 11 centres in the USA, with 1,383 eligible patients randomised to the nine treatment groups, between January 2001 and January 2004. The inclusion and exclusion criteria were reported and the length of follow up was 16 weeks. The primary endpoints were the percentage of days abstinent, the proportion of patients who did not relapse to heavy drinking (defined as five drinks or more per day for men and four or more for women), and the proportion of patients with a good clinical outcome (defined as abstinent or moderate drinking, with a score of three or less on the Drinker Inventory of Consequences questionnaire).

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
The summary measures of benefit were the increase in the percentage of days abstinent, the number of patients avoiding heavy drinking, and the number of patients attaining a good clinical outcome (as defined above).

Cost data:
The economic analysis included the costs required for the implementation of the intervention, including those for office space, labour, medications, and laboratory tests. A micro-costing method was used and resource use was obtained from the COMBINE trial. The details of the costing were reported elsewhere (Zarkin, et al. 2005, see 'Other Publications of Related Interest' below for bibliographic details). All costs were derived from official national sources. They were adjusted for inflation using the consumer price index and were reported in US dollars ($) for the price year 2007.

Analysis of uncertainty:
The parameter uncertainty was investigated, using a deterministic approach. Pharmaceutical prices and labour costs were varied individually, in one-way sensitivity analysis, and together, in two-way sensitivity analysis. Cost-effectiveness acceptability curves, for the three benefit measures, were generated using probabilistic sensitivity analysis.

Results
The mean total costs per patient ranged from $409.25 for medical management plus placebo to $1,312.96 for medical management plus naltrexone, acamprosate, and the combined behavioural intervention.

An incremental analysis was conducted, with the interventions ranked in order of increasing costs. All interventions, except medical management plus placebo, medical management plus naltrexone, and medical management plus naltrexone and acamprosate were eliminated from the analysis because they were more costly and less effective than another intervention.

Compared with medical management plus placebo, medical management plus naltrexone resulted in an incremental cost of $42.24 per point increase in the percentage of days abstinent, $2,846.85 per patient who avoided heavy drinking, and $1,689.74 per patient with a good clinical outcome. Compared with medical management plus naltrexone, medical management plus naltrexone and acamprosate resulted in an incremental cost of $663.80 per point increase in the percentage of days abstinent, $8,095.12 per patient who avoided heavy drinking, and $7,543.18 per patient with a good clinical outcome.

With increase in the percentage of days abstinent as the benefit measure, medical management plus placebo had the highest probability of being the most cost-effective strategy at a willingness-to-pay (WTP) of $50 or less. Medical management plus naltrexone had the highest probability of being cost-effective at a WTP of $50 to $350.

With the other two benefit measures, medical management plus naltrexone had the highest probability of being the most cost-effective interventions at a WTP of $8,000 or less and at greater WTP values, medical management plus naltrexone and acamprosate had the highest probability (0.5) of being the most cost-effective intervention.

These results were sensitive to variation in the price of naltrexone.

Authors' conclusions
The authors concluded that medical management plus naltrexone and acamprosate was the most effective strategy, but had a low probability of being the most cost-effective.

CRD commentary
Interventions:
The selected interventions were those included in the COMBINE trial. Alternative interventions were not investigated and the authors correctly acknowledged this as a limitation of their study.

Effectiveness/benefits:
The use of a RCT as a source for the clinical data was appropriate, given the strengths of this design. The details of the randomisation procedures, power calculations, method of analysis, comparability of patients groups, and statistical analysis to account for potential biases, were not reported, which makes it difficult to assess the quality of these data. The measures of benefit were disease specific and did not capture the impact of the interventions on a patient's quality of life.

Costs:
The authors clearly defined the perspective and appear to have included all the relevant costs. The micro-costing methodology might have created too much detail for all the cost components to be listed, but without these details it is difficult to replicate the analysis for other settings. The medical services component of the consumer price index would have been more appropriate for inflating the costs. The price year was reported and this will facilitate future reflation exercises. Discounting was not relevant, given the short time horizon.

Analysis and results:
The base-case results were clearly presented, using an incremental approach. The parameter uncertainty was addressed, using deterministic and probabilistic sensitivity analyses and producing cost-effectiveness acceptability curves. Limitations of the study were discussed, including whether or not the analysis reflected everyday clinical practice.

Concluding remarks:
Despite some limitations with data transparency, the methods appear to have been appropriate. The conclusions reached by the authors reflect the scope of their analysis.

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MeSH
Adult; Alcohol Deterrents /adverse effects /economics /therapeutic use; Alcoholism /economics /rehabilitation; Behavior Therapy /economics; Combined Modality Therapy /economics; Cost-Benefit Analysis; Drug Costs /statistics & numerical data; Drug Therapy, Combination; Female; Humans; Male; Middle Aged; Naltrexone /adverse effects /economics /therapeutic use; Taurine /adverse effects /anals & derivatives /economics /therapeutic use; Temperance /economics

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