

SPECIAL REPORT

Alzheimer's Disease: Financial and Personal Benefits of Early Diagnosis

\$7.9 trillion

is the potential cost savings for the current U.S. population from early diagnosis of Alzheimer's.

An Evolving Understanding of Alzheimer's Disease

The search for biological markers, or biomarkers, of Alzheimer's disease is a major area of research that is transforming the way that scientists and physicians understand the disease. What was once a disease based on symptoms is becoming a disease based on changes in the brain. Due in large part to the discovery of Alzheimer's biomarkers and the development of biomarker tests, today the diagnosis of Alzheimer's is occurring earlier in the disease process. Individuals are no longer being diagnosed only in later stages of the disease. Individuals can be identified using biomarkers during the mild cognitive impairment due to Alzheimer's disease (MCI due to AD) stage (for more information about MCI, see page 10). In the future, if biomarker changes are detected and validated in preclinical populations, individuals who are not yet showing symptoms may also be identified as being on the Alzheimer's disease continuum.

This Special Report examines the potential effects of a future with widespread biomarker-based diagnosis of Alzheimer's during the MCI due to AD stage.

Changing Diagnostic Criteria

Alzheimer's disease was historically defined as beginning once dementia symptoms appear, and diagnosis was only confirmed on autopsy by elevated levels of beta-amyloid and tau in the brain. However, due to the development of biomarkers, proposed revised diagnostic guidelines were published in 2011 by the National Institute on Aging (NIA) and the Alzheimer's Association.²⁰⁻²³ These guidelines incorporated biomarker tests in addition to clinical symptoms and gave researchers tools for diagnosing

The Alzheimer's Disease Continuum

The Alzheimer's disease continuum encompasses the full course of the disease. It begins with a period during which an individual experiences brain changes due to Alzheimer's, but symptoms have not yet appeared. It continues through a period of changes in cognitive, functional and physical abilities that happen because of these brain changes. Alzheimer's disease is fatal, so the continuum ends only with an individual's death due to or with Alzheimer's. Between the beginning of Alzheimer's disease and the emergence of overt symptoms, the Alzheimer's continuum represents a decades-long window of hope. It is during this window of time that researchers believe treatments to prevent symptoms or slow or cure the disease will be most effective.

Alzheimer's disease earlier in the Alzheimer's continuum. This move from a symptom-based definition to a biology-based definition of Alzheimer's disease is leading to a better understanding of the underlying mechanisms of the disease and aiding in the development of new interventions to delay or prevent disease progression.

The 2011 guidelines proposed three stages of Alzheimer's disease that exist on a continuum: preclinical Alzheimer's disease, a stage after brain changes have begun but before symptoms are present; MCI due to AD, a stage characterized by both brain changes and mild cognitive symptoms that do not significantly affect everyday living; and dementia due to Alzheimer's disease, a stage with brain changes and significant memory, thinking and behavioral problems that interfere with an individual's daily life.²⁰⁻²³

2018 NIA-Alzheimer's Association Research Framework

A working group convened by the NIA and the Alzheimer's Association is currently reviewing the latest available research evidence to determine whether the 2011 diagnostic guidelines should be refined, and this work is expected to be published in 2018.⁴⁸⁷ However, the 2018 NIA-Alzheimer's Association framework will be intended for research purposes only; it will need to be validated and possibly further updated before being used in clinical practice. The new research framework will define Alzheimer's disease as a continuum starting with underlying brain processes, which can be observed using biomarkers in living people and by postmortem findings, and continuing through the later stages of MCI due to AD and dementia due to Alzheimer's.⁴⁸⁷

One way to conceptualize Alzheimer's biomarkers is to divide them into three categories (the A/T/N system) based on the underlying brain changes measured.⁴⁸⁸ Beta-amyloid deposits in the brain can be measured by amyloid positron emission tomography (PET) imaging and by cerebrospinal fluid (CSF) tests of specific forms of the amyloid protein (collectively known as the A biomarkers). Neurofibrillary tangles can be approximated by CSF levels of phosphorylated tau and cortical tau PET imaging (the T biomarkers). Nonspecific biomarkers of neurodegeneration or neuronal injury, which may be due to Alzheimer's or other pathologies, are elevated levels of CSF total tau, decreased glucose metabolism shown on fluorodeoxyglucose (FDG) PET imaging, and brain atrophy shown with structural magnetic resonance imaging (MRI) (the N biomarkers).⁴⁸⁹

Like the 2011 guidelines, the new research framework will propose a classification system using Alzheimer's disease biomarkers.⁴⁸⁷ An individual with evidence of one or more amyloid biomarkers, with or without symptoms, but no evidence of a tau biomarker, would be defined as having an "Alzheimer's pathologic change." An individual with both amyloid and tau biomarkers, with or without symptoms, would be considered to have "Alzheimer's disease." Applying normal/abnormal cut points to each of the biomarker categories yields four Alzheimer's biomarker profiles:

- a) A+/T-/N-
- b) A+/T-/N+
- c) A+/T+/N-
- d) A+/T+/N+

TABLE 18

Research Framework Utilizing Biomarker Profiles and Cognitive Stages

Biomarker Profile	Cognitive Stage		
	Cognitively Unimpaired	Mild Cognitive Impairment (MCI)	Dementia
A-/T-/N-	Normal Alzheimer's biomarkers, cognitively unimpaired	Normal Alzheimer's biomarkers with MCI	Normal Alzheimer's biomarkers with dementia
A+/T-/N-	Preclinical Alzheimer's pathologic change	Alzheimer's pathologic change with MCI	Alzheimer's pathologic change with dementia
A+/T-/N+	Alzheimer's and concomitant suspected non-Alzheimer's pathologic change, cognitively unimpaired	Alzheimer's and concomitant suspected non-Alzheimer's pathologic change with MCI	Alzheimer's and concomitant suspected non-Alzheimer's pathologic change with dementia
A+/T+/N- A+/T+/N+	Preclinical Alzheimer's disease	Alzheimer's disease with MCI (prodromal Alzheimer's)	Alzheimer's disease with dementia

Table from a draft of the 2018 NIA-Alzheimer's Association research framework.⁴⁸⁷

A combination of ATN that does not include A+ (for example, A-/T+/N-) indicates that a person is not on the Alzheimer's continuum.

The 2018 research framework also will include a cognitive staging dimension that is independent of the biomarker profile. The cognitive staging dimension is divided into three traditional categories: cognitively unimpaired, MCI and dementia. Dementia is further subdivided into mild, moderate and severe stages. Under the 2018 framework, individuals would be characterized by both a biomarker profile and a cognitive stage. The biomarker profile and cognitive stage are combined to assess an individual's subsequent risk of short-term cognitive decline (Table 18).⁴⁸⁷

Biomarkers of Alzheimer's Disease

The use of biomarkers in all stages of Alzheimer's disease will facilitate the development of treatments that target the underlying brain changes at each stage. Depending on the stage, such treatments might prevent or delay the onset or progression of clinical symptoms.

