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Research Report

JODI L. LIU, LAWRENCE BAKER, ANNIE CHEN, JESSIE WANG, FEDERICO GIROSI

Modeling Early Detection and Geographic Variation in Health System Capacity for Alzheimer's Disease–Modifying Therapies

Widespread availability of effective disease-modifying therapies (DMTs) would be a breakthrough in slowing the progression of early-stage Alzheimer's disease (AD) to later stages of dementia. As an AD DMT has received traditional approval from the U.S. Food and Drug Administration (FDA) and more candidates are on the horizon (Reardon, 2023; FDA, 2023), with a third having promising Phase 3 clinical trial results (Sims et al., 2023), questions remain about how these therapies will be priced, covered by insurance, and delivered.

KEY FINDINGS

- There is substantial variation in health care system capacity across the United States to detect, diagnose, and treat early-stage Alzheimer's disease (AD) with disease-modifying therapies.
- The estimated wait times and the number of patients treated are sensitive to patient uptake of brief cognitive assessments.
- Estimated average wait times vary by state and can be three times longer in rural areas compared with urban areas.
- Care models that enable primary care practitioners (PCPs) to diagnose and evaluate patients for treatment eligibility would make the biggest impact on reducing wait times for specialists and increasing the number of people treated from 2025 through 2044 in our analysis. Improved triage of patients using blood-based biomarker tests could further reduce caseloads for specialists.
- Widespread delivery of AD-modifying therapies will require a combination of strategies to communicate the value of detection and treatment to patients, integrate PCPs into the detection and diagnosis pathway, and address capacity disparities across the United States.

Medicare covers therapies with traditional approval from the FDA and, under the Centers for Medicare & Medicaid Services' (CMS's) National Coverage Determination, also requires collection of real-world evidence through registries (CMS, 2023). Reimbursement levels for AD DMTs will have critical influence on patient uptake of therapies and on provider decisions related to the allocation of capacity and health care system infrastructure to detect, diagnose, and treat eligible patients.

Early-stage AD—mild cognitive impairment (MCI) and mild dementia due to AD—is often undiagnosed (Mattke, Jun, et al., 2023). About 12.1 million people in the United States are estimated to have MCI or cognitive impairment with no dementia (CIND) (Hudomiet, Hurd, and Rohwedder, 2023; U.S. Census Bureau, 2023), which could be due to AD or other causes; however, prevalence estimates vary widely (Ward et al., 2012). Factors affecting patient care-seeking for diagnosis include attitudes toward dementia, including stigma and problems with communication, as well as physicians' lack of knowledge and concerns about misdiagnosis (Bradford et al., 2009). These factors contribute to the underdiagnosis of dementia, with potentially more than 50 percent of people with dementia not receiving cognitive evaluations (Boustani et al., 2003; Kotagal et al., 2015), and missed or delayed diagnoses are even more common among minority populations (Amjad et al., 2018; Blinka et al., 2023; Lin et al., 2020). Very early detection of cognitive impairment is limited because cognitive assessments are typically initiated after subjective memory complaints and/or observations of cognitive impairment by family or friends. As AD DMTs become available, patient uptake of cognitive assessments would likely increase, although the extent of the increase would depend on the effectiveness of patient outreach against such factors as stigma and trust in providers.

The purpose of this study is to demonstrate the implications of several uncertain factors and geographic variation that will affect the delivery of AD DMTs. The three research questions we address in this report are the following:

1. How does primary care capacity for early detection of patients with MCI due to AD affect the delivery of Alzheimer's therapies?
2. How do varying patient care-seeking behaviors for cognitive assessment affect the delivery of Alzheimer's therapies?
3. What is the variation in health system capacity for early detection, diagnosis, and treatment of early-stage AD across the United States?

The simulation results in this report are not meant to predict what will actually happen with treatment delivery in the future, which will hinge on coverage and reimbursement decisions. Rather, the simulation results illustrate a selected set of possible scenarios under specific—and uncertain—conditions and demonstrate the relative impact of varying patient uptake and capacity and how they interact to influence the delivery of AD DMTs.

Overview of Approach

We used a simulation model to assess patient demand and provider supply for the delivery of AD DMTs, based on methods used in prior analyses (Liu et al., 2017; Hlavka, Mattke, and Liu, 2018; Liu et al., 2019; Baxi, Girosi, and Liu, 2019). We expanded on prior modeling in two ways. First, we included the capacity of primary care practitioners (PCPs) who perform brief cognitive assessments. Prior models focused only on the capacity of specialists and assumed that PCP capacity was unconstrained (Liu et al., 2017; Mattke et al., 2020; Mattke and Hanson, 2022); however, PCPs serve an important role in early detection and may be a potential bottleneck as well as a potential resource in the diagnostic pathway. In this study, we investigated the impact of changes in PCP capacity and patient uptake of brief cognitive assessments in primary care settings on the delivery of therapies.

Second, our model utilizes county-level data, taking into account the geographic variations in patient populations and health system capacities. This approach allows us to capture local variation and provide a more accurate assessment of capacity constraints and wait times. Furthermore, national-level estimates that do not account for geographic

heterogeneity are likely to underestimate overall capacity constraints and mask important variation at local levels. For example, for an area with high capacity with an adjacent area with low capacity, people could have differential access to care and may travel further for care; however, averaging across those two areas would underestimate possible constraints.

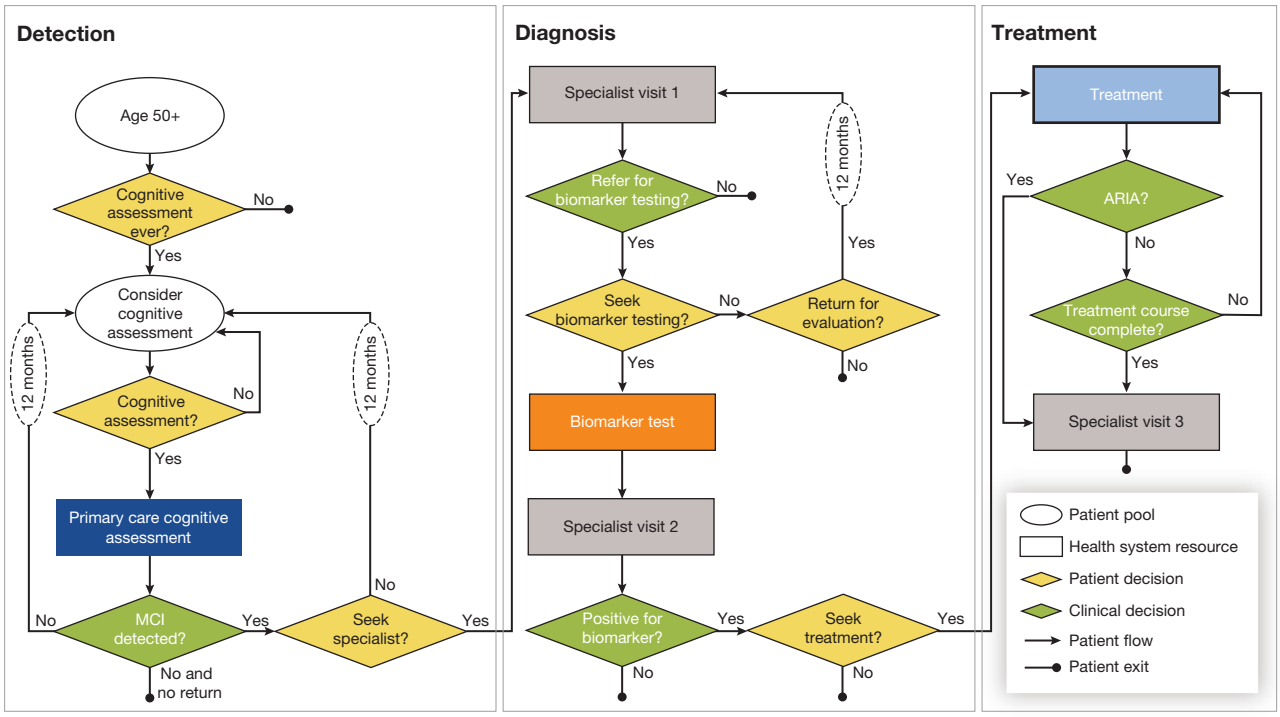
Conceptual Framework

The conceptual framework underlying the simulation model is shown in Figure 1. The clinical pathway is represented by three phases: detection, diagnosis, and treatment. Although this pathway is a simplified flow between clinical steps that not all patients may follow exactly, these steps are typical of a patient journey. Each rectangle represents a health care resource with finite capacity. Each diamond represents a decision, with yellow diamonds indicating patient decisions and green diamonds indicating clinical decisions.

In this framework, the detection phase begins with the population aged 50 and older, which reflects the age eligibility criterion used in several late-stage clinical trials of AD DMTs (U.S. National Library of Medicine, 2021, 2022, 2023). We assume that some individuals would never seek a brief cognitive assessment, and they exit the model. Other individuals would consider cognitive assessment each year, because of subjective memory complaints or at routine visit. We assume that this cognitive testing would be a brief cognitive assessment performed by a PCP. The Alzheimer's Association defines a *brief cognitive assessment* as a short evaluation for cognitive impairment, in which the practitioner may ask the patient about cognitive concerns, observe cognitive function, seek input from family and friends, consider physical exams and medical and family histories, and use a structured assessment tool such as the Montreal Cognitive Assessment (MoCA) (Alzheimer's Association, 2019). We assume that PCPs are primary care physicians, as well as nurse practitioners (NPs) and physician assistants (PAs)

FIGURE 1

Conceptual Framework of the Clinical Pathway Through Detection, Diagnosis, and Treatment



NOTE: ARIA = amyloid-related imaging abnormalities.

who work in primary care settings. PCPs are a critical component of the clinical pathway because most people would likely be first seen in a primary care setting and have cognitive impairment detected by a PCP before getting referred to a specialist.[1] If an individual screens positive (i.e., scores within the range for MCI), they would be referred to a dementia specialist for further evaluation. Those who do not undergo a subsequent cognitive assessment, those who screen negative, or those who do not seek a specialist each year might consider seeking cognitive assessment again in the following year.

In the diagnosis phase, dementia specialists would evaluate patients. We assume that dementia specialists are neurologists, geriatricians, and geriatric psychiatrists. Following a positive screen for MCI from a brief cognitive assessment, more comprehensive neuropsychological (or neurocognitive testing) is recommended (Petersen et al., 2018). To diagnose MCI due to AD, a specialist may order imaging and would consider reversible causes of cognitive impairment. If reversible causes of cognitive impairment or non-Alzheimer's etiology are not identified, then they may refer patients for biomarker testing to detect the presence of amyloid, which is a hallmark of AD. To determine eligibility for currently approved AD DMTs, a confirmatory biomarker test with an amyloid positron emission tomography (PET) scan is needed.[2] If determined to be eligible, patients would be referred to treatment. In the treatment phase, there would be routine monitoring for ARIA that could result in discontinuation of treatment.

Simulation Model

Our model simulates the progression of patients through the clinical pathway and disease states. In the clinical pathway, inflows into the health system resources are determined by patient uptake and clinical decisions, and outflows depend on health system capacity for the service. Clinicians and patients rely on the results of diagnostic tests to make decisions, which may yield false negatives or false positives. When patients receive a referral to the next stage of the clinical pathway, they may choose to (1) pursue the referral and seek further care, (2) not follow up with the referral (but they may return in the clinical pathway), or (3) exit the clinical pathway altogether. The flows through the clinical pathway are updated monthly in the model.

The model uses county-level data, parameters drawn from the literature, and assumptions about the clinical flow. Many of the assumptions follow from prior studies that were informed by expert input (Liu et al., 2017, 2019). For this expanded analysis, which includes modeling of primary care and patient uptake of cognitive assessment, we consulted ten different subject-matter experts. The experts were a convenience sample of clinicians and health services researchers with expertise in primary care, family medicine, nursing, neurology, geriatrics, psychiatry, radiology, and telemedicine. Example questions from our semi-structured interview protocol are shown in Appendix C. The assumptions used in this analysis reflect our team's compilation and judgment of the input provided from the interviewees and from prior published studies.

For all simulation scenarios, we assume that AD DMTs are available and reimbursed by payers starting in 2025. We modeled DMTs delivered by monthly intravenous (IV) infusions for 18 months. With treatment, we assume that the progression from MCI due to AD to Alzheimer's dementia reduces by 30 percent. Table 1 shows key parameters and the assumed value, including mid, low, and high levels for parameters that were varied in this analysis. See Table A.1 in Appendix A for a summary of all model parameters and assumptions.

We use transition probabilities reported in the literature as the fraction of people who move to the next disease state each year. The disease states are normal cognition, MCI, Alzheimer's dementia, and death; see Table A.2 in Appendix A for the annual transition probabilities. MCI may arise due to AD or other causes.

