4-1-2017

Direct and indirect cost of managing alzheimer's disease and related dementias in the United States

Arijita Deb
West Virginia University

James Douglas Thornton
West Virginia University

Usha Sambamoorthi
West Virginia University

Kim Innes
West Virginia University

Digital Commons Citation

Deb, Arijita; Thornton, James Douglas; Sambamoorthi, Usha; and Innes, Kim, "Direct and indirect cost of managing alzheimer's disease and related dementias in the United States" (2017). *Clinical and Translational Science Institute*. 595.
https://researchrepository.wvu.edu/ctsi/595

Published in final edited form as:

Expert Rev Pharmacoecon Outcomes Res. 2017 April ; 17(2): 189–202. doi:10.1080/14737167.2017.1313118.

Direct and indirect cost of managing alzheimer's disease and related dementias in the United States

Arijita Deb[a], **James Douglas Thornton**[a], **Usha Sambamoorthi**[a], and **Kim Innes**[b]

[a]School of Pharmacy, Department of Pharmaceutical Systems and Policy, West Virginia University, Morgantown, USA

[b]School of Public Health, Department of Epidemiology, West Virginia University, Morgantown, USA

Abstract

Introduction—Care of individuals with Alzheimer's Disease and Related Dementias (ADRD) poses special challenges. As the disease progresses, individuals with ADRD require increasing levels of medical care, caregiver support, and long-term care which can lead to substantial economic burden.

Areas covered—In this expert review, we synthesized findings from studies of costs of ADRD in the United States that were published between January 2006 and February 2017, highlighted major sources of variation in costs, identified knowledge gaps and briefly outlined directions for future research and implications for policy and program planning.

Expert commentary—A consistent finding of all studies comparing individuals with and without ADRD is that the average medical, non-medical, and indirect costs of individuals with ADRD are higher than those without ADRD, despite the differences in the methods of identifying ADRD, duration of the study, payer type and settings of study population. The economic burden of ADRD may be underestimated because many components such as direct non-medical costs for home safety modifications and adult day care services and indirect costs due to the adverse impact of ADRD on caregivers' health and productivity are not included in cost estimates.

Keywords

Dementia; alzheimer's disease; economic burden; direct cost; indirect cost

---

CONTACT Kim Innes, kinnes@hsc.wvu.edu, Department of Epidemiology, West Virginia University, School of Public Health, Robert C. Byrd Health Sciences Center (North), Morgantown, WV 26506-9127, USA.

Declaration of interest

KE Innes disclosure: NIH/NIGMS U54GM104942, Alzheimer's Research and Prevention Foundation. JD Thornton disclosure: NIH Research Training Program in Behavioral and Biomedical Sciences 5 BBS T32 GM 081741-08. U Sambamoorthi disclosure: NIH/NIGMS U54GM104942. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

ORCID

Arijita Deb http://orcid.org/0000-0002-4570-0364(/p)(p)James Douglas Thornton http://orcid.org/0000-0001-6017-7500(/p)(p)Usha Sambamoorthi http://orcid.org/0000-0001-8311-1360(/p)(p)Kim Innes http://orcid.org/0000-0002-6395-7972

1. Introduction

Dementia is an umbrella term used to describe a level of neurocognitive impairment that can affect a person's activities of daily living. Multiple etiologies, including Alzheimer's disease (AD), vascular disease, presence of Lewy bodies, frontotemporal disease, and brain injury, can lead to dementia. Alzheimer's disease and related dementias (ADRD) are generally characterized by progressive loss of memory and cognitive functioning; functional impairment in the performance of daily activities such as eating, making meals, bathing, and paying bills; and manifestation of neuropsychological symptoms such as depression, anxiety, agitation, apathy, delirium, and psychosis [1]. The most common cause of dementia among adults aged 65 years and older is AD that accounts for 60–80% of all dementias [2]. Other, less common forms of dementia are vascular dementia (VD), frontotemporal dementia (FTD), and Lewy body dementia (LBD) that comprise approximately 10%, 10%, and 4% of dementia cases, respectively [2,3]. It is expected that demographic shifts in the United States due to the rapid growth of the elderly population will increase the number of individuals afflicted with AD by threefold in the next 30 years [4].

As the disease progresses, individuals with ADRD require increasing levels of care and support, including medical treatment, prescription drugs, medical equipment, home safety modifications, safety services, personal care, adult day care, and, ultimately, full-time residential services. Currently, there is no cure for ADRD, and effective disease-modifying treatments remain elusive. Therefore, ADRD can impose a high financial burden on payers, patients and their families, health-care delivery systems, and society as a whole. According to recent estimates from the Alzheimer's Association, the total direct medical expenditures associated with ADRD in the United States will increase from $236 billion in 2016 to more than $1 trillion in 2050 due to projected increases in the elderly population [2]. These figures do not take into account informal care and other indirect costs, including the unpaid care needed for those with ADRD and currently provided by almost 16 million Americans. For example, in 2015, unpaid caregivers provided approximately 18.1 billion hours of assistance, and this care has been valued conservatively at $221.3 billion [2].

With the rising economic burden of ADRD in the United States, it is important for health policy planners and other decision makers to gain a comprehensive understanding of the economic burden of AD/ADRD in the US population. In recent years, several studies have assessed the direct and indirect cost associated with ADRD [5–19]. Most studies have differed considerably in their definitions (AD/ADRD), data sources, cost estimation approaches, components of costs, and the stage at which costs were captured. A rigorous review and synthesis of studies that include both direct and indirect costs of AD/ADRD in the US population is lacking. In this critical review, we describe the various measures for assessing economic burden of ADRD, synthesize the findings from recent studies regarding costs of ADRD in the US population, highlighted major sources of variation in costs, identified knowledge gaps, and briefly outlined directions for future research and implications for policy and program planning.

2. Literature search

In this paper, we reviewed articles on direct and indirect costs of ADRD in the United States that were published in English between January 2006 and February 2017. To identify qualifying studies, we searched three scientific databases via EbscoHost (Medline, PsycINFO, and Web of Science) and scanned bibliographies of relevant review papers and identified articles. Search strings included different combination of the keywords ‘dementia,’ ‘alzheimer*’ together with ‘economic,’ ‘expenditure,’ and ‘cost.’ One example of such a combination was (dementia OR alzheimer*) AND (‘economic’ OR ‘expenditure’ OR ‘cost’). Cost studies that did not target adults with ADRD, or did not include cost data, were excluded. We excluded conference abstracts, doctoral and master’s theses, and ‘gray’ literature. Of the 46 potentially relevant abstracts and citation indices scanned, 31 potentially eligible papers were identified for closer review. A total of 17 published articles met our eligibility criteria and were included in this review (Tables 1 and 2). Of these, nine studies [5–13] were on individuals with AD diagnosis, four studies [16,19–21] were on individuals with ADRD. These studies identified ADRD using International Classification of Diseases-9th edition clinical modification (ICD9-CM) codes for AD, VD, FTD, LBD, and unspecified dementias (senile dementia uncomplicated, senile dementia w/delusional or depressive features, senile dementia w/delusional features, senile dementia w/depressive features, dementia in conditions classified elsewhere, dementia in conditions classified elsewhere without behavioral disturbance, or senility w/o psychosis and presenile dementia) and four studies [14,15,17,18] were based on individuals with dementia identified using cognitive screening measures.