Neuroimaging Biomarkers

A number of studies comparing imaging data with autopsy findings have demonstrated that beta-amyloid PET imaging accurately reflects levels of amyloid deposits (called neuritic plaques) in the brain.⁴⁹⁰⁻⁴⁹⁷ Three amyloid PET radiotracers are currently approved by the U.S. Food and Drug Administration (FDA) — florbetapir, flutemetamol and florbetaben (approved in 2012, 2013 and 2014, respectively) — to aid in the diagnosis of Alzheimer's disease. While elevated levels of beta-amyloid detected via PET cannot be used in clinical practice to conclusively diagnose the disease, they give clinicians reason to conduct additional Alzheimer's testing. In addition, in a person with persistent MCI with an unknown cause, the presence of beta-amyloid detected by PET greatly increases the likelihood of that person having MCI due to AD and thus being in the early stages of Alzheimer's. Likewise, non-elevated levels of beta-amyloid indicate a reduced likelihood that cognitive impairment is due to Alzheimer's and may be reason for clinicians to explore other diagnoses.⁴⁹⁸

To aid clinicians in determining when to use amyloid PET imaging, the Amyloid Imaging Taskforce of the Alzheimer's Association and the Society of Nuclear Medicine and Molecular Imaging published appropriate use criteria (AUC) that detail the types of patients and clinical circumstances under which amyloid PET imaging should be used to increase the certainty of an Alzheimer's diagnosis.⁴⁹⁹⁻⁵⁰⁰

It is important to know that amyloid PET imaging is not right for everyone and that it is not currently covered by Medicare or most insurance companies.

What Are Biomarkers?

A biomarker, or biological marker, is a measurable indicator of a biological state or condition in the human body. Clinicians use biomarkers to determine the presence or absence of disease, assess the risk of developing a disease and understand how an individual has responded to a treatment. For example, a high blood glucose (blood sugar) level may be diagnostic of diabetes and lowering that level can indicate the success of a prescribed diet or medication.

Researchers are investigating several promising biomarkers for Alzheimer's disease. These include, but are not limited to, the amount of accumulation of the proteins beta-amyloid and tau in the brain. These proteins can be measured using brain imaging or the levels in cerebrospinal fluid or blood. Other biomarkers are changes in brain size and activity.

Identifying and then validating biomarkers for Alzheimer's disease is critical for several reasons. One is that biomarkers facilitate early diagnosis and treatment. Many researchers believe that early intervention — either at the mild cognitive impairment (MCI) stage or even in the proposed preclinical stage before symptoms appear — offers the best chance of slowing or stopping the progression of Alzheimer's and therefore the best chance of preserving brain function.

Biomarkers also have an important role in the discovery of treatments. Biomarkers enable researchers to enroll in clinical trials only those individuals with the biomarker changes targeted by a treatment. For example, if a treatment targets beta-amyloid accumulation, researchers would want to enroll only those individuals with high levels of beta-amyloid accumulation as shown on biomarker tests. In addition, biomarkers make it possible for researchers to monitor the effects of treatments. Researchers can compare results of biomarker tests conducted during clinical trials with results of biomarker tests conducted before clinical trials to find out if a treatment has slowed or stopped the brain changes targeted. It's important to note that the most effective biomarker test or combination of tests may differ depending on the stage of the disease and other factors.

Research on new strategies for earlier diagnosis, including ongoing efforts to identify and validate biomarkers for Alzheimer's disease, is among the most active areas in Alzheimer's science.

The Imaging Dementia — Evidence for Amyloid Scanning (IDEAS) Study, led by the Alzheimer's Association, is currently assessing the impact of amyloid PET imaging on patient management and health outcomes in people with MCI or dementia of uncertain origin. Preliminary results indicate that amyloid PET imaging does have a substantial impact on how clinicians diagnose the cause of cognitive impairment and select the most appropriate course of follow-up. In both the MCI and dementia groups, changes in patient management were observed in more than 60 percent of individuals who underwent amyloid PET imaging.⁵⁰¹

Three other Alzheimer's neuroimaging biomarkers are currently used for research and in some cases are used to aid in clinical diagnosis. Elevated cortical tau shown with PET imaging⁵⁰²⁻⁵⁰⁴ is a biomarker for neurofibrillary tangles; decreased glucose metabolism shown by FDG-PET imaging and atrophy shown by structural MRI are biomarkers for neurodegeneration or neuronal injury.⁵⁰⁵

CSF and Blood Biomarkers

Additional types of biomarkers currently being studied in Alzheimer's disease and used mainly for research purposes are found in CSF and blood. CSF biomarkers reflect the rates of both protein production and clearance at one point in time rather than the cumulative damage assessed by neuroimaging biomarkers, but nevertheless may provide insight into the pathological changes of Alzheimer's.⁴⁸⁷ A lower CSF level of a specific form of the amyloid protein, known as A β ₄₂, is a biomarker for beta-amyloid deposition in the brain.⁵⁰⁶⁻⁵⁰⁸ Elevated CSF levels of phosphorylated tau^{507,509} and total tau⁵¹⁰ are biomarkers of neurofibrillary tangles and neurodegeneration, respectively. Candidate blood biomarkers, currently in the early stages of development, include neurofilament light protein as a proxy for neurodegeneration⁵¹¹ and specific forms of the amyloid protein as a screening tool for the accumulation of beta-amyloid in the brain.⁵¹²⁻⁵¹⁴

It is important to note that while much research has been conducted on biomarker levels in white populations, less is known about these markers in diverse populations.^{487,515} Therefore, a better understanding of how biomarkers behave and correlate with underlying disease and clinical symptoms in African-Americans, Asian-Americans, Hispanic-Americans and other groups underrepresented in clinical studies is a high priority for researchers.

Benefits of Early Detection and Diagnosis for People Living with Alzheimer's and Caregivers

An early and accurate diagnosis has many benefits.⁵¹⁶⁻⁵¹⁷ One benefit is accurate determination of what may be causing an individual's cognitive decline.

As clinically approved biomarkers become more widespread, more individuals who receive a diagnosis of MCI may be able to undergo biomarker testing to see if their cognitive changes are indeed due to Alzheimer's disease. Currently, biomarker testing is not reimbursed as part of normal clinical care by the Centers for Medicare & Medicaid Services (CMS) or most insurance plans. The only ways to obtain amyloid PET imaging, for example, are through a coverage with evidence development study (such as the IDEAS Study), participation in another research study or through private pay. Until biomarker testing is used routinely, individuals who receive a diagnosis of MCI can be followed closely by their medical teams to ensure that any subsequent cognitive changes indicative of an underlying progression of Alzheimer's disease are detected promptly.

In cases where cognitive impairment is detected but Alzheimer's biomarker results are within the normal range, additional tests can be performed to identify the cause of the cognitive problems when it is something other than Alzheimer's. When further testing shows reversible or treatable causes (for example, depression, obstructive sleep apnea or vitamin B₁₂ deficiency) rather than Alzheimer's disease, early diagnosis can lead to treatment and improvement of cognition and quality of life.