TABLE 1
Key Parameters and Assumptions

Parameter	Value	Rationale and Source
Patient uptake of cognitive assessment: • Share of cognitively impaired individuals[a] who ever consider cognitive assessment • Share of cognitively normal individuals who ever consider cognitive assessment • Share of cognitively impaired individuals who seek cognitive assessment each year • Share of cognitively normal individuals who seek cognitive assessment each year	 • 85% (low 70%, high 90%) • 25% (low 15%, high 50%) • 90% (low 80%, high 90%) • 35% (low 10%, high 40%)	These parameters reflect the team's judgment and target the following values collected from expert inputs: Approximately 20% of the population age 50 and older would seek cognitive assessment in the initial year (low 10%, high 30%).
Patient uptake of evaluation and treatment: • Share of patients who follow up with a dementia specialist for further evaluation • Share of referred patients who would seek this confirmatory biomarker testing with an amyloid PET scan • Share of those who do not seek biomarker testing who would return to the specialist in the following year • Share of patients with clinically relevant amyloid burden who would seek treatment with an infusion therapy	 • 50% • 80% • 50% • 80%	Based on expert input
Capacity for a clinical activity: • PCPs for cognitive assessment • Dementia specialists for diagnosis • PET scans for biomarker testing • Outpatient RNs and LPNs for infusions	 • 5% (low 1%, high 10%) • 5% • 50% • 20%	 • Based on expert input and lower bound based on presence of AD at office visits (Santo and Kang, 2023) • Based on expert input (Liu et al., 2017) • Based on expert input (Liu et al., 2017) • Aligned with the historical number of infusions (Centers for Disease Control and Prevention [CDC], 2017; Liu et al., 2017)
Sensitivity and specificity • MoCA for detecting MCI • Amyloid PET for detecting amyloid	 • 0.84, 0.79 • 0.92, 0.88	 • Roalf et al., 2013; Abd Razak et al., 2019 • Salloway et al., 2017
• Share of MCI patients who have clinically relevant amyloid burden consistent with Alzheimer's pathology	• 42%	• Janssen et al., 2021
• Share of patients receiving infusion therapy who develop ARIA and discontinue treatment	• 4%	• Salloway et al., 2022

[a] Cognitively impaired individuals includes those with MCI and Alzheimer's dementia.

NOTE: LPN = licensed practical nurse; RN = registered nurse.

Patient Demand and Capacity Estimates

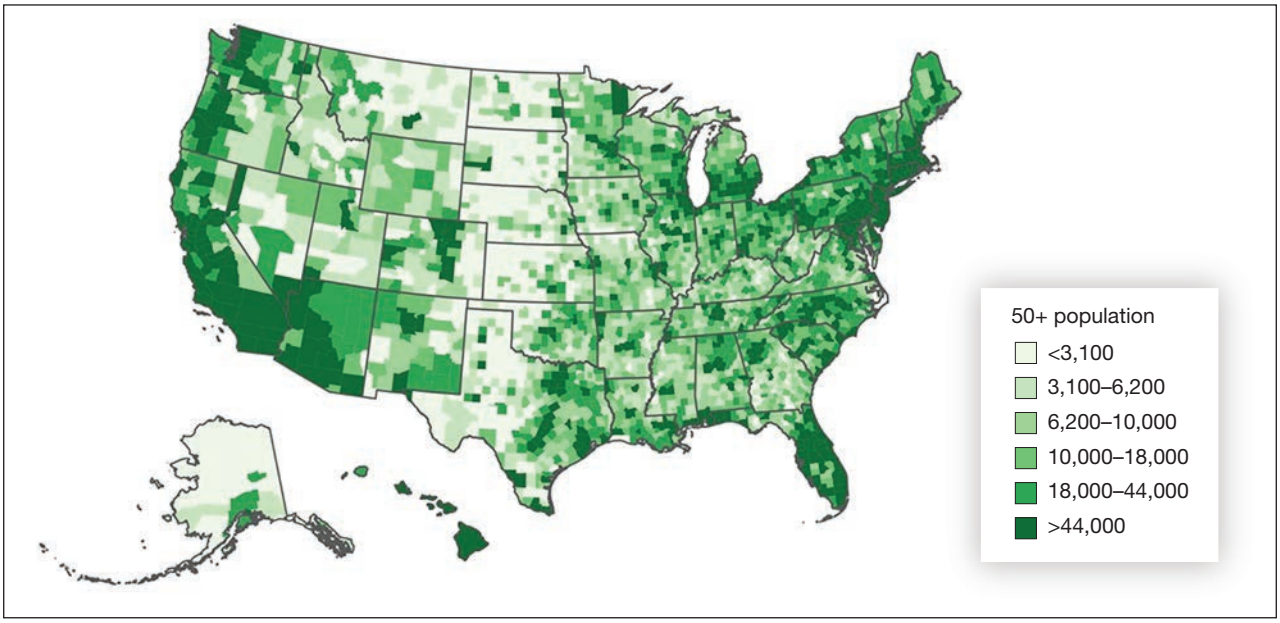
Population

We used 2020 county-level population data by five-year age bins from the Census Bureau as the baseline population (U.S. Census Bureau, 2023) (Figure 2). The baseline MCI and Alzheimer's dementia populations were derived by applying age-specific prevalence rates (Hudomiet, Hurd, and Rohwedder, 2022, 2023) to the population. In each projected year, we add a new cohort of 50-year-olds based on national population projections (U.S. Census Bureau, 2021).

We assume that individuals aged 50 and older are potentially eligible for treatment. Figure 3 illustrates the estimated patient demand at each step of the clinical pathway in the first simulation year assuming no capacity constraints—i.e., there are no wait times for any service.

FIGURE 2

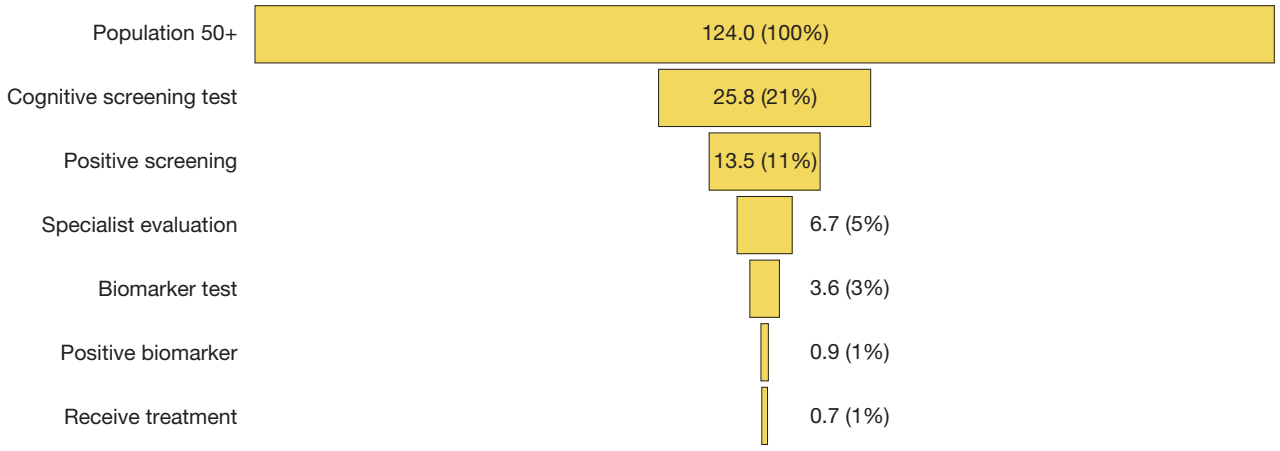
Population Age 50 and Older, by County, in 2020



SOURCE: Data based on July 1, 2020, estimates from U.S. Census Bureau, 2021.

FIGURE 3

Estimated Patient Demand Without Capacity Constraints in 2025 (millions)



Health System Capacity

The primary source of data for health system capacity in the model is the Area Health Resources File (AHRF) 2021–2022, which includes county-level data on the health care workforce and health facilities (U.S. Department of Health and Human Services, Health Resources and Services Administration, undated). To estimate the health care workforce in future years, we calculated annual growth rates from the Health Resources and Services Administration (HRSA) health workforce projections from 2020 to 2035. We carry forward the 2035 annual growth rate for each subsequent year through 2044.

Primary Care Workforce

We used the number of PCPs in each county in 2020 from the AHRF as the baseline primary care workforce. We define PCPs as primary care physicians,[3] as well as NPs and PAs who work in primary care settings, which are 61.6 percent of all NPs and 23.1 percent of PAs (American Association of Nurse Practitioners, 2022; National Commission on Certification of Physician Assistants, 2020). To estimate the workforce in future years, we used a combined projection of primary care physicians, NPs, and PAs in the HRSA health workforce projections.

We estimated that a PCP provides 2,051 visits a year on average, derived from the National Ambulatory Medical Care Survey (NAMCS) and Association of American Medical Colleges (AAMC) physician specialty data report (Santo and Kang, 2023; AAMC, 2021). Of those visits, our status quo assumption is that PCPs spend 1 percent of their capacity on brief cognitive assessment, which is approximately equal to the presence of AD at office visits reported in the NAMCS (Santo and Kang, 2023). Based on expert input, we varied this assumption between 1 and 10 percent in alternative scenarios, with 5 percent as the mid-level assumption.

Specialist Workforce

The dementia specialist workforce in our model consists of neurologists, geriatricians, and geriatric psychiatrists. We used data in the AHRF for neurologists, general internal medicine physicians, family medicine physicians, and psychiatrists involved in patient care. Based on the 2022 AAMC physician specialty data report (AAMC, 2022), we estimated that geriatricians represent about 2.6 percent of all internal medicine physicians and family medicine physicians. Similarly, we estimated that geriatric psychiatrists represent 2.9 percent of psychiatrists (Beck et al., 2018). We used the HRSA health workforce projections for adult psychiatry, geriatric physicians, and neurology physicians to project the number of dementia specialists.

We assume that each dementia specialist provides 1,576 visits a year (Santo and Kang, 2023; AAMC, 2022). Following prior expert input, we assume that the share of visits a specialist spends on diagnosis and evaluation of MCI due to AD is 5 percent.

PET Scanners

We used AHRF data on the distribution of PET scanners in hospitals in each county in 2020. The total number of PET scanners in hospitals from the AHRF (705) is comparable to the number reported by the Organisation for Economic Co-operation and Development (OECD), which also reports that 41 percent of PET scanners are in hospitals (OECD, 2023). We benchmarked the number of PET scanners, 2,371 scanners in all settings (Lam et al., 2021), using a ratio (2,371/705) to scale up the county estimates. To estimate the number of PET scanners in future years, we linearly fit the number of total PET scanners from 2011 to 2020 OECD data and extrapolated to 2044 to calculate annual growth rates.

Based on 2020 OECD data, we calculated the average number of PET scans per PET scanner to be 1,166 per year. Following prior analyses based on expert input, we assumed that the share of PET scans for determining patient eligibility for AD DMTs is 50 percent (Liu et al., 2017).

Infusion Workforce

We assumed that IV infusions would be administered by RNs and LPNs and used this workforce to define infusion capacity. We used county-level AHRF data on full-time and part-time RNs and LPNs in short-term general hospitals, short-term non-general

hospitals, and long-term hospitals. We then included RNs and LPNs who work in outpatient settings, which is 20 percent of all RNs and 15.2 percent of all LPNs, respectively (U.S. Bureau of Labor Statistics, 2022; Coffman, Chan, and Bates, 2015). To estimate the infusion workforce in future years, we used the HRSA health workforce projections for RNs.

We estimated that the average number of infusions an RN or LPN provides is 1,440 per year (Rondinelli et al., 2014). We assumed that the share of infusions for AD DMTs is 20 percent, which approximates the historical number of injections and infusions of therapeutic and/or prophylactic substances, excluding cancer chemotherapy and biologic response modifiers, reported in the 2011 and 2013 NAMCS and National Hospital Ambulatory Medical Care Survey (NHAMCS) (CDC, 2017).

Smoothing Capacity Across Counties

We accounted for the possibility that individuals may seek health care services in counties other than their county of residence. To approximate this care received across counties, we implemented a smoothing approach that distributes capacity for PCPs, dementia specialists, PET scanners, and outpatient RNs and LPNs across counties within the same state. Without smoothing, simulating patients and capacity using the raw capacity data would imply that no one accesses service outside their county of residence, which would be unrealistic. However, it is challenging to simulate exactly how much care is accessed in other counties. See Appendix B for technical details on our smoothing algorithm. Briefly, we used a smoothing algorithm that effectively shares the capacity from counties with higher capacity to adjacent counties with lower capacity. The smoothing process iterates until a predefined level of access across the state is reached. To parameterize a reasonable level of equal access within each state, we used the Gini index with a threshold of 0.2 (Teng et al., 2011). For example, a given state may have PET scanners only in few urban centers and have a Gini of 0.7. Our smoothing algorithm would allow adjacent counties (and counties adjacent to those counties) to share that capacity until the Gini is 0.2 in the state, approximating people accessing care in other counties. We also allowed 10 percent of the population in each state to access services in any county within the state. For the four health care resources in the model, Figure 4 shows the raw capacity in counties from the AHRF and the capacity after our smoothing algorithm. Resources that are more concentrated (i.e., have more unequal access geographically), such as PET scanners, are smoothed more than resources that are less concentrated, such as PCPs.