3. Identification of ADRD

One of the challenges in deriving precise estimates of costs of ADRD is the difficulty of identifying patients with ADRD. In the absence of specific biomarkers for differentiating the various subtypes of dementia, diagnosis of ADRD has remained essentially a clinical diagnosis based on patient’s cognitive and functional history, clinical examinations, and neuropsychological testing. As illustrated in Table 3, studies have used varying criteria and methods for defining ADRD. The most commonly used diagnostic criteria for identifying dementia are those detailed in the Diagnostic and Statistical Manual of Mental Disorders (DSM); these criteria were developed by the American Psychiatric Association and require (1) a continued gradual decline in memory function and (2) cognitive deficits in one or more domains which impair social and occupational functioning [23]. AD is often diagnosed using the National Institute on Neurological and Communicative Disorders and Stroke and the Alzheimer Disease and Related Disorders Association (NINCDS-ADRDA) criteria originally proposed in 1984 [24]. These criteria require a gradual and continued decline in two or more areas of cognition that is supported by clinical examination, neuroimaging tests, and cognitive screening tests such as Mini-Mental State Examination, Clinical Dementia Rating, Blessed Dementia Rating Scale, and other neuropsychological tests. Many registry-based studies that have assessed the economic costs of AD have identified patients using the NINCDS-ADRDA criteria for ‘probable’ AD and/or the DSM-III-R or DSM-IV criteria [5,18,23–25].

Alternatively, studies using the Health Retirement Survey (HRS), a nationally representative survey of adults aged 50 or older, determined probability of dementia with predictive modeling [14,15]. In these studies, probable dementia was identified using in-home clinical assessments on a sample of adults, and these data were then used to extrapolate ADRD prevalence in the population. However, given that these estimates are based in part on documented limitations in cognition and function, ADRD may be underestimated among individuals with mild symptoms/early stage disease.

In studies using the Medicare Current Beneficiary Survey (MCBS), a survey of nationally representative sample of beneficiaries enrolled in Medicare, ADRD has been determined using any of the three criteria: (1) self or proxy reports, (2) medications, and (3) the International Classification of Diseases-9th edition clinical modification (ICD9-CM) codes for ADRD [21] (Table 3). In other investigations relying on Medicare [20], Medicaid [16,26], and other commercial insurance claims databases [6,7], ADRD was likewise identified using the ICD9-CM codes recorded in inpatient, outpatient, skilled nursing home, and home health-care claims.

Limitations of most existing studies with respect to ADRD identification include lacking or inadequate information on ADRD severity as well as under diagnosis or misdiagnosis of ADRD leading to over or under estimation of costs. Claim-based studies use inpatient and outpatient claims to identify ADRD and do not have high sensitivity and specificity in identifying ADRD [27,28]. Therefore, there is potential to misclassify ADRD cases. In one study comparing the Medicare costs estimates for patients with ADRD to the costs of patients without ADRD, ADRD is identified in two different ways: one using Medicare claims and the other using clinical examinations [28]. Researchers reported that using Medicare claims resulted in substantial overestimation of the costs attributed to ADRD as compared to using clinical examinations to identify patients with ADRD [28]. In this study, using Medicare claims to identify ADRD was associated with a 110% increase in costs for those with ADRD as compared to a 68% increase when using clinical examinations to identify ADRD [28]. Similarly, a study using 5% Medicare claims data found that a considerable number of Medicare beneficiaries with VD or Parkinson’s dementia were misdiagnosed as AD, comprising almost 25% of reported AD cases [29]. Such misdiagnosis resulted in an incremental annual Medicare expenditure of $9500–$14,000 among the patients; this excess expenditure was largely eliminated after correcting for misdiagnoses [29]. Research has also shown that the chronology of AD diagnosis has substantial impacts on health-care costs. For example, patients who initially receive a diagnosis of cognitive impairment other than AD and are later diagnosed with AD incur significantly higher health-care costs as compared to those who receive AD as their initial diagnosis [30].

4. Economic burden of ADRD: direct medical, nonmedical, and indirect costs

The economic burden of a disease is often assessed by measuring costs of the disease for society or part of society. Costs of a disease are typically grouped into direct and indirect costs. Direct medical costs of ADRD are associated with the use of resources for medical care including hospital visits, physician visits, emergency department visits, pharmacy, and short-term skilled nursing facility care. Direct nonmedical costs include those associated, paid formal home-health care, transportation costs to health-care providers and costs of making necessary modifications to one’s diet, house, car, or related items. Indirect costs include costs due to premature death or loss of productivity, as well as costs of informal (unpaid) care.

4.1. Estimates and projections of national economic burden of ADRD

Estimates for the total direct medical costs of ADRD at the national level have been calculated by multiplying per capita cost estimates by the expected prevalence of ADRD in the population. For direct medical expenditures, the costs of care for prevalent ADRD in year 2010 in the United States were estimated as $109 billion [14]. Due to the accelerated aging of the population, this cost is projected to reach $259 billion by 2040, assuming that the current prevalence of ADRD and per capita direct medical cost of ADRD remain stable [14]. On the other hand, if recent declines in ADRD prevalence continue, estimated direct costs of prevalent ADRD would increase to only $154 billion by 2040, a more modest, but still substantial (70%) increase [31]. Thus, the broad variation in estimates of future direct costs of ADRD in part reflects differential assumptions regarding projected ADRD prevalence, cost of medical services for ADRD, and longevity of the population. As illustrated in the section on per-capita direct medical costs, variations in per-capita direct medical costs can also contribute to the variations in the national cost estimates.

In terms of indirect costs, the aggregate cost in 2010 for informal caregiving for ADRD in the United States was estimated at $159 billion dollars and $215 billion dollars using the forgone wage and replacement cost approach, respectively. This estimate exceeds the direct cost estimate of $109 billion in 2010 [14]. Assuming that the prevalence of ADRD remains constant at 2010 levels, these costs would increase to $379 billion and $511 billion, respectively, by 2040 [14]. Alternatively, using the same approach to valuing caregiver time but assuming a continued decline in ADRD prevalence, informal caregiving costs would increase to $226 and $305 billion, respectively, by 2040 [31].

4.2. Per-capita direct health-care costs of ADRD

In the United States, direct health-care costs are borne by insurers (both private and public) as well as by patients and their families. Currently, 68% of the total direct health-care costs of ADRD are covered by Medicare, a federal insurance program, and Medicaid, a federally subsidized insurance program administered by the states [2]. In 2015, Medicare spent an estimated $226 billion and Medicaid paid an estimated $44 billion on total direct health-care costs for individuals with ADRD [2]. The direct health-care costs can be further divided by the type of service such as inpatient visit, outpatient visit, physician office visit, pharmacy, emergency department, diagnostic and laboratory tests, long-term care, home care, and hospice care. For individuals with ADRD, long-term or nursing home care costs are a particularly critical component of total health-care costs.

The direct health-care costs of ADRD have typically been reported over variable time periods. These include prevalence-based costs, post-diagnosis costs, lifetime costs, and end-of-life costs. As costs of chronic conditions may follow a U-shape curve, peaking during the initial diagnosis and end-of-life periods, cost estimates may vary depending on at what stage the costs were captured.

4.2.1. Prevalence-based costs—The economic burden of ADRD has been measured using a snapshot of costs in 1 year known as the prevalence-based cost approach. Under this approach, costs are estimated for all individuals with ADRD in a given year (both incident and prevalent cases); such estimates are often used for budgetary allocations and for policy and program planning. In a study using HRS data, researchers reported that in 2010, the total per capita annual direct health-care costs of dementia were $28,501 [14]. Using the Medical Expenditures Panel Survey, community-dwelling adults over the age of 65 with ADRD had 44% higher total health-care expenditures compared to patients without ADRD [19]. As can be seen from Table 1, there is a considerable variation in these costs based on the data sources, setting, and stage of ADRD.

4.2.2. Costs around the time of ADRD diagnosis—Nearly 30% of ADRD diagnoses occur during hospitalization for another serious condition such as cardiovascular disease, cerebrovascular diseases pneumonia, kidney disease, or infection [20]. Therefore, studies that focus on the immediate period after diagnosis can show higher costs (Table 1). Interestingly, studies assessing the direct medical costs around the time of ADRD diagnosis have shown that direct medical expenditures among individuals with ADRD were already significantly higher in the pre-diagnosis period than their non-ADRD counterparts perhaps due to diagnostic workup, early manifestations of cognitive impairment, and higher comorbidity burden (Table 1). In a recent study using 5% sample of Medicare claims, Lin et al. found that Medicare expenditures were 42% higher in the ADRD cohort in the 1-year pre-diagnosis period as compared to the matched non-ADRD cohort.

