The clinical effectiveness and cost-effectiveness of bupropion and nicotine replacement therapy for smoking cessation: a systematic review and economic evaluation


Authors' objectives
To assess the clinical effectiveness, cost-effectiveness and adverse events of bupropion sustained-release (BSR) and nicotine replacement therapy (NRT) for smoking cessation.

Searching
The authors searched a number of different databases and websites up to May 2001 (a detailed search strategy was provided). The bibliographies of retrieved articles and submissions were also checked. Both unpublished and published data were sought, and there were no language restrictions.

Study selection
Study designs of evaluations included in the review
Systematic reviews updated with randomised controlled trials (RCTs) were included in the review. To investigate adverse events, other study types were included in the review: cohort studies, case-controlled studies, uncontrolled studies, surveys, surveillance data, case reports and case series.

Specific interventions included in the review
Studies were included if they examined bupropion (150 or 300 mg/day) immediate release and SR formulations, used to aid smoking cessation alone, or as part of combination therapy with motivational support, or as part of combination therapy with motivational support and NRT. The main comparator was placebo, but other eligible comparators were no treatment, other pharmacological agents, and non-pharmacological interventions such as acupuncture.

Participants included in the review
Smokers of any age or gender were included in the review.

Outcomes assessed in the review
The main clinical outcome measure assessed was the number of participants who were not smoking at 6, 12 or more months after the start of therapy. In addition, the incidence and severity of all adverse events were included in the review.

How were decisions on the relevance of primary studies made?
Two reviewers independently screened all the titles and abstracts for relevance. Full papers were obtained and the relevance of each article was assessed according to predefined criteria. Any discrepancies were resolved by consensus, consulting a third reviewer if necessary. Non-English language papers were not selected for inclusion in the review.

Assessment of study quality
The quality of the systematic reviews was assessed using criteria developed for DARE; the quality of the RCTs was assessed using criteria based on CRD report 4 (see Other Publications of Related Interest). Checklists for assessing the quality of studies that reported adverse events were provided in an appendix. One reviewer assessed the quality of the included studies, while another reviewer checked it independently. Any discrepancies were resolved by consensus, consulting a third reviewer if necessary.

Data extraction
One reviewer extracted relevant data into an Access database, while a second reviewer independently checked the accuracy. Details of the studies, study design, participants, interventions and results were tabulated.
Methods of synthesis
How were the studies combined?
For the assessment of clinical effectiveness, the data were pooled where possible using Peto’s fixed-effect model and/or a random-effects model. Odds ratios (ORs) with 95% confidence intervals (CIs) were reported. A narrative summary was provided for the assessment of adverse events and safety.

How were differences between studies investigated?
The authors examined heterogeneity between the studies using a chi-squared test. Where possible, subgroup analyses were conducted for different participant groups.

Results of the review
To assess clinical effectiveness, 3 systematic reviews and 13 individual RCTs (including 2 unpublished RCTs) were included in the review. Four systematic reviews and 112 individual studies relating to adverse events and safety were also included.

Overall, the quality of the systematic reviews and individual RCTs included in the review was good, while the quality of the data on adverse effects and safety were variable.

Two systematic reviews and 7 RCTs (including 2 unpublished RCTs) assessed the effectiveness of NRT. NRT as an aid to smoking cessation was found to be more effective than placebo: the OR was 1.74 (95% CI: 1.64, 1.86) when using Peto's method or 1.79 (95% CI: 1.65, 1.93) when using a random-effects model. The results for abstinence at 12 months or longer were similar. The majority of data came from studies investigating the use of NRT gum and NRT patches, although there were no data to indicate that other forms of NRT were less efficacious. In addition, there were no data to indicate subgroup differences in the response to NRT.

Two systematic reviews, 3 RCTs and 4 unpublished trials assessed the effectiveness of BSR. BSR as an aid to smoking cessation was also found to be more effective than placebo: the ORs were 2.52 (95% CI: 1.99, 3.19) and 2.45 (95% CI: 1.72, 3.49) for fixed-effect (Peto) and random-effects models, respectively. The results were similar for all durations of follow-up. There was evidence from single subgroup populations that BSR was as effective in smokers with chronic obstructive pulmonary disease, cardiovascular disease and in those who had failed in the past to achieve abstinence with BSR, as in the general smoking population.

Evidence to support one intervention over the other was relatively weak.

Overall, the incidence of adverse events with NRT was very low, while the review identified seizure as the most significant and important potential adverse effect of BSR.

Cost information
The results from 17 economic studies were included in the review. Based on decision analysis modeling, NRT and/or BSR were found to be cost-effective in comparison with many accepted health care interventions. The incremental cost per life-year saved was about £1,000 to £2,400 for NRT, £640 to £1,500 for BSR, and £900 to £2,000 for NRT plus BSR.

Authors’ conclusions
Both NRT and BSR are effective interventions for assisting smoking cessation, but their relative effectiveness still needs further research. Information on how to maximise effectiveness in practice is still lacking, but probably involves motivational support. The authors also concluded that, overall, the safety of NRT was more favourable than BSR.

CRD commentary
The inclusion or exclusion criteria were clearly defined in terms of the study design, participants, intervention and outcomes of interest. The search strategy was well conducted. However, although the strategy did not limit the search to English language studies, non-English studies were excluded, thus introducing language bias into the review. The
validity of the included studies was adequately assessed, with detailed descriptions of quality presented in the text and in tabular format. The review methodology was generally well conducted with adequate steps taken to minimise other sources of bias. However, pooling the data by meta-analysis may not have been appropriate in some cases due to clinical heterogeneity. Overall, the conclusions of the review appear to accurately reflect the data presented.

**Implications of the review for practice and research**

**Practice:** The authors stated that both NRT and BSR are effective interventions to assist smoking cessation, although NRT offers more favourable safety than BSR.

**Research:** The authors stated that studies comparing the effectiveness of BSR and NRT are needed. Ideally, these studies should include a high level of motivational support.

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**Other publications of related interest**

NHS Centre for Reviews and Dissemination. Undertaking systematic reviews of research on effectiveness. CRD’s guidance for those carrying out or commissioning reviews. York: University of York, NHS Centre for Reviews and Dissemination; 2001. Report No.: CRD report 4 (2nd ed.).

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on
the reliability of the review and the conclusions drawn.