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Assessing the Preparedness of the Korean Healthcare System Infrastructure for an Alzheimer's Treatment

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Key Findings

- Potential disease-modifying therapies could prevent or delay the progression of early-stage Alzheimer's disease to manifest dementia.
- The complexity of identifying and evaluating treatment-eligible patients combined with the high prevalence of the disease might overwhelm the capacity of healthcare systems without advance planning and preparation.
- We use a simulation model to assess the preparedness of South Korea's healthcare system infrastructure to diagnose and treat people with mild cognitive impairment due to Alzheimer's disease if a future therapy becomes available.
- If a therapy becomes available in 2022, we estimate that average annual wait times for diagnosis and treatment in South Korea could peak at 14 months and persist until 2028 in the absence of practices to leverage scarce dementia specialists' capacity more efficiently and increase capacity for biomarker testing and treatment delivery.
- Depending on policies, we estimate that 39,000 to 130,000 Koreans could progress from mild cognitive impairment due to Alzheimer's disease to Alzheimer's dementia while on wait lists.
- South Korea also faces the challenge of strong aversion to lumbar punctures and high rates of elderly residents in rural areas with limited access to specialty care.
- Expanding capacity would require coordinated efforts among multiple stakeholders to increase awareness and investment, and to implement policies that ensure adequate capacity to deliver a future Alzheimer's therapy.
- Several efforts are under way in South Korea that could be leveraged for this objective, such as the National Dementia Responsibility Policy, free cognitive screening and consultation at regional dementia centers and training programs for dementia specialists.

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Introduction

Alzheimer's disease is a chronic neurodegenerative disorder that leads to cognitive and functional decline, dementia, and premature death. No disease-modifying treatment exists at the moment and numerous clinical trials have failed in the past. However, on August 7, 2020, Biogen and Eisai announced that the U.S. Food and Drug Administration has accepted the Biologics License Application for aducanumab with priority review, with a Prescription Drug User Fee Act (PDUFA) action date on March 7, 2021. Thus, the first disease-modifying treatment might become available next year and several other therapies are currently in varying stages of clinical trials. Table 1 summarizes the additional Alzheimer's disease-modifying therapies that are currently in Phase 2 and Phase 3 clinical trials.

TABLE 1. *ALZHEIMER'S DISEASE-MODIFYING THERAPY CANDIDATES IN PHASE 2 AND PHASE 3 CLINICAL TRIALS, AS OF AUGUST 2020*

CANDIDATE	SPONSOR	CLINICAL TRIAL PHASE	EXPECTED PRIMARY COMPLETION DATE	NATIONAL CLINICAL TRIAL IDENTIFIER
Anti-beta-amyloid antibodies				
Gantenerumab	Hoffman-La Roche	Phase 3	May 2022	NCT03443973, NCT03444870
BAN2401	Eisai/Biogen	Phase 3	February 2022	NCT03887455
Anti-tau antibodies				
BIIB092	Biogen	Phase 2	March 2024	NCT03352557
RO7105705	Genentech	Phase 2	July 2020	NCT03289143
LY3303560	Eli Lilly	Phase 2	August 2021	NCT03518073
TRx0237	TauRx Therapeutics	Phase 3	December 2021	NCT03446001
Vaccines				
AADvac1 (anti-tau)	Axon Neuroscience	Phase 2	June 2019	NCT02579252
Other Mechanisms				
PQ912	Vivoryon Therapeutics	Phase 2	December-2023	NCT03919162, NCT04498650
PTI-125	Cassava Science	Phase 2	September 2021	NCT04388254, NCT04079803
Azeliragon	vTv Therapeutics	Phase 2/3	April 2023	NCT03980730

*SOURCE: Author's review of ClinicalTrials.gov website as of August 13, 2020. *Phase 2 has been completed with positive results presented at the AAT-AD/PD 2020 conference.*

NOTES: Anti-beta-amyloid and anti-tau antibodies are monoclonal antibodies that are typically administered by intravenous infusions or subcutaneous injections. Alzheimer's vaccines are injections of antigens with the aim of triggering antibody responses against Alzheimer's proteins. Other mechanisms include a glutaminyl cyclase inhibitor, a molecule targeting filamin A proteins, and an inhibitor receptor for advanced glycation end-products (RAGE). Aducanumab is omitted from the table as it has completed its clinical trial program.

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This development is of particular importance for Korea, as it is rapidly ageing, like other East Asian countries, and the risk of developing the disease increases with age. The old-age dependency ratio increased from 10.1 percent in 2000 to 19.6 percent in 2018, making Korea the fastest aging country among OECD members. Projections show with the rapid aging process, Korea will become the oldest OECD country in 2075 (OECD, 2017). Approximately 750,000 Koreans currently have dementia as of 2018, of which about 75 percent have dementia due to Alzheimer's disease and the Korean government estimates that dementia prevalence will increase to 3 million by 2050 (J. Lee et al., 2020). In response, addressing the burden of dementia has long been a policy priority in Korea. Starting in 2008, the government has implemented several national dementia strategies and the current administration has reemphasized that commitment with a focus on supporting dementia care (see Box 3 for details).

However, making such a treatment available creates an unprecedented challenge for healthcare systems because of the combination of a complex evaluation process to determine treatment eligibility and the prevalence of the disease. The disease must be diagnosed in early stages for the treatment to slow down the progression of cognitive decline and the diagnostic process involves neurocognitive testing and advanced imaging. As many as 1.7 million Koreans may live with mild cognitive impairment (MCI) today (H. Cho & Kim, 2020), which is the stage at which treatment would ideally start. Most of them have not been evaluated and diagnosed because of the limited symptoms and treatment options. In previous studies, we have analyzed the preparedness of the healthcare systems in the U.S., Australia, Canada, Japan and six European countries (Germany, France, Italy, Spain, Sweden, and the U.K.) and predicted substantial obstacles to access in all of them, resulting in wait times and potentially avoidable disease progression (Hlávka, Mattke, & Liu, 2018; Jodi L. Liu et al., 2019; J.L. Liu, Hlávka, Hillestad, & Mattke, 2017; Soeren Mattke, Hlávka, Yoong, Wang, & Goto, 2019).

This report presents an analysis of the preparedness of the Korean healthcare system to identify and treat people with early-stage Alzheimer's disease (MCI due to AD and mild dementia due to Alzheimer's disease) when a disease-modifying therapy becomes first available. Following our earlier studies, we draw on publicly available data and expert insights to refine a simulation model that quantifies the capacity of the healthcare system to diagnose and treat people with early-stage Alzheimer's disease. We present projections for several scenarios under high-level assumptions; none of the scenarios are meant to provide precise predictions of the future given uncertainties related to the profile of a new therapy, patient uptake, and future capacity growth. Our goal is to demonstrate the magnitude of the potential capacity challenges in order to inform strategies for expanding capacity.

The following sections present our conceptual framework, simulation model, and projections. We discuss the design of the model and show historical and projected capacity trends that affect case finding, diagnosis and treatment. We show the impact of capacity constraints on wait lists, waiting times, and the number of people progressing from MCI due to Alzheimer's disease to full-blown dementia due to Alzheimer's disease. It is our hope that the analysis will facilitate dialogue among stakeholders and help ensure timely access in the era, in which a disease-modifying therapy becomes available.