Following the diagnosis of ADRD, the Medicare expenditures increased 3 times within 1-year and by 1.7 times by 2 years [30]. Similar pattern was observed in another study using Medicare Advantage Prescription Drug plan dataset. This study revealed that during the year prior to diagnosis of ADRD, total medical expenditures were 44% higher, 1 year after diagnosis, the total medical expenditures were 2 times higher, and 2 years after diagnosis, the total medical expenditures were 1.7 times higher in the AD versus non-AD cohort [12]. In addition, the perceptions of physicians, patients, and family members regarding ADRD may also affect health-care utilization following an ADRD diagnosis. Therefore, in a prospective multicenter study, researchers followed community dwelling Medicare beneficiaries at multiple centers in the northern Manhattan area of New York and clinically examined them to diagnose incident AD; however, both patients and their providers were blinded to the diagnosis of AD [18]. Nonetheless, Medicare expenditures were 65% higher in those diagnosed with AD than in those not diagnosed in the 2 years preceding diagnosis. After diagnosis, Medicare expenditures doubled in the AD cohort, whereas it only increased by 43% in the non-AD cohort.

4.2.3. End-of-life costs—Table 1 also presents end-of-life costs associated with ADRD. In a study using a prospective cohort of nursing home residents with advanced AD, Goldfeld et al. reported that the average total Medicare expenditures increased by 65% in the year prior to death, with costs progressively increasing as death approached ($1061: 365–271 days before death; $1605: 270–121 days before death; $2297: 120–91 days before death, and $3877: 90–0 days before death) [9]. The major drivers for end-of-life Medicare costs were hospitalizations (30.2%) and hospice care (45.6%) [9]. One retrospective cohort study using the HRS data assessed Medicare and Medicaid costs among patients with versus without dementia in the 5 years prior to death [15]. While there was no significant difference in the adjusted total Medicare spending in the dementia versus non-dementia group, average Medicaid spending was nearly 8 times higher in those with versus without ADRD [15]. Medicaid is the primary payer for long-term care for Medicaid eligible patients. Many patients who are not initially eligible for Medicaid may, after ‘spending down’ their assets, ultimately transition to Medicaid-supported long-term care. In contrast, Medicare does not support nursing home care, the major driver of end-of-life costs in adults with ADRD. Thus, it is not surprising that excess Medicare expenditures associated with ADRD are lower than excess Medicaid costs.

4.2.4. Life-time costs—Individuals with ADRD experience gradual declining health with an average life-expectancy of 8–10 years [32]. Cost estimates of ADRD may depend on the time during which costs are captured; therefore, it is important to estimate life-costs of ADRD [21]. As can be seen from Table 1, in a cohort-based simulation study assessed the lifetime costs of AD using the MCBS data. This study estimated the average lifetime Medicare expenditures using an estimated 5.1 year duration of dementia and found that the average lifetime Medicare expenditures was 13% higher ($101,810 vs. $89,835) and the average lifetime Medicaid expenditures was 69% higher ($27,028 vs. $15,955) per AD patient as compared to non-AD control group [21]. Not surprisingly, it was also reported that lifetime costs could be lowered with shorter duration of AD [21].

4.3. Type of direct health-care costs specific to ADRD

4.3.1. Formal home-health care costs—The unique characteristics of ADRD influence the drivers of direct health-care costs for ADRD. Due to the progressive decline in cognitive and functional status, many older patients with ADRD need home–health care and may spend their last years of life in long-term care facilities (Table 1). The annual number of paid home-health visits in the first year following ADRD diagnosis averaged 30 versus 13 among those without an ADRD diagnosis [20]. As the disease progresses, use of formal home-health care use also increases. For example, in a prospective cohort study of elders with early stage AD at baseline, the percentage of patients receiving paid home health increased from 9.9% at the time of diagnosis to 34.5% by 4 years. The incremental total costs for paid home care in 2010 was $5678, accounting for 20% of the incremental direct costs associated with ADRD [14]. In one prospective study of Medicare beneficiaries, it was observed that excess costs of ADRD were largely due to home-health care, skilled nursing care, and durable medical equipment [18].

4.3.2. Nursing home costs—On average, individuals with mild-to-moderate ADRD aged between 70 and 80 years spend 3 years in a nursing home while those with severe ADRD spend 4 years in nursing home [33]. Therefore, a substantial portion of the direct costs associated with ADRD is for nursing home stays. In the United States, almost 75% of the oldest adults with ADRD (≥80 years) are nursing home residents as compared to only 4% of those without ADRD [33]. Therefore, it is not surprising that nursing home costs account for a major portion of the incremental total direct expenditures associated with ADRD [14]. For example, using HRS, a study reported that nursing home care costs accounted for 49% of the total direct medical costs of ADRD [14].

In the United States, Medicare does not cover long-term care stays; therefore, many ADRD patients rely on Medicaid to cover their long-term care expenditures. For example, in a retrospective cohort study of older Indiana Medicaid beneficiaries, 93% of the incremental Medicaid expenditures associated with ADRD were for nursing home stays [16]. Many ADRD patients required skilled nursing home care. It has been reported that during the year after diagnosis, skilled nursing home care costs were 9 times higher ($6755 vs. $727) 1 year after diagnosis in the ADRD cohort compared to no ADRD cohort [30].

4.4. Out-of-pocket spending by patients and their families

Although Medicare provides health-care coverage for most of the elderly in the United States, many elderly and their families pay for medical care out of their pockets. Out-of-pocket spending includes spending on health insurance premiums, deductibles, coinsurance, and copayments for medical care and prescription drugs; certain services or equipment only partially covered or not covered by insurance; non-prescription medications; transportation to health-care providers; and uncovered structural or lifestyle modifications. According to the Global Health Observatory (GHO) data, out-of-pocket health-care expenditures by patients and/or their families comprised 45% of total health-care expenditures in 2014 [34]. Among Medicare beneficiaries, health insurance premiums account for 42% of the total out-of-pocket spending, with payments toward cost-sharing and non-covered services and goods accounting for the remaining 58% [35]. It is important to assess the magnitude of out-of-pocket expenditures because high out-of-pocket expenditures can also lead to worse health outcomes because of access issues. For example, individuals with high out-of-pocket costs may be more likely to stop taking their medications [36], less likely to use preventive care, and less likely to use outpatient services for their health care [37,38].

Estimation of out-of-pocket health-care expenditures burden is especially important for those with chronic conditions such as ADRD because these individuals may require long-term medical care, residential services, and prescription drugs. Despite its importance, only few studies have evaluated out-of-pocket spending in the US population [13–15,39]. In an article not specific to ADRD, Hurd et al. examined average out-of-pocket spending among a nationally representative sample of older adults (HRS) with dementia [14]. In this study, out-of-pocket spending included costs borne by the patient and the families for the following services: nursing home, hospital, medical visits, outpatient surgery, home-health care, rehabilitation, prescription drugs, and dental services. This study found that adults with dementia spent on the average $6838 out-of-pocket, an amount that was only slightly attenuated by adjustment for demographic factors and coexisting conditions (adjusted mean = $6194, 95% CI $4522, $7866). This figure may represent an underestimate because out-of-pocket spending estimates did not include health insurance premiums and the study did not focus on those with ADRD [14]. Using data from the MCBS, it was estimated that patients with ADRD and their families spent an average of $10,495 out-of-pocket for ADRD care, with those residing in long-term care facilities or assisted living facilities spending 6 times as much as community dwelling patients with ADRD [2]. In another HRS study of decedents with likely/probable dementia, mean out-of-pocket costs for last 5 years of life totaled $61,522 for those with dementia and these individuals spent nearly 32% of their expenditures out-of-pocket [15]. Researchers using data from the nationally representative Aging, Demographics, and Memory Study found that individuals with dementia had more than 3 times annual out-of-pocket spending relative to those with normal cognition [39]. None of these studies examined out-of-pocket burden as measured by the percent of income spent on medical and nonmedical care.

