

The Costs of Alzheimer's Disease and the Value of Effective Therapies

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Abstract

Every 69 seconds, a person in the United States develops Alzheimer's disease (AD). By 2050, this rate is expected to double. Total direct costs of AD and dementia (AD/D) are estimated at \$183 billion, and are expected to increase to \$1.1 trillion by 2050. In 2010, unpaid care was valued at an estimated \$202 billion. Caregivers of patients with AD are usually family members, and provide up to 70 hours of care per week. By delaying institutionalization of an AD patient, a savings of \$2029 per month in direct healthcare costs could be realized; therefore, caregiver support is a significant factor in controlling costs. It is important for those with AD/D to have prescription plans that optimize access to AD/D therapies. Among older adults who previously did not have prescription coverage, 80% are now enrolled in Medicare Part D. Three preferred AD/D agents (donepezil, extended release galantamine hydrochloride, and memantine hydrochloride) have been identified by an expert panel. It is important, given the clinical course of AD, especially with progression to moderate-to-severe disease, that physicians continue to have access to preferred medications as demonstrated through evidence-based clinical evaluations. Many Medicare Part D beneficiaries are subject to a gap in prescription coverage known as the "donut hole," including 64% of patients with AD. Because of the increased out-of-pocket expenditures associated with this coverage gap, some patients stop taking their medication completely or reduce medication use. It is critical to avoid lapses in maintenance therapy, as functional and cognitive abilities cannot be regained. Numerous clinical trials have demonstrated the pharmacoeconomic benefits of appropriate and preferred AD therapies; greater therapeutic availability may lead to better adherence and therefore improved outcomes.

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For author information and disclosures, see end of text.

An estimated 35.6 million people worldwide have Alzheimer's disease and other dementias (AD/D).¹ The total costs associated with dementia are \$604 billion (2010 US dollars), or approximately 1% of the world's gross domestic product.¹ The majority (70%) of global costs come from Western Europe and North America.¹ In the United States, total direct costs of AD/D are \$183 billion (2011 US dollars), and are expected to increase to \$1.1 trillion by 2050. The estimated value of informal care is approximately \$202 billion (2010 US dollars).² It is estimated that 5.4 million Americans have AD. An estimated 5.2 million are at least 65 years old, while 200,000 are less than 65 years old and suffering from younger-onset Alzheimer's.² The Alzheimer's Association estimates that half a million Americans less than 65 years of age have some form of dementia, and 40% of them have AD. Every 69 seconds, a person in the United States develops AD. By 2050, this rate will double to a new AD case every 33 seconds.³ In 2003, approximately 31% of caregivers listed AD as their patient's primary disorder; this figure escalated to 49% in 2009. These rising figures are attributed not only to an increasing prevalence of AD, but also an increasing public awareness and understanding of the condition, resulting in more frequent and earlier diagnoses.³

AD Caregiver Burden

The majority of care for AD patients comes from their families. Approximately 94% of those who assist a patient with AD/D care for a relative, and 21% of those live in the same household as the patient.³ This care carries a significant cost, not only financial, but emotional and physical. Compared with noncaregiver controls matched by age, gender, race, and marital status, AD caregivers are harnessed with a constellation of physical, psychological, emotional, and financial burdens.⁴⁻⁷ AD caregivers visit their physicians 46% more and have 71% more prescriptions than noncaregivers.⁴ Six percent of AD caregivers care for their spouse.³ Studies reveal that the acute psychological stress of caring for a spouse with AD may result in higher diastolic blood pressure,⁵ higher plasma norepinephrine,⁷ and may elicit a hypercoagulable state in the elderly who have cardiovascular disease.⁶ More than 40% of family members and other unpaid caregivers of patients with AD rate their stress levels as high to very high, and a third of family

caregivers exhibit symptoms of depression. In their patients' last year of life, 59% of these caregivers described themselves as "on call" 24 hours a day.²

Family members are typically the primary caregivers of dementia patients, providing up to 70 hours of care per week. Direct costs of caring for dementia in the community have been estimated at 4.5 times less than that in facilities. Because each month's delay in institutionalization may save as much as \$2029 in direct healthcare costs, counseling, education, and support of caregivers are important cost controls in dementia management.⁸ Moreover, recognition of AD symptoms by caregivers can facilitate appropriate therapy for the severity of AD while patients are still under the care of loved ones.

