Harvard
Center for
Risk
Analysis

JUNE 1999

Volume 7
Issue 4

Risk in Perspective

The Cost-Effectiveness of New Drugs for Alzheimer s Disease

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Do the clinical benefits of the drugs justify their costs?

Alzheimer's disease (AD) is a devastating illness, affecting patients' cognition, memory, judgment, speech, ambulation, and continence. It typically leads to impaired functioning, and is associated with high rates of depression, agitation, and psychosis. It has a high prevalence, affecting 4 million Americans, approximately 10 percent of Americans 65 years of age or older, and between 25 and 45 percent of those 85 years or older. With the aging of the U.S. population, it is projected to affect more than 10 million individuals by 2040. The burdens that AD places on family caregivers and the nation's health care system are substantial.

In recent years, drugs that temporarily halt or slow the decline in cognitive deterioration associated with the disease have been developed and approved by the Food and Drug Administration, and work on other medications is underway.

As the health care system grows ever more concerned with demonstrating that new drugs offer value, there has been an increased emphasis on costs in addition to traditional concerns about risks and clinical effectiveness. For new medications for Alzheimer's disease this means confronting new questions: Do the clinical benefits of the drugs justify their costs? To what degree do potential economic benefits related to decreased medical and supportive care for Alzheimer's disease patients offset the costs of medications? Would dollars spent on AD medications produce greater effects if they were targeted to alternative interventions?

To address such questions, we conducted a cost-effectiveness analysis of a new drug, donepezil, for mild and moderate Alzheimer's disease compared to the option of no treatment.

Cost-Effectiveness Analyses

Cost-effectiveness analyses (CEAs) show the relationship between the resources used (costs) and the health benefits achieved (effects) for a health or medical intervention compared to an alternative strategy. The cost-effectiveness ratio (C/E) reflects

the difference in the interventions' costs divided by the difference in their health effectiveness. CEAs allow for comparisons across a broad spectrum of interventions and clinical conditions, as long as the numerators and denominators from different ratios are reported in similar terms and are obtained by similar methods. The method has been used to study a broad range of drugs, including treatments for hypertension, complications from AIDS, and a variety of psychiatric conditions.

We followed recommendations of the Panel on Cost-Effectiveness in Health and Medicine which call for analysts to adhere to standard methodologic conventions, including use of a "reference case," in order to enhance the transparency of study methods, and to improve the reliability and comparability of results.

The study was conducted from a societal perspective, accounting for all costs and health effects resulting from the intervention regardless of who bears or receives them. Costs were defined in net terms: that is, they include both the costs and potential savings resulting from use of an intervention. We included the costs of health care resources (medications, acute hospital care, physician services, nursing home care), non-health care resources (support services provided by paid caregivers) and the provision of unpaid care by family members. The effectiveness of care was measured in terms of quality-adjusted life years or "QALYs." Future costs and QALYs were discounted at a 3 percent annual rate.

Estimates for the model came from a variety of sources. To estimate disease progression, we used data from a national longitudinal database of Alzheimer's disease patients. To measure the effect of donepezil on the transition probabilities, we analyzed data from a randomized, placebo-controlled clinical trial. Cost estimates were based on published estimates. The cost of the drug was based on the average wholesale price. All costs were expressed in 1997 dollars.

To measure health-related quality of life, we relied upon the preference-weighted instrument, the Health Utilities Index, which was administered in a companion, cross-sectional study of 528 caregivers of AD patients, stratified by disease stage (201 mild, 175 moderate, and 142 severe) and setting of care (354 community and 164 nursing home). Due to limitations in patients' abilities to respond to questions themselves, we asked primary caregivers to complete the HUI:2 questionnaire as proxy respondents.

The various inputs were incorporated in a "state-transition," or "Markov" model to characterize the progression of individuals with AD through different disease stages and residential settings.

Results of the Study

Figure 1 shows the results of our model. The figure shows that in our model the cost-effectiveness of the drug depends largely on assumptions about the duration of the drug effect. Assuming that the drug effect lasts 18-months, the C/E ratio is $9,400/QALY for mild AD and 77,000/QALY for moderate AD. Threshold analyses show that savings would be achieved in mild AD if the drug effect persists for 24 months; for moderate AD patients, the model predicts that the drug will not achieve savings regardless of the duration of the drug effect, though the C/E ratio would fall below $50,000/QALY if the drug effect lasts beyond 24 months.

