

Commissioned Paper on AD/ADRD Health Economics and Public Policy

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Summary

The financial burden Alzheimer's disease and Alzheimer's disease-related dementias (AD/ADRD) place on patients, families and the health care system has been well documented. If current disease prevalence rates persist, the economic burden of AD/ADRD is projected to increase drastically due to population aging. For many people with AD/ADRD, the majority of care is delivered by unpaid, informal care givers. The intensity and complexity of caregiving for persons with AD/ADRD may result in substantial "spillover" cost and health effects on family members and other informal caregivers. As AD/ADRD progresses, both formal and informal care costs increase. From an economic perspective, studies have highlighted the importance of delaying AD/ADRD onset with shortened disease duration and delaying disease progression to more costly stages. Simulation studies also indicate that changing the disease prevalence or trajectory may substantially reduce future economic burden of AD/ADRD. However, more data are needed to determine whether any savings generated from early detection and early treatment will be large enough to offset downstream long-term costs. Future AD/ADRD disease-modifying therapies are likely to create many reimbursement and access challenges, and the U.S. health system is unprepared. Health care payers and policymakers should develop strategies to contain AD/ADRD costs and ensure patient access to high-value products and services. In the era of disease-modifying therapies, increasing disease awareness and improving access to dementia care, especially among underserved populations, will be continuing goals for AD/ADRD outreach programs.

1. Introduction

Alzheimer's disease and Alzheimer's disease-related dementias (AD/ADRD) are not only an aging issue but also a public health issue that affects society as a whole. The financial burden AD/ADRD places on patients, families and the health care system has been well documented. AD/ADRD cost-of-illness studies are critical to identifying types of care that drive the economic burden of the disease and should be more closely scrutinized for the purpose of improving care efficiency. Such data can also guide the development of policy recommendations to ameliorate delays and disparities in the delivery of timely, effective dementia care.

Currently there are more than 130 innovative treatment agents for AD/ADRD in clinical trial,¹ offering hope that some may slow or halt the disease progression. On the other hand, novel agents with potentially high prices coupled with a large and growing aging population with AD/ADRD could exacerbate economic burden of the disease. Furthermore, uncertainty in long-term treatment effectiveness poses additional challenges in value assessment, coverage and reimbursement for health care payers.

This paper focuses on the health economics and policy of AD/ADRD. *Sections 2 and 3* of the paper summarize key findings in the health economics literature on current disease burden, future projections, and cost drivers of AD/ADRD care, and identify knowledge gaps for future research. *Section 4* discusses the value of AD/ADRD interventions from a broad societal perspective and highlight reimbursement and health care delivery issues. All discussion focuses on the US population, and therefore, the evidence cited throughout the paper is drawn from US studies, when possible, unless otherwise indicated.

2. Economic burden of AD/ADRD: current estimates and future projections

2.1 AD/ADRD impose a substantial burden on patients, their informal caregivers and the health care system

It is well recognized that AD/ADRD have substantial social and economic impacts beyond the individuals living with the condition. The socioeconomic costs of AD/ADRD generally can be divided into two categories: direct health care costs of persons with AD/ADRD (i.e., formal costs) and unpaid, informal care provided by their family and friends (i.e., informal costs). According to the Alzheimer's Association, direct health care payments (e.g., medical services, prescriptions, long-term care and hospice) in 2019 for U.S. individuals with AD/ADRD are estimated at \$290 billion,² although the estimates may be on the high end. Of these, Medicare and Medicaid are the primary payers, covering \$146 billion (51%) and \$49 billion (17%), respectively.² Patient out-of-pocket payments for health insurance premiums, deductibles, copayments and services not covered by other sources are also substantial, estimated at \$63 billion (22%) in 2019.² The estimated economic burden of AD/ADRD may vary significantly by definition of the disease (e.g., based on clinical symptoms or pathologic and biomarker findings) and by case definition (e.g., identified by self-report, diagnosis in claims, or use of an AD/ADRD prescription medicine, or some combination thereof).³ Therefore, policymakers should be aware of methodologic differences in calculating AD/ADRD burden, when using these estimates in policy development.

Alzheimer's disease and Alzheimer's disease-related dementias (AD/ADRD) are associated with substantial informal care costs. For many people with AD/ADRD, the majority of care is delivered by their spouses, adult children, and other informal care providers.⁴⁻⁶ The

medical condition can impose a significant financial, physical, and emotional toll on informal/family caregivers. Caring for persons with AD/ADRD often involves a wide variety of tasks, ranging from personal care to day-to-day household duties to medication management. Data from the 2016 Behavioral Risk Factor Surveillance System (BRFSS) showed that 60% of caregivers of persons with AD/ADRD helped manage personal care (e.g., feeding, dressing, and bathing) and 77% helped manage household activities (e.g., cleaning, managing money, or preparing meals).⁷ Nearly 30 % of caregivers of persons with AD/ADRD reported providing 20 or more hours of care per week.⁷ The intensity and complexity of caregiving for persons with AD/ADRD may result in substantial “spillover” cost and health effects on family members and other informal caregivers.⁸ In 2018, informal caregivers of persons with AD/ADRD provided more than 18.5 billion hours of unpaid assistance, valued at \$234 billion, according to the Alzheimer’s Association.² However, these data may underestimate informal care costs in AD/ADRD because they account only for current foregone wages.

