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WHAT CAN ECONOMICS SAY ABOUT ALZHEIMER'S DISEASE?

Amitabh Chandra
Courtney Coile
Corina Mommaerts

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ABSTRACT

Alzheimer’s Disease (AD) affects one in ten people aged 65 or older and is the most expensive disease in the United States. We describe the central economic questions raised by AD. Although there is overlap with the economics of aging and health, the defining feature of the “economics of Alzheimer’s Disease” is an emphasis on choice by cognitively impaired patients that affects health and financial well-being, and situations in which dynamic contracts between patients and caregivers are useful but difficult to enforce. A focus on innovation in AD prevention, treatment, and care is also critical given the enormous social cost of AD and present lack of understanding of its causes, which raises questions of optimal resource allocation and alignment of private and social incentives. The enormous scope for economists to contribute to our understanding of AD-related issues including drug development, efficient care delivery, dynamic contracting, long-term care risk, financial decision-making, and the design of public programs for AD suggests a rich research program for many areas of economics.

Amitabh Chandra
John F. Kennedy School of Government
Harvard University
79 JFK Street
Cambridge, MA 02138
and NBER
amitabh_chandra@harvard.edu

Courtney Coile
Department of Economics
Wellesley College
106 Central Street
Wellesley, MA 02481
and NBER
ccoile@wellesley.edu

Corina Mommaerts
Department of Economics
University of Wisconsin-Madison
1180 Observatory Drive
Madison, WI 53706
and NBER
cmommaerts@wisc.edu

Alzheimer's Disease (AD), a progressive neurocognitive disease of the brain that eventually causes dementia, is the costliest disease in the United States. AD is projected to account for in excess of $350 billion or 8 percent of total US health care spending in 2021, roughly the same amount as cancer and heart disease combined (Alzheimer's Association 2021; Centers for Disease Control 2021). Much of this goes to long-term care, as nearly half of nursing home residents have a dementia diagnosis and 70 percent of AD patients die in a nursing home (Harris-Kojetin et al. 2016; Joyce et al. 2018). Informal caregiving costs are of a similar order of magnitude. AD affects an estimated 6 million Americans and is projected to affect 14 million by 2050 (Hebert et al. 2013); worldwide, dementia affects 50 million people and has a social cost of 1.1 percent of global GDP (WHO 2020). As seen in Figure 1, AD rates rise rapidly with age – more than 10 percent of those over age 65 and 40 percent of those over age 85 have AD (Hudomiet, Hurd, and Rohwedder 2018) – and there are substantial racial disparities (Mayeda et al. 2016). Individuals with AD likely hold trillions of dollars of assets given the $35 trillion held by households over age 70 (Eisen and Tergesen 2021).

Figure 1: Dementia incidence by age and race-ethnicity, 2000-2013

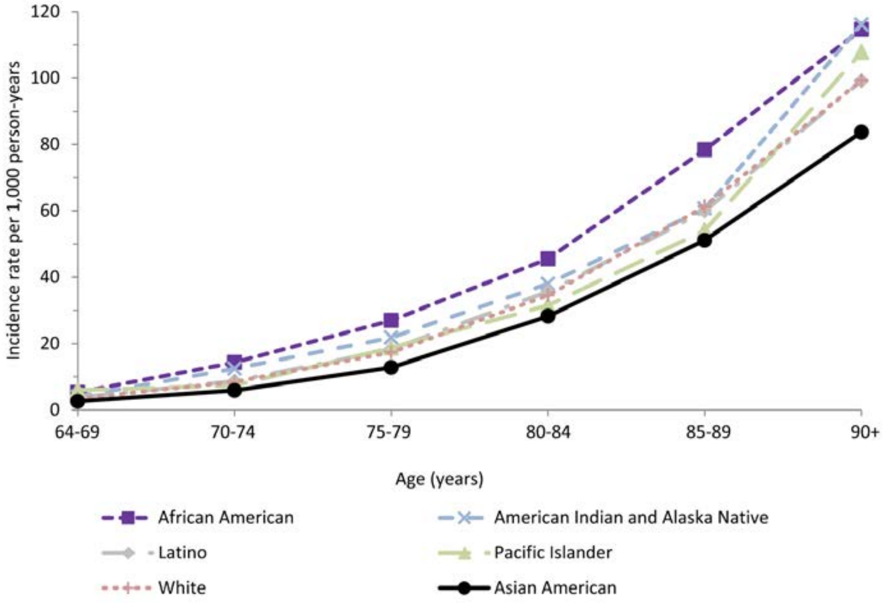

Fig. 2. Dementia incidence rates per 1000 person-years by age and race-ethnicity, 2000–2013.

Reprinted from Mayeda et al., 2016. Figure shows annual incidence (new cases per 1,000 people, a flow measure), which is different than prevalence (a stock measure).

Although the enormous costs of AD are evident, it may not be immediately clear why the disease merits special attention from economists. How is the "economics of Alzheimer's Disease" anything more than the application of the economics of aging and health to a specific disease, or different from the economics of cancer? What can a social science discipline like economics have to say about a particular medical condition?

The defining feature of the economics of AD is an emphasis on cognitive decline and decision-making by cognitively impaired patients that affects health and financial well-being. Such decision-making may be different from “behavioral bias,” and raises a host of issues where dynamic contracts between patients, caregivers, insurers, and providers of financial services are useful for well-being but difficult to enforce, highlighting a role for regulation. Existing economic theory as well as new models may be needed to explain the behavior of cognitively impaired patients, their family members, and the firms that provide services to this population.

The other central topic in the economics of AD is innovation in prevention and treatment. Issues like the role of basic science as a public good and need for adequate incentives for innovation, although not exclusive to AD, are uniquely relevant here. The social value of AD innovation to current and future generations is enormous, but the underlying etiology of AD is not well understood and represents a fundamental market failure, as the value of such insights cannot be appropriated and so are less likely to be developed. This leaves pharmaceutical firms without clear targets to pursue and society without knowledge of how to reduce AD through prevention. Economics can offer insights into the optimal allocation of resources to basic science, research on therapeutics, and behavioral interventions, and into policies for aligning private and social incentives for innovation, prevention, and treatment.

In this essay, we describe the central economic questions raised by AD. We begin by presenting a simple economic framework that lays out how an individual at risk of developing AD might approach care, insurance, and saving decisions as well as how the social planner might evaluate investments in AD research. This framework serves as the roadmap for our subsequent discussion of AD innovation, care and insurance, and financial decision-making. Our primary goal is to elucidate areas in which there is scope for economists to engage with AD-related issues. Though we often refer to AD, our discussion is broadly relevant to other dementias and the full spectrum of cognitive impairment. We discuss existing AD-related research, but also draw heavily on non-AD-specific work to elucidate the potential for future work on AD. In discussing areas for future research, we highlight both questions that can be readily addressed with existing economic tools and questions that may require methods and tools to be adapted or developed.

1 Conceptual framework for the economics of Alzheimer’s Disease

We begin this essay with a simple economic framework to ground our discussion of the central economic questions raised by AD. Equation (1) below describes a two period model of utility over consumption and health in which individuals face a probability π of becoming sick with AD in the second period, and individuals derive utility over non-health consumption c in both periods and health h in the second period:

$$V = u(c_1) + \beta[(1-\pi)u(c^w, h^w) + \pi u^s(c^s, h^s)] \tag{1}$$

where β is the discount factor, w and s superscripts denote individuals who are well and sick with AD, respectively, and utility is increasing and concave in all arguments. Developing AD results in a reduction in health ($h^s < h^w$), can be costly to manage ($c^s < c^w$), and may also alter one's underlying preferences u^s.

Several tools are available to the individual and society to improve well-being in the face of AD risk, including:

- Technologies R_1 to reduce the probability π of developing AD. This is typically achieved through research and development of new therapeutics that might remove the likelihood of Alzheimer's completely, but could also include broader notions of technologies, such as lifestyle changes and public health interventions.
- Technologies q chosen by individuals and regulations R_2 to improve health h^s in the AD state. These technologies could consist of higher quality care, which could incorporate formal (nursing home care and home aides) or informal (family members) sources of care, as well as medical treatments, some of which may also reduce π and thus be affected by research and development R_1. Regulations could include nursing home staffing ratios or licensing requirements for home health aides.
- Technologies and regulations to improve financial well-being in the AD state c^s. This is traditionally achieved through insurance arrangements offered by the market or government to smooth consumption over time and between healthy and sick states. Regulation R_2 can also affect financial well-being in the AD state, for example, through screening of financial transactions to identify predatory schemes.

Rewriting Equation (1) with these technologies gives:

$$V(R_1, R_2) = u(c_1) + \beta[(1 - \pi(R_1))\, u(c^w, h^w \mid R_1, R_2) + \pi(R_1) u^s(c^s, h^s(q) \mid R_1, R_2)] \qquad (2)$$

These technologies come with costs: research and development R_1 can carry enormous price tags and added uncertainty; regulation R_2 can add to the cost of services; high quality care and treatments q for those with AD can be prohibitively expensive; and insurance markets for care related to AD are rife with market failures that result in inefficiently high coverage costs. In the language of economics, improving welfare within this framework involves a budget constraint, which makes the economics of AD ultimately a problem of resource allocation. Although some of these technologies are individual-level allocations (e.g., the decision to use higher quality care or purchase insurance), others are regulatory in nature or more similar to public goods that may require collective solutions through government intervention (e.g., research and development for therapeutics). This suggests (at a minimum) two decision-makers to this problem: an individual decision problem conditional on society's choices of research and development R_1 and the regulatory environment R_2, and society's decision problem accounting for individual decision-making in response.[1]

Solving this problem backwards, individuals with AD in the second period choose spending on care q (beyond the necessary level of care L), conditional on their first period choice of insurance coverage x, savings a, and society's choice of R_1 and R_2:

$$\max_{q} u^s(c^s, h^s(q) \mid a, x; R_1, R_2) \quad \text{subject to } c^s = a - (1 - x)(L + q)$$

which yields the optimality conditions $(1 - x)\frac{\partial u^s}{\partial c^s} = \frac{\partial u^s}{\partial h^s}\frac{\partial h^s}{\partial q}$ that optimal spending on care q is at the point where $(1 - x)$ dollars for consumption yields the same marginal benefit as a marginal increase in health implied by a dollar spent on q.[2]

Given this second period solution, individuals in the first period choose how much of their resource endowment y to save (a) and how much insurance coverage x to purchase that pays out in the second period in the AD state, conditional again on society's choice of R_1 and R_2:

$$\max_{a,x} u(c_1) + \beta[(1 - \pi(R_1))\, u(c^w, h^w \mid R_1, R_2) + \pi(R_1) u^s(c^s, h^s(q) \mid R_1, R_2)]$$

$$\text{subject to } y = c_1 + a + \tau + x p_x$$

This yields a standard Euler equation $\frac{\partial u}{\partial c_1} = \beta(1 - \pi)\frac{\partial u}{\partial c^w} + \beta\pi\frac{\partial u^s}{\partial c^s}$ that balances the marginal benefit of a dollar prior to retirement with the expected discounted marginal benefit of a dollar in the second period. It also yields the optimality condition for insurance coverage $p_x\frac{\partial u}{\partial c_1} = \beta\pi(L + q)\frac{\partial u^s}{\partial c^s}$ that optimal insurance coverage is at the point where p_x dollars for consumption in the first period yields the same expected discounted marginal benefit as $(L + q)$ dollars in the sick state.[3]

The collective problem facing a social planner for a population of size N is then:

$$\max_{R_1, R_2, \tau} \textstyle\sum_N V(R_1, R_2) \quad \text{subject to } R_1 = N\tau \tag{3}$$

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[1] There are, of course, many other agents making important decisions regarding the economics of AD including family members' decisions to provide care and health care provider and pharmaceutical company decisions. We abstract from these decision-makers here, but elaborate on their role in later sections.

