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China's healthcare system's readiness to provide high-quality memory care and access to a disease-modifying Alzheimer's treatment

Soeren Mattke, M.D., D.Sc., Joanne Yoong, Ph.D., Kah-Hung Yuen, Wei Kok Loh

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China's healthcare system's readiness to provide high-quality memory care and access to a disease-modifying Alzheimer's treatment

The USC Brain Health Observatory

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OVERVIEW AND OBJECTIVES OF THE STUDY

With the recent U.S. FDA approval of lecanemab as the first new Alzheimer's treatment with clear evidence for clinical benefit (Van Dyck et al., 2023), patients and their families have found new hope. However, as history has taught us, the approval of a new drug does not guarantee widespread adoption of complex treatments for large numbers of patients. The first direct-acting antiviral drugs for hepatitis C, for example, not only created a fiscal shock because of the high unit cost of the treatments and the large number of prevalent patients but also resulted in wait times because of a lack of specialists, who could correctly identify treatment eligible patients, as initial treatments were only effective in certain subtypes of the disease. A similar case was sacubitril/valsartan, the first novel drug for congestive heart failure in many years, whose adoption was slower than expected despite evidence of a reduction of over 20 percent in mortality and hospital admission rates. An important reason was that primary care clinicians, who manage most heart failure patients, found the drug's complex uptitration and monitoring process to be incompatible with their workflow.

Alzheimer's treatments face similar challenges. Because no disease-modifying option existed so far, the pool of prevalent cases is large, and a delivery ecosystem has not evolved. As we had shown in recent reports, even in the G7 countries capacity of memory services is insufficient, which will create substantial bottlenecks for treatment delivery (Hlavka et al., 2019; J. Liu et al., 2017; Mattke 2019), and subsequent reviews (Mattke, Ullrich, & Wang, 2020; Mattke & Wang, 2020) have shown that capabilities and coverage add to the obstacles resulting from capacity constraints.

> *"Taking care of a patient with high blood pressure takes three minutes, but half an hour for a patient with dementia. The payment is the same, so it is difficult to attract talents to this field"*
>
> Neurologist, Guangdong

The challenge is that currently medical care for dementia is mainly focused on diagnosis and counseling. If patients are formally evaluated at all, they may undergo neurocognitive testing to document and quantify the degree of impairment and rarely imaging and biomarker testing to identify the etiology. With the current lack of widely available disease-modifying treatment options, physicians are typically limited to managing symptoms and counseling patients and their families on the expected course of their disease and the consequences for their lives, and the time requirements for such difficult conversations often impede their depth.

At the same time, the complexities of determining treatment eligibility and monitoring treatment response and side effects mean that Alzheimer's care will likely have to remain in the hands of specialists, who are scarce because of the limited professional and financial incentives to train in this specialty. Thus, the advent of a disease-modifying treatment for Alzheimer's disease will meet an unprepared healthcare delivery system.

This project builds on this earlier work and estimates supply and demand of diagnostic services to identify patients, who are potentially eligible for a disease-modifying treatment, in China and analyzes how policy, practice organization and payment models could be changed to accommodate the substantial increase in demand that the treatment will bring about.

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TECHNICAL APPROACH

METHODS

The study used a combination of desk research and expert interviews to describe the current patient journey in China, to capture obstacles to access that result from this journey and to identify potential changes to payment models and care delivery that might improve access. Desk research covered the websites of national and multilateral organizations that publish health system capacity data and reports, advocacy organization, payers and specialty societies as well as research published in peer-reviewed journals and technical reports. A total of 44 expert interviews were held with policy experts, clinical and health services researchers, clinicians and payer representatives in China using a semi-structured interview protocol. The data retrieved in this search were used in our existing capacity simulation model to predict wait times and queues under different scenarios.

We developed a stylized patient journey (Figure 1) to capture the current pathway that dementia patients take through identification based on screening or memory complaints, evaluation with neurocognitive testing, imaging, and biomarkers and then finally diagnosis and treatment delivery and monitoring.

Figure 1: Stylized patient journey

For each step of the patient journey, we analyzed China's status quo regarding coverage, capacity, and capabilities:

- Coverage
  - Are the services under each step currently covered by health insurance?
  - Are payment levels adequate to ensure actual delivery of the service?
- Capacity
  - Does current capacity deliver services sufficient to meet expected demand?
  - Would the capacity actually be devoted to the respective care step, given prevailing incentives and organization of care?
- Capabilities
  - Do providers have appropriate training, tools, and technology to perform the required services?

We used a simulation model to predict the match of demand for and supply of services along a patient's journey and implications for wait times and disease progression for the nation and the selected jurisdictions. We comment on possible changes to coverage, capacity and capabilities that might be required to reduce the obstacles to access to a disease-modifying treatment for Alzheimer's disease as well as memory care in general.