In addition to caregiving time costs, studies have considered health effects and productivity impacts on caregivers of persons with AD/ADRD. Prior research has shown that approximately one in five informal caregivers of someone with AD/ADRD have difficulty with medical/nursing tasks, compared to one in ten caregivers of persons without dementia, and are more likely to report a high degree of physical and emotional strain owing to their caregiving tasks.⁹ Family caregivers of persons with AD/ADRD are more likely than caregivers of persons without dementia to help with patients’ emotional or mental health problems and challenging behavioral issues,¹⁰ and they may have an increased risk of anxiety, depression, and sleep disorders.^{6,11-15} Caregivers of persons with AD/ADRD also may experience economic hardship as a result of lost work and care expenses.^{6,11-15} For example, national survey data indicate that

employed caregivers of persons with AD/ADRD are more likely to need to go to work late or leave early, reduce their work hours because of care responsibilities, or give up working entirely, compared with caregivers of persons without dementia.¹⁰

The amount of time caregivers spend assisting patients with activities of daily living may increase and the health impact on the caregiver may intensify as a result of worsening patient symptoms.^{14,16} Caregiver burden is likely to intensify as persons with AD/ADRD approach the end of life.¹⁷ Further, the burden of informal care also may be different when patients transition from home to a nursing facility where caregiving tasks typically shift from providing comprehensive care to emotional support, interacting with facility staff, and advocating for appropriate care. Future research is needed to better characterize the dynamic of caregiver spillover effects in relation to AD/ADRD disease severity, end-of-life care, and care setting. Interventions targeting caregivers of persons with AD/ADRD are beyond the scope of this article and discussed in another paper in this Commissioned Papers series.¹⁸

Future research is need to better quantify indirect costs of persons with AD/ADRD and employer costs due to AD/ADRD caregiving. Despite extensive evidence on AD/ADRD direct health care costs and informal care costs, indirect costs of the disease are less clear. Indirect costs refer to production losses in the working population (e.g., impaired work productivity, sick leave and early retirement). Although indirect costs may be less substantial in AD/ADRD because most of the affected population are older adults in retirement, these costs are relevant to individuals with early onset disease and individuals delaying retirement. Moreover, much less is known about AD/ADRD caregiving-related costs to employers. These may include the replacement costs for employees who quit due to their caregiving responsibilities and costs of absenteeism and workday interruptions.¹⁹ Researchers have proposed an alternative approach to

estimating informal care costs, which monetizes change in well-being due to caregiving and calculates “welfare costs.”²⁰ For example, one study calculated the value of time, the implications for future employability and wages, and any intrinsic benefits that accrue to caregivers.²⁰ This approach yielded 20% higher informal care costs, compared to the traditional approach that accounted only for current foregone wages.²⁰ Future research should explore alternative approaches to estimating costs associated with AD/ADRD caregiving. As an example, studies could evaluate the impact of the Family and Medical Leave Act (FMLA), which provides eligible employees with up to 12 weeks of unpaid, job-protected leave per year for specified family members with a serious health condition, such as AD/ADRD.

2.2 *Economic burden of AD/ADRD is projected to rise, if current prevalence rates persist*

Although the magnitude of specific estimates varies, studies consistently suggest substantial AD/ADRD cost increases in the future due to population aging, if current disease prevalence rates persist (Table 1). A RAND study using data from the Health and Retirement Study estimated that total annual monetary costs of dementia may increase from \$268-\$324 billion in 2010 to \$638-\$770 billion in 2040.²¹ In contrast, a well-validated microsimulation model, namely the Future Elderly Model, indicated a higher future disease burden. The model projected that from 2010 to 2050 the number of individuals ages 70+ with AD may increase from 3.6 to 9.1 million, and annual costs may increase from \$307 billion (\$181B formal, \$126B informal costs) to \$1.5 trillion.²² At the individual level, the Future Elderly Model projected that per patient annual health care costs for AD may increase from \$42,000 in 2010 to \$106,000 in 2050.²² Similar trends are suggested by Alzheimer’s Association’s estimates: total direct annual health care costs for persons with AD/ADRD may increase from \$290 billion in 2019 to more

than \$1.1 trillion in 2050 (2019 dollars).² This rise reflected four-fold increases in Medicare and Medicaid, as well as patient out-of-pocket spending.

TABLE 1 Estimated Costs of AD/ADRD (in billions)

Year	Hurd et al. ²¹ (2010 dollars)	Zissimopoulos et al. ²² (2010 dollars)	Alzheimer's Association ² (2019 dollars)
Direct health care			
2010	\$109	\$181	--
2018/2019	--	--	\$290
2040	\$259	--	--
2050	--	\$1140	\$1100
Informal care			
2010	\$159-\$215	\$126	--
2018/2019	--	--	\$234
2040	\$379-\$511	--	--
2050	--	\$361	--
Total			
2010	\$268-\$324	\$307	--
2018/2019	--	--	\$524
2040	\$638-\$770	--	--
2050	--	\$1501	--