[2] The solution for individuals without AD is trivially $c^w = a$.

[3] With actuarially fairly priced insurance and equivalent marginal utility functions in the sick and healthy states ($u^s(c^s) = u(c^w)$), which could arise if $u^s() = u()$ and consumption and health are separable, for example), this would result in full insurance; departures from this result could arise from market or behavioral frictions or state-dependent utility functions.

where R_1 is funded by per-capita taxes and N could consist of the current population of a country, the world, or even many generations of individuals.[4] This simple framework does not explicitly formalize the constraints related to R_2, but these could include constraints both chosen by the social planner on individual choice (e.g., regulating the types of financial products available to consumers) and on the ability of the planner to impose optimal regulation that emerge from a political process (Acemoglu and Robinson 2013). To the extent that R_1 is costly and the gains to research and development are uncertain (e.g., $\pi'(R_1)$ is not always increasing in R_1), this problem generates a trade-off between investing in technologies to reduce the probability of AD (or improve health if one has AD) and improving mechanisms that provide high quality care and financial protection conditional on experiencing the disease (q, x). Current generations will favor investments in the latter, but a broader view of society may favor the former.

Thus far, this framework is not unique to AD and could be used to understand decision-making and welfare for other diseases, such as cancer. Our discussion becomes specific to AD when we consider particular features of AD, such as a potential inability of cognitively challenged patients to make optimal decisions about care q or financial decisions about time (for example, within an expanded model with multiple periods in the AD state). These issues suggest the importance of alternative arrangements like altruistic agents or longer-term contracts. The latter, however, may be particularly difficult to enforce for populations with AD because of the inability of a cognitively challenged patient to monitor quality of care. The regulatory environment R_2 may provide another mechanism for assuring quality in care settings or financial services. AD may also alter one's preference structure u^s in unforeseeable ways, thus making planning for such an event more challenging. Lastly, unlike many other diseases, the etiology of AD is poorly understood and at the time of this writing there are no meaningful therapies for reducing π or improving h^s. Given the long arc of therapeutic development R_1 from basic science research to drug commercialization for AD, incentives to innovate by private pharmaceutical companies may be particularly misaligned with social incentives.[5]

This simple framework organizes our discussion. Our starting point in Section 2 is a brief review of the disease that informs h^s and the probability of getting the disease π. In Section 3, we turn to the challenge of producing technologies R_1 that reduce π or improve h^s through research and development. In Section 4, we discuss care choices q, insurance choices x, and regulations R_2 for health care and long-term care for AD. Section 5 discusses savings choices a and the challenges of financial decision-making and regulation from a broader life cycle perspective.

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[4] In the (perhaps more realistic) case of the social planner aggregating over many future generations, the discount rate δ of future generations becomes important (i.e., $\max \sum_g \sum_{N_g} \delta^t V(R_1, R_2)$).

[5] For example, if the social planner maximizes Equation (3) over many generations and discounts the utility of future generations by 2 percent (close to the social discount rate used in climate change), then the allocation that maximizes social welfare would likely be one that invests far more than current levels in R_1 to reduce (or ideally eliminate) the risk of AD.

2 Background on AD

We begin with a brief overview of key facts about AD that may be useful to economists interested in doing research in this area. A more extensive discussion is available in Mucke (2009) and Masters et al. (2015).

Alzheimer's Disease (AD) is a progressive neurocognitive disease of the brain that eventually causes dementia, which is not a disease but rather a general term for a loss of cognitive functioning that interferes with daily activities. AD is the most common cause of dementia, accounting for 60-80 percent of cases (Alzheimer's Association 2021). Relative to other causes of dementia, AD is uniquely characterized by the presence of specific biochemicals -- amyloid plaques and neurofibrillary tau-based tangles -- in the brain.

The progression of AD can be divided into three phases: preclinical disease, mild cognitive impairment (MCI), and Alzheimer's dementia. During the preclinical phase, biological signs of AD are present in the brain, but the individual maintains normal cognitive function. During the MCI phase, the individual has memory lapses, diminished planning and problem-solving skills, and other deficits, but maintains independence in instrumental activities of daily living (IADLs) like driving and managing finances. In the dementia phase, cognitive impairment is severe and the individual loses the ability to perform IADLs and basic activities of daily living (ADLs) like dressing and feeding, and becomes increasingly reliant on caregivers.

A biological diagnosis of AD relies on biomarkers, the presence of which (even in the absence of clinical symptoms) may reflect AD's true prevalence. Whereas until recently biological diagnosis was possible only via autopsy after death, there are now two tests that enable detection of biochemicals associated with AD: a positron emission tomography (PET) scan, which can look for amyloid deposits in the brain; and a spinal tap, which can detect changes in amyloid components and tau levels in cerebrospinal fluid. A clinical diagnosis of AD is based on physicians' application of clinical guidelines to assess patients with AD symptoms.[6] Cognitive impairment beyond what would be expected due to age is required; however, individuals without AD may experience normal age-related cognitive decline that eventually impedes their decision-making ability.[7] AD is generally diagnosed clinically, often with biomarker testing to confirm the diagnosis. Economists will primarily use the clinical definition of AD, as it is central to decision-making and more likely to be available in datasets, but should note that the prevalence of clinically diagnosed AD will understate the true prevalence of the disease.

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[6] Guidelines created by the American Psychiatric Association (Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, or DSM-V) and the National Institute on Aging and the Alzheimer's Association (NIA-AA) are available.

[7] Cognitive abilities are often measured in terms of fluid intelligence (reasoning with novel information) and crystallized intelligence (reasoning that relies on previous knowledge). Crystallized intelligence rises and fluid intelligence declines with age. As many real-world tasks rely on both in combination, performance often exhibits a hump-shaped pattern with respect to age, peaking in mid-life (Agarwal et al. 2009). For an introduction to cognitive aging, see Institute of Medicine (2015).

The average duration of AD from clinical diagnosis to death is 8-10 years, while preclinical and MCI stages can last two decades (Masters et al. 2015; Scharre 2019). Individuals with MCI have a 10-15 percent chance of developing Alzheimer's dementia each year (Michaud, Siahpush, and Murman 2017).

The risk of AD (π) is large. In the population age 65 and above, the estimated prevalence of AD is 10-30 percent and the incidence 1-3 percent (Masters et al. 2015). Age is the most important risk factor for AD, with incidence rates doubling every 5 to 6 years (Ziegler-Graham et al. 2008).

Women account for two-thirds of AD cases, but it is not known how much of the imbalance results from their longevity advantage vs. other factors (Beam et al. 2018). Relative to whites, Blacks are twice as likely and Hispanics one and one-half times as likely to develop AD or other dementias (Alzheimer's Association 2021). Racial disparities could stem from a higher prevalence of comorbidities like heart disease and diabetes, genetic and social factors, or bias in measurement of cognitive function (Anderson 2004; Manly and Mayeux 2004). Educational attainment is strongly associated with lower dementia risk (Meng and D'arcy 2012), potentially due in part to changes in brain structure that provide a "cognitive reserve" (Langa 2018).

A general lack of meaningful treatments for AD may be a consequence of the root causes of AD not being well understood, in contrast to understanding of other large diseases like cancer, heart disease, and diabetes. Prominent theories attribute disease progression to the build-up of amyloid plaque, tau tangles, or both, while another theory posits a role for immune system activation. Genes are a known risk factor, particularly for early-onset AD, which represents only a small share of cases.

3 Innovations to reduce prevalence and disease burden

With these key facts in mind, we now consider how economics can add to our understanding of AD. We begin with a discussion of disease prevalence (π), disease burden ($h^s - h^w$), and technologies to reduce prevalence and burden(R_1). The greater disease prevalence and burden the higher the social value of R_1 technologies and more pressing the need to investigate whether the correct incentives are in place to promote innovation. Innovations in diagnostic tools, medicines, and behavioral interventions are relevant, although the salient issues may differ in each case, as discussed below.

3.1 Measurement of disease burden

The concept of health capital (Grossman 1972), a standard way for economists to think about health, may be useful for calculating the burden of AD. Health capital is defined as the present discounted value of lifetime health, health at each future age being the probability of being alive at that age multiplied by the average quality of life among those alive at that age (or quality weight, ranging from 0 to 1) multiplied by the value of a year of life in perfect health. Quality weights may be estimated from health survey data by regressing self-reported health status on a set of disease indicators to obtain the estimated effect of each condition on health, then multiplying these coefficients by disease prevalence rates by age to obtain an age-specific quality weight (Cutler and Richardson 1999). Economists have estimated the value of a statistical life (or year of life) by estimating the wage premium for risky jobs and or consumers' willingness to pay for safety improvements as well as by contingent valuation (Viscusi 1993). The health capital model can be used to quantify the health cost of AD by using quality weights that include vs. exclude the risk of AD. The model can also be used to understand race and gender differences in prevalence and to project the benefit of treatments and lifestyle changes that delay disease onset or reduce its impact on quality of life.

Disability-free life expectancy, another health measure used by economists, could yield insights into the impact of AD on health. It is calculated like standard life expectancy, except that the probability of being alive at future ages is multiplied by the age-specific probability of being non-disabled. Defining disability as difficulty performing activities of daily living or instrumental activities of daily living, Chernew et al. (2017) estimate that changes in disease prevalence for AD and Parkinson's between the early 1990s and late 2000s led to a 0.13-year decrease in life expectancy and a 0.10-year decrease in disease-free life expectancy, mostly due to the change in AD. Combined with a value of statistical life, estimates such as these can also be used to evaluate disease burden or societal willingness to pay for changes in disease prevalence or burden.

In practice, micro-simulation models are useful for estimating changes in health and health care costs that might result from changes in disease prevalence. Zissimopoulus, Crimmins, and St. Clair (2015) estimate substantial benefits from medical treatments that delay the onset of AD.

3.2 Behavioral interventions

Economics may also be useful for developing a better understanding of behavioral and social factors that affect the probability of developing AD (π) or muting its effects h^s. As noted above, the root causes of AD not being well understood, there may be modifiable risk factors for the disease. Behavioral interventions to prevent AD or slow disease progression, analogous to reducing cancer by not smoking and avoiding sun exposure, could be highly cost-effective given the high cost of AD and potentially low cost of behavioral modifications. It is also plausible that investments in public health, safety net, or education programs could affect AD. In our conceptual framework, all of these may be thought of as R_1 technologies that reduce the prevalence or burden of disease.

Unfortunately, an evidence base establishing the efficacy of behavioral interventions, particularly evidence from randomized controlled trials, is lacking. For example, medical conditions including hypertension and later-life depression are associated with increased risk of AD (Launer 2019; Diniz et al. 2013), as are behavioral risk factors including poor sleeping patterns, smoking, and lack of exercise (Mayo Clinic 2018) and environmental factors like air pollution (Block et al. 2012; Underwood 2017). Yet two recent reports conclude that current evidence does not justify large-scale public health investments aimed at preventing dementia, even as they acknowledge encouraging but inconclusive evidence that cognitive training, blood pressure management, and physical activity may protect against disease (AHRQ 2017; NAS 2017).

Given the paucity of reliable evidence for this potentially important channel, economists could usefully employ quasi-experimental methods to validate whether epidemiological risk factors represent causal effects or incidental associations. If the former, one can think about policy levers to manipulate them, if the latter, they are useful only for predicting the future risk of AD.

A research program would resemble the work economists have done to assess the causal effect of education on mortality (Cutler and Lleras-Muney 2008) or in-utero exposure on later health (Currie 2011). In these literatures, quasi-random variation may derive from sibling differences (Johnson and Schoeni 2011), events like the 1918 influenza epidemic (Almond, 2006), or policy changes (Lleras-Muney 2005). Bishop, Ketcham, and Kuminoff (2018), in a study of air pollution and dementia that leverages variation in exposure arising from the Clean Air Act, illustrate how this approach could be used for AD-related work, and Banks and Mazzona (2012) exploit compulsory schooling laws in the United Kingdom to show the effect of education on cognitive ability in old age. Research identifying an association between state of birth and AD mortality (Glymour et al. 2011) highlights the need for future research to uncover specific childhood exposures or public programs that may account for this relationship.