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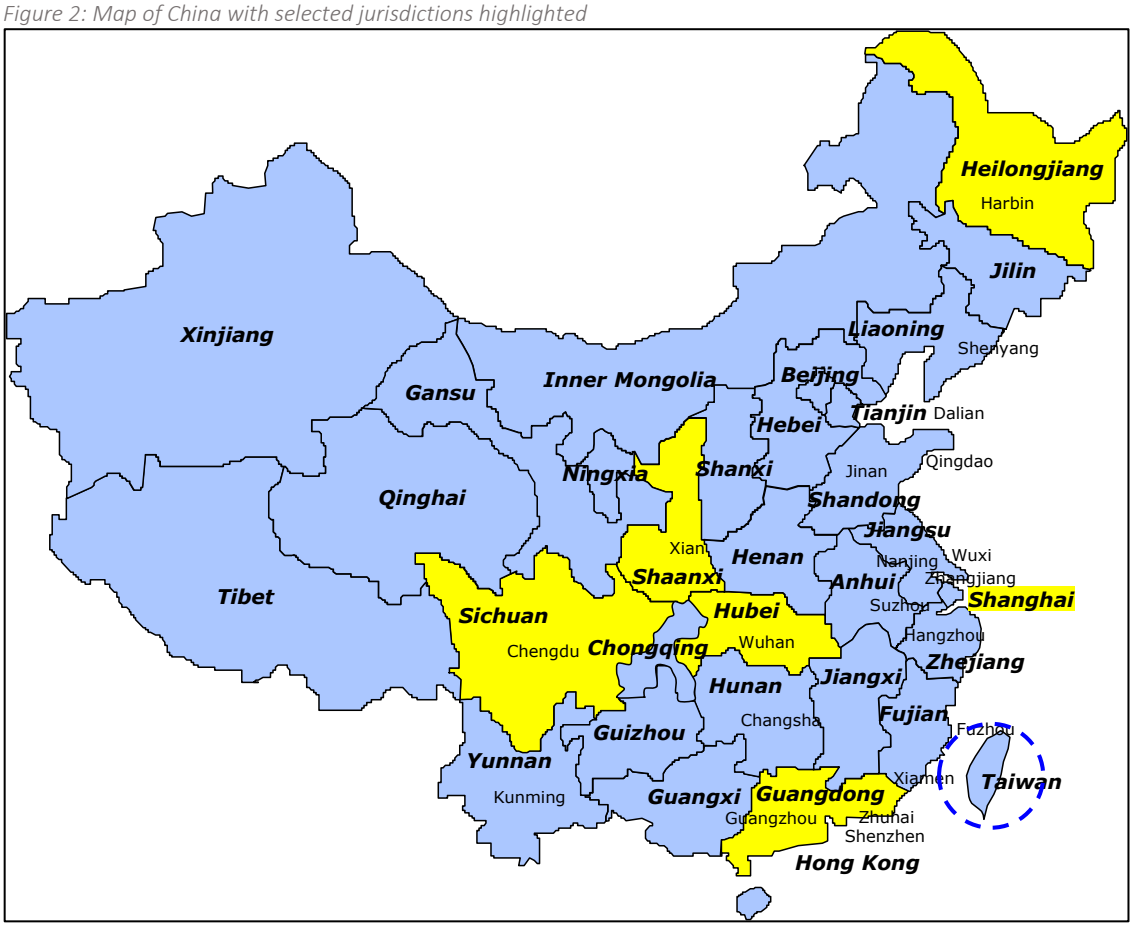
GEOGRAPHIC COVERAGE

Because of the size and diversity of China and the devolved nature of decision making on healthcare, we have summarized national data and policies, and focused on five out of 23 provinces that represent the economic and geographic diversity (see Figure 2) of the nation, as well as Shanghai as one of the directly administered municipalities (Table 1).

Table 1: Population and economic development of the included jurisdictions and the nation (2019 or most recent)

	Population size	Population density = Population size / Land area in km^2	Share of population 65 and older	GDP per capita (Yuan)	GDP rank (Out of 23 provinces)
Guangdong	113,460,000	631.00	8.62	88,781	6
Hubei	59,170,000	318.29	13.03	71,109	7
Sichuan	83,410,000	171.63	15.79	48,883	15
Shaanxi	38,644,000	213.30	11.38	63,477	9
Heilongjiang	37,731,000	82.96	12.86	33,977	22
Shanghai	24,237,800	3,822.70	14.40	157,279	2
National	1,395,380,000	148.06	11.9	64,521	

Figure 2: Map of China with selected jurisdictions highlighted



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Sichuan is a landlocked province located in southwestern China. It is the second largest province in China in terms of land area (485,000 km^2) with a population of 83.67 million (National Bureau of Statistics of China, 2021), which is similar to Germany. Its GDP per capita is 48,883 RMB (or 7682.50 USD) and close to 54% of the population reside in urban areas. The province has 2,336 hospitals, of which 65% (1,507) are general hospitals, 25% (582) are specialized hospitals and the remaining 10% are TCM hospitals. In the rural areas, there are over 1,000 community health service centers, 4,400 township health centers and 55,000 village clinics. Urban and rural healthcare institutions provide 272,000 and 360,000 beds respectively. Sichuan has seven accredited medical schools (Ministry of Education Clinical Medicine Professional Certification Working Committee, 2022). Currently, there are 2.21 physicians per 1000 persons in Sichuan.

