
Treatment Expectations in Alzheimer's Disease

While people with Alzheimer's disease (AD), and their caregivers, do not expect treatment to reverse dementia, they do expect that it will show its effects in cognition, function, behaviour, social interactions and leisure activities. People expect a mix of stabilization and improvement. For patients with mild dementia, some hope of recovery is a common expectation, whereas in patients with moderate dementia, the aim is to stabilize the disease. This article discusses the variety of methods that exist to help patients and caregivers understand the goals of treatment, and understand what is achievable.

By Kenneth Rockwood, MD, MPA, FRCPC

Alzheimer's disease (AD) is a devastating diagnosis for people to hear. The initial shock is mitigated somewhat by the idea that treatment is possible. Quickly, however, patients and caregivers wonder just what can be expected of treatment. This article discusses what most patients and caregivers expect, how the idea of what to look for can be incorporated into daily practice, and some potential future directions for this vital aspect of counseling in dementia.

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Expectations of Treatment

We have several sources of information about treatment expectations, including studies undertaken with two cholinesterase inhibitors: donepezil and galantamine.

ACADIE. In the Atlantic Canada Alzheimer's Disease Investigation of Expectations (ACADIE) study, my colleagues and I investigated treatment expectations.¹ In that one-year, open-label study of donepezil, we asked patients and caregivers to set goals for treatment, using goal attainment scaling as the primary outcome.² We also had the treating clinicians set goals, blind to what the patients/caregivers had done. Several trends emerged, including that patients and caregivers set more goals,

and different goals, than did the physicians. They set more goals in part because they tended to "split" where clinicians tended to "lump." For example, a patient/caregiver dyad might set separate goals for remembering recent events and remembering short lists for shopping that a physician would group as "problems with new learning."

In the ACADIE study, patients/caregivers also set more goals because they set goals that were different from those set by clinicians. For example, they set more goals in the areas of leisure and social activities than did clinicians, who tended to focus more on cognition, function and behaviour. This illustrates that while patients and caregivers

expect to see effects in cognition, behaviour and function, they are not content with such goals on their own. Hobbies, in particular, were an important source of goals for patients and caregivers, but were not common amongst the goals set by clinicians. Of note, while they were not expected to regain their prior competence, caregivers especially hoped that patients would reacquire their lost interest.

A similar pattern was seen with the progressive loss of interest in social activities. Indeed, reviewing the way that goals were scaled makes evident that such loss often occurs stereotypically (see Table 1). The pattern of loss thereby informs what people would like to “get back” as the disease progresses. Thus, for example, the family of a patient with moderate dementia might desire being able to take their loved one to a social engagement without fear of embarrassment, whereas in mild dementia, more often the goal is for patients to enjoy themselves, and fully participate when they are out.

TOPS. This emphasis on social engagement and its recovery is also a theme that is evident in the Top Symptoms (TOPS) study.³ TOPS was also an open-label study of donepezil in people with mild-to-moderate AD. The study was conducted over six months in primary-care practices across

Table 1

Pattern of Loss in Social Behaviour as Dementia Develops

Initial effects	Patients begin to lose interest in common social activities. They will initiate them less often, but remain content to go, and are interested when they are there. They will commonly talk about the activity afterwards.
Early effects	Patients rarely initiate social activities, but are still content to go. They enjoy the activities while they are there. They usually do not talk about them afterwards, but sometimes admit to embarrassment.
Common in established mild dementia	Patients no longer initiate social activities, and are usually content to go, generally enjoying the activities as long as they last. Afterwards, however, they rarely talk about them. May remember, or even dwell on hurtful aspects of the experience (e.g., forgetting a familiar name).
Seen later in mild dementia	Patients begin to resist going to social events, even if they seem to have a good time while there. Often little remembrance of the event, even within the same day.
Suggests moderate dementia	Patients routinely resist social events, and when there, often ask to leave, even after only a few minutes. Can often enough act in a stubborn manner that family members worry about taking them out.
Common in moderate dementia	Patients actively resist going out and can even be belligerent. Often, families will limit outings to very familiar environments.