3.3 Medicines

Although transformational medicine for AD might delay the onset of the disease and, ideally, reverse its course, affecting both π and h^s, there is little evidence that this goal is within reach near term. We review the current state of AD medicines and opportunities to accelerate innovation before discussing relevant economic incentives.

There are currently five FDA-approved treatments for AD. Four work to prevent the breakdown of neurotransmitters, the signaling devices neurons release to communicate with each other, which die as AD progresses. These drugs have a small effect on cognition and no effect on disease progression. The FDA’s June 2021 approval of a new drug (Biogen’s Aduhelm) for treating AD is the first such in two decades. The decision was controversial as the drug removes amyloid, which is implicated in AD, but has not been conclusively shown to improve cognition or functioning in AD patients. The relative paucity of AD treatments is not for lack of effort; pharmaceutical companies, biotechnology companies, and academic centers have tested hundreds of drugs in clinical trials (Cummings, Morstorf, and Zhong 2014). In 2019, 132 potential therapeutics were in the development pipeline (Cummings et al. 2019).

AD drug developers face several unique hurdles, the most significant being lack of understanding of the underlying etiology of the disease. AD patients experience a build-up of amyloid and tau in the brain, but it is not known if these biomarkers, individually or in combination, are a cause or effect of AD. Most drug development targets one or the other of these processes, but there are also therapeutic approaches that target the immune system, the genes implicated in AD, and neurons in the brain as well as non-traditional approaches.[8] This lack of understanding distinguishes the development of AD medicines from the development of new drugs for cancer, for example. Whereas cancer is many diseases involving different kinds of cancer cells, researchers' ability to identify proteins or enzymes that direct cell growth and replication for some cancers has enabled them to develop targeted therapies that block these messages and disrupt cancerous growth. AD researchers do not know whether blocking formation of amyloid deposits or tau tangles in the brain will slow disease progression.

The average cost of AD drug development is estimated (based on a host of assumptions) to be $5.6 billion, largely due to high preclinical and phase 3 trial costs (Cummings, Reiber, and Kumar 2018). This number greatly exceeds R&D costs for other drugs, for which the median cost of development is estimated to be $2.5 billion (DiMasi, Grabowski, and Hansen 2016). One reason for the high cost is the long trial time needed to see results, the average length of AD drug development being 13 years. We discuss the economic issues raised by these challenges in the next section.

Despite the challenges posed by not knowing the precise etiology of AD, many biotechnology and pharmaceutical companies persevere because of the promise of windfall profits. Given the large market, lack of competitors, and relatively poor prognosis for AD patients, demand for AD drugs is enormous, even for a medicine with a small or uncertain impact on disease burden. In the case of Aduhelm, for example, spending on the drug by the US Medicare program (which insures people over age 65 and those receiving disability insurance benefits) could be $29 billion per year if just one-quarter of beneficiaries who currently take an AD medication were to take this new drug (Cubanski and Neuman 2021).

3.4 Incentives for behavioral interventions and therapeutics

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[8] Immune system: As it is unknown whether the increased immune cells researchers see in AD are protective or harmful, both anti-inflammatory and pro-inflammatory strategies are being tested; trials of NSAIDs (i.e., ibuprofen), aspirin, and the immunosuppressant prednisone have all failed to reduce cognitive decline in mild AD, but other trials of anti-inflammatory and immune system stimulator drugs in AD patients are still underway. Genes: Lab tests of drugs targeting APOE4 appear to have met with some success, and early stage trials of high-risk individuals with two APOE4 genes are ongoing (Weill Medical College of Cornell University 2019); editing of BACE-1 or other genes that relate to the formation of amyloid plaques have been suggested, but not yet moved to human trials. Neurons: Regenerative biology and stem cell approaches aim to increase the number of neurons in the brain, reversing damage caused by AD; although success has been demonstrated in laboratory models, these approaches have thus far gained less traction than the amyloid and tau strategies, especially in the United States. Non-traditional: Blood from young donors having been prescribed off-label after studies found that it improved age-related cognitive impairment in mice, several trials are underway, although the FDA has recommended against this approach; Chinese regulators granted conditional approval to a mixture of carbohydrates extracted from kelp after a trial showed some effect on cognition among patients with mild AD (Trial Site News 2020).

We next discuss innovation in the development of R_1 technologies. Doing so requires an understanding of the production function that converts basic science research into patents and subsequently into medicines. Basic science refers to fundamental research detached from a particular disease or therapy. A prominent discovery of this type is the gene editing technology CRISPR. Discoveries resulting from basic science research typically cannot be patented because they refer to natural processes.[9] Disease-specific research often builds on insights gained through basic science research to develop diagnostic tools or treatments for specific diseases. Promising technologies are patented at this stage, and those that prove safe and efficacious in clinical trials receive FDA approval.

There are in the economics of pharmaceutical innovation three open questions as to whether economic incentives are sufficient for private firms to bring AD drugs to market. The first relates to the level of funding for basic science research, an area ripe with market failure. As the inability to patent discoveries discourages participation by private firms, public funding is necessary.

Government funding of basic science may be considered a “push incentive” as it lowers the cost of drug development by providing well-defined targets for disease-specific research as well as for tools like gene editing. There is evidence that public funding leads to commercializable insights, but the optimal level of basic science funding is unclear (Li, Azoulay, and Sampat 2017; Azoulay et al. 2019). A new area of research for economists is to measure the performance of the review process for basic science funding, there being a tradeoff between expert and unbiased reviewers, the former being more likely to identify more successful applications, but potentially less likely to bet on diverse (or high-risk, high-reward) ideas (Li 2017; Begley 2019).

Increasing amounts of public funding have been devoted to AD in recent years, the National Institute of Health being projected to spend \$3.1 billion on Alzheimer’s research in 2021, up from about \$450 million in 2011 (NIH 2021). Despite this commitment to research, little progress has been made developing therapeutics to prevent or slow the progression of AD due to the ongoing ambiguity about its cause and lack of validated surrogate endpoints (analogous to using cholesterol in heart-disease). Both obstacles are basic science hurdles unlikely to be resolved by private companies. This raises the possibility that reallocating some disease-specific funding, including funding for translational science, to basic science research on the fundamental biology of aging or regenerative biology might yield better insights over the long term, which is more aligned with the social planner’s preferences. Put differently, the market failure is in basic science research, not in translational research from which firms can appropriate the value of their investments.

The second question relates to the economics of “pull incentives,” which work by increasing the economic viability of R&D, principally through patents and FDA-granted exclusivity periods

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[9] For example, a 2013 US Supreme Court decision ruled that genes cannot be patented because they are “a product of nature”; as nothing new is created when a gene is discovered, there is no intellectual property to be protected.

during which generics cannot enter. Policies that increase expected profits will increase innovative activity in an area. The Orphan Drug Act, for example, increased potential profits by protecting manufacturers from generic competition for a longer period of time (pull incentive) while lowering R&D costs through tax credits (another push incentive) (Bagley et al. 2018).

Because the marginal costs of manufacturing drugs is relatively small compared to the large fixed costs of research and development, a variety of incentives, such as patents and exclusivity periods, are granted by governments to permit above-marginal cost pricing in order to induce innovation. Patents protect intellectual property by preventing competitors from using, making, or selling it for a specified period of time (usually 20 years from the date the patent was filed). In exchange for these rights, the patent holder discloses the existence of its innovation to the public. The key challenge here is whether the effective patent length is sufficient to make the expected value of an R&D investment profitable. The time required to bring a product to market after filing a patent effectively results in pharmaceutical companies having much briefer periods of patent exclusivity than other industries; the longer the clinical trials, the shorter the patent exclusivity life. For example, evidence from Budish, Roin, and Williams (2015) shows incentives to be greater for drug companies to develop drugs to treat late compared to early stage cancers because the latter require longer clinical trials to confirm their effectiveness at extending patients' lives.

Pull incentives operate by giving market power to an entrepreneur, which translates to higher prices. The high price for a meaningful medicine for AD will partially reflect the value of the medicine including any cost savings. Schemes such as Ramsey pricing may be of particular interest for a transformational drug for AD (one that helps almost all patients and would be unconscionable to deny), pointing to the importance of economic insights from price theory and industrial organization, entrepreneurial finance, and the economics of innovation.

It remains an open question whether more generous protections are needed to bring transformative treatments for AD to market. The slow progression of the disease makes for a shorter period of market exclusivity, although the large potential market size could nevertheless provide a sufficient return on investment. A better understanding of the root causes of the disease would increase the probability of success of any given drug investment. Venture capitalists play a large role in this enterprise, but not much is known about the quality of their decision-making, even though their decisions profoundly shape the medicines that come to market (Lerner and Nanda 2020; Chandra, Foroughi, and Mostrom 2020a). Williams' (2017) overview of the patent system through the lens of an economist includes frameworks for thinking about the incentives underlying the patent system.

It is important to note that there are few pull incentives for discovering non-therapeutic ways to prevent AD (e.g., better sleep habits) as such ideas will be difficult to patent. This leads to underinvestment in such discoveries and increases the need for push incentives to discover behavioral interventions. The importance of these interventions should not be discounted, their effect in other settings being impressive. Consider, for example, the evidence for lowering salt intake and other risk factors on mortality from coronary disease (as noted by Ford et. al. (2007) and Chandra and Skinner (2012)) and the advice to stop smoking on lung cancer.

The key challenge with pull incentives like patents, which reduce dynamic inefficiency, is the static inefficiency created by monopoly pricing (which can be overcome by generous public provision of health-insurance, as noted by Lakdawalla and Sood (2009)). This tradeoff is a central topic in economics (Finkelstein 2004). Among related insights on how innovation responds to pull incentives is Dubois et al.'s (2015) finding that on average it takes the promise of $2.5 billion of additional revenue to induce one more medicine; we emphasize the "on average" component of this statement. The distributional effects of price discrimination, which will likely occur for AD medicines owing to varying efficacy across individuals and varying willingness-to-pay across countries, although well understood by economists, are less clearly appreciated in the policy community (Chandra and Garthwaite 2017), highlighting another area in which economic insights can be powerful. A question that often arises is whether pull incentives in other nations induce innovation. Although this is possible, the market for medicines in other nations pales against that of the United States; Australia's market is 3 percent, Canada's 5 percent, and Germany's about 10 percent of the US market (Kleinrock and Muñoz 2020), suggesting a critical role for US incentives to induce innovation regardless of where companies are based.

The third question relates to follow-on innovation in AD. Patents can generate incentives for inventions, declaration of an invention to the public accommodating learning, but not copying, as well as follow-on innovation by competitors once a patent expires, both of which can increase social welfare. Too expansive or lengthy a patent could induce further innovation initially, but discourage follow-on innovations in life saving treatments as well as reward infra-marginal medicines more than is required to be launched. Because AD treatment will likely involve multiple drugs for multiple targets, the tradeoffs surrounding infra-marginal medicines and follow-on innovation may be particularly salient for research and development. Frameworks used by economists, as summarized by Lakdawalla (2018), are central to making these determinations.

The key point for inducing new treatments for AD is that, being a complicated disease it is unlikely that a single treatment will be effective. As with oncology treatments, society will have to ensure that a variety of treatments come to market, different treatments for different targets. Combination therapies also reflect the complementary effects medicines can have, the value of one medicine being increased by the presence of another. This feature may provide incentives for firms to partner to capture the value of combination therapies while also increasing the likelihood of static deadweight loss from less competition. Understanding the tradeoffs between long-run social welfare and short-run deadweight loss is an area in which economists have a unique comparative advantage (Kakani, Chernew, and Chandra 2020).