Just North-East of Sichuan lies Shaanxi, another landlocked province. Shaanxi's population of 39.52 million people (National Bureau of Statistics of China, 2021) is similar to California's, but its territory is 181,173 km^2, roughly half the size of California. Approximately 60 percent of the population lives in urban areas and GDP per capita is 63,477RMB (or 9977 USD). Shaanxi has four accredited medical schools (Ministry of Education Clinical Medicine Professional Certification Working Committee, 2022) and 1,186 hospitals, of which about 64% (n=756) are general hospitals, 22% (262) are specialized hospitals and 14% (168) are TCM hospitals. Shaanxi has 666 community health service centers, 1532 township health centers and 23,747 village clinics. Shaanxi has 2.3 licensed doctors per 1000 persons and 128,530 and 137,284 beds in healthcare institutions for rural and urban areas, respectively.

Below Shaanxi is Hubei, located in Central China. Hubei has a population of 57.75 million (National Bureau of Statistics of China, 2021), which is much larger than that of Shaanxi but about the same land area of 185,900 km^2. Around 61% of the population lives in urban areas and GDP per capita is 71,109RMB (or USD 11177). Hubei has 11 accredited medical schools (Ministry of Education Clinical Medicine Professional Certification Working Committee, 2022) and 998 hospitals consisting of 562 (about 56%) general hospitals, 310 (31%) specialized hospitals and 126 (13%) TCM hospitals. In the rural areas, Hubei has 1148 community health service centers, 1129 township health centers and 23,242 village clinics. Hubei has 2.17 licensed doctors per 1000 persons and 219,518 and 183,782 beds in healthcare institutions for rural and urban areas, respectively.

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Guangdong. on the Southern coast of China, has a land area of 179,810 km^2 and GDP per capita of 88,781RMB (or 13954 USD ranked 6th of the 23 provinces) but twice the population, 126.01 million (National Bureau of Statistics of China, 2021) (71.4% in urban areas) as Shaanxi. Guangdong has nine accredited medical schools (Ministry of Education Clinical Medicine Professional Certification Working Committee, 2022) and 1582 hospitals, of which about 57% (911) are general hospitals, 31% (501) are specialized hospitals and 22% (170) TCM hospitals. In the rural areas, Guangdong has 2625 community health service centers, 1,180 township health centers and 25,788 village clinics. There are 2.12lcensed doctors per 1000 persons and 170,032 and 375,164 beds in health care institutions for rural and urban areas, respectively.

Heilongjiang, China's most northeastern province, has a population of 31.85 million (National Bureau of Statistics of China, 2021) (60.9% in urban areas) and a land area of 454,810 km^2 (similar to Sichuan) and GDP per capita of 33,977RMB (or 5340 USD). Heilongjiang has four accredited medical schools (Ministry of Education Clinical Medicine Professional Certification Working Committee, 2022) and 1125 hospitals, of which 67% (755) are general hospitals, 18% (201) specialized hospitals and 15% (169) TCM hospitals. Heilongjiang has 631 community health service centers, 966 township health centers, and

10,448 village clinics. There are 2.12 physicians per 1000 persons and 96,732 and 165,843 beds in healthcare institutions for rural and urban areas, respectively.

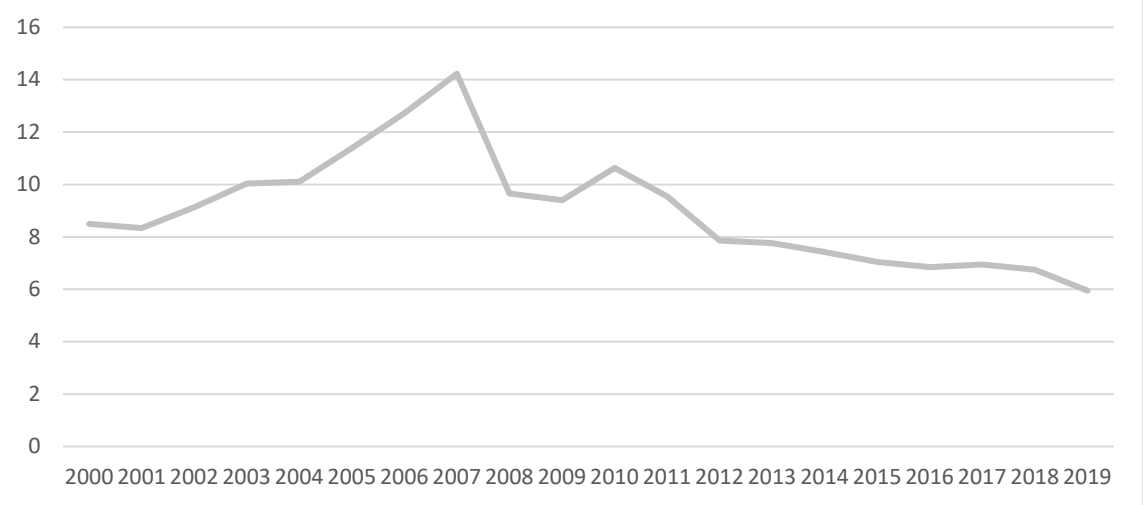
Lastly, Shanghai, on the east coast of China, has a population of 24.87 million (National Bureau of Statistics of China, 2021) (88.3% in urban areas), a land area of 6,340 km,^{2} and GDP per capita of 157,279RMB (or 24719 USD). This makes Shanghai not only the most populous urban area in China but also the most prosperous in terms of GDP per capita. Shanghai has four accredited medical schools (Ministry of Education Clinical Medicine Professional Certification Working Committee, 2022) and 312 hospitals. Of the 312 hospitals, 54% (169) are general hospitals, 39% (122) specialized hospitals, and only about 7% (21) TCM hospitals. Shanghai has 1,066 community health service centers and 1,179 village clinics. There are 2.93 physicians per 1000 persons and 146,454 beds in health care institutions.

