

tion in North America, and whether a net public health benefit was expected from reintroduction of this amphetamine product.

Why are the scientific data that form the basis of regulatory decisions in Canada considered proprietary? The New Drug Committee should have met in public, its reports and transcripts should have been posted on the Web, and other scientists, health care professionals and members of the public should have been allowed to make submissions. The committee's report provides a glimpse of the thinking behind regulatory decision-making. A glimpse is not enough: full participation and access to information are needed.

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Questioning the evidence

I am writing about a recent article in the CMA Leadership Series on Elder Care, distributed with the Nov. 8, 2005, issue of *CMAJ*.¹

As one who has been studying the

research and marketing related to Alzheimer's disease (AD) treatments for nearly a decade, I found the article disturbing. The discussion on the benefits of the AD drugs are nearly opposite to what the best evidence says.

The writer states that "In numerous randomized clinical trials (RCTs), cholinesterase inhibitors (ChEIs) have consistently been shown to improve or delay the decline of cognitive functioning, delay the emergence of challenging behaviours and slow the loss of activities of daily living. In RCTs, benefits have been shown to last over a period of up to 2 years, with data from open-label trials suggesting a longer benefit."¹

However, the company-sponsored trials upon which this statement relies are problematic and overstate the case for the role of these drugs in managing AD. The latest meta-analyses find that the effects of ChEIs are marginal to non-existent.²

I found the discussion of side effects almost laughable: "Before initiating treatment, physicians should discuss reasonable expectations with the patient and their caregiver. Patients should be warned of possible side effects, noting that they are often mild and fleeting."¹

When I have read the monographs of the key AD drugs, the effects such as nausea, vomiting, anorexia and stomach upset are as high as 30%. In fact some commentators have joked that these drugs are more effective as weight-loss pills than altering the rate of cognitive decline. Here is an example of some of the side effects related to an AD drug, rivastigmine (taken from the product monograph):

Exelon's use is associated with significant gastrointestinal adverse reactions, including nausea and vomiting, anorexia, and weight loss. In the controlled clinical trials, 47% of the patients treated with an Exelon dose in the therapeutic range of 6 to 12 mg/day developed nausea (compared with 12% in placebo). A total of 31% of Exelon-treated patients developed at least one episode of vomiting (compared with 6% for placebo). The rate of vomiting was higher during the titration phase ... than in the maintenance phase ... Five percent of patients discontinued for vomiting, compared to less than 1% for patients on placebo.³

I don't know any physician who would dismiss these effects as "mild and fleeting."

I would echo the words of one researcher, Jason Karlawish, who remarked on a flawed study on donepezil with: "Would it be churlish to wonder out loud how this paper is different from an advertisement?"⁴ I have to admit I am on the verge of losing a lot of respect for the *CMAJ* unless it stops distributing this kind of clearly biased and non-evidence-based fluff. I cannot see how it is in the best interests of physicians to have such articles published under the banner of *CMAJ*.

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[The author responds:]

Mr. Cassels raises 2 major objections relating to comments I made about the treatment of AD with ChEIs.¹ His first objection refers to the quality of the evidence supporting the use of these medications. The second objection relates to the tolerability of these drugs, specifically, addressing the issue of gastrointestinal side effects.

With regards to the evidence supporting the use of ChEIs, to date there are 22 RCTs with ChEIs published in leading peer-reviewed journals, including the *New England Journal of Medicine*, the *Journal of the American Medical Association*, the *Lancet*, *Neurology* and *JAGS*, that have consistently shown a modest benefit for patients with AD. All these trials were carried out under