Medical Benefits

There are medical benefits to being diagnosed with MCI due to Alzheimer's early in the disease process.⁵¹⁶ When individuals receive a diagnosis of MCI due to AD, they can begin health measures to preserve their existing cognitive function for as long as possible. For example, prevention of stroke and minimization of vascular risk factors through control of blood pressure and diabetes, as well as smoking cessation, may reduce the risk of progression from MCI to dementia.⁵¹⁸ Aerobic exercise, mental activity and social engagement may also help to delay further cognitive decline in MCI.⁵¹⁸

If a diagnosis of Alzheimer's is confirmed, the earlier that a diagnosis is obtained, the earlier that treatment of symptoms with medications or other interventions can start, enabling individuals to better manage their symptoms and optimize their ability to function. (It is important to note, however, that the current medications for the cognitive symptoms of Alzheimer's have not been shown by clinical trials to provide benefit in the MCI due to AD stage.) While current therapies do not prevent, halt or reverse Alzheimer's disease, they can temporarily improve and prolong cognitive function in many individuals with Alzheimer's dementia.⁵¹⁹⁻⁵²⁰ An early diagnosis of Alzheimer's also maximizes the chances of participation in a clinical trial, which may also provide medical benefits, as discussed in the Clinical Trial Participation section (see page 63).

In addition, receiving an Alzheimer's diagnosis early in the disease process gives the individual time to assemble medical and caregiving teams to provide support and help prevent or treat medical concerns, such as dental problems, incontinence and pneumonia, that can occur with Alzheimer's. This proactive approach includes discussions about the treatment and management of coexisting medical conditions, which represent a significant and expensive problem in individuals with undiagnosed Alzheimer's. An early diagnosis also enables potential safety issues, such as problems with driving or wandering, to be addressed ahead of time. For example, increased caregiver awareness of higher fall risk for individuals living with dementia may lead to fewer falls and other accidents.

Emotional and Social Benefits

Early diagnosis offers a number of emotional and social benefits.⁵¹⁷ Once a diagnosis of MCI due to AD or Alzheimer's dementia has been made, individuals and family members can learn what to expect for the future and plan accordingly. In addition, early diagnosis allows individuals to maximize time spent engaging in activities that are meaningful to them and interacting with the most important people in their lives. It can also open doors to the many training, education and support programs available to individuals and family members and facilitate relationships with others living with Alzheimer's.

For affected individuals and family members, a diagnosis can also reduce anxiety and provide a sense of relief and closure as worrisome symptoms are finally given a name.⁵²¹ In fact, in a survey of public perceptions and awareness about Alzheimer's, nearly 90 percent of Americans said they would want to know if the cause of their symptoms was Alzheimer's.⁵²² Among those age 60 and older, it was even higher: 95 percent of participants said they would want to know. Similarly, the survey showed that 97 percent of Americans would want to know if a family member had Alzheimer's.

Planning for the Future

Early diagnosis gives individuals more time to plan for the future while they are cognitively able to make decisions and understand available choices.^{516,522} It also empowers individuals and their families to make the best choices for the future, such as moving closer to members of one's support team. Additional types of planning include legal, financial and end-of-life, as well as the assembly of a care team.

Legal planning includes taking inventory of existing legal documents and reviewing and updating them as necessary. It also includes making plans for finances and property, and for identifying an individual's future health care and long-term care preferences. Finally, legal planning includes designating another person to make decisions on behalf of the individual when he or she is no longer able to do so.

Financial planning includes preparing for the costs associated with the care of an individual with Alzheimer's. An individual may also want to review government benefits, including veterans benefits, as well as any long-term care insurance policies. Financial planning also includes deciding who will help the individual with routine financial responsibilities such as paying bills, handling benefits claims, making investment decisions, managing bank accounts and preparing tax returns when an individual is no longer able to complete these tasks.

For an individual diagnosed early in the disease when he or she may still be working, additional financial plans, including a reassessment of the family budget, may be needed to prepare for the loss of future income. Alternative plans for financing children's education and a spouse or partner's retirement may be necessary. In addition, it is important for employed individuals to investigate the benefits they may be able to access through their employer before they stop working. It may also be possible to tap into financial resources from retirement plans prior to retirement age without penalty, or receive pension payments prior to retirement age, if the worker is defined as disabled under the plan's guidelines. An elder law attorney or a financial adviser may help individuals to understand their options.

End-of-life planning, although often difficult and emotional, is another important aspect of preparation that early diagnosis affords. When an individual with MCI due to AD or Alzheimer's dementia expresses his or her wishes while still able to make decisions, it helps family members ensure that these requests will be followed when the time comes. Legal documents called advance directives, which include a living will and a health care power of attorney, allow an individual to document his or her preferences regarding treatment, end-of-life care, comfort care and funeral arrangements.

To learn more about planning for a future with Alzheimer's disease, visit alz.org/i-have-alz/plan-for-your-future.asp.

Clinical Trial Participation

An early diagnosis of MCI due to AD or Alzheimer's dementia maximizes the chances that an individual can enroll in a clinical trial or participate in other forms of scientific research. Participation in research helps to accelerate progress and provides valuable insights into potential treatments that may halt or slow the progression of the disease.

The novel therapy tested in a clinical trial may provide benefits to the individual who is participating whether or not it is proven effective. Regardless of effectiveness, the knowledge that one is contributing to important research and helping future generations with the disease has its own psychological benefits. Additional benefits of clinical

trial participation include receipt of high-quality care at leading institutions, often at no cost; close monitoring and management of symptoms; and opportunities for education about Alzheimer's through regular contact with trial staff.⁵¹⁶

To learn more about participating in clinical trials and to find studies that might be right for you, visit alz.org/TrialMatch.

Financial Benefits of Early Diagnosis

Currently, most people who are diagnosed with Alzheimer's have received a clinical diagnosis without the support of biomarker confirmation. This means that many people who are diagnosed with Alzheimer's may in reality have MCI or dementia due to other causes. Regardless of underlying cause, however, diagnosis of individuals earlier in the symptomatic stages — MCI and dementia — could result in a reduction in health care costs at both the individual and national levels. A number of analyses have examined the potential economic benefits of early diagnosis of Alzheimer's, and there is general agreement that early diagnosis will save costs.^{517,523-525} For example, a cost-benefit analysis based on long-term care cost data from Wisconsin suggests that early diagnosis and treatment of Alzheimer's has financial benefits at both the state and federal levels, and that benefits are highest when individuals are identified at the earliest stages.⁵²⁴ Early diagnosis could also maximize the economic benefits that are projected to result from the availability of potential disease-modifying treatments, when available.^{262,485-486}

Model of Reduction in Health Care Costs Resulting from Early Diagnosis

To learn more about the potential cost savings associated with earlier diagnosis, the Alzheimer's Association commissioned Precision Health Economics to study the effect on medical expenditures (including medical, pharmaceutical and institutional long-term care costs) of the introduction of early detection measures that would lead to the diagnosis of individuals with Alzheimer's at the MCI stage rather than the dementia stage or not at all.

The study used The Health Economics Medical Innovation Simulation (THEMIS), which utilizes data from the Health and Retirement Study (HRS), a nationally representative sample of adults age 50 and older, to estimate health care spending. Individuals were tracked from age 50 through death, and the probability of an individual being diagnosed with Alzheimer's was determined through a regression model based on an individual's cognitive performance, functional limitations, other health conditions and demographics. The model included the entire U.S. population alive in 2018, and early detection measures were assumed to begin in 2020.

