Cost-effectiveness of sibutramine in the LOSE Weight Study: evaluating the role of pharmacologic weight-loss therapy within a weight management program


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 sibutramine in conjunction with a weight management programme (WMP) for the treatment of overweight and obese individuals. The WMP consisted of a physician-supervised, multidisciplinary programme for which enrollees paid $100. The intervention included five monitored care visits with a prevention specialist and attendance at two or more group-format weight management seminars. Individuals also participated in two education programmes offered by the American Heart Association. Study participants who completed 6 months of the study received a $50 gift cheque. Those patients who completed 12 months of the study received an additional $100 gift cheque.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients aged 18 years or older who had either a body mass index (BMI) of greater than 30 kg/m² or a BMI of 27 - 29.9 kg/m² with one or more co-morbidities, including diabetes, hypertension and/or hyperlipidaemia.

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

Dates to which data relate
The sample of patients from which the effectiveness and resource use data were derived was enrolled from January 1999 to June 2000. The price year was 2004.

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 included in the effectiveness study.

Study sample
Power calculations were performed in the preliminary phase of the study. These suggested that a sample of 285 individuals per group was required to detect a 10% difference in change in body weight between the groups using a
2-tailed alpha of 0.05 and a power of 75%. Of the 1,564 individuals initially screened at Kaiser Permanente of Colorado, 976 (62%) did not meet the inclusion criteria or were not interested in the programme. Thus, 588 patients were included. Of these, 296 (21% men) were assigned to the intervention group and 292 (15% men) were assigned to the control group. The intervention group had a mean age of 47.2 (+/- 10.7) years (age range: 19 - 79) and the mean BMI was 38.6 (+/- 7.0) kg/m2. The control group had a mean age of 49.6 (+/- 10.4) years (age range: 23 - 72) and the mean BMI was 36.8 (+/- 5.6) kg/m2. Twenty-one patients in the intervention group and 44 in the control group withdrew consent at the beginning of the study.

**Study design**
This was a randomised, prospective controlled trial that was carried out at a managed care organisation in Colorado, USA. Allocation of patients to the study groups was based on a computer-generated random numbers table. Study assignments were placed in envelopes that were opened on completion of the baseline visit. The overall length of follow-up was 12 months, but the primary outcome was also assessed at 6 months. Data on some patients were not available due to loss to follow-up (60 in the intervention group and 80 in the control group), lack of efficacy, adverse events and protocol violations. However, patients were considered in the final analysis if they had received at least one dose of study medication (for those in the intervention group) or if they had a body weight recorded at least 4 weeks after randomisation. No blinding was used.

**Analysis of effectiveness**
The analysis of the clinical study was conducted on an intention to treat basis. It included 281 patients in the intervention group and 220 in the control group. The outcome measures used were weight loss at 12 months and percentage change in weight. The study groups were not well matched at baseline. For example, of the evaluable patients, those assigned to the sibutramine plus WMP group were significantly older and had higher BMI values than those receiving the WMP alone.

**Effectiveness results**
The mean weight loss at 12 months was 13.7 (+/- 15.0) pounds (range: -85 - 20) in the intervention group and 5 (+/- 13.2) pounds (range: -79 - 20) in the control group, (p<0.001).

The percentage change in weight was -6% (+/- 6.7) in the intervention group versus -2.2% (+/- 5.5) in the control group, (p<0.001).

In the control group, 80.9% of participants had a weight loss of less than 5%, compared with 52.7% for those assigned to the intervention group.

In contrast, 19.6% of the intervention group had a weight loss of at least 10%, compared with 10% of those in the control group.

**Clinical conclusions**
The effectiveness analysis showed that sibutramine plus a WMP was significantly more effective than a WMP alone in terms of weight loss.

**Measure of benefits used in the economic analysis**
The summary benefit measure used was the mean change in body weight and the percentage change in weight. These were derived directly from the effectiveness analysis.

**Direct costs**
The analysis of costs was carried out from the perspective of a managed care organisation. It included the costs of outpatient visits (including medical office and emergency department visits), hospitalisations, professional services.
claims (e.g. oxygen, ambulance, outside physician referrals), and prescription medications. The quantities of resources used were presented for the majority of items but unit costs were, in general, not provided. Resource use was estimated using data retrieved from electronic medical records, and administrative claim and clinical databases maintained and used by the managed care organisation. Resource consumption referred to a 24-month period, including the 12 months before and after study enrolment.

The costs were estimated using Medicare’s resource-based relative value scale fee schedule and the reimbursement rates of diagnosis-related groups. The costs for professional claims were based on billed amounts. The prescription costs came from average wholesale prices. An expert panel comprising 3 to 5 physicians, 2 clinical pharmacists, and a health promotion specialist determined whether outpatient visits and hospitalisations were related to obesity for the 12 months before and 12 months after study enrolment. This allowed the calculation of obesity-related health care resource consumption. All costs were updated to 2004 values using the Consumer Price Index. Discounting was not applied as the costs were incurred within 2 years.

### Statistical analysis of costs

The Wilcoxon rank sum test was used to test the statistical significance of resource use and cost-differences. A regression analysis was also carried out to isolate the effect of the medications and cost of therapy while controlling for other factors.

### Indirect Costs

The indirect costs were not included in the cost analysis.

### Currency

US dollars ($).