As stated above, as many as three quarters of all patients with ADRD will require care in a long-term care facility [40]. Therefore, it is not surprising that individuals with ADRD spent a major proportion of their out-of-pocket costs on long-term care facilities [35]. Long-term facility costs account for much of the cost-sharing among Medicare beneficiaries who also qualified for Medicaid [41], suggesting that even with dual coverage of Medicare and Medicaid, individuals with ADRD face a significant financial burden.

High out-of-pocket expenditures can be borne not only by ADRD patients but also by their caregivers. These expenditures may include travel, medical supplies, food, and groceries. According to the Usage and Attitudes Family Caregiver Survey, nearly 50% of caregivers spent over $5000 annually [42]. Such expenditures can exact a toll on the caregivers by reducing their ability to pay for food, housing, health-care, and other basic needs and thus lead to significant declines in caregiver health and well-being [10,11,43].

4.5. Indirect costs

As stated above, another component of ADRD costs is the indirect costs that include costs due to loss of productivity as well as costs of informal (unpaid) care. Typically, indirect costs exclude costs specific to disease treatment [44]. In general, valuation of the productivity losses for elderly and specifically for patients with ADRD are scarce. As friends and family members provide nearly 75% of all caregiving for patients with ADRD [10,45], productivity loss is not limited to patients with ADRD but also affects informal caregivers who provide care for patients with ADRD [5,8,17]. As summarized in Table 2, in an epidemiological study using the HRS data, Friedman et al. reported that older adults with probable ADRD received 171 h of informal care per month versus 66 h for those without ADRD [46]. However, medical care provided by unpaid caregivers is not always included in costs estimations for ADRD.

The informal cost of care for ADRD is usually measured by valuing the time lost due to unpaid caregiving using the human capital approach. Initially, informal caregiving time is assessed in terms of caregiving hours per day or per week. Caregiving time is then valued in terms of either the *replacement cost* of hiring paid formal care or the *opportunity cost due to lost wages* (foregone wages). The former is measured by monetizing caregiving hours based on market wages paid to formal (paid) caregivers [13,14]; the latter is measured by valuing caregiving time in terms of the caregiver’s expected market wage based on the caregiver’s age, education, previous income, or occupation [5,8,14,15,17]. Details on data source, informal cost estimation approach, wage estimates, and per capita cost estimates can be seen in Table 2.

Estimates of informal caregiving may vary depending on whether the replacement costs or the foregone wage approach is used. Using the same cohort of patients, average adjusted annual informal caregiving was valued at $13,188 (2010 USD) using the replacement costs approach and $27,789 (2010 USD) using the foregone wages approach by Hurd and colleagues in an analysis of the HRS data [14]. The foregone wage approach has been used in other studies to estimate informal caregiver costs (see Table 2) [5,8,15,17].

The estimate of indirect costs due to ADRD requires the consideration of factors other than productivity losses. Indirect ADRD costs need to include caregiver's health-care resource utilization and health-care costs. It has been reported that members of households with AD patients were estimated to have significantly greater total annual medical, pharmacy, and total health-care costs than did those without AD patients [11]. For all caregivers of ADRD patients, average annual medical care costs have also been shown to rise as care recipient's condition progressed [10].

5. Expert commentary

5.1. Key findings

A consistent finding of all studies comparing individuals with and without ADRD is that the average medical, nonmedical, and indirect costs of individuals with ADRD are higher than those of individuals without ADRD [6,7,12,15,18–21], despite the differences in source of payment (Medicare, Medicaid, out-of-pocket), time period (lifetime vs. annual) and study population (e.g. decedents vs. all adults, AD vs. all forms of dementia), and stage of disease. Because of the long duration and the progressive cognitive and functional impairment characterizing ADRD, nursing home and home health-care services accounted for a substantial portion of the direct costs associated with ADRD. Nursing home stays, home health-care services, and informal caregiving accounted for more than three-fourth of the total costs associated with ADRD [14]. For community-dwelling individuals with ADRD, the indirect costs of ADRD far exceeded the direct costs of ADRD due to the high need for formal and informal caregiver services in these vulnerable populations [14,15]. In the United States, the combined direct and indirect costs of ADRD is higher than those of other serious chronic illnesses, including stroke, diabetes, heart disease, hypertension, lung disease, cancer, psychiatric problems, and arthritis in the US population [15].

5.2. Major sources of variation in costs

One important source of variation in the cost estimates stems from the differences in the method of determining ADRD across studies. Studies using administrative claims data such as Medicaid, Medicare, MarketScan, and PharMetrics have identified AD/ADRD based on diagnosed ADRD, whereas studies using survey data such as the HRS have assessed ADRD based on cognitive screening measures and registry-based studies have used clinical examinations to determine AD/ADRD. Studies that use claims data to identify ADRD at a particular point in time need to be particularly cautious in defining AD, because both underreporting (mild cases) and misdiagnosis are common, potentially leading to inaccurate estimates of care costs for individuals with AD [28,29]. In addition, because the onset of AD is insidious, cognitive decline is typically gradual, and compensatory behaviors can mask early symptoms, capturing 'true' incident cases of AD can be challenging. The higher estimates of medical expenditures generated using claims based versus registry data likely reflect differences in stage of disease at diagnosis; while registries capture incident ADRD, claims data are more likely to reflect those with more advanced disease [18,20].

Other sources of variations in the cost estimates of studies are due to the determination of costs using approaches such as prevalence-based costs [14] versus incidence-based costs [20]. Studies that assessed annual costs of ADRD after incidence usually have higher estimates as compared to studies that have assessed costs using prevalence based approach. Other sources of variations in costs are due to the differences in the population setting (community vs. nursing home) and differences in the source of pay (Medicare, Medicaid, out-of-pocket).

6. Five-year view

6.1. Knowledge gaps and implications for future research

Direct nonmedical costs play a particularly important role in ADRD because as the disease progresses, home-safety modifications, safety services, personal care, adult day care, and full-time residential services are typically required [8,14]. Because studies generally do not include many of these costs, the cost burden of ADRD may be underestimated.

There remains a significant knowledge gap regarding estimation of indirect costs. Studies assessing the indirect costs of ADRD have primarily focused on the productivity loss or replacement cost of informal caregivers. However, caregiver burden is multidimensional [47]. Importantly, the chronic stressors associated with caregiving for ADRD patients can have significant adverse effects on caregiver health, increasing risk for depression, anxiety, hypertension, cardiovascular disease, dementia, and ultimately, mortality [48–51]. Therefore, to better capture the economic burden of ADRD, future studies need to measure loss in caregiver productivity, caregivers' health, absenteeism, and employment. This information can help inform the development of programs and policies to more effectively address the burden of informal caregivers who provide care for ADRD patients.

Many studies have used insurance claims to estimate costs of ADRD. Claim-based databases are important because policy makers and payers also have developed new payment models (shared savings), performance evaluation (Centers for Medicare and Medicaid Services's Star Rating System, National Quality Forum performance measures), payment reduction (e.g. 30-day readmissions for certain chronic conditions), and other policies to ensure high-quality patient-centered care. With these shifts, administrative claims data have become vital to population health management. As most of the direct home health-care costs in the United States are borne by Medicare and most of the long-term care costs are borne by Medicaid, studies using only Medicare, Medicaid, or private insurance claims databases may underestimate the direct medical costs of care for ADRD.