Most AD/ADRD cost-of-illness studies estimate the economic burden in the patient population as a whole, but it should be noted that the disease risk and burden differ by race and ethnicity.²³ Observational data consistently suggest higher AD/ADRD incidence and prevalence rates among blacks and Hispanics than among non-Hispanic whites;^{24,25} however, how AD/ADRD care costs vary by race and ethnicity is less understood.²³ One descriptive, unadjusted analysis reported that in 2014, annual Medicare payments for beneficiaries with AD/ADRD may be higher among blacks (\$27,900) and Hispanics (\$22,100) compared to whites (\$20,700).² However, this study did not account for differences in patient characteristics such as age and comorbidity burden. One study of Medicaid beneficiaries with AD/ADRD found that

non-Hispanic blacks may incur \$600 higher annual care costs compared to non-Hispanic whites, and that 80% of the cost difference may be attributable to race.²⁶ The analyses also found that blacks with AD/ADRD had more inpatient care and more comorbidities, which may explain the cost difference by race.²⁶ This analysis, while adjusting for comorbidities, may not be generalizable to the broader AD/ADRD population because the sample was Medicaid patients enrolled in four states (California, Florida, New Jersey, and New York) in 2004. More recent, nationally representative data are needed to understand AD/ADRD health care and cost disparities by race and ethnicity. Additional research is needed to evaluate racial and ethnic disparities in AD/ADRD diagnosis and treatment delays, the effects of such delays in patient health outcomes and costs, and strategies to address these disparities. Moreover, given the expected growth of minority populations, it would be helpful to project future economic burden of AD/ADRD by race and ethnicity. These projections should take into account differences in patient characteristics such as comorbidity profiles. Racial and ethnic disparities in AD/ADRD are a complex issue and this topic is discussed in more detail in another paper in this Commissioned Papers series.²⁷

2.3 Individuals with AD/ADRD incur higher health care costs, including out-of-pocket expenses, than those without the condition, even before they receive the diagnosis

It is well established that individuals with AD/ADRD incur higher health care costs compared to people without the condition, despite variation in the magnitude of specific estimates. Unadjusted, descriptive analyses using data from the 2011 the Medicare Current Beneficiary Survey showed that average annual health care costs for Medicare beneficiaries age 65 and older with AD/ADRD were roughly \$49,000 per person, compared to \$14,000 for

beneficiaries without the condition (2018 dollars). A more refined estimate produced by the Future Elderly Model projected annual health care costs for individuals over age 70 with AD at \$42,000, compared to \$15,000 for non-AD individuals at that age (2010 dollars).²²

One analysis of the Health and Retirement Study with linked Medicare fee-for-service claims data estimated that dementia's five-year *incremental* cost to the traditional Medicare program was approximately \$15,700 per patient (2017 dollars), with nearly half incurred in the first year after diagnosis.²⁸ The estimates are consistent with findings in an earlier study, reporting that the average duration of dementia is about five years, with *lifetime* Medicare costs of \$13,400 and Medicaid costs of \$12,400 (2010 dollars).²⁹ A systematic review of nine studies indicated wide ranges for AD/ADRD-attributable costs in private Medicare managed care plans, with estimates varying from \$3,700 to \$8,700 in prevalent cases and \$8,900 to \$38,800 in 1-year immediate post-diagnosis incident cases.³⁰ The excess costs of treating persons with AD/ADRD were driven by higher health care utilization, including more hospitalizations, longer hospital stays, and more post-acute skilled nursing facility and home health care, compared to individuals without the disease.^{28,31-33}

Despite Medicare and Medicaid covering a large proportion of health care costs, individuals with AD/ADRD have a much higher out-of-pocket cost burden. The Future Elderly Model estimated *annual* out-of-pocket health care costs at roughly \$10,000 among individuals with AD patients, compared to \$2,800 among non-AD individuals (2010 dollars).²² The annual costs translate into significant financial burden over a patient's lifetime. One study estimating *lifetime* out-of-pocket costs reported that persons with dementia spent \$39,000 more (2014 dollars) from age 65 to death, when controlling for length of life, demographics, lifetime

earnings and comorbidities.³⁴ These out-of-pocket costs were mostly driven by spending on nursing home care, rather than doctor visits or prescription drugs, for example.³⁴

A number of studies have found that, before an AD/ADRD diagnosis, individuals may begin using more healthcare services and accruing high expenditures. For example, using Medicare claims data from a large, national sample, one study reported that Medicare expenditures were 42% higher among beneficiaries with AD/ADRD (\$15,100 vs. \$10,600) and 41% higher among those with mild cognitive impairment (MCI) (\$13,700 vs. \$9,700) than in propensity-score matched control subjects during the year before diagnosis (Figure 1).³³ Acute inpatient expenditures, which may reflect declining health status, appeared to be the primary determinant of the cost differences prior to receiving a coded diagnosis in claims. The study also showed that Medicare expenditures of AD/ADRD beneficiaries started to increase at least 12 months before their diagnosis and peaked during the first few months after diagnosis; they then decreased but remained at a higher level than before diagnosis.³³ Studies of pre-diagnosis AD/ADRD costs based on smaller cohorts or cohorts with shorter follow-up generally show similar trends.³⁵⁻⁴⁰ These studies generally rely on administrative claims data to evaluate health care costs before a formal AD/ADRD diagnosis is recorded. There are some well-known limitations to administrative claims, such as potential under-diagnosis and under-coding of AD/ADRD.³ Nonetheless, the findings reflect how AD/ADRD are being diagnosed and coded in real-world settings.