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Patient Journey and Simulation Model

PATIENT JOURNEY

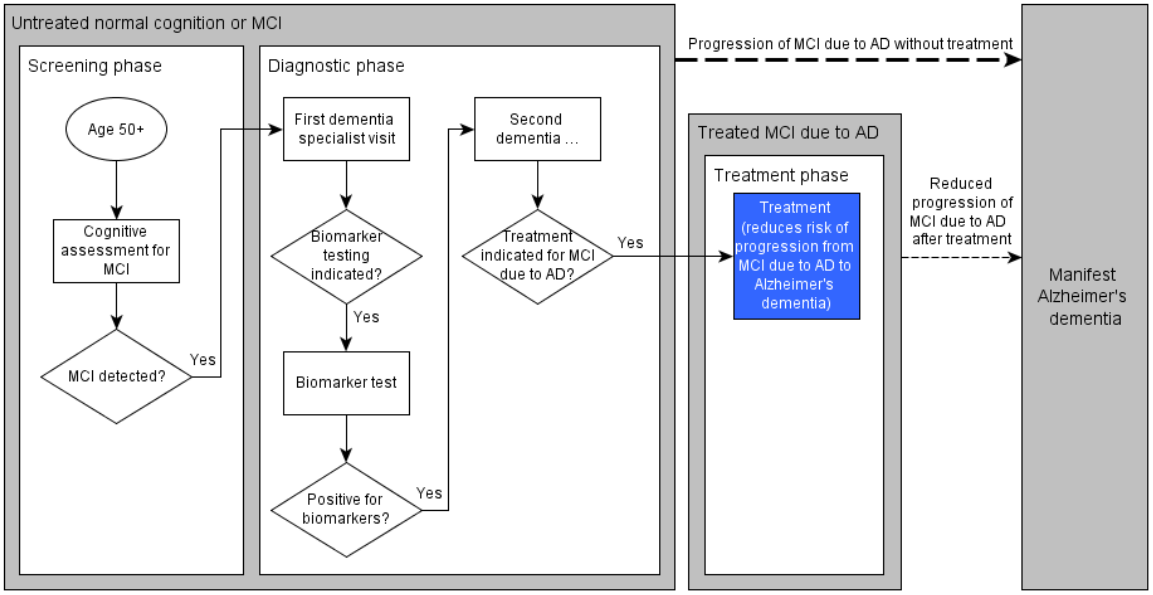
We used a stylized patient journey of the path to a disease-modifying therapy as the basis for our simulation model (Figure 1). We assume that patients will enter this pathway at the stage of mild cognitive impairment, either because they sought medical advice for a memory complaint or because screening suggested early cognitive decline, our Screening Phase. They will then undergo evaluation for the etiology of the cognitive

decline, our Diagnostic Phase, and finally be treated if shown to be eligible, our Treatment Phase. The disease continues to progress while patients are passing through the steps of this journey.

In this patient journey, older adults would undergo cognitive assessment with a short instrument such as the Folstein Mini—Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975), Modified Mini-Mental State Examination (Tombaugh, McDowell, Kristjansson, & Hubley, 1996), or the Montreal Cognitive Assessment (Ciesielska et al., 2016) and an assessment of functional deficits in primary care settings. Next, people who exhibit MCI, but no manifest dementia, would be further evaluated to ensure no other treatable causes exist, such as depression, substance use or hypothyroidism.

Having ruled out other treatable or reversible etiologies for MCI, patients would be referred to a dementia specialist for further evaluation, including additional cognitive and functional assessments, and possible referral to testing for the presence of amyloid and/or tau biomarkers to determine if the MCI is likely to be due to Alzheimer's disease (Diagnostic Phase). After a positive biomarker test, a dementia specialist would determine whether treatment was indicated. If indicated, patients could be treated with a therapy that would reduce the risk of progression from MCI to dementia due to Alzheimer's disease (Treatment Phase). For people with untreated MCI due to Alzheimer's disease, the disease would continue to progress. Compared to treated MCI patients, untreated MCI patients have a higher risk of progressing to a later stage of the disease with manifest dementia, at which point the assumed treatment would no longer be effective.

FIGURE 1. *STYLIZED PATIENT JOURNEY*



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SIMULATION MODEL

Our simulation model is a Markov model that simulates transitions between disease states and a systems dynamic model that simulates healthcare system capacity constraints within the MCI state, as used in our previous analyses. In this model, individuals move through the disease states—from no cognitive impairment (i.e., no MCI and no dementia due to Alzheimer's disease) to MCI to dementia due to Alzheimer's disease—according to transition probabilities derived from the literature (see Appendix Table A.1).

Within the MCI state, people are diagnosed (for MCI due to Alzheimer's disease) and treated based on a system dynamics model with outflows constrained by infrastructure capacity. We model three capacity constraints: dementia specialists, biomarker testing facilities, and treatment delivery facilities. For the two dementia specialist visits in the diagnostic phase of our framework, the model is optimized such that specialists do not take on a new patient for an initial visit if they do not have the capacity to provide confirmatory visits for existing patients in the same year.

We use Korean data on the population, disease prevalence, mortality, and historical workforce and infrastructure in the model. See Appendix Table A-1 for the parameter values and their respective sources.

MODEL ASSUMPTIONS

As no actual disease-modifying therapy for Alzheimer's disease exists today, we are using expert-guided assumptions to model a hypothetical therapy in the future. For this analysis of the Korean health care system, we start with the same assumptions for treatment effectiveness, uptake, and disease transitions as in our prior studies, but modify them to the Korean context as noted.

To adapt assumptions for Korea, we consulted with several experts familiar with clinical practice, care delivery, patient needs, and the policy environment. The experts were identified by a targeted search of the literature and websites of academic institutions and by snowball sampling in which interviewees recommended other experts for our recruitment process. We selected interviewees based on their clinical specialty, expertise, and contributions to the field. The interview questions were related to the following domains: clinical pathway, detection, and diagnosis, treatment and monitoring, data, and policies and practices. These assumptions include the types of specialists involved in the diagnosis of MCI due to Alzheimer's disease, and the relative role of PET and CSF to measure biomarkers.

The key assumptions in our analysis are as follows:

- A disease-modifying therapy for patients with MCI due to Alzheimer's disease becomes available in 2022.[1] Our analyses are based upon an anti-beta-amyloid monoclonal antibody therapy. We further assume that the therapy would be delivered by intravenous administration.
- We assume that individuals age 50 and older are eligible for annual cognitive screening, unless they have been diagnosed with MCI or manifest dementia. We modeled the population 50 years and older because most later-stage clinical trials include ages as low as 50 (e.g., Phase 3 trial of BAN2401, NCT03887455).[2] Screening starts in 2021 as patients and providers anticipate the approval of the therapy. Annual screenings may be conducted by general practitioners. We assume their capacity to conduct cognitive screening and functional assessments would be unconstrained. We assume that 50 percent of individuals age 50 and older would consent to screening each year. Of those who screen positive for MCI or are known to have MCI, we assume 50 percent would seek further evaluation from a dementia specialist. These proportions are based upon expert input collected in the original development of the model.

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[1] *Our U.S. and European analyses, which were published in 2017 and 2018, assumed that a therapy would become available in 2020.*

[2] *Our U.S. and European analyses assumed that the age eligibility would be 55 and older. For this analysis, similar to our analysis of Canada and Japan, we lowered the age range to 50 as current clinical trials tend to start enrolling at that age (e.g., Phase 3 trial of BAN2401, NCT03887455) and some trials targeting later age groups have been terminated.*

- Further evaluation would be conducted by a dementia specialist, whom we assume to include 80 percent of neurologists and 35 percent of psychiatrists. Individuals would be referred to testing for biomarkers if the evaluation confirmed MCI and did not find an alternative explanation for MCI (e.g., severe depression) or a reason to not pursue treatment (e.g., presence of another life-limiting disease). Of those with confirmed MCI that is possibly due to Alzheimer's disease, we assume that 90 percent of patients would seek biomarker testing, based on expert input in the original development of the model.
- In Korea, we assume that biomarker testing may be performed with a Positron Emission Tomography (PET) scan for amyloid deposits in the brain, or with a cerebrospinal fluid (CSF) test.[3] Based on input from Korean experts regarding the potential availability of PET scanners and patient preferences, our assumption is that 95 percent of tests would be performed using PET and 5 percent would be performed using CSF. We assume that 45 percent of people with MCI have clinically relevant biomarker levels that warrant anti-beta-amyloid monoclonal antibody therapy (Doraiswamy et al., 2014; Ong et al., 2015).
- If an individual's amyloid level is clinically relevant, she or he returns to a dementia specialist who determines whether treatment is indicated. If there are no contraindications and the individual consents, the individual is referred for treatment. Of people with MCI who test above a certain amyloid level, we assume that 80 percent would have no contraindications for treatment (based on expert input).
- We assume that the therapy would be delivered by intravenous infusion every four weeks for 18 months, following the protocol for aducanumab. We further assume that treatment reduces the relative risk of progression from MCI due to Alzheimer's disease to dementia due to Alzheimer's disease by 30 percent after treatment.