The model did not assume that biomarkers were used in the diagnostic process; indeed, timely diagnosis is possible now, even without widespread use of biomarkers. For this reason, the language used to describe Alzheimer's in this section differs from the rest of this Special Report. Most notably, the term "MCI due to AD" is not used because it is closely tied to biomarker confirmation of diagnosis. In addition, "Alzheimer's dementia" refers to Alzheimer's in the dementia stage, regardless of whether the diagnosis has been confirmed with biomarker testing. Unless otherwise stated, "Alzheimer's" refers to the symptomatic stages of the disease — MCI or dementia — regardless of whether the diagnosis has been confirmed with biomarker testing.

The model included three scenarios: 1) the current status quo, in which many people never receive a diagnosis or tend to receive it later in the disease process, typically in the dementia stage and too often when dementia is quite advanced; 2) a partial early diagnosis scenario, in which individuals with Alzheimer's have a higher likelihood of receiving a diagnosis and receiving it during the MCI stage rather than the dementia stage; and 3) a full early diagnosis scenario, in which all individuals with Alzheimer's receive a diagnosis in the MCI stage. Based on existing medical literature, differences in expected costs come from two primary sources: 1) there is a "spike" in costs during the period immediately before and after diagnosis, and this spike is smaller when diagnosis is made during the MCI stage, and 2) medical and long-term care costs are lower in people with diagnosed and managed MCI and dementia than in people with unmanaged MCI and dementia.

For a full description of the model, see page 67.

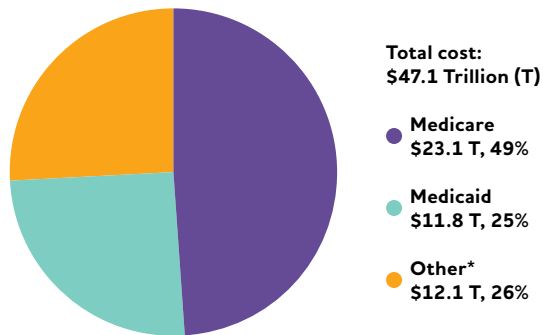
Results

Under the current status quo, the cumulative total cost of medical and long-term care expenditures for all individuals alive in the United States in 2018 who will develop Alzheimer's is projected to be \$47.1 trillion. This projection is the present value of future costs^{A23} and includes medical and long-term care costs calculated from the year prior to the development of MCI and continuing until death. This does not include the costs of everyone who actually has Alzheimer's disease because it does not include 1) people who are alive now and already in the dementia stage or 2) people who have brain changes on the Alzheimer's continuum but have not yet entered the MCI stage of the disease. Under the assumptions of the model, this total cost represents \$23.1 trillion in Medicare costs, \$11.8 trillion in Medicaid costs and \$12.1 trillion in other costs (for example, out-of-pocket expenses)^{A24} (Figure 14).

Under the partial early diagnosis scenario, in which individuals with Alzheimer's have a 70 percent chance of being diagnosed every 2 years, starting in the MCI stage (yielding a total diagnosis rate of 88 percent),

FIGURE 14

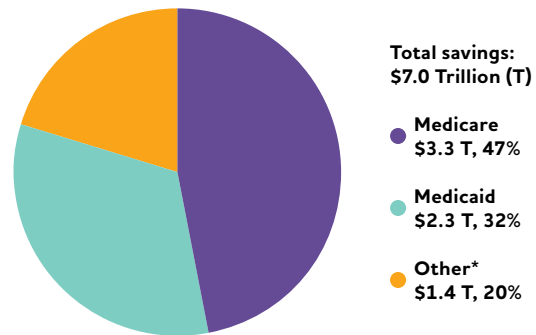
Projected Total Medical Costs (in Trillions of 2017 Dollars, Present Value of Future Savings^{A23}) Under the Current Status Quo, by Category of Expenditures^{A24}



*The "Other" category includes all costs outside of Medicare and Medicaid, such as out-of-pocket expenses and private insurance.

FIGURE 15

Projected Total Medical Savings (in Trillions of 2017 Dollars, Present Value of Future Savings^{A23}) Under the Partial Early Diagnosis Scenario Compared with the Current Status Quo, by Category of Expenditures^{A24}

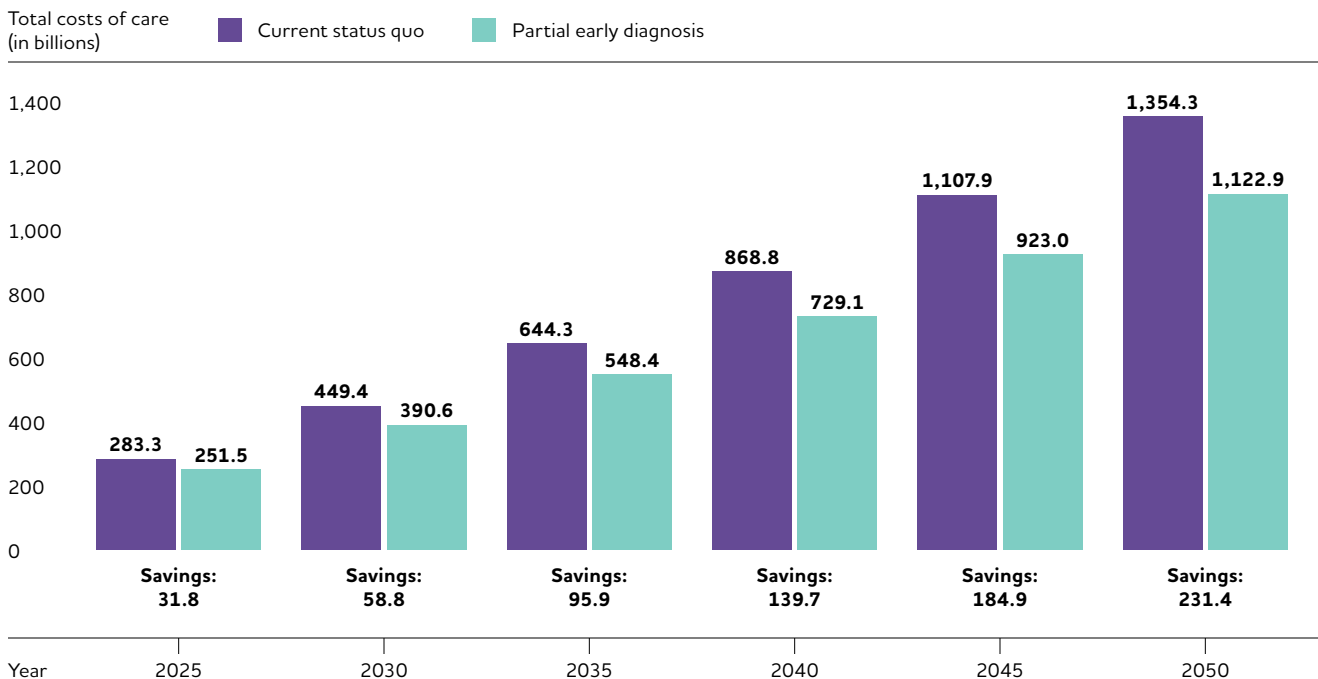


*The "Other" category includes all savings outside of Medicare and Medicaid, such as out-of-pocket expenses and private insurance.