Therefore, to improve economic analysis of the direct and indirect costs of ADRD, efforts should be directed toward linking various registries of AD/ADRD and surveys with multiple administrative claims datasets from all payers. In this context, the all payer claims database (APCD) initiatives that are being implemented can offer great value for individuals covered by multiple health-care plans because of the industry-wide coding standards of health-care encounters. These databases will assist practitioners in patient care by providing a ‘360-degree’ view of patients’ health care and ‘actionable intelligence’ that can offer specific guidance for improving chronic disease management. Indeed, use of health analytics involving large databases has been shown to bring about improvements such as increased adherence to guideline-based care, enhanced surveillance and monitoring, and decreased medication errors [52]. As of January 2016, 18 states have an APCD to help policy decision makers with cost containment and quality improvement strategies [53]. Unfortunately, establishment of APCDs has been met with resistance, and in 2015, the US Supreme Court ruled that self-insured group health plans are not required to comply with ACPD data requests [54]. Despite this setback, APCD implementation may not be significantly affected since many states have already received buy-in from these self-insured group health plans [55].

Additionally, long-term, prospective studies that track ADRD costs over time are needed because cost estimates can differ significantly based on ADRD severity. By helping to delineate the components, trajectories, and major drivers of costs and burden associated with ADRD from disease onset to end-of-life, findings from these studies will aid in program planning and help identify optimal timing for intervention.

6.2. Potential impact of emerging technology and treatment on ADRD burden

With the advances in neuroimaging technologies including volumetric magnetic resonance imaging, single-photon emission computed tomography, positron emission tomography imaging, cerebrospinal fluid beta, tau metabolites, and other serum markers, it may soon be possible to detect the ADRD at a prodromal or preclinical stage before the signs of the first clinical symptoms [56]. A recent predictive economic model has shown that the use of a neuroimaging technique for detection of early indicators of AD pathophysiology (with 90% sensitivity and specificity) and a disease modifying treatment that retards AD progression by 50% would reduce the lifetime risk of AD in elderly adults from 10.5% to 5.7% [57]. Technological innovations for ADRD caregivers may reduce the caregiver burden. For example, intelligent assistive devices currently under development such as cognitive aids, environmental sensors, video and audio technologies to support daily life activities and monitor the safety of individuals with dementia have the potential to significantly reduce the burden of informal and formal caregiving for dementia [58].

7. Implications for future policy and program planning

The development and implementation of high impact policy and programs to reduce the escalating economic burden of ADRD requires a comprehensive understanding of the direct and indirect costs of ADRD throughout the disease trajectory. As long-term institutionalized care accounts for a significant portion of the federal and state spending on ADRD, policies should be implemented to shift long-term care from institutional settings to home- and community-based settings [59]. This would necessitate implementation of new home- and community-based services and inclusion of such services in state Medicaid plans, as well as expansion of financial compensation programs for caregivers of patients with ADRD. Additionally, policy makers should facilitate the adoption of intelligent assistive devices and other technology-based services to reduce the burden on caregivers.

Acknowledgments

Funding

This paper was funded by NIH/National Institute of General Medical Sciences (NIGMS) U54GM104942, Alzheimer's Research and Prevention Foundation, and NIH Research Training Program in Behavioral and Biomedical Sciences 5 BBS T32 GM 081741-08.

References

Papers of special note have been highlighted as either of interest (•) or of considerable interest (••) to readers.

1. Tarawneh R, Holtzman DM. The clinical problem of symptomatic Alzheimer disease and mild cognitive impairment. Cold Spring Harb Perspect Med. 2012; 2(5):a006148. [PubMed: 22553492]
2. Alzheimer's Association. 2016 Alzheimer's disease facts and figures. Alzheimer's & Dementia. 2016; 12(4):459–509. •• This report provides background, context, and key statistics for dementia in the United States.
3. Vann Jones SA, O'Brien JT. The prevalence and incidence of dementia with Lewy bodies: a systematic review of population and clinical studies. Psychol Med. 2014; 44(4):673–683. [PubMed: 23521899]
4. Hebert LE, Weuve J, Scherr PA, et al. Alzheimer disease in the United States (2010-2050) estimated using the 2010 census. Neurology. 2013; 80(19):1778–1783. •• Using incidence data from the Chicago Health and Aging Project (CHAP), this study estimated the expected prevalence of Alzheimer's disease in the United States for the next four decades. [PubMed: 23390181]
5. Zhu CW, Scarmeas N, Torgan R, et al. Clinical characteristics and longitudinal changes of informal cost of Alzheimer's disease in the community. J Am Geriatr Soc. 2006; 54(10):1596–1602. [PubMed: 17038080]
6. Joyce AT, Zhao Y, Bowman L, et al. Burden of illness among commercially insured patients with Alzheimer's disease. Alzheimer's Dement. 2007; 3(3):204–210. [PubMed: 19595939]
7. Kuo TC, Zhao Y, Weir S, et al. Implications of comorbidity on costs for patients with alzheimer disease. Med Care. 2008; 46(8):839–846. [PubMed: 18665064]
8. Zhu C, Torgan R, Scarmeas N, et al. Home health and informal care utilization and costs over time in Alzheimer's disease. Home Health Care Serv Q. 2008; 27(1):1–20. [PubMed: 18510196]
9. Goldfeld KS, Stevenson DG, Hamel MB, et al. Medicare expenditures among nursing home residents with advanced dementia. Arch Intern Med. 2011; 171(9):824–830. [PubMed: 21220646]
10. Zhu CW, Scarmeas N, Ornstein K, et al. Health-care use and cost in dementia caregivers: longitudinal results from the Predictors Caregiver Study. Alzheimer's Dement. 2015; 11(4):444–454. [PubMed: 24637299]
11. Suehs BT, Shah SN, Davis CD, et al. Household members of persons with Alzheimer's disease: health conditions, healthcare resource use, and healthcare costs. J Am Geriatr Soc. 2014; 62(3):435–441. [PubMed: 24576203]
12. Suehs BT, Davis CD, Alvir J, et al. The clinical and economic burden of newly diagnosed alzheimer's disease in a medicare advantage population. Am J Alzheimer's Dis Other Demen. 2013; 28(4):384–392. [PubMed: 23687180]

