The cost-effectiveness of sibutramine in non-diabetic obese patients: evidence from four Western countries

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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
In this study sibutramine treatment combined with diet and lifestyle advice was compared with placebo combined with the same standardised non-pharmacological treatment, for long-term weight reduction in obese individuals with a body mass index of at least 30 kg/m² and without co-morbidities. All individuals participated in a comprehensive weight reduction programme that included up to 20 group educational sessions and 3 individual dietary counselling sessions in addition to the usual information on healthy nutrition, physical activity and behavioural modification. Sibutramine was prescribed at 10- and 15-mg doses. Further details of the intervention strategies were described elsewhere (Warren et al. 2004, see 'Other Publications of Related Interest' below for bibliographic details).

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The hypothetical population comprised a cohort of 1,000 obese patients. The authors reported the age and gender distribution of the patients, which differed across countries, reflecting the prevalence rates of obese patients and/or those who were prescribed sibutramine treatment in each setting.

Setting
The practice setting for the study was outpatient care. The economic study was carried out for Finland, Germany, Switzerland and the UK.

Dates to which data relate
The effectiveness data used in the model came from studies published between 1983 and 2006. The dates for the resource use and cost data were not reported, but they are available from the authors on request. The price year was 2004.

Source of effectiveness data
The clinical and epidemiological data included:

- the efficacy rates of treatment,
- the incidence rates of diabetes,
- the reduction in the relative risk of developing diabetes,
the relative risks of mortality for diabetics,

the risks of coronary heart disease (CHD),

the relative risks of mortality for CHD,

the reduction in risk factors for CHD, and

the effects due to weight changes before and after the intervention.

**Modelling**

A model was used to combine weight loss rates with the risk of coronary heart disease and diabetes, and to combine these with mortality rates. The costs and utilities were accumulated over time. The time horizon was 5 years. Other model details were explained elsewhere (Warren et al. 2004 and Brennan et al. 2006, see ‘Other Publications of Related Interest’ below for bibliographic details).

**Sources searched to identify primary studies**

The pivotal effectiveness evidence, such as the proportions of patients who respond to treatment or who were withdrawn through lack of efficacy, as well as weight losses for responders, were based on patient level data from the SAT clinical trial. The SAT trial was a large multi-centre double-blind, randomised controlled trial (Hauner et al. 2004, see ‘Other Publications of Related Interest’ below for bibliographic details). To predict the risk of a CHD event, data from 26 controlled trials were used in conjunction with the Framingham equations on more than 5,000 individuals receiving sibutramine. Data from sibutramine studies and published evidence were used to estimate the reduction in diabetic incidence following weight losses (Colditz et al. 1995 and Sjostrom et al. 1999, see ‘Other Publications of Related Interest’ below for bibliographic details). The authors made assumptions about the relative risk mortality and risk reductions in function of weight changes.

**Methods used to judge relevance and validity, and for extracting data**

The process used to identify the data was not reported. No inclusion criteria for any of the parameters. The method used to select the estimates was neither reported, nor discussed.

**Measure of benefits used in the economic analysis**

The measure of benefit used was the quality-adjusted life-years (QALYs). These were based on the SAT trial which was designed specifically to examine the relationship between weight loss and quality of life. This relationship was derived from an analysis of Short Form 36 (SF-36) observations on obese individuals (Hauner et al. 2004). Life-years were transformed into QALYs using age-adjusted utility measurements obtained from a UK study in all evaluations, except the Finnish adaptation which incorporated the Finnish specific utility measures derived from the Health 2000 survey. Country-specific life tables were used. The SF-36 scores were converted to a utility index using the Brazier algorithm and utility multipliers were used to represent the reduced quality of life associated with CHD events and diabetes. The benefits were discounted according to country practice and guidelines (i.e. 5% for the Finnish, German and Swiss evaluations, and 3.5% for the UK).

**Direct costs**

The direct costs included were health state, treatment and monitoring costs for each country. The categories reported were the cost of a nonfatal CHD event in the year of occurrence, the annual cost of continued care following a CHD event, the cost of a fatal CHD event, annual diabetes costs, and sibutramine treatment (10 and 15 mg) per month. Guidelines were used to assign monitoring costs in some evaluations, while others were based on the results of expert panels. The costs for CHD and diabetes were based on published literature and have been provided by the economists involved in each of the evaluations. Resource use was not reported, but details are available from the authors upon request. The costs were discounted according to country practice and guidelines (i.e. 5% for the Finnish, German and...
Swiss evaluations, and 3.5% for the UK). The price year was 2004.

**Statistical analysis of costs**
No statistical analysis of the quantities or costs was reported.

**Indirect Costs**
Productivity costs were not included in the analysis.

**Currency**
Euro (EUR). To enable a comparison of the results, the costs were converted to euros using the Purchasing Power Parity Index.

**Sensitivity analysis**
Univariate sensitivity analyses and different scenarios were evaluated and the results summarised. Analyses were undertaken under the assumption that health state costs for CHD and diabetes were 20% lower than the base-case. Some ranges were selected according to their confidence interval, while others were arbitrarily assigned.

**Estimated benefits used in the economic analysis**
The total incremental QALYs gained per 1,000 patients was 50.5 for Finland, 51.5 for Germany, 54.4 for Switzerland and 48.5 for the UK.