Medicare Beneficiaries With Dementias Have Significant Comorbidities

Medicare beneficiaries at least 65 years of age with AD/D typically have 1 or more comorbid conditions impacting healthcare utilization and cost (Table 1).² Patients with AD/D and serious comorbidities are more likely to be hospitalized than those without AD/D. Also, patients with AD have longer hospital stays, and their overall healthcare expenditures are higher.² Based on results from a 2004 survey, the average prescription drug cost for a community-dwelling Medicare patient with AD/D was \$3198 versus \$2203 (2010 US dollars) for that of a non-AD/D patient.² A study of 2006 Medicare claims compared AD/D and non-AD/D costs per service in patients with coronary heart disease, diabetes, congestive heart failure (CHF), and cancer requiring hospital care, physician care, skilled nursing facility care, and home healthcare.² All costs were higher for patients with AD/D and a serious medical condition than those without AD/D and a serious medical condition, with the exception of payments for physician visits in patients with CHF (which were lower in those with AD/D). In 7 of the 16 comparisons, costs for patients with AD/D were more than double that of those without AD/D.

The Concentration and Persistence of Expenditures in AD/D Medicare Beneficiaries

Due to its high cost and increasing prevalence, AD/D is a great concern to Medicare and Medicaid. In order to identify cost-containment targets, Lin et al recently

Table 1. Comorbidities of Medicare Beneficiaries at Least 65 Years of Age With AD or Other Dementia in 2004²

Comorbidity	Percentage
Hypertension	60
Coronary heart disease	26
Stroke	25
Diabetes mellitus	23
Osteoporosis	18
Congestive heart failure	16
Chronic obstructive pulmonary disease	15
Cancer	13
Parkinson's Disease	8

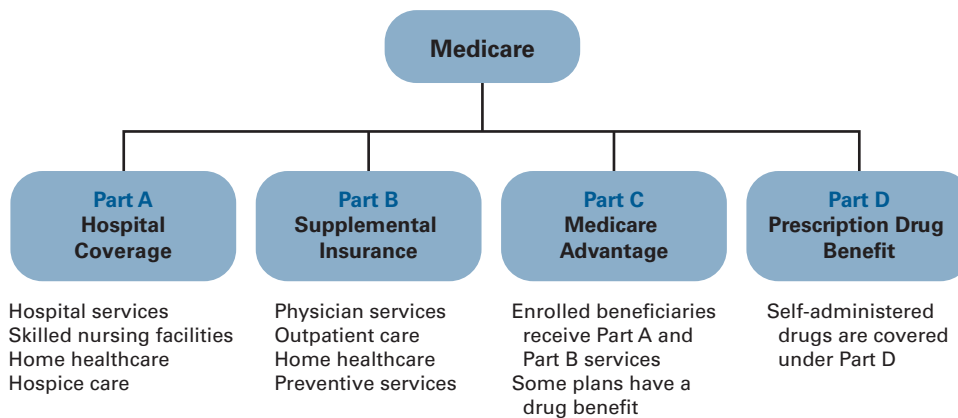
AD indicates Alzheimer's disease.
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researched the extent of concentration and persistence in total healthcare and prescription drug expenditures among elderly patients with AD/D. They analyzed cross-sectional data of expenditures incurred by the top 10%, 25%, and 50% of beneficiaries to predict expenditure persistence over a 2-year period.⁹ Nearly half of the total health expenditures and one-third of all drug expenditures were incurred by the top 10% of beneficiaries. The largest expenditure in the top 10% group was inpatient care, while in the bottom 50% group, physician visits and prescription drugs were the major cost drivers. Persistence in expenditures was very strong, particularly for prescription drugs. The strongest predictors of persistence were comorbidities and prior expenditures.

On average, Medicare patient payments for healthcare services are also significantly higher for those with AD/D compared with those without AD/D. Similarly, long-term care service costs are significantly higher for patients with AD/D. Increased hospitalization and physician service costs are the primary drivers of persistent and higher expenditures in patients with AD/D.