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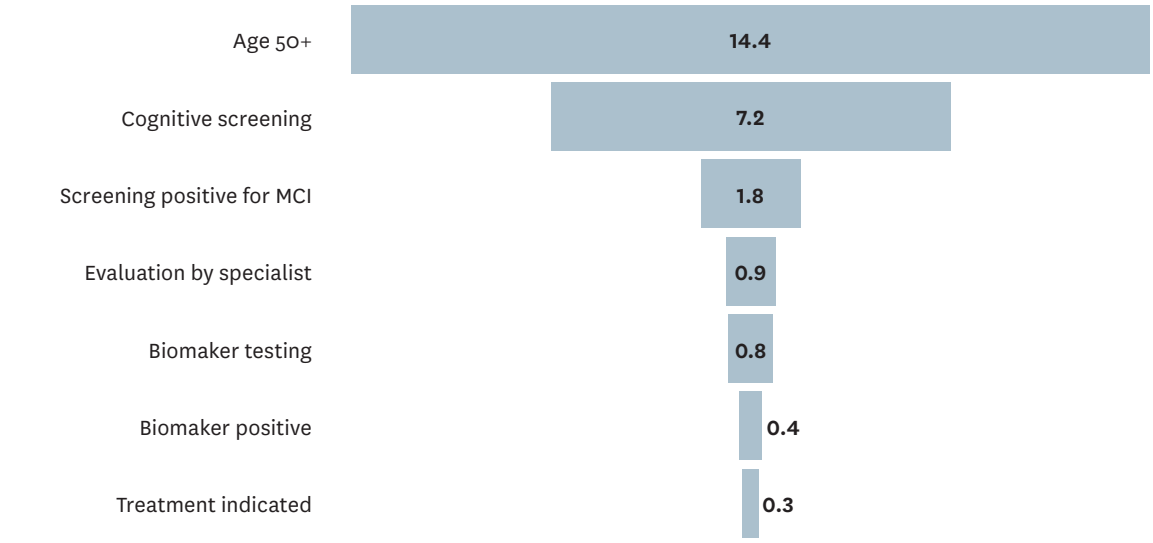
Current Patient Demand and Capacity Estimates

PATIENT DEMAND

Figure 2 shows the expected patient demand in the screening and diagnostic phases of the clinical pathway. We estimate that there would be 1.8 million Koreans who would either be known to have or screen positive for MCI in 2021. Of those, 0.9 million patients would seek evaluation by a specialist, 0.8 million would undergo biomarker testing, 0.4 million would test positive for amyloid pathology and 0.3 million patients would be determined eligible for treatment.

[3] *OWe applied the same assumption in our prior analysis in Japan, but a different assumption in the United States, where a PET scan is the only currently FDA-approved modality for clinical use. In our analyses of European countries, we assumed that 90 percent of biomarker testing would be performed by CSF biomarker testing and only 10 percent would be PET imaging for patients with contraindications to lumbar puncture.*

FIGURE 2: EXPECTED PATIENT DEMAND IN SCREENING AND DIAGNOSTIC PHASES IN 2021 (MILLIONS)



SPECIALIST WORKFORCE

Based on expert input, we expect that two categories of specialist physicians will be involved in Alzheimer's diagnosis in Korea: neurologists and psychiatrists. We use specialist data from the Healthcare Bigdata Hub which is organized by the Health Insurance Review & Assessment Service of Korea for the number of neurologists and psychiatrists in the country from 2013 to 2019 (HIRA, 2020). We project future workforce pool using historical trends of the physician workforce and use medium fertility population forecasts from Korean census data until 2050 (KOSTAT, 2020). Based on expert input, we assume that 80 percent of neurologists and 35 percent of geriatric psychiatrists would be able to evaluate patients with suspected Alzheimer's disease (**Table 2**). This estimate reflects the share of specialists, whom our experts would consider capable of evaluating patients with cognitive decline, rather than the much smaller share of physicians, who are currently specializing in memory care. Of note, geriatric medicine was only recently established as a specialty in Korea, and only a negligible number of physicians has completed training (Kim, 2002).

TABLE 2. *PROJECTED WORKFORCE OF SPECIALISTS THAT MAY DIAGNOSE EARLY ALZHEIMER'S DISEASE*

YEAR	NEUROLOGISTS	PSYCHIATRISTS
2020	1,571	1,315
2030	2,197	1,731
2040	2,824	2,147
2050	3,450	2,562

SOURCE: Health Insurance Review & Assessment Service of Korea (http://opendata.hira.or.kr).

NOTE: We assume that 80 percent of neurologists and 35 percent of psychiatrists would be able to evaluate patients with suspected Alzheimer's disease in Korea.

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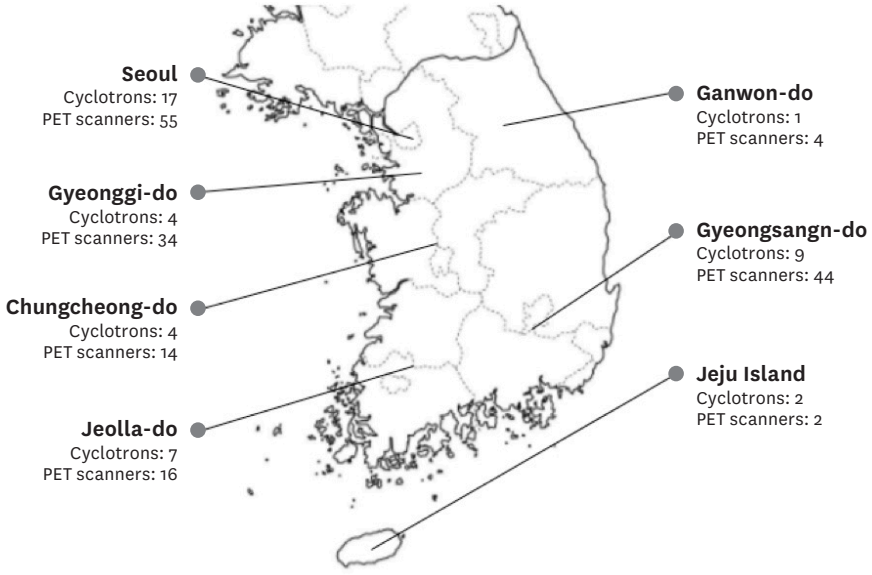
DIAGNOSTIC TECHNOLOGY

A diagnosis of Alzheimer's disease requires confirmation of its biologic hallmarks based on biomarkers (beta-amyloid and/or tau) (Portet et al., 2006), which can be obtained with two diagnostic technologies: PET scans with tracers that bind to beta-amyloid in the brain, and CSF measurement of beta-amyloid and tau levels (Moore et al., 2014; Okamura et al., 2018). Currently, both technologies are approved but not reimbursed in Korea. However, Koreans commonly pay for PET scans out of pocket. Given a strong reluctance of Koreans to undergo a lumbar puncture, we assume that 95 percent of biomarker test-eligible patients will undergo a PET scan. We assume that the remaining 5 percent of patients will undergo a CSF test that reports both amyloid beta and tau biomarker levels. Our model does not apply any constraint on CSF tests, while capacity is constrained for PET scans (given limited excess capacity and slight decrease in the number of devices).

In **Figure 3**, we show the locations of the 169 PET scanners and 44 cyclotrons in Korea by province.

FIGURE 3: *PET SCANNERS AND CYCLOTRONS IN KOREA (AS OF 2019)*



SOURCE: The number of cyclotrons by province in 2018 is from expert input (Korean Association for Radiation Application) and the number of PET scanners by province in 2019 is from the Health Insurance Review & Assessment Service (http://opendata.hira.or.kr/).

INFUSION DELIVERY

Our base case assumption is that a disease-modifying therapy would be delivered intravenously, since many Alzheimer's disease treatments in clinical trials are delivered as intravenous drugs. As such therapies are delivered every few weeks for a period of 12 to 24 months, we model a therapy that would be administered every four weeks for a total of 19 infusions per patient over the course of 18 months. We recognize that other modalities and treatment durations may eventually be adopted in clinical practice. We explore an alternative scenario in which infusion delivery is not a barrier, as some candidate treatments are delivered subcutaneously or orally.