HEALTH SYSTEM OVERVIEW

OVERVIEW OF ORGANIZATION AND GOVERNANCE

China is the world's fourth largest country by size and, with roughly 1.4 billion inhabitants, the most populous one. After years of rapid economic growth (Figure 3)(The World Bank, 2023), China is an upper-middle income country and the world's second largest economy, projected to overtake the U.S. within a few years.

Figure 3: Annual GDP growth [%] in China 2000-2019



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The current healthcare system has its roots in a reform program launched in 2009 that aims to introduce universal coverage and to modernize the delivery system with the intent to promote a "harmonious society". The reform reinstates a strong role of the government in a major departure of the market-oriented approach of the prior two decades (Yip et al., 2012). The three main reform areas are universal health insurance, drug pricing, and public hospitals (G. G. Liu et al., 2017). The central government set a policy and legislative framework for China's health system based on the principle of ensuring universal access to basic services and delegates the organization and provision of care to local governments (Fang, 2020a).

FINANCING HEALTHCARE

Total health expenditure was 5.9 trillion RMB in 2018 (around 900 billion USD), which accounts for 6.57% of GDP. About a quarter (27.74%) of health expenditure is financed by central and local government, 43.66% is paid by public insurance plans and 28.61% of health expenditure comes from out-of-pocket payments.

Health Insurance

In 2009, China introduced universal public health insurance to ensure equal access to basic health services (Yip et al., 2019) and has achieved near-universal coverage through three insurance schemes (Finch, 2013). The Urban Employee Basic Medical Insurance is mandatory for workers in urban areas and is financed mainly from employee (2% of annual wage up to an amount that is tied to local wages) and employer payroll taxes (around 6% of annual wage with differences by province) with minimal government funding (Fang, 2020a). Insurance coverage is restricted to the employee and does not include family members. The voluntary New Cooperative Medical Scheme and Urban-Rural Resident Basic Medical Insurance, which are being merged, cover rural residents and urban, self-employed individuals, children, students, and elderly adults, respectively (Li, 2011). Both schemes have nominal premiums and are heavily subsidized by the government. Cost sharing in the form of deductibles and copayments can be substantial, especially for inpatient care and prescription drugs, whereas copayments for office visits are nominal (Fang, 2020a). While there is no limit on cost-sharing, leading to a high proportion of 28 percent of share of out-of-pocket contributions, the overall annual benefit is capped (National Health Commission, 2021). Each province designs its own packages for the three publicly financed insurance plans, with substantial differences in copayment and annual benefit. For example, under the Beijing Urban Employee Basic Medical Insurance, deductible and copayment for inpatient care are 1500 RMB[1] and 15% of charges, respectively. (for inpatient care charges between 1300 RMB to 30,000RMB) with a 500,000 RMB maximum annual benefit. Most publicly financed insurance plans have lower copayments for secondary and tertiary hospitals than primary hospitals. Copayments for primary, secondary, and tertiary hospitals in Beijing are 15%, 13%, and 10% respectively. The voluntary New Cooperative Medical Scheme and Urban-Rural Resident Basic Medical Insurance tend to have higher copayments and lower annual caps under each province's plan. For example, under the Beijing Urban-Rural plan, the copayment for inpatient care is 25% for primary hospitals with a 250,000 RMB annual benefit cap (People's Government of Haidian District, 2018).

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Safety net programs for individuals, who cannot afford insurance premiums or copayments, are funded by local governments and charities. In 2018, 76.7 million people (approximately 5.5% of the population) received such assistance for health insurance premiums, and 53.6 million people (3.8% of the population) received funds for copayments (National Health Commission, 2021).

Preventive services for maternal and child health, such as screening programs and childhood vaccinations, are covered through a separate benefit without co-payments. Supplemental private insurance policies for co-pays and non-covered services are being sold, mostly to higher income individuals and as a workplace benefit. According to a recent review, private insurance coverage increased to around twelve percent of the population in 2013 from around four percent between 2004 and 2006 (R. Wu et al., 2020), with rates as high as 35 percent in large cities (Fang et al., 2012).

[1] 1,000 Chinese Yuan are approximately 150 U.S. Dollar as of January 2023

Social Care Insurance

Neither in-home nor institutional care are traditionally covered under public insurance. Not only financing but also provision of long-term care is seen as a family responsibility and consequently the delivery infrastructure for formal care remains underdeveloped. The idea of a genetic connection, the so called "Ties of Blood". is a core value of traditional Chinese culture, which requires the young generations to support the elders financially and emotionally (Yuan, 2000). Even for patients and families with means, wait times for admission into a facility can take long (Z. Feng et al., 2020). According to the 2019 Report on Alzheimer's Disease Patients Family in China, over two-thirds of dementia patients rely on themselves or their families for their care (Chinese Aging Well Association, 2020).

Children support their parents not only for cultural reasons, but also for legal ones. According to the People's Republic of China law on Protection of the Rights and Interests of the Elderly (Standing Committee of the Eight National People's Congress, 1996), elderly care should be based on home care. It is the children's responsibility and legal obligation to support the elderly financially, physically, and emotionally.

