Appendix A
METHODOLOGY

The Alzheimer's Association report, *Changing the Trajectory of Alzheimer's Disease: How a Treatment by 2025 Saves Lives and Dollars*, presents information about the impact of Alzheimer's disease based on data from a model developed for the Alzheimer's Association by The Lewin Group. The report offers information about the current trajectory, a delayed onset trajectory and a slowed progression trajectory included in a separate Appendix. This Appendix describes the model and the research findings used to develop it.

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The Lewin Group Model

The Lewin Group Model projects the trajectory and impact of Alzheimer's disease given various scenarios, including the current scenario, in which there are no known treatments that can change the course of the disease, and alternate scenarios, in which hypothetical treatments could become available to delay the onset and/or slow the progression of the disease. Based on data from scientific research and national surveys, the model projects the number of people age 65 or older who have or will have Alzheimer's disease in single years through 2050; the number and proportion who will be in the mild, moderate or severe stage of the disease in any year during that period; and the cost of their care to all payers and to specific payers, including Medicare, Medicaid, individuals with Alzheimer's and their families, and others (such as private insurance, HMOs and those who cover the costs of uncompensated care).

Methodology

The Lewin Group model combines analytical techniques reported by Sloane et al.[1] for examining the potential impact of breakthrough treatments for Alzheimer's disease; incidence rates (the percent of individuals that develop Alzheimer's disease over the course of a year) reported by Evans et al.[2] and resulting prevalence rates (the percent of individuals who have Alzheimer's disease) reported by Hebert et al.;[3,4] estimates of stage of disease reported by Graham et al.;[5] per capita costs of care for Medicare beneficiaries age 65 and older from the 2008 Medicare Current Beneficiary Survey (MCBS) Cost and Use file;[6] and mortality rates and estimates of differential costs by stage of disease (mild, moderate and severe) based on a previous analysis by The Lewin Group.[7]

The model begins with a national count of individuals with Alzheimer's disease and projects the number of individuals with Alzheimer's by stage of disease for each single year to 2050 using incidence rates, population projections from the United States Census Bureau,[8] estimated rates of progression from mild to moderate and moderate to severe Alzheimer's disease and differential mortality rates. Cost figures from the MCBS[6]

are applied to the prevalence estimates to determine the total costs of caring for individuals with Alzheimer's disease and other dementias in total and by specific payer.

The model projects national data and does not take into account regional, state or local differences in incidence, prevalence, stage of disease, mortality or costs.

Number of Americans with Alzheimer's Disease

Incidence and Prevalence. To develop incidence and prevalence rates, the model starts with incidence rates reported by Evans et al.[2] and prevalence rates reported by Hebert et al.[3,4] These rates are based on findings from the same population-based, longitudinal research study. The Hebert et al. projections through 2050 indicate a declining prevalence within age groups as a result of increased educational attainment among future cohorts of people age 65 and older (educational attainment is associated with a lower likelihood of developing Alzheimer's). To approximate the Hebert et al. prevalence projections, the incidence rates from Evans et al. are adjusted downward over time based on the increasing proportion of people age 65 and older with a high school education.

Stage of Disease. To establish baseline figures for the proportion of people with Alzheimer's disease that are in the mild, moderate or severe stage of the disease, the model uses findings from the Canadian Study of Health and Aging reported by Graham et al.[5] The Canadian study was chosen to determine these baseline figures because the comparable figures reported by Hebert et al.[3,4] are for a sample of individuals with incident disease and therefore include a higher proportion of individuals with mild disease than would be found in a sample that also contained prevalent cases.

Progression between Stages of Disease. The model assumes that without new treatments that could delay the onset or slow the progression of Alzheimer's disease, the transition probability from the mild to the moderate stage of the disease is 45 percent annually, and the transition probability from the moderate to the severe stage of the disease is 28 percent annually. These baseline transition probabilities were developed

for a previous analysis by The Lewin Group[7] to convert the single transition probability from Sloane et al.,[1] which estimates the transition rate from the mild stage to a combined moderate/severe stage, into two probabilities that estimate the transition from the mild to the moderate stage and from the moderate to the severe stage. Not accounting for deaths, this transition rate implies staying in a mild stage for approximately two years and a moderate stage for four years.

Mortality Rate. The model uses age-specific mortality rates from the Social Security Administration to project the number of people age 65 and older that will die of all causes.[9] Several studies have found higher mortality rates for individuals with Alzheimer's disease.[10,11,12] Based on these findings, the model assumes differential mortality rates of 1.2 for individuals in the mild stage of Alzheimer's disease; 1.5 for individuals in the moderate stage of the disease; and 2.0 for individuals in the severe stage.

Costs of Caring for People with Alzheimer's Disease and Other Dementias

Community-Based Care. The model uses per capita costs to all payers for the care of people with and without Alzheimer's disease and other dementias and costs of care to specific payers from an analysis of data from the 2008 MCBS.[6] In the MCBS data, Medicare beneficiaries age 65 and older were identified as having Alzheimer's disease or other dementias based on responses of the beneficiary or a proxy to an MCBS question about whether a doctor said the person had Alzheimer's disease or dementia and/or the presence of diagnostic codes for Alzheimer's disease and other dementias on Medicare claims for any Medicare service in 2008. The costs of all kinds of medical care, nursing home and other residential care, home and community-based services, and medications are included. These data provided the overall per capita spending for those with and without Alzheimer's disease and other dementias by various payers (Medicare, Medicaid, individual out of pocket, private insurance, HMOs, other payers and uncompensated care). These per capita costs are reported annually in the Alzheimer's Association *Alzheimer's Disease Facts and Figures*, available at www.alz.org/facts.