### Sensitivity analysis

Univariate analyses were performed on clinical and economic variables, and non-parametric statistical procedures were used for variables that were not normally distributed. A multivariate sensitivity analysis was also carried out to determine the strongest predictors of total health care costs. For incremental cost-effectiveness ratios, a non-parametric bootstrap with 1,000 replications was performed.

### Estimated benefits used in the economic analysis

See the 'Effectiveness Results' section.

### Cost results

The health care costs were significantly greater for the sibutramine plus WMP group, compared with the WMP only group, for obesity-related physician visits, total prescriptions, obesity-related prescriptions, total health care expenditures and obesity-related health care expenditures.

Since these comparisons reflect differences between the groups without controlling for baseline differences, the authors stated that it may not be appropriate to draw conclusions on the basis of these findings. Thus, the cost analysis focused on the magnitude of the change from 12 months before enrolment to 12 months after enrolment.

There were no differences in overall health care resources used in outpatient visits, hospitalisations, or professional service claims from 12 months before enrolment to 12 months after enrolment in both groups. However, as expected, the intervention group had a greater change in prescription medication than the control group (median change: 9 versus 2; p<0.001).

The median change in total costs was $1,279 (range: 2,399 - 131,090) in the intervention group and $271 (range: -4,217 - 27,197).
Similar results were obtained when obesity-related costs were considered. The median change in obesity-related costs was $408 (range: -6,077 - 4,868) in the intervention group and $31 (range: -6,091 - 3,519) in the control group, (p<0.001).

**Synthesis of costs and benefits**

Average and incremental cost-effectiveness ratios (ICERs) were calculated to combine the costs and benefits.

The average cost per each pound of weight loss was $32 for sibutramine plus the WMP and $12 for the WMP alone.

The mean ICER of sibutramine plus WMP over the WMP alone was $44 (95% confidence interval, CI: 44 - 46; median 42) per additional pound lost when obesity-related costs were divided by weight loss.

The ICER was $101 (95% CI: 99 - 102) per additional percentage change in body weight when obesity-related costs were divided by the percentage weight loss.

The ICER was $194 (95% CI: 188 - 200) when total health care costs were divided by the weight loss and $399 (95% CI: 391 - 406) when divided by the percentage weight loss.

In the multivariate analysis, the strongest predictor of total health care costs was the study arm, with those participants receiving sibutramine plus WMP having an estimated annual cost of $474 more than those in the control group, (p<0.001). Interaction terms were evaluated in the model but were not significant. The univariate analysis suggested that the ICER was sensitive to changes in the price of sibutramine.

**Authors' conclusions**

Sibutramine plus a weight management programme (WMP) led to a significant greater reduction in weight than the WMP alone. However, such weight loss was achieved at higher cost than that associated with patients receiving the WMP alone.

**CRD COMMENTARY - Selection of comparators**

The selection of the comparator (i.e. the WMP) was appropriate as it represented a typical treatment strategy for overweight or obese patients. The main characteristics of the WMP were reported. The dosage of sibutramine was not reported. You should decide whether this is a valid comparator in your own setting.

**Validity of estimate of measure of effectiveness**

The effectiveness evidence came from a clinical trial, which was appropriate for the study question. Information on the methods of sample selection and randomisation was reported. The study groups were not comparable at baseline, which might affect the validity of the comparison. It was unclear whether the study sample could have been considered representative of the patient population, although the data came from a large managed care organisation which should have enhanced the representativeness of the patients included in the study. The majority of potentially eligible patients were not, however, interested in the study, thus caution is required when extrapolating the results of the analysis to all overweight or obese patients. These issues tend to limit the validity and robustness of the primary estimates.

**Validity of estimate of measure of benefit**

The summary benefit measure was specific to the disease considered in the study. It is not comparable with the benefits of other health care interventions. The impact of the treatments on quality of life was not investigated.

**Validity of estimate of costs**

The analysis of the costs was consistent with the perspective adopted. Thus, only direct medical costs were included in
the analysis. Resource consumption was estimated from the sample of patients included in the effectiveness analysis, thus it reflected actual treatment patterns. The source of the costs was appropriate given the perspective of the managed care organisation. Data on the quantities of resources used were given, which increases the possibility of replicating the cost analysis in other settings. However, the unit costs were not provided. Statistical analyses of the costs were performed. The cost estimates were specific to the study setting, thus caution is required when extrapolating the cost results to other contexts. The price year was reported, which makes reflation exercises in other time periods possible. The authors noted that the inclusion of indirect costs might have favoured the intervention group since a higher BMI is usually associated with longer absenteeism and greater productivity losses. Discounts for managed care organisations and patients' reimbursements for drug costs were not taken into consideration.

Other issues
The authors reported the results from other studies, but did not make explicit comparisons with their findings. They stated that their findings may be generalisable to settings where WMPs are available and patients pay for part of their anti-obesity medications. The authors noted some strengths of their analysis, such as the inclusion of the full range of obese individuals (also individuals with a BMI greater than 40), the use of data from a clinical trial, and the fact that resource consumption was derived from the actual use of resources rather than from patient self-reports. Limitations to the validity of the study were also considered. For example, the short-term follow-up period or the imbalance of study groups at baseline, despite the randomisation procedure.

Implications of the study
The study results suggested that a significant weight loss can be achieved with sibutramine plus a WMP at an extra cost. Reimbursement agencies might consider covering such additional costs. The authors suggest that long-term studies of sibutramine should be carried out to examine weight loss over a 1-year period.

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Other publications of related interest


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