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Effectiveness of selective serotonin reuptake inhibitors

As a family physician I see many patients with mood disorders and selective serotonin reuptake inhibitors are an important therapeutic option for them. I have the clinical impression that drugs in this class can be very effective, and I prescribe them often. I was thus interested to read what the systematic review by Barbui and colleagues revealed about their effectiveness.¹

I was disappointed and puzzled by the bizarre primary outcome measure selected by the authors: the proportion of patients who left a study early for any reason. Consider the ideal situation in which no one in either study arm drops out; it would be impossible for the active treatment to be better than placebo even if all treated subjects went into remission. How can this be a measure of effectiveness?

In my practice, the biggest challenge is persuading patients to persist with therapy through the first few days of unpleasant side effects until the beneficial effects become manifest. I consider early dropout to be a failure of my persuasive powers and not an indication that the therapy is ineffective. I believe that it is important to distinguish between dropout in the first days of treatment, which is a consequence of the predictable and often transitory unpleasant side effects, and delayed dropout, which may reflect treatment failure. The authors failed to stratify their analysis on the time of dropout

and their analysis is thus not informative with respect to dropout for the important end points of treatment failure or persistent side effects.

As a clinician I am primarily interested in the effectiveness of a drug in those who actually take it. It is thus disappointing that the authors gave short shrift to their secondary outcome measures, all of which showed a significant benefit of active treatment.

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[The authors respond:]

We selected leaving the study early for any reason as the primary outcome for our systematic review¹ because patients frequently stop taking or change their antidepressant medication. In Italy, for example, a recent survey showed that of more than 2800 adults observed for 6 months after receiving their first antidepressant prescription, 60% received only occasional prescriptions after their first one.² We therefore reasoned that treatment adherence might represent a clinically useful outcome measure in meta-analyses of randomized controlled trials, as we thought that under experimental conditions this outcome might integrate patients' and clinicians' judgments of efficacy, safety and tolerability into a global measure of effectiveness and acceptability. Similar reasoning was recently used in a clinical trial of antipsychotic drugs.³

We acknowledge that this outcome measure may only offer a "down-to-earth" evaluation of a drug's effective-

ness and acceptability, but this limitation can be seen as a strength in a field of research where efficacy is typically quantified as a score on a rating scale: in clinical practice, physicians seldom define patient improvement with rating scales.

For patients with moderate to severe major depression, one of the first goals is to keep them on treatment. Therefore, the main clinical question of our systematic review was whether paroxetine is better than placebo at keeping patients on treatment. Staying on treatment can also be seen as a hard measure with little measurement error. In addition, we investigated the effectiveness of paroxetine in those who actually took it and we also used standard measures of depression.

The main clinical message of our analysis is that the effect of antidepressants in patients with moderate to severe depression is modest. Physicians should consider combining pharmacologic and nonpharmacologic treatments such as psychological and psychosocial interventions backed by scientific evidence.^{4,5} Similarly, patients should not receive the message that modifications of thought, mood and behaviour can be achieved by pharmacologic means only.

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A “take with a grain of salt” label for Holiday Review articles

For the past decade *CMAJ* has published a series of articles inspired by the holiday season in a section called the Holiday Review. Some of these articles consist of quirky questions addressed with real data whereas others are, in the words of *CMAJ*'s editors, “evidence-free exaggeration and premeditated preposterousness.” Although these articles are a welcome holiday diversion for many physicians, confusion has sometimes arisen because these articles are indexed in MEDLINE as if they were real research articles.

To see if these articles have been mistaken for evidence-based articles, I searched Google Scholar for citations of Holiday Review articles published in 1999–2006 and then reviewed these citations. In some instances, the authors citing Holiday Review articles clearly understood that they were citing a tongue-in-cheek “study.” However, in at least 4 instances, the citing authors appear to have mistakenly cited

evidence-free articles as if they were real studies: a citation¹ of a case report in which the patient was a cartoon character,² a citation³ of my own completely evidence-free paper⁴ and 2 other citations^{5,6} of Holiday Review spoof studies.^{7,8} If *CMAJ*'s Holiday Review articles are to continue being indexed in MEDLINE, perhaps it would be prudent to insert a note at the end of each evidence-free abstract stating that the article is for entertainment purposes only and is not a real study.

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[A *CMAJ* Deputy Editor responds:]

We thank Christopher Naugler for bringing this to our attention. Normally, spoof science does not appear in PubMed searches. However, Naugler's findings show that the system we have been using is neither inclusive nor foolproof. In the future, we will include a disclaimer in the titles of our Holiday Review science articles.

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Health Check program

One of the major tools to reduce the prevalence of hypertension and improve hypertension control is to reduce the amount of sodium added to our foods during processing. Recently we estimated that hypertension could be prevented in 1 million Canadians by reducing sodium additives to a healthy level.¹ However, a reduction in sodium additives will not happen overnight. A collaborative and progressive approach to reducing sodium consumption by 2020 was recently endorsed by 17 Canadian health organizations, including the Canadian Medical Association, the Heart and Stroke Foundation of Canada and Blood Pressure Canada.

Education of the public is critical, as is the development of foods with less sodium. The Health Check program of the Heart and Stroke Foundation of Canada has already resulted in significant amounts of sodium being removed from many foods. As a result of Health Check's work with the Campbell Soup Company, for example, Blood Pressure Canada recently awarded the company a certificate of excellence for sodium reduction.

Health care practitioners, the food industry and health groups like the Heart and Stroke Foundation of Canada need to continue to work together to make a healthier diet a reality, and Health Check is an important program that is taking us toward that goal. Health advocates need to focus their energies on companies that continue to add large quantities of salt and other harmful substances to our foods rather than on organizations striving to make Canadians healthier.²

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Competing interests: Norm Campbell received travel assistance from McCain Foods to speak at the regional meeting of the Atlantic Dietitians of Canada in 2007. There was no contact with McCain Foods about the talk or its content.

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