The results suggest that the cost of the drug may be partially or completely offset by a reduction in the costs of care due to a deceleration in the progression of patients to more severe and more costly disease stages and settings. From a societal standpoint, donepezil

could be a cost-effective or even cost saving treatment for mild AD patients. The cost-effectiveness ratios are higher in moderate AD, and more sensitive to assumptions about the drug duration. For purposes of comparison, Table 1 shows the cost-effectiveness of selected interventions focusing on the elderly.

To our knowledge, this is the first study of Alzheimer's disease treatments to use formally the recommendations of the Panel on Cost-Effectiveness in Health and Medicine. Our model underscores the uncertainty surrounding the drug's cost-effectiveness given available data. If the magnitude of the drug effect is varied one standard error in either direction, the results change substantially. If the duration of the drug effect is varied from six months to two years, the cost-effectiveness ratio changes by several orders of magnitude.

What should decision makers make of such uncertainty on cost-effectiveness? For one, the uncertainty can be incorporated into judgments which include other complex factors, including patients' response to the drug, toleration of side effects, availability of caregiver support, patients' and families' financial situation, and the availability of insurance coverage. Ultimately, whether it is worth roughly $1500 (the annual cost of the drug) per patient per year to enhance cognitive functioning temporarily in a patient with AD is a determination that turns in part on considerations of cost-effectiveness. The value of a modeling exercise and a cost-effectiveness analysis lies in its ability to shed light on this issue by projecting costs and health effects based on the best available data, by making all assumptions explicit, and by appraising the degree of uncertainty in the assessment.

Elucidating the uncertainty can also help identify gaps in our knowledge and serve to improve future research. This study highlights the absence of direct evidence on the drug's impact on costs, quality of life, and nursing home placement, and the lack of long-term efficacy data from controlled studies. Decision makers would likely benefit from such information and future researchers would do well to consider collecting and analyzing such data.

Interpretation of the results from the standpoint of any individual payer, however, is complicated by the patchwork nature of the reimbursement system. Much of the direct cost associated with AD is paid for out-of-pocket by patients and their families. Indeed, the largest share of AD-related direct costs -- comprised of custodial home and nursing home care -- is generally not reimbursed by insurers. Medicare, which provides health insurance for most older Americans, does not pay for most nursing home care -- or for most outpatient prescription drugs for that matter. Thus, it remains unclear whether these results would hold from the perspective of a particular managed care plan or other health insurer.

Cost-effectiveness analysis can serve as an important tool for evaluating costs, risks, and clinical effectiveness in a rigorous and systematic way. As new drugs for AD are developed and used, and as considerations of cost-effectiveness become more important, clinicians and other health care decision makers would benefit by becoming more discerning consumers of this information.

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FURTHER READING

Neumann PJ, Hermann RC, Kuntz KM, Araki SS, Duff SB, Leon J, Berenbaum PA, Goldman PA, Williams LW, Weinstein MC. Cost-Effectiveness of Donepezil in the Treatment of Mild or Moderate Alzheimer's Disease. Neurology 1999;52:1138-45.

Neumann PJ, Kuntz KM, Leon J, Araki SS, Hermann RC, Hsu MA, and Weinstein MC. Health Utilities in Alzheimer's Disease: A Cross-Sectional Study of Patients and Caregivers. Medical Care, 1999;37:27-32.

Weinstein MC, Siegel JE, Gold MR, Kamlet MS, Russell LB for the Panel on Cost-Effectiveness in Health and Medicine. Recommendations of the panel on cost-effectiveness in health and medicine. JAMA. 1996;276(15):1253-1258.