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Given the lack of publicly available infusion data in Korea, we use an index approach consistent with our prior European, Canadian, and Japanese analyses. Our estimates of the capacity to deliver infusions are based on the relative capacity of the Korean health care system based on four indicators: hospital beds, active nurses, magnetic resonance imaging (MRI) scanners, and PET scanners (see Appendix Table A.-2). We use Organisation for Economic Co-operation and Development (OECD) data to develop a capacity index for Korea relative to the United States (OECD, 2018), which we use to scale the per-capita infusion capacity projected for the United States and assume the same relative rate of growth in infusion capacity as in the United States. As in our prior analyses, we assume that existing infusion clinics can expand capacity by 10 percent to accommodate new patients, while 80 percent of the capacity in new infusion clinics would be dedicated to administering the Alzheimer's therapy.

Simulation Results under Selected Capacity Scenarios

BASE CASE SCENARIO

Figure 4 shows the projected wait times for receipt of a disease-modifying therapy, assuming such a treatment becomes available in 2022. We estimate average peak wait times of 14 months initially, mostly because of capacity limitation for specialist visits due to their limited number. At the currently projected capacity for specialist visits, we do not expect wait times for biomarker testing given South Korea's large number of PET scanners relative to the population. Minimal waiting times for infusion delivery will persist until 2028. By 2029, we project that the backlog of cases will have been cleared so that patients can access treatment without wait.

FIGURE 4: *PROJECTED WAIT TIMES FOR ALZHEIMER'S DISEASE DIAGNOSIS, TESTING, AND TREATMENT*

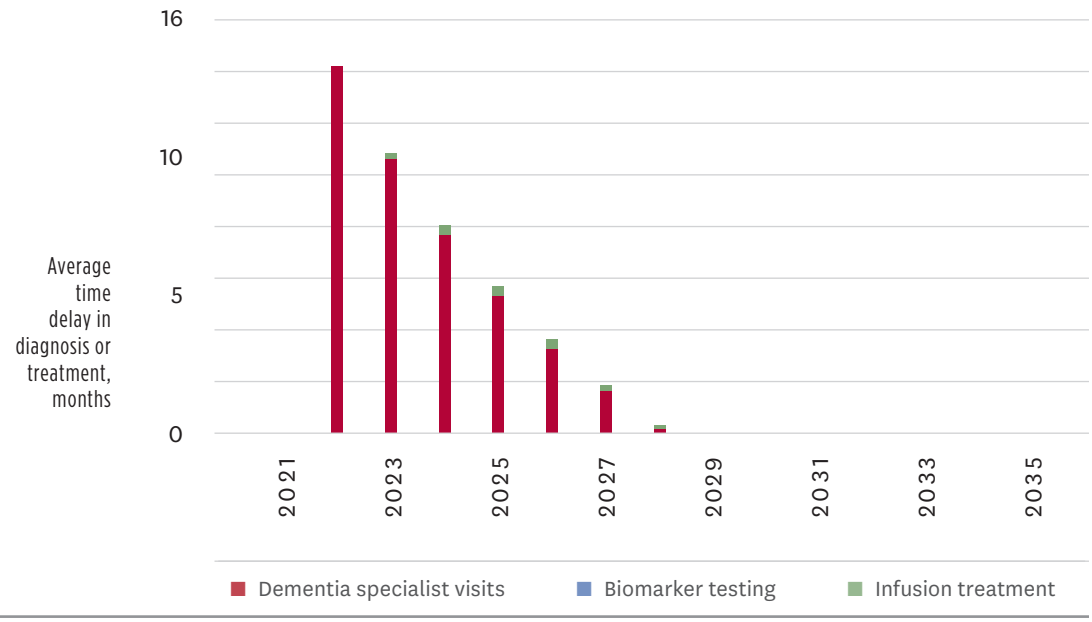

Figure 5 illustrates the effects of the capacity constraints on the number of patients in the respective queues. Initially, over five hundred thousand Korean patients are estimated to wait for their specialist

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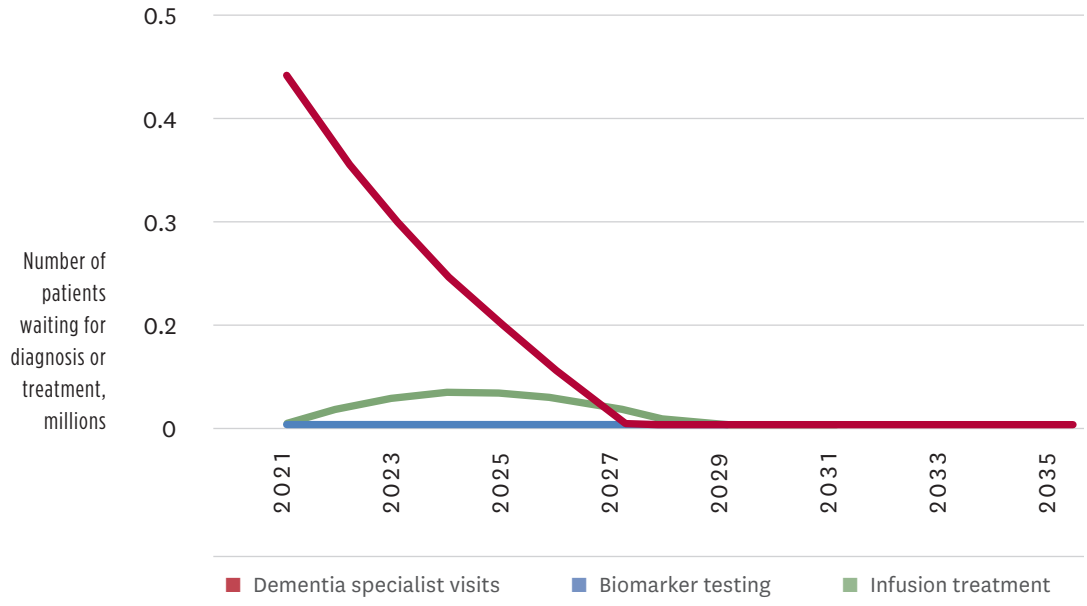
appointment, but that wait list is projected to clear by 2028. Up to 47,000 patients would have to wait for treatment delivery in the first few years.

FIGURE 5: *PROJECTED WAIT LISTS FOR ALZHEIMER'S DISEASE DIAGNOSIS, TESTING, AND TREATMENT*



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ALTERNATIVE SCENARIOS

We assess alternative scenarios that reflect efforts to expand capacity in order to eliminate some of the barriers to diagnosis and treatment of people with MCI due to Alzheimer's disease. The assumptions for three alternative scenarios are shown in **Table 3**.

TABLE 3. *CAPACITY ASSUMPTIONS ACROSS SCENARIOS*

SCENARIO	SPECIALISTS	BIOMARKER TESTING	INFUSIONS
Base case	*80% of neurologists and 35% of psychiatrists with 5% excess capacity for visits*	*95% PET with historical capacity projected forward, 5% CSF with no capacity constraint*	*Level estimated using a general health care capacity index, with current capacity projected forward*
Alternative 1: *Increase in specialists*	*20% increase in specialists*	*Same as base case*	*Same as base case*
Alternative 2: *Increase in specialists and shift to CSF testing*	*20% increase in specialists*	*85% PET with historical capacity projected forward, 15% CSF with no capacity constraint*	*Same as base case*
Alternative 3: *Increase in specialists, shift to CSF testing and investment in infusion delivery facilities (or non-intravenous administration)*	*20% increase in specialists*	*85% PET with historical capacity projected forward, 15% CSF with no capacity constraint*	*No capacity constraint*

Alternative scenario 1 illustrates the case of an increase in specialist capacity or improved triaging of patients at the primary care level. Given the long training times for dementia specialists, net increases in capacity seem unlikely in the short run, but increased task shifting to other specialists, primary care providers and other healthcare professionals could lessen the burden. The introduction of a blood-based test (Sebastian Palmqvist et al., 2020) for Alzheimer's disease biomarkers would allow identifying patients with MCI due to other causes earlier in the process and thus reducing specialist referrals. (S. Mattke, Cho, Bittner, Hlavka, & Hanson, 2020). Recently, a Korean blood-based test kit, "MDS-OAß Test", received approval from the Korean FDA (Dominguez et al., 2019).