3.5 Incentives for diagnosis

Diagnostic tests for AD using biomarkers can serve several purposes. For a patient who develops symptoms of AD, tests can be used to improve the accuracy of a clinical diagnosis, even experienced clinicians rendering inaccurate diagnoses in 10 to 15 percent of cases (Thal et al. 2006). Biomarkers can be used to track disease progression in AD patients, enabling doctors to understand whether and how quickly patients' conditions are worsening.

Drug developers can use biomarkers in clinical trials to assess the efficacy of an intervention more quickly than is possible with clinical outcomes, increasing efficiency and reducing cost (Thal et al. 2006). Relatedly, biomarkers may help to identify patients the course of whose disease is more amenable to modification by existing therapies. Better diagnostics and new therapies for AD thus being complementary goods, pharmaceutical companies may be inclined to purchase companies that can diagnose AD, particularly if the buyer's medicine uses the same biomarker revealed by the diagnostic.

It is less clear whether diagnostic tests for identifying AD early in its course should be administered routinely. Insurance companies argue that using PET scans for early diagnosis is expensive and unnecessary because there are no treatments to slow disease progression (Apostolova 2016). Our framework suggests that this is not quite right; even if it is not possible to modify the trajectory of the disease, there are other decisions involving consumption, labor supply, and bequests that patients who know they have AD may want to change. Of course, screening may also lead to unnecessary psychological strain, as many individuals who never developed clinical AD during their lifetimes have been found during post-mortem examination to have abnormal amyloid deposits (Mormino and Papp 2018). The net benefit of earlier screening is therefore not a simple determination for individuals; at a societal level, earlier and better diagnosis may induce innovation by revealing market size and heterogeneity in the disease. The value of tests, particularly those more informative of the probability of developing clinical AD, may thus be considerable.

Further development of AD diagnostics should focus on two goals. The first is to find tools, such as a blood or saliva test that could be administered at an annual checkup, that enable earlier, less invasive, less costly detection of the disease.[10] To be useful, such tests would need to have a high positive predictive value. The second goal is to better characterize the disease trajectory to aid in AD treatment and research. Further validation of specific biomarkers is needed before they can be used as a surrogate endpoint, that is, a marker known or likely to produce clinical

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[10] Other easy-to-administer tests might serve a dual role for diagnosis and prevention. Neurotrack, for example, provides a Cognitive Health Program that works to improve brain function now in an attempt to delay decline later. Taking the form of a mobile application that can be used on tablets and smartphones, the program includes such measures as eye tracking, processing speed, and recognition memory to identify areas in which users might be at most risk of cognitive decline or at risk for dementia.

benefit and that can be used to support drug approval (Brioch, Weiergräber, and Hampel 2011).[11]

3.6 Genoeconomics

The emerging field of genoeconomics, which lies at the intersection of molecular genetics and economics, offers some promise for identifying targets for medicines or diagnostic tools that may lower the cost of development (Benjamin et al. 2007). AD is caused by a specific genetic mutation in fewer than one percent of cases, but it is possible that multiple genes, not simply single genes like APOE4, are implicated. Polygenic scores (PGS) serve to summarize the effect of multiple genes on AD risk (by predicting, using genome-wide association studies, an individual's probability of developing AD). A robust PGS would enable individuals who receive a risk-score for Alzheimer's to take actions to mitigate the onset (including, if one was available, submitting to a therapeutic as well as making decisions about savings, long-term care, and other considerations depending on their genomic risk).

One way this literature might reveal targets for drug development is by noting the causal association between genes, including PGS, and decision-making by AD patients. This is sharper than looking only at the link between AD and PGS because it is limited to genes that affect cognition and behavior as opposed to genes that affect biomarkers like amyloid. Shin, Lillard, and Bhattacharya (2019), for example, report a positive correlation between the PGS for AD and the share of wealth held in "hands off" assets like certificates of deposit, and Han et al. (2020) find that volunteering helps to mitigate cognitive decline associated with polygenic risk for AD. Shin et al. (2021) report similar results for activities like reading and playing card games. Linnér and Koellinger (2020) find the PGS for AD, parental lifespan, and smoking to be associated with survival and perhaps be better predictors than some conventional actuarial risk factors; they also find greater genetic mortality risk to be associated with reduced probability of long-term care purchase.

Future research could explore whether the genetic risk of AD is related to latent parameters like time preference or risk aversion. PGS for AD could be used as an instrument for cognition, though Benjamin et al. (2012) caution about the possible violation of the exclusion restriction, a gene often affecting more than one medical condition. The genoeconomic literature is fairly small. It remains to be seen which areas hold the most promise for AD research because replication is a first-order problem in these studies (Beauchamp et al. 2011), but the topic is certainly attracting attention from economists who have noted linkages between genes and behaviors.

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[11] One biomarker that has garnered enthusiasm in recent years is the neurofilament light chain, a marker of general damage to brain cells. It is not specific to AD, having been observed in increased amounts in many conditions including other dementias and traumatic brain injuries. Although it would not be useful in distinguishing AD from other conditions, serial measurements of such a marker may help to predict whether the disease is worsening or improving.

4 Health care and long-term care for Alzheimer's Disease

Given that current therapeutics have small to negligible effects on the development and trajectory of the disease, many of the pressing questions for individuals currently suffering from AD relate to health care and long-term care decisions (q in the conceptual framework), care delivery and regulation R_2, and insurance x. We now turn to the economics of this care.

4.1 An overview of the market for care under cognitive constraints

In the market for health care, consumers choose among services offered by providers. While there are many reasons why market outcomes in health care may be sub-optimal, such as market power or asymmetric information, most economic research on these topics assume that consumers rationally choose the best option according to their preferences. But what happens when consumers lack the cognitive capacity to act according to their preferences and become dependent on other agents and entities to act on their behalf? More generally, how should we conceptualize economic decision-making under cognitive constraints, when individuals may not remember past experiences or be able to assess quality, respond to prices, or even be sure where or who they are? A more precise understanding of how cognitive capacity affects choice may lead to a better understanding of whether cognitive constraints can be understood as bounded rationality, time-inconsistent preferences, or something else entirely (see Mullainathan (2002) for a memory-based model of bounded rationality and Handel and Schwartzstein (2018) for a review of tests of various behavioral models of decision-making).

One way to characterize the problem of consumer choice under cognitive constraints is as a principal-agent problem in which an agent facilitates choice by advising or even acting on behalf of a cognitively constrained individual (see McGuire (2000) for a review of physician agency). The key challenge in principal-agent problems is that the principal (the individual needing care) and agent (e.g., a family member or health care provider) may have different incentives and information.

One agent is the family, typically adult children who act as caretakers or guardians for their elderly parents (see Lundberg and Pollak (2007) for an overview of family economics and models of family interaction). A literature in family economics that tests for children's altruistic motives versus exchange motives finds evidence of both (e.g., Altonji, Hayashi, and Kotlikoff 1997; McGarry 1999). Applying these tests to families with AD could provide a relatively extreme test case: for example, do altruistic motives appear in children of parents with AD (who may not even recognize their children) even without the prospect of bequests? Economists could also contribute to the literature on family bargaining models to understand, for example, whether parental cognitive decline leads to changes in bargaining power, health care decisions, and, ultimately, health outcomes.

Another agent is the state, which uses regulation and legal guardianship to discipline health care and long-term care practices. For example, the government sets minimum quality standards, such as staffing ratios in nursing homes, to safeguard against low quality care, monitors the quality of health care providers, and regulates insurance markets by defining what constitutes minimum coverage (and in the case of fee-for-service Medicare, by supplanting the market completely on prices and quantities).[12] Regulatory checks may be particularly valuable for the AD population, some of whom may not have others to act in their interest. Legal guardianship and associated ethical issues have been the subject of much scholarly work and debate among non-economists (e.g., Teaster, Schmidt, and Lawrence 2010; Wright 2019), but there is little to no work by economists. The interaction between economic models of decision-making for individuals experiencing cognitive decline and prevailing legal agency arrangements could provide important insights into the role of regulation and legal autonomy for individual well-being. As fertility rates continue to decrease, the availability of children to act as advocates for parents with AD will inevitably decline, imparting further value to an understanding of these safeguards.

An alternative solution to the problem of consumer choice under cognitive constraints may be to appeal to mechanism design. Insights from contract theory suggest that more complex, and likely dynamic, contracts could come closer to achieving “cognitively frictionless” outcomes. For example, some providers (e.g., “continuing care” communities) offer long-term, dynamic contracts to individuals prior to cognitive decline that define care arrangements for all future care need contingencies, thus avoiding active choice during cognitive decline. Reputation effects (Arrow 1963) and other safeguards, such as family advocates or regulation, may still be necessary to sustain agreed upon levels of quality care. Government-sponsored data collection and monitoring could have the dual benefit of ensuring regulatory adherence and providing measurements of provider reputation. Better understanding of the dynamic incentives of these types of contracts and the role of reputation and regulation would help to solve the problem of consumer choice under cognitive constraints.

In sum, the economics of health care delivery may be quite complex for individuals with AD and could benefit greatly from economists’ insights in areas ranging from contract theory to family economics to law and economics.

4.2 Health care for individuals with AD

Diagnosis of AD often occurs in a primary care setting, and care as the disease progresses takes place in a host of settings including in-home, hospitals, and nursing homes (see Norton (2016) for a review of the economic literature on health and long-term care as it relates to population aging). Care is paid by large rate-setting insurers like Medicare and Medicaid (the US program that provides health insurance for low-income individuals and covers long-term care expenses for the indigent) as well as private payers and out-of-pocket. This complex network of payers and providers on the supply side coupled with potentially cognitively impaired consumers on the demand side affords many opportunities for economists to study how the incentive structures of these players interact to produce care for AD patients (see Gaynor, Ho, and Town (2015) for an introduction to the industrial organization of health care markets).

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[12] See Musumeci and Chidambaram (2020) for an overview of nursing home regulations including a summary of their evolution over time and recent changes in light of the COVID-19 pandemic.

Classic demand theory makes stark predictions about consumer behavior, for which cognitively compromised populations could be an extreme test case. For example, demand theory suggests that higher quality hospitals should attract greater market share. Chandra et al. (2016) find evidence to support this theory, in contrast to the notion of "health care exceptionalism" (Arrow 1963), but whether standard demand forces also apply to cognitively vulnerable populations is an open question. Demand theory also suggests that insurance leads to ex-post moral hazard in the form of overuse of low-value care, and that cost-sharing can mitigate moral hazard and lead to more efficient levels of care (at the cost of lower risk protection). There is increasing evidence, however, that cost-sharing also leads to cuts in *high*-value care (Chandra, Gruber, and McKnight 2010; Brot-Goldberg et al. 2017). These findings are suggestive of "behavioral hazard" in which patients mistakenly cut back on high value care in response to cost-sharing (Baicker, Mullainathan, and Schwartzstein 2015), with ultimately negative consequences for health including mortality (Chandra, Flack, and Obermeyer 2021). These hazards are particularly important to study in the context of AD patients, whose decreased cognitive capacity may make them more prone to such mistakes.[13] More generally, in the presence of behavioral hazard the key question for AD patients is whether the price-elasticity of demand is a sufficient statistic for patient welfare.[14]

Health insurance can also generate inefficiencies in the form of fiscal externalities consequent to the presence of many different insurers that cover different types of care or different life stages. Chandra, Gruber, and McKnight (2010), study the effects of an increase in patient cost-sharing for a supplemental insurance plan that covered physician visits and drugs, and found that the change led to savings for the supplemental insurer, but higher hospital costs, which accrued to Medicare. A similar fiscal externality can arise intertemporally when different insurers provide coverage at different ages, such as private insurance coverage prior to age 65 and Medicare thereafter (Fang and Gavazza 2007). Given that health care for AD can span decades, this issue may be particularly acute for AD care. For instance, a private insurer may not want to cover an expensive but effective early-stage intervention for AD (e.g., diagnostic testing or a preventive medicine) because the later stage savings accrue to Medicare or Medicaid (Cutler et al. 2017).