A safety net exists in that the government will pay full cost of the living and care expenses for people who meet a series of specific requirements ("Three Nos": no ability to work, no source of income, and no family or relatives to support them). In rural areas, these benefits are referred as the "Five Guarantees" (food, clothing, housing, medical care, and burial expenses). Approximately 2.5% of residents 60 years and older were covered under these social assistance schemes in 2014 (Z. Feng et al., 2020). Publicly financed long-term care accounts for about 0.1% of total GDP in China, which is lower than the OECD average (Maisonneuve & Martins, 2015) of 0.8%, and 60% of public funds come from the Public Welfare Lottery Fund run by the central government, 25% is contributed by local governments and the remaining 15 percent from other sources.

Recently, the government has started pilot programs with long-term care insurance. (Zhu & Österle, 2019) To ensure older people receive affordable care provided by either public or private institutions, the Chinese Ministry of Human Resources and Social Security published the "Guidelines on Carrying out Long-Term Care Insurance System Pilots" in 2016 and selected 15 provinces and cities for these pilots (Peng et al., 2022). These programs are financed directly by the government through UEBMI (Urban Employee Basic Medical Insurance) and URRBMI (Urban-Rural Resident Basic Medical Insurance) with varied benefit package and policies.

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Guangdong : Insurance pilots lead to insights for future dementia coverage

Guangdong province, in South China, is host to one of China's pioneering 2016 long-term care insurance (LTCI) pilots. Guangzhou a city of about 9 million residents, officially started providing LTCI in August 2017, enrolling about 50% of its 1.7 million residents over the age of 60. Inclusion of individuals with dementia was a particular feature of this pilot program. In order to quality for LTCI benefits, eligibility included moderate to severe physical dependence and diagnosis of moderate or severe dementia. The restricted eligibility excludes people with mild dementia, or people with moderate-to-severe dementia but mild physical dysfunction.

In the original pilot design, home care provided mainly focused on support for basic activities of daily living and nursing care. However, beneficiaries with dementia were found to have less need for both of these services than those without dementia, leading to the inclusion of such as dementia-appropriate supports. Evaluators also suggested that persons with dementia may have found it harder to access benefits that are mainly based on physical impairment and not cognition or behavioral disturbance. As a result, cognitive training, occupational therapy, and dementia care have been added to the services list in the Guangzhou pilot, and more comprehensive assessments for cognition and behavioral problems have been recommended. (J. Wu et al., 2020)

CARE PROVISION

Medical Care

Delivery of medical care in China occurs mostly in hospitals and outpatient health centers and traditional Chinese medicine is commonly practiced alongside Western medicine. While China pioneered the universal provision of basic clinical and public health services with great achievements in maternal and child health and infectious diseases, a robust primary care system for the era on noncommunicable diseases is only beginning to take shape (Li, Krumholz, et al., 2020).

> *"We are severely limited in terms of manpower and institutional capacity in rural areas, as skilled physicians prefer private hospitals in cities like Harbin or employment in southern provinces. Even if you have money, you may not be able to find suitable providers*"
>
> Policy Expert, Heilongjiang

There are three types of primary care clinicians in China (Li et al., 2017). Physicians complete 12 years of school and three years of medical school and so-called Assistant Doctors three years of technical medical training after nine years of school. Both have to pass a national exam and undergo regular recertification. Village Doctors have a less standardized training pathway and are only permitted to practice in village clinics that serve rural areas, often supported by community health workers (Fang, 2020b). Village Doctors (formerly referred to as Barefoot Doctors) are commonly unlicensed (Li, Krumholz, et al., 2020). Village doctors tend to be independent practitioners, who are paid on a fee-for-service basis combined with incentives to support care delivery in poor and sparsely populated areas (Hu et al., 2017).

In urban areas, there is a hierarchy of primary care facilities (Li et al., 2017). Community health stations serve as satellites for community health centers. While these community institutions are meant to be the main point for primary care, health services are also delivered by family practitioners in community hospitals (referred to as Tier 1 hospital) and by physicians and nurses in Tier 2 (secondary care) and 3 (tertiary care) hospitals. Patients are free to choose their primary care clinician but co-payments and wait times increase with the level of the institution (World Health Organization. Regional Office for the Western, 2015). Clinicians are typically employees of the facility. Historically, strong incentives existed for both managers and physicians to increase revenue and profits, as their compensation was tied to a facility's financial performance, recent reforms introduced targets and incentives for cost control and patient satisfaction, as well as alternative payment models, such as capitation payments and global budgets (Yip et al., 2019).

> *"Many diseases, such as colds, can actually be treated in the community, but ordinary people still choose to go to big hospitals. We also see that there is indeed overtreatment in the hospitals. To make the common people truly believe in community doctors, unless the policy is changed, doctors in tertiary hospitals should be serve some time in community hospitals. Aside from talent, equipment needs transformation. It would be great if all the medicines and examinations were as accessible in the community as the tertiary hospitals."*
>
> University Researcher, Sichuan

Formal registration of patients with family practices, who serve as gatekeepers and care coordinators, started in 2016 (Yip et al., 2019), and patients may, and commonly do, seek out physicians without referrals or coordination. The primary care sector remains under-resourced, as it offers over half of outpatient visits while receiving only about 18 percent of the funds (Yip et al., 2019). As a result, primary care centers often lack basic infrastructure (Li et al., 2017), such as labs, electrocardiogram and x-ray machines, and the objective and perceived quality of care remains substandard. Studies have shown high