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Canada and included 101 patients and their physicians. The patients and their physicians completed a TOPS checklist. Caregivers and physicians were blind to each other’s responses. Even so, four symptoms topped both lists. Problems remembering was the most common symptom reported (97%). Next were problems with temporal orientation (89%) and repetitiveness (85%). None of these items is particularly surprising, and accords to the idea of the heavy cognitive burden of AD.

The next most important problem—and a clear expectation of a positive treatment effect—is so-called “cognitive activation.” On the TOPS checklist, this was described as the patient being “present,” “in tune,” or “more like himself/herself” and was checked in 84% of cases. In ACADIE, we also noted this from the qualitative evaluations of what goals people set, and what they talked about. While initially people did not know to expect it of treatment, it quickly

became apparent that the report of “dad’s back” or “my father is more like himself” was a robust indicator of successful treatment.

In addition to these four symptoms that were identified more than 80% of the time by physicians and caregivers, four more were present on each group’s “top ten” list. These were problems in spatial orientation, leisure, attention and apathy. These expectations were met to varying degrees, as will be

should expect: some symptoms will get better, some will stabilize, and some will get worse. It was also reassuring to see that, in general, people who improved on the TOPS checklist also improved on the Alzheimer’s Disease Assessment Scale—Cognitive subscale (ADAS-Cog) which is the standard neuropsychological measure used in drug trials for mild-to-moderate AD.⁴

VISTA. The most recent study to look at treatment expectations

listening carefully, setting goals and adjudicating them likewise is an important part of therapy. In short, for many problems faced by patients and caregivers, identifying them is an important step to resolving them. The study also found that improvement on the ADAS-Cog was reflected in improvement in goal attainment. What it also made clear, however, was that the same could not be said when the ADAS-Cog worsened. Many people with clinical improvement had worse ADAS-Cog scores, which suggests that some of the standard ways in which we test anti-dementia drugs might underestimate the extent of clinical benefit. Given its design, the VISTA trial also shows that the effects are not just due to placebo, but that cholinesterase inhibition—here with galantamine—is a clinically important treatment.

These studies offer some lessons for routine office practice. One is that, however good the ADAS-Cog (and the much shorter and more widely used Mini-Mental State Examination [MMSE])⁶ might be, they are inadequate for detecting the full range of treatment benefits which are important to AD patients and caregivers.

detailed in the full TOPS publication. Of note, for the current purposes, the TOPS study showed the most consistent improvement in cognitive activation, attention, and apathy. What is also helpful to note, from a clinical standpoint, is that symptomatic changes were often consistent within patients. In other words, in most patients, either no symptoms improved (38%) or most symptoms improved (20%). Still, that leaves a substantial proportion in whom some, but not all symptoms will improve, and that is what people

of patients and caregivers is the Video Imaging Synthesis in Treating Alzheimer’s disease (VISTA) study. This was a randomized, placebo-controlled trial that also used goal attainment scaling as the primary outcome.⁵ The active compound was galantamine and the duration was four months, with a four-month, open-label extension. The study makes two important points. First, the treatment was clinically meaningful, and could be detected by clinicians using a goal-setting approach. Second, the process of

Lessons for Office Practice

These studies offer some lessons for routine office practice. One is that, however good the ADAS-Cog (and the much shorter and more widely used Mini-Mental State Examination [MMSE])⁶ might be, they are inadequate for detecting the full range of treatment benefits which are important to AD patients and caregivers. To capture this range—and to know too when patients are not responding so that we can offer

medication changes—it is important to define targets for treatment.