Percentages do not total 100 due to rounding.

FIGURE 16

Projected Total Medical and Long-Term Care Costs and Cost Savings (in Billions of 2017 Dollars) by Diagnosis Scenario and Year



the cumulative total cost of medical and long-term care expenditures is projected to be \$40.1 trillion. Thus, increasing early detection and diagnosis of Alzheimer's, even partially, results in significant cost savings. Compared with the current status quo, it yields a total cumulative savings of \$7.0 trillion. Under the assumptions used in the model, these savings include \$3.3 trillion in Medicare savings, \$2.3 trillion in Medicaid savings and \$1.4 trillion in other savings (for example, out-of-pocket expenses and private insurance^{A24}) (Figure 15).

Under the full early diagnosis scenario, in which 100 percent of individuals with Alzheimer's receive a diagnosis during the MCI stage, the cumulative cost is projected to be \$39.2 trillion, yielding a total cumulative savings of \$7.9 trillion. Thus, nearly all of the potential savings of early diagnosis can be realized under the partial early diagnosis scenario.

The model also projected total costs of Alzheimer's in specific years (Figure 16). Under the partial early diagnosis scenario, total savings are projected to be \$31.8 billion in 2025 and \$231.4 billion in 2050. Greater cost savings are realized as an increasing number of individuals with Alzheimer's are diagnosed during the MCI stage rather than the dementia stage.

The model also projected how the average per-person medical and long-term care costs of individuals with Alzheimer's would be affected by early diagnosis. Under the current status quo, an individual with Alzheimer's has total projected health and long-term care costs of \$424,000 (present value of future costs^{A23}) from the year before MCI until death. Under the partial early diagnosis scenario, the average per-person cost for an individual with Alzheimer's is projected to be \$360,000, saving \$64,000 per individual. Under the assumptions of the model, this represents \$30,000 in Medicare savings, \$20,000 in Medicaid savings and \$13,000 in other savings (for example, out-of-pocket expenses and private insurance)^{A24} (Figure 17).

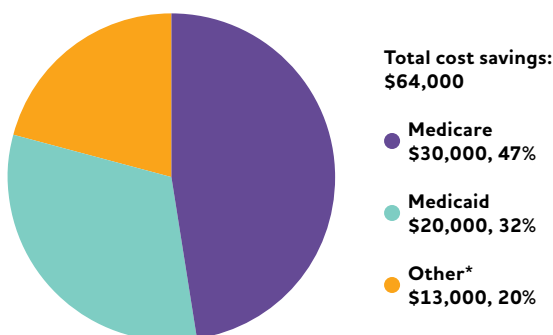
The results of this model underscore the economic benefits — to the government, to individuals, and to the medical and long-term care systems overall — of an early and accurate diagnosis of Alzheimer's. Furthermore, they suggest that diagnosing all individuals who have Alzheimer's is not necessary to achieve large cost savings, and that savings can be achieved with a realistic diagnosis rate goal.

Conclusions

The development of biomarkers for Alzheimer's disease is making it possible to detect the disease and provide an accurate diagnosis earlier than at any other time in history. Early diagnosis of Alzheimer's provides a number of important benefits to diagnosed individuals, their caregivers and loved ones, as well as society as a whole. In addition to providing significant medical, emotional and social benefits and facilitating participation in important clinical trials, early diagnosis enables individuals to prepare legal, financial and end-of-life plans while they are still cognitively able to make decisions and share their wishes. Based on the economic projections presented here, early diagnosis, even without biomarker confirmation, will also yield significant cost savings in medical and long-term care for both the U.S. government and diagnosed individuals. Given the numerous benefits, continued biomarker development and validation rightly remains a top priority of Alzheimer's disease research.

FIGURE 17

Projected Total Medical Savings per Diagnosed Individual (in 2017 Dollars, Present Value of Future Savings^{A23}) from One Year Before Diagnosis to End of Life Under the Partial Early Diagnosis Scenario Compared with the Current Status Quo, by Category of Expenditures^{A24}



*The "Other" category includes all costs outside of Medicare and Medicaid, such as out-of-pocket expenses and private insurance.

Percentages do not total 100 due to rounding.

The Precision Health Economics study used The Health Economics Medical Innovation Simulation (THEMIS), a peer-reviewed model,⁵²⁶⁻⁵³³ to provide projections of the effect of early diagnosis of Alzheimer's disease on future medical and long-term care costs. THEMIS is a microsimulation that uses population data from the Health and Retirement Study (HRS), a nationally representative sample of people 50 years of age and older, and tracks individuals from enrollment at age 50 until death to estimate disease and comorbidity burdens, life expectancy and functional status, and health care spending. People age in the model under a Monte Carlo simulation in which individuals' health states depend on current health states and on a set of random health shocks that vary with individuals' own risk factors (for example, their age, health behaviors and current disease conditions).^{A25}

Diagnosis Rates and Probability of Diagnosis

For this study, the impact of early diagnosis on medical expenditures was estimated by modeling an environment where Alzheimer's diagnosis is more likely to occur in the MCI stage, rather than in the dementia stage or not at all. The model included the entire U.S. population born in or prior to 2018, and early detection measures were assumed to begin in 2020. (Because THEMIS includes only those age 50 and older, to be diagnosed with Alzheimer's in the model, an individual would need to be at least 50 years old by 2068.) Two hypothetical scenarios were simulated: 1) a partial early diagnosis scenario and 2) a full early diagnosis scenario.

The probability of an individual being diagnosed with MCI or Alzheimer's dementia was determined through a probit regression model based on an individual's cognitive performance, functional limitations, other health conditions and demographics.^{A26} HRS respondents were stratified into age groups. Within each age group, the proportion of individuals with the highest probability of being diagnosed with Alzheimer's was identified, using a randomized process, such that the proportion was consistent with the prevalence of amnesic MCI for that age group in the Mayo Clinic Study of Aging.⁵¹⁵

Under the partial early diagnosis scenario, these identified individuals had a 70 percent probability of being diagnosed with Alzheimer's every 2 years, beginning in the MCI stage. Because this is a probability model in which individuals who are undiagnosed remain eligible to be diagnosed in later years until they die, the model yields a total diagnosis rate of 88 percent under this scenario.

Under the full early diagnosis scenario, all individuals identified in the probit regression model as having Alzheimer's were considered to have been diagnosed in the MCI stage. While a 100 percent diagnosis rate is

an unrealistic expectation, it was simulated to provide an estimate of the true extent of the problem and the upper bound of potential cost savings.

Effect on Costs

The underlying THEMIS model includes estimations of health and long-term care spending that were based on data from the Medical Expenditure Panel Study (MEPS) and the Medicare Current Beneficiary Survey (MCBS). The current study required looking at what would happen to those costs if individuals were diagnosed earlier in the disease process. Studies show that costs of MCI and dementia peak around the time of diagnosis.^{439-442,534-536} Accordingly, the model assumed that if an individual with Alzheimer's was diagnosed during the MCI stage rather than the dementia stage, the peak costs would occur surrounding the MCI diagnosis. Thus, for diagnosed individuals, costs from the year they were diagnosed under the hypothetical scenarios until the year they would have been diagnosed under the status quo were adjusted from the underlying THEMIS model to be consistent with the pre- and post-diagnosis costs of dementia reported in a recent Medicare expenditure study.^{440,A27} Costs after the point at which individuals would have been diagnosed under the status quo remained the same as determined by the underlying THEMIS model.