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rates of underdiagnosis and undertreatment of common chronic conditions, such as blood pressure (Lu et al., 2017) and diabetes (Wang et al., 2017), and survey data show low levels of satisfaction and trust (Li et al., 2017). According to the Healthy China 2030 plan (C. P. s. G. o. t. P. s. R. o. China, 2016), strengthening the primary healthcare system is a critical element of improving access to and quality of care, a theme that was commonly brought up in our interviews. Similar recommendations have been made in a recent review by Li et al. (Li, Krumholz, et al., 2020)

Like primary care physicians, specialists are mostly hospital-based with a similar compensation structure. Public hospitals deliver around 90 percent of all inpatient and outpatient services, and many patients prefer care at large hospitals even for simple problems and primary care, as their quality is perceived as superior. (Yip et al., 2012) While fees in public sector institutions are regulated, emerging private sector clinics and hospitals may bill privately paying patients at higher rates, but have to accept the regulated rates for patients in public insurance schemes.

> *"Guangzhou has strong economic capabilities and government investment. When the income of a community doctor in Guangzhou increases, he is willing to work in the community. With strong efforts, the community was able to develop and retain people, and then strengthen various trainings. The community health service centers in Guangzhou are particularly good, the general medicine curriculum is solid, and the teachers are also good."*
>
> Geriatrician, Guangdong

Traditional Chinese medicine (TCM) has been used for the prevention and treatment of neurodegenerative disease in China and other Asian countries for more than 3000 years (Division of Aging and Health, 2019a). Dementia patients could choose acupuncture therapy or be recommended to eat more lecithin-rich foods (Zeng, 2020). Recent research has also revealed that gingko biloba may help to treat patients afflicted with Alzheimer's Disease (Jarrell et al., 2018). There were a total of 1.324 million beds, 683,000 licensed (assistant) physicians and 131,000 licensed physicians collectively in all 72,355 TCM institutions at the end of 2020. These numbers were higher than in 2019. However, the total number of consultations in TCM institutions was 920 million visits, a decrease of 250 million visits as compared to year 2019 (National Health Commission, 2021).

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Social Care

The last two decades have witnessed a substantial expansion of the social care infrastructure, in particular on the institutional care side. A combination of incentives and reduction of regulatory burden stimulated public private partnerships to build nursing homes and permitted for-profit and not-for-profit companies to operate government-owned facilities (Z. Feng et al., 2020). The number of nursing home beds increased by about 10 percent annually in the second decade of this century, mostly in urban centers (Shum et al., 2015). Growth was so fast that only about half of beds were estimated to be occupied in 2015 because of a combination of lack of affordability, concerns about quality, and staff shortages (Z. Feng et al., 2020).

While the official framework for a three-tier long-term care system calls for 90 percent of the elderly to receive formal and informal care at home, seven percent through community-based services and only three percent in nursing homes (Wang et al., 2018), the development of a robust infrastructure for home and community-based care has been lagging relative to the rapid increase in nursing home beds (Z. Feng et al., 2020).

Hubei – Public-Private Partnership Pilots Support Integrated Elderly Care

In Hubei province, Yichang City has worked closely with the Asian Development Bank to support the development of the elderly care system under the first sovereign public-private partnership ADB loan in China. A mainstream third-tier city that typifies mid-sized cities and second largest city in the province after the capital city of Wuhan, Yichang's approach has been to actively take on public-private partnerships.

With ADB knowledge sharing technical assistance (KSTA) and two loan projects, Yichang has developed and implemented an overarching holistic eldercare strategic plan that aims to build a comprehensive elderly care system integrating medical care with a three-tiered model (home-, community- and institution-based) to address the needs of low- to middle-income elderly (including expanding dementia care). Strategically the plan has focused on the addition of home care and elderly care facilities as well as supporting human resources development and technological innovation such as a city-wide elderly-care communication platform.

The number of elderly care beds in the city has increased from 18,000 in 2014 to 35,520 in 2022; while the proportion of nursing beds increased from 22% to 63% during the same period. The city has also allotted 150 hectares of land for elderly care services, with 176 community- and home-based elderly care service institutions and 71 "happiness canteens" or canteens catering specifically for the elderly since 2014. The strategic plan also includes the improvement of overall dementia care capacity and completion of a dementia care center by 2023.

In light of its commitment to innovation, Yichang City was recently named a National Key Contact City in June 2022 (Asian Development Bank, 2022).

DEMOGRAPHIC TRENDS

Few countries have developed as fast as China with an average annual GDP growth of nine percent since 1970, which lifted 770 million people (Lifang, 2018) out of poverty and into the middle class (The World Bank, 2023). However, the rapid industrialization that made that growth possible has profound demographic implications, as China has become one of the fastest ageing countries because of the combined effect of increasing life expectancy and low fertility (China Power Team, 2020). In addition, industrialization has led to substantial migration into the coastal cities in the South and East.

INCREASING LIFE EXPECTANCY

The combination of reduced poverty, improved maternal and child health, and broad accessibility of basic medical care has increased life expectancy in China dramatically from 44 years at birth in 1961 to 77 years in 2018 (Figure 4), which is higher than that of its high-middle income peers and on par with Central Europe and the Baltics.