Alternative scenario 2 reflects expanded use of CSF biomarker testing such that less than 85 percent of biomarker testing is conducted using PET and more than 15 percent using CSF. This would be possible, if resources were dedicated to performing lumbar punctures and to conducting assays. It may be possible that capacity for CSF testing could rapidly be expanded if planning, policies, regulations, and reimbursements encourage investments, and an educational campaign changed reluctant attitudes towards lumbar punctures. This may require training, developing standard protocols, and establishing laboratory networks with adequate reimbursement. If more than 15 percent of biomarker testing were based on CSF testing, wait times for confirmatory biomarker testing would be completely eliminated.

In alternative scenario 3, the elimination of the infusion delivery constraint could reflect adequate capacity growth of infusion services, or a therapy that does not require intravenous delivery (i.e., could be administered subcutaneously or orally). Eliminating the infusion constraint may be possible if increasing infusion center capacity becomes a priority, and/or if home infusions are utilized more widely. **Table 4** illustrates projected wait times under the base case and alternative scenarios.

TABLE 4. *SUMMARY OF PROJECTED WAIT TIMES FOR ALZHEIMER'S DISEASE DIAGNOSIS, TESTING, AND TREATMENT, BY SCENARIO*

SCENARIO	2021	2025	2030	2040
Base case	14.2	3.6	0	0
Alternative 1: *Increase in specialists*	10.8	1.7	0	0
Alternative 2: *Increase in specialists and shift to CSF*	10.4	0.7	0	0
Alternative 3: *Increase in specialists, shift to CSF and investment in infusion delivery (or non-intravenous administration)*	10.4	0	0	0

DEMENTIA DUE TO ALZHEIMER'S DISEASE CASES AVOIDED IN THE BASE AND ALTERNATIVE SCENARIOS

Figure 6 shows the cumulative incident dementia due to Alzheimer's disease cases between 2022 and 2050 in the base case and alternative scenarios. These changes would help to avoid around two percent of additional cases of dementia due to Alzheimer's disease. If all constraints were removed, up to 130,000 cases of dementia due to Alzheimer's disease could be averted in Korea between 2022-2050, assuming that the treatment reduces the risk of progression from MCI due to Alzheimer's disease to manifest dementia by 30 percent.

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FIGURE 6: *CUMULATIVE INCIDENT CASES OF DEMENTIA DUE TO ALZHEIMER'S DISEASE CASES AVERTED, 2022-2050*

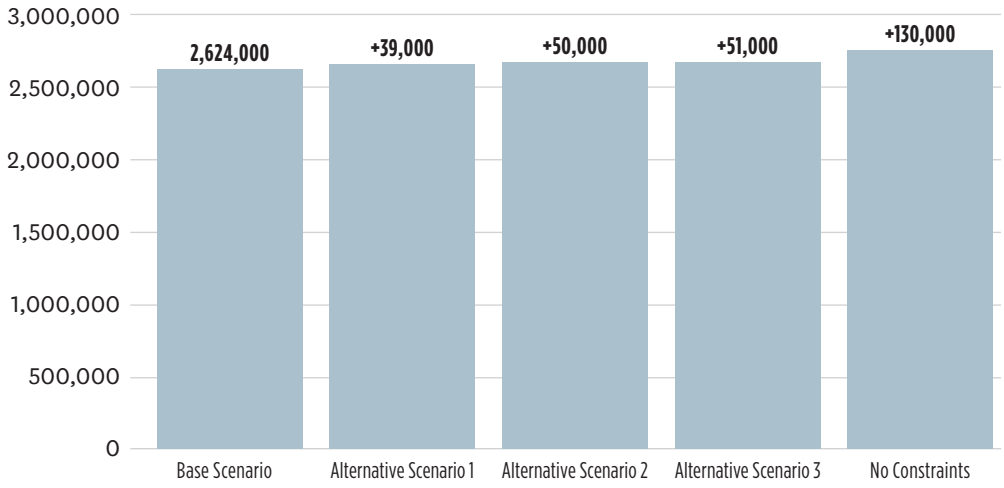
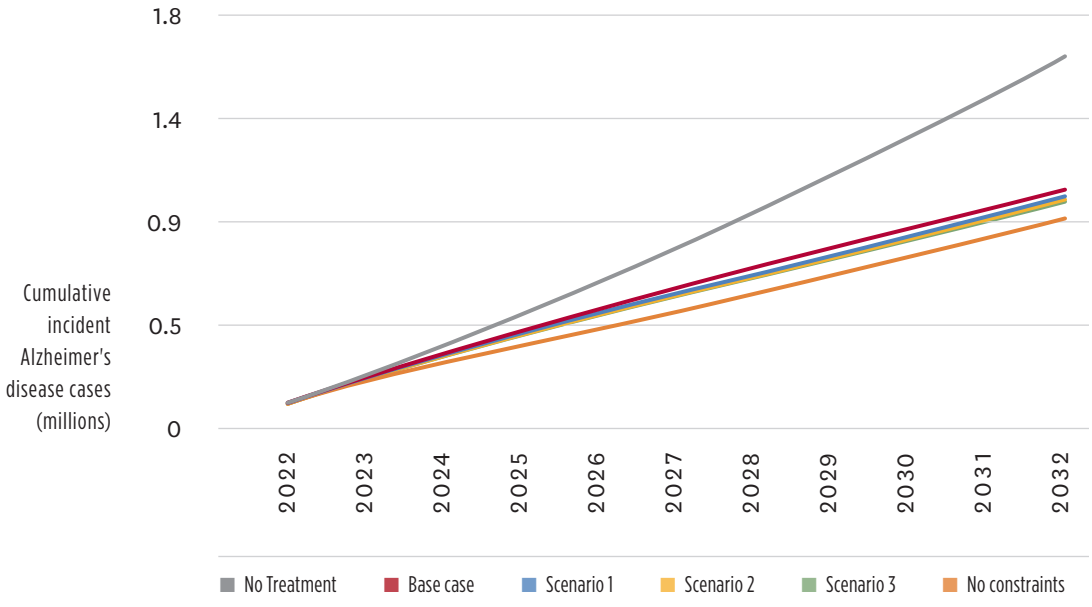


Figure 7 displays the trajectories of incident dementia cases caused by Alzheimer's disease in Korea for the first ten years after the projected market entry of a disease-modifying treatment under different scenarios. The gray line on top reflects the expected cumulative incidence in the absence of a treatment and the red line depicts the situation under our base case assumptions. The graph illustrates the fact that waiting times in Korea would be determined by access to specialists. When specialist capacity is raised by 20% (scenario 1), neither increasing utilization of CSF testing (scenario 2) nor greater infusion capacity (scenario 3) has a meaningful effect. Only removing the specialist constraint fully (no constraints) has a noticeable impact on the predicted incidence.

FIGURE 7: *TRAJECTORIES OF INCIDENT CASES OF DEMENTIA DUE TO ALZHEIMER'S DISEASE UNDER DIFFERENT SCENARIOS, 2022-2032*



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Limitations

Our analysis has several limitations and our estimates should therefore be seen as illustrative of the magnitude of the problem rather than precise predictions of wait times and disease progression.

We use a stylized clinical pathway that simplifies actual care patterns and make many assumptions about hypothetical scenarios in future states of the world. However, our stylized model is intended to provide a range of estimates to help identify potential capacity constraints if an Alzheimer's disease-modifying therapy becomes available in the near future.

We use assumptions for treatment effectiveness and indications. As the efficacy of a therapy is unknown at this time, we use the assumption of a 30 percent reduction in relative risk of transitioning from MCI to dementia due to Alzheimer's disease. The actual efficacy may be different and might affect patient uptake and the number of dementia due to Alzheimer's disease cases that could be avoided. We assume that the therapy would be indicated for people with MCI due to Alzheimer's disease; we do not include pre-symptomatic individuals and we assume the therapy would not be effective for people who have developed manifest dementia. If the therapy were indicated for pre-symptomatic individuals, the subsequent wait times could be longer. Patient uptake in response to a new disease-modifying therapy would also depend on a variety of factors, such as awareness, efficacy of the therapy, side effects, stigma associated with a MCI or dementia diagnosis, and costs.