A year later, Lin et al compared hierarchical condition category (HCC) risk-adjustment measures used by the Centers for Medicare & Medicaid Services (CMS) against other measures in predicting Medicare costs of AD/D patient care. The CMS-HCC and Chronic Illness and Disability Payment System–Medicare had higher overall and subgroup predictive power for total expenditures compared with other diagnosis-based measures.¹⁰ The prescription drug HCC also exhibited greater predictive power compared with other measures in identifying AD/D patients with extremely high drug expenditures. These CMS-HCC and prescription HCC

■ **Figure.** The Medicare Landscape¹¹



measures are more accurate in cost prediction than other measures for determining overall costs of AD/D to Medicare. These studies encourage making and documenting the AD/D diagnosis when it is present.

AD/D Management Payer and Formulary Intricacies

A number of government payer entities exist; they span all settings through which funds are channeled for the management of AD/D. The **Figure** depicts how Medicare is designed to disburse funds.¹¹ Medicaid is primarily the responsible payer for long-term care in nursing homes.

Among older adults, who prior to the availability of Medicare Part D did not have prescription coverage, 80% are enrolled in Medicare Part D today.⁸ Because of the benefit of pharmacologic therapy in AD, it is important for patients with AD/D to have prescription plans that optimize therapeutic access. In 2006 (at the beginning of Medicare Part D), a Novartis Pharmaceuticals survey revealed that just 56% of clinician respondents felt they knew enough about Medicare Part D to comment on it, and 72% expected that it would increase medication-related problems.⁸

Medicare drug plans that elect to follow United States Pharmacopeia (USP) guidelines provide at least 2 medications in each AD class. Therefore, they have 2 cholinesterase inhibitors (ChEIs) and memantine on formulary. In addition, there are 6 protected classes. Most medications in those classes need to be available for patients with AD; these include all antidepressant, anticonvulsant, and antipsychotic medications.⁸ Despite these guidelines, accessibility is still a problem. Access can be impeded by prior authorization requirements, while some drugs are excluded from coverage by law (eg, benzodiazepines) and cannot be appealed.⁸ Benzodiazepines are slated to be covered in 2013. Those drugs

that are not excluded by law and are not on a plan formulary can be appealed.

Further research is needed to determine which CNS medications, particularly AD/D-indicated medications, are the most tolerable, efficacious, and cost-effective in the elderly. Recently, an expert panel evaluated 78 medications in 4 indications, including dementia, to identify preferred medications.¹² Using available clinical evidence, medications were classified by an expert panel as preferred if they were found both effective and imposing less risk to the patient compared with available alternative drugs. Three preferred AD/D agents were identified: donepezil, extended-release galantamine hydrochloride, and memantine hydrochloride.

A Model Guidelines Expert Panel for the 2010-2015 USP reviewed and updated the Medicare Model Guidelines, which includes categories and classes that Medicare Part D plans can implement when developing formularies for benefit years 2012-2014. This Expert Panel served as an advisory body to the Nomenclature, Safety, and Labeling Expert Committee. The Nomenclature, Safety, and Labeling Expert Committee was ultimately responsible for the Model Guidelines, based on the recommendations of the Expert Panel. The experts appointed to the panel included clinical pharmacists and pharmacologists, formulary specialists, healthcare practitioners and academicians, pharmaceutical industry representatives, providers, beneficiaries, drug information experts, and others.¹³ For antidementia agents, there were no revisions to the class of ChEIs (eg, donepezil, galantamine, rivastigmine).¹⁴ However, because memantine is the sole drug in the class formerly titled “glutamate pathway modifiers,” this class name was revised to align with the FDA-established pharmacologic class—N-methyl-D-aspartate (NMDA) receptor antagonist.

Medicare Prescription Coverage Impacts AD/D Drug Utilization

Under Medicare Part D, many beneficiaries are subject to a gap in prescription coverage known as the “donut hole” once they have expended their prescription drug benefit and prior to qualifying for catastrophic coverage. Beneficiaries within the gap originally paid 100% of the costs of branded prescriptions and, most often, 100% of the costs of generic medications.