The simulated population included everyone alive in 2018. Cognition was assessed beginning at age 50, and diagnosis was possible anytime from that point until death. Costs were assessed for all people who will develop Alzheimer's (diagnosed and undiagnosed) starting the year before early diagnosis (or, for those who are undiagnosed, the year before they would have been diagnosed under the full early diagnosis scenario) and ending in the year of the patient's death.

End Notes

- A1. Number of Americans age 65 and older with Alzheimer's dementia for 2018 (prevalence of Alzheimer's in 2018): The number 5.5 million is from published prevalence estimates based on incidence data from the Chicago Health and Aging Project (CHAP) and population estimates from the 2010 U.S. Census.³⁰
- A2. Proportion of Americans age 65 and older with Alzheimer's dementia: The 10 percent for the age 65 and older population is calculated by dividing the estimated number of people age 65 and older with Alzheimer's dementia (5.5 million) by the U.S. population age 65 and older in 2018, as projected by the U.S. Census Bureau (52.8 million) = approximately 10 percent.¹⁴⁵ Please note that the proportion of Americans age 65 and older with Alzheimer's dementia has gone down slightly in recent years despite the number of Americans with Alzheimer's dementia in this age range going up; this is because of the large number of baby boomers who have started to enter this age range and increased the overall number of seniors, but at the early low risk years in this range.²²⁹
- A3. Percentage of total Alzheimer's dementia cases by age groups: Percentages for each age group are based on the estimated 200,000 people under 65,³⁰ plus the estimated numbers for people ages 65 to 74 (0.9 million), 75 to 84 (2.5 million), and 85+ (2.1 million) based on prevalence estimates for each age group and incidence data from the CHAP study.
- A4. Differences between CHAP and ADAMS estimates for Alzheimer's dementia prevalence: ADAMS estimated the prevalence of Alzheimer's dementia to be lower than CHAP, at 2.3 million Americans age 71 and older in 2002,¹⁴⁸ while the CHAP estimate for 2000 was 4.5 million.⁵³⁷ At a 2009 conference convened by the National Institute on Aging and the Alzheimer's Association, researchers determined that this discrepancy was mainly due to two differences in diagnostic criteria: (1) a diagnosis of dementia in ADAMS required impairments in daily functioning and (2) people determined to have vascular dementia in ADAMS were not also counted as having Alzheimer's, even if they exhibited clinical symptoms of Alzheimer's.¹⁴⁹ Because the more stringent threshold for dementia in ADAMS may miss people with mild Alzheimer's dementia and because clinical-pathologic studies have shown that mixed dementia due to both Alzheimer's and vascular pathology in the brain is very common,⁶ the Association believes that the larger CHAP estimates may be a more relevant estimate of the burden of Alzheimer's dementia in the United States.
- A5. Number of women and men age 65 and older with Alzheimer's dementia in the United States: The estimates for the number of U.S. women (3.4 million) and men (2.0 million) age 65 and older with Alzheimer's in 2013 is from unpublished data from CHAP. For analytic methods, see Hebert et al.³⁰ The numbers for men and women do not add to 5.5 million due to rounding.
- A6. Prevalence of Alzheimer's and other dementias in older whites, African-Americans and Hispanics: The statement that African-Americans are twice as likely and Hispanics one and one-half times as likely as whites to have Alzheimer's or other dementias is the conclusion of an expert review of a number of multiracial and multiethnic data sources, as reported in detail in the Special Report of the Alzheimer's Association's 2010 *Alzheimer's Disease Facts and Figures*.
- A7. State-by-state prevalence of Alzheimer's dementia: These state-by-state prevalence numbers are based on an analysis of incidence data from CHAP, projected to each state's population, with adjustments for state-specific age, gender, years of education, race and mortality.²⁰⁹ Specific prevalence numbers for 2018 were derived from this analysis and provided to the Alzheimer's Association by a team led by Liesi Hebert, Sc.D., from Rush University Institute on Healthy Aging.
- A8. Number of new cases of Alzheimer's dementia this year (incidence of Alzheimer's in 2018): The East Boston Established Populations for Epidemiologic Study of the Elderly (EPESE) estimated that there would be 454,000 new cases in 2010 and 491,000 new cases in 2020 (see Hebert et al.²¹⁰). The Alzheimer's Association calculated the incidence of new cases in 2018 by multiplying the 10-year change from 454,000 to 491,000 (37,000) by 0.8 (for the number of years from 2010 to 2018 divided by the number of years from 2010 to 2020), adding that result (29,600) to the Hebert et al. estimate for 2010 (454,000) = 483,600.²¹⁰ Rounded to the nearest thousand, this is 484,000 new cases of Alzheimer's dementia in 2018. The same technique for linear interpolation from 2010 to 2020 projections was used to calculate the number of new cases in 2018 for ages 65-74, 75-84 and 85 and older. The age group-specific Alzheimer's dementia incident rate is the number of new people with Alzheimer's per population at risk (the total number of people in the age group in question). These incidence rates are expressed as number of new cases per 1,000 people using the total number of people per age group (e.g., 65-74, 75-84, 85+) for 2018 from population projections from the 2000 U.S. Census as the denominator.⁵³⁸
- A9. Number of seconds for the development of a new case of Alzheimer's dementia: Although Alzheimer's does not present suddenly like stroke or heart attack, the rate at which new cases develop can be computed in a similar way. The 65 seconds number is calculated by dividing the number of seconds in a year (31,536,000) by the number of new cases in a year (483,600)^{A8} = 65.2 seconds, rounded to 65 seconds. Using the same method of calculation for 2050, 31,536,000 divided by 959,000 (from Hebert et al.²¹⁰) = 32.8 seconds, rounded to 33 seconds.
- A10. Criteria for identifying people with Alzheimer's or other dementias in the Framingham Study: From 1975 to 2009, 7,901 people from the Framingham Study who had survived free of dementia to at least age 45, and 5,937 who had survived free of dementia until at least age 65 were followed for incidence of dementia.¹⁷³ Diagnosis of dementia was made according to Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) criteria and required that the participant survive for at least 6 months after onset of symptoms. Standard diagnostic criteria (the NINCDS-ADRDA criteria from 1984) were used to diagnose Alzheimer's dementia. The definition of Alzheimer's and other dementias used in the Framingham Study was very strict; if a definition that included milder disease and disease of less than six months' duration were used, lifetime risks of Alzheimer's and other dementias would be higher than those estimated by this study.
- A11. Projected number of people with Alzheimer's dementia: This figure comes from the CHAP study.³⁰ Other projections are somewhat lower (see, for example, Brookmeyer et al.⁵³⁹) because they relied on more conservative methods for counting people who currently have Alzheimer's dementia.^{A4} Nonetheless, these estimates are statistically consistent with each other, and all projections suggest substantial growth in the number of people with Alzheimer's dementia over the coming decades.
- A12. Projected number of people age 65 and older with Alzheimer's dementia in 2025: The number 7.1 million is based on a linear extrapolation from the projections of prevalence of Alzheimer's for the years 2020 (5.8 million) and 2030 (8.4 million) from CHAP.³⁰
- A13. Annual mortality rate due to Alzheimer's disease by state: Unadjusted death rates are presented rather than age-adjusted death rates in order to provide a clearer depiction of the true burden of mortality for each state. States such as Florida with larger populations of older people will have a larger burden of mortality due to Alzheimer's — a burden that appears smaller relative to other states when the rates are adjusted for age.