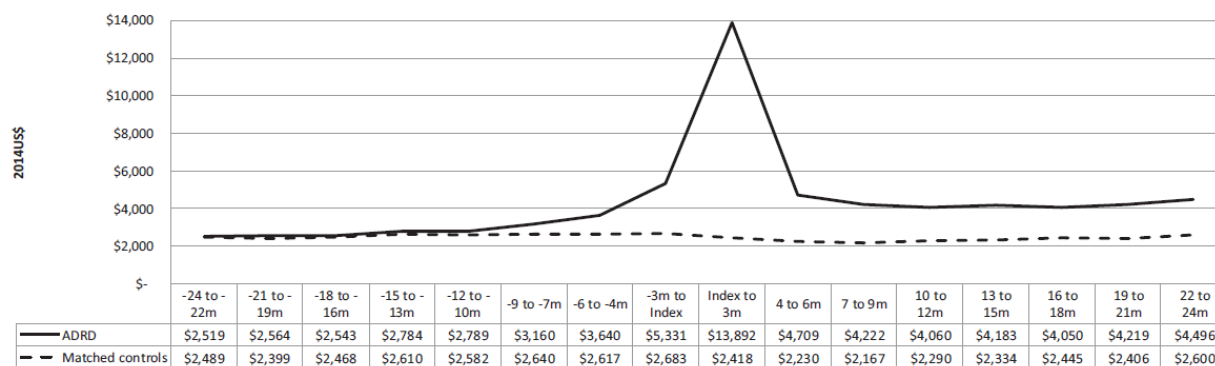


FIGURE 1 Trends In Quarterly Medicare Expenditures Before and After Diagnosis in Participants with ADRD (Solid Line) and Matched Controls (Dotted Line)³³

2.4 Comorbidities are highly prevalent among persons with AD/ADRD, and AD/ADRD can make the management of other chronic conditions more difficult and expensive

Almost all older adults with AD/ADRD (>90%) have at least one other chronic condition. Some common chronic comorbidities among Medicare beneficiaries with AD/ADRD include coronary artery disease (38%), diabetes (37%), chronic kidney disease (29%), congestive heart failure (28%) and chronic obstructive pulmonary disease (25%).² Although chronic conditions are prevalent among older adults in general, evidence indicates that older adults with AD/ADRD have a higher comorbidity burden than those without the condition.^{31,41,42} One analysis reported an average of 8.1 comorbid conditions among AD patients, compared to 6.5 among non-AD controls with similar demographic characteristics, based on data from a large sample of Medicare beneficiaries with employer-sponsored supplemental coverage.³¹ This study also showed that individuals with AD may be more likely than demographically matched controls to have mental health conditions, neurologic conditions, cognitive disorders, cerebrovascular disease, diabetes with acute complications, and injuries.³¹

The high comorbidity burden is a key contributing factor to the higher health care costs among individuals with AD/ADRD. One study of Medicare data has analyzed the top five chronic conditions with the highest excess costs for persons with AD: polyneuropathy, diabetes with neurologic/peripheral circulatory manifestation conditions, major depressive, bipolar and delusional disorders, mononeuropathy/other neurologic condition/injuries, and pelvic inflammatory disease, and other specified female genital disorders.³¹ For example, the risk-adjusted cost difference between AD and demographically matched non-AD subjects was estimated at \$4,800 among people who also had polyneuropathy.³¹ Excess health care costs attributable to AD ranged from \$1,500 to \$3,000 for selected common comorbid conditions in this analysis.³¹

Studies also have reported more frequent hospitalizations for comorbid conditions among AD/ADRD patients, and some of these admissions may be preventable with proactive outpatient care.^{41,43-46} For example, data from the Health and Retirement Study and linked Medicare claims suggested that individuals with dementia may be 30% more likely to have a preventable hospitalization for Ambulatory Care Sensitive Conditions than those without a neuropsychiatric disorder, after controlling for demographic, clinical and health risk factors.⁴⁴ Preventable hospitalizations for Ambulatory Care Sensitive Conditions are often measured using the Agency for Healthcare Research and Quality Prevention Quality Indicators.⁴⁷ These include acute (e.g., bacterial pneumonia, urinary tract infection, and dehydration) and chronic (i.e., diabetes, hypertension, heart failure, angina without a cardiac procedure, and asthma/chronic obstructive pulmonary disease) conditions. By definition, an inpatient admission for any of the Ambulatory Care Sensitive Conditions is considered potentially “avoidable” had timely and effective care been received in an ambulatory care setting.⁴⁸ One Medicare claims analysis reported that

beneficiaries with AD/ADRD may be at higher risk of potentially avoidable hospitalizations for diabetes complications and hypertension, compared to matched controls without AD/ADRD.⁴⁵ Medicare expenditures averaged \$43,000 for AD/ADRD beneficiaries with potentially avoidable hospitalizations related to diabetes long-term complications, compared to \$35,000 among matched controls who were hospitalized for the same condition but did not have AD/ADRD.⁴⁵ Another Medicare study reported that 14% of hospitalizations for AD/ADRD patients may be potentially avoidable and that these preventable hospitalizations for Ambulatory Care Sensitive Conditions in the AD/ADRD population cost Medicare \$2.58 billion in 2013.⁴⁹ Overall, there is solid evidence suggesting that AD/ADRD can complicate the management of other comorbidities and increase care costs.

As the disease progresses, AD/ADRD patients may lose their self-care skills and have difficulty complying with care management instructions (e.g., adherence to medications and diets). However, current treatment guidelines for common chronic conditions generally emphasize patient self-management, which is especially problematic for persons with AD/ADRD. This situation is particularly challenging for AD/ADRD patients who live alone or lack support networks (e.g., family, informal caregiver).

