

Societal Impact of Research Funding for Women’s Health in Alzheimer’s Disease and Alzheimer’s Disease–Related Dementias

Technical Appendixes

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Preface

These technical appendixes accompany the report titled *Societal Impact of Research Funding for Women's Health in Alzheimer's Disease and Alzheimer's Disease-Related Dementias* (Baird et al., 2021) and provide additional information about the data sources and microsimulation model used in that report, which can be found at www.rand.org/t/RRA708-1.

Technical Appendix A. Selection of Data Sources

Table A.1. Availability of Key Variables Among Potential Data Sources

	Panel Study of Income Dynamics	National Longitudinal Survey of Youth, 1979	Medical Expenditure Panel Survey
N	24,000 people	12,686 people	30,000 households
Age ranges	Born 1951-present	Born 1957-1964	Range of ages
Received diagnosis of			
Alzheimer's specifically	No (just diagnosis of permanent loss of memory/ mental ability)	No	Yes
Health spending	Yes (aggregated)	No	Yes
Health condition limits activities	Yes	Snapshot	Yes
Extra care needed	Snapshot	No	Yes
Disability insurance participation	Yes	Yes	No
Paid nurse to come to home this year	Yes	No	Yes

Note: "Snapshot" indicates a variable is capture incidentally (e.g. in a single year or at milestone ages) rather than every survey wave (annual/biennial).

Technical Appendix B. Model

Overview of the Model

This microsimulation model is based on a synthetic starting cohort with 999,988 individuals aged 35-99. We use the fraction of individuals that are each age and gender in the U.S. population from the Census Bureau (U.S. Census Bureau, 2020) and multiply that fraction by 999,988 to determine how many individuals in our simulation sample are that age and gender. Conditional on age and gender, individuals in the starting cohort are sorted into one of eight states:

1. Alive without AD/ADRD and not institutionalized
2. Alive without AD/ADRD and institutionalized
3. Alive with AD/ADRD in mild stage and not institutionalized
4. Alive with AD/ADRD in mild stage and institutionalized
5. Alive with AD/ADRD in moderate stage and not institutionalized
6. Alive with AD/ADRD in moderate stage and institutionalized
7. Alive with AD/ADRD in severe stage and not institutionalized
8. Alive with AD/ADRD in severe stage and institutionalized.

The distribution of the 8 states in the population is derived by simulating a cohort of 100,000 females and 100,000 males aged 34 for 66 years through our health model until everyone dies in our simulation. This is used to calculate the initial conditions of the population. Setting the number of individuals in the starting cohort at 1000,000, we multiply 1000,000 with the distribution to assign individuals with AD/ADRD status, ADRD severity, and nursing home status. This determines by age and gender the fraction of individuals within each of the 8 states. We take each age and gender group and assign the proportion of people in each state reflected by those simulations. We ended up with 999,988 individuals for the starting cohort due to the discrete nature of the states.

There are three components in this model:

1. Simulating and predicting the proportion of people diagnosed with Alzheimer's Disease/Alzheimer's Disease and Related Disorders (AD/ADRD), the progression of the disease, care status, and mortality.
2. Generating aggregate projections of individual-level outcomes, including total non-nursing home health care costs (including formal home care), nursing home costs, productivity loss of informal caregivers, and quality of life loss.
3. Estimating the impact of additional research funding on economic costs, using return on research funding investment.

Data Sources Used for Estimation

Medical Expenditure Panel Survey

The Medical Expenditure Panel Survey (MEPS), beginning in 1996, is a set of large-scale surveys of individuals and families, their medical providers (doctors, hospitals, pharmacies, etc.), and employment status across the United States (Agency for Healthcare Research and Quality, 2020). The Household Component (HC) of the MEPS provides data from individual households and their members, which is supplemented by data from their medical providers. The Household Component collects data from a representative sub sample of households drawn from the previous year's National Health Interview Survey (NHIS). Institutionalized population is not included in the MEPS, which implies that we can use the MEPS to estimate health care costs only for the individuals living in communities. Information collected during household interviews includes demographic characteristics, health conditions, health status, use of medical services, and health insurance status. Each year the household survey includes approximately 12,000 households or 34,000 individuals. We estimate expenditures and utilization using 2011-2017 data.

Health and Retirement Study

The Health and Retirement Study (HRS) is a longitudinal panel survey of Americans over the age of 50 occurring every two years (The University of Michigan, 2020). It's a complex and rich source to explore health transitions relating to aging. We used from the waves 1 (1990) through wave 12 (2014-2016) to estimate the proportion of people being institutionalized. We use the dataset created by RAND (RAND HRS, version Q) as our basis for the analysis. When appropriately weighted, the HRS is representative of U.S. households where at least one member is at least 51.

Centers for Medicaid & Medicare Services Data

The CMS Medicare Beneficiary Summary File (base and chronic conditions components) was used to estimate the age incidence rate of AD/ADRD. The master beneficiary summary file (MBSF) base segment includes Medicare enrollment information for the universe of Medicare beneficiaries. It also contains demographic data (date of birth, date of death, sex, race, and ethnicity) and limited socio-economic information (Medicare/Medicaid dual eligibility status and Part D (drug coverage) cost-sharing status). The MBSF chronic conditions segment contains data on 27 chronic conditions, two of which are Alzheimer's disease (AD) and Alzheimer's disease related dementia (ADRD), and for each condition, it includes the date of first diagnosis as well as indicators for whether the diagnosis is active in the current year. With date of first diagnosis, incident cases can be identified separately from prevalent cases in any year. We used data these annual files 2016 and 2017 so we would have one complete year from birthday to birthday for

each beneficiary, and from these we identified age-specific incidence rates for AD and ADRD. We used the 2017 data to estimate age-specific mortality rates, conditional on AD/ADRD status and the time since AD/ADRD diagnosis. Thus, estimates of age-specific incidence rate and age-specific mortality rates conditional on AD/ADRD duration were made using the universe of individuals who were at least 65 years of age and enrolled in Medicare (Research Data Assistance Center, 2020a; Research Data Assistance Center, 2020b).