More generally, underinvestment in preventive measures (Ellis and Manning 2007) may prove to be an important source of inefficiency for AD given the long horizon of the disease. Some research suggests that a healthy diet and exercise can improve later AD outcomes and reduce

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[13] Moral hazard in this case is not along the extensive margin of whether individuals without needs use any services (as most AD patients have significant care needs), but rather the intensive margin of over-using additional health care services, such as diagnostic screening or aggressive surgery when non-surgical treatment options exist.

[14] See Keane and Thorp (2016) for a review of the literature on health care decisions under complex choice environments, and Ericson and Sydnor (2017) for a review of theory and evidence on how consumer constraints, such as confusion (which may be a relevant friction for individuals suffering from AD), affect health insurance choice and interact with market forces, such as adverse selection.

AD costs (Pope, Shue, and Beck 2003), yet these investments can be costly or unpleasant for individuals. Because downstream savings from these investments largely accrue to insurers, individuals may not find the preventive measures worth the immediate costs, leading to underinvestment in preventive care. Economic frameworks and causal methods provide a useful lens through which to understand incentives for early stage AD interventions as well as identify whether and when to recommend different diagnostic tests (e.g., Einav et al. 2020).

The importance of provider-side incentives may also be amplified in the case of care for AD patients, particularly if cognitively impaired individuals cannot act as a check against supply side forces. Payment structures for care illuminate this issue. Because health care providers are often paid for care rendered (e.g., fee-for-service) and not for outcomes (e.g., pay-for-performance), they face financial incentives to maximize payments at the expense of higher costs and, sometimes, lower quality. A stark example of this is the payment structure for end-of-life care for AD patients in nursing homes. Many such patients are dually eligible for Medicare and Medicaid. Medicaid typically pays a relatively low per-diem rate for each nursing home resident regardless of the intensity of care needs, whereas Medicare reimburses at a higher rate, but covers only 100 days of post-acute nursing home care. Because end-of-life AD patients are typically more costly than other patients (see French et al. (2019) for a review of end-of-life medical expenses), nursing homes face incentives to transfer patients near death, who need more intensive care, to hospitals, temporarily shifting their reimbursement to Medicare, which pays higher reimbursement rates (Goldfeld, Hamel, and Mitchell 2013).[15] This not only increases the cost of care, but is associated with increased use of "questionable medications" for AD patients (Tjia et al. 2014) and is generally inconsistent with the goals of patient comfort (Gozalo et al. 2015).

Studies suggest that Medicare payment structures with pay-for-performance features (e.g., Medicare Advantage plans) result in lower-cost AD care as well as fewer burdensome hospital transfers (Goldfeld, Hamel, and Mitchell 2013).[16] There is also evidence that coordinated care plans for individuals with AD, which, among other things, assign a care manager to coordinate the wide range of provider services, can result in positive health outcomes (see Hughes, Lepore, and Wiener (2017) for a review). These plans have not been widely implemented, however, in part because typical reimbursement systems once again do not incentivize coordinated care (Boustani et al. 2019). Nonetheless, the recent trend towards alternative payment models in Medicare, such as Accountable Care Organizations (ACOs) and bundled payments (e.g., McWilliams et al. 2015; Finkelstein et al. 2018), suggest an appetite for payment redesign for

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[15] This not only relieves the nursing home from high-intensity care during the hospitalization, but also shifts the reimbursement to Medicare for 100 days after the patient returns to the nursing home.

[16] Others have cautioned against an interpretation of "hopeless" spending, showing that it is virtually impossible to predict death from health spending and suggesting that it is not clear that care for those who ex-post died was futile (Einav et al. 2018).

AD care.[17] If quality care for AD patients is expensive to provide and not observable, however, it is not fully understood how these payments will affect AD patients' well-being. More generally, it is unclear whether the policy goal of reducing spending by altering provider payment structures is necessarily aligned with better outcomes for patients with AD (Mukamel et al. 2007).

The complex forces highlighted in this section likely create situations in which quality of care is particularly compromised for minority patients, a point amplified by the substantial gaps that exist for minority patients even for relatively common medical conditions. Work in this area could build on the approaches used by Alsan, Garrick, and Graziani (2019) to study the effect of racial congruity between patients and their physicians on health, Baicker and Staiger (2005) on the conditions for which public assistance can improve patient outcomes, and Skinner et al. (2005) and Chandra, Kakani, and Sacarny (2020b) on the role of geography and provider differences in quality as an explanation for racial disparities in health care.

4.3 Long-term care and caregiving

Long-term care involves providing support for activities of daily living (ADLs) including bathing, dressing, eating, and walking as well as instrumental activities of daily living (IADLs) like taking medications, managing money, and shopping for groceries. This care is commonly provided in-home or in a nursing home, but also in assisted living facilities, adult day care centers, and other settings along the care continuum.[18] Of individuals diagnosed with AD, one third live in a residential care setting (18 percent in nursing homes), although two thirds die in nursing homes (Kasper et al. 2015; Mitchell et al. 2005).[19] In 2019, nursing home care averaged $90,000-$100,000 per year and formal home care cost around $23 per hour, or roughly $53,000 annually for 44 hours per week. These long-term care costs rival the medical care costs of the disease. Medicare does not cover most long-term care costs, most of which fall on the Medicaid program, individual savings, families, and to a lesser extent private insurance.

4.3.1 Measuring the cost of informal care

The formal costs of AD care paint an incomplete picture of the economic burden of long-term care for individuals with AD because they do not factor in the substantial costs that spill over onto families in the form of informal care. In 2010, an estimated 7.4 billion hours of informal care was provided to 3.6 million individuals with AD (Friedman et al. 2015), and of the AD population receiving care in the community 78 percent of care hours were informal (Kasper et

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[17] An example of this is the Program of All-Inclusive Care for the Elderly (PACE). PACE providers receive capitation payments from Medicare and Medicaid to provide a full spectrum of health care services to frail elderly, more than half of whom have dementia (Mukamel et al. 2007).

[18] The number of dementia special care units (SCUs) within nursing homes has increased over the past decade to the point that it constitutes the largest type of specialized long-term care (Cadigan et al. 2012).

[19] In contrast, most deaths from cancer occur at home or in a hospital (Mitchell et al. 2005).

al. 2015). Most AD caregivers are female spouses or children, and many live with the individual with AD. Thirty percent of these caregivers provide in excess of 20 hours of care per week, the majority of them helping with both ADLs and IADLs (Alzheimer's Association 2019), while fulfilling other demands on their time; 60 percent also work part or full time and a quarter are also caregivers to young children (Alzheimer's Association 2021). Informal care for AD may be particularly costly (compared to informal care for other illnesses) due to the round-the-clock needs of many patients and emotional toll of memory-related illness on caregivers.

Measuring the cost of informal care is difficult because these costs do not have an explicit market or monetary value. One simple method, which attempts to quantify the monetary *savings* from an hour of informal care, is to price it at its replacement cost, such as the market rate for purchased home care (roughly \$20 per hour). A second simple method, which attempts to quantify the *cost* of an hour of informal care, is to price it at the cost of foregone wages if the caregiver had worked in the labor market instead of providing care. Hurd et al. (2013) estimate the cost of informal care for individuals with dementia using the ”replacement cost” method to be around \$28,000 annually, and using the ”foregone wages” method around \$13,000 annually. Using the former method, the 7.4 billion hours of informal care for AD is "worth" \$148 billion, on aggregate, or roughly as much as the total formal payments for health care.

The true value of informal care is somewhere in between, and may include other non-monetary costs such as caregiver health (Coe and Van Houtven 2009). An alternative method is an economic model that incorporates replacement costs, potential foregone wages, and other opportunity costs (such as leisure and health) in a unified framework of caregiver well-being. At a basic level, it specifies caregiver utility over monetary consumption and leisure and a budget constraint over labor income, consumption, and care costs. Caregivers make decisions about how to spend their time, comparing the value of each hour spent doing something else instead of caring, including potentially working (i.e., lost productivity), but also enjoying leisure, against the cost of purchasing the care on the formal market.

Caregiving can affect labor supply at both the intensive and extensive margins. Caregivers experience not only a reduction in work hours due to time spent caregiving (the intensive margin), but may leave the workforce entirely or choose a worse paying (or less satisfying) job to achieve greater flexibility or closer proximity to caregiving obligations (the extensive margin).[20] There may also be dynamic effects of caregiving on downstream labor outcomes in the presence of human capital depreciation or labor market frictions in finding a new job. Using a model with these features, Skira (2015) estimates welfare costs of caregiving to be seven times greater than foregone wages.

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[20] Van Houtven et al. (2013) find some evidence of both margins of labor supply adjustment in response to caregiving demands, while Løken, Lundberg, and Riise (2017) find only intensive margin responses.

Future work in this area could tailor models of caregiving to the particularities of AD (for example, the need for emotionally taxing, inflexible round-the-clock care)[21] It could also be fruitful to exploit variation in the timing of AD onset to estimate a causal effect of AD on own or caregiver labor supply, following Fadlon and Nielson (2021).

4.3.2 Prices, costs, and selection among long-term care options

The availability of informal care and other long-term care options for individuals with AD raises questions about selection. How do individuals decide between nursing home, informal, and paid in-home care? To what extent do they care about price versus health outcomes? These questions have implications not only for individual welfare, but also for social policy given that social programs pay many of these costs and there are substantial cost differences between modes of care. One question that economists have made progress answering is whether individuals' long-term care decisions are price-elastic. The answer appears to be yes. Coe, Goda, and Van Houtven (2015) and Mommaerts (2018), for example, find evidence of substitution towards nursing home care and away from informal care when the out-of-pocket cost of nursing home care decreases. These studies, however, focus on the general long-term care population and an open question is how individuals with AD, who are likely cognitively constrained or may need round-the-clock care or specialized memory care, approach these choices.

A related question is whether choices between long-term care options generate selection, and the ramification of selection for providers. For example, the increase in the number of assisted living facilities over the past few decades may draw healthier, cheaper patients out of nursing homes and leave nursing homes with a sicker pool of patients. With typically fixed reimbursement rates from Medicare and Medicaid that do not vary with patient health, this could generate increased financial strain for nursing homes. An important area for research is how selection into various care options interacts with providers' payment and cost structures, especially with the advent of new care arrangements like memory care units (Cadigan et al. 2012).

Another open question is whether long-run costs differ between long-term care options. For example, although home-based care is typically less costly than nursing home care, it is unclear whether home care results in long-run savings in total health care costs.[22] Recent quasi-

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[21] The model can be expanded to account for an AD individual's welfare and preference for informal care via either the addition of "warm glow" utility or a more complex model of family interactions (e.g., Barczyk and Kredler 2018; Mommaerts 2020).

[22] This is particularly relevant for state Medicaid policies, which have expanded home care in recent decades. The primary setting for Medicaid-covered long-term care was historically nursing homes, but in the past 40 years states have gradually shifted Medicaid funds toward long-term care benefits and services in the home. This shift partly reflects a strong preference to remain in the community (reinforced by the Supreme Court's Olmstead decision in 1999), but a second justification is economic: many policymakers believe that nursing home care is excessive for many individuals with less intensive long-term care needs and allowing them to remain in the community may reduce long-term care costs.

experimental evidence from the Netherlands shows overall health care spending to be unchanged for individuals at the margin of home care and nursing home care because the latter causally generates fewer hospitalizations (Bakx et al. 2020). Moreover, home care may be more difficult to target, which may increase costs (Lieber and Lockwood 2019). Evidence from community care demonstrations in the 1980s suggest that long-term care costs actually increased when home care was provided in lieu of nursing home care, in large part because home care is more difficult than nursing home care to target to appropriate individuals (Kemper, Applebaum, and Harrigan 1987). More evidence of the effects of different care settings on cost is needed, particularly for AD patients, whose health and long-term care needs may differ from those suffering from other ailments.

