

## The Pharmacoeconomics of Alzheimer's Disease

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### *Presentation Summary*

Alzheimer's disease (AD), the leading cause of disability in people older than 75 years of age, has direct and indirect medical costs estimated at \$100 billion per year. Yet underdiagnosis, coding, and reimbursement barriers result in most patients with AD receiving inadequate care. The vast majority of managed care organizations (MCOs) still lack formal disease management programs for AD. In several documented studies, the total costs for managing patients with AD increased significantly over age- and comorbidity-matched controls without AD. Importantly,

these extra costs include not only nursing home care but also medical claims for inpatient stays, emergency department visits, and outpatient care. The extra costs are especially high in those patients with comorbidities such as diabetes or heart failure. Emerging pharmacoeconomic data indicate potential savings in medical care costs associated with early treatment of AD and the potential cost effectiveness of cholinesterase inhibitors such as donepezil. These studies document that Medicare MCOs are in need of directed efforts to improve medical management for members with AD.

Alzheimer's disease (AD) is the most common cause of functional disability in people older than 75 years of age and is the fourth leading cause of death.<sup>1</sup> Estimates from the early 1990s indicate the current annual direct and indirect costs for AD may be as high as \$100 billion.<sup>2,3</sup> Thus, AD ranks third after cancer and heart disease in terms of total cost to society.<sup>4</sup>

Approximately 2 million to 4 million elderly individuals in the United

States have AD.<sup>5,6</sup> Although the exact number of affected elderly patients is uncertain, most researchers estimate the following: up to 6% of those older than age 65 may have AD; the prevalence increases every year after the age of 65; and up to 40% of the population older than age 85 may be afflicted with AD.<sup>1,5-7</sup>

With the world population rapidly aging, the number of AD cases is expected to double or triple by 2050. Some researchers predict that 14 mil-

lion Americans will have AD by 2040.<sup>6</sup> The AD-related increases in healthcare costs over the next several decades will have tremendous implications for payers and providers alike. However, many professionals in today's healthcare settings—including those in managed care settings—fail to recognize the economic impact of AD.

This article will explore reasons for the underrecognition of AD and will then examine in detail the acute and chronic costs attributable to this disease. The evaluation of such costs are critical in any justification of specialized AD case management approaches aimed at improving AD care.

### **Positioning AD on the Managed Care Radar**

Managed care organizations (MCOs) often examine priorities for potential disease management programs by determining the top 20 to 30 cost drivers in their healthcare systems. Such rankings provide a natural economic context for the analysis. However, despite the high prevalence of AD in the elderly, these listings of expensive conditions invariably do not include AD, even when the MCO evaluation focuses on diseases of the elderly.

There may be several reasons for this common, and glaring, omission. Dementia is vastly underrecognized by physicians and caregivers, and even by spouses or close family members of the patient with AD. Because family members often miss the signs of cognitive failure, the dementia is not brought to the attention of a physician.<sup>7</sup> In many cases, the early symptoms are mistaken for normal aging or senility.<sup>6</sup> A recent survey of AD caregivers reported an average 22-month delay between first recognition of symptoms and diagnosis.<sup>8</sup>

Failure of primary care physicians to recognize the patient with early AD is a common occurrence. This diagnostic gap can be attributed to inadequate training and experience in AD

diagnosis (including insufficient knowledge of tools such as mental status testing, evaluation of cognitive function, and diagnostic algorithms for dementia).<sup>9</sup> In inpatient clinical settings the AD or dementia diagnosis may be masked by comorbidities, eg, the elderly patient admitted to the hospital with a broken hip or aspiration pneumonia may also have AD, but the diagnosis is usually missed or neglected. In addition, diagnosis-related groups (DRGs) for acute complicating conditions of AD, such as aspiration pneumonia, may be reimbursed at a higher rate, creating coding disincentives for the use of DRGs related to dementia.

Structural barriers within the medical system may also contribute to the late diagnosis and undercoding of AD. Providers are not reimbursed adequately for counseling and other services required for quality AD management, resulting in much of this care simply not being provided. Frequently, for example, fee-for-service and capitated payments for a Medicare patient are insufficient to cover the time required for extensive counseling, caregiver support, or treatment of early AD. Thus, physicians may focus on management of more acute—and more easily reimbursed—primary diagnoses.