Simulation Scenarios

Table 2 shows a summary of selected scenarios. See Table A.3 in Appendix A for the detailed assumptions in each scenario. We included a "status quo" scenario that reflects patient demand and health system capacity estimated at current levels.[4] The "base case" scenario reflects our mid-level assumptions for patient uptake and health system capacity.

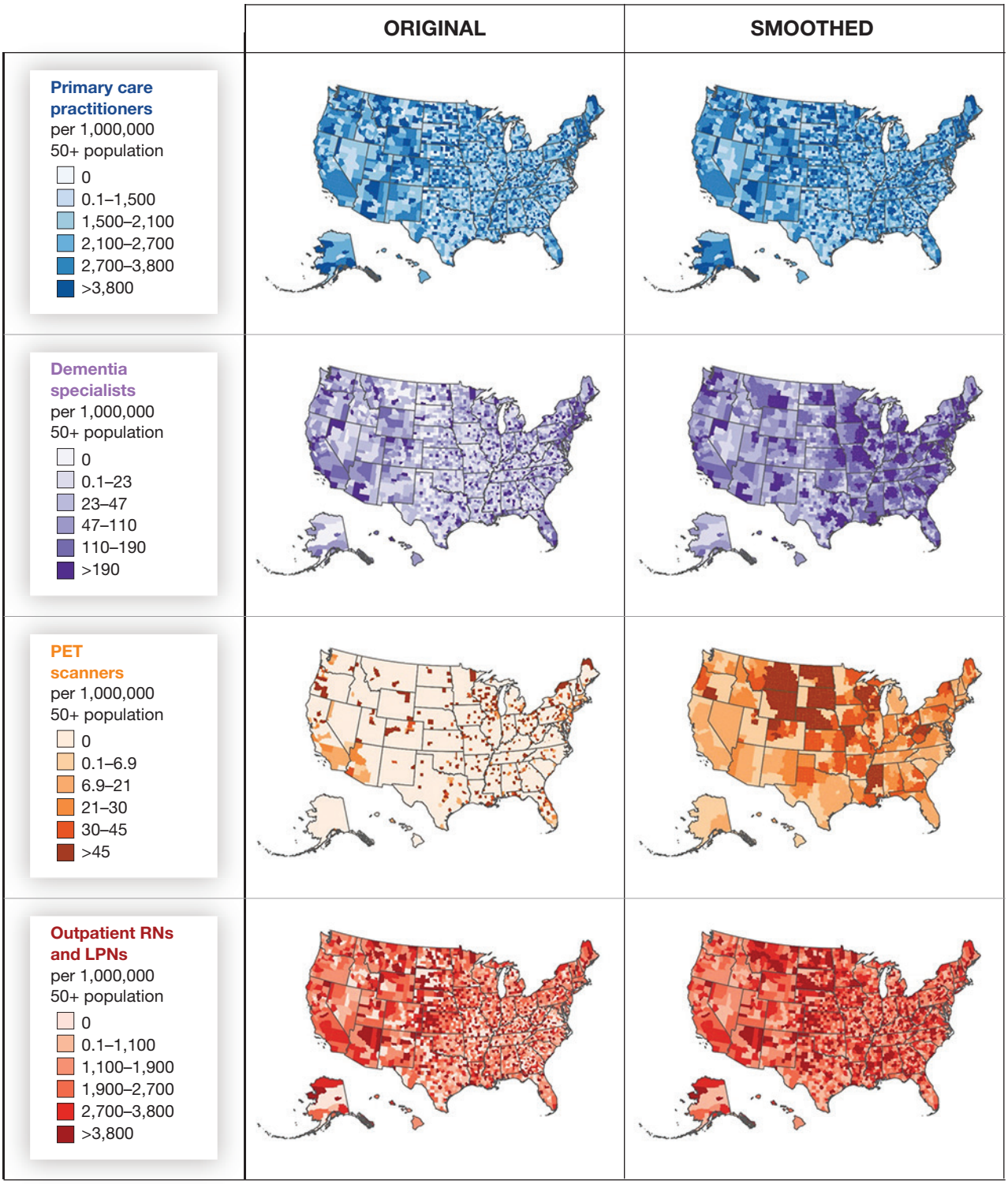
In alternative PCP capacity scenarios, we varied the capacity and role of the primary care workforce in detection and diagnosis. In "low PCP" and "high PCP," PCP capacity for detection is 1 and 10 percent, respectively (base case 5 percent). In "blood biomarker," PCPs order blood-based biomarker tests that allow for triaging patients with MCI and Alzheimer's pathology. In "dementia specialists plus PCPs," we assume that diagnosis and treatment management are protocolized such that PCPs and specialists can evaluate patients.

In alternative patient uptake scenarios, we varied patient uptake of brief cognitive assessments. The mid-level uptake assumptions result in 20 percent of the age 50+ population who seek a brief cognitive assessment in the first year (Table A.3 in Appendix A). The low-level and high-level uptake assumptions result in 10 percent and 30 percent, respectively, of the age 50+ population who seek a brief cognitive assessment in the first year.

For comparison, we have included a "no constraints" scenario in which we assume that there is enough capacity to serve all patients seeking detection, diagnosis, and treatment with no wait times.

FIGURE 4

Health System Capacity per Capita Among the Population Aged 50 and Older, by County, Before and After Smoothing, 2020



SOURCE: Unsmoothed data based on U.S. Department of Health and Human Services, Health Resources and Services Administration, undated.

TABLE 2
Simulated Scenarios

Scenario	Patient Uptake	Primary Care Capacity
Status quo	Estimated current level carried forward	Estimated current level carried forward
Base case	Mid uptake	Mid capacity
Low PCP	Mid uptake	Low PCP capacity
High PCP	Mid uptake	High PCP capacity
Blood biomarker	Mid uptake	PCP triage of MCI due to AD using blood-based biomarker test
Dementia specialists plus PCPs	Mid uptake	Combined dementia specialist and PCP capacity for diagnosis and treatment management based on protocolized evaluations
Low uptake	Low uptake of brief cognitive assessment	Mid capacity
High uptake	High uptake of brief cognitive assessment	Mid capacity
No constraints	Mid uptake	No constraints

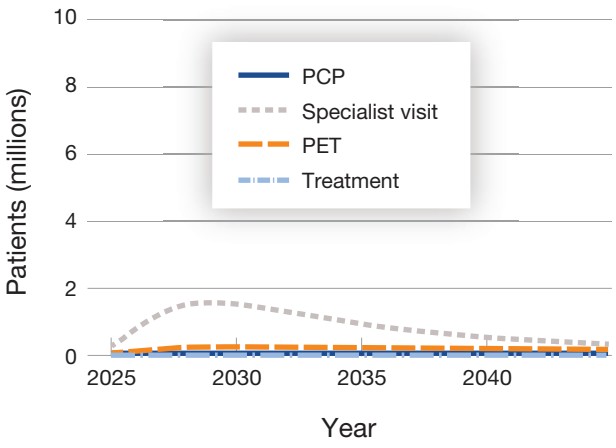
This report is accompanied by a web-based tool that allows users to adjust key parameters to explore different scenarios. See www.rand.org/t/TLA2643-1.

Simulation Results

Status Quo

In the status quo scenario, the main capacity constraint is access to dementia specialists. We estimate up to about 1.6 million patients waiting in 2028 (Figure 5), with average wait times of 19 months (Figure 6). There are shorter waits for PET scanners of about two to seven months, and no waits for PCPs and infusions. We estimate that 1.5 million patients with MCI due to AD would be treated between 2025 and 2044.

FIGURE 5
Estimated Number of People Waiting, by Year, in Status Quo (millions)



Base Case: Mid Patient Uptake and Capacity

Relative to the status quo scenario, there are more patients waiting (reflecting the assumptions in which increased patient demand outpaces increased capacity) but also more patients treated in the base case scenario. Under the base case assumptions, the main capacity constraint is also access to dementia specialists, with 0.8 million patients waiting initially in 2025 and up to about 5.4 million waiting in 2032 (Figure 7). There are no waits for PCPs. Because of long queues for specialists, on average, there are shorter waits for PET scanners that follow the waits to see a specialist, of about three to ten months, and no waits for infusions. The total average wait times are about 18 months in 2025, and they peak at about 55 months in 2030 (Figure 8). The queues and wait times begin declining after 2030 as the prevalent population of people with MCI due to AD clears the queues; in later years, the eligible population reflects people with incident MCI due to AD. We estimate that 2.1 million patients with MCI due to AD would be treated between 2025 and 2044.

FIGURE 6

Estimated Average Wait Times, by Year, in Status Quo (months)

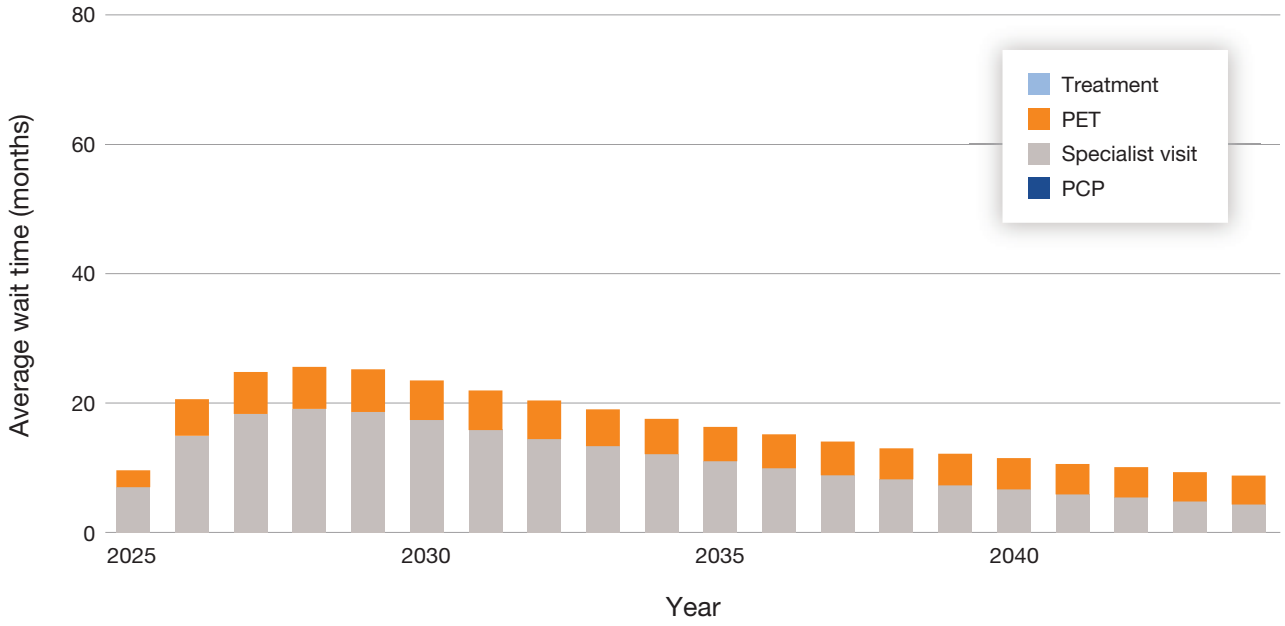
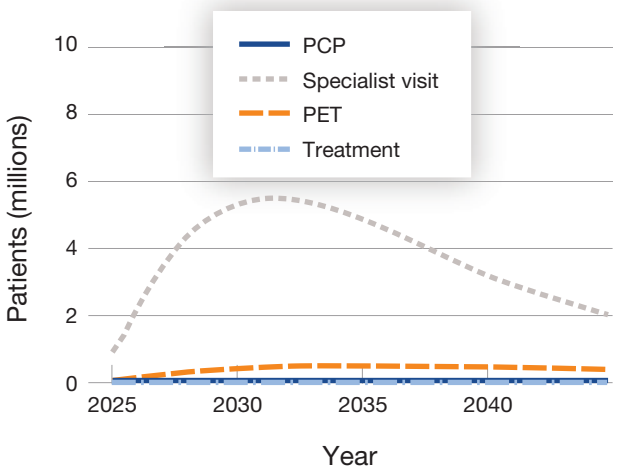


FIGURE 7

Estimated Number of People Waiting, by Year, in Base Case (millions)