A growing body of literature has recognized the burden of multiple chronic conditions among older adults.^{50,51} In the Medicare population, 26% of beneficiaries with AD/ADRD have four or more other chronic conditions, compared to 4% among beneficiaries without AD/ADRD.² Although some patients may benefit from disease-specific interventions, for people with multimorbidity, coordinated services across multiple conditions are essential to maximize health care efficiency.⁵² Studies have established that managing individual health conditions in

isolation may be ineffective and inefficient, and in some cases, adherence to treatment guidelines for one disease may even adversely exacerbate another.^{53,54}

Future research should address comorbidity mix, treatment burden, and competing care demands among persons with AD/ADRD in order to improve patient outcomes and care efficiency. Such analyses may require new data sets that link across multiple sources, such as administrative claims, electronic health records, and patient registries. As an example, the linkage between Medicare and Medicaid claims records and the National Alzheimer's Coordinating Center Uniform Data Set has not been established yet. Linking these data sources would allow additional research to identify vulnerable subgroups with the greatest AD/ADRD and comorbidity burden, evaluate disease progression rates for patients on current standard of care based on real-world data, and provide a baseline for comparison when new treatments become available.⁵⁵

3. Bending the curve: understanding drivers of direct health care costs for AD/ADRD

3.1 Medicare expenditures for beneficiaries with AD/ADRD are concentrated in a small group of high-cost patients with prominent comorbidities

The cost drivers discussed in *Sections 3.1 and 3.2* primarily focus on direct health care costs. Prior research on the concentration of Medicare expenditures has shown that a small fraction of beneficiaries account for a large share of health care expenditures,⁵⁶ and that a subset of beneficiaries with high expenditures exhibit persistently high expenditures over time.⁵⁷ This phenomenon is also observed in the AD/ADRD population. One analysis of Medicare Current Beneficiary Survey linked with Medicare claims data documented that the highest-spending 10% of beneficiaries with AD/ADRD accounted for nearly half of total health expenditures and one-

third of drug expenditures.⁵⁸ The study also showed that expenditure persistence was very strong in the Medicare AD/ADRD population, especially for prescription drugs.⁵⁸ One-third of AD/ADRD beneficiaries who ranked in the top 10% for total health expenditures remained in the top 10% in the next year, but only 15% became the bottom 50% in the next year. For drug expenditures, 49% of AD/ADRD beneficiaries in the highest-spending 10% retained this ranking in the next year and only 3% became the lowest-spending 50%. Compared with the trends in the general Medicare population, findings from this study suggest that overall and drug expenditures among Medicare beneficiaries with AD/ADRD may be slightly less concentrated, whereas the degree of year-to-year persistence of high expenditures appears similarly strong.

The predictability of medical and drug expenditures can create incentives for favorable selection of individuals with low-cost risk and for avoidance of those with high-cost risk.^{59,60} On the other hand, expenditure predictability also creates opportunities to focus AD/ADRD disease management strategies on specific subpopulations. In this Medicare analysis, comorbidity burden strongly predicted high-expenditure persistence, and inpatient care accounted for the largest proportion of expenditures among high-cost AD/ADRD patients.⁵⁸ These findings highlight the importance of reducing expenditure growth and persistence for high-cost AD/ADRD beneficiaries with prominent comorbidities.

3.2 Inpatient, long-term care and end-of-life care costs are high in AD/ADRD

Past findings consistently have reported more frequent hospitalizations and longer hospital stays among individuals with AD/ADRD than those without the condition, and that hospital admissions represent the largest component of health care expenditures in the AD/ADRD population.^{32,41,61,62} Furthermore, inpatient care constitutes more than half of total

expenditures among the most expensive AD/ADRD patients.⁵⁸ Some hospitalizations are expected as part of the natural course of treatment, whereas others may not need to happen if patients' medical conditions, such as diabetes, hypertension and asthma, are being managed properly in outpatient settings. In addition, unplanned hospital readmissions within 30 days of discharge are another type of hospitalization that potentially could have been avoided with appropriate post-discharge care.²

A number of studies have highlighted the significance of potentially avoidable hospitalizations and unplanned hospital readmissions in the AD/ADRD population.^{33,41,43-46} For example, one study estimated that in 2013, 410,000 Medicare fee-for-service AD/ADRD patients were hospitalized for potentially avoidable conditions or readmitted for unplanned reasons within 30 days of discharge, costing Medicare roughly \$4.7 billion.³³ This study reported that in 2013 one in 10 Medicare fee-for-service AD/ADRD patients had potentially avoidable hospitalizations and one in seven (14%) hospitalizations for these patients may be potentially preventable.³³ In addition, almost one in five hospitalized AD/ADRD patients (18%) had unplanned 30-day readmissions in 2013.³³

Hospitalizations for potentially avoidable conditions and unplanned readmissions may be indicative of access barriers, problems in continuity of care, inefficient resource use, and poor patient outcomes.^{41,46,63} Additional time spent in the hospital may increase suffering and the risk of adverse events. For example, these hospitalizations may endanger the health of individuals with AD/ADRD, such as causing delirium and “post-hospital syndrome” that may increase the risk of cognitive decline, institutionalization, and death.⁶⁴⁻⁶⁶ Therefore, reducing unnecessary admissions to the hospital is clearly an important and underserved need in AD/ADRD care.