Employing a medical claim code for senile dementia (290.0, a psychiatric code) leads to lower payments. Some medical carriers and MCOs may also reimburse less for AD (International Classification of Diseases-9 code 331.0). Also, most general practitioners do not have the time or training to administer a Mini-Mental State Examination (MMSE). Consequently, they are not only ill-equipped to implement care but full reimbursement also may be refused. This may explain why many primary care physicians feel more comfortable coding for hypertension rather than AD as a cause for the outpatient visit.

In the coming years, new physician incentives for recognition and man-

agement of dementia may be created by changes in reimbursement policies, which pay more for high-risk members in MCOs. Today, most indirect healthcare costs for AD are currently borne by patients, their families, and society; Medicare and Medicaid pay for the majority of the direct healthcare costs. As the elderly population continues to grow,<sup>10</sup> new AD management or case management approaches are needed. Investments in new programs must include an increased focus on early diagnosis and effective case management. The new AD management programs will also require expanding investments in pharmaceutical agents such as “cognitive enhancers” and psychotropics, which may be effective in facilitating case management and reducing costs. In addition, clinical practice guidelines and formularies must be developed.

The cost information reviewed in the remainder of this article is intended to present data supporting the notion that AD deserves a place on the list of most costly diseases in MCOs and therefore requires a disease management or specialized case management approach.

**The (Hidden) Costs of Dementia**

How costly is dementia? One large staff-model health maintenance organization (HMO) tracked the total healthcare costs for all adult enrollees.<sup>11</sup> Not surprisingly, the average costs for adults with chronic conditions were at least double (range of 80% to 300%) the costs for adults without chronic conditions. In Medicare patients, the age-adjusted mean costs for chronic conditions, such as arthritis, depression, diabetes, respiratory disease, and hypertension, were between \$5700 and \$6700—a change in cost ranging from 122% to 175%. In this large managed care population, the absolute mean cost of care was highest for dementia—\$9824—representing a 175%

increase over costs of care for the age-adjusted nondementia population.

In another recent study, 0.5% of the managed care population with codes for dementia or AD accounted for 3.6% of total healthcare expenditures within the plan.<sup>12</sup> The percentage of patients with AD probably is much larger, considering the administrative data used for this study probably underestimate the prevalence of AD by a factor of 10.

Similarly in a recent case-control study involving more than 80,000 Medicare enrollees in 4 geographical locales, the mean total cost for 677 patients with dementia was \$13,687 per member compared with \$9276 for 677 matched controls.<sup>13</sup> As indicated in Table 1, almost 75% of the higher costs among cases were attributable to inpatient costs for which the MCO would be responsible.

Much of the excess cost highlighted in this study is likely generated by the interaction of the dementia with a comorbidity. When patients with AD had 1 comorbidity, such as heart disease or diabetes, the total cost of patient management was \$10,435 per member compared with a total cost of \$526 for the control member without AD with the same diagnosis of heart disease or diabetes. With 2 comorbidities, the cost differential between

**Table 1.** Excess Medical/Prescription Costs of Alzheimer’s Disease in Managed Care

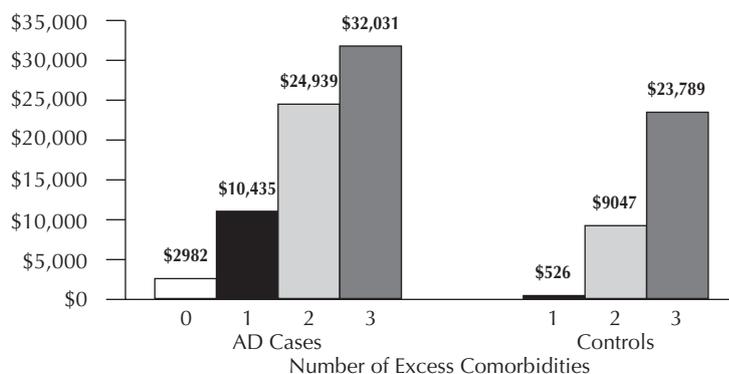
Type of Service	Cases (\$) (n = 677)	Controls (\$) (n = 677)	P
Medical claims	12,824	8591	< 0.001
Inpatient	9529	6377	< 0.001
Emergency department	545	221	< 0.001
Office visits	470	484	0.826
Prescription claims	663	685	0.695
Total	13,487	9276	< 0.001

