
# Effectiveness of donepezil in treating Alzheimer's disease

I congratulate Drs Steele and Glazier[1] for their excellent Critical Appraisal article, which appeared in the April issue. As a geriatrician with special interest in dementia who is participating in multinational trials of new drugs for treating Alzheimer's disease, I believe this article is of special importance and has perfect timing.

Aside from the Mini-Mental State Examination, few physicians have had experience with psychometric testing for diagnosing dementia. Moreover, the nature of psychometric testing itself presents certain issues of interpretation that need to be considered. It is, therefore, difficult to evaluate the real relevance of results based on that type of assessment. In this regard, there are two main issues on which I would like to comment.

Although the psychometric tests used in the donepezil trial[2] are widely used in dementia-related new drug trials, those tests are rather limited and might not reflect the real changes observed in treated patients. Specifically, neither of the tests provide an accurate measurement of "lack of initiative" or "apathy." Characteristically, a large percentage of patients with Alzheimer's disease have prominent apathy (lack of initiative) affecting all aspects of daily life, from their capacity to engage in daily activities to their capacity to follow and participate in conversations and any other aspect of social and private life. In my opinion, apathy is one of the cognitive functions most responsive to donepezil therapy in patients with mild to moderate Alzheimer's disease, and yet, we are not measuring it.

Unlike other diagnostic tests, cognitive testing is based on an interviewer's (physician's or psychometrist's) interpretation of a patient's performance. Those scales have been validated, their reliability has been assessed, and there are standards to guide evaluation of a particular response, but data collection and evaluation are substantially more subjective than, for instance, a fasting blood glucose result.

The Clinician's Interview-Based Impression of Change scale (CIBIC-plus), which is being used in most trials of Alzheimer's drugs, uses comparisons of performance obtained at baseline in the trial with performance at each subsequent visit. It is relevant to note that this test attempts to provide an overall evaluation of not only cognitive, functional, and behavioural-mood data but also medical, side effects, and compliance issues that might affect the final score. Moreover, the test does not provide specific questions, it merely outlines the areas (as mentioned above) on which an interviewer should obtain information. It is up to each interviewer to formulate the questions and, not being written, the questions will vary from visit to visit.

The test includes results for both patient's performance during the visit and caregiver's opinion (patient and caregiver are interviewed separately, patient first). Often, the information is contradictory, and it is up to the interviewer to decide which results better reflect a patient's condition and evolution since the start of the trial. With that information, the interviewer then gives a final evaluation (ranging from marked worsening to marked improvement) that is largely subjective and frequently conservative. Thus, it is not surprising to find a very small variation in the score.

In this era of evidence-based medicine, it is important to consider the above observations before interpreting the results of current clinical trials on drugs for Alzheimer's disease, because they might not have the same weight as conclusions derived from clinical trials in other types of medical conditions. I would be reluctant to withhold donepezil treatment in appropriately diagnosed patients on the basis of questionable "clinical improvements." Unfortunately, we do not currently have more accurate cognitive assessment-evaluation methods and therefore need to be aware of the intrinsic limitations of the current methods.

For now, donepezil is the only relatively safe drug available for treating Alzheimer's disease and, although we know it will not cure the condition or

be miraculous, it might provide some help. In the absence of a better option, it is worth trying.

*—Angeles Garcia, MD, PHD, FRCPC*
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**References**

1. Steele LS, Glazier RH. Is donepezil effective for treating Alzheimer's disease? *Can Fam Physician* 1999;45:917-9.
2. Rogers SL, Doody RS, Mohs RC, Friedhoff LT. Donepezil improves cognition and global function in Alzheimer disease: a 15-week, double-blind, placebo-controlled study. The Donepezil Study Group. *Arch Intern Med* 1998;158:1021-31.

# Are there benefits to treating these conditions?

I am writing to comment on the article by Keast et al[1] from the February issue. I would have written this letter sooner, but I was hoping someone else would do it more eloquently than I can. So far, however, no comments have been published.

This article is a simple, elegant, absolutely worthless piece of research. I got the impression that the authors were justifying the waste of valuable resources caused by the parade of patients who go to their doctors with cold symptoms. I make three points in debunking this study.

First, coding a visit as "otitis media" or "bronchitis" does not necessarily mean the person actually had the condition. Canadian physicians are notorious for overdiagnosing these conditions. Thus, we end up prescribing far more antibiotics than many of our European counterparts.

Second, just what is bronchitis or otitis media? Where do we draw the line between a cough and bronchitis, a red ear and otitis media, a runny nose and sinusitis, or a sore throat and pharyngitis? One of the tenets of good research is an accurate definition of the disease in question.

Third, let's assume we have useful definitions of these conditions, and the patients indeed had complications of upper respiratory tract infection (or bronchitis, otitis media, sinusitis, pharyngitis). These conditions are not substantially ameliorated by prescription medications (including antibiotics). The only exceptions seem to be exacerbations of chronic bronchitis and high probability strep throat (or better yet, strep throat proven with a swab culture), which make up only a small fraction of presenting cases.

I really take issue with this article, as it seems to use what we are doing to justify what we are doing (silly and circular logic and a trap for researchers). Articles of this type serve only to reinforce a wasteful and useless health care practice, both in physicians' and patients' minds. The real question that should be addressed is: what are the benefits of treating these conditions?

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**Reference**

1. Keast DH, Marshall JN, Stewart MA, Orr V. Why do patients seek family physicians' services for cold symptoms? *Can Fam Physician* 1999;45:335-40.

## *Response*

Dr Milburn not only missed one of the main points of our article, he also seems to have missed one of the main points of family medicine. The paper sought to examine the reasons patients see their family physicians for cold symptoms and found that most patients were worried about developing complications and that some were seeking relief from symptoms.

Implicitly the paper was based on the premise that eliciting and responding to patients' underlying reasons for a visit leads to better care, better patient outcomes, and fewer subsequent visits. This premise is supported by numerous well-executed studies.[1,2] This line of thinking is widespread in North America. In Europe, which is even more advanced, physicians routinely code both diagnosis and underlying reason for the encounter.[3]

The purpose of our paper was not to examine diagnostic criteria in the manner that epidemiologists would but rather to focus on the underlying reasons for utilization.

Take the example in our paper of the mother of a child who has cold symptoms. The mother might know how to treat the cold symptoms (and indeed our study showed that such symptoms were treated for 7 days on average before a physician's opinion was sought) but might be worried about possible pneumonia or meningitis. Dr Milburn seems to imply that such a visit is a waste of resources. I do not agree. Patients do not often come to their family doctors with a diagnostic label. They come with symptoms and fears that require clinicians to take the problem and the fears seriously. Anything less indicates a misunderstanding of the