- A14. Number of family and other unpaid caregivers of people with Alzheimer's or other dementias: To calculate this number, the Alzheimer's Association started with data from the BRFSS survey. In 2009, the BRFSS survey asked respondents age 18 and over whether they had provided any regular care or assistance during the past month to a family member or friend who had a health problem, long-term illness or disability. To determine the number of family and other unpaid caregivers nationally and by state, we applied the proportion of caregivers nationally and for each state from the 2009 BRFSS (as provided by the CDC, Healthy Aging Program, unpublished data) to the number of people age 18 and older nationally and in each state from the U.S. Census Bureau report for July 2017. Available at: <https://www.census.gov/data/tables/2017/demo/popest/state-detail.html>. Accessed on Dec. 26, 2017. To calculate the proportion of family and other unpaid caregivers who provide care for a person with Alzheimer's or another dementia, the Alzheimer's Association used data from the results of a national telephone survey also conducted in 2009 for the National Alliance for Caregiving (NAC)/AARP.⁵⁴⁰ The NAC/AARP survey asked respondents age 18 and over whether they were providing unpaid care for a relative or friend age 18 or older or had provided such care during the past 12 months. Respondents who answered affirmatively were then asked about the health problems of the person for whom they provided care. In response, 26 percent of caregivers said that: (1) Alzheimer's or another dementia was the main problem of the person for whom they provided care, or (2) the person had Alzheimer's or other mental confusion in addition to his or her main problem. The 26 percent figure was applied to the total number of caregivers nationally and in each state, resulting in a total of 16.139 million Alzheimer's and dementia caregivers.
- A15. The 2014 Alzheimer's Association Women and Alzheimer's Poll: This poll questioned a nationally-representative sample of 3,102 American adults about their attitudes, knowledge and experiences related to Alzheimer's and dementia from Jan. 9, 2014, to Jan. 29, 2014. An additional 512 respondents who provided unpaid help to a relative or friend with Alzheimer's or a related dementia were asked questions about their care provision. Random selections of telephone numbers from landline and cell phone exchanges throughout the United States were conducted. One individual per household was selected from the landline sample, and cell phone respondents were selected if they were 18 years old or older. Interviews were administered in English and Spanish. The poll "oversampled" Hispanics, selected from U.S. Census tracts with higher than an 8 percent concentration of this group. A list sample of Asian-Americans was also utilized to oversample this group. A general population weight was used to adjust for number of adults in the household and telephone usage; the second stage of this weight balanced the sample to estimated U.S. population characteristics. A weight for the caregiver sample accounted for the increased likelihood of female and white respondents in the caregiver sample. Sampling weights were also created to account for the use of two supplemental list samples. The resulting interviews comprise a probability-based, nationally representative sample of U.S. adults. A caregiver was defined as an adult over age 18 who, in the past 12 months, provided unpaid care to a relative or friend age 50 or older with Alzheimer's or another dementia. Questionnaire design and interviewing were conducted by Abt SRBI of New York.
- A16. Number of hours of unpaid care: To calculate this number, the Alzheimer's Association used data from a follow-up analysis of results from the 2009 NAC/AARP national telephone survey (data provided under contract by Matthew Greenwald and Associates, Nov. 11, 2009). These data show that caregivers of people with Alzheimer's or other dementias provided an average of 21.9 hours a week of care, or 1,139 hours per year. The number of family and other unpaid caregivers (16.139 million)^{A14} was multiplied by the average hours of care per year, which totals 18.379 billion hours of care. This is slightly lower than the total resulting from multiplying 1,139 by 16.139 million because of rounding.
- A17. Value of unpaid caregiving: To calculate this number, the Alzheimer's Association used the method of Amo et al.⁵⁴¹ This method uses the average of the federal minimum hourly wage (\$7.25 in 2017) and the mean hourly wage of home health aides (\$18.00 in July 2017).⁵⁴² The average is \$12.63, which was multiplied by the number of hours of unpaid care (18.379 billion) to derive the total value of unpaid care (\$232.129 billion; this is slightly higher than the total resulting from multiplying \$12.63 by 18.379 billion because 18.379 is a rounded number for the hours of unpaid care).
- A18. Higher health care costs of Alzheimer's caregivers: This figure is based on a methodology originally developed by Brent Fulton, Ph.D., for The Shriver Report: A Woman's Nation Takes on Alzheimer's. A survey of 17,000 employees of a multinational firm based in the United States estimated that caregivers' health care costs were 8 percent higher than non-caregivers'.⁵⁴³ To determine the dollar amount represented by that 8 percent figure nationally and in each state, the 8 percent figure and the proportion of caregivers from the 2009 BRFSS^{A14} were used to weight each state's caregiver and non-caregiver per capita personal health care spending in 2014,⁵⁴⁴ inflated to 2017 dollars. The dollar amount difference between the weighted per capita personal health care spending of caregivers and non-caregivers in each state (reflecting the 8 percent higher costs for caregivers) produced the average additional health care costs for caregivers in each state. Nationally, this translated into an average of \$705. The amount of the additional cost in each state, which varied by state from a low of \$523 in Utah to a high of \$1,051 in the District of Columbia, was multiplied by the total number of unpaid Alzheimer's and dementia caregivers in that state^{A14} to arrive at that state's total additional health care costs of Alzheimer's and other dementia caregivers as a result of being a caregiver. The combined total for all states was \$11.367 billion. Fulton concluded that this is "likely to be a conservative estimate because caregiving for people with Alzheimer's is more stressful than caregiving for most people who don't have the disease."⁵⁴⁵
- A19. Lewin Model on Alzheimer's and dementia costs: These numbers come from a model created for the Alzheimer's Association by the Lewin Group. The model estimates total payments for health care, long-term care and hospice — as well as state-by-state Medicaid spending — for people with Alzheimer's and other dementias. The model was updated by the Lewin Group in January 2015 (updating previous model) and June 2015 (addition of state-by-state Medicaid estimates). Detailed information on the model, its long-term projections and its methodology are available at alz.org/trajectory. For the purposes of the data presented in this report, the following parameters of the model were changed relative to the methodology outlined at alz.org/trajectory: (1) cost data from the 2011 Medicare Current Beneficiary Survey (MCBS) were used rather than data from the 2008 MCBS; (2) prevalence among older adults was assumed to equal the prevalence levels from Hebert et al.³⁰ and included in this report (5.5 million in 2018),^{A2} rather than the prevalence estimates derived by the model itself; (3) estimates of inflation and excess cost growth reflect the most recent relevant estimates from the cited sources (the Centers for Medicare and Medicaid Services [CMS] actuaries and the Congressional Budget Office); and (4) the most recent (2014) state-by-state data from CMS on the number of nursing home residents and percentage with moderate and severe cognitive impairment were used in lieu of 2012 data.
- A20. All cost estimates were inflated to year 2017 dollars using the Consumer Price Index (CPI): All cost estimates were inflated using the seasonally adjusted average prices for medical care services from all urban consumers. The relevant item within medical care services was used for each cost element. For example, the medical care item within the CPI was used to

inflate total health care payments; the hospital services item within the CPI was used to inflate hospital payments; and the nursing home and adult day services item within the CPI was used to inflate nursing home payments.