In addition to having more hospital stays, older adults with AD/ABRD use more post-acute skilled nursing facility care and long-term care, and incur higher costs for these services than other older adults. Although Medicare covers post-acute care in a skilled nursing facility and hospice care, it does not cover nursing home care. Long-term care expenses, including adult day services, residential care facilities, and nursing home care, are typically paid out-of-pocket by the patient/family, by Medicaid, or supplemental insurance. Prior research has reported that Medicare fee-for-service beneficiaries with AD/ABRD had four times as many skilled nursing facility stays per year, compared to those without dementia (283 vs. 73 stays per 1,000 beneficiary in 2014).⁶⁷ Average annual per capita nursing home care costs for Medicare beneficiaries with AD/ABRD were estimated at \$16,000, compared to \$780 among non-AD/ABRD beneficiaries (2018 dollars), based on unadjusted, descriptive data.⁶⁸ Data from the Health and Retirement Study and linked Medicare fee-for-service claims suggested that yearly per person nursing home costs (excluding payments by Medicare and out-of-pocket spending) attributed to dementia were roughly \$14,000 (2010 dollars), after adjusting for demographic characteristics and coexisting conditions.²¹ For Medicare-Medicaid dually eligible beneficiaries with AD/ABRD, Medicaid pays for a large proportion of their nursing home and other long-term care services. Unadjusted, descriptive data showed that average annual per person Medicaid payments for dually eligible beneficiaries with AD/ABRD were 23 times as high as those without dementia (\$8,600 vs. \$365, in 2018 dollars).⁶⁸ Although Medicaid covers nursing home care, coverage of other long-term care and support services, such as assisted living, home-based skilled nursing care and help with personal care, varies by state. States also differ substantially in the beneficiary eligibility criteria and benefits in their Medicaid programs. Further research is

needed to understand variability in use and costs of long-term care services covered by Medicaid across states among the AD/ADRD population.

Prior research has documented substantial health care costs for AD/ADRD individuals in their last years of life. Data from the Health and Retirement Study with linked Medicare fee-for-service claims showed that total costs in the last five years of life were 57% higher among individuals with dementia compared to other older adults (\$287,000 vs. \$183,000, in 2010 dollars).⁶⁹ The study also indicated that dementia may increase out-of-pocket medical expenditures in the last five years of life by \$27,000, and that families of individuals with dementia paid a greater proportion of family assets for end-of-life care than families of patients without dementia.⁶⁹ Moreover, the average length of hospice stay for individuals with a primary diagnosis of dementia may be >50% longer than for individuals with other primary diagnoses (112 days vs. 74 days), based on data from the 2008-2011 National Hospice Survey.⁷⁰ Longer hospice stays result in higher care costs, estimated at \$2,100 among AD/ADRD patients, compared with \$160 for all other Medicare beneficiaries (2018 dollars).⁷⁰ These findings highlight substantial financial burden for AD/ADRD end-of-life care among patients and their families. Although not specific to Medicare beneficiaries with AD/ADRD, the Medicare Payment Advisory Commission has raised concerns about potential misuse of hospice care, which may lead to substantial cost increase over time.⁷¹

3.3 AD/ADRD costs rise with increasing disease severity

It is well established that the economic impact of AD/ADRD increases with advanced disease not only for patients but also for caregivers, health care payers, and society (Figure 2).⁷² Observational data have shown that costs of AD/ADRD increase with advanced stages in which

patients have worse cognition, more functional impairment, and more behavioral symptoms.⁷³⁻⁷⁵

The most common staging of AD/ADRD is defined as mild/early stage (first year or two), moderate/middle stage (second to fourth or fifth years), and severe/late stage (fifth year or later), although symptoms and length of stages vary.⁷⁶ In a systematic review of 27 studies to identify cost drivers in dementia, 17 studies analyzed costs by disease severity.⁷⁷ The systematic review indicated that different measures and different cut-off points have been used to define dementia severity, including cognitive function (Mini Mental State Examination, Alzheimer's Disease Assessment Scale Cognition, and Clinical Dementia Rating; n=12), activities of daily living (ADL; n = 2), behavioral symptoms (Behavioral and Psychological Symptoms of Dementia; n=1), and mortality risk score (n = 1).⁷⁷ Eight studies in the review stratified costs by severity measures such as MMSE, CDR, and BPSD, and the data consistently showed that costs rose with increasing disease severity.⁷⁷ The mean costs were estimated at \$22,000 for mild stage, \$43,000 for moderate stage, and \$52,000 for severe stage of dementia.⁷⁷

		Cost				
		Preclinical Stage	Prodromal Stage	Mild Dementia	Moderate Dementia	Severe Dementia
Impact	Patients	Low	Moderate	Moderate	High	High
	Caregivers	Low	Low	Moderate	High	High
	Family	Low	Low	Moderate	Moderate	High
	Payers	Low	Low	Moderate	Moderate	High
	Society	Low	Low	Moderate	Moderate	High

FIGURE 2 Cost Impacts of AD/ADRD along Disease Continuum, by Stakeholder⁷²

3.4 Changing the disease prevalence or trajectory may substantially reduce future economic burden of AD/ADRD

Although currently there are no disease-modifying treatments to slow AD/ADRD progression, a number of studies have modeled the economic impact of future interventions.^{2,22,78,79} Using data from the Health and Retirement Study, a RAND study estimated that declining dementia prevalence rates may reduce monetary costs of the disease by \$153-\$205 billion in 2040, from \$379-\$511 billion to \$226-\$306 billion, depending on the method used to value informal care.⁷⁸ Another study, commissioned by the Alzheimer's Association, estimated that a hypothetical treatment introduced in 2025 that delayed AD onset by five years would decrease the number of persons with AD in 2050 by 42% (from 13.5 million to 7.8 million). The study also projected that a five-year delay in AD onset as a result of the treatment would reduce 33% of total health care costs in 2050 (from \$1.1 trillion to \$734 million), including 44% of reductions in out-of-pocket costs (from \$198 million to \$110 million). Results of a microsimulation produced by the Future Elderly Model projected that medical advances that delayed AD onset for 5 years may reduce disease prevalence rate by 41% and decrease total costs (including formal and informal care) by 40% in 2050.²² Specifically, the model projected that by 2050, a 1-year delay in AD onset may result in projected savings of \$219 billion, a 3-year delay may save \$415 billion, and a 5-year delay may save \$599 billion (2010 dollars), relative to the status quo.²²

Studies also have suggested economic benefits resulted from avoided AD/ADRD cases and shortened disease duration. One analysis of the Medicare Current Beneficiary Survey with linked CMS claims further demonstrated that a cohort with later dementia onset may have

shorter duration of the disease (average: 3.8 vs. 6.4 years), lower Medicare costs (\$8,300 vs. \$15,600) and lower Medicaid costs (\$7,600 vs. \$14,300) over the course of illness (2005 dollars), compared to a cohort with earlier dementia onset.²⁹ The results suggest that delaying dementia onset with more compressed disease duration in older age may result in lower formal care costs.