In 2007, beneficiaries reached the donut hole if they expended \$2400 in benefits and did not qualify for catastrophic coverage until reaching \$3850 in prescription costs.¹⁵ Such coverage gaps prove detrimental to therapeutic adherence. In that same year, 26% of beneficiaries hit the coverage gap and 15% of those who hit the gap eventually qualified for catastrophic coverage. A total of 64% of beneficiaries with AD were affected by the coverage gap; 49% hit the gap and 15% eventually reached catastrophic coverage. Of all beneficiaries who hit the gap, 15% stopped taking their medication completely, 5% switched to an alternative in the same class, and 1% reduced medication use (subtherapeutic dosing). Of AD beneficiaries who hit the gap, 8% stopped taking the medication completely, 4% switched to an alternative in the same class (which will probably increase due to generic introductions), and 2% reduced medication use. After reaching catastrophic coverage, 33% of beneficiaries with AD resumed medication, but 60% remained off medication. Physicians are often unaware of the high percentage of patients who are covered but have stopped taking medication.

Closure of the coverage gap will benefit all Medicare beneficiaries, but especially patients with AD/D. Starting in January 2011, the cost of branded drugs were initially discounted 50% by manufacturers who participate in rebate programs.¹⁶ This discount will eventually rise to 75% of total coverage, and by the year 2020, patients will pay 25% out of pocket for both brand and generic drugs, which equates to the same coverage prior to the coverage gap. Patients reaching catastrophic coverage will continue to pay just 5% total out-of-pocket drug costs at this point.

Long-Term Care and AD/D Versus Non-AD/D Cost Differences

The major payer for nursing home care is Medicaid; however, Medicare Part A does cover subacute nursing home care up to 100 days.¹⁷ Several bright spots are on the horizon for increasing the identification and treatment of patients with AD/D and those with cognitive impairments. For example, Medicare administrators previously regarded

AD/D claims as “mental healthcare” as opposed to “medical” services, resulting in 50% reimbursement versus 80%, respectively.¹⁷ Discrepancies led Stuart et al to compare the nursing home costs of patients with AD/D to those without AD/D. Medicare expenditures per person month (PPM) were compared for 640 residents diagnosed with dementia and 636 with no dementia for 1 year pre- and 2 years post-nursing home admission. Medicare expenditures peaked in the month immediately preceding admission and dropped to preadmission levels by the third month in the facility.¹⁷

Adjusted PPM costs following admission for the dementia group as a whole were 79% of the Medicare costs of treating residents without dementia. For the subgroup of residents admitted without a Medicare-qualified stay (MQS), those with dementia had Medicare costs of just 63% of those without dementia.¹⁷ Overall Medicare costs PPM were not different between the 2 groups admitted with an MQS. The researchers determined that whether nursing home residents were admitted with an MQS was the single most important factor in assessing treatment cost differentials between residents admitted with and without dementia. Implementing MQS criteria in patient evaluations can be used to curtail costs, as can other mental assessment tools that identify AD/D.

In addition, the CMS introduced a new Minimum Data Set (MDS) in October 2010. Implementation of the MDS is a requirement for all nursing homes that participate in Medicare and Medicaid programs. Within the MDS 3.0 is a requirement to complete the Brief Interview for Mental Status.¹⁸ This is a screening device used to evaluate memory function in residents. Residents are asked to repeat 3 words, provide the year, month, and day of the week, and then repeat the 3 words. Residents are scored on a scale of 0 to 15 for this cognitive pattern test. It is expected that once identified, an appropriate care plan can be developed for those with dementia. Because the MDS must be completed at predetermined intervals and with any change in resident status, it presents another opportunity to assess AD and the impact of pharmacologic therapy.

Healthcare Reform Improves AD/D Patient Identification and Management

In an effort to reduce costs through improved communication and utilization of resources, physicians are being encouraged to embrace electronic record utilization because standardized records facilitate accurate communication of patient diagnoses and therapies. Clinicians are eligible to provide services to either Medicare or Medicaid and will be offered \$44,000 and \$63,750 incentives, respectively, to

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participate.¹⁹ These incentives will be distributed incrementally to encourage meaningful use, which is preliminarily defined within the contexts of clinical decision support, e-prescribing, health information exchange, and quality reporting.