QALYs directly attributable to weight losses, CHD events avoided and diabetes incidence were in the range of 61%, 27% and 12%, respectively.

**Cost results**
The total incremental costs were EUR 614,031 for Finland, EUR 706,148 for Germany, EUR 583,742 for Switzerland and EUR 572,449 for the UK.

The proportion of total incremental costs derived from the three separate elements was comparable with the majority of the costs being accrued through treatment and monitoring costs.

**Synthesis of costs and benefits**
The incremental cost-effectiveness ratios (ICERs) estimated from the weight loss element alone, assuming no benefits, were accrued through reductions in CHD or diabetes. The ICERs ranged from EUR 21,400 per QALY for the UK evaluation to EUR 29,400 per QALY for the German evaluation.

When including the potential benefits from all three elements, the central estimates were EUR 12,149 for Finland, EUR 13,707 for Germany, EUR 10,734 for Switzerland and EUR 11,811 for the UK.

The results were most sensitive to changes in utility directly attributable to weight losses, with ICERs increasing (decreasing) by an average of 90% (28%) when using the lower (upper) confidence intervals.

**Authors’ conclusions**
The study showed that benefits associated with sibutramine-induced weight loss were obtained at a reasonable cost, and suggested that sibutramine treatment could be considered a viable option for pharmacotherapy treatment alongside diet and exercise.
CRD COMMENTARY - Selection of comparators
The comparator used was justified, mainly because a non-pharmacological treatment based on diet and lifestyle advice is the current practice in the settings analysed by the authors. You should decide if the comparator represents current practice in your own setting or whether other weight reducing drugs could also be relevant.

Validity of estimate of measure of effectiveness
The authors selectively combined data from existing models with data from several published studies of varying design, expert opinion and authors'-assumptions. No systematic search for data was reported, so the possibility of selection bias cannot be eliminated. A positive feature of the study was that randomised clinical trials, which are an adequate source to estimate effectiveness, were used to derive the effectiveness and treatment effects on weight change. However, a systematic review was not performed in order to evaluate all the effectiveness evidence.

Validity of estimate of measure of benefit
The estimation of health benefits (QALYs) was modelled based on the SAT trial, which was designed specifically to examine the relationship between weight loss and quality of life. The methods to estimate the utility weights were described and the source reported as they were taken from a published paper (Hauner et al. 2004). With the exception of Finland, where specific utility measures were available, UK age-specific utilities were generally used to derive the QALYs.

Validity of estimate of costs
Given that a single provider perspective was adopted, all the relevant cost categories and their associated costs seem to have been taken into consideration. The resource use data, unit costs and sources of resource use were not reported, but details can be obtained from the authors on request. This would make it difficult to rework the analysis for other settings. The price year was adequately reported. The costs were discounted according to country practice and guidelines (5% for the Finnish, German and Swiss evaluations, and 3.5% for the UK), which would appear appropriate as the time horizon was greater than one year. Some sensitivity analyses were conducted to assess the robustness of the cost estimates used, but these were not reported in full.

Other issues
The authors compared their findings with those from other studies and found the results to be in agreement. The results of the study do not appear to have been presented selectively. The authors' conclusions would appear to reflect the scope of their analysis. However, they also reported some limitations to their study. First, the ratio of men and women in the evaluations differed according to the settings and the model accounted for changes to this ratio by recalculating the risk of CHD or incidence of diabetes by gender. Second, the main cost-savings differed by country, reflecting the difference in health services provided in each setting, but these have little impact on the results. Third, the placebo arm in the SAT study was used as a proxy for diet and lifestyle advice given in primary care, but individuals in a real primary care setting are unlikely to receive an intervention of a similar magnitude, which could lead to an overestimation of the true comparator. Fourth, it is unlikely that sibutramine treatment would be withdrawn from individuals who continued to respond in clinical practice, and the benefits for responders to treatment are likely to have been underestimated. Finally, weight regain after cessation of treatment/diet and exercise might not occur immediately, as assumed in the model, and the evidence demonstrated that individuals were able to maintain sibutramine-induced weight losses for up to 6 months after cessation of treatment.

Implications of the study
According to the authors, current licensing indicates that sibutramine treatment should be offered as part of a long-term integrated therapeutic approach that includes dietary and behavioural modification as well as increased physical activity.

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Bibliographic details

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Other publications of related interest
Because readers are likely to encounter and assess individual publications, NHS EED abstracts reflect the original publication as it is written, as a stand-alone paper. Where NHS EED abstractors are able to identify positively that a publication is significantly linked to or informed by other publications, these will be referenced in the text of the abstract and their bibliographic details recorded here for information.


Indexing Status
Subject indexing assigned by NLM

MeSH
Adult; Age Distribution; Aged; Appetite Depression/economics; Cohort Studies; Coronary Disease/economics/prevention & control; Cost-Benefit Analysis; Cyclobutanes/economics; Diabetes Mellitus/economics/prevention & control; Double-Blind Method; Female; Finland; Germany; Great Britain; Humans; Male; Middle Aged; Obesity/drug therapy/economics; Quality-Adjusted Life Years; Sensitivity and Specificity; Sex Distribution; Switzerland

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