4. Value of AD/ABRD interventions and reimbursement challenges

4.1 Delaying AD/ABRD disease progression may result in economic benefits, but more data are needed to determine whether any savings generated from early detection and early treatment will be large enough to offset downstream long-term costs

Early diagnosis is an essential first step to managing AD/ABRD because it helps optimize treatment and allows patients and their families and caregivers to plan and make decisions for the future.⁸⁰⁻⁸² Some evidence suggests that early diagnosis of AD/ABRD might result in economic benefits. For example, a study commissioned by the Alzheimer's Association has estimated potential cost savings of early diagnosis in two scenarios.⁸³ In the first scenario in which a subset (88%) of individuals who would develop AD at some point in their lives were diagnosed in the MCI stage rather than the dementia stage or not at all, the study estimated that \$7 trillion could be saved in direct health care costs.⁸³ In the second scenario in which all individuals who would develop AD received the diagnosis in the MCI stage, the study indicated that a larger saving (\$7.9 trillion) may be achieved.⁸³ The study indicated that the potential savings were attributable to a smaller spike in costs immediately before and after diagnosis and lower medical and long-term care costs for individuals who have diagnosed and managed MCI and dementia compared with individuals with unmanaged diseases.⁸³ However, this study did

not account for *how* to accomplish early diagnosis. The cost of achieving early diagnosis and the mechanism for expected savings are unclear, thus limiting the usefulness of the estimates.

Simulation studies also have suggested that early detection of AD/ADRD in the MCI phase may generate reasonable value on cost-effectiveness grounds. A UK-based simulation model has shown that compared with no early assessment, identifying patients in early-stage AD (which was assumed to include a visit to a general practitioner, two specialist visits, laboratory tests, and a magnetic resonance imaging or computed tomography scan) could produce downstream cost savings (\$3100 per patient, with an additional \$5300 in savings attributable to reductions in caregiver time costs) and health benefits, despite significant up-front costs.⁸⁴ These findings are consistent with a U.S. study, simulating the potential benefits of early AD detection followed by treatment, which indicates that early assessment may reduce costs.⁸⁵

It is worth noting that the economic value of detecting AD/ADRD in its early stages rely on targeting resources to individuals most likely to benefit from intensive workup and follow-up care. The use of imaging tests, such as positron emission tomography, in the diagnosis of AD has demonstrated limited economic value, especially in the absence of effective disease-modifying treatment agents.^{86,87} To improve diagnostic efficiency, one study has suggested that primary care physicians use a combination of brief cognitive tests (e.g., the Mini-Mental State Examination and the Montreal Cognitive Assessment) and blood-based biomarker tests to identify individuals with early stage AD and triage them for further evaluation.⁸⁸ Routine, universal screening for cognitive impairment is unlikely to generate reasonable economic and clinical value. A 2019 U.S. Preventive Services Task Force report has indicated the lack of empirical evidence that screening for cognitive impairment or early diagnosis of cognitive impairment improves patient, caregiver, family, or clinician decision-making.⁸⁹ The Report also

concluded that there was scarce evidence related to screening for and treating MCI among community-dwelling older adults ages 65 and older.⁸⁹

In addition to early diagnosis, researchers also have conducted economic evaluation of early treatment for AD/ADRD. Overall, findings in the health economics literature suggest that delaying the disease progression to full-blown AD/ADRD may result in economic benefits, but it remains unclear whether any savings generated from early detection and early treatment will be large enough to offset downstream long-term costs. A recent study estimating the cost-effectiveness of a hypothetical, disease-modifying therapy for MCI due to AD reported that the treatment may be associated with \$11,330 incremental costs (2017 dollars) and 0.224 incremental quality-adjusted life years, compared to usual care.⁹⁰ In the base-case analysis, the hypothetical MCI treatment had an incremental cost-effectiveness ratio of \$50,542 per quality-adjusted life year, suggesting reasonable value for money based on commonly cited cost-effectiveness benchmarks (i.e., below \$100K-150K per quality-adjusted life year⁹¹). Although this is a methodologically rigorous study, some model inputs and assumptions play a critical role in influencing the results, as in any cost-effectiveness analyses. For example, MCI intervention cost was assumed to be \$5,000 per year in the study. This assumption likely underestimated costs of future MCI therapy, given the prices of recently approved biologics or specialty drugs in the U.S. In addition, the study assumed that the disease modifying treatment would reduce the risk of conversion from MCI to AD by 20%. Uncertainty in treatment effectiveness and sub-optimal treatment adherence in real-world settings also have important implications for the therapy's economic value.