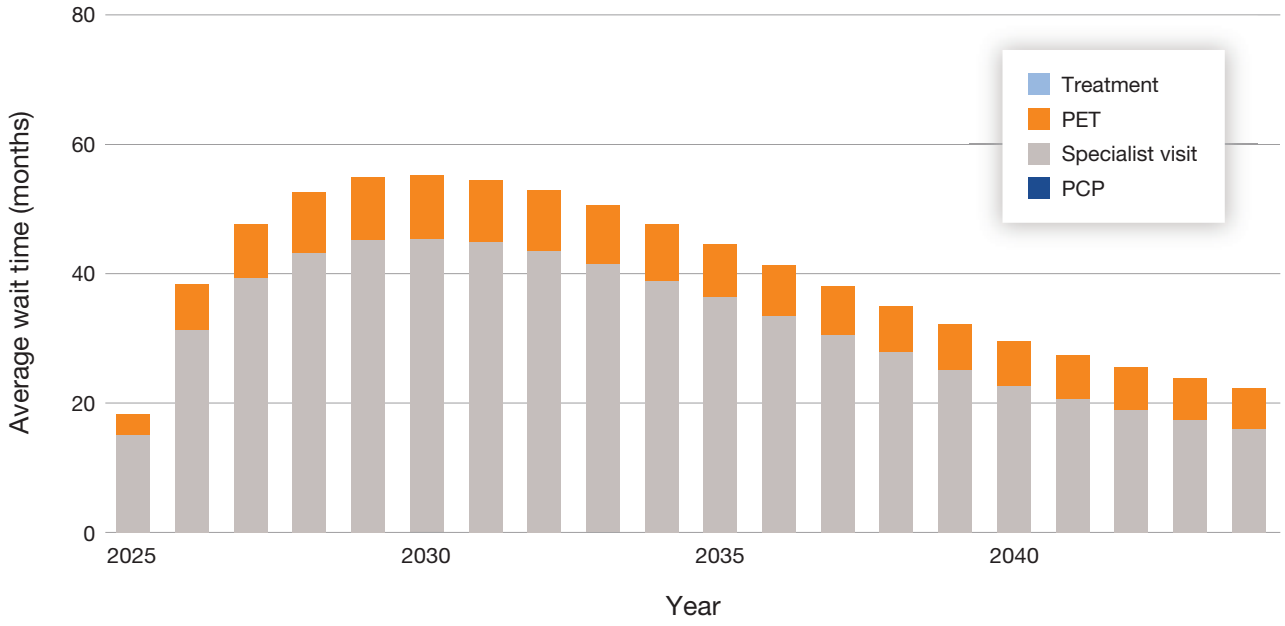
Varying the Capacity and Role of Primary Care

With lower PCP capacity for brief cognitive assessments, we estimate average wait times for PCPs of between one and seven months from 2025 to 2035 and less than one month after 2035 (top left panel of Figure 9). However, total average wait times (peaking at about 52 months in 2031) are similar to the base case because the specialist wait times are shifted to PCPs—i.e., increased waits for PCPs are offset by decreased waits for specialists. Higher PCP capacity (top right panel of Figure 9) does not alter total time to receive treatment relative to the base case, because specialists are the most limited resource. Scenarios with both lower and higher PCP capacity result in a similar number of patients treated as the base case.

However, there may be ways to engage PCPs to dramatically decrease specialist wait times, either by improving the accuracy of PCP cognitive assessments or by allowing PCPs to perform clinical tasks usually undertaken by specialists. We modeled the impact of administering a blood-based biomarker test for amyloid to all patients who score as having MCI based on a MoCA in primary care settings (bottom left panel of Figure 9). This improves triage by decreasing the number of false positives from patients who do not have MCI or who have MCI due to reasons other than AD, greatly reducing specialist wait times. However, average wait times for specialists are still long, with total average wait times peaking at about 33 months

FIGURE 8

Estimated Average Wait Times, by Year, in Base Case (months)



NOTE: The wait time in a given year reflects the average wait time for patients who enter the queue in that year.

in 2030. The estimated number of patients with MCI due to AD treated between 2025 and 2044 increased to 2.6 million.

Under a scenario in which PCPs could undertake diagnostic and evaluation activities typically done by specialists, such as more comprehensive neurocognitive testing and ordering advanced imaging, then queues for specialists could be effectively eliminated (bottom right panel of Figure 9). However, PET scanners become the rate-limiting step in most geographies, with average wait times ranging from nine to 23 months. We estimate that 3.4 million patients with MCI due to AD would be treated between 2025 and 2044.

Varying Patient Uptake of Brief Cognitive Assessments

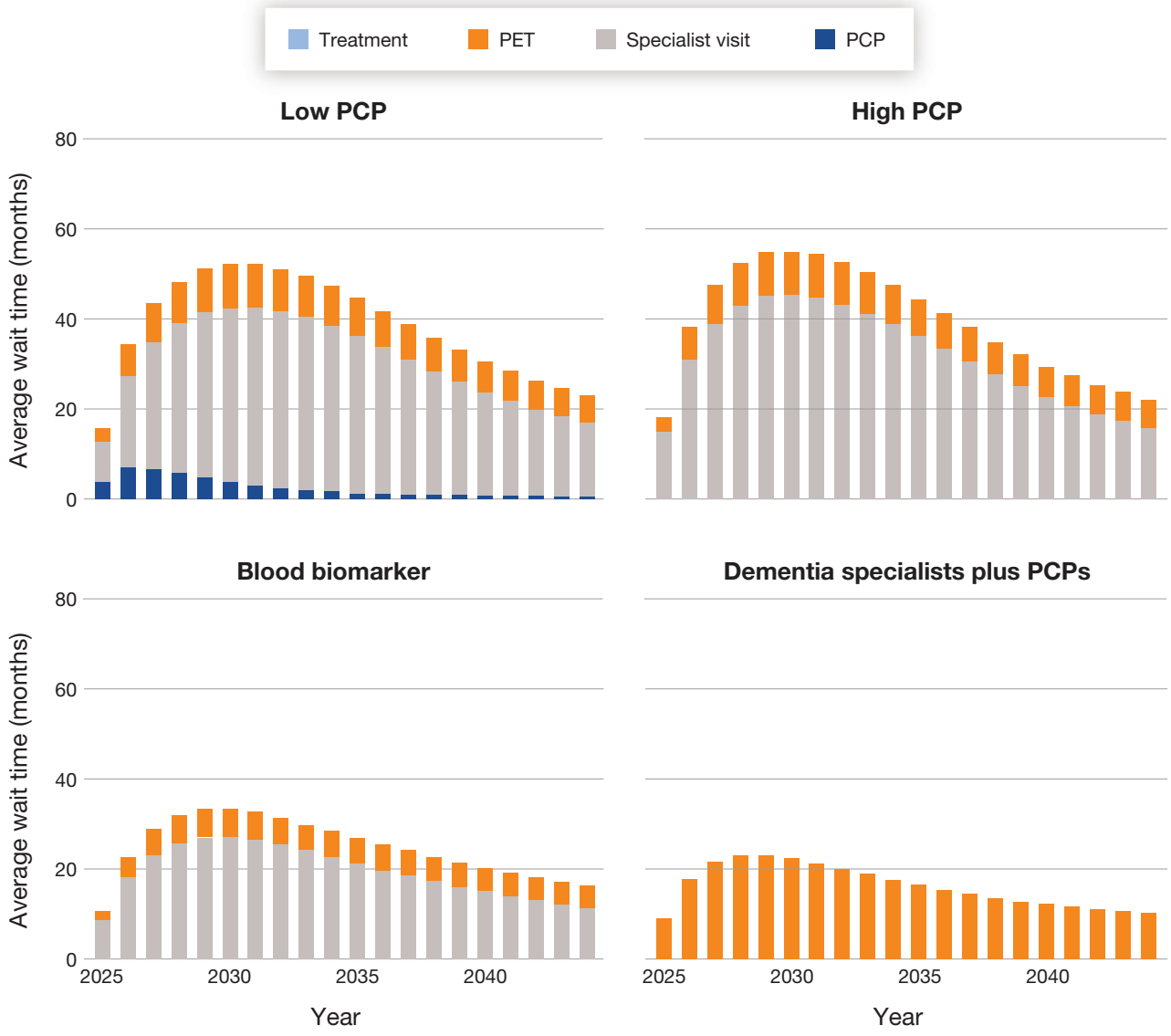
Lower patient uptake of brief cognitive assessments decreases the number of patients getting referred to specialists and average wait times (Figure 10). However, fewer patients (1.9 million between 2025 and 2044) are treated relative to the base case. Higher patient uptake increases the number of patients dramatically, and total average waits peak at about 80 months in 2033. Because of the long wait times, the estimated number of patients treated is similar to the lower-uptake scenario (1.9 million between 2025 and 2044) and lower than the base case.

Comparing Scenarios

Figure 11 shows the total number of patients who have MCI due to AD and are treated and the average wait time over the 2025 to 2044 period for each scenario. Relative to the status quo, the base case, scenarios varying PCP capacity (low PCP and high PCP), and scenarios varying patient uptake (low uptake and high uptake) all increase the total number of patients treated from about 1.7 million to about 2.2–2.5 million, but there are substantial increases in average wait times as patient uptake increases. Without other interventions, high uptake can negatively impact the total number of patients treated, as queues becomes so long that many patients' disease has progressed before it can be addressed by treatment or patients die. When the PCPs are generally not rate limiting, varying PCP capacity alone makes

FIGURE 9

Estimated Average Wait Times, by Year, in Alternative PCP Scenarios (months)



very little difference to total wait times; however, this could change with alternate sets of assumptions with low PCP capacity combined with high patient uptake.

Expanding the role of PCPs in detection and diagnosis of MCI due to AD has the potential to reduce wait times and increase the number treated. The blood biomarker scenario reduces overall average wait times (to 23 months) and increases the number treated (to 3.0 million) relative to the base case (37 months and 2.5 million, respectively). The "dementia specialists plus PCPs" scenario moves the estimates further toward the "no constraints" scenario (4.9 million treated), with 16 months for the overall average wait time and 3.9 million patients treated.

Geographic Variation in Wait Times

In each scenario, the wait times vary geographically. Figure 12 illustrates the variation in wait times by urbanicity in the base case scenario. Wait times are longer in rural and suburban counties compared with

FIGURE 10

Estimated Average Wait Times by Year in Alternative Patient Uptake Scenarios (months)