Source: Reference 13.

cases and controls was even more pronounced (Figure). The increased medical costs attributable to AD in these patients illustrate a key point: Dementia complicates management of other chronic conditions. For example, patients with AD who have dia-

betes will probably not take their insulin or follow their diets. Similarly, patients with AD who have heart failure may be noncompliant with diet and medication. As reflected in the high AD costs in the studies cited, greater costs for hospitalization and acute care result.

**Figure.** Alzheimer's Disease Increases the Cost of Patient Management—Especially in Those with Comorbid Conditions



AD = Alzheimer's disease.  
Source: Reference 13.

When a patient with AD is admitted to the hospital, costs continue to increase. The cognitive impairments, limited mobility, and incontinence associated with dementia lengthen the stay, for example, by increasing noncompliance with diagnostic tests, risk of infection, and risk of accidents such as falls. Even if cognitive impairment in the elderly is not specifically diagnosed as AD, it can be a clear risk factor for extended hospitalization. A study of more than 900 senior citizens in California found that the 17% of the population who had some degree of cognitive impairment were twice as likely to be hospitalized, with a length of stay exceeding 6 days.<sup>14</sup>

For clinicians and MCO administrators who consider that skilled nursing facilities and long-term care constitute the primary costs of AD, excessive rates of hospitalization for patients with AD may be surprising. Because there are many opportunities for the average MCO to better control AD costs through improved medical management,<sup>15</sup> data on excess direct inpatient costs of dementia are crucial to MCO managers seeking productive areas for disease management investment.

**Table 2.** Projected Savings as a Result of Treatment-Related Changes in Cognitive Function

Initial MMSE Score	Annual Cost Savings if MMSE Is Raised by:			
	+10	+5	+2	+1
20	\$1965	\$1242	\$587	\$312
15	\$3666	\$2424	\$1186	\$638
12	\$5630	\$3805	\$1876	\$1008
Initial MMSE Score	Annual Cost Savings if MMSE Is Prevented from Falling by:			
	-10	-5	-2	-1
20	\$365	\$765	\$2424	\$7537
15	\$744	\$1611	\$5113	\$13,733
12	\$1164	\$2494	\$7407	\$16,125

MMSE = Mini-Mental State Examination.  
Source: Adapted from reference 16.

### The Role of Effective Treatment and Case Management in Reducing Total AD Costs

Can improved medical management in patients with diminished cognitive function improve their clinical and economic outcomes? This question is relevant to pharmacoeconomic evaluations and formulary discussions related to drugs approved for use in AD.

One exploratory analysis of the potential dollar savings attributable to

AD treatments found that savings could indeed be correlated with the projected degree of cognitive improvement as measured by MMSE scores.<sup>16</sup> Utilization data for 64 patients with probable AD were collected, and the total costs of care were estimated as regression functions of the MMSE scores. Based on this analysis, the potential savings in illness costs were estimated by comparing costs at various baseline and intervention-level values. For example, if a patient had an initial MMSE of 12, which reflects moderately severe AD, a drug or treatment that prevented a 2-point decline in the MMSE in 1 year was calculated to produce an annual cost savings of \$7407. Similarly, a drug capable of raising an MMSE of 12 by 2 points would have saved \$1876. The potential savings, as summarized in Table 2, were greatest for moderately to severely demented patients with AD. Based on these projected figures, the potential cost savings to the typical MCO as a result of using effective AD therapeutic agents can be millions of dollars.

To determine if such savings are really achieved in MCOs, a retrospective analysis of actual medical and prescription claims for patients with AD treated in a multisite MCO was recently performed.<sup>17</sup> Seventy patients treated with the cholinesterase inhibitor donepezil, which is recommended for individuals with mild-to-moderate cognitive deficits associated with AD, were studied.<sup>18,19</sup> The total cost of claims for patients in the 13 months before treatment was compared with the total cost 3 months after treatment initiation. The exact length of drug exposure was variable and institutional care was not reimbursed.