Modeling health and economics statuses

Incidence of AD/ADRD

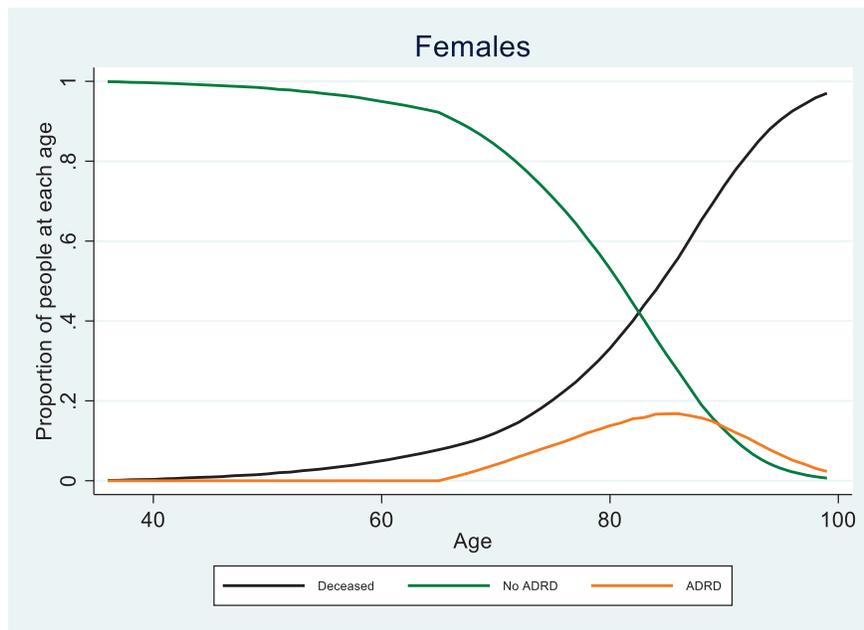
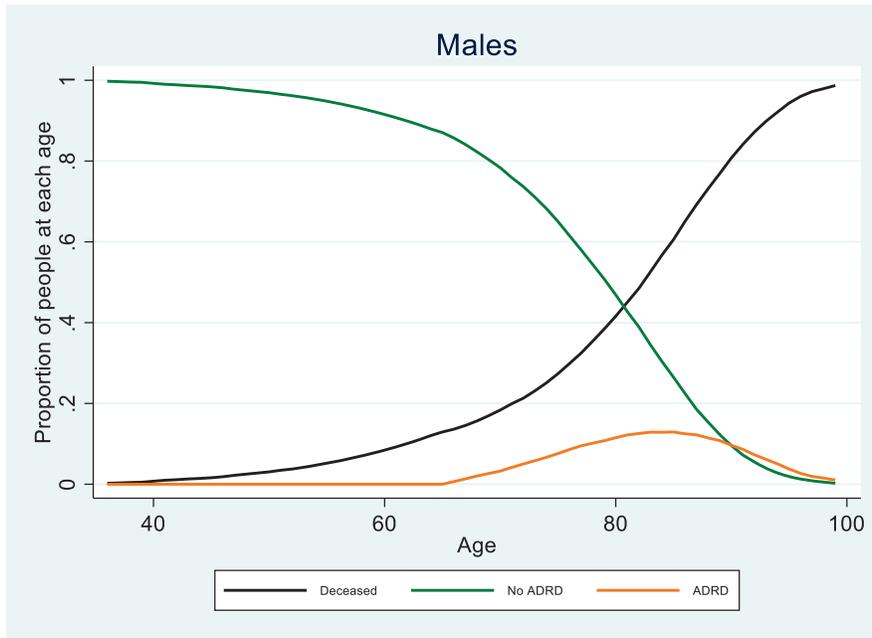
We model the probability of having onset of AD/ADRD for each individual. To do so, we estimated the following probability in equation B.1 for each gender g and age t using CMS data.

$$\psi_{gt} = \Pr(\text{AD/ADRD at age} = t + 1 | \text{alive at age} = t + 1, \text{no ADRD at age } t, \text{gender})$$

(B.1)

We do not assign anyone younger than or equal to 65 years old to AD/ADRD state ($i = 66 - 99$); that is, our model does not consider early-onset AD/ADRD patients. AD/ADRD is an absorbing state in our model, which means that once an individual is diagnosed, he/she lives with the condition until death. With these probabilities estimated, in the microsimulation model we take uniform random draws (u_{gt1}) from 0 and 1 for each individual at each age that did not have AD/ADRD in the prior year, model them as having been diagnosed with AD/ADRD in that year if the random draw is less than the probability, i.e. if $u_{gt1} < \psi_{gt}$. Figure B1 presents our simulated proportion of people at each age in each state of alive with AD/ADRD, alive without AD/ADRD, and deceased. The fraction of people with AD/ADRD peaks shortly after age 80.

Figure B.1. AD/ADRD Case Trend in Males and Females



Severity of AD/ADRD

Transition probabilities between AD/ADRD severity stages are based on Davis et al. (2018), Table 4. Davis et al. model seven states: normal, mild cognitive impairment, mild AD, moderate AD, severe AD, non-AD cognitive impairment, and death. We assign normal, mild cognitive impairment, and non-AD cognitive impairment into a category of non-AD/ADRD. The definition of mild AD/ADRD state by Davis et al. is having a clinical dementia rating (CDR) less

than 2, whereas patients in moderate AD state have CDR of 2 and patients in severe AD/ADRD state have CDR of 3.¹ The transition probabilities in Davis et al. (2018)'s Table 4 allow patients transition from more severe stages back to a milder stage to capture measurement noise. For age 65, we use the transition probabilities in Table 4 panel A. For age 75 and older, we use the transition probabilities in Table 4 panel B. For ages between 65 and 75, we use a linear interpolation of the transition probabilities. For example, the unconditional transition probability from mild to moderate for age 68 would be set to $0.19 + (0.21-0.19)/10*3=0.196$.