A21. Medicare Current Beneficiary Survey Report: These data come from an analysis of findings from the 2011 Medicare Current Beneficiary Survey (MCBS). The analysis was conducted for the Alzheimer's Association by Avalere Health.⁴²⁷ The MCBS, a continuous survey of a nationally representative sample of about 15,000 Medicare beneficiaries, is linked to Medicare claims. The survey is supported by the U.S. Centers for Medicare & Medicaid Services (CMS). For community-dwelling survey participants, MCBS interviews are conducted in person three times a year with the Medicare beneficiary or a proxy respondent if the beneficiary is not able to respond. For survey participants who are living in a nursing home or another residential care facility, such as an assisted living residence, retirement home or a long-term care unit in a hospital or mental health facility, MCBS interviews are conducted with a staff member designated by the facility administrator as the most appropriate to answer the questions. Data from the MCBS analysis that are included in *2018 Alzheimer's Disease Facts and Figures* pertain only to Medicare beneficiaries age 65 and older. For this MCBS analysis, people with dementia are defined as:

- Community-dwelling survey participants who answered yes to the MCBS question, "Has a doctor ever told you that you had Alzheimer's disease or dementia?" Proxy responses to this question were accepted.
- Survey participants who were living in a nursing home or other residential care facility and had a diagnosis of Alzheimer's disease or dementia in their medical record.
- Survey participants who had at least one Medicare claim with a diagnostic code for Alzheimer's or other dementias in 2008. The claim could be for any Medicare service, including hospital, skilled nursing facility, outpatient medical care, home health care, hospice or physician, or other health care provider visit. The diagnostic codes used to identify survey participants with Alzheimer's or other dementias are 331.0, 331.1, 331.11, 331.19, 331.2, 331.7, 331.82, 290.0, 290.1, 290.10, 290.11, 290.12, 290.13, 290.20, 290.21, 290.3, 290.40, 290.41, 290.42, 290.43, 291.2, 294.0, 294.1, 294.10 and 294.11.

Costs from the MCBS analysis are based on responses from 2011 and reported in 2017 dollars.

A22. Differences in estimated costs reported by Hurd and colleagues: Hurd et al.⁴²⁶ estimated per-person costs using data from participants in ADAMS, a cohort in which all individuals underwent diagnostic assessments for dementia. *2018 Alzheimer's Disease Facts and Figures* estimated per-person costs using data from the Medicare Current Beneficiary Survey (MCBS). One reason that the per-person costs estimated by Hurd et al. are lower than those reported in *Facts and Figures* is that ADAMS, with its diagnostic evaluations of everyone in the study, is more likely than MCBS to have identified individuals with less severe or undiagnosed Alzheimer's. By contrast, the individuals with Alzheimer's registered by MCBS are likely to be those with more severe, and therefore more costly, illness. A second reason is that Hurd et al.'s estimated costs reflect an effort to isolate the incremental costs associated with Alzheimer's and other dementias (those costs attributed only to dementia), while the per-person costs in *2018 Alzheimer's Disease Facts and Figures* incorporate all costs of caring for people with the disease (regardless of whether the expenditure was related to dementia or a coexisting condition).

A23. Present value of future costs: Present value is a calculation to determine the current value of a future amount of money. In this study, present value was used when presenting cumulative costs over time. Cumulative costs are in 2017 dollars and calculated

using (a) an annual 3 percent discount rate to account for the anticipated value of the money over time and (b) a medical growth rate — the anticipated real growth rate of medical expenditures above and beyond inflation — of 3.1 percent.

A24. Breakdown of total medical savings: Where the literature only calculated reductions in Medicare costs, rather than total costs, the total and Medicaid costs were assumed to change by the same proportions. For example, if Medicare savings were 20 percent, it was assumed that total medical and Medicaid expenses also decreased 20 percent.

A25. THEMIS Monte Carlo simulation: One hundred Monte Carlo repetitions were used for each scenario, where each repetition consisted of an entire run of the simulation with a different random seed. In a given year (for example, 2024), sample individuals may have diseases and functional status limitations that put them at risk of developing new diseases and disabilities, or even dying. THEMIS uses a health transition model to simulate how population health will evolve given existing health conditions and assumptions about treatment and diagnosis for individuals. In addition, while mortality reduces the population over the course of the time step, the sample is "refreshed" by introducing those who turn 50 in 2024 and who now age into the target population. This forms the set of sample individuals for the next time step and the process is repeated for subsequent years.

A26. Variables used to determine individuals' probability of being diagnosed with Alzheimer's: Cognitive performance was assessed in the HRS using the Telephone Interview for Cognitive Status (TICS). Normal cognitive performance was defined as a TICS score of 12 or above; MCI was defined by a TICS score between 7 and 11; and dementia was defined as a TICS score below 7.⁵⁴⁶ The functional limitations that contributed to an individual's probability of being diagnosed with Alzheimer's were difficulty (a) taking medications, (b) using the telephone and (c) handling money. Other health conditions included in determining the risk for developing Alzheimer's were diabetes, hypertension and stroke. The following demographic variables were also used: sex, age, race/ethnicity and education level.

A27. Cost adjustments: Adjusting the model's underlying cost estimates for those receiving an early diagnosis had two parts. The first part was a once-per-lifetime reduction in the two-year period centered on the time of diagnosis of \$8,140 (2014 dollars), which is the difference between the costs of being diagnosed during the dementia stage and the MCI stage.⁴⁴⁰ The second part of the cost adjustment is the cost per patient-year following a diagnosis in the MCI stage, calculated at \$14,286 (2014 dollars). To illustrate the second part of the cost adjustment, assume an individual is diagnosed at age 75 under the status quo and diagnosed at age 65 in the early diagnosis scenarios. Under this example, the costs between age 66 and age 75 will be \$14,286 times the medical cost growth factor. The medical cost growth — the real growth in medical expenditures above and beyond inflation — was assumed to be 3.1 percent per year, so as an example, the medical cost growth factor 10 years in the future would be 1.031 E+10.

The Alzheimer's Association is the leading voluntary health organization in Alzheimer's care, support and research. Our mission is to eliminate Alzheimer's disease through the advancement of research; to provide and enhance care and support for all affected; and to reduce the risk of dementia through the promotion of brain health.

Our vision is a world without Alzheimer's disease.®

Alzheimer's Association
225 N. Michigan Ave., Fl. 17
Chicago, IL 60601-7633

Alzheimer's Association
Public Policy Office
1212 New York Ave., N.W., Suite 800
Washington, DC 20005-6105

800.272.3900
alz.org®

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