13. Yang Z, Levey A. Gender differences: a lifetime analysis of the economic burden of alzheimer's disease. Women's Health Issues. 2015; 25(5):436–440. [PubMed: 26363924]
14. Hurd MD, Martorell P, Delavande A, et al. Monetary costs of dementia in the United States. New England J Med. 2013; 368(14):1326–1334. •• A landmark study using data from the Health and Retirement Survey (HRS) which conducted a detailed evaluation of the nursing home costs, Medicare costs, out-of-pocket costs, and costs of formal and informal caregiving for older adults with dementia aged 70 years and above. [PubMed: 23550670]
15. Kelley AS, McGarry K, Gorges R, et al. The burden of health care costs for patients with dementia in the last 5 years of life. Ann Intern Med. 2015; 163(10):729–736. •• This study estimated the direct and indirect costs of dementia in the last 5 years of life and compared the costs with the end-of-life costs of other most commonly occurring chronic conditions like heart disease and cancer, using data from the Health and Retirement Survey (HRS). [PubMed: 26502320]
16. Bharmal MF, Dedhiya S, Craig BA, et al. Incremental dementia-related expenditures in a medicaid population. Am J Geriatr Psychiatry. 2012; 20(1):73–83. [PubMed: 22183012]
17. Rattinger GB, Schwartz S, Mullins CD, et al. Dementia severity and the longitudinal costs of informal care in the Cache County population. Alzheimer's and Dementia. 2015; 11(8):946–954.
18. Zhu CW, Cosentino S, Ornstein K, et al. Medicare Utilization and expenditures around incident dementia in a multiethnic cohort. J Gerontol Ser Biol Sci Med Sci. 2015; 70(11):1448–1453.
19. Deb A, Sambamoorthi U, Thornton JD, et al. Direct medical expenditures associated with Alzheimer's and related dementias (ADRD) in a nationally representative sample of older adults – an excess cost approach. Aging Ment Health. 2017:1–6.
20. Lin PJ, Zhong Y, Fillit HM, et al. Medicare expenditures of individuals with alzheimer's disease and related dementias or mild cognitive impairment before and after diagnosis. J Am Geriatr Soc. 2016; 64(8):1549–1557. [PubMed: 27295430]
21. Yang Z, Zhang K, Lin PJ, et al. A longitudinal analysis of the lifetime cost of dementia. Health Serv Res. 2012; 47(4):1660–1678. •• Life-time costs of dementia for Medicare and Medicaid were evaluated using a cohort-based simulation model for various scenarios of age of onset and duration of illness. [PubMed: 22171532]
22. US Bureau of Labor Statistics. Consumer price index for all urban consumers: medical care services. 2017. Available at https://data.bls.gov/cgi-bin/surveymost?cu
23. Zhu CW, Scarmeas N, Torgan R, et al. Longitudinal study of effects of patient characteristics on direct costs in Alzheimer disease. Neurology. 2006; 67(6):998–1005. [PubMed: 16914696]
24. Miller EA, Rosenheck RA, Schneider LS. Assessing the relationship between health utilities, quality of life, and health care costs in alzheimer's disease: the catie-ad study. Curr Alzheimer Res. 2010; 7(4):348–357. [PubMed: 19715552]
25. Murman DL, Eye AV, Sherwood PR, et al. Evaluated need, costs of care, and payer perspective in degenerative dementia patients cared for in the United States. Alzheimer Dis Assoc Disord. 2007; 21(1):39–48. [PubMed: 17334271]
26. Gilligan AM, Malone DC, Warholak TL, et al. Health disparities in cost of care in patients with Alzheimer's disease: an analysis across 4 state medicaid populations. Am J Alzheimer's Dis Other Demen. 2013; 28(1):84–92. [PubMed: 23196405]
27. Gorina Y, Kramarow EA. Identifying chronic conditions in medicare claims data: evaluating the chronic condition data warehouse algorithm. Health Serv Res. 2011; 46(5):1610–1627. [PubMed: 21649659]
28. Taylor DH, Østbye T, Langa KM, et al. The accuracy of medicare claims as an epidemiological tool: the case of dementia revisited. J Alzheimers Dis. 2009; 17(4):807–815. [PubMed: 19542620]
29. Hunter CA, Kirson NY, Desai U, et al. Medical costs of Alzheimer's disease misdiagnosis among US Medicare beneficiaries. Alzheimer Dement. 2015; 11(8):887–895.
30. Gilden DM, Kubisiak JM, Sarsour K, et al. Diagnostic pathways to Alzheimer disease costs incurred in a medicare population. Alzheimer Dis Assoc Disord. 2015; 29(4):330–337. [PubMed: 25635340]
31. Hurd MD, Martorell P, Langa K. Future Monetary Costs of Dementia in the United States under alternative dementia prevalence scenarios. J Popul Ageing. 2015; 8(1–2):101–112. •• Expanding

on a previous study, this article estimated the future monetary costs of dementia in the United States by using two different prevalence rate scenarios. [PubMed: 25926904]

32. Brookmeyer R, Corrada MM, Curriero FC, et al. Survival following a diagnosis of alzheimer disease. Arch Neurol. 2002; 59(11):1764–1767. [PubMed: 12433264]
33. Arrighi HM, Neumann PJ, Lieberburg IM, et al. Lethality of Alzheimer disease and its impact on nursing home placement. Alzheimer Dis Assoc Disord. 2010; 24(1):90–95. [PubMed: 19568155]
34. World Health Organization. Out-of-pocket expenditure on health as a percentage of private expenditure on health (US$). 2016. Available at http://www.who.int/gho/health_financing/out_pocket_expenditure/en/
35. Cubanski, J., Swoope, C., Damico, A., et al. How much is enough? Out-of-pocket spending among medicare beneficiaries: a chartbook. 2014. Available at http://files.kff.org/attachment/how-much-is-enough-out-of-pocket-spending-among-medicare-beneficiaries-a-chartbook-report
36. Tamblyn R, Eguale T, Huang A, et al. The incidence and determinants of primary nonadherence with prescribed medication in primary carea cohort studyprimary nonadherence with prescribed medication in primary care. Ann Intern Med. 2014; 160(7):441–450. [PubMed: 24687067]
37. Hoffman C, Schwartz K. Eroding access among nonelderly U.S. adults with chronic conditions: ten years of change. Health Aff (Millwood). 2008; 27(5):w340–348. [PubMed: 18647762]
38. Thorpe KE, Ogden LL, Galactionova K. Chronic conditions account for rise in Medicare spending from 1987 to 2006. Health Aff (Millwood). 2010; 29(4):718–724. [PubMed: 20167626]
39. Delavande A, Hurd MD, Martorell P, et al. Dementia and out-of-pocket spending on health care services. Alzheimer Dement. 2013; 9(1):19–29.
40. Gruber-Baldini AL, Stuart B, Zuckerman IH, et al. Treatment of dementia in community-dwelling and institutionalized medicare beneficiaries. J Am Geriatr Soc. 2007; 55(10):1508–1516. [PubMed: 17727648]
41. Walsh, E., Freiman, M., Haber, S., et al. Cost drivers for dually eligible beneficiaries: potentially avoidable hospitalizations from nursing facility, skilled nursing facility, and home and community based services waiver programs. 2010. Available at https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-andReports/Reports/downloads/costdriver stask2.pdf
42. Caring.com. Nearly Half of Family Caregivers Spend Over $5,000 Per Year on Caregiving Costs. 2014. Available at https://www.caring.com/about/news-room/costs-of-caregiving-2014
43. Feinberg, L., Reinhard, SC., Houser, A., et al. Valuing the invaluable: 2011 update, the growing contributions and costs of family care-giving. Vol. 51. Washington, DC: AARP Public Policy Institute; 2011. p. 1-28.
44. Garrison LP Jr, Mansley EC, Abbott TA 3rd, et al. Good research practices for measuring drug costs in cost-effectiveness analyses: a societal perspective: the ISPOR drug cost task force report–part II. Value Health. 2010; 13(1):8–13. [PubMed: 19883405]
45. Brodaty H, Donkin M. Family caregivers of people with dementia. Dialogues Clin Neurosci. 2009; 11(2):217–228. [PubMed: 19585957]
46. Friedman EM, Shih RA, Langa KM, et al. US prevalence and predictors of informal caregiving for dementia. Health Aff (Millwood). 2015; 34(10):1637–1641. [PubMed: 26438738]
47. Carretero S, Garces J, Rodenas F, et al. The informal caregiver's burden of dependent people: theory and empirical review. Arch Gerontol Geriatr. 2009; 49(1):74–79. [PubMed: 18597866]
48. Levine C. Depression in Caregivers of Patients with Dementia: A Greater Role for Physicians. J Gen Intern Med. 2003; 18(12):1058–1059. [PubMed: 14687266]
49. Kolanowski AM, Fick D, Waller JL, et al. Spouses of persons with dementia: their healthcare problems, utilization, and costs. Res Nurs Health. 2004; 27(5):296–306. [PubMed: 15362141]
50. Schulz R, Beach SR. Caregiving as a risk factor for mortality: the caregiver health effects study. Jama. 1999; 282(23):2215–2219. [PubMed: 10605972]
51. Tremont G. Family caregiving in dementia. Med Health R I. 2011; 94(2):36–38. [PubMed: 21456372]
52. Chaudhry B, Wang J, Wu S, et al. Systematic review: impact of health information technology on quality, efficiency, and costs of medical care. Ann Intern Med. 2006; 144(10):742–752. [PubMed: 16702590]

53. National Conference of States Legislatures. Collecting health data: all-payer claims databases. 2016. Retrieved 10/12/2016, from http://www.ncsl.org/research/health/collecting-health-data-all-payer-claims-database.aspx

54. Gobeille, V. Liberty Mut Ins Co, 577 US 1. 2016. Available at https://www.supremecourt.gov/opinions/15pdf/14-181_5426.pdf

55. National Academy for State Health Policy. Overview of state programs that utilize an assessment of Self-Funded ERISA Plans and/or Third Party Administrators. 2016. Available at http://nashp.org/states-with-assessments-on-self-funded-plans-andor-third-party-administrators/

56. Dubois B, Hampel H, Feldman HH, et al. Preclinical Alzheimer's disease: definition, natural history, and diagnostic criteria. Alzheimer's & Dementia: the Journal of the Alzheimer's Association. 2016; 12(3):292–323.