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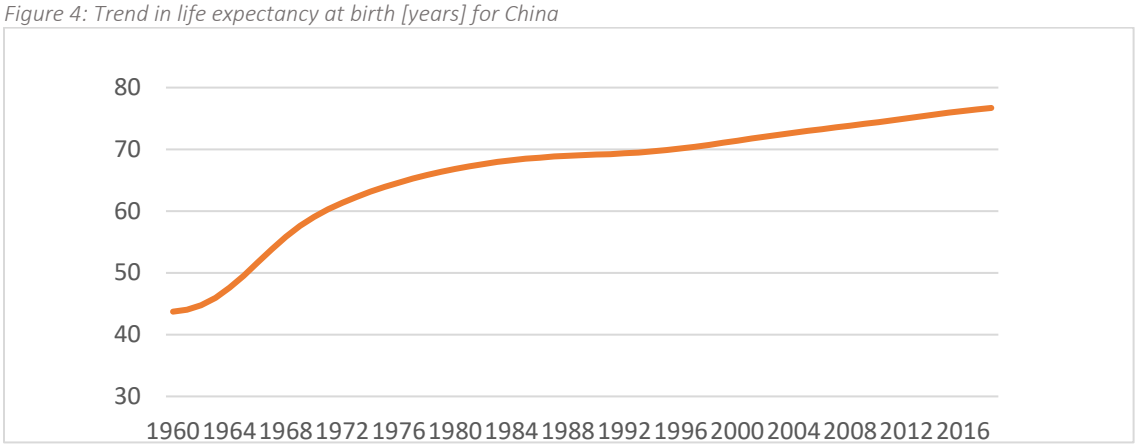
Figure 4: Trend in life expectancy at birth [years] for China

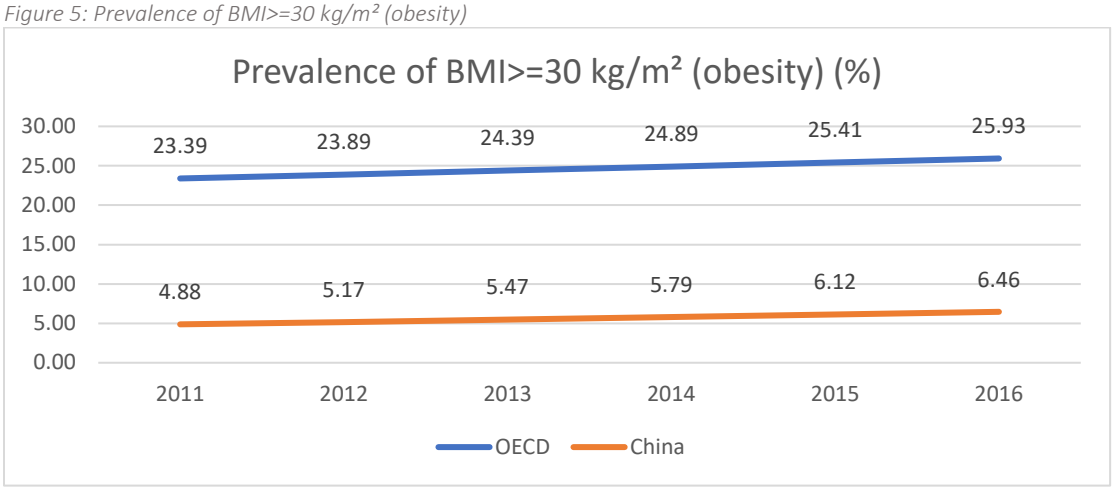


Source: World Bank (The World Bank, 2023)

RISK FACTORS

With growing wealth and longer lifespans, many Chinese people adopted Western-style diets and lifestyles resulting in a growing burden of cardiovascular risk factors and noncommunicable diseases that also increase dementia risk (Jia, Du, et al., 2020). As Figure 5 shows, obesity rates in China, while still comparatively low, have increased by 32 percent from 2011 to 2016. The weighted average (using population size as weights) OECD prevalence of smoking any tobacco product among persons aged >= 15 in year 2015 was 10.05% and 25.26% (47.6% for men and 1.8% for women) for China (World Health Organization, 2020).

Figure 5: Prevalence of BMI>=30 kg/m² (obesity)



Source: NCD Risk Factor Collaboration (NCD Risk Factor Collaboration, 2023)

While burden of hypertension (Figure 6) and diabetes (Figure 7) have stabilized in OECD countries, prevalence continues to grow in China. Combined with the above-mentioned insufficient control of these diseases and population ageing (described below), China is likely to experience a growing burden of cardiovascular disease and dementia.