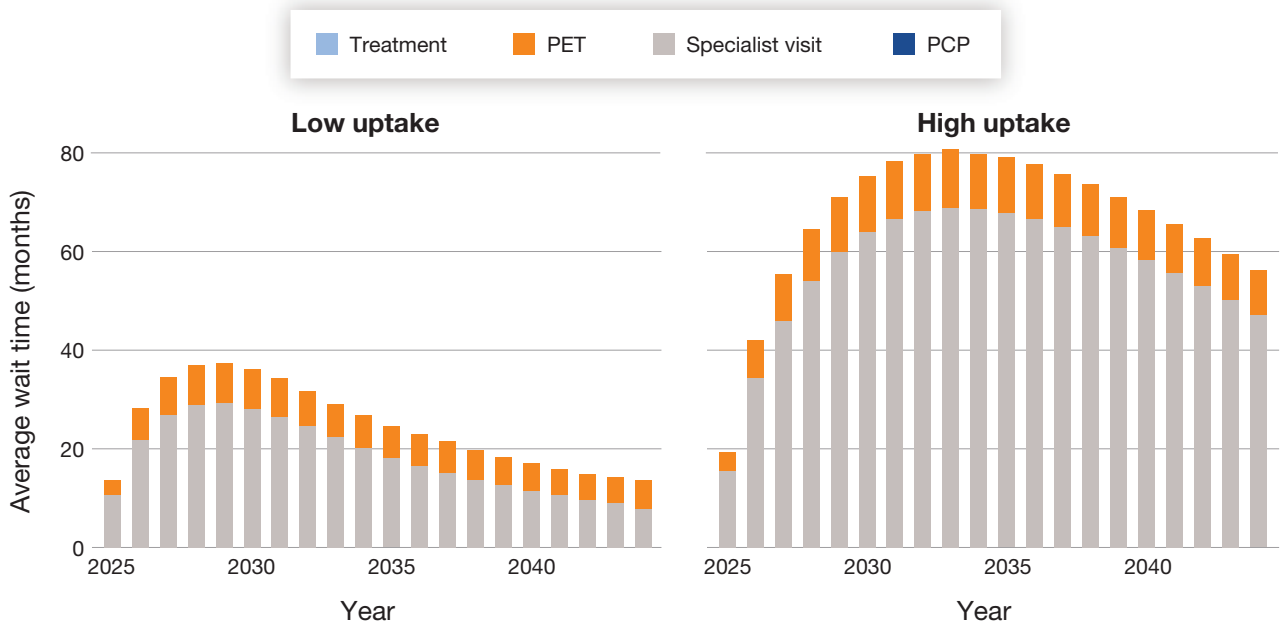


FIGURE 11

Comparison of Treated Patients and Average Wait Time in Scenarios, 2025–2044

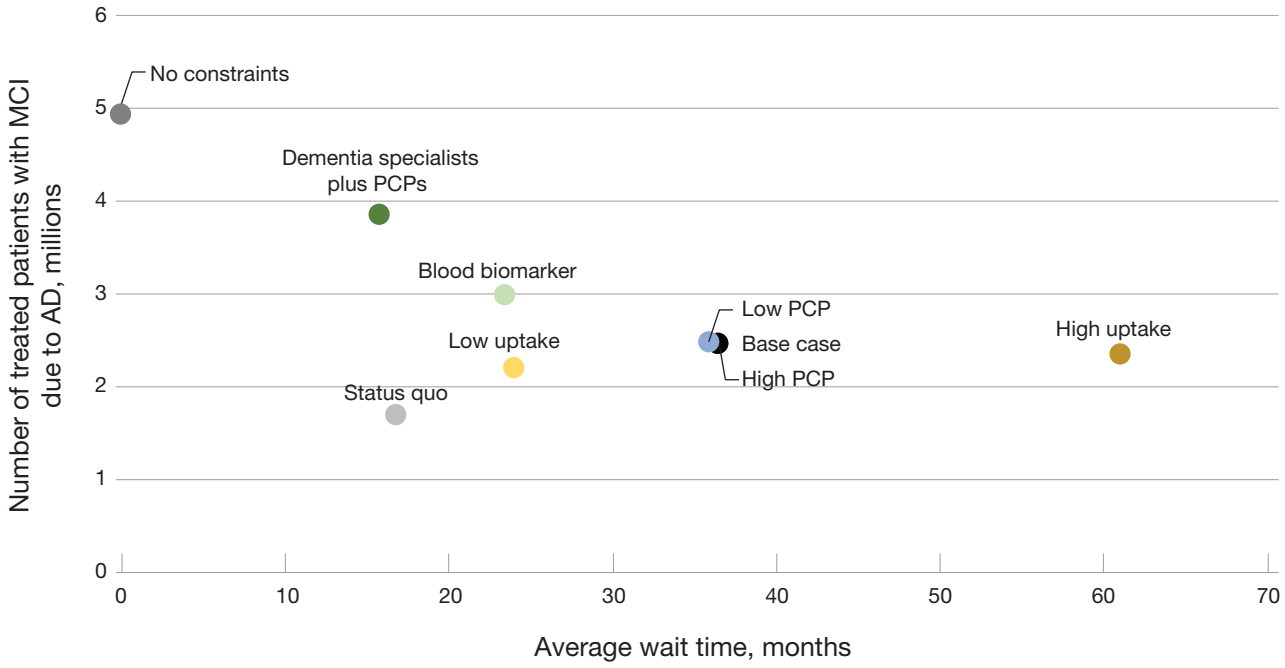
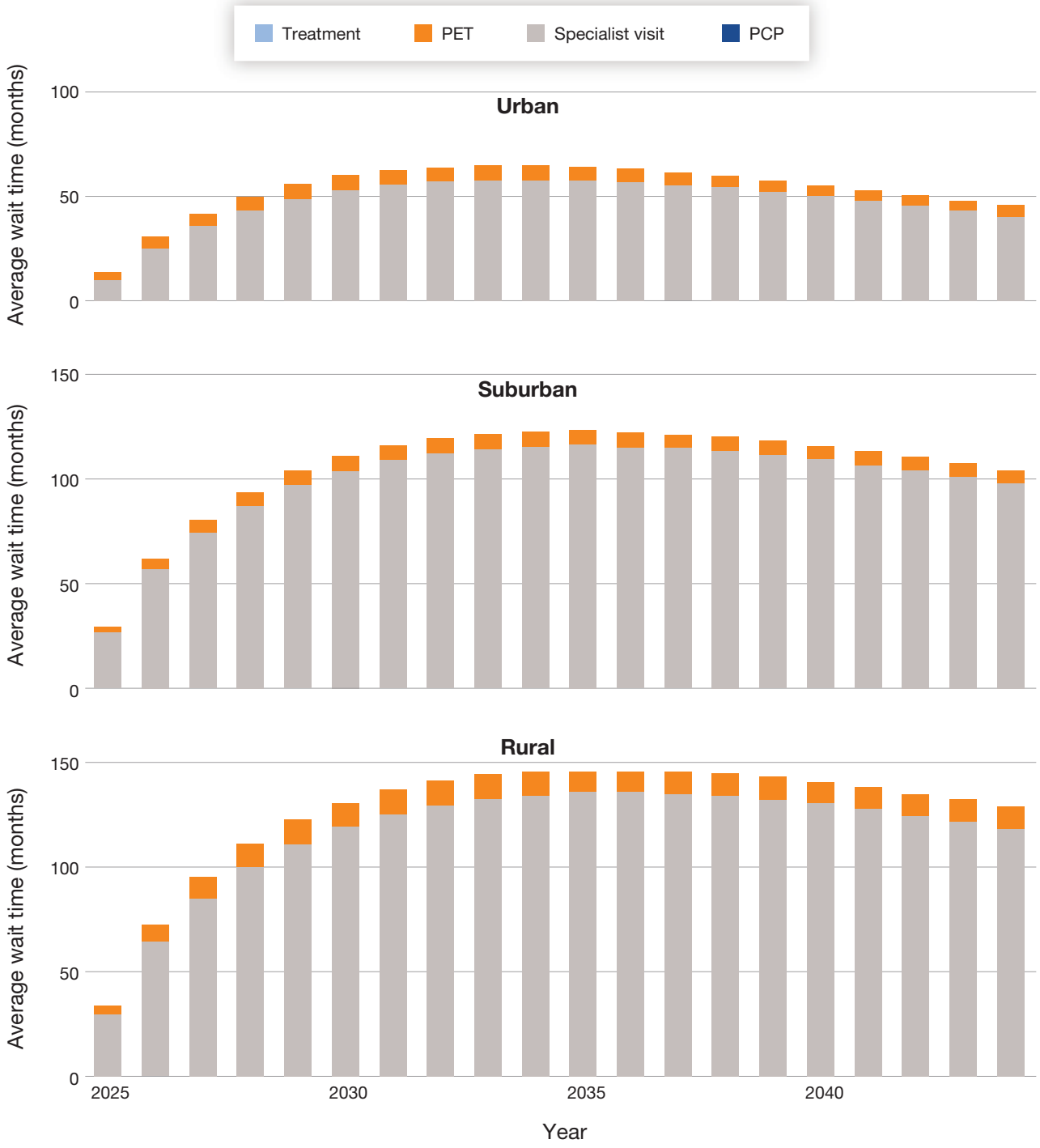


FIGURE 12

Estimated Average Wait Times by Urbanicity of Counties in Base Case (months)



NOTE: We categorized counties into three groups based on the 2013 Rural/Urban Continuum Codes (U.S. Department of Agriculture Economic Research Service, 2023): urban = metropolitan ("01", "02", "03"), suburban = non-metropolitan adjacent to a metropolitan area ("04", "06", "08"), and rural = non-metropolitan not adjacent to metropolitan areas ("05", "07", "09").

urban counties, with the peak of wait times being more than three times longer in rural areas than in urban areas. Although wait times are longer in rural and suburban counties, the number of patients waiting is fewer due to the smaller population sizes in those areas (data not shown).[5] Small increases in specialist and PET scanner access for rural and suburban areas could dramatically decrease wait times.

Figure 13 shows the variation in wait times by state in the base case scenario. Average waits are shorter in areas with greater specialist access, such as New England and parts of the Midwest. However, average waits are much longer than average in parts of the South and Mountain West, particularly in states with lower numbers of specialists per capita.

Limitations

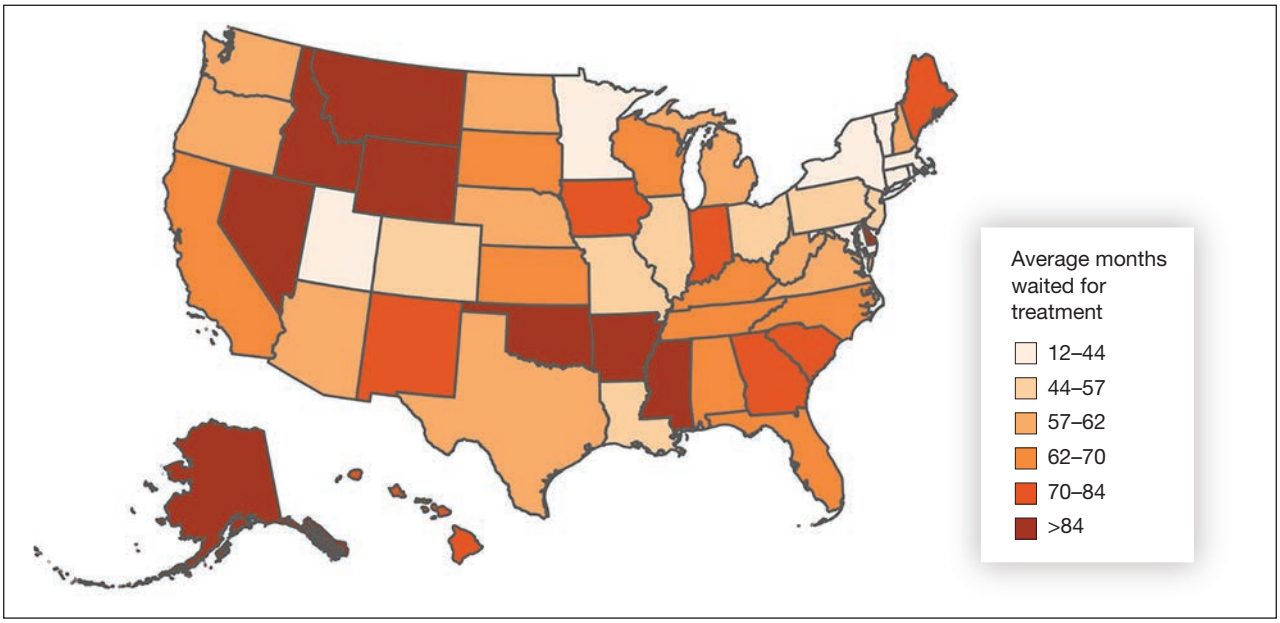
This analysis has several limitations. We modeled a simplified clinical pathway that captures only certain patient journeys. For example, we assumed that a proportion of individuals who are cognitively normal at baseline never undergo assessment—i.e., they do not re-enter the model even if they develop cognitive impairment in future years. This contributes to underestimation of the number of patients going through the clinical pathway. Although the model does not encompass all possible patient journeys, it does allow for comparisons of the relative impact of policies and strategies aiming to engage patients and increase the allocation of health system resources. For example, some stakeholders may focus on improving communication of the value of early detection and treatment to patients, while others may focus on enhancing the capabilities of PCPs to dedicate resources for early detection or embedding new technologies to streamline detection.

While we benchmarked our assumptions of patient uptake of cognitive assessment on available information about how often cognitive assessments are performed in Medicare annual wellness visits, how often people have routine visits to PCPs, and expert input, there is limited information on how patients' care-seeking behaviors for cognitive assessment would change if AD DMTs were widely available and covered by insurance.[6] If AD DMTs were available and reimbursed by payers, patient care-seeking would be strongly influenced by factors that include price, effectiveness, and side effects of therapies that are still to be determined.

In this analysis, we estimated the number of dementia specialists based on estimates of neurolo-

FIGURE 13

Average Wait Times in the Base Case, by State, 2025–2044



gists, geriatricians, and geriatric psychiatrists, and we did not distinguish between these three types of specialists. These specialists will vary in their likelihoods of seeing patients who may have early-stage AD and of prescribing AD DMTs and monitoring the course of treatment. Our assumptions on dementia specialist capacity for diagnosis, evaluation, and treatment with AD DMTs reflect the average across these types of specialists. Further work would be needed to better understand difference between the specialist types.

Although we included two scenarios that increased the role of PCPs by using blood-based biomarkers and combining PCP and specialist capacity for diagnosis and treatment management, we did not assess the time, training, infrastructure changes, and other considerations that would be needed to enable PCPs to dedicate resources to these activities. Integrating blood-based biomarkers into workflows may be relatively straightforward but would still require time, while having PCPs engage in diagnosis and treatment management would require substantial investments in training and workflow adjustments, as well as the right conditions in terms of reimbursement and workforce to take over some existing tasks.

This simulation model is not an agent-based model and does not contain heterogeneity in patient characteristics beyond disease states and county of residence. An agent-based approach would allow for further exploration of how subgroups of patients may have different uptake behaviors and access to providers. For example, it is documented that Black and Hispanic patients are more likely to have missed or delayed dementia diagnoses (Lin et al., 2020).

The geographic smoothing of capacity between counties that we use in this analysis is a rough approximation of people accessing services outside their county of residence. We constrained people to use resources only within their state of residence, but people may also choose to travel outside their state for care. Furthermore, it is possible that our smoothing algorithm assumes greater access to services than what is achievable in reality given barriers to travel. Future work is needed to better understand travel patterns and how they would affect the dynamics between patient demand and provider supply. Future sensitivity analyses could also explore confidence intervals around estimates.

In this study, we did not vary all possible assumptions. For example, we did not vary assumptions related to confirmatory biomarker testing. Of the four resources we examined, PET scanners are the most unequally distributed across the United States; scanners are typically centrally located in urban areas. Future analyses could examine alternative scenarios for making access to confirmatory biomarker testing more equitable, such as by using cerebrospinal fluid (CSF) testing or improved biomarkers, as well as how other biomarkers, such as apolipoprotein E (ApoE) status, could be part of patient and provider decisionmaking for evaluation and treatment management.

The focus of this study is on AD DMTs. Other than treatment, we did not assess potential benefits of early detection, such as care planning, treatment of symptoms, and financial and legal planning.