4.3.3 Quality of long-term care

Another important aspect of long-term care for AD that economists are well positioned to study is the market for quality long-term care, particularly in formal care settings. A persistent concern among policymakers is that many long-term care facilities provide low-quality care and patients are not well informed about the wide variation in quality when making long-term care decisions.[23] In general, economic theory suggests that if consumers can evaluate their quality, facilities have an incentive to compete with higher quality care; if consumers cannot evaluate their quality, facilities may underinvest in quality care (Akerlof 1970). Empirical evidence confirms this for the broader long-term care population. For example, nursing home "report cards" lead to increased demand for higher quality facilities (at least when the report cards are easily interpretable), and competition among providers has meaningful effects on quality, but only when consumers have good information about the quality of candidate nursing homes (Grabowski and Town 2011; Werner, Konetzka, and Polsky 2016; Zhao 2016).

Complicating this basic theory is that because consumers of long-term care differ in cost, providers may have an incentive to use quality as a screening device. For example, lower Medicaid reimbursement rates lead to lower quality care for Medicaid patients (Hackmann 2019) and even rationing of Medicaid patients by nursing homes (He and Konetzka 2014). Moreover, the quality effects discussed above arise mainly in short-stay nursing home populations typically covered by Medicare, for which profit margins are higher than for long-stay residents typically covered by Medicaid (Grabowski and Town 2011). It is not obvious how these incentive structures for quality care apply to the AD population. In hospital settings, for example, AD patients typically generate low to negative profits, and Colla et al. (2016) show that competition is associated with *lower* quality AD care, perhaps as a way to discourage these unprofitable patients. On the other hand, special care units for AD patients in nursing homes have been shown to provide higher quality care, albeit at a higher price point (Joyce et al. 2018).

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[23] For example, although approximately 5 percent of nursing homes had zero out of roughly 175 types of "deficiencies" in 2016, more than 20 percent of facilities received scores for the most egregious deficiencies of "actual harm or jeopardy" (Harrington et al. 2018).

A related and understudied issue is the role of cognitive constraints in the demand for quality care. This is particularly relevant for the AD population, as individuals with AD may be less aware and or able to advocate for quality care.[24] As discussed in Section 4.1, one solution could be long-run contracts (like continuing care communities) in which individuals make care arrangement contingencies well in advance of cognitive decline. It is unclear, however, whether these types of contracts are incentive-compatible once an individual suffers from dementia. Alternatively (or in addition), there may be a role for regulation in ensuring the quality of long-term care providers. While regulation may benefit individuals who have difficulty optimizing over choices,[25] it could reduce welfare for unconstrained individuals by limiting choice. The effects of regulation may also depend crucially on the ability of the regulator to set prices. If regulated prices are too low, perhaps because of monopsonistic price setting by the state, quality can suffer (Chandra and Garthwaite 2019).

4.3.4 Long-term care workforce

Long-term care is highly labor-intensive. The workforce is predominantly composed of direct care workers including nursing, home health, and personal aides who are typically low skilled, low paid, and often immigrant workers. The United States is currently facing a major shortfall of such workers (Zallman et al. 2019). Studies have shown that low pay is linked both to this shortage and to lower quality care (Ruffini 2020) and that tight labor markets lead to lower staffing levels and higher mortality rates in long-term care facilities (Stevens et al. 2015). However, a significant fraction of long-term care provider financing is dictated by low Medicaid reimbursement rates that do not allow much room to adjust pay to improve quality or respond to cost shocks. For example, Cawley, Grabowski, and Hirth (2006) found that exogenous increases in labor costs (through minimum wage law increases) led to substitution away from labor towards other inputs like psychoactive drugs for nursing home patient care.

The shortage of long-term care workers is projected to worsen as demand for long-term care grows among the older US population. A ripe area for study is the effectiveness of various policy levers to expand this workforce. For example, changes to immigration policy, labor market policies (e.g., minimum wage policy), and regulatory conditions could all play a major role in the future supply of long-term care workers, as could more ambitious changes to the organization of the occupation, such as the formation of career ladders or a path to citizenship for immigrants who deliver long-term care. Immigration reform may, at first glance, seem unrelated to the well-being of AD patients, but may prove central in the coming decades.

4.4 Insurance for long-term care

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[24] This is exacerbated by the increasing use of psychotropic drugs on AD patients. These drugs not only decrease awareness among AD patients, but studies have found increases in mortality among AD patients to be directly related to use of these drugs (Briesacher et al. 2013).

[25] For example, regulations such as minimum staffing regulations and nursing home inspections have had modest success in improving the quality of care in nursing homes (Werner and Konetzka 2010).

In the United States, insurance against medical expenditures operates in a largely distinct market from insurance against long-term care expenditures. Whereas medical expenditures for AD care are relatively well insured, long-term care expenditures pose one of the greatest uninsured financial risks to the elderly (Brown and Finkelstein 2011). Crucially, Medicare does not cover most long-term care expenses.[26] Of the $310 billion in aggregate formal long-term care expenditures in 2013, 8 percent was paid by private long-term care insurance, 72 percent by public insurance (mostly Medicaid, the means-tested program for the impoverished), and 19 percent out-of-pocket (Reaves and Musumeci 2015).[27] These expenditures are not spread evenly across elderly individuals: while fewer than 50 percent of individuals will ever enter a nursing home, there is a long right tail in the duration of nursing home stays among those who do, with 15 percent of stays lasting more than five years (Brown and Finkelstein 2009). These tail events are those for which insurance is most valuable, and AD patients are the population most often in need of this very long-term care.[28]

4.4.1 Private long-term care insurance

Despite the potential value of insurance in this setting, the private market for long-term care insurance in the United States is small and provides incomplete coverage.[29] Average applicants are in their mid-sixties and payouts typically do not begin until years later. The average annual premium for an individual policy was $2,700 in 2015 and covered roughly $150 per day of nursing home or home care for up to four years (LifePlans, Inc. 2017). Given that nursing home care typically costs upwards of $100,000 per year, policyholders still pay for a substantial fraction of their care out-of-pocket. In 2015, only about 10 percent of individuals aged 65 and over had coverage through private long-term care insurance.

Many explanations for the poor functioning of this market have been offered, and developments in the prevalence and treatment of, and information about AD could exacerbate these issues. One explanation is the aggregate risk inherent in insuring against contingencies that can occur far in the future. Long-term care insurance contracts are written and signed years, often decades before AD risks are realized, and there is a great deal of uncertainty over what the long-term care landscape will look like in the coming decades (Cutler 1996). For example, unexpected advances in technologies and treatments for, and increased rates of prevalence of AD could result in (unexpectedly) higher future costs to insurers. To safeguard against this risk, insurers can impose higher premiums or “quantity rationing,” such as payout

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[26] Medicare covers 100 days of post-acute care, but only after a hospitalization lasting at least three days.

[27] These numbers correspond to long-term care expenditures for all underlying ailments, not only AD.

[28] For example, among a sample of AD patients mean nursing home use was three years (Welch, Walsh, and Larson 1992).

[29] See Lambregts and Schut (2020) for a review of the literature on long-term care insurance demand that includes other countries.

caps, that ultimately result in less attractive, incomplete insurance for policyholders (Brown and Finkelstein 2007).[30]

Another explanation is the role of private information about the risk of developing AD. When the insured have greater knowledge about their underlying risk than insurers, adverse selection can result whereby higher risk (i.e., higher cost) individuals purchase insurance, which drives up prices and results in lower risk individuals being priced out of the market. At its worst, this could lead to the market unraveling. A first-order question is the degree to which advances in genetic and diagnostic technologies for AD will exacerbate adverse selection in the long-term care insurance market (e.g., with polygenic scores; see Linnér and Koellinger (2020)). Adverse selection could be exacerbated if individuals are able to privately obtain this information or insurers are not allowed to price on it. If, on the other hand, insurers are able to use these tools to screen applicants, greater price discrimination and ultimately a pool of uninsurable higher risk individuals could result.[31] Empirical evidence includes Hendren's (2013) finding that insurers use health conditions (including AD diagnoses) to screen and reject high risk individuals in the long-term care insurance market, and the findings by Zick et al. (2005) and Taylor et al. (2010) that individuals who learn that they have a variant of the APOE4 gene that increases the risk of developing AD are significantly more likely to purchase long-term care insurance.[32] The Genetic Information Nondisclosure Act currently bans the use of genetic tests in health insurance pricing, but does not regulate the use of genetic testing (or biomarkers) in long-term care insurance pricing (Arias et al. 2018). Thus, the full effect of current and future AD testing advances on the functioning of the long-term care insurance market remains an open and pressing question.

Private information may also take the form of unobservable care needs, which can lead to moral hazard. Because some care is valuable even to those who don't need it (e.g., housekeeping and errands), there are incentives for insured individuals to over-use these services, which in equilibrium leads to higher-cost, lower-value insurance.[33] One solution to this type of problem is to create a targeting mechanism such that only those who truly need care will use it (Nichols and Zeckhauser 1982). An example of this would be a policy that covers only nursing home and not home care. Among individuals who strongly prefer to remain in their home, this policy would attract only those who truly need long-term care and screen out those who do not. Although this would reduce moral hazard, it comes at the cost of inferior coverage

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[30] Reinsurance, which insurers can purchase to insure this aggregate risk, is also small in this market. Financial vehicles that transfer risk from insurers to capital markets, similar to longevity bonds, could be an alternative possibility (Kiff 2020; MacMinn and Brockett 2017; Blake and Burrows 2001).

[31] Theoretically, Peter, Richter, and Thistle (2017) show that mandatory disclosure laws are optimal and information bans suboptimal.

[32] Similarly, Oster et al. (2010) show that genetic testing for Huntington's disease (another degenerative disease) results in selective purchase of long-term care insurance.

[33] Moral hazard problems of this sort also occur in health insurance (e.g., additional screenings, unnecessary procedures) when it is not obvious to insurers whether the patient needs the screening, but patients derive value (e.g., peace of mind) from the extra services, as well as in disability insurance in cases in which it is difficult for disability examiners to ascertain whether an applicant is truly disabled.

because individuals, including those who need it, would be unable to obtain coverage for home care. In contrast, indemnity insurance that provides cash payouts for care would allow individuals to choose their preferred care arrangements, but would likely have poor targeting and moral hazard properties (Lieber and Lockwood 2019).

Complicating the moral hazard concern in the context of AD is the underlying assumption of rationality in those suffering from AD, an assumption that has been challenged in the literature even for patients without AD (Brot-Goldberg et al. 2017; Chandra, Flack, and Obermeyer 2021). More broadly, behavioral constraints including limited financial literacy, incorrect beliefs concerning the risks and costs associated with AD, narrow framing, procrastination, and the perceived risk of insurer bankruptcy may not only affect moral hazard, but also contribute to the limited demand and high lapse rates for private insurance (Brown, Goda, and McGarry 2012, 2016; Gottlieb and Mitchell 2019). How MCI or mild dementia changes or contributes to these behavioral issues would be an interesting area for future work on long-term care insurance demand.