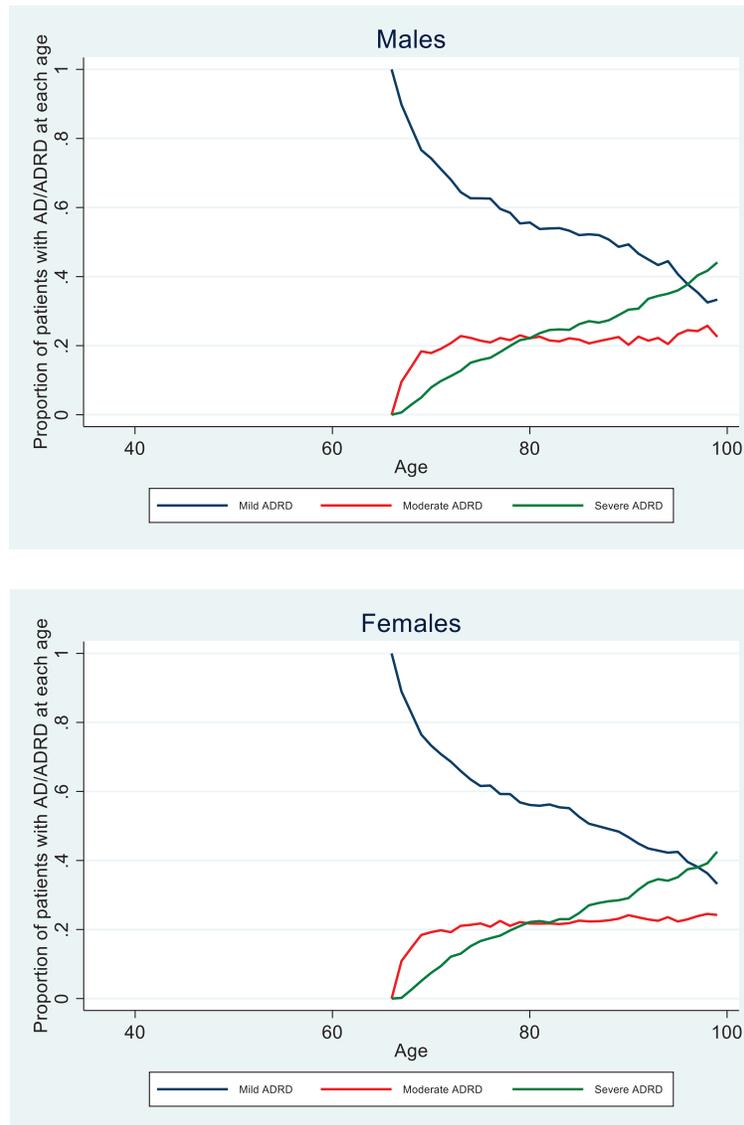
These represent the unconditional probabilities of transitioning, specifically, allowing for a transition into death. Our model instead is conditional on surviving at that age, and so we must adjust the transition probabilities. We do so recognizing that $Pr(transition|alive) = \frac{Pr(transition,alive)}{Pr(alive)}$. The numerator on the right hand side is contained in the numbers in Davis et al. Table 4. We must divide by the probability the person survives between the two years. We describe in the next section how mortality transition probabilities by age, gender, and AD/ADRD severity are calculated, which we use there.

With the adjustments to represent the conditional probability of transitioning into a different severity of AD/ADRD, we have probabilities of each transition. We take a random uniform draw u_{gt2} between 0 and 1. Then, for example, for a person who had mild AD/ADRD in the prior year, he/she is assigned to severe AD/ADRD if the random draw is less than the transition probability of mild to severe stage, i.e. if $u_{gt2} < Pr(mild\ to\ severe|alive)$. A random draw of people who had mild AD/ADRD in the prior year are assigned to moderate disease severity in an amount that exceeds the transition probability of mild to severe but is less than the sum of the transition probabilities for all transitions from mild: mild to moderate and mild to severe.

$$Pr(mild\ to\ severe|alive) < u_{gt2} \\ < Pr(mild\ to\ severe|alive) + Pr(mild\ to\ moderate|alive)$$

Figure B2 presents the simulated proportions of individuals in each severity group, conditional on being diagnosed with AD/ADRD.

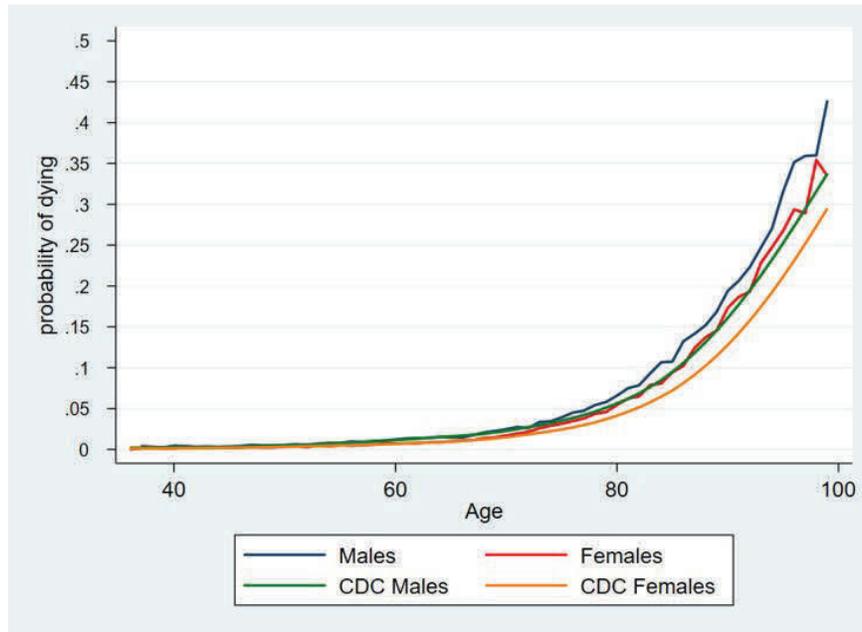
Figure B.2. AD/ADRD Stage Trend in Males and Females



Probability of Dying

We used the United States Life Table in 2017 released by Centers for Disease Control and Prevention (CDC) to assign probabilities of dying to individuals without AD/ADRD each year, conditional on age and gender.² For patients with AD/ADRD, probability of dying is assigned based on AD/ADRD stage, age, and gender. We generated the transition probabilities to death based on Davis et al. (2018) and adjusted for age and gender using the CDC probabilities of dying for the general population, so that the probabilities of dying for AD/ADRD patients are always higher than people without AD/ADRD conditional on age and gender. Figure B3 compares our simulated death probabilities with the CDC life tables.