On the infrastructure side of the model, we focus on three capacity constraints. We do not model capacity challenges related to cognitive screening, CSF testing, other imaging such as magnetic resonance imaging (MRI), radiologists and nuclear medicine specialists, and treatment monitoring. For example, there is limited access to physicians in some provinces, which could make MCI detection more challenging. There will likely be challenges with the capacity considerations that we did not model, and successful delivery of a novel disease-modifying therapy will depend on a host of practitioners and planners to coordinate services. However, we focus on specialists, biomarker testing for diagnosis, and infusion delivery because these are likely to be the most pressing barriers and possibly the most difficult to overcome.

Our estimated capacity of specialists to conduct these visits reflects the theoretical capability and willingness of the specialists to provide the services. Although not all neurologists and psychiatrists may choose to provide evaluation and diagnostic services to people with MCI, we made a simplifying assumption that these specialists could conduct 5 percent more visits overall than visits in the status quo. In addition, these specialists typically see different types of patients. Neurologists tend to see patients with disorders in the brain and nervous system and psychiatrists see patients who have mood and or behavioral issues. As our model does not stratify patients by age, i.e., we consider the entire cohort of people ages 50 and older and assess patients based on average age of the cohort each year and other characteristics such as rates of patient uptake and contraindications. For example, younger people may be less likely to seek further evaluation from a specialist, while older people would be more likely to be frail or have comorbidities that could preclude them from the treatment, but we use uniform patient uptake assumptions that reflect an average patient. Including age strata would allow for subgroup analysis but would be unlikely to change the overall findings of our study given the uncertainties around the therapeutic profile, efficacy, and patient uptake.

Although we use a proxy measure for infusion capacity, future capacity growth in Korea is difficult to predict, it is likely that providers would add infusion capacity, if an intravenous treatment were approved and covered by health insurance.

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Discussion

A disease-modifying therapy for Alzheimer's disease may become available for the first time in the coming years. Such a therapy has the potential to greatly reduce the number of dementia due to Alzheimer's disease cases by delaying or preventing disease progression. However, this preventive paradigm implies that the population impact of a therapy will depend on a country's ability to identify people who would benefit from therapy and to administer it in a timely fashion.

Our analysis suggests that up to 130,000 Koreans could progress from MCI due to Alzheimer's disease to dementia due to Alzheimer's disease between 2022 and 2050 while on wait lists for diagnosis, testing, and treatment if a therapy became available in 2022. The wait times are most pronounced in the first few years, with the annual average waiting times peaking at 14 months in the year prior to launch, and wait times, albeit limited, could persist for decades. Peak wait times in Korea are projected to be similar to those in the U.K. (14 months) and Germany (11 months) and shorter than in the U.S. (19 months) and Canada (28 months).

As the fastest ageing of the OECD countries, Korea has embarked on several policy initiatives that can become the basis for efforts to reduce wait times for access to a disease-modifying therapy for Alzheimer's diseases. Most notably, as part of its call for action on research and development, the Government's National Dementia Responsibility Policy calls for better models for care for and prevention of dementia.

EARLY DETECTION

Korea has a unique program that provides free cognitive screening and consultation to residents age 60 and over. Currently, 256 dementia centers are spread throughout the country providing various dementia related programs for older Koreans. Promoting regular cognitive screening could become an avenue through which patients with Alzheimer's disease could be identified at an early stage (see Box 1).

Box 1: Improving preventive care through dementia centers

The National Institute of Dementia was established by the Ministry of Health and Welfare and the National Medical Center in 2012, with an aim to create an effective dementia service network for elderly Koreans. From 2017, regional dementia centers were built around the country, reaching 256 centers in only two years. These dementia centers provide a wide array of community-based services. By December 2019, more than 2.6 million Koreans have visited these centers and around 60% of all diagnosed dementia patients in Korea report, having utilized the services provided by these centers (H. Cho & Kim, 2020).

The centers provide free cognitive screening tests for those aged 60 and over, encouraging regular examination of cognitive health. Community residents are able to talk to an onsite specialist after the screening and can get a referral for further testing if necessary. Centers also provide various activities, such as engaging in memory-related quizzes, puzzles, and singing, to help older adults remain cognitively active. Educational programs further provide dementia-related knowledge.

These centers also offer programs for family members of dementia patients. Consultations with an expert are available as well as screening tests for caregiver stress, such as the Patient Health Questionnaire-9 (PHQ-9), the Neuropsychiatric Inventory Questionnaire (NPI-Q), and the

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Differential Ability Scales (DAS). Gatherings or group sessions are available for families with dementia patients. A survey by the National Institute of Dementia show users have been especially pleased with programs for family members (H. Cho & Kim, 2020).

For the future, dementia centers are aiming to expand services to hard-to-reach patients, such as single household members and residents in rural areas, by providing at-home services. Certain regions with high rate of elderly residents are assigned as a dementia reassurance village *where additional services are provided in connection with the centers. These villages are planned to expand along with the dementia centers.*

WORKFORCE EXPANSION

As in many other countries, limited capacity of dementia specialists is the most limiting obstacle to evaluating patients with MCI for treatment eligibility in Korea. Expanding specialty capacity is also the hardest constraint to address, because specialist training takes many years and current training pipelines do not even keep up with the growing needs of aging populations under established treatment options. An alternative is to qualify non-specialist healthcare professionals, such as general practitioners, or physicians in adjacent specialties, such as internal medicine, in the evaluation and diagnosis of memory complaints. Korea has a one-year training program for healthcare professionals, who seeks to get specialized training in dementia care (see Box 2). While currently participants are mostly neurologists and psychiatrists, these programs could form the basis for training physicians in other areas in diagnostic evaluation of MCI. A challenge to recruiting physicians from other specialties into dementia care is that Korea has a comparatively low number of physicians per capita. According to OECD data, Korea had 2.3 physicians per 1,000 people in 2017 compared to the OECD average of 3.4, and the number of medical graduates is declining.

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Box 2: Annual training programs for dementia specialists

In South Korea, the elderly population has been increasing dramatically for the past decades, leading to an increasing demand for geriatricians and dementia specialists. Although geriatrics is yet to be defined as a separate specialty, the steady increase in memberships of geriatric associations implies the growing interest among clinicians. The first association, the Korean Geriatric Society, was established in 1968, followed by several others that that play a significant role in advancing geriatric research and related policies.

Among them, the Korea Dementia Association (founded in 1996) and the Korean Association for Geriatric Psychiatry (founded in 1994) focus mainly on dementia. Starting from 2009, the associations provide a joint training program for physicians and other clinicians each year, who plan to work with dementia patients. The program provides training on screening, diagnosis, treatment and care of dementia patients, tailored to the different needs of patients in dementia centers, hospitals and nursing homes. The program also teaches details of government dementia policy and goes through case studies.

Program participants undergo through a qualifying exam to receive a certificate. While all neurologists and psychiatrists in Korea are formally certified to treat dementia patients, this program provides with additional training, and allows other specialists, such as internal medicine, to get trained in dementia care.

Dementia care training programs have been introduced for other clinicians as well. In 2003, a curriculum for dementia nurses was established, which consists of 100 hours of lectures and 150 hours of apprenticeship training (Ko, Lee, & Baumann, 2007). There are also shorter courses for nurses specialized in dementia, provided by the Ministry of Health and Welfare. Undergraduate level geriatric courses and postgraduate geriatric training have been developed in several medical schools. (K. H. Cho et al., 2004)

DIAGNOSTIC CAPACITY

In contrast to other countries that we studied, the capacity to confirm the Alzheimer's pathology with biomarkers is not a pressing concern in Korea. While patients are strongly averse to undergoing lumbar punctures, which limits the potential of using CSF testing as a scalable and inexpensive modality for biomarker testing, the PET scanner capacity is relatively high (**Figure 8**). Japan and the U.S. are the only G7 countries with a higher number of scanners per million population. The reason for this relatively high number is a willingness of Koreans to pay for dementia scans out-of-pocket.

As a result, we project limited wait times for biomarker testing, even if specialist throughput increases, as in our scenarios. Moreover, our estimates suggest that shifting as little as about 15 percent of patients to CSF testing for would eliminate wait times for confirmatory tests completely. Developing standardized protocols for CSF testing for Alzheimer's disease biomarkers will increase the reliability and adoption of CSF testing in Korea (Park et al., 2017; Park et al., 2015).