There are many ways to set goals. The goal attainment scaling procedure is in most settings too time-consuming for primary care, but there are ways to adapt it. In Nova Scotia (and other provinces in Atlantic Canada), drug reimbursement for cholinesterase inhibitors is tied to physicians completing a form. The form has them record the MMSE and the Functional Assessment Staging Tool (FAST).⁷ The MMSE and FAST help determine eligibility. For identifying treatment response, however, physicians record target symptoms. Three symptoms need to be identified, and these can be adequately summarized in a single sentence each. For example, considering some of the common symptoms described in Table 2, descriptions of target symptoms might be “dad repeats himself 20 times a day more if there’s an upcoming appointment.” Or “mom gets lost sometimes just going to the corner store. We have to watch her all the way.” At follow-up, in 3 to 6 months, these statements form the basis for individualized scales, and physicians simply record on a Likert scale anchored at a score of 4 (“no change”) whether the symptom is “much better” (a score of 1) to “much worse” (a score of 7). Thus the goal of treatment is not

Table 2

Common Expectations of Treatment and Patterns of Response

Misplacing objects	This is inquired about often, but very uncommonly responds to treatment.
Repetitive questioning	Often set as a goal of treatment, and often met. Often signifies a robust treatment response.
Temporal disorientation	Common, often met, even when other goals might not be.
Spatial disorientation	Common, inconstantly met; often not related to meeting other goals.
Being more engaged/aware/ having better initiative	A common goal, often met, and generally a sign of a robust treatment response.

specified, but discussions around improvement are anchored to specific, observable, quantifiable events that are relevant to patients and families. While the process requires some time to complete, it requires no more time, and is less arbitrary, than deciding whether an individual should continue to receive treatment based on their score on the MMSE, a screening test.

Physicians who routinely use a target-symptoms approach report many benefits. For deciding about reimbursement, the chief advantage is being able to make decisions on good clinical grounds. Moreover, the approach aids clinical decision-making in general, as physicians commonly notice that patterns establish themselves fairly quickly. For example, patients who have problems with the television remote control often have problems with the microwave and the telephone.

Even though families will commonly report these separately, a clear pattern of impaired visuospatial functioning is evident. This set of deficits often is most forcefully a problem in patients who stay on their own during the day. It is easy to imagine the prior coping mechanism of calling dad to heat up the prepared meal in the microwave, and coming home to find him happily watching television, now entirely disrupted. In our experience, this pattern often responds to treatment with a cholinesterase inhibitor. Understanding such patterns, and being able to counsel and to help gratifyingly enhances the clinical encounter.

Future Possibilities

Understanding the treatment expectations of people with dementia, being able to counsel them about those expectations, and translating the expectations

into specific, clinically relevant treatment goals, enhance physicians' abilities to help patients and families. Still, it places demands on physicians' time, and such demands can be impossible to meet. How to provide symptom-specific expertise directly to patients and families is a challenge. Patients and families are widely distributed, but they want and need a lot of information. Specialist groups have expertise, but not the reach. Family physicians have the reach, but not the time. To help solve this conundrum, plans are now in the works to distribute the TOPS checklist, and provide specific continuing medical education around that approach to following treatment effects. In addition, a website (www.dementiaguide.ca) has

been created. [Disclosure: I founded the company and am majority owner of it.] It provides information on the 60 common symptoms in dementia, as well as detailed information about each, in terms of their definition, staging and pathophysiology, as well as management. Specific continuing health education programs are also being designed for this, so that physicians can recognize the one-page summary of treatment effects that the website generates for their use. The intention is that patients and caregivers, who have the time to work with the site, can gain access to expert information on symptoms of interest to them. We envisage a role for the family physician to help patients and families track symptoms. In short, we hope that the website

will give physicians a head start in the clinical interview, by being able to focus on specific concerns that families have already identified. The future appears to hold many possibilities for a symptom-based approach to dementia treatment. This should allow a better understanding that present therapies have much to offer many patients with dementia, and that there can be some expectation of treatment success, even when such therapy falls short of a cure.

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