Healthcare reform is shifting payment, by paying for improved outcomes as opposed to quantity of services rendered. The testing of innovative payment and service delivery models will occur through the Center for Medicare & Medicaid Innovation. Such new structures as Accountable Care Organizations (ACOs) will focus on outcomes, including those important for patients with AD/D, such as reducing nursing home placement, and emergency department and hospital utilization.

Healthcare reform is also promoting comparative effectiveness research (CER).²⁰ CER is set to compare pharmacotherapeutic and disease management strategies. With the passage of the American Recovery and Reinvestment Act of 2009, the Institute of Medicine (IOM) was tasked with prioritizing CER study topics, which must be taken into account by the Department of Health and Human Services within the next 2 years. The third primary research area is psychiatric disorders, which includes AD/D. IOM recommendations for CER in AD/D include comparing the effectiveness and costs of alternative detection and management strategies for dementia in community dwelling individuals and caregivers. Also recommended are efficacy comparisons of pharmacologic and nonpharmacologic treatments for managing AD/D behavioral disorders in home and institutional settings.²¹

Pharmacoeconomic Outcomes in AD Treatment

Given the heavy burden of AD/D due to high utilization of nursing home care, perhaps the best advocates for appropriate AD/D therapy access are State Medicaid programs, caregivers, and patients themselves. It has been demonstrated through numerous published clinical trial results that the positive pharmacotherapeutic effects on cognition, behavioral, and functional status reduce medication mismanagement costs, excess comorbidity costs, hospitalization risk and length of stay, and caregiver, long-term care, and nursing home placement costs.²² Oftentimes, however, the cost of treatment is separated from the cost of care. This misalignment of incentives results in inappropriate access to therapy.

At this year's Alzheimer's Association Annual Meeting, McCarten et al presented findings from the Dementia Demonstration Project (DDP), which demonstrated cost benefits through employing specially trained registered nurses (dementia care coordinators) to lead screenings, evaluations, and DDP patient management teams.²³ Patient eligibility

requirements were age of at least 70 years, medical stability, ability to comply with screening, and no prior cognitive impairment diagnosis. Decline in median per patient outpatient care costs from 1 year before to 1 year after diagnosis was more than 54% in DDP patients versus 25% in non-DDP patients. Median number of line-item outpatient costs dropped 53% in DDP patients versus 32% in non-DDP patients.

There is a generalized perception among healthcare providers that AD treatments are relatively ineffective and do not significantly impact outcomes.²⁴ However, many patients with age-related illnesses, such as diabetes mellitus and hypertension, are treated to reduce the risk of complications and not for immediate clinical improvement. Geldmacher concluded that sustaining function and quality of life by reducing declines in function, behavior, and cognition is a comparable AD treatment goal.²⁴ He also conducted meta-analyses of data from double-blind placebo controlled trials to demonstrate the cost-effectiveness of AD pharmacotherapy. Per-patient 1-year cost savings in those with mild-to-moderate AD treated with donepezil (vs placebo) are depicted in [Table 2](#).²⁴ A net cost savings of \$1097 for donepezil versus placebo was realized, primarily from caregiver time saved in assistance with daily living, caregiver hospitalizations, and physician visits. In another study, total societal cost per patient was \$224 less for patients with moderate-to-severe AD treated with donepezil for 6 months; again, primarily due to caregivers' time savings.²⁴ AD patients with related dementias were hospitalized 2.5 times more than patients without dementia. Active, problematic behavioral patients with AD incur higher costs, which may be reduced through pharmacotherapy.

Memantine added to an existing donepezil regimen has demonstrated superior efficacy to donepezil alone²⁵; however, its cost-effectiveness as an adjunctive therapy in moderate-to-severe AD had not been demonstrated prior to the study by Weycker et al.²⁶ They developed a microsimulation model to depict cognitive function changes and associated clinical and economic outcomes, as assessed over time by the Severe Impairment Battery. All patients entering the model were community based and received a score between 5 and 14 on the Mini-Mental State Exam. Duration of treatment was assumed to be 12 months. Cognitive function was assumed to revert to natural history levels upon termination of therapy. Outcomes and costs (formal and informal services) were evaluated monthly until death for each treatment regimen. During the year of memantine therapy, pharmacotherapy costs increased, but lifetime costs

of formal and informal services decreased. Clinical improvement was reflected through cost-effectiveness. Memantine added to an existing donepezil regimen also appeared more effective in less advanced disease.