Alternatively, better triaging of patients earlier in the diagnostic pathway could reduce demand for confirmatory tests. Currently available cognitive tests that are suitable for primary care settings have reasonable sensitivity to detect MCI, but limited specificity for MCI due to Alzheimer's disease. In a recent review (Lam, Hlávka, & Mattke, 2019), we concluded that there was limited potential to improve specificity of simple cognitive tests, because the patterns of early cognitive decline due to different etiologies are not distinct enough to be differentiated with such tools. However, blood-based tests for the biomarkers of Alzheimer's disease might allow identifying patients with cognitive decline due to other etiologies at the primary care level. We estimated that using a fully automated blood test for amyloid-ß with published performance (S. Palmqvist et al., 2019) in patients with suspected MCI could be used to triage patients for confirmatory testing, thus reducing the need for PET scans substantially (S. Mattke et al., 2020). A blood-based biomarker test for Alzheimer's disease (Dominguez et al., 2019) is already approved, albeit not reimbursed, in Korea.

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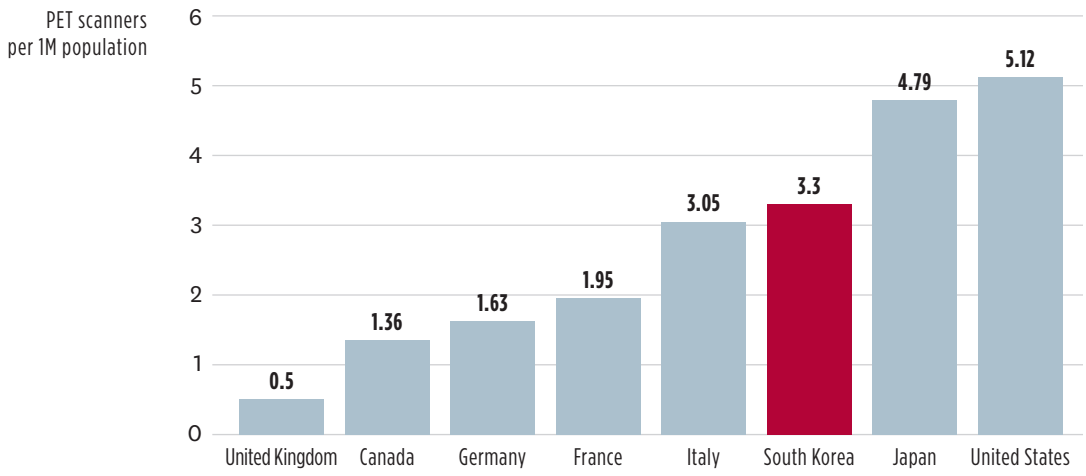
FIGURE 8: *PET SCANNER CAPACITY IN KOREA COMPARED TO G7 COUNTRIES*



GEOGRAPHIC IMBALANCES

An important consideration in analyzing the health system infrastructure to deliver an Alzheimer's disease treatment in Korea is that the national view may disguise regional imbalances between supply and demand of dementia services. Differential migration of younger populations towards urban areas has led to a disproportionate share of the elderly in rural-remote Korea, where around 17-23 percent of the population are over 65 years old compared to 14.3 percent in predominantly urban areas (KOSTAT, 2020). In many agricultural regions the elderly represent more than 70-80% of the total population (Choi, 2011). The elderly in rural areas also tend to have lower education levels leading to a higher risk for dementia (D. Y. Lee et al., 2002).

At the same time, rural areas tend to have fewer healthcare resources per capita. In 2019, 29% of the total number of physicians were located in the city of Seoul and the share increased to 54% for the Seoul Capital Area (i.e. Seoul, Incheon, and Gyeonggi Province) (HIRA, 2020). Similarly, advanced imaging technology are predominately installed in urban areas. 52% of PET scanners and 45% of MRI scanners are in the Seoul Capital Area and among the 703,468 hospital beds, 63% are built in urban areas.

While installing additional fixed infrastructure in rural areas may not be economically viable, technology innovations, such as mobile PET scanners and tele-consultation models, may present options to improve access to memory care, if the prerequisite approvals can be obtained. At-home services organized by regional dementia centers and dementia reassurance villages will expand dementia diagnosis and care services to rural regions.

Conclusion

In spite of recent setbacks, there is cautious optimism that a disease-modifying therapy for Alzheimer's disease will be available soon. Many countries do not have sufficient infrastructure to deliver such a therapy to a large population of people with MCI due to Alzheimer's disease, and Korea is no exception.

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Without efforts to expand capacity, we estimate that projected wait times for access to treatment could peak at 14 months, which is comparable to Japan and the United Kingdom. The comparatively low density of dementia specialists contributes most to those wait times. In addition, Korea faces the challenge of disproportionate aging in rural areas that have limited infrastructure for specialty care.

At the same time, the fact that Korea is the fastest aging OECD country spawned numerous initiatives to advance dementia care. The current administration's dementia plan is a comprehensive national dementia strategy with the aim of reducing the financial burden on dementia patients and families (see Box 3). The willingness to increased coverage for dementia care signals a commitment to make a disease-modifying Alzheimer's treatment accessible.

Box 3: Reducing out-of-pocket medical costs for dementia patients

In 2008, the Ministry of Health and Welfare announced the first national strategy for dementia which became the start of a series of dementia policies in South Korea. In 2017, the Moon administration announced the National Dementia Responsibility Policy *stating that society rather than patients and families should bear most of the financial burden of dementia care. Under this policy, the above-mentioned dementia centers were established as were 24-hour dementia call centers providing consultation and information to dementia patients and family members. Long-term care services were expanded to a wider range of dementia patients and medical centers specialized in dementia diagnosis and care increased. A budget of around 200 billion KRW (approximately 171 million USD) was committed to a ten-year R&D plan to promote research in various areas, including development of disease-modifying treatments.*

One of the most important components of the policy was the reduction of out-of-pocket medical costs for dementia patients. The plan aimed to reduce the share of dementia related out-of-pocket burdens from 60% to 10%, indicating the remaining 90% being covered by the National Health Insurance. Effective immediately, the out-of-pocket cost of screening tests was reduced to by half (150,000 KRW) and the cost of MRI scans was reduced from 600,000 KRW to 330,000 KRW. Costs for long-term care services and equipment such as wheelchairs, beds, portable toilets, etc. were subsidized. National Health Insurance data show that 85.8% of the overall medical cost for dementia were covered by the government in 2019, (J. Lee et al., 2020).

The new dementia policy has been credited for reducing the financial burden on patients and families and increasing public awareness, but it increased government spending on dementia care by 42% in 2019 compared to the previous year.

The changes necessary to expand capacity will not happen without the concerted and coordinated effort of multiple stakeholders, given the need for increased awareness, capital investment, care model innovation, and changes to regulation and reimbursement. Without these changes, we estimate that up to 130,000 Koreans will progress from MCI to manifest dementia due to Alzheimer's disease while waiting for treatment between 2022 and 2050. With a disease-modifying therapy for Alzheimer's disease potentially being available soon, preciously little time remains left for stakeholders to take action and remedy the capacity gap. Failure to do so in a timely and decisive manner will likely result in hundreds of thousands of potentially avoidable cases of dementia due to Alzheimer's disease.

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References

Cho, H., & Kim, J. (2020). *National Institute of Dementia Annual Report 2019 [2019 중앙치매센터 연차보고서]. National Institute of Dementia, Ministry of Health and Welfare.* Retrieved from https://www.nid.or.kr/info/dataroom_view.aspx?bid=208

Cho, K. H., Chung, Y., Roh, Y. K., Cho, B., Kim, C. H., & Lee, H. S. (2004). Health Care for Older Persons: A Country Profile – Korea. *Journal of the American Geriatrics Society, 52*(7), 1199-1204. doi:10.1111/j.1532-5415.2004.52322.x

Choi, H. (2011). Present and Future of Korean Geriatrics. *Journal of the Korean Geriatrics Society, 15*(2), 71-79. doi:10.4235/jkgs.2011.15.2.71

Ciesielska, N., Sokolowski, R., Mazur, E., Podhorecka, M., Polak-Szabela, A., & Kedziora-Kornatowska, K. (2016). Is the Montreal Cognitive Assessment (MoCA) test better suited than the Mini-Mental State Examination (MMSE) in mild cognitive impairment (MCI) detection among people aged over 60? Meta-analysis. *Psychiatr Pol, 50*(5), 1039-1052.