Last, this study did not assess several important factors that could influence access to care. For example, we did not directly assess the roles of financial barriers to patient uptake and reimbursement to provider capacity allocations. Furthermore, future technological and policy developments could substantially change access to care. Our aim with the alternative scenarios is to provide a range of what may be possible for uptake and capacity allocations, but these are still a narrow set of possible scenarios for a simplified clinical pathway that does not reflect all care pathways that people with cognitive impairment may take.

Discussion

Our results suggest that engaging the primary care workforce in the diagnostic process would be vital to accelerate the delivery of AD DMTs, which will overwhelm neurology and geriatric practices that often already have wait lists for appointments. While there are primary care–led memory clinic models (Bender et al., 2022; Lee et al., 2014; Callahan et al., 2011; Boustani et al., 2005), widespread engagement of PCPs in this process faces challenges with the need to establish content expertise in cognitive assess-

ment and the trade-offs of shifting resources away from other activities. A recent work group of national experts recommended the following three strategies to encourage the use of brief cognitive assessments in primary care: providing suitable assessment tools, integrating assessments into routine workflows, and implementing payment policies that promote use of assessments (Mattke, Batie, et al., 2023). While PCPs are technically capable of performing cognitive assessments and neuropsychological testing, most do not do them regularly, given trends toward billing higher volumes of services and the time it takes to do testing. Expanding the role of PCPs in detection and diagnosis would require training and experience, and the extent of PCP engagement would realistically be limited by competing demands and potential provider burnout. Furthermore, the role of primary care in detection and diagnostic activities will depend on reimbursement levels and the development of guidelines and standard protocols to streamline workflows.

Triage of patients could be improved with the use of blood-based biomarkers for AD, development of blood biomarkers for other types of dementia, and digital biomarkers. The use of these biomarkers would need to be integrated into workflows, ideally in primary care settings. While improved availability and accuracy of biomarkers for detection would allow for better triage, protections for information generated by biomarkers will need to be considered, especially if they are widely used at early stages of AD. The protections should consider implications for individual privacy, health insurance, employment, and genetic relatives.

Patient care-seeking levels will matter for the delivery of AD DMTs and can exacerbate capacity bottlenecks. How uptake increases among eligible individuals who would benefit from treatment, individuals with MCI from other causes, the "worried well," and those with later-stage dementia affects estimated wait times and the total number treated. In addition to policies and programs focused on building capacity, improved patient awareness and provider training are essential to reduce stigma and enable clear communication about cognitive decline. An area that needs more research is how computer-based testing could be integrated for initial assessments and could help reduce the need for more comprehensive evaluation to identify patients who are not eligible for treatment.

Geographic variation in patients and capacity result in large differences in estimated wait times. Rural areas and certain states have specialist shortages that limit access to diagnosis and evaluation. Our estimates of long wait times for rural populations reflect disparities in access to specialists because people already have difficulty getting appointments. Our analysis also draws attention to states in which addressing capacity constraints would be most critical. Under our base case assumptions, the states with the longest wait times are Alaska, Arkansas, Idaho, Mississippi, Montana, Nevada, Oklahoma, and Wyoming, which result largely from low levels of dementia specialists per the population aged 50 and older. Primary care models and telehealth models could help improve access to care in these areas. Further analyses of capacity constraints at sub-national levels could help county and state officials and health system leaders consider ways to collaborate and jointly allocate resources.

There is the possibility that effective Alzheimer's therapies will be available but system-level barriers to access would mean that people with cognitive impairment would not benefit from the therapies. However, our estimates are not meant to predict exactly what treatment delivery will look like in the future. Rather, the dynamic modeling of alternative scenarios can help inform where bottlenecks in the system may occur and how components of the clinical flow could be organized to best serve patients. Our analysis suggests that strategies to alleviate the patient caseload on specialists for evaluation and diagnosis are needed. Further work is needed to evaluate how primary care–led models of care can widely and effectively evaluate and manage treatment for people with early-stage AD, as well as how technological advancements, such as improved biomarkers and computerized testing, can be integrated into workflows to better serve patients.

APPENDIX A

Model Parameters, Assumptions, and Projections

Table A.1 shows model parameters for assumptions related to patient uptake, clinical decisions, capacity, and tests.

Transition probabilities (Table A.2) are derived from Davis et al., 2018. We calculated an annual transition matrix for people aged 50 years or older by weighting two transition matrices (for age 65 and age 75) based on the share of 50+ population aged less than 70 or 70 and older. We considered mild, moderate, and severe Alzheimer's dementia as one state.

Figure A.1 shows the projected workforce and PET scanners used in the simulation.

Table A.3 shows the patient uptake and primary care capacity assumptions in each scenario.

TABLE A.1

Model Parameters and Assumptions

Parameter	Value	Description
Patient Uptake Assumptions		
Share of age 50+ population that seeks a brief cognitive assessment:		Parameters below adjusted to target 20% of the population seeking a brief cognitive assessment in the first year, which is based on expert input; range provided by experts: 12%–64%. The low assumptions target 10% and the high assumptions target 30% in the first year.
• for those with cognitive impairment who ever seek assessment	85%	Low assumption is 70%. High assumption is 90%.
• for those with normal cognition who ever seek assessment	25%	Low assumption is 15%. High assumption is 50%.
• for those with cognitive impairment who seek assessment in a given year	90%	Low assumption is 80%. High assumption is 90%.
• for those with normal cognition who seek assessment in a given year	35%	Low assumption is 10%. High assumption is 40%.
Share of MCI population who choose to visit dementia specialist (initially or a return visit the next year)	50%	Assumption based on expert input; range provided by experts: 30%–80%.
Share of MCI population referred for biomarker test who seek testing	80%	Assumption based on expert input; range provided by experts: 80%–95%.
Share of AD-MCI patients eligible for treatment who seek treatment	80%	Assumption based on expert input; range provided by experts: 60%–90%.
Clinical Parameters		
Share of MCI patients with other health conditions who would preclude treatment	10%	Assumption based on expert input.
Share of MCI patients who have clinically relevant amyloid burden	42%	Estimated from Janssen et al., 2021.
Share of MCI patients under treatment who discontinue due to ARIA	4%	Estimated based on 6.2% of patients treated with aducanumab and who developed ARIA over 76 weeks (Salloway et al., 2022).

Table A.1—Continued

Parameter	Value	Description
Capacity Assumptions		
Average number of visits by a PCP per year	2,051	Estimated from the number of visits to PCP in 2019 from the NAMCS and the number of PCP in 2019 from the AHRF.
Share of PCP visits for cognitive assessment	5%	Assumption based on expert input; range provided by experts: 1%–10%. Low assumption is 1%, based on the presence of AD at office visits in 2019 (Santo and Kang, 2023). High assumption is 10%.
Average number of visits by a dementia specialist per year	1,576	Estimated from the number of visits to surgical and medical specialists in 2019 from the NAMCS and the number of medical specialists (patient care) in 2020 from the AHRF.
Share of dementia specialist visits for diagnosis, evaluation, and treatment management	5%	Assumption based on expert input; range provided by experts: 0%–20%.
Share of PET scans for amyloid detection	50%	Assumption based on expert input (Liu et al., 2017).
Average number of infusions by a full-time outpatient RN or LPN per year	1,440	Estimated from the number of times per shift spent on initiating and managing treatments for an ambulatory RN (Rondinelli et al., 2014).
Share of infusions for administering AD DMTs	20%	Assumption to align with the historical number of infusions used in prior modeling (CDC, 2017; Liu et al., 2017).
Test Parameters		
Brief cognitive assessment, sensitivity and specificity	0.84 and 0.79	Sensitivity and specificity of MoCA to detect MCI (Roalf et al., 2013; Abd Razak et al., 2019)
Blood-based biomarker, sensitivity and specificity	0.89 and 0.69	Sensitivity and specificity of blood-based biomarker test to detect amyloid (Palmqvist et al., 2019).
Amyloid PET scan, sensitivity and specificity	0.92 and 0.88	Sensitivity and specificity of PET to detect amyloid (Salloway et al., 2017).

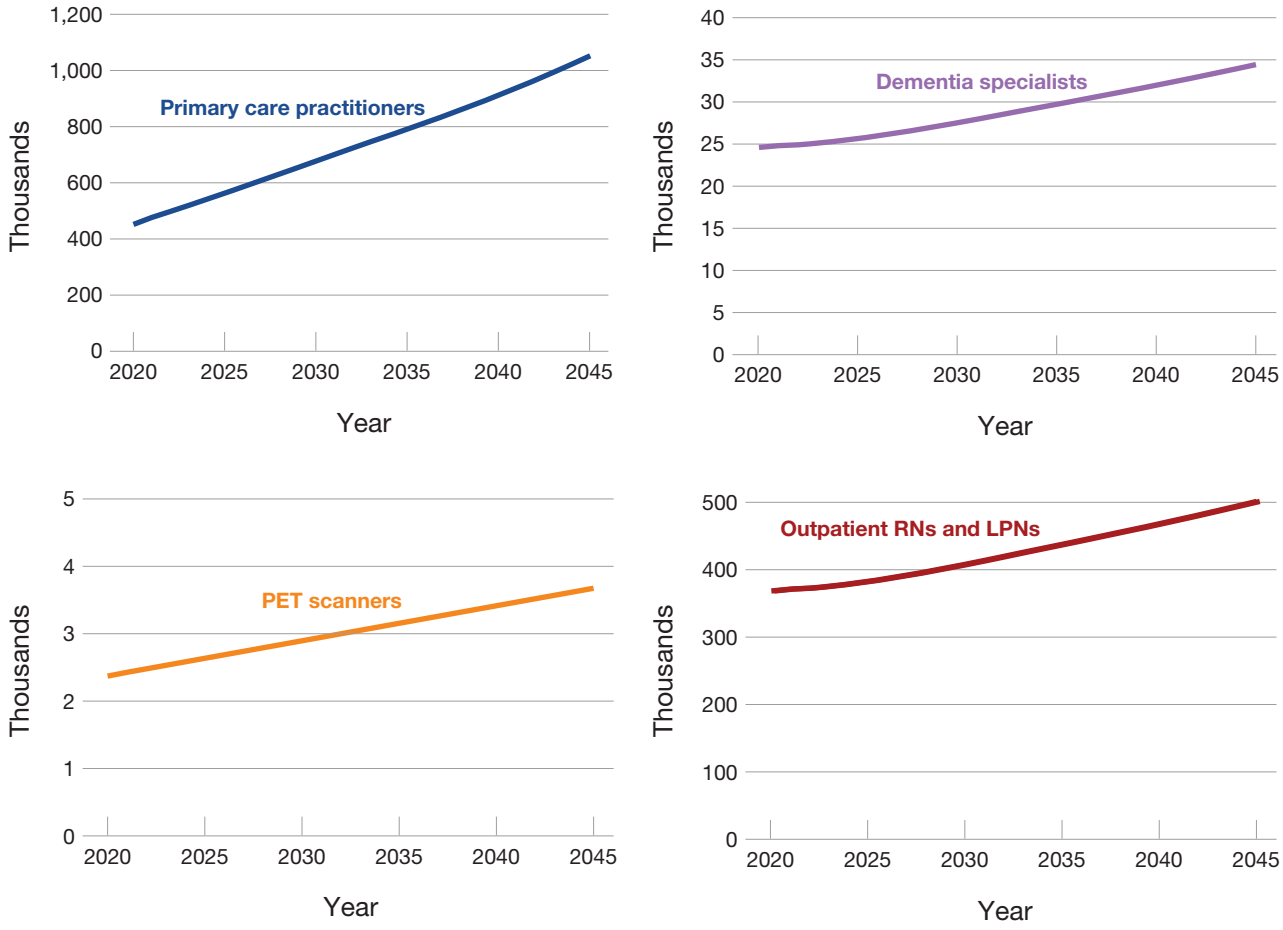
TABLE A.2
Annual Transition Probabilities

	Normal Cognition	MCI Not Due to AD	MCI Due to AD, Untreated	MCI Due to AD, Treated	Alzheimer's Dementia	Death
Normal cognition	0.917	0.03	0.039	0	0	0.01
MCI not due to AD	0	0.92	0	0	0	0.08
MCI due to AD, untreated	0	0	0.77	0	0.216	0.014
MCI due to AD, treated	0	0	0	0.835	0.151	0.014
Alzheimer's dementia	0	0	0	0	0.938	0.062
Death	0	0	0	0	0	1

SOURCE: Derived from Davis et al., 2018.

FIGURE A.1

Projected Capacity, 2020–2045



SOURCE: Features data from U.S. Department of Health and Human Services, Health Resources and Services Administration, undated; U.S. Department of Health and Human Services, Health Resources and Services Administration, 2023; OECD, 2023; Lam et al., 2021.