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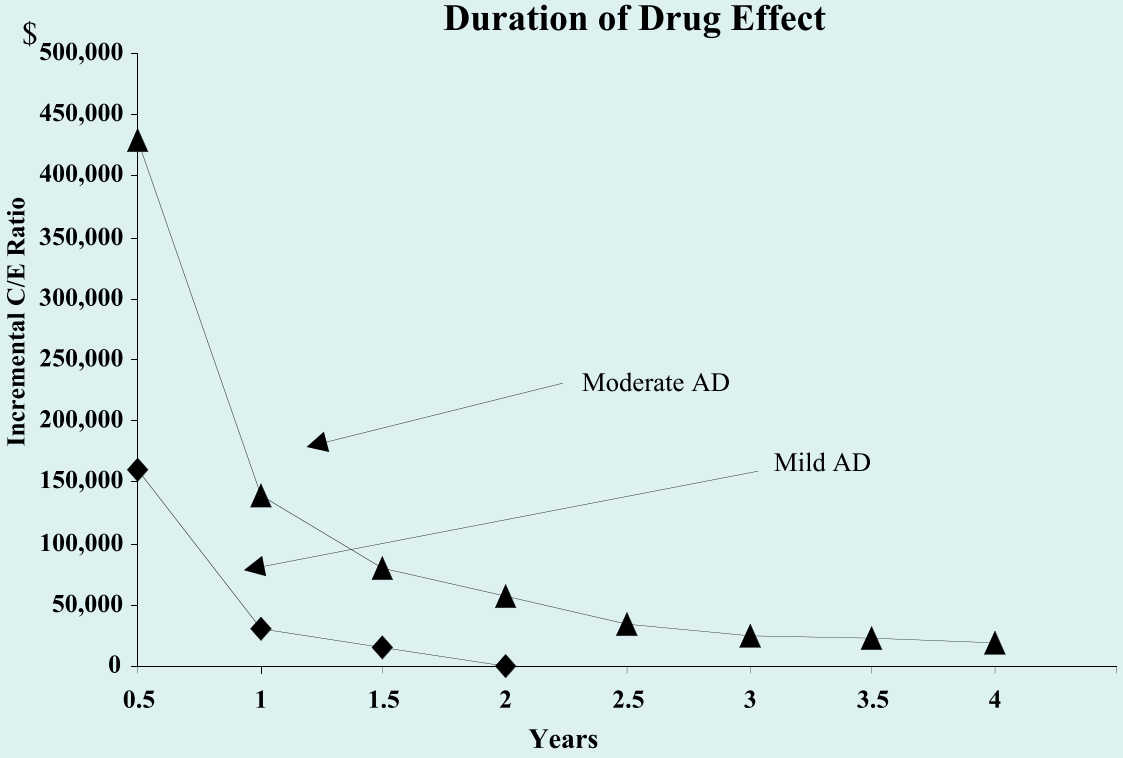

Adapted from Neumann et al. Cost-effectiveness of donepezil in the treatment of mild or moderate Alzheimer's disease. Neurology 1999;52:1138-1145.

Figure 1

Cost-effectiveness of selected interventions for the elderly

Intervention	Δ C/ ΔQ*
Screen and treat with hormone replacement therapy if bone mass density <0.9g/cm2 for osteoporosis vs. no intervention for perimenopausal 50-year-old white women with intact uteri	$ 7,600
Comprehensive treatment of noninsulin-dependent diabetes mellitus with goal of normoglycemia vs. standard diabetes care for population, age 19-75, with newly diagnosed diabetes	$18,000
Annual fecal occult blood test for colorectal cancer vs. no screening for population ages 50-75	$19,000
Coronary angiography vs. medication only for acute myocardial infarction (AMI) patients age 55-84, with positive exercise test and prior AMI	$20,000-$86,000
Thrombolytic therapy with t-PA for AMI vs. thrombolytic therapy with streptokinase for patients with AMI who were candidates for thrombolytic therapy	$34,000
Tissue plasminogen activator (t-PA) vs. treatment with stretokinase for eligible patients post-AMI	$43,000
Annual pap smear vs. pap smear very 3 years for women age 65 and older	$66,000
Coronary artery bypass graft and revascularization if indicated vs. medication only for AMI patients age 55-84, with negative exercise test and no prior AMI	$68,000-$270,000

*All cost-effectiveness ratios were adjusted to 1997 dollars using the medical care component of the Consumer Products Index, rounded to the nearest thousand.

Adapted from Neumann et al. Cost-effectiveness of donepezil in the treatment of mild or moderate Alzheimer's disease. Neurology 1999;52:1138-1145.

Table 1