

## Is bupropion (Zyban) causing deaths?

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**TO THE EDITOR:** From 1 February to 30 June 2001, 277 602 prescriptions for the smoking cessation drug bupropion hydrochloride (Zyban, GlaxoSmithKline) were processed. The Health Insurance Commission approved 343 737 prescriptions for bupropion between 1 February and 30 June.<sup>1</sup> Comparing this figure with the 277 602 processed scripts, some 66 135 (19.2%) scripts went unfilled. One reason for this may have been extensive publicity given to reports of deaths and numerous adverse reactions following bupropion use.

The website of the Australian Drug Reactions Advisory Committee (ADRAC) reports that, as at 22 June, there had been 18 reports of deaths in patients aged from 30 years to 69 years who were using or who had recently stopped using bupropion.<sup>2</sup> ADRAC summarised intelligence on these deaths thus:

... there were a variety of reported causes of death and not a single consistent mode of death. In addition to being smokers, several patients had other existing risk factors for unexpected death such as alcohol abuse, diabetes or cardiomyopathy. Eleven of the 18 patients had an alternative explanation for death that was at least as plausible as a possible effect of bupropion. In four reports, the available information was very limited and it was not possible to assess the cause of death. Further information is being sought on three cases to aid assessment of the cause of death.<sup>2</sup>

Smokers are at 3.1 times greater risk of dying (from any cause) than non-smokers and twice as likely to die from coronary disease and stroke.<sup>3</sup> People with depression are three times as likely to be daily smokers<sup>4</sup> and have double the suicide rate of non-smokers.<sup>5</sup>

In Australia, sudden coronary fatalities occur at a rate of about 450 per million people aged under 65,<sup>6</sup> perhaps at a rate of 355 per million in non-smokers and about double that in smokers. In three months (the period of recommended bupropion use), one would expect 180 deaths per million smoker-users. Thus, among 277 602 Australian smokers, 50 might die during any given three-month period without any added risk from bupropion.

This estimate helps to place the 18 fatalities reported to ADRAC in context.

The 277 602 scripts represent about 9.5% of Australia's 2.9 million regular smokers. These people, their families and doctors deserve to have their anxieties about the risks of using bupropion addressed. We would urge the government to commission urgently a case-control study of morbidity and mortality among smokers and their relationships to use or non-use of bupropion.

**Competing interests:** SC has received funding from SmithKlineBeecham (now GlaxoSmithKline) for the preparation of professional and public educational material on smoking in Australia.

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## Carotid stenting or endarterectomy for stroke prevention

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**TO THE EDITOR:** I read with interest the article by Hender and colleagues recently published in the Journal.<sup>1</sup> I agree with the authors' conclusion that there is presently insufficient evidence to suggest the widespread use of endoluminal treatment for carotid artery disease. However, there are a number of problems with the authors' interpretation of our recent article

comparing the outcome of surgical and endoluminal treatment of symptomatic carotid stenosis.<sup>2</sup>

Firstly, the figures in the Box are completely misleading. The percentages of adverse outcome quoted for patients undergoing endoluminal treatment are those that were found for cases receiving endarterectomy, while the figures quoted for endarterectomy are the findings for endoluminal treatment. [A correction of this error was published in the 3/17 December 2001 issue of the Journal, page 672.] Hence, any reader simply looking at the Box would be left with the false conclusion that the outcome of endoluminal treatment is superior.

Secondly, the authors refer to our article<sup>2</sup> as a "meta-analysis". In our article we went to some trouble to explain that a meta-analysis was not possible, as only one small randomised trial had been published at that time. Instead, we had to use reports from single centres and we discussed the difficulties of comparing the results when patients had not been randomised.

Thirdly, the results of the CAVATAS trial were published in June 2001.<sup>3</sup> A surprising finding was that the perioperative stroke rate (defined as a neurological deficit lasting seven days or more) for patients undergoing either carotid angioplasty (with or without stenting) or conventional endarterectomy was the same (around 10%). In fact, the disabling stroke rate of around 6% after either endovascular treatment or endarterectomy was three times higher than that found in the North American randomised trial of endarterectomy.<sup>4</sup>

Finally, the authors refer to our patients undergoing carotid *stenting*, whereas the majority of the patients referred to in fact received angioplasty alone.

1. Hender KM, Anderson JN, Chong W. Carotid stenting or endarterectomy for stroke prevention? *Med J Aust* 2001; 175: 430-431.
2. Golledge J, Mitchell A, Greenhalgh RM, Davies AH. Systemic comparison of the early outcome of angioplasty

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