TABLE A.3

Patient Uptake and Primary Care Capacity Assumptions in Alternative Scenarios

Scenario	Patient Uptake	Primary Care Capacity
Status quo	Estimated current uptake of brief cognitive assessment: • 65% of cognitively impaired and 10% of cognitively normal ever seek cognitive assessment • 60% of cognitively impaired and 10% of cognitively normal seek cognitive assessment each year (7% seek assessment in the initial year)	Estimated current capacity: • 1% of PCP visits
Base case	Mid uptake of brief cognitive assessment: • 85% of cognitively impaired and 25% of cognitively normal ever seek cognitive assessment • 90% of cognitively impaired and 35% of cognitively normal seek cognitive assessment each year (20% seek assessment in the initial year)	Mid capacity: • 5% of PCP visits
Low PCP	Mid uptake (same as base case)	Low PCP capacity (same as status quo): • 1% of PCP visits
High PCP	Mid uptake (same as base case)	High PCP capacity: • 10% of PCP visits
Blood biomarker	Mid uptake (same as base case)	PCP triage of MCI due to AD using blood-based biomarker test
Dementia specialists plus PCPs	Mid uptake (same as base case)	Combined dementia specialist and PCP capacity for diagnosis and treatment management based on protocolized evaluations
Low uptake	Low uptake of brief cognitive assessment: • 70% of cognitively impaired and 15% of cognitively normal ever seek cognitive assessment • 80% of cognitively impaired and 10% of cognitively normal seek cognitive assessment each year (10% seek assessment in the initial year)	• Mid capacity (same as base case)
High uptake	High uptake of brief cognitive assessment: • 90% of cognitively impaired and 50% of cognitively normal ever seek cognitive assessment • 90% of cognitively impaired and 40% of cognitively normal seek cognitive assessment each year (30% seek assessment in the initial year)	• Mid capacity (same as base case)
No constraints	• Mid uptake (same as base case)	• No constraints

APPENDIX B

Technical Details

Smoothing Capacities

The raw capacity data from AHRF represent the amount of health care resources available in each U.S. county. Because individuals are not constrained to access health resources in the county where they reside, the AHRF data do not accurately represent the actual level of access to health resources. Therefore, in order to make our simulation model realistic, we need to account for the fact that the actual (or realized) distribution of resources is far less unequal than the one represented by the raw AHRF data.

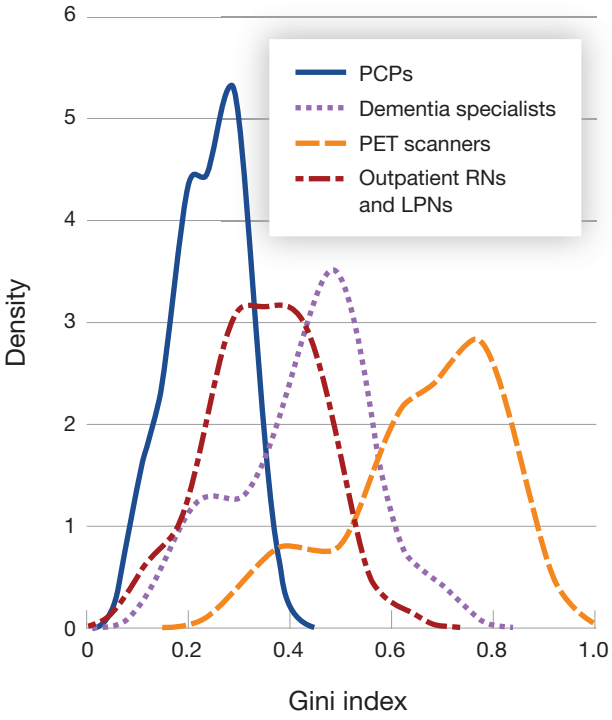
In order to provide a measure of the degree to which health resources are unequally distributed across counties, we computed the Gini index for the four health care resources considered in this report using the raw AHRF county-level data; their distribution across the U.S. states is shown in Figure B.1. The Gini index is commonly used as a measure of income inequality, with 0 representing perfect equality and 1 representing perfect inequality (Semega and Kollar, 2022). International comparisons commonly use the following thresholds to describe the Gini index: <0.2 as perfect income equality, 0.2–0.3 as relative equality, 0.3–0.4 as adequate equality, 0.4–0.5 as high disparity, and above 0.5 as severe disparity (Teng et al., 2011). In the context of health care capacity, a high value of the Gini index means that the resources are highly unequally distributed, or equivalently highly concentrated in few counties.

Not surprisingly, the distribution shows that PET scanners and dementia specialists are unequally distributed in most states, with Gini indices much above 0.4, which is already considered a high value. While the Gini index of actual resource use is not known, we assumed in this report that it would be roughly around 0.2, corresponding to relative equality based on the commonly used thresholds above. However, it would require further study to determine the level that best approximates actual access levels.

Our overall strategy is therefore to geographically smooth the density of health resources (i.e., the capacity per capita) provided by the AHRF data in such a way that the final Gini index for all the four health resources we considered was approximately 0.2. The effect of smoothing is to redistribute resources from areas with high capacity to areas of low capacity. This simulates the fact that individuals in areas with zero or low capacity will travel to areas with higher capacity and that the resulting utilization pattern is as if some resources were moved from high- to low-capacity areas.

FIGURE B.1

Distribution of Gini Index over States



While geographic smoothing is a well-studied topic, we could not use standard methods to smooth the density of resources across counties, because these methods fail to maintain the total capacity constant (Lawson et al., 2016).

Technically, the smoothing algorithm has two components:

- The first component is the smoothing formula for the density of resources experienced by the population of any given county. The formula requires knowledge of the amount of resources available in nearby counties, as well as an estimate of the number of people who may seek care in each of those counties.

- The second component is a model that produces realistic estimates of how many people seek care in each county. In this context, *realistic* means that the model captures (1) the fact that people may benefit from seeking care in counties with higher capacity than their own county of residence and (2) the fact that there are barriers to travel that limit the amount of resource sharing across counties. Without any smoothing, we would underestimate access to resources because we would be assuming that no one travels to other counties for care.

We describe each component in the following subsections.

Smoothing Formula

Each county i has a population P_i and is endowed with an amount C_i of a health resource (e.g., PET scanners). The resource C_i is shared equally across all individuals who are in the county at a given time. The nominal density (derived from AHRF) of the resource is $d_i = \frac{C_i}{P_i}$. However, as people travel to seek care, the population in county i is $P_i^* \neq P_i$ and comprises residents who have not traveled and travelers from other counties. Therefore, the *local density*, that is, the realized density experienced by the combination of residents and travelers who are in county i, is $d_i^{loc} = \frac{C_i}{P_i^*}$.

As a result of travel, residents of county i end up consuming an amount of the resource $C_i^* \neq C_i$: Those who have not left the county have to share the endowment C_i with travelers from other counties, and those who have traveled share parts of the resource endowment of other counties. Therefore, residents of county i experience an *effective density* $d_i^* = \frac{C_i^*}{P_i}$, where *effective* captures the fact that, from the point of view of residents of county i, the "endowment of the health resource is C_i^*, not C_i. The effective density d_i^* is the smoothed version of the density we are looking for.

To derive the formulas for the smoothed density d_i^*, we assume that we know the travel patterns. We denote by ω_{ij} the proportion of residents of county i who travel to county j seeking better access to a health care resource. The number of people traveling from county i to county j is stored in the matrix p, which we refer to as the *travel matrix*:

$$p_{ij} = \omega_{ij} P_j$$

After traveling, the population of a county includes the residents who have not traveled and travelers from other regions. The size P_i^* of this population is therefore

$$P_i^* = \sum_j p_{ij}$$

The amount of resource C_i^* consumed by the residents of county i is equal to the following:

$$C_i^* = p_{ii} d_i^{\text{loc}} + \sum_{j \neq i} p_{ij} d_j^{\text{loc}} = \sum_j \frac{p_{ij}}{P_j^*} C_j$$

The first term in the formula above accounts for the residents who do not travel: There are p_{ii} of them, and the amount of resource per capita available to them is $d_i^{loc} = \frac{C_i}{P_i^*}$. The second term accounts for the travelers. There are p_{ij} residents of county i who travel to county j, where the local density of the resource is d_i^{loc}.

The formula for C_i^* makes clear that allowing residents to travel is equivalent to having residents stay in their county but redistributing the health resource across counties using a linear smoothing operation: The endowment of a county is replaced by a weighted average of the endowments of the other counties, with weights defined by the travel matrix p. It is easily verified that $\sum_i C_i^* = \sum_i C_i$ so that the total capacity remains constant. The smoothed, effective density is therefore derived as

$$d_i^* = \frac{C_i^*}{P_i} = \frac{1}{P_i} \sum_j \frac{p_{ij}}{P_j^*} C_j$$

Therefore, to smooth the densities of resources, in addition to the raw capacity data C_i, all we need is the travel matrix p.

Estimating the Travel Matrix

To determine the number p_{ij} of residents of county i who travel to county j, we developed a simple model of traveling behavior based on the following assumptions:

- Individuals benefit from accessing a health resource, and they are willing to travel to maximize this benefit (which we also refer to as *utility*).

- The utility associated with accessing a health resource in a certain county is proportional to the local density of the resource in that county.
- There are barriers to travel, which can be quantified by a cost parameter.
- The cost of travel is proportional to the distance traveled, and the cost per unit of distance is a parameter γ.
- The utility and costs of traveling are aggregated at the county level, so that the determination of how many people travel is also made at the county level.

Based on the assumptions above, if p_{ij} individuals travel from county i to county j, they receive a total utility of $d_j^{\text{loc}} p_{ij}$ and experience a travel cost equal to $\gamma p_{ij} D_{ij}$, where D_{ij} is the distance between counties i and j. Therefore, we can write the utility accruing to county i from the travel pattern p_{ij} as

$$U_i = \sum_j p_{ij}\left(d_j^{\text{loc}}(p) - \gamma D_{ij}\right)$$

where we highlight the fact that d_j^{loc} depends on the entire travel matrix p.

The travel matrix p is determined by using an iterative best-response approach, where the utility of a county is maximized while taking the choices from all other counties as given, and cycling through all the counties until an equilibrium is reached where no county has the incentive to change their travel pattern. The existence of an equilibrium is guaranteed by noticing that this problem is an instance of a congestion game (Rosenthal, 1973), where the utility that accrues to each player from utilizing a scarce resource depends on the number of players utilizing the same resource. Congestion games have the property that a pure Nash equilibrium always exists, and it can be determined using the best-response iterative procedure described above.

The only free parameter in this procedure is the parameter γ, which represents the barriers to travel, and acts as a smoothing parameter: For larger values of γ, people travel less and less smoothing takes place, while for smaller values of γ, people can move more freely and resources are widely shared, leading to a more equal distribution of resources. Each value of γ determines the Gini index of the distribution of resources in a state, and, therefore, when we establish a target for the Gini index, we can back out the corresponding value of γ.

An example of the smoothing algorithm applied to the PET scanner capacity in Texas is shown in Figure B.2. The top and bottom panels of the figure show, respectively, the raw and smoothed number of PET scans per million in Texas. In the northern region of Texas, many patients are able to take advantage of a fairly highly density of PET scans in few counties, so the smoothed density is fairly high in this region. Individuals who live at greater distance from PET scanners, such as those in western Texas or those living near the borders, are the ones who have the most limited access to PET scanners.