Dominguez, J. C., De Guzman, M. F., Laurilla Uy, J. G., Megan F Yu, J., Ligsay, A., Kang, S., & Kim, S. (2019). P4-549: PLASMA-BASED BIOMARKER MDS-OAβ DIFFERENTIATES ALZHEIMER'S DISEASE FROM OTHER ETIOLOGIES. *Alzheimer's & Dementia, 15*, P1527-P1528. doi:10.1016/j.jalz.2019.08.096

Doraiswamy, P. M., Sperling, R. A., Johnson, K., Reiman, E. M., Wong, T. Z., Sabbagh, M. N., . . . Pontecorvo, M. J. (2014). Florbetapir F 18 amyloid PET and 36-month cognitive decline:a prospective multicenter study. *Molecular Psychiatry, 19*(9), 1044-1051. doi:10.1038/mp.2014.9

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. *Journal of psychiatric research, 12*(3), 189-198.

HIRA. (2020). Healthcare Bigdata Hub, Health Insurance Review & Assessment Service [보건의료빅데이터개방시스템, 건강보험심사평가원]. Retrieved from http://opendata.hira.or.kr/

Hlávka, J. P., Mattke, S., & Liu, J. L. (2018). *Assessing the Preparedness of the Health Care System Infrastructure in Six European Countries for an Alzheimer's Treatment* (RR-2503-BIOG). Retrieved from Santa Monica, CA: https://www.rand.org/pubs/research_reports/RR2503.html

Kim, J. M. (2002). Dementia care in Korea. *Dementia, 1*(2), 135-139.

Ko, S. H., Lee, M. C., & Baumann, S. L. (2007). Reducing the Burden of Dementia in Korea. *Nursing Science Quarterly, 20*(2), 178-182. doi:10.1177/0894318407299893

KOSTAT. (2020). Statistics Korea Database. Retrieved from http://kostat.go.kr/portal/eng/

Lam, J., Hlávka, J., & Mattke, S. (2019, July 14, 2019). *Estimated Impact of Diagnostic Tools for Primary Care Settings on Demand for Specialist Visits for Patients with Prodromal Alzheimer's Disease.* Paper presented at the Alzheimer's Association International Conference, Los Angeles, CA.

Lee, D. Y., Lee, J. H., Ju, Y. S., Lee, K. U., Kim, K. W., Jhoo, J. H., . . . Woo, J. I. (2002). The Prevalence of Dementia in Older People in an Urban Population of Korea: The Seoul Study. *Journal of the American Geriatrics Society, 50*(7), 1233-1239. doi:10.1046/j.1532-5415.2002.50310.x

Lee, J., Kang, M., Nam, H., Kim, Y., Lee, O., & Kim, K. (2020). *Korean Dementia Observatory 2019 [대한민국 치매현황 2019]. National Institute of Dementia, Ministry of Health and Welfare, NIDR-1902-0028.* Retrieved from https://www.nid.or.kr/info/dataroom_view.aspx?bid=209

Liu, J. L., Hlávka, J. P., Coulter, D. T., Baxi, S. M., Mattke, S., & Gidengil, C. A. (2019). *Assessing the Preparedness of the Canadian Health Care System Infrastructure for an Alzheimer's Treatment.* Retrieved from https://www.rand.org/pubs/research_reports/RR2744.html

Liu, J. L., Hlávka, J. P., Hillestad, R., & Mattke, S. (2017). *Assessing the Preparedness of the U.S. Health Care System Infrastructure for an Alzheimer's Treatment.* Retrieved from Santa Monica, CA: https://www.rand.org/pubs/research_reports/RR2272.html

Mattke, S., Cho, S. K., Bittner, T., Hlavka, J., & Hanson, M. (2020). Blood-based biomarkers for Alzheimer's pathology and the diagnostic process for a disease-modifying treatment: Projecting the impact on the cost and wait times. *Alzheimers Dement (Amst), 12*(1), e12081. doi:10.1002/dad2.12081

Mattke, S., Hlávka, J. P., Yoong, J., Wang, M., & Goto, R. (2019). *Assessing the Preparedness of the Japanese*

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Health Care System Infrastructure for an Alzheimer's Treatment. Retrieved from https://cesr.usc.edu/research/publications

Moore, A., Patterson, C., Lee, L., Vedel, I., Bergman, H., Canadian Consensus Conference on the, D., & Treatment of, D. (2014). Fourth Canadian Consensus Conference on the Diagnosis and Treatment of Dementia: recommendations for family physicians. *Can Fam Physician, 60*(5), 433-438. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/24829003

OECD. (2017). *Pensions at a Glance 2017: OECD and G20 Indicators.* Retrieved from OECD Publishing, Paris:

OECD. (2018). OECD Statistics. Retrieved from https://stats.oecd.org/

Okamura, N., Harada, R., Ishiki, A., Kikuchi, A., Nakamura, T., & Kudo, Y. (2018). The development and validation of tau PET tracers: current status and future directions. *Clinical and translational imaging, 6*(4), 305-316. doi:10.1007/s40336-018-0290-y

Ong, K. T., Villemagne, V. L., Bahar-Fuchs, A., Lamb, F., Langdon, N., Catafau, A. M., . . . Rowe, C. C. (2015). Abeta imaging with 18F-florbetaben in prodromal Alzheimer's disease: a prospective outcome study. *J Neurol Neurosurg Psychiatry, 86*(4), 431-436. doi:10.1136/jnnp-2014-308094

Palmqvist, S., Janelidze, S., Quiroz, Y. T., Zetterberg, H., Lopera, F., Stomrud, E., . . . Hansson, O. (2020). Discriminative Accuracy of Plasma Phospho-tau217 for Alzheimer Disease vs Other Neurodegenerative Disorders. *JAMA*. doi:10.1001/jama.2020.12134

Palmqvist, S., Janelidze, S., Stomrud, E., Zetterberg, H., Karl, J., Zink, K., . . . Hansson, O. (2019). Performance of Fully Automated Plasma Assays as Screening Tests for Alzheimer Disease-Related beta-Amyloid Status. *JAMA Neurol.* doi:10.1001/jamaneurol.2019.1632

Park, S. A., Chae, W. S., Kim, H. J., Shin, H. S., Kim, S., Im, J. Y., . . . Min, K. D. (2017). Cerebrospinal Fluid Biomarkers for the Diagnosis of Alzheimer Disease in South Korea. *Alzheimer Dis Assoc Disord, 31*(1), 13-18.

Park, S. A., Kang, J. H., Kang, E. S., Ki, C. S., Roh, J. H., Youn, Y. C., . . . Kim, S. Y. (2015). A consensus in Korea regarding a protocol to reduce preanalytical sources of variability in the measurement of the cerebrospinal fluid biomarkers of Alzheimer's disease. *J Clin Neurol, 11*(2), 132-141. doi:10.3988/jcn.2015.11.2.132

Portet, F., Ousset, P. J., Visser, P. J., Frisoni, G. B., Nobili, F., Scheltens, P., . . . Disease, M. C. I. W. G. o. t. E. C. o. A. s. (2006). Mild cognitive impairment (MCI) in medical practice: a critical review of the concept and new diagnostic procedure. Report of the MCI Working Group of the European Consortium on Alzheimer's Disease. *J Neurol Neurosurg Psychiatry, 77*(6), 714-718. doi:10.1136/jnnp.2005.085332

Tombaugh, T., McDowell, I., Kristjansson, B., & Hubley, A. (1996). Mini-Mental State Examination (MMSE) and the Modified MMSE (3MS): a psychometric comparison and normative data. *Psychological Assessment, 8*(1), 48.

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About This Report

This report illustrates the magnitude of healthcare system infrastructure challenges for diagnosis and treatment of early-stage Alzheimer's disease with a future potential disease-modifying therapy in South Korea. This research was funded by an unrestricted grant of Eisai, Inc. to the University of Southern California. For questions about this report, please contact Dr. Soeren Mattke at mattke@usc.edu.

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For more information about our data, please see this report's technical appendix at cesr.usc.edu/research/publications.

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