Conversion from sustained-release to immediate-release bupropion: patient tolerability and economic impact
Mayo J L, Cahill G M, Lott R S

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 study compared the use of a single dose of sustained-release bupropion 200 mg (GlaxoSmithKline) versus a single dose of immediate-release bupropion 150 mg (generic).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients from the authors' setting who were converted from sustained release to generic immediate-release bupropion. In particular, patients who were converted to immediate-release bupropion from 1 July to 31 December 2001 and were administered sustained-release bupropion for at least 30 days before the conversion were included in the study. If poor compliance with bupropion treatment was documented in the patients' pharmacy refill records, they were excluded from the study.

Setting
The setting was a medical centre (the Boise Veterans Affairs Medical Center). The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were collected from patients' medical records that documented a conversion from 1 July to 31 December 2001. Data were collected from the medical records for at least 6 months after conversion. The dates to which the cost data referred were not reported, nor was the price year.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
Although not explicitly reported, the costing appears to have been carried out prospectively on the same sample of patients as that used in the effectiveness study.

Study sample
The sample size was not determined in the planning phase of the study. All patients who met the inclusion and exclusion
criteria were eligible for the study. Overall, 103 patients were found to be eligible and were included in the study. The mean age of the patients was 55.4 (+/- 12.1) years. Thirty-one per cent of the patients were older than 60 years.

Study design
The analysis was based on a retrospective, single-centred cohort study, specifically a retrospective medical record review. Data from medical records were collected for each patient, for 1 month before conversion and for 6 months after.

Analysis of effectiveness
It was not reported whether all of the patients included in the study were considered at analysis. The primary outcomes assessed were the mean daily doses taken by patients when receiving sustained-release bupropion at conversion and immediate-release bupropion 6 months after conversion. Differences in these outcomes were compared using Student's t-test. Further outcomes were the mean single dose of immediate-release bupropion and the frequency of adverse events (i.e. seizure, headache, agitation or anxiety, chest pain, gastrointestinal complaints and death). The rates of adverse events were compared using the chi-squared test. A p value less than or equal to 0.05 was declared statistically significant.

Effectiveness results
The results were reported separately for those aged over 60 years, for patients who received bupropion for smoking cessation, and for patients who received it because of a psychiatric diagnosis.

Mean daily doses of sustained-release bupropion at conversion did not differ significantly from mean daily doses of immediate-release bupropion at 6 months after conversion, (p=0.73).

Although four deaths occurred during the study period, they were found to be unrelated to bupropion therapy or the change in dosage form.

Four patients (5.6%) out of 71 under the age of 60 years and 3 patients out of 32 over the age of 60 experienced nonfatal adverse events after conversion. The difference was not statistically significant, (p=0.485, chi-squared test). Patients aged 60 years and older received smaller mean daily doses of immediate-release bupropion at the end of the follow-up period compared with patients younger than 60 years, but the difference in mean doses was not statistically significant (279.7 +/- 91.5 mg versus 303.2 +/- 84.9 mg; p=0.223, Student's t-test).

Compared with patients with psychiatric diagnoses, patients who received bupropion for smoking cessation did not demonstrate a statistically significant adverse event rate (6% versus 8.1%; p=0.810, chi-squared test). The mean daily doses of immediate-release bupropion at the end of the follow-up period also did not vary significantly (300 +/- 75 mg for the smoking-cessation group versus 295 +/- 90 mg for the group with psychiatric diagnoses; p=0.832, Student's t-test).

The most frequent dosage of immediate-release bupropion at the end of the follow-up period was 300 mg/day in each group. Dosages different from 300 mg/day were administered to 4 patients (25%) in the smoking-cessation group and 36 patients (41%) in the group of patients with psychiatric diagnoses.

Clinical conclusions
The authors concluded "conversion from sustained-release bupropion to immediate-release bupropion appears to be safe". The analysis proved that immediate-release bupropion can be administered to patients without them experiencing disproportionate adverse events including seizure.

Measure of benefits used in the economic analysis
No summary measure of benefit was used in the economic analysis. The study was, in effect, a cost-consequences
analysis.

**Direct costs**
Only the drug costs were included in the analysis. The unit costs and the quantities were not explicitly reported. Although quantities were most probably derived from the single study (medical records of patients), the source of the cost data was not reported. In addition, the authors did not explicitly state the price year. Discounting was not relevant, as the costs were incurred during less than 2 years, and was not conducted.

**Statistical analysis of costs**
The costs were treated deterministically.

**Indirect Costs**
The indirect costs were not included in the analysis.

**Currency**
US dollars ($).

**Sensitivity analysis**
No sensitivity analysis was carried out.

**Estimated benefits used in the economic analysis**
See the 'Effectiveness Results' section.

**Cost results**
The total intervention costs were not reported. It was only reported that the reduction in drug acquisition costs of bupropion after conversion amounted to $48,910 for all 103 patients.

**Synthesis of costs and benefits**
The costs and benefits were not combined.

**Authors’ conclusions**
The conversion from sustained-release to immediate-release bupropion resulted in decreased drug acquisition costs.

**CRD COMMENTARY - Selection of comparators**
The choice of the comparators was explicitly justified. You should decide if they represent widely used technologies in your own setting.

**Validity of estimate of measure of effectiveness**
The analysis was based on a retrospective review of medical records. It was not possible to comment on the internal validity of the effectiveness results since there was insufficient information on the way the medical records were constructed and whether they contained rigorous data on the patients. The study sample was representative of the study population and details of the patients were given. However, as the sample size was not determined in the planning phase and no power calculations were undertaken, it is possible that the sample size was relatively small and inadequate to detect an accurate increase in adverse events resulting from changes in dosage form. The retrospective, observational
nature of the study design suggests a low internal validity.

Validity of estimate of measure of benefit
No summary measure of benefit was used. The reader is referred to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

Validity of estimate of costs
The perspective adopted was not reported, but it was not societal since the indirect costs were not included; only the drug costs were included. The unit costs were not reported, thus impeding the reproducibility of the study to other settings. The source of the cost data was not reported, and the costs were treated deterministically. No sensitivity analysis was conducted to assess the robustness of the estimates used. The quantities were derived directly from medical records, but no statistical analysis on the quantities was performed. The price year was also not reported. The inadequate cost analysis limits the interpretation of the study findings.

Other issues
The authors did not compare their findings with those from other studies. However, this might have been due to a lack of published literature in this specific area. The issue of generalisability of the results to other settings was not directly addressed. The authors do not appear to have presented their results selectively. The study enrolled patients who were converted from brand-name sustained-release bupropion to generic immediate-release bupropion, and this was reflected in the authors' conclusions.

The authors reported a number of limitations to their study. For example, the analysis was based on a retrospective study and the sample size was relatively small. Power calculations have demonstrated that, based on seizure rates, a sample size of at least 1,000 patients would be needed to detect one seizure episode. Combined with the fact that bupropion-induced seizures are infrequent at daily doses less than 450 mg, the study was not sufficiently powered to detect increases in the rate of seizure. In addition, while it was reported that the study sample comprised mainly male patients, it is documented that women face an increased risk. It is therefore possible that the likelihood of adverse events was underestimated in the study.

Implications of the study
The authors did not make any explicit recommendations for changes in policy. However, they recommended that further research should be undertaken to explore similar substitutions. Future studies should be based on larger sample sizes with representative proportions of women, and should focus on the evaluation of changes in the effectiveness of bupropion after conversion.

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