Results from this analysis showed the sum of medical claims for those 70 patients in the pretreatment period was \$302,057. In the period after the start of treatment, as also shown in Table 3, the total medical treatment costs were \$182,711. All categories of major medical claims,

especially outpatient and office visit claims, were reduced in the post-donepezil period. On a median per diem basis, which minimizes the individual differences in length of follow up, the medical costs were \$1.22/day lower after treatment with donepezil than before treatment ( $P = 0.02$ ).

In terms of prescription claims, the summed costs were \$38,317 in the pretreatment period and \$58,279 in the posttreatment period. On a median per diem basis, prescription costs were \$2.59/day lower before treatment with donepezil ( $P < 0.001$ ).

Overall, the adjusted median daily cost of treatment for AD was \$5.15/day before donepezil initiation and \$6.58/day after donepezil treatment. Although the higher cost of medication increased the overall costs, the reductions in medical costs produced an estimated cost offset of 65%. This analysis compares post-treatment results with pretreatment

**Table 3.** Total Costs in Year Before and After Donepezil Treatment for Patients with AD

	Summed Costs (\$) Pre-Donepezil	Summed Costs (\$) Post-Donepezil
	(N = 70)	
Medical Claims		
Inpatient	161,446	132,199
Outpatient	36,379	9523
Office	43,248	9829
Home	7422	2297
ED/Urgent care	11,463	9868
Outpatient surgical	15,985	9699
Other	26,114	9296
All medical	302,057	182,711
Prescription Claims		
Psychotropics	6624	8156
Donepezil	—	31,354
Other drugs	31,693	18,769
All prescriptions	38,317	58,279

AD = Alzheimer's disease; ED = emergency department.  
Source: Reference 17.

data from an earlier disease phase, ie, the pretreatment period; thus the results are likely to be conservative. Considering the inevitable progression of the disease over any given 2-year period, the potential for treatment-related cost reductions in long-term care, caregiver burden, and quality of life (none of which were evaluated in this study) may further demonstrate the overall cost effectiveness of donepezil treatment. Obviously, larger prospective randomized studies are needed to further demonstrate the pharmacoeconomic benefits of cholinesterase inhibitors.

Pharmacoeconomic assessments of donepezil in other clinical settings also suggest that donepezil may be cost effective when used in the treatment of AD. For example, in a recent survey of caregivers of patients with AD, results indicated that overall direct medical costs did not increase with donepezil therapy and, in fact, the acquisition cost of the drug was balanced by reduced institutionalization costs.<sup>20</sup>

Importantly, the impact of anti-dementia treatments, such as donepezil, on the AD caregiver burden may also have economic implications. In a recent 9-month analysis, caregivers of patients receiving donepezil not only reported significantly lower levels of difficulty in providing routine types of care (eg, assistance with walking, transportation, finances, household tasks), they also reported fewer hospital stays (4% versus 6% in the group providing care for patients with AD not taking donepezil), fewer emergency department visits (4% versus 10%), lower overall direct healthcare costs (\$331 versus \$402), and fewer missed days of work (4.7 days versus 7.2 days).<sup>21</sup> If caregivers are receiving healthcare coverage through the same MCO as the patient with AD, as may be the case with elderly spouses, this additional impact of AD drug therapy may be significant.

### Summary

AD is still greatly underrecognized in most clinical settings. Most practicing clinicians have not been trained in the diagnosis and management of AD and, until recently, had little to offer their elderly patients with AD. However, there is increasing awareness of the clinical and economic toll of this disease, and recent data demonstrate that AD is a major cost driver in the treatment of elderly patients with comorbidities.

Emerging evidence also indicates that early diagnosis and thus early drug treatment may reduce the substantial cost and the high levels of caregiver burden associated with this chronic disease. These pharmacoeconomic and cost-of-illness data should prompt MCOs to consider implementation of formal care management pathways similar to those available for other costly chronic diseases such as diabetes, depression, and heart disease. In fact, because patients with AD who have comorbidities may generate the highest per-member costs, modifying existing disease management programs to include the identification and treatment of patients with AD may provide many MCOs with a reasonable first step toward improved AD management.