Allowing a Portion of the Population to Have No Barriers to Travel

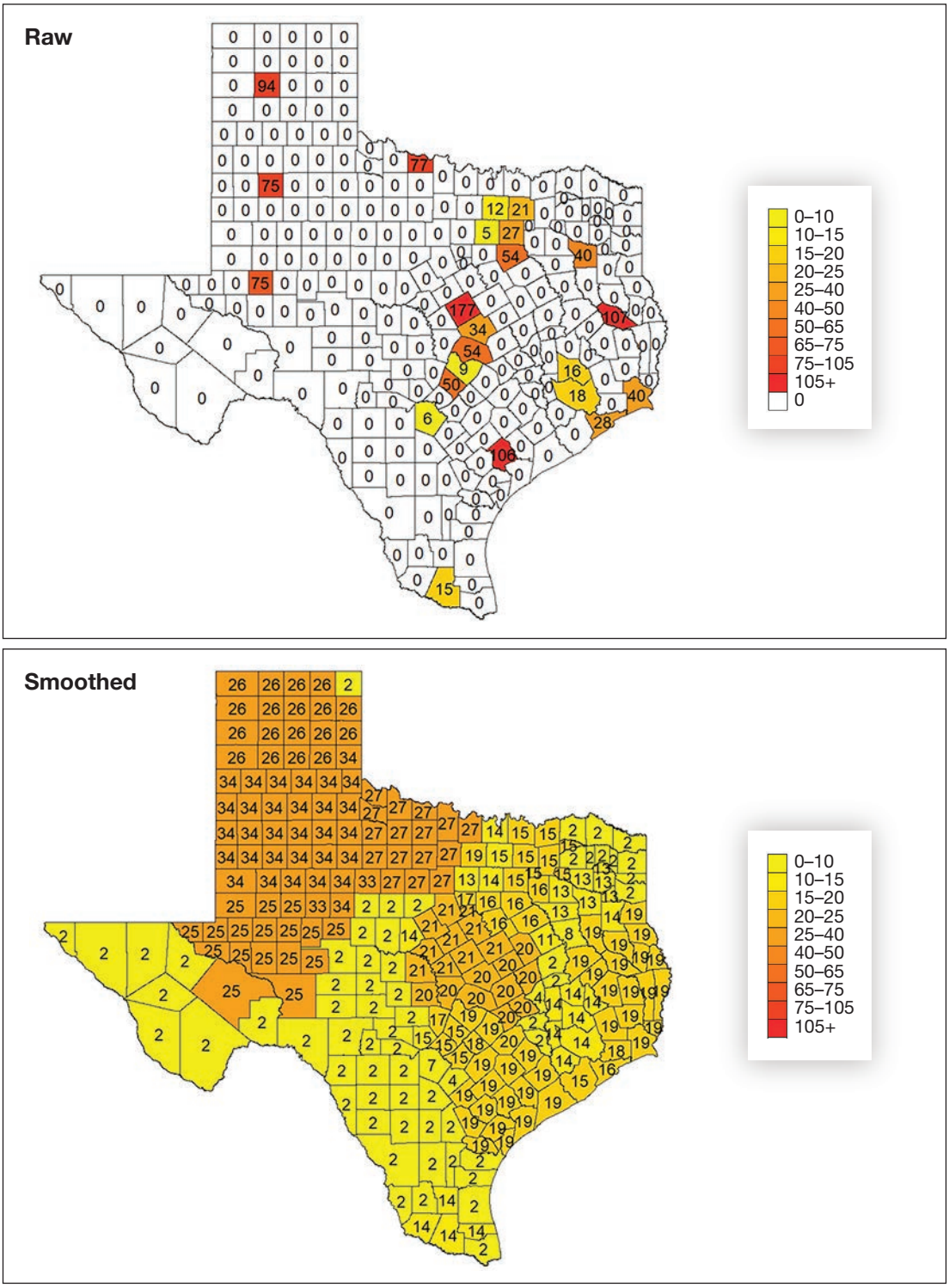
The model described above assumes that the barrier to travel is a function of distance and that all individuals in a county face the same level of barrier. But barrier to travel could vary. For example, some individuals may choose to fly to get care, and they do not necessarily fly to the nearest counties with higher capacity. To make the model more realistic and introduce some heterogeneity in travel patterns, we made a small modification to the model above and assumed that in each county, there is a small proportion of the population (10 percent) that faces no barriers to travel. In reality, some counties may have a higher or lower proportion of the population that faces no barriers to travel; however, we assumed 10 percent for all counties for simplicity. As a result, the final density pattern is modeled as a weighted average of the uniform density pattern that would result if everybody could travel freely (with weight 0.1) and the smoothed pattern corresponds to a cost of travel equal to γ.

Alternative Methodologies

The smoothing algorithm described in this appendix is not the only methodology we could have used. On the simpler side, we could have developed an algorithm that redistributed the total capacity according to some "distance decay," similar to what is often done in building catchment areas (Luo and Qi, 2009).

FIGURE B.2

Raw and Smoothed PET Scanner Density per Million, in Texas



The main drawback of such a method would be the failure to take into account any congestion effect.

A more sophisticated approach would have been to incorporate the congestion effects directly into the simulation: As people queue and waiting times become longer, people would switch the location where they access services, seeking shorter queues. The advantage of this approach is that it would directly incorporate the wait times observed in the simulation. However, while in principle feasible, this would have made the simulation much more complex and resource-intensive to run. Because not enough is known about cross-county travel patterns for receiving care related to cognitive impairment, it is not obvious that this would have led to increased accuracy. In addition, this type of modeling would have been more appropriate in the context of a microsimulation, which models behaviors at individual levels. The current approach, based on a utility maximization principle, could easily be adapted and incorporated into this a microsimulation. However, a full microsimulation is well beyond the scope of this study.

Steps in the Simulation

The simulation model represents patients as groups of people who move through the health system resources in the clinical pathway. A group is defined by its size (i.e., the number of people in the group), its health states (i.e., the proportion of the people in the group who have normal cognition, MCI, or dementia), its location in the clinical pathway, and the timestep at which it entered the queue for each resource. Groups can be split at points in the clinical pathway. For instance, if 30 percent of individuals in a group of 200 people do not seek a specialist after a positive cognitive assessment, then the group would be split into a group of 140 who seek a specialist and a group of 60 who do not. Groups can also be combined. For example, if two groups of 300 arrive at a unit at the same time, then they can be combined into a group of 600, preserving the health state proportions.

The logic for how groups flow through the model is defined for each unit described below. The timestep for moving between units is monthly.

- A **Service Unit** represents a health care resource, which can be PCPs, specialists, PET scanners, and outpatient RNs and LPNs. Each Service Unit has a predefined capacity for each timestep and geography. At each timestep, any group arriving at a Service Unit is put at the back of its queue. The Service Unit serves a number of patients from the front of the queue that is equal to its capacity, splitting groups when necessary. When there are multiple uses of the same resource, such as multiple visits to specialists, each use has a priority attached. The Service Units first serves in order of priority and then in order of arrival. There are two types of Service Units:
  - A **Test Unit** administers a clinical assessment or test. Tests are defined by sensitivity, specificity, and a set of health states they are attempting to test for. Test results can either be positive or negative and will generate false positives and negatives. Results are determined by multiplying the population in each health state by its sensitivity or specificity. After testing, patients move on different paths, with patient and clinical decisions made based on the test results, not the true underlying health states. In addition, patients make decisions such as whether to return for cognitive assessment. We modeled decisions as probabilistic, implemented as proportions (e.g., a group of 100 with 30 percent probability to seek a specialist and 70 percent probability to return for assessment next year would result in a group of 30 moving to the specialist queue and a group of 70 returning to the cognitive assessment pool).
  - A **Treatment Unit** modifies health states. This unit moves individuals from an (untreated) MCI due to AD state to a treated MCI due to AD state. The treated MCI due to AD state has a lower probability of developing Alzheimer's dementia.
- A **Pool Unit** represents groups waiting to make decisions. At each timestep, a fraction of the groups in the pool leaves the pool, and this fraction can vary by health state. In the model,

the cognitive assessment pool represents people who are eligible for cognitive assessments but have not yet undergone one that year. We assume that people with cognitive impairment are more likely to receive cognitive assessments than people with normal cognition, and so those with cognitive impairment leave the pool at a higher rate.

- A **Wait Unit** represent groups with wait times of a fixed length, such as waiting 12 months before returning for a cognitive assessment.
- An **Outflow Unit** tracks groups who permanently leave the clinical pathway when they die, decide to stop seeking care, or finish treatment. This allows the simulation to keep track of individuals after treatment and to continue to advance their health states.

Health state changes are simulated through a simple transition matrix. Once per year, we apply the transition matrix to the health states for every group, yielding the new health states for the next year. Deaths are moved to the Outflow Unit. Health state advancement occurs annually because monthly health state transitions are computationally intensive and yield similar results to annual transitions.

This model can simulate different geographic levels, including nationally, by state, or by county. Each geography is an independent simulation with its own population and capacity inputs, though geographies use the same parameters (such as the accuracy of testing). In the first model timestep, everyone who is age 50 and older in each geography enters the model. In subsequent timesteps, people who turn age 50 enter the model. Not everyone who enters the model receives treatment—e.g., there are patient decisions on whether to visit a provider.

At the end of the simulation, the model outputs the following three metrics:

- **Queue sizes** are the number of people waiting in a queue for a unit in each geography and timestep. Queue sizes are reported nationally by summing across all geographies.
- **Individuals treated** is the number of people with MCI due to AD who receive treatment. We did not count treated individuals who do not have MCI due to AD (but were incorrectly determined to have MCI due to AD—i.e., a false positive) because they do not derive benefit from treatment. The number of individuals treated is reported nationally by summing across all geographies.
- **Wait times** are the average amount of time people wait to get served for a unit in each geography and timestep. This is complex to compute because patients can loop through the clinical flow several times or elect not to follow referrals. To get around this problem, we first calculated the wait time at a unit for each group as the difference between when the group entered the queue for the unit and when they were served by the unit. We then aggregated these group-level waits to estimate average waits. When reporting wait times by year, we averaged across the unit and year of entry. We reported aggregate waits over a period of time by averaging across the time period and summing the unit waits. At the end of the simulation, not everyone will have exited their queues. This can bias the estimated wait time downwards because their actual wait time is longer and extends beyond the end of the simulation. To solve this issue, we ran additional years (e.g., five more years) to clear most people who entered queues and extrapolate the wait times for people who remain in the queue based on capacity, the number of people ahead of them, and the number of people ahead of them who will die (and therefore leave the queue).

APPENDIX C

Example Questions from Semi-Structured Interview Protocol

A. Cognitive Assessment

1. What type of cognitive assessments do primary care providers typically perform? E.g., Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA).
2. What share of PCP visits do you think could be allocated to perform cognitive assessments on the population aged 50+?
3. How would telehealth affect PCP capacity to perform cognitive assessments?
4. Assuming one or more AD therapies is available with reasonable effectiveness, what share of the population age 50+ do you think would seek cognitive assessment each year?
5. If a blood-based biomarker test for the detection of beta-amyloid was available, would you expect PCPs to administer these tests and triage patients for specialist referral? How might this affect patient uptake for cognitive screening?
6. Of patients with MCI based on a cognitive assessment, what share would be referred to and seek further evaluation with a dementia specialist?

B. Diagnosis and Patient Eligibility for Treatment

7. What share of specialist visits could be allocated to evaluating patients with MCI to determine eligibility for amyloid biomarker testing and treatment?
8. How would telehealth affect specialist capacity to evaluate patients with MCI?
9. We expect a patient's trajectory through the diagnostic steps would be affected by a combination of clinical judgment and patient uptake.
   a. Of MCI patients evaluated by dementia specialists, what share would be referred for biomarker testing? Of those, what share of patients would get tested?
   b. If there are no specific contraindications for the therapy, are there conditions or circumstances for which you would expect treatment to not be recommended?
   c. Of patients with a clinically relevant amyloid burden based on biomarker testing, what share would receive treatment?

C. Treatment

10. We assume that an AD therapy administered by intravenous (IV) infusion would likely occur in outpatient infusion centers.
    a. Who would likely administer infusions? E.g., what type of nurses: all registered nurses, advanced practice registered nurse with NPI [National Provider Identifier], nurse practitioner with NPI, clinical nurse specialist with NPI?
    b. Is it reasonable to assume that the capacity to administer IV infusions would be limited by the nursing workforce?
    c. Would it be reasonable to assume that current nurses have some excess capacity to administer infusions? E.g., 10%?
    d. How easily could people be newly trained to administer infusions?

Is there anything we did not discuss today that you feel is important for us to understand the clinical practice and relevant capacity issues from your point of view?

Notes

[1] We considered including a pathway by which people would skip the PCP visit and go directly to a specialist, which may occur for some people with preferred provider organization plans or traditional Medicare. However, this would be rare for people with normal cognition and possibly those with MCI, unlikely for rural populations who have limited access to specialists because of shortages of specialists, and limited because of difficulties getting appointments with specialists even in urban areas.

[2] CSF can also be used as a biomarker test; however, the AD DMT clinical trials to date have used amyloid PET scans for confirmatory biomarker testing.

[3] We used AHRF data that draw from the American Medical Association Physician Masterfiles and excludes physicians aged 75 and older. We focused on primary care physicians in patient care and excluded hospital residents.

[4] In the status quo, we assume that the annual patient uptake for a brief cognitive assessment is about 7 percent, reflecting approximately 16 percent of people age 65 and older undergoing cognitive assessment each year (Alzheimer's Association, 2019) and rare occurrences of cognitive assessment for those under age 65. The share of PCP visits for brief cognitive assessment is 1 percent, which is the presence of AD at office visits (Santo and Kang, 2023).

[5] In 2025, we estimate that 84.5 percent of the age 50+ population resides in urban counties, 10.3 percent in suburban counties, and 5.2 percent in rural counties.

[6] Information on patient care-seeking behaviors collected from the American Life Panel is from unpublished RAND Corporation research by Susann Rohwedder, Péter Hudomiet, and Michael D. Hurd.

Abbreviations

AAMC	Association of American Medical Colleges
AD	Alzheimer's disease
AHRF	Area Health Resources File
ARIA	amyloid-related imaging abnormalities
CDC	Centers for Disease Control and Prevention
CMS	Centers for Medicare & Medicaid Services
CSF	cerebrospinal fluid
DMT	disease-modifying therapy
FDA	U.S. Food and Drug Administration
HRSA	Health Resources and Services Administration
IV	intravenous
LPN	licensed practical nurse
MCI	mild cognitive impairment
MoCA	Montreal Cognitive Assessment
NAMCS	National Ambulatory Medical Care Survey
NHAMCS	National Hospital Ambulatory Medical Care Survey
NP	nurse practitioner
OECD	Organisation for Economic Co-operation and Development
PA	physician assistant
PCP	primary care practitioner
PET	positron emission tomography
RN	registered nurse

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AAMC—*See* Association of American Medical Colleges.

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About This Report

This report illustrates how patient uptake and health care system capacity will affect the delivery of Alzheimer's disease–modifying therapies. It expands and updates prior work by examining the role of primary care and geographic variation in capacity across the United States.

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1776 Main Street
P.O. Box 2138
Santa Monica, CA 90407-2138
(310) 393-0411, ext. 7775
RAND_Health-Care@rand.org

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