4.4.2 Substitute sources of long-term care insurance

Most individuals without formal insurance rely on alternative sources of insurance against AD risk including precautionary savings, Medicaid, and informal insurance provided by family. Precautionary savings can come with high opportunity costs given that it cannot be used for other purposes, although Lockwood (2018) shows that bequest motives reduce this opportunity cost by providing value to unused savings. Housing equity may also substitute for long-term care insurance (Davidoff 2010), and Hanewald, Post, and Sherris (2016) find reverse mortgages to be preferred to long-term care insurance. Bundling long-term care insurance with other financial products like annuities (Brown and Warshawsky 2013; LIMRA 2017; Murtaugh, Spillman and Warshawsky 2001) or reverse mortgages (Shao, Chen, and Sherris 2019) may be another appealing way to hedge risk and reduce adverse selection problems.

The Medicaid program provides long-term care coverage to individuals with extremely low income and assets. Although this clearly crowds out demand for private insurance among poor households, Brown and Finkelstein (2008) and De Nardi et al. (2016) show that even for wealthy households there is a non-trivial chance of eventually ending up on Medicaid that generates crowd-out of private insurance for much of the wealth distribution. Braun, Kopecky, and Koreshkova (2019), however, find administrative costs and adverse selection to be the main drivers of non-purchase for wealthier households.

The perhaps largest substitute for formal long-term care insurance is the family. A series of papers show that the expectation of informal care from family members acts as implicit insurance that suppresses demand for formal insurance (Mommaerts 2020; Coe, Goda, and Van

Houtven 2015; Mellor 2001).[34] This is not a perfect substitute for insurance as informal care comes with its own costs and can lead to further selection problems in the formal insurance market (Ko 2021). As rates of AD grow and the availability of informal caregivers decreases (e.g., due to lower fertility rates; see Wettstein and Zulkarnain (2019)), more research will be needed to assess the role of the family in insuring care for AD including the feasibility of structuring insurance payouts as cash payments instead of expense reimbursement (Norton 2016; Lieber and Lockwood 2019; Mommaerts 2020). Studying this and related issues across a range of countries as they experience different rates of demographic change may be a promising way forward.

Going forward, more comprehensive social insurance for long-term care, which exists in many European countries, could provide a solution to the challenges of offering private insurance for AD care (Weiner et al. 2020).[35] A classic benefit of social insurance is its ability to mitigate adverse selection issues by imposing mandatory participation. Moreover, social insurance may be better equipped to weather the aggregate risk associated with AD and its associated expenditures because it can more easily spread the risk across generations. However, a classic downside of social insurance is that it could exacerbate moral hazard concerns, particularly if it comes with the generous benefits typical in other countries. The Netherlands, for example, recently scaled back its long-term care program due to ballooning costs often attributed to excessive use (Maarse and Jeurissen 2016). European programs will be useful case studies for the United States as it grapples with how to insure an aging population in the coming decades amid an evolving AD landscape.

A final point to consider in insuring AD care, both privately and publicly, is whether preferences support (fully) insuring the state of the world in which one needs long-term care for AD. If the marginal utility of (non-health) consumption is much lower when one is suffering from AD (meaning an extra dollar of non-health consumption is less valuable with AD than an extra dollar of non-health consumption without AD), insurance coverage that financially protects individuals against low non-health consumption in these states of the world may not be welfare improving. This notion of state-dependent utility has been studied in a variety of contexts with mixed results (Ameriks et al. 2020; Finkelstein, Luttmer, and Notowidigdo 2013). One reason for the mixed results is that differing health conditions may result in different changes in the marginal utility of consumption. For example, whereas Finkelstein, Luttmer, and Notowidigdo (2013) focus on chronic conditions like heart disease and cancer, an illness like AD that affects cognition and memory may alter preferences for non-health consumption in markedly different ways. Preference structure in the specific context of AD is an important input for understanding demand for long-term care insurance and a key part of financial decision-making, the topic of the next section.

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[34] See Klimaviciute, Pestieau, and Schoenmaeckers (2019) for evidence from Europe and De Donder and Pestieau (2017) for a theoretical treatment of optimal social insurance in the presence of informal care and private insurance.

[35] The CLASS Act, an attempt in 2010 to create a voluntary social long-term care insurance program as part of the Affordable Care Act, was ultimately repealed over concerns about adverse selection.

5 Financial decision-making

The risk of developing AD can also have important implications for financial decision-making beyond that related to health care. Within the conceptual framework in Section 1, this can manifest as decisions about how much to save (in assets a) from the first period to the second as well as about how to make decisions within the sick state of the world. Although the conceptual framework distills the AD state as a single period, AD can last many years and require not only decisions between consumption goods within a period (such as the trade-off between c^s and q), but also savings and investment over the course of the disease. In this section, we discuss these topics and the role financial literacy and financial mistakes play in the lives of cognitively compromised individuals. We conclude with a discussion of the regulatory environment for financial services for this population.

5.1 Saving and dissaving

How much do households save for retirement and spend down their assets during retirement, and how much should they save and dissave? The risk of AD may affect these decisions. We briefly review the relevant economic theory before turning to the implications of AD.

In the standard life-cycle model of consumption, labor supply, and saving, forward-looking individuals who seek to maximize lifetime utility accumulate wealth during their working years and decumulate assets during retirement in order to equate the marginal utility of consumption over time. This is in a similar vein to the optimality condition over assets in Section 1 (Attanasio and Weber 2010). A large literature has identified numerous empirical phenomena not easily explained in the context of the simple model. These include low levels of retirement wealth for the typical household, heterogeneity in retirement wealth among similar households, an observed drop in consumption at retirement, and low rates of wealth decumulation in retirement (Browning and Crossley 2001; Poterba, Venti, and Wise 2011). These revelations have spurred the development of more complex life-cycle models that incorporate elements such as uncertainty in longevity, earnings, and medical expenses, capital and insurance market imperfections, bequest motives, behavioral features, and access to social insurance programs (Hubbard, Skinner, and Zeldes 1994, 1995; Dynan, Skinner, and Zeldes 2002) to help explain these phenomena.

The role of health care expenditure risk in saving and dissaving decisions is of particular relevance in the context of AD. Medical expenditures of the elderly are substantial and rise with age. De Nardi, French, and Jones (2016) report that average annual medical expenditures rise from about $7,000 at age 65 to more than $25,000 at age 90 and above.[36] Expenditures are highly skewed, with the top five percent of spenders responsible for more than one-third of total spending, and average annual spending of nearly $100,000 within that group. Long-term care, which features prominently in the treatment of those with AD, accounts for one-fifth of

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[36] This expenditure risk is compounded if it occurs during working years and affects labor supply and earnings. We discuss labor supply in section 5.4.

total health care spending among those aged 65 and above as well as most of the growth in spending with age. Research using augmented life-cycle models confirms the importance of medical expenditure risk in both asset accumulation (Hubbard, Skinner, and Zeldes 1994, 1995) and asset decumulation decisions (Palumbo 1999; De Nardi, French, and Jones 2010; Laitner, Silverman, and Stolyarov 2018). However, slow rates of decumulation have also been found in non-US contexts in which health and long-term care costs are well insured (Van Ooijen, Alessie, and Kalwij 2015; Asher et al. 2017).

Beyond health expenditure, the risk of developing AD may affect saving and dissaving decisions through changes in utility. In our framework, the marginal utility of consumption could be higher in the AD state (as $c^s < c^w$ due to the cost of managing the disease), implying greater savings in preparation for such a state. AD may also modify the utility function from $u()$ to $u^s()$. Ameriks et al. (2020) show that a life-cycle model augmented with long-term care state-dependent utility generates even greater asset accumulation pre-retirement and continued asset accumulation during retirement. The literature on health-dependent utility is, however, far from settled, so expanding our understanding of these issues within the context of AD would be a fruitful step forward.

Both normal aging and AD may affect other utility parameters. Huffman, Maurer, and Mitchell (2019) find that individuals diagnosed with a cognitive deficit have higher discount rates, but whether this reflects the effect of reduced life expectancy or the impact of cognitive impairment on decision-making remains unclear. In their survey of aging and preferences, Sunde and Dohmen (2016) note that much of the decreasing risk tolerance with age is, according to Bonsang and Domen (2015) and Falk et al. (2018), related to cognitive decline. Tymula et al. (2013) find that older adults' choices exhibit more inconsistency. Future work examining how and why cognitive decline affects critical parameters of the utility function would be useful.

Cognitive decline associated with AD may also manifest as constraints on decision-making capacity. This may affect dissaving decisions as well as portfolio choice and financial mistakes (discussed in the following subsections) (Banks, O'Dea, and Oldfield 2010). The behavioral economics literature offers various departures from standard models of decision-making including "bounded rationality" and "bounded willpower," or such factors as overconfidence, loss aversion, time-inconsistent preferences, and self-control problems (Laibson 1997; Mullainathan and Thaler 2001; Mullainathan 2002).[37] Numerous studies find that financial tools like defaults in employer-provided pension plans can influence individual behavior in the presence of some of these behavioral phenomena (e.g., Beshears et al. 2009). Understanding whether and how cognitive constraints map to these alternative models of behavior is an open and important question for future research.

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[37] Keane and Thorp (2016) highlight the many inconsistencies between the predictions of rational choice models and consumer behavior in the areas of retirement saving and health insurance purchase; their extensions of rational models to account for irrational behavior and "confusion" might be of use in modeling cognitive decline.

5.2 Portfolio allocation

Households make other financial decisions during and in preparation for retirement that may interact with AD, including portfolio choice and annuity purchases.[38]

Annuities are a potentially attractive investment because they allow insured individuals to convert a lump sum of wealth into a guaranteed stream of income that lasts as long as they live, providing protection against longevity risk. Annuities also offer a higher rate of return than traditional investments because payments go only to surviving annuitants and the initial investment is not returned upon the buyer's death (the "mortality credit"; Brown (2009)). Given these advantages, the small size of the private annuity market has been viewed as puzzling (Benartzi, Previtero, and Thaler 2011). Among the explanations that have been advanced for this are bequest motives, degree of annuitization provided by Social Security and defined benefit pensions (Dushi and Webb 2004), adverse selection (Finkelstein and Poterba 2004), behavioral biases (Brown et al. 2008, 2011), and medical expenditure risk (Sinclair and Smetters 2004), particularly among households dissatisfied with the care provided by Medicaid and consequently holding liquid assets to insure against out-of-pocket medical spending (Ameriks et al. 2011).

The risk of developing AD could affect demand for annuities in multiple ways. Although concerns about the medical and long-term care expenditure risk from AD could amplify the lack of demand, annuities, because they offer a more hands-off dynamic contract than per-period savings decisions, may be an appealing way to structure long-run finances in the face of cognitive decline. A "hybrid" annuity product that provides protection against both longevity risk and long-term care expenditure risk may generate higher demand (Murtaugh, Spillman and Warshawsky 2001) and improve long-run financial well-being for cognitively constrained individuals.

Portfolio choice involves deciding not only what fraction of retirement wealth to annuitize, but also how to allocate non-annuitized assets across asset classes that vary in risk, return, and liquidity. A long line of research beginning with Merton (1969) and Samuelson (1969) examines optimal portfolio composition. Although a classic result from this literature (for a review, see Kaschützke and Mauer (2016)) is that individuals should invest a constant fraction of their wealth in the risky asset regardless of age, empirical evidence suggests that retired individuals shift their portfolio towards less risky assets as they age (Ameriks and Zeldes 2004; Guiso, Haliassos, and Jappelli 2002).

Again, health expenditure risk and cognitive decline, both hallmarks of the risk of developing AD, may affect portfolio allocation. Studies have found some association between poor health and safer portfolios (Rosen and Wu 2004; Love and Smith 2010), that households decrease financial risk with age as a hedge against increasing health risk (Edwards 2008), that health

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[38] See Kaschützke and Maurer (2016) for a useful review of the literature on asset decumulation and portfolio choice during retirement.

shocks are associated with a shift out of housing wealth and into low-risk assets like bank accounts and CDs (Coile and Milligan 2009), and that households facing reduced medical expenditure risk because they hold a Medigap or other supplemental health insurance policy are more likely to hold risky assets (Goldman and Maestas 2013). Yogo (2016) establishes within a life-cycle model that stochastic health depreciation can explain these empirical findings.