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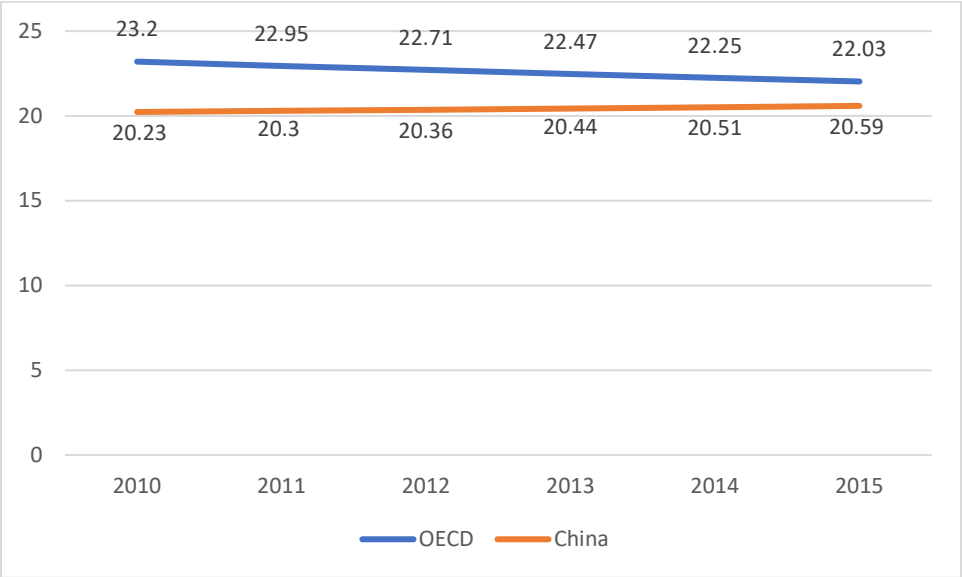
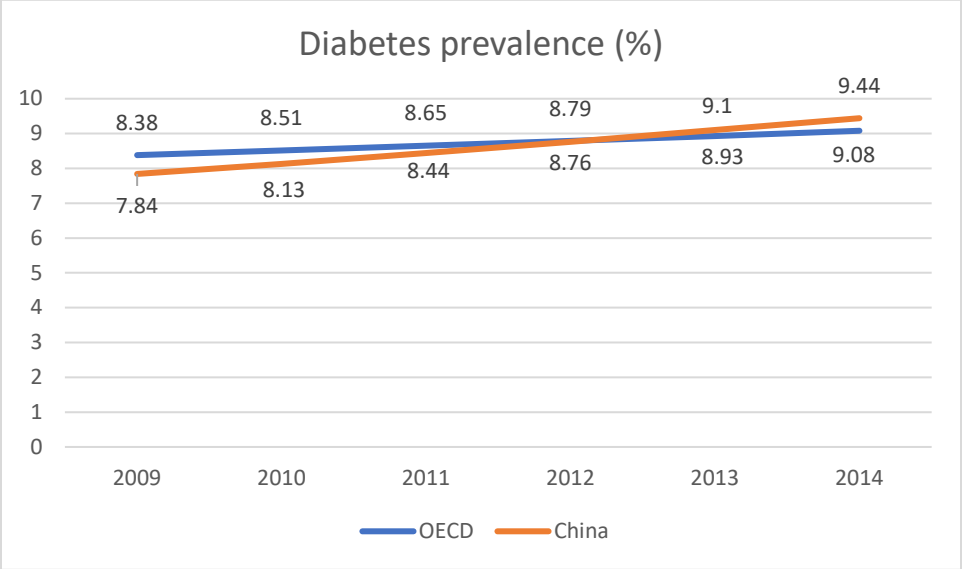
Figure 6: Prevalence of raised blood pressure



Source: NCD Risk Factor Collaboration (NCD Risk Factor Collaboration, 2023)

Figure 7: Diabetes prevalence



Source: NCD Risk Factor Collaboration (NCD Risk Factor Collaboration, 2023)

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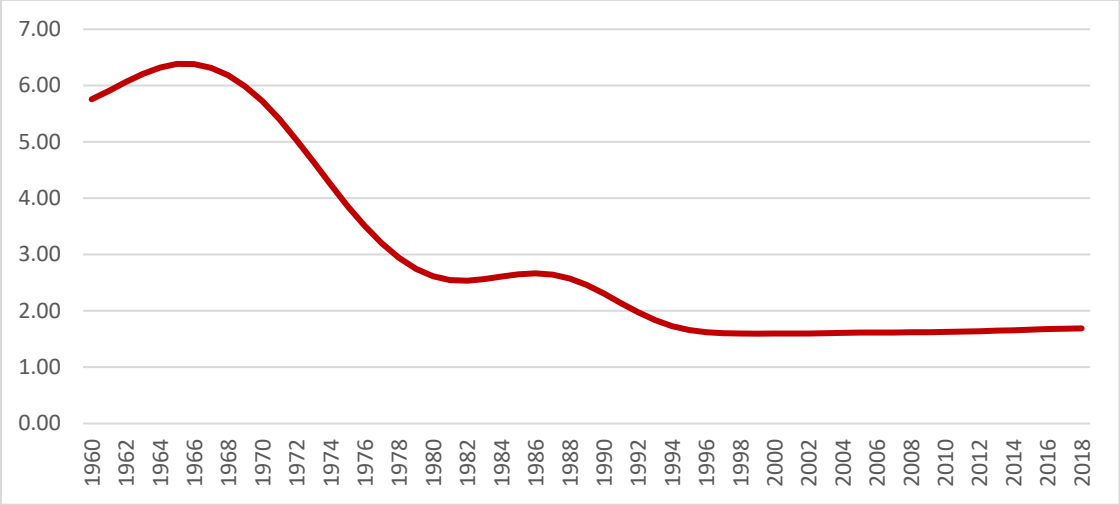
LOW FERTILITY

China is unusual for a rapidly growing economy as its fertility rate declined early in its development phase