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### ... DISCUSSION HIGHLIGHTS ...

#### Underrecognition and Undercoding

*Dr. Parker:* I agree that AD is extremely underreported in managed care. One way of capturing more data on AD is to list it as a primary diagnosis and as a cause of death. It shouldn't just be listed as pneumonia or a fall.

*Dr. Fillit:* The coding issues are of great importance. In my experience I have found that some carriers consider the codes for AD as psychiatric codes and, therefore, reimburse at 63% of the medical cost. Copayments can recover some costs,

but the additional paperwork requires staff time.

**Dr. Moak:** Coding errors and inconsistencies may also prevent healthcare systems from capturing their true costs for AD. For MCOs with psychiatric carveouts, AD is not considered a psychiatric disorder and whenever patients with AD are coded for atypical psychosis, atypical depression, or some other psychiatric code, the physician can never determine the actual AD costs. Studies of care costs based on Medicare claims data, for example, typically focus on the 331 code for AD, not the 290 series for senile dementia. This approach may result in an underestimation of psychiatry costs.

**Dr. McCarten:** Financial disincentives are not the only reason AD is not diagnosed. Residents in academic centers, for example, have no incentive to avoid the diagnosis. Therefore, we can assume the diagnosis is missed or not made in primary care.

**Dr. Fillit:** Unquestionably, underdiagnosis is the first problem. The undercoding simply compounds the problem.

**Dr. Parker:** Physicians may be reluctant to diagnose AD because there is a lack of a support system, such as resources for referrals, support groups, 800 numbers, and newsletters, to help the patient's family.

### Opportunities for Complication Prevention, Cost Reduction

**Dr. Fillit:** As I understand, the behavioral carveouts don't cover AD because the complications are medical, chronic, progressive, and costly. And yet on the medical side, it's considered a psychiatric disorder. So it falls through the cracks. I believe, as an internist and a geriatrician, that AD is a primary care medical disease. The complications are medical: uri-

nary incontinence, malnutrition, aspiration pneumonia, immobility, accidents, falls, and hip fractures. We need to move AD management into the mainstream of primary care rather than try to convince behavioral management companies to cover AD.

*“For MCOs with psychiatric carveouts, AD is not considered a psychiatric disorder and whenever patients with AD are coded for atypical psychosis, atypical depression, or some other psychiatric code, the physician can never determine the actual AD costs.”*

—Gary Moak, MD

**Dr. Moak:** Most of the opportunities for prevention of psychiatric morbidity occur at the primary care level. Preventing delirium, for example, is a major opportunity to control costs, but in a system with a mental health carveout there may be no incentive at the primary care level to head off this staggering problem.

**Dr. Fillit:** Demonstrating the ability to avoid hospitalizations will be critical in showing care managers the value of AD management. There are now a few demonstration projects, including the National Chronic Care Consortium and Kaiser Permanente in Southern California. As someone who has cared for 2000 to 3000 of these patients over the past 20 years, I believe adequate secondary and tertiary prevention can indeed avoid many hospitalizations.

**Dr. Rabins:** I consider prevention of delirium as one of the most effective ways to reduce costs, in addition to the prevention of drug interactions and increased education in managing comorbidities for family members.

**Dr. McCarten:** Treatment of patients with moderately severe AD can

reduce costs, but this doesn't change the course of the disease. What's the incentive for an HMO to keep a patient out of a nursing home for 2 years by putting him or her on medication?

*Dr. Fillit:* There are several key issues related to the impact of nursing home placement on managed care costs. First, in the treatment period before placement, there may be direct medical and hospitalization costs that can be avoided by treatment. Second, there are some subacute nursing home costs that fall under Medicare HMO reimbursement, such as the first 100 days of care. With proper treatment many of these costs may also be avoided. HMOs are often not at risk for long-term care costs; these are often covered by Medicaid or privately paid. However, these long-term care patients will still often become ill and be hospitalized. During the time these patients remain in the HMO, they may also continue to generate high costs for the MCO. Many of these patients are frail and can have as many as 6 hospitalizations per year toward the end of their lives. Of course, HMOs cannot automatically cancel enrollment for patients sent to long-term care. These extremely high, direct costs at the end of life—\$25,000 or more per year per patient—may still provide the incentives needed by managed care to invest in secondary or tertiary prevention, even in severe cases. I also foresee more managed care involvement in long-term care programs.