57. Sperling RA, Aisen PS, Beckett LA, et al. Toward defining the preclinical stages of Alzheimer's disease: recommendations from the national institute on aging-alzheimer's association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimer's & Dementia. 2011; 7(3):280–292.

58. Bharucha AJ, Anand V, Forlizzi J, et al. Intelligent assistive technology applications to dementia care: current capabilities, limitations, and future challenges. Am J Geriatr Psychiatry. 2009; 17(2): 88–104. [PubMed: 18849532]

59. Shih RA, Concannon TW, Liu JL, et al. Improving dementia long-term care: A policy blueprint. Rand Corporat. 2014

Key issues

- Identifying patients with ADRD is very challenging. Due to differences in diagnostic criteria and application, ascertainment and categorization of ADRD may vary across studies, leading to potential misclassification and inaccurate cost estimates.
- Despite the definitional differences, studies comparing patients with and without ADRD have consistently reported that the average medical, non-medical, and indirect costs of individuals with ADRD were higher than those without ADRD.
- Nursing home costs and formal home-healthcare costs are the major contributors of the total direct costs of ADRD.
- Out-of-pocket expenditures on medical and non-medical services also impose a significant burden on patients and their caregivers. Yet there is no precise estimate of out-of-pocket expenditures burden as measured by income spent out-of-pocket.
- The overall economic burden of ADRD may be underestimated because many non-trivial components of costs such as direct non-medical costs and indirect costs are not included in the cost estimates.

Table 1

Per capita direct cost estimates of Alzheimer's diseases and related dementias (ADRD) used in cost of illness studies in the United States.

Study	Follow-up time	Data source	ADRD/AD/Dementia	Study design	Control group	Adjusted per capita cost estimates
Deb, Sambamoorthi et al. [19]	1 year	MEPS	ADRD	Retrospective	Yes	In 2013 US dollars: Total health-care costs per year: (ADRD vs. non-ADRD) $14,508 vs. $10,096 In 2015 US dollars (author's calculation[a]): Total health-care costs per year: (ADRD vs. non-ADRD) $15,216 vs. $10,588
Lin, Zhong et al. [20]	2 years pre- and post-diagnosis	5% sample of Medicare claims	ADRD	Retrospective	Yes	In 2014 US dollars: Total Medicare costs per year: (AD vs. non-AD) 2 years pre-diagnosis: $10,533 vs. $10,102 1 year pre-diagnosis: $15,091 vs. $10,662 1 year post-diagnosis: $27,126 vs. $9274 2 years post-diagnosis: $17,257 vs. $9,930 In 2015 US dollars (author's calculation [a]): Total Medicare costs per year: (AD vs. non-AD) 2 years pre-diagnosis: $10,791 vs. $10,349 1 year pre-diagnosis: $15,460 vs. $10,923 1 year post-diagnosis: $27,790 vs. $9501 2 years post-diagnosis: $17,679 vs. $10,173
Zhu, Cosentino et al. [18]	2 years pre- and post-diagnosis	Community dwelling Medicare beneficiaries in northern Manhattan	Dementia	Prospective multicenter	Yes	In 2012 US dollars (author's calculation [a]): Excess Medicare costs per quarter: 2 years pre-diagnosis: $1003 (ref = no dementia) 2 years post-diagnosis: $1895 (ref = pre-diagnosis) In 2015 US dollars: Excess Medicare costs per quarter: 2 years pre-diagnosis: $1085 (ref = no dementia) 2 years post-diagnosis: $2049 (ref = pre-diagnosis)
Kelley, McGarry et al. [15]	5 years before death	HRS	Dementia	Retrospective	Yes	In 2010 US dollars: Total costs in the last 5 years: (dementia vs. no dementia) Medicare costs: $86,430 vs. $98,326 Medicaid costs: $35,346 vs. $4552

Study	Follow-up time	Data source	ADRD/AD/Dementia	Study design	Control group	Adjusted per capita cost estimates
						Out-of-pocket costs: $61,522 vs. $34,068 In 2015 US dollars (author's calculation [a]): Total costs in the last 5 years: (dementia vs. no dementia) Medicare costs: $100,084 vs. $113,860 Medicaid costs: $40,930 vs. $5271 Out-of-pocket costs: $71,241 vs. $39,450
Hurd, Martorell et al. [14]	1 year	HRS	Dementia	Retrospective	Yes	In 2010 US dollars: Total annual costs attributable to dementia: Direct medical costs: $28,501 Medicare costs: $2752 Out-of-pocket costs: $6194 Nursing home costs: $13,876 Formal Homecare costs: $5678 In 2015 US dollars (author's calculation [a]): Total annual costs attributable to dementia: Direct medical costs: $33,004 Medicare costs: $3187 Out-of-pocket costs: $7173 Nursing home costs: $16,086 Formal homecare costs: $6575
Suehs, Davis et al. [12]	1 year pre- and 2 years post-diagnosis	MAPD plan members	AD	Retrospective	Yes	In 2011 US dollars: Excess annual total health-care costs: (ref = non-AD) 1 year pre-diagnosis: $2331 1 year post-diagnosis: $9333 2 years post-diagnosis: $5761 In 2015 US dollars (author's calculation [a]): Excess annual total health-care costs: (ref = non-AD) 1 year pre-diagnosis: $2619 1 year post-diagnosis: $10,486 2 years post-diagnosis: $6473
Yang, Zhang et al. [21]	Lifetime cost (5-year duration)	Medicare Current Beneficiary Survey	ADRD	Cohort-based simulation	Yes	In 2005 US dollars: Total lifetime costs (ADRD vs. non-ADRD): Medicare: $101,810 vs. $89,835 Medicaid: $27,028 vs. $15,955 In 2015 US dollars (author's calculation [a]): Total lifetime costs (ADRD vs. non-ADRD): Medicare: $143,982 vs. $127,047 Medicaid: $38,224 vs. $22,564
Bharmal, Dedhiya et al. [16]	1 year	Indiana Medicaid	ADRD	Retrospective	Yes	In 2004 US dollars: Incremental Medicaid costs: $9829 In 2015 US dollars (author's calculation [a]): Incremental Medicaid costs: $14,567

Study	Follow-up time	Data source	ADRD/AD/Dementia	Study design	Control group	Adjusted per capita cost estimates
Goldfeld, Stevenson et al. [9]	0–90, 91–120, 121–270, 271–365 days before death	CASCADE study	AD	Prospective cohort	No	In 2007 US dollars: Total Medicare costs among NH residents: 0–90 days before death = $3877 91–120 days before death = $2297 121–270 days before death = $1605 271–365 days before death = $1061 In 2015 US dollars (author’s calculation [a]): Total Medicare costs among NH residents: 0–90 days before death = $4999 91–120 days before death = $2962 121–270 days before death = $2069 271–365 days before death = $1368
Kuo, Zhao et al. [7]	1 year	MarketScan Medicare Supplemental	AD	Retrospective	Yes	In 2003 US dollars: Total health-care costs (AD vs. non-AD): $13,936 vs. $10,369 In 2015 US dollars (author’s calculation [a]): Total health-care costs (AD vs. non-AD): $21,686 vs. $16,135
Joyce, Zhao et al. [6]	1 year from first diagnosis of AD	PharMetrics Patient-Centric Database	AD	Retrospective	Yes	In 2003 US dollars: Total health-care costs (AD vs. non-AD): $21,150 vs. $4053 In 2015 US dollars (author’s calculation [a]): Total health-care costs (AD vs. non-AD): $32,912 vs. $6307

[a] Authors converted costs to 2015 US dollars using the Consumer Price Index for Medical Care Services [22]. MEPS: Medical Expenditure Panel Survey; HRS: Health and Retirement Study; MAPD: Medicare Advantage Prescription Drug; CASCADE: Choices, Attitudes, and Strategies for Care of Advanced Dementia at the End-of-Life.