Before calculating total costs, the model takes this overall figure for individuals with Alzheimer's disease and other dementias and estimates nine separate per person cost figures for each payer based on the age of the individual (65-74, 75-84, and 85+) and his/her stage of disease (mild, moderate and severe). First, the model stratified the per capita spending by age of the individual based on Medicare claims data,[13] which showed that Medicare spending by those with Alzheimer's and dementia decreases as the individual gets older. Specifically, relative to the overall per person costs for those with Alzheimer's, costs were 121.1 percent for those aged 65-74; 103.4 percent for those aged 75-84; and 86.1 percent for those aged 85 and older.

Second, per person costs by age are then stratified by stage of disease. The cost of care data from the 2008 MCBS are not reported by stage of disease. Thus, the model uses estimates of differential costs of care by stage of disease based on findings from Leon et al.[14] and Small et al.[15] Both studies found that average costs of care increased by stage of disease. In the model, the relative per person cost adjustment for disease stage varies by age group based on the distribution of relative prevalence for each severity level. The adjustments for stage of disease in the model are as follows:

Disease Stage Stratification of Age-Specific Per-Person Costs

	65-74	75-84	85+
Mild	0.75	0.68	0.64
Moderate	1.00	0.90	0.86
Severe	1.50	1.36	1.29

Nursing Home Care. Beyond the costs associated with community-based care, the model estimates the additional costs of nursing home care using per capita costs of those with Alzheimer's and other dementias living in nursing homes from the 2008 MCBS Cost and Use data,[6] less the cost of their community-based care. Costs are estimated separately for Medicare, Medicaid, individuals (out of pocket) and other sources (private insurance, uncompensated and other payers). For nursing home costs, the model does not adjust for age or stage of disease because, unlike medical costs, the cost of nursing home custodial care rarely varies by individual. The model does adjust for the rate of institutionalization, and this adjustment varies by stage of disease. Based on a previous analysis by The Lewin Group,[7] the model assumes nursing home residency for 4.1 percent of those in the mild stage, 29.1 percent in the moderate stage and 42.9 percent in the severe stage.

Inflation. All per capita costs derived from the 2008 MCBS were inflated to 2014 dollars; all resulting total cost figures for each year through 2050 were then inflated to constant 2015 dollars based on the projection of general inflation by Centers for Medicare and Medicaid Services (CMS) actuaries.[16] For this report, the Association chose not to increase costs over time to reflect the impact of general inflation. However, health care inflation over and above general inflation ("excess cost growth") is captured in the costs shown in constant 2015 dollars. For Medicare, the model uses the projection of excess cost growth as determined by CMS actuaries.[16] Excess cost growth for Medicaid and all other payers is based on historical averages as reported by the Congressional Budget Office.[17]

Hypothetical Treatment Scenarios

Delayed Onset of Alzheimer's Disease. Under the model, a hypothetical treatment could delay the onset of Alzheimer's disease anywhere from 1 to 10 years from the baseline trajectory and could become available in any year from the present to 2050. For this report, the Alzheimer's Association chose to delay the onset of Alzheimer's disease by five years beginning in 2025, as is consistent with the goal of the *National Plan to Address Alzheimer's Disease*.[18] The Association assumed a 100 percent take-up rate.

Individuals who do not get Alzheimer's disease because of the availability of a treatment will, nonetheless, still have health care costs. The model accounts for the continued, albeit lower, health care spending of such individuals before reporting the amount of savings that would be achieved by the existence of a treatment that delays onset. Consistent with the methodology concerning those with Alzheimer's disease, these costs are based on per person costs of seniors who do not have dementia from the 2008 MCBS Cost and Use data,[6] stratified by age based on 2000 Medicare claims data.[13]

Slowed Progression of Alzheimer's Disease. A treatment that slowed the progression of Alzheimer's disease would mean that individuals would transition from the mild to moderate stages and the moderate to severe stages at a slower rate than under the baseline trajectory. The model allows for the selection of any transition rates and such a treatment could become available in any year through 2050. For the Appendix to this report, the Alzheimer's Association chose to slow progression beginning in 2025 (again, consistent with the goal of the National Plan), so that 10 percent of people with Alzheimer's disease would transition from the mild to the moderate stage annually and 5 percent would transition from the moderate to the severe stage annually. These figures are based on a hypothesis by Sloane et al.[1] that a medication might reduce the annual transition rate between mild to a combined moderate/ severe stage from 28 percent to 10 percent. The Association assumed a 100 percent take-up rate.

Costs of a Hypothetical Treatment. In determining savings under either a delayed onset or slowed progression treatment scenario, the model can account for the estimated costs of the hypothetical treatment. However, the Alzheimer's Association chose not to include those costs in this report because the possible treatments range so widely from a relatively low cost treatment, such as a change in diet or exercise, to a relatively high cost treatment, such as a single medication or a combination of medications that would be taken several times a day over a long period of time. Further, payments for a treatment could vary widely over future years due to regulatory changes and reimbursement policies would be very difficult to forecast with any certainty.

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