Lopez et al studied the long-term effects of concomitant memantine and cholinesterase inhibition in AD. They examined time to nursing home admission and death in 943 patients with probable AD who had at least a 1-year follow-up evaluation. Of the 943 patients, 140 (14.9%) used ChEIs and memantine, 387 (45%) used only ChEIs, and 416 (40.1%) used neither.²⁷ Compared with those who never used cognitive enhancers, patients who used ChEIs had a significant delay in nursing home admission. This effect was significantly augmented with the addition of memantine. ChEIs alone, or in combination with memantine, had no significant association with time to death. Patients taking ChEIs and memantine were more than 7 times less likely to be admitted to a nursing home during follow-up than those taking ChEIs alone. In patients on ChEI monotherapy, nursing home admission itself, however, was a predictor of time to death.

Based on Lopez's findings, a cost-utility analysis was performed by Lachaine et al from the Montreal University of Pharmacy to evaluate the economic impact of delayed time to nursing home admission with memantine and a ChEI compared with a ChEI alone.²⁸ From both societal and healthcare system perspectives, combination therapy was assessed as a cost-effective strategy compared with a ChEI alone, leading to increased benefit and lower costs.

New Pharmaceutical Products Expected to Impact AD Management Strategies

Currently, several changes are expected to impact the pharmacologic management of AD. These include the availability of generic donepezil (November 2010) and the additions of donepezil 23 mg (approved in July 2010) and extended-release memantine (approved in June 2010). The broad impact of new AD medications remains to be fully elucidated; however, it is expected that reduced out-of-pocket costs and copays will increase access to AD medication, including combination therapy. The increase in options and reduction in patient out-of-pocket expenditures is expected to lead to better adherence and improved outcomes.

Conclusions

Pharmacotherapy in AD, though not curative, may reduce the slope of decline, delay emergence, and promote diminished behavioral-associated disturbances. Patients

■ **Table 2. Per-Patient 1-Year Cost Savings With Donepezil for Mild-to-Moderate AD²⁴**

Cost Savings With Donepezil Therapy Versus Placebo (US\$)^a	
Direct Patient Costs	
Donepezil (study medication)	(1280)
Patient hospitalization	(216)
Patient emergency department	(23)
Patient healthcare professionals	5
Patient concomitant medications	0
Patient social services	1158
Patient accommodation (living arrangement)	65
Total Patient	(291)
Caregiver Costs	
Caregiver hospitalization	145
Caregiver emergency department	(11)
Caregiver healthcare professionals	216
Caregiver medications	5
Caregiver patient care time	1018
Caregiver missed work	15
Total Caregiver	1388
Net Cost Savings	1097
^a Calculated over 12 study months as placebo group cost minus donepezil group cost. Reprinted with permission from Geldmacher DS. <i>Manag Care</i> . 2005; 14:44-52, 54.	

who receive an early diagnosis and sustain pharmacotherapeutic adherence and routine care can maintain longer independence and have reduced healthcare costs. Because a significant portion of the benefits of AD pharmacotherapy fall outside the benefits of payers, those most impacted, such as State Medicaid programs, caregivers, and AD patients, may prove the strongest advocates of appropriate access to therapy. Lastly, healthcare reform may provide resources and financial incentives to improve outcomes; this includes a move toward value-based benefit designs and ACOs that assure medication access and availability of combination therapy through low out-of-pocket costs. Studies demonstrate that combination therapy with donepezil and memantine is associated with improved efficacy, delayed time to nursing home admission, and reduced overall costs compared with a ChEI alone. The availability of generic donepezil presents additional cost savings. Focus on improving outcomes in patients with AD and their caregivers may be managed in a holistic manner rather than within isolated silos.

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