Table 2

Per capita indirect cost estimates of Alzheimer's diseases and related dementias (ADRD) used in cost of illness studies in the United States.

Study	Data source	ADRD/AD/Dementia	Study design	Approach used to estimate caregiver cost	Wage used to estimate value caregiver time	Per capita indirect cost estimates (adjusted unless otherwise specified)
Kelley, McGarry et.al. [15]	Health and Retirement Study	Dementia	Retrospective	Foregone wage	State-average costs of home health-care services	In 2010 US dollars: Five-year informal care costs (dementia vs. non-dementia): $83,022 vs. $38,272 In 2015 US dollars (authors' calculation[a]): Five-year informal care costs (dementia vs. non dementia): $90,241 vs. $41,600
Zhu, Scarmeas et al [10]	Predictors 2 Study	AD	Retrospective	Personal medical costs	–	In 2010 US dollars: Total health-care costs of caregivers: Year before baseline: $2585 Average across entire study period: $3068 In 2015 US dollars (authors' calculation [a]): Total health-care costs of caregivers: Year before baseline: $2993 Average across entire study period: $3553
Yang, Levey [13]	Medicare Current Beneficiary Survey	AD	Retrospective	Replacement cost	Used the replacement cost inputs from Hurd et al (2013)	In 2013 US dollars: Lifetime informal care costs: Female family member of a male AD patient: $54,956 Male family member of a female AD patient: $8659 In 2015 US dollars (authors' calculation [a]): Lifetime informal care costs: Female family member of a male AD patient: $57,639 Male family member of a female AD patient: $9082
Rattinger et al. [17]	Cache County Dementia Progression Study	Dementia	Retrospective	Foregone wage	Utah median hourly wage as reported in the US Bureau of Labor's Occupational Employment Statistics	In 2012 US dollars: Average daily costs of informal dementia care at start of study observation[b]: $40.07 In 2015 US dollars (authors' calculation [a]): Average daily costs of informal dementia care at start of study observation[b]: $41.37
Suehs, Shah et al. [11]	Humana Medicare Advantage Prescription Drug plan	AD	Retrospective	Personal medical costs of household members	–	In 2011 US dollars: Annual health-care costs for household members (AD vs non-AD): $7168 vs. $6301 In 2015 US dollars (authors' calculation [a]): Annual health-care costs for household members (AD vs non-AD): $8054 vs. $7079
Hurd, Martorell et al. [14]	Health and Retirement Study	Dementia	Retrospective	Forgone wage and replacement cost	Average wages for persons with similar demographic	In 2010 US dollars: Average annual costs of informal caregiving time: Foregone wage approach: $13,188

Study	Data source	ADRD/AD/Dementia	Study design	Approach used to estimate caregiver cost	Wage used to estimate value caregiver time	Per capita indirect cost estimates (adjusted unless otherwise specified)
					characteristics; and average hourly rates charged by home health agencies in the respondent's state of residence	Replacement cost approach: $27,789 In 2015 US dollars (authors' calculation [a]): Average annual costs of informal caregiving time: Foregone wage approach: $14,335 Replacement cost approach: $32,179
Zhu, Scarmeas et al. [8]	Predictors Study	AD	Retrospective	Forgone wage	National average hourly earnings for all private industries	In 2004 US dollars: Average annual costs of informal care: Among users at baseline[b]: $20,590 Among users in year 4: $43,031 In 2015 US dollars (authors' calculation [a]): Average annual costs of informal care: Among users in baseline[c]: $25,835 Among users in year 4: $53,992
Zhu, Scarmeas et al. [5]	Predictors Study	AD	Retrospective	Forgone wage	National average hourly earnings for all private industries	In 2004 US dollars: Average annual informal care cost: Unadjusted cost: $25,381 In 2015 US dollars (authors' calculation[a]): Average annual informal care cost: Unadjusted cost: $31,846

[a] Authors converted costs to 2015 US dollars using the Consumer Price Index for Medical Care Services [22].

[b] Baseline severity of ADRD in informal care users, as assessed with Mini-Mental State Exam was 20.7.

[c] Baseline severity of AD in informal care users, as assessed with Mini-Mental State Exam was 21.7.

Table 3

Diagnostic definitions of Alzheimer's diseases and related dementias used in cost of illness studies in the United States.

Studies	Source	AD/ADRD/Dementia	Diagnostic definitions
Zhu, Scarmeas et al. [5], Zhu, Torgan et al. [8], Zhu, Scarmeas et al. [10]	Predictors Study	AD	Clinician-based diagnosis of: (1) Primary degenerative AD based on DSM-III-R criteria, (2) Probable AD based on NINCDS-ADRDA criteria, and (3) Modified MMSE score of 30 or greater
Zhu, Cosentino et al. [18]	Washington Heights-Inwood Columbia Aging Project	AD	Clinician-based diagnosis of: (1) Dementia based on DSM-IV criteria (2) Probable AD based on NINCDS-ADRDA criteria
Goldfeld, Stevenson et al. [9]	CASCADE study	Dementia	Clinician-based diagnosis of: (1) Cognitive Performance Score equal to 5 or 6, (2) Cognitive impairment due to dementia (any type), (3) Global Deterioration (4) Scale score of 7 ascertained by nurse interview, and (5) Length of NH stay >30 days
Murman, Eye et al. [25]	Neurology and geriatric medicine practices in the state of Michigan, USA	AD	Clinician-based diagnosis of: (1) Probable AD based on the NINCDS-ADRDA criteria
Yang, Zhang et al. [21], Yang and Levey [13]	MCBS	AD	Based on (1) Self or proxy reported diagnosis of ADRD, (2) ICD-9-CM codes of 290 or 331.0, and (3) Self or proxy reported prescriptions for prescription for drugs including donepezil, rivastigmine, galantamine, and memantine
Hurd, Martorell et al. [14], Kelley, McGarry et al. [15]	Health and Retirement Study	Dementia	(1) Probable dementia was determined based on an algorithm using multiple cognitive measures
Joyce, Zhao et al. [6]	PharMetrics Patient-Centric Database	AD	At least one claim with a diagnosis of AD (ICD. 9.CM 331.0)
Kuo, Zhao et al. [7]	MarketScan Medicare Supplemental and Coordination of Benefits Database	AD	(1) At least one claim with a diagnosis of AD (ICD.9.CM 331.0) and/or (2) At least one pharmacy claims for tacrine, donepezil, galantamine, rivastigmine, or memantine
Bharmal, Dedhiya et al. [16]	Medicaid claims	Dementia	At least one claim with any dementia-specific ICD-9 code (046.1, 290.0, 290.1x–290.4x, 291.2, 294.1x, 331.0, 331.1x, 331.2, or 331.82)
Gilligan, Malone et al. [26]	Medicaid claims	AD	At least one claim with ICD-9 code of 331.0 in any section of the inpatient, long-term care, or outpatient Medicaid claim files
Suehs, Davis et al. [12], Suehs, Shah et al. [11]	Medicare Advantage Prescription Drug	AD	At least one claim with a diagnosis of AD (ICD. 9.CM 331.0)
Lin, Zhong et al. [20]	5% Medicare sample–claims	ADRD	ICD-9-CM codes of 331.0, 331.11, 331.19, 331.2, 331.7, 290.0, 290.10, 290.11, 290.12, 290.13, 290.20, 290.21, 290.3, 290.40, 290.41, 290.42, 290.43, 294.0, 294.10, 294.11, 294.20, 294.21, 294.8, 797

DSM: Diagnostic and Statistical Manual of Mental Disorders; ICD-9-CM: International Classification of Diseases, Ninth Revision, Clinical Modification; MMSE: Mini-Mental State Examination; NH: Nursing Home; NINCDS-ADRDA: National Institute of Neurological, Communicative Disorders and Stroke–Alzheimer Disease and Related Disorders Association; MCBS: Medicare Current Beneficiary Survey.