4.2 Future AD/ADRD disease-modifying therapies could make a significant budget impact, in light of the size of the eligible population, presenting coverage and reimbursement challenges for health care payers who must develop strategies to contain costs while ensuring access to products and services that provide value for patients and their caregivers

As described in Sections 1.1 and 1.2, AD/ADRD pose a substantial economic burden on the health care system and the estimated total health care costs may exceed \$1 trillion by 2050. The projected cost growth is primarily due to increased life expectancy and population aging, especially the increased number of persons age 85 and older (the “oldest old”) with AD/ADRD. Therefore, the size of the eligible population challenges payers and policymakers to address coverage and reimbursement for AD/ADRD disease-modifying therapies, when they become available. Health care payers must develop strategies to contain costs while ensuring access to products and services that provide value for AD/ADRD patients and their caregivers. Even if the novel AD/ADRD treatment agents demonstrate cost-effectiveness compared to standard of care, their potentially high prices may present a financial barrier to persons with AD/ADRD. It has been documented in other disease areas, such as cancer, that high out-of-pocket burden may result in suboptimal use and adherence to therapy.^{92,93} Because treatments for AD/ADRD may continue for years, the long-term financial burden to patients, families, and the health care system should also be considered.

Future AD/ADRD treatments will create reimbursement challenges not only for Medicare and Medicaid but for private payers as novel agents are targeting (younger) patients with early-stage diseases. If treatments delay or prevent AD/ADRD onset at older ages, the economic benefits may not accrue to private payers covering persons under age 65. Although private payers will be under great pressure to pay for new AD/ADRD therapies, they may receive little

realized savings. Future research should develop novel payment models for AD/ADRD drugs addressing these challenges.

4.3 Barriers to timely AD/ADRD interventions are high. Policy actions are needed to improve access to dementia care and increase dementia care workforce

Studies have suggested that roughly half of the population with AD/ADRD receive a formal diagnosis and, of these, only half are treated with anti-dementia medications.² Although undiagnosed AD/ADRD in its early stages is a general phenomenon, it may be more common among non-Hispanic blacks and Hispanics than among non-Hispanic whites.^{23,63,94-97} Delays in AD/ADRD diagnosis can exacerbate disability, reduce treatment effectiveness, prevent timely care, and increase health care costs.^{98,99} Racial and ethnic minority populations with AD/ADRD also may experience additional barriers such as less knowledge about the disease and inferior access to health care services.¹⁰⁰ Additional research on vulnerable populations is needed to evaluate the effects of exposure to AD/ADRD risk factors from different parts of the life course. Policy efforts, such as the Healthy Brain Initiative (a partnership between the Alzheimer's Association and the Centers for Disease Control and Prevention),¹⁰¹ are critically important to promote early detection and diagnosis of AD/ADRD. Outreach programs to increase AD/ADRD awareness and improve care access remain essential.

Currently there are more than 130 AD treatment agents in clinical trial. When a high-cost, novel treatment agent for AD becomes available, many access challenges will rise with respect to the large and growing patient population. For example, therapeutic advances in AD/ADRD raise an important policy question: how prepared is the U.S. health care system to meet unprecedented demand for disease-modifying treatments? To anticipate future trends,

RAND researchers developed a Markov model that simulated the effects of capacity constraints on access to care for individuals with suspected AD. The model projected that patients would have to wait an average of 18.6 months for receiving AD treatment in 2020. Delay in access to care could result in 2.1 million people who might develop AD between 2020 and 2040 while waiting for evaluation and treatment. Projections of this simulation model showed insufficient capacity of dementia specialists (e.g., neurologists, geriatricians, and geriatric psychiatrists) to evaluate and diagnose AD. Furthermore, access to AD diagnostic imaging tests (e.g., amyloid positron emission tomography scan) and to infusion centers to deliver the treatment also constitute a barrier that would increase waiting times. This study highlights important capacity constraints in the U.S. health care system, suggesting that policy actions are needed to improve access to dementia care and increase dementia care workforce.

5. Conclusion

The economic impacts of AD/ADRD on patients, families and the health care system are well-recognized. Studies consistently have shown that individuals with AD/ADRD incur higher health care costs, including out-of-pocket expenses, than people without the condition. The higher costs of caring for persons with AD/ADRD are in part due to their high comorbidity burden and poor comorbidity management. Furthermore, AD/ADRD can make the management of other chronic conditions more difficult and expensive because, as the disease progresses, patients may lose self-care skills and have difficulty complying with comorbidity management instructions. Indeed, Medicare data suggest that AD/ADRD expenditures are concentrated in a small group of high-cost patients with prominent comorbidities and that inpatient costs for comorbidities are high in this population. As AD/ADRD progresses, both formal (especially

inpatient, nursing home and end-of-life care) and informal care costs increase. If current prevalence rates persist, the economic burden of AD/ADRD is projected to increase drastically due to population aging.

From an economic perspective, studies have highlighted the importance of delaying AD/ADRD onset with shortened disease duration and delaying disease progression to more costly stages. Simulation studies also indicate that changing the disease prevalence or trajectory may substantially reduce future economic burden of AD/ADRD. Further research should project future economic burden of AD/ADRD by race and ethnicity, given the expected growth of minority populations and the different disease risks.

Delaying AD/ADRD disease progression to more costly stages may reduce care expenditures, but more data are needed to determine whether any savings generated from early detection and early treatment will be large enough to offset downstream long-term costs. Future AD/ADRD disease-modifying therapies are likely to create many reimbursement and access challenges and the U.S. health system is unprepared. Health care payers and policymakers should develop strategies to contain AD/ADRD costs and ensure patient access to high-value products and services. In the era of disease-modifying therapies, increasing disease awareness and improving access to dementia care, especially among underserved populations, will be continuing goals for AD/ADRD outreach programs.

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