*Dr. McCarten:* The avoidance of hospitalization must remain the key factor of the pharmacoeconomic equation. Improvements in quality of life alone are insufficient.

### Pharmacy Perspectives

*Mr. Sosa:* Managed care pharmacies with fixed budgets particularly watch

for diseases such as diabetes and congestive heart failure. The large number of new drugs being introduced for the treatment of AD is increasing the awareness of this disease.

*Dr. Fillit:* MCO pharmacists should consider that patients with AD taking cholinesterase inhibitors also use psychotropics. Psychotropics will be prescribed for many patients not coded as AD. Late-onset schizophrenia is rare, so it's likely that most geriatric patients who are taking psychotropics and are in managed care plans have dementia. This is another pharmacy cost for dementia and another way for MCOs to identify this disease by tracking patients on psychotropics.

*Dr. Relkin:* Tracking these indicators of putative patients with dementia works best in a managed care environment and can be difficult for private and academic practices. Using medical informatics to identify overutilizers and to identify cases of dementia is a wonderful opportunity for managed care.

*Dr. Rabins:* Do individuals on cholinesterase inhibitors use fewer antipsychotic medications?

*Dr. Fillit:* There are some data on this. In the study by Small et al,<sup>6</sup> an evaluation of caregivers revealed less use of psychotropics, sedative hypnotics, and anxiolytics in patients treated with cholinesterase inhibitors. Some studies are now evaluating actual claims data to better understand the potential pharmacy budget implications.

*Dr. Rabins:* Did the effect continue beyond 1 year, when the measurable effects of cholinesterase inhibitors on cognition usually start to decline?

*Dr. Fillit:* No, it was a 6-month study, which is another reason to interpret it with caution.

**Dr. Rabins:** What about antidepressant use in patients with AD?

**Dr. Fillit:** About 30% of people with AD suffer depression as a comorbidity, so pharmacy data on antidepressant use could also assist managed care pharmacies to identify patients with AD. Of course the pharmacy data on all of these drugs can be used to identify patients with AD.

**Dr. Rabins:** Is there any evidence that cholinesterase inhibitors prevent delirium?

**Dr. Reichman:** Data on one of the new agents, galantamine, indicate the cholinesterase inhibitors may actually prevent or delay the onset of behavioral problems. If this effect is significant, the indirect cost savings could be substantial.

**Dr. Fillit:** Phase IV studies are under way. Also, data on other agents show this class has positive effects on function and caregiver outcomes and, perhaps, costs.

### Beyond the Direct Costs of Illness

**Dr. Reichman:** We must recognize that the costs of AD extend well beyond the direct costs affecting insurance companies and managed care. Not recognizing early-stage AD can greatly increase societal costs, such as patients making poor financial decisions or being involved in car accidents that lead to higher insurance premiums and liability protection.

**Dr. Parker:** The cost to the family can be significant. Many caregivers must leave work early or work part-time, which can reduce their own social security credits or pensions. A caregiver's productivity may decline as a result of care-related phone calls or emergencies. Treatment of caregivers' headaches, gastrointestinal distress,

and back and leg pain associated with caregiving also adds to the overall cost to the healthcare system. Caregivers also use more prescription drugs than do noncaregivers.

**Dr. Fillit:** Women, and sometimes men, who are caring for their parents and their own children simultaneously are called the "sandwich generation." Because these employed caregivers are often in MCOs, the costs to both business and managed care can be enormous. A corporation I'm affiliated with has an assistance program for employees who are caregivers of patients with AD, although we found that few caregivers knew about the program.

**Dr. McCarten:** With so many individuals working past the age of retirement, we now have more patients with dementia making mistakes on the job.

**Mr. Sosa:** Certainly the indirect costs and the caregiver issues impact the big picture, but I think most MCOs are still struggling with the direct cost scenario. From a practical managed care perspective, improving membership retention and establishing a mutual commitment between patient and physician may be the critical factors in dealing with these societal issues.

**Dr. Rabins:** The same point about membership retention may also apply to caregivers and children.

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