Are there gender differences in smoking cessation, with and without bupropion: pooled-and meta-analyses of clinical trials of Bupropion SR

Scharf D, Shiffman S

CRD summary
This review found that Bupropion SR is an effective smoking cessation aid for both men and women. However, women have less success at quitting than men, regardless of whether treated with Bupropion SR or placebo. Given that the quality of the original studies was not assessed, a limited search was employed and the review methods were not reported, the reliability of the authors' conclusions is weakened considerably.

Authors' objectives
To examine gender differences in smoking cessation with and without treatment with Bupropion SR.

Searching
MEDLINE and PsycLIT were searched using the keywords given. It was not reported whether and language restrictions were applied or when the searches were performed. In addition, abstract booklets from meetings (Society for Research on Nicotine and Tobacco, and College on Problems of Drug Dependence 2000-3) were searched and the reference lists of identified articles were checked.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were the only studies eligible for inclusion in the review.

Specific interventions included in the review
Studies of Bupropion SR provided at an accepted therapeutic dose of 300 mg/day for a minimum of 6 weeks were eligible for inclusion. The studies had to have a placebo comparator. Studies that also used other pharmacological smoking cessation aids were excluded.

Participants included in the review
Studies were only eligible for inclusion if they included both male and female smokers, and if participants lost to follow-up were considered as smokers. Most of the studies included healthy participants from the general population, although in one study participants had chronic obstructive pulmonary disease and in another the participants had cardiovascular disease. The mean age of the participants in the included studies ranged from 39 to 55 years and the mean number of cigarettes per day ranged from 17 to 28.

Outcomes assessed in the review
Studies in which smoking status was verified with biochemical measures, and smoking abstinence could be defined according to point prevalence or continuous abstinence since target quit date, were eligible for inclusion. Most of the studies reported outcomes at between 4 and 7 weeks, the longest being 26 weeks.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection. When insufficient information was reported to determine eligibility for inclusion, the primary authors of the studies were contacted for further information.

Assessment of study quality
The authors did not state that they assessed validity.
Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

If a study reported data on both continuous abstinence and point prevalence, then the point prevalence outcome was extracted for the analyses. The preferred time of outcome assessment was abstinence at the end of treatment, rather than the longer term 6-month follow-up abstinence, because it was reported more frequently.

Methods of synthesis
How were the studies combined?
The included studies were combined using a random-effects meta-analysis model to estimate the effects of treatment on cessation outcomes, grouped by gender, and also the effects of gender, grouped by treatment. An individual level analysis, using logistic regression analysis, was also performed using variables for treatment, gender, treatment by gender interaction and 'study' to further examine the effects of treatment for men and women.

How were differences between studies investigated?
The authors stated that they tested the meta-analysis for heterogeneity, although they did not explicitly state how they did so. The analyses were re-run excluding the study that was heterogeneous. Subgroup analyses were performed for studies reporting only short-term outcomes (10 weeks or less) and for studies that only included healthy populations. A 'study' dummy variable was fitted to the logistic regression model; this controlled for any differences in population, outcome assessment and design.

Results of the review
Twelve RCTs (n=4,421) were included in the review.

The meta-analysis of the effects of treatment on cessation, grouped by gender, showed that Bupropion SR was effective in comparison with placebo at helping smokers quit. Bupropion SR was effective for not only men and women combined (odds ratio, OR=2.49, 95% confidence interval, CI: 2.06, 3.00), but also for men only (OR 2.53, 95% CI: 1.88, 3.40) and for women only (OR 2.47, 95% CI: 1.92, 3.17). The meta-analysis of the effects of gender, grouped by treatment, suggested that women were less successful at quitting smoking than men, regardless of treatment (OR 0.77, 95% CI: 0.66, 0.89).

Analyses of the individual level data showed that more smokers quit when treated with Bupropion SR than with placebo. The effect was observed for men (OR 2.54, 95% CI: 2.08, 3.10), women (OR 2.45, 95% CI: 1.99, 3.02), and men and women combined (OR 2.49, 95% CI: 2.16, 2.88). Analysis of the gender-by-treatment interaction suggested that men and women benefited equally from Bupropion SR treatment (OR=1.01).

An exploration of heterogeneity left the results essentially unchanged.

Authors' conclusions
Bupropion SR is an effective smoking cessation aid for women. However women, have less success at quitting than men, regardless of whether they have been treated with Bupropion SR or placebo.

CRD commentary
The review question was clearly defined in terms of the study design, participants, interventions and outcomes of interest. The search, which was not reported in full, comprised searches of two electronic databases accompanied by handsearches; this might have led to the omission of other relevant studies. In addition, since it was unclear whether any language restrictions were applied, it is difficult to assess the potential for language bias. The methods used to select the studies and extract the data were not described, so it is not known whether any efforts were made to reduce bias or reviewer error. The validity of the included studies was not assessed, thus it was not possible to assess the reliability of the results of individual studies. However, all of the studies included randomisation, placebo control and biochemical
verification of the outcomes.

Studies reporting adequate data were combined in meta-analyses: first, grouped by gender, which appears appropriate, and then grouped by treatment, which appears inappropriate as the power of randomisation of the original studies is lost. Individual level data were also analysed appropriately. The second author of the review declared conflicts of interest. Given that the validity of the original studies was not assessed, a limited search strategy was employed, and the fact that no review methods were reported, the reliability of the authors’ conclusions is weakened considerably.

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

Practice: The analysis supported the current smoking cessation guidelines statement that Bupropion SR more than doubles success with smoking cessation, without making separate recommendations for men and women.

Research: The authors stated that future research should continue to investigate gender differences in smoking cessation treatment outcomes.

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