A number of studies have established a strong relationship between cognition and portfolio choice, although whether this represents a causal effect is not yet well understood. These studies generally find higher cognitive ability to be associated with riskier portfolios (McArdle, Smith, and Willis 2011; Kézdi and Willis 2003, Christelis, Jappelli, and Padula 2010; Grinblatt, Keloharju, and Linnainmaa 2011). Pak and Babiarz (2018), however, conclude on the basis of an analysis that exploits variation in cognition driven by seasonal affective disorder that there is no causal effect of cognition on portfolio choice. In a rare example of AD-specific research on this topic, Shin, Lillard, and Bhattacharya (2019) find that AD risk is associated with increased holding of "hands off" assets like CDs.

A useful next step for this literature would be to examine how portfolio allocation is affected by cognitive decline. By exploiting plausibly exogenous variation in the onset or timing of MCI or AD, researchers could potentially gain a better understanding of the causal relationship between cognition and asset holdings. Given the higher levels of AD in Black and Hispanic populations as well as among the less educated, it would also be useful to explore how AD may contribute to wealth disparities.

5.3 Financial literacy and financial mistakes

Financial literacy may enhance individuals' ability to make better financial decisions (Lusardi and Mitchell, 2014).[39] It peaks in midlife and declines at older ages (Finke, Howe, and Huston 2017), an effect that may reflect declining cognitive abilities of which AD is an extreme form (Lusardi, Mitchell, and Curto 2014). Financial education can improve financial literacy and affect financial behaviors (Kaiser et al. 2020), but this treatment may be more effective for younger individuals who lack crystallized intelligence than for older individuals experiencing declining fluid intelligence.

A nascent literature explores age patterns in financial decision-making and the effects of AD on decisions. Consistent with age patterns in financial literacy, financial mistakes like excess interest rate and fee payments increase with age (Agarwal et al. 2009), financial capacity as reflected in checkbook management declines as AD progresses (Triebel et al. 2009; Sudo and Laks 2017), and Medicare beneficiaries with AD are more likely to select a suboptimal prescription drug plan (Keane et al. 2021).

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[39] Gomes, Haliassos, and Ramadorai (2020) provide a recent and wide-ranging review of household finance that includes a discussion of financial literacy and cognitive abilities.

In the case of couples, cognitive decline is associated with a larger decrease in wealth when the affected spouse is the financial decision-maker (Angrisani and Lee 2018). Couples tend to transition the management of finances to the non-impaired spouse (Hsu and Willis 2013) and women to acquire financial literacy as they approach widowhood (Hsu 2016).

Becoming a victim of financial fraud may be a particularly costly financial mistake. More than one-third of older individuals report attempted or successful fraud over the past five years, with attempted or actual unauthorized use of an account accounting for most of the incidents (DeLiema et al. 2020). In 2017, US financial institutions reported 63,500 cases of elder financial exploitation to the government, representing $1.7 billion in suspicious activity, but only a "tiny fraction of actual incidents of elder exploitation" (CFPB 2019). A number of studies suggest that weak cognitive skills put older individuals at greater risk of financial fraud (Judges et al. 2017; Gamble et al. 2014; Spreng, Karlawish, and Marson 2016).

Research on the effect of AD on financial decision-making could have important policy implications. Nicholas et al. (2021) find that individuals with AD are more likely to miss bill payments up to six years before diagnosis and develop subpar credit scores 2.5 years before diagnosis. This suggests that routine financial monitoring could be used to help detect AD at an early stage. If financial mistakes in the early stages of AD are sufficiently common and costly, this could suggest a need for more early screening for AD (e.g., via imaging) even in the absence of an effective medical treatment.

Economists could be helpful in designing and assessing the impact of policies to protect older individuals with diminished cognitive capacity from financial mistakes or exploitation (i.e., regulations R_2 in the conceptual framework of Section 1). Potential regulatory remedies include greater oversight of financial products, stronger fiduciary requirements, and financial "driver's licenses" (Agarwal et al. 2009). Choice architecture might be used to encourage a greater reliance on "hands off" assets like CDs or annuities for older asset holders, and greater screening of financial transactions for suspicious patterns of activity could allow for earlier detection of fraud.

A variety of contractual and legal models could also be used to protect the interests of cognitively impaired individuals. Long-term wealth management contracts or financial advance directives might allow non-impaired individuals to direct their future financial transactions. Legal models including power of attorney, the Social Security Representative Payee Program, and guardianship delegate to an authorized representative the ability to make financial and/or legal decisions on behalf of impaired individuals. The Payee Program is currently used by 9 percent of beneficiaries with AD and 2 percent with MCI (Belbase, Sanzenbacher, and King 2020), and an estimated 1.3 million adults in the United States are under legal guardianship (National Council on Disability 2018). Use of such models involves trading off the potential benefit from an altruistic agent making better decisions against the loss of autonomy, risk of error in determining which individuals need such protection, and potential for abuse (Krauss and Sales 1997). Empirical work in the vein of Doyle's (2007) analysis of foster care would be helpful in assessing the effect on well-being of guardianship or other models. Economists could also develop new models of financial decision-making that reflect the reality that many older people receive assistance with these tasks from adult children.

5.4 Labor supply

AD may have implications for the labor supply of affected individuals due to the risk of onset before retirement. Although early onset of AD (before age 65) is rare, affecting less than 1 percent of the working-age population (Ferri et al. 2005; Vieira et al. 2013), experiencing some level of cognitive impairment is more common. Estimates of MCI prevalence vary (Ward et al. 2012; Roberts and Knopman 2013), but several studies suggest that the rate is about four percent among individuals in their early 60s and that as much as 30 percent of this group may have a mild cognitive disorder (Kumar et al. 2005; Anstey 2008). One in nine adults between the ages of 45 and 64 self-report cognitive decline (CDC 2019). The risk to labor supply may also be growing over time as labor force participation rates at older ages rise (Coile 2018).

Economists could estimate how MCI affects work and retirement trajectories and lost earnings (Moschetti et al. 2015), which are part of the societal cost of AD. Economists are also well-positioned to explore how the Americans with Disabilities Act (ADA), workplace policies, and access to Social Security Disability Insurance benefits help workers cope with cognitive decline, building on general research on these topics conducted in the past (Acemoglu and Angrist 2001; Hill, Maestas, and Mullen 2016). Recent research estimating work capacity by comparing individuals' self-reported functional abilities to the functional requirements of occupations (Garcia, Maestas, and Mullen 2019) could be adapted to assess the work capacity of those with MCI.

6 Accelerating research on the economics of AD

AD is not only a costly, but also a highly complex disease, both biologically and from a public policy point of view. The prevalence of AD at older ages is high and the number of affected individuals is rising over time due to population aging. AD is different from other costly diseases in that there are currently no effective treatments and no proven behavioral interventions for public health officials to recommend. AD robs people of their decision-making capacity and ability to manage activities of daily living, eventually leaving them totally dependent on caregivers, whose lives are also profoundly affected by the disease. There are other diseases with high prevalence, from diabetes to HIV to cancer, but none match the medical and care needs of AD.

The economist's toolkit is well-suited, perhaps uniquely so, to distill complicated and difficult problems into manageable pieces, and AD poses a thicket of challenging and interrelated problems for which economic frameworks that incorporate core principles of incentives and cost-benefit trade-offs can be extremely useful. Solving the social planner's problem with respect to AD is an extremely difficult task, but there are concrete areas in which progress can be made through the application of economic theory and empirical methods.

One such area involves the level of investment in scientific research and AD treatment and prevention. The principle of allocative efficiency requires equating the marginal benefit of the last dollar spent in each area, basic research, disease-specific research, patient care, and prevention. The marginal value of public funds approach might also be useful for welfare analysis in this area (Finkelstein and Hendren 2020). Evaluating AD policy using these economic principles is newly urgent given the recent approval of a new AD drug with potential sales of $50 billion per year. Considering the present discounted value of future AD spending, would $50 billion be better spent on basic research that could lead to a transformational drug?

Economists are also primed to think about incentives, and the potential for misalignment of private and social incentives is particularly high for AD drug development given the lack of understanding of the disease etiology. Which push and pull incentives are needed to increase the probability of successful AD drugs coming to market? Economists, particularly those willing to collaborate with biologists or neuroscientists,[40] can also add to our understanding of AD's causes through quasi-experimental studies that exploit exogenous variation in AD risk factors or research using PGS scores.

Another broad area relates to the choices and behavior of cognitively impaired individuals. Is decision-making under cognitive constraints better modeled within the rational-agent framework, a behavioral framework, or is neither fully adequate? Exploring this question, through experiments and in collaboration with psychologists and neuropsychologists, may have more general spillovers on how economists think about choice inconsistencies and poor decision-making by the non-AD population.

This inquiry would open up new areas for research in optimal regulation. How, for example, does the presence of altruistic agents and dynamic contracts affect the well-being of AD patients, and how does the answer to this question inform the design of regulation in financial services, health care, and long-term care to overcome inefficiencies in market outcomes? These inter-related questions include asking further questions, such as: What models from family economics best explain the behavior of AD patients and their family members? Can self-enforcing contracts that approximate benevolent guardianship be designed for patients in the AD state? Under what set of circumstances would direct provision of AD care by the state be superior or inferior to market-based care? Which regulations (i) have positive spillovers for non-AD patients who also benefit from their protections, and (ii) would reduce welfare by constraining market offerings? Economists have a comparative advantage in modeling strategic behavior, devising incentive-compatible contracts, and measuring costs and benefits of government policies.

The rich agenda for future AD-related research that we envision encompasses a wide variety of research questions, and accordingly will draw on many kinds of data (only some of which we

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[40] A recent example of productive interdisciplinary cross-fertilization is the *Journal of Economic Perspectives*' symposium on economics and epidemiology (Avery et al. 2020; Murray 2020),

discuss here). Among survey data, the Health and Retirement Study (HRS) offers especially rich data on memory and cognition, PGS and biomarker data, and clinical assessments of dementia for some respondents (HRS 2021; Ofstedal, Fisher, and Herzog 2005). "Sister studies" in other countries offer some of the same features. Administrative data, such as Medicare claims records, offer detailed healthcare utilization data, much larger sample sizes, and the potential to identify dementia from ICD codes (Moura et al. 2021). New researcher-established linkages, for example, between Medicare claims and consumer credit data (Nicholas et al. 2021) or Medicare and Medicaid claims (Hackmann and Pohl 2020), open the door to many key research questions.[41] Investments by the NIA and other funders in more data linkages of this sort, for example, linking credit data to the HRS or earlier life course data to data on older adults, could greatly enhance the scope of AD-related questions that economists can tackle. Using data from countries that provide access to linked administrative data covering numerous domains (e.g., health care, tax, and public benefit records) for the entire population could also prove useful.

In sum, there is enormous scope for economists to contribute to the understanding of AD and generate research findings of great value to policy makers facing critical decisions about basic and AD-specific research funding, prescription drug access and price regulation, public long-term care insurance, and the regulatory environment. Such work could also lead to advances in the discipline of economics more broadly, particularly research on modeling the behavior of cognitively impaired consumers. These topics overlap with many areas of economics including health economics, public economics, behavioral economics, industrial organization, and theory. Despite the dismal nature of Alzheimer's Disease, the prospect of economists improving our understanding of the disease appears to be bright.

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[41] The link between Medicare and Medicaid records is particularly fruitful for AD research, and long-term care more generally, given that Medicaid is a major payer of care for AD. That many studies have thus far been unable to observe the Medicaid side of the payer market has resulted in a major gap in our knowledge of the payer side of AD care.

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