Figure B.3. Probabilities of Dying in Simulated Cohort and in U.S. General Population



In addition to using Davis et al. (2018) to parameterize transitions between severity of AD/ADRD (as discussed in the previous section), we also use their paper to calculate the probabilities of dying at any given age, depending on gender and AD/ADRD severity. To do so, we use both Table 3 from Davis et al. (to examine differences by gender) and Table 4 (to differences by severity of AD/ADRD).

We start by using the AD/ADRD severity distribution conditional on age groups (65-74, 75-84, 85-94, 95+) from Davis et al. (2018) Table 3. To generate stage distribution for every age, we first assign median age for the severity distribution (70, 80, 90, 97). Next, we get female/male ratio for every severity group using the severity distribution conditional on gender from Davis et al. (2018). For example, when examining moderate AD/ADRD, Table 3 reports 418 women in the moderate group, and $681-418=263$.

$$\frac{\Pr(\text{moderate}|\text{female})}{\Pr(\text{moderate}|\text{male})} = \frac{418/(4962 + 1684 + 2001 + 418 + 183 + 1088)}{263/(18103 - (4962 + 1684 + 2001 + 418 + 183 + 1088))} = 1.1943 \quad (B.2)$$

We do this for each of the three severity groups to get the difference for women and men.

Next, we use this in combination with the overall CDC life tables for mortality rate. Below is an example using an individual age 70 with moderate disease severity. Using the law of total probability, we can rewrite the probability of having moderate AD/ADRD as in equation B3.

$$\begin{aligned}
& \Pr(\text{moderate}|\text{age } 70) \\
&= \Pr(\text{moderate}|\text{age } 70, \text{female}) \Pr(\text{female}|\text{age } 70) \\
&+ \Pr(\text{moderate}|\text{age } 70, \text{male}) \Pr(\text{male}|\text{age } 70) \quad (B.3)
\end{aligned}$$

We assume that the change in probability of being in a given severity stage by gender is constant over age (as we do not have age-specific values). Therefore, we can use

$$\begin{aligned}
& \Pr(\text{moderate}|\text{female}, \text{age} = 70) = 1.1943 \times \\
& \Pr(\text{moderate}|\text{male}, \text{age} = 70) \quad (B.4)
\end{aligned}$$

We can substitute equation B.4 into equation B.3. Furthermore, we use the 2017 CDC life tables to calculate $\Pr(\text{female}|\text{age} = 70)$ and $\Pr(\text{male}|\text{age} = 70)$. We also use the probability of being in a given severity stage by age from Davis et al.; for example, $\Pr(\text{moderate}|\text{age } 70) = 197/(3953 + 1371 + 1352 + 197 + 89 + 1421)$. This leaves us with one unknown in equation B3, namely $\Pr(\text{moderate}|\text{male}, \text{age} = 70)$. We solve for this and then solve for $\Pr(\text{moderate}|\text{female}, \text{age} = 70)$.

We repeat the steps above and we have $\Pr_{i,j}(\text{stage} = i|\text{male}, \text{age} = j)$ and $\Pr_{i,j}(\text{stage} = i|\text{female}, \text{age} = j)$, where $i = \text{mild}, \text{moderate}, \text{severe}$ and $j = 70, 80, 90, 97$. These values of j are chosen as the mid-points in the Davis et al. ranges. We perform linear interpolation to get the probabilities of all ages between 70 to 97 and linear extrapolation for age 65 to 69 and age 98 to 99.

We need these probabilities of being in a given severity stage by age and gender so as to adjust for the mortality rates. Davis et al. (2018) also report transition probabilities to death at age 65 and 75 for women and men combined, given the severity of ADRD. Similar to the approach in part 3.2, we use the transition probabilities to death in Table 4 panel A for patients age 65. For age 75 and older, we use the transition probabilities to death in Table 4 panel B. For ages between 65 and 75, we use a linear interpolation of the transition probabilities.

However, we are still missing the probability of dying in the next year for those without AD/ADRD for a given age and gender for these two ages, as well as more generally, the probability of dying at other ages for each gender and severity. For the former, we combine these transition probabilities to death with the probabilities of dying in any given age conditional on gender from CDC life tables, stage distribution conditional on age and gender from previous steps, and use the equation (B.5) below to get, for a given age and gender, $\Pr(\text{die}|\text{no ADRD}, \text{at age} = i, \text{gender})$. We do so by again using the law of total probability. This is shown in equation B.5.

$$\begin{aligned}
& \Pr_i(\text{die at age} = i + 1 | \text{alive at age} = i, \text{gender}) \\
&= \Pr(\text{die} | \text{no ADRD}, \text{at age} = i + 1, \text{gender}) \times \Pr(\text{no ADRD} | \text{at age} = i, \text{gender}) \\
&\quad + \Pr(\text{die} | \text{mild ADRD}, \text{at age} = i + 1, \text{gender}) \\
&\quad \times \Pr(\text{mild ADRD} | \text{at age} = i, \text{gender}) \\
&\quad + \Pr(\text{die} | \text{mod ADRD}, \text{at age} = i + 1, \text{gender}) \times \Pr(\text{mod ADRD} | \text{at age} = i, \text{gender}) \\
&\quad + \Pr(\text{die} | \text{severe ADRD}, \text{at age} = i + 1, \text{gender}) \\
&\quad \times \Pr(\text{severe ADRD} | \text{at age} = i, \text{gender}) \quad (B.5)
\end{aligned}$$

From equation B.5, we can back out the probability of dying given not having AD/ADRD. We estimated $\Pr(\text{die} | \text{no ADRD}, \text{at age} = i, \text{gender})$ separately at age 65 and age 75.

For the calculation of the probability of death at any age and gender for each severity group, we assume a linear adjustment to the underlying CDC mortality curve by severity, age, and gender. To do so, we calculated the hazard by the following equation (B.6) for $i = 65, 75$ and $j = \text{mild}, \text{moderate}, \text{severe}$:

$$\begin{aligned}
& \text{Hazard}_{i,j} = \Pr_{i,j}(\text{die at age} = i + 1 | \text{alive at age} = i, \text{stage} = j, \text{gender}) - \\
& \Pr(\text{die at age} = i + 1 | \text{alive at age} = \\
& i, \text{no ADRD}, \text{gender}) \quad (B.6)
\end{aligned}$$

We used linear interpolation to get hazard rates between age 65 and 75 and set constant hazards for $\text{age} \geq 75$ as the hazard of age 75. Finally, equation (B.7) below gives us the estimation for probabilities of dying conditional on any given age, AD/ADRD stage and gender:

$$\begin{aligned}
& \Pr_{i,j}(\text{die at age} = i + 1 | \text{alive at age} = i, \text{stage} = j, \text{gender}) \\
&= \Pr_i(\text{die at age} = i + 1 | \text{alive at age} = i, \text{no ADRD}, \text{gender}) \\
&+ \text{Hazard}_{i,j} \quad (B.7)
\end{aligned}$$

As before, we then took random uniform draws between 0 and 1, and if the uniform draw was below the probability, we assigned that person in the simulation to die that year.

Living in Nursing Homes

We estimated the probabilities of being institutionalized in a nursing home conditional on age using all available waves (through wave 12) the RAND HRS version Q. We first estimated the probability of moving into a nursing home for the non-AD/ADRD population. We did so

separately for women and men by fitting a general, non-linear monotonic increasing function of age on the probability of nursing home entry. Specifically, we used a logistic function (symmetric sigmoid shape) using Stata's nl package with the log4 model.

$$\Pr(NH|Non - AD, gender) = b_0 + \frac{b_1}{1 + \exp(-b_2 * (age - b_3))} \quad (B.8)$$

Where $\Pr(NH|Non - AD, gender)$ is the probability of nursing home entry for non-AD/ADRD persons. We estimated this for individuals age 50-94, and then predicted the smooth line from the estimated parameters to calculate the probability of nursing home entry or non-AD/ADRD populations.

We used the same data to calculate the probability of nursing home entry for AD/ADRD patients. Here, we had fewer data points, and so we did not estimate the probability of nursing home entry with a non-linear function. Instead, we estimated how much higher the probability of nursing home entry was for AD/ADRD patients compared to non-AD/ADRD patients with a linear time trend, as described in equation B.9.

$$\Pr(NH) = a_0 + a_1(Age - 65) + a_2AD + a_3(Age - 65) \times AD \quad (B.9)$$

For any age and gender then, we can adjust and calculate the probability of nursing home by adding $\widehat{a}_2 + \widehat{a}_3(Age - 65)$ to the probability of nursing home entry calculated for the non-AD/ADRD population using the logistic function (symmetric sigmoid shape) described above. However, this does not yet depend on AD/ADRD severity but is the average across severity for any given age/gender. To adjust for severity, we use the transition probabilities of being institutionalized from Spackman et al. (2012), Table 4. Spackman and colleagues provide transition probabilities by severity, but do not allow them to differ by age or gender. We use these to benchmark the *difference* in the probabilities of nursing home entry. That is, they calculate $\Pr(NH|Mild AD) = 0.01$, $\Pr(NH|Moderate AD) = 0.034$, and $\Pr(NH|Severe AD) = 0.066$.

From this we, calculate the difference in the probabilities. From the law of total probability, we have for any given age and gender

$$\begin{aligned} \Pr(NH|AD) = & \Pr(NH|mild AD)\Pr(mild AD) + \Pr(NH|mod AD)\Pr(mod AD) \\ & + \Pr(NH|severe AD)\Pr(severe AD) \end{aligned} \quad (B.10)$$

The key is that we have $\Pr(NH|AD)$ calculated from the HRS for each age and gender. We additionally have $\Pr(mild AD)$, $\Pr(mod AD)$, and $\Pr(severe AD)$ estimated for every age and gender from Davis et al. (2018). From the Spackman et al. differences, we have two more equations (the differences between moderate and mild as well as the difference between severe

and mild, for example), which leaves us with three equations and three unknowns ($Pr(NH|mild AD)$, $Pr(NH|mod AD)$, and $Pr(NH|severe AD)$), which we solve for at each age and gender. This gives us a full set of probabilities of nursing home entry for every age and gender, for non-AD/ADRD, as well as AD/ADRD by severity. Figure B4 and B5 present the simulated care trends.

Figure B.4. Care Trend in Non-AD/ADRD Males and Females

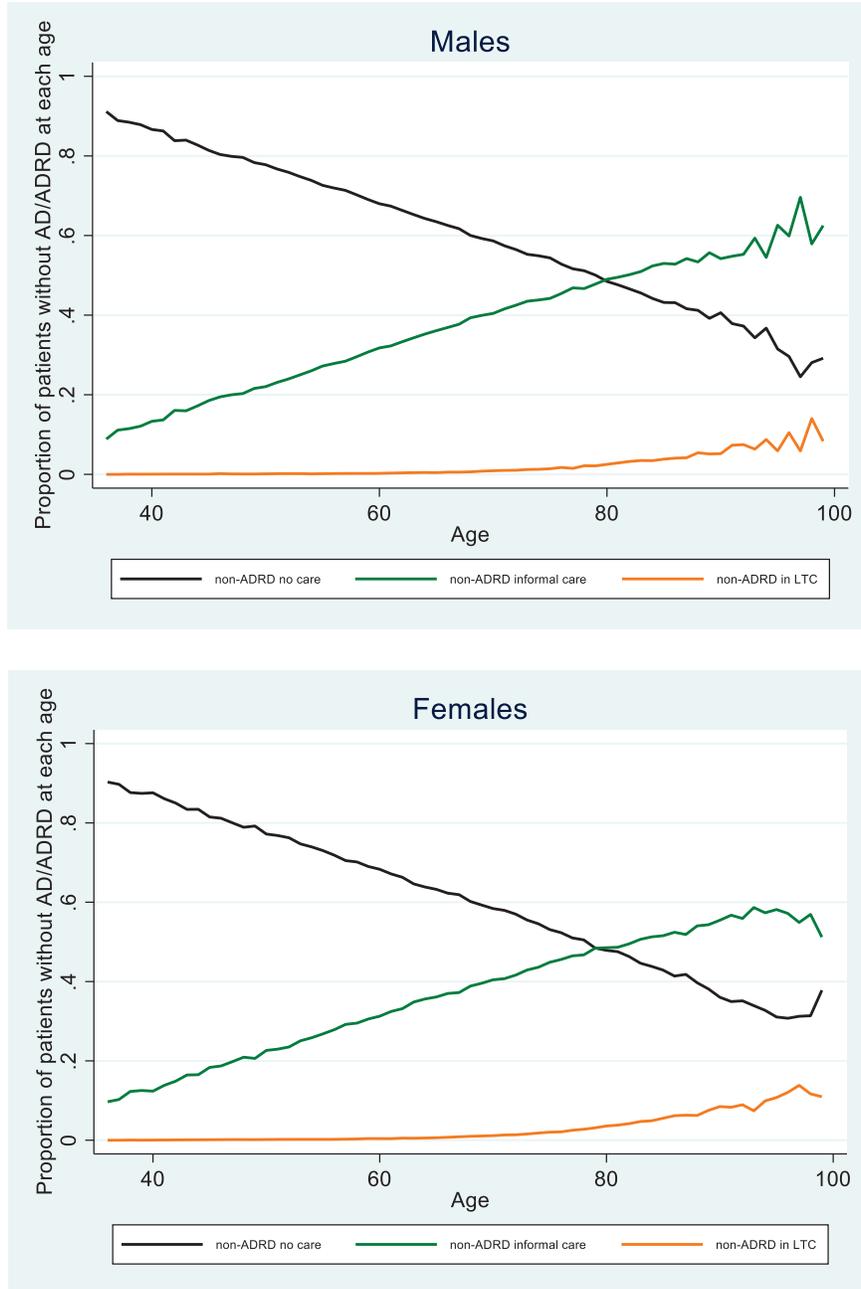
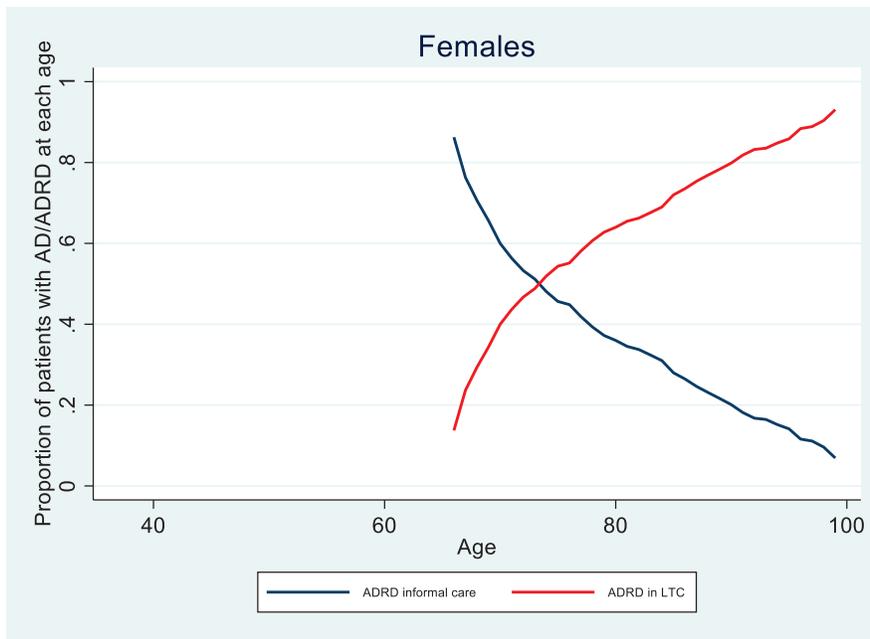
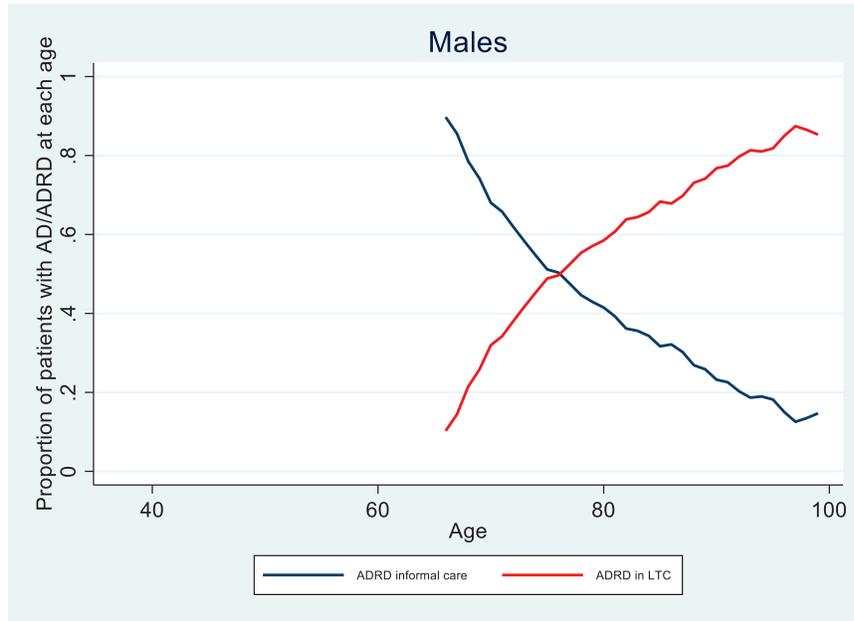


Figure B.5. Care Trend in AD/ADRD Males and Females



Receiving Informal Home Care

We assumed that all community-dwelling AD/ADRD patients receive some informal home care, regardless of disease severity. For people without AD/ADRD living in the communities, we randomly assigned 15 percent of non-AD/ADRD individuals in the community younger than 65 years old and 45 percent of non-AD/ADRD individuals older than 65 years old to be receiving informal home care that year, based on Kaye (2013). (Kaye, 2013)

Cost Model

All costs were projected over 30 years assuming the investment is a one-time cost incurred in 2019. Future medical costs were normalized to 2017 USD using the Personal Consumption Expenditures (PCE) Health index. We adjusted for time preferences and the opportunity cost of investment by discounting future costs and QALYs at an annual rate of 5 percent. Figures B.6 and B.7 show the average costs—across both AD/ADRD and non-AD/ADRD patients—by age, based on our simulations. We describe each in turn.

Figure B.6. Average Cost Conditional on Age for Males

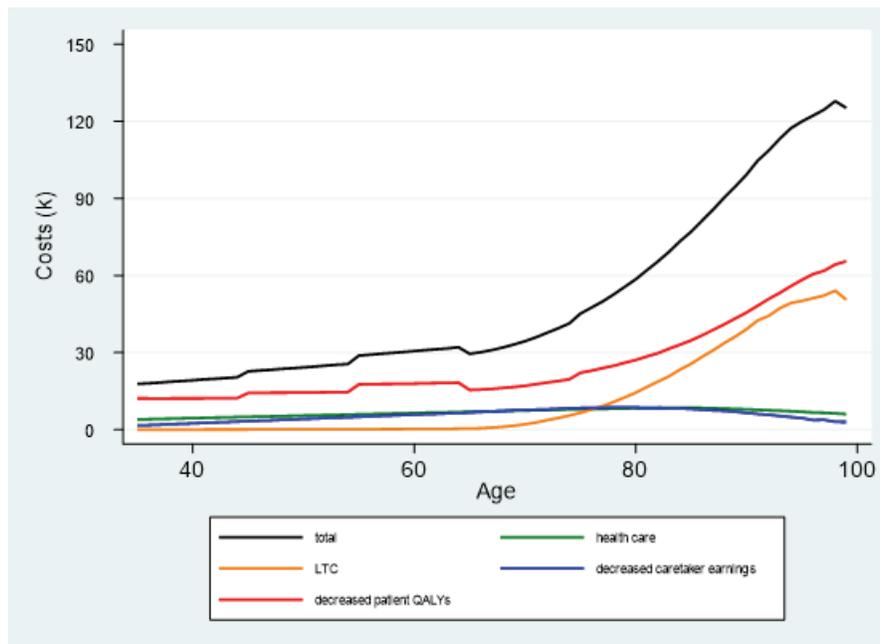
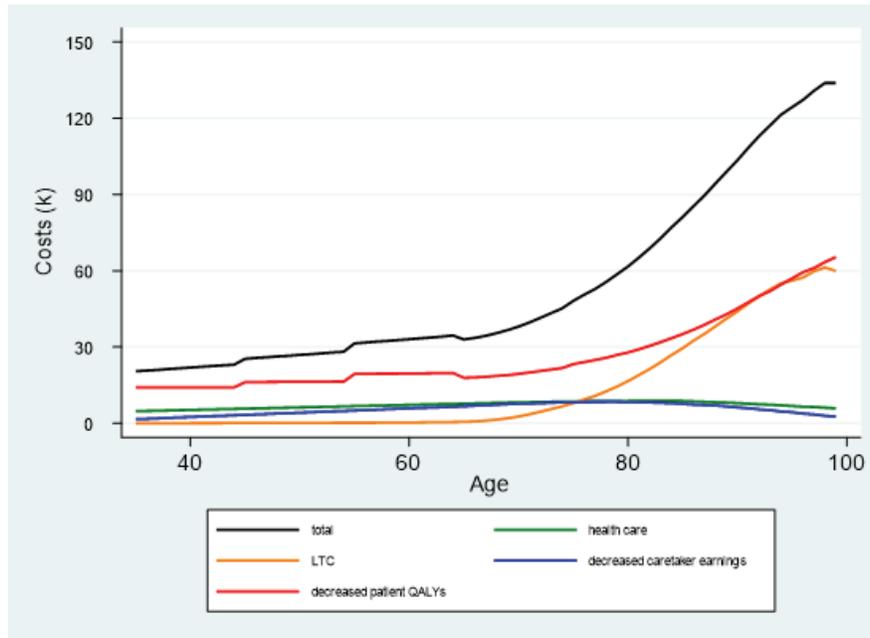


Figure B.7. Average Cost Conditional on Age for Females



Health Care Costs

We estimated the average health care costs (not including nursing home stays) conditional on age and gender using the 2011-2017 Medical Expenditure Panel Survey (MEPS) for individuals without AD/ADRD. For AD/ADRD patients, we assigned them the average health care costs of AD/ADRD patients conditional on gender. There is no variation in the assigned health care costs based on age for AD/ADRD patients because of the difficulty to estimate those from the small sample size of AD/ADRD patients in MEPS (although we also found little difference in the health care costs when we did estimate, likely because the MEPS does not include nursing home stays or costs). In view of the impact of insurers on medical spending, we used ordinary least squares regression to estimate total medical spending (medical spending from all payment sources) controlling for year, age, gender, and insurer type (Medicaid, Medicare, Tricare and private insurers). Instead of modelling the status of receiving formal home care and assigning formal home health care costs conditionally, we assigned the total health care costs that include formal home care. Informal home health care is not included in the total health care costs from MEPS but estimated using productivity loss of caregivers in the next section. Since MEPS is representative of only the US civilian non-institutionalized population, health care costs for individuals in nursing homes were estimated separately. However, we chose to assign the same average total health care costs for institutionalized population on the assumption that their health care costs (not including the costs of the nursing home) do not differ from community-dwelling individuals.

Productivity Loss of Informal Home Caregivers

Costs of informal home care are calculated using the productivity loss of informal home caregivers. All informal caregiver earnings are based on those of non-Hispanic white males to correct for gender and race-based labor market discrimination. The hourly wage for non-Hispanic white males estimated from MEPS is around \$23.86 for workers younger than 65 and \$23.60 for workers older than 65. The steps of calculating the productivity loss are as follows:

1. We assign 30 percent of caregivers for individuals receiving informal home care to be older than age 65. The percentage of caregivers older than age 65 (30 percent) is similar in individuals without AD/ADRD and AD/ADRD patients who receive informal home care (“2020 Alzheimer’s disease facts and figures,” 2020; Spillman et al., 2014).
2. The average hours spent on caretaking for AD/ADRD patients, not conditional on receiving informal home health care is based on Friedman et al. (2015) exhibit 2. For individuals without AD/ADRD and AD/ADRD patients in mild stage receiving informal home care, the hours per month caregivers spent are 65.8. We assign AD/ADRD patients in moderate stage with 89.3 hours per month of informal caregiving and 171.1 hours per month for AD/ADRD patients in severe stage.
3. By multiplying the hourly wage of non-Hispanic white males estimated from MEPS with the average informal caregiving hours from step 2, we get productivity loss in a year of informal home caregivers for AD/ADRD patients in different stages, calculated as follows:
 - a. Mild AD/ADRD or non-AD/ADRD, caregivers younger than 65: $23.86 \times 65.8 \times 12 = 18839.856$
 - b. Mild AD/ADRD or non-AD/ADRD, caregivers older than 65: $23.58 \times 65.8 \times 12 = 18618.768$
 - c. Moderate ADRD, caregivers younger than 65: $23.86 \times 89.3 \times 12 = 25568.376$
 - d. Moderate ADRD, caregivers older than 65: $23.58 \times 89.3 \times 12 = 25268.328$
 - e. Severe ADRD, caregivers younger than 65: $23.86 \times 171.1 \times 12 = 48989.352$
 - f. Severe ADRD, caregivers older than 65: $23.58 \times 171.1 \times 12 = 48414.456$

Nursing Home Costs

The cost of living in nursing homes is set at \$90,520 annually for non-AD/ADRD individuals and AD/ADRD patients in mild and moderate stage. This rate is based on the reported national average for a private room in the Market Survey of Long-Term Care Costs published by MetLife Mature Market Institute in 2012 (MetLife Mature Market Institute, 2012). For AD/ADRD patients in severe stage, we assign the costs of living in nursing homes twice as much as the average rate (\$181,040/year). The rise in costs is to reflect the intensity of care and unaccounted health care costs for severe AD/ADRD patients.

Quality of Life Loss

The value of one quality of life year (QALY) is set between \$50,000 to \$150,000 by the Institute for Clinical and Economic Review, and we choose to use \$100,000 in our model.

Although \$50,000 threshold is arguably the “rule of thumb” in cost-effectiveness analysis in health care sector, but we believe that this value is an underestimation since it has never been adjusted for advances in technology, increased costs of care, and change in valuations about life over time.

We assign health utilities based on Health Utilities Index Mark 2 (HUI2) to the general population conditional on age and gender from Fryback et al. (2007) table 3, and AD/ADRD patients conditional on disease severity based on Neuman et al. (1999) table 2. Although Neuman et al. (1999) also report health utilities of caregivers for AD/ADRD patients, the utility levels are almost identical to those from Fryback et al. of the general population conditional on age and gender, so we choose to not consider lost QALYs from caregivers in our model.

We calculated lost QALYs for both non-AD/ADRD and AD/ADRD patients by subtracting their health utilities from 1, i.e. perfect quality of life. If someone is living in a nursing home, an additional 0.1 is added to the lost QALYs (Zissimopoulos, Crimmins and St Clair, 2014). Persons who die in the simulation will have a lost QALY of 1 in the year they die, and for all the subsequent years in the time horizon. Below is an example of the calculation of lost QALYs for an individual with mild AD/ADRD not living in a nursing home.

$$1 - 0.69 \text{ (HUI2 for mild AD/ADRD patients)} = 0.31$$

If this individual enters a nursing home, the lost QALYs would be:

$$1 - 0.69 \text{ (HUI2 for mild AD/ADRD patients)} + 0.1 = 0.41$$

If the individual dies, the lost QALYs each year would be 1.

Return on Investment

Initially the target return on investment was set between 5 and 15 percent, and parameters were varied to achieve an ROI in this range. This proved a difficult task to calibrate, given small changes in the parameter could generate small changes in the outcomes (that is, only affecting a few people in our simulation), which when multiplied out represented large differences. For example, a small change which resulted in one person out of the one million people in our microsimulation having only one fewer year in a nursing home out of the thirty years simulated would represent a large shift in cost savings. With one million people in our sampling frame, and nearly 200 million in the underlying US population, each individual in the microsimulation sample represents nearly 200 people in the US population. Thus, the one fewer year of nursing home for one person, valued at \$100,000, would represent a cost reduction of \$100,000 times 200, or \$20 million for the economy. Therefore, we instead focused on pre-chosen health improvements, and evaluated the (typically much larger than 10-15 percent) ROIs associated

with those health improvements, as well as the probability of success necessary for that cost improvement to yield an expected ROI of 15 percent. These methods are described below.

Calculation of Return on Investment

The return on investment, or ROI, is calculated using the following equation B.11:

$$ROI = 100 * \left(\frac{cost_s - cost_n - Investment}{Investment} \right) \quad (B.11)$$

Where

- $cost_s$: US healthcare costs for age 35 and older under *status quo* health
- $cost_n$: US healthcare costs for age 35 and older with the new health improvement
- $Investment$: increase in investment.

Expected ROI Under Uncertain Probability of Success

The return on investment process described in the previous section assumes that the investment will with certainty yield the health improvement and thus the cost savings. However, this is not a realistic representation of the risky nature of investments into health. We thus additionally frame an investment as a Bernoulli trial, that is, a binary outcome with a probability of success P achieving the given health improvement (and associated reductions in healthcare costs), or $(1 - P)$ probability of having no health improvement and remaining at the *status quo* healthcare costs. We write this as follows, where $cost_i$ is the healthcare cost under investment:

$$E[cost_i] = P * cost_n + (1 - P) * cost_s \quad (B.12)$$

We can combine equation B.12 with the ROI by connecting it to a specific ROI. For example, we can estimate the probability of success that is related to an expected ROI of 15 percent by

$$15 = E \left[100 * \left(\frac{cost_s - cost_i - Investment}{Investment} \right) \right] \quad (B.13)$$

At the investment decision point, the only uncertainty is what the cost under investment ($cost_i$) will be—either $cost_n$, the new healthcare cost under health improvement from the investment, with probability P , or $cost_s$, the *status quo* healthcare cost, with probability $(1 - P)$. Solving for the expected cost in the equation, we have

$$E[cost_i] = cost_s - 1.15 * Investment \quad (B.14)$$

Putting the two equations together, we can solve for P as

$$cost_s - 1.15 * Investment = P * cost_n + (1 - P) * cost_s$$

$$\Rightarrow P = \frac{1.15 * Investment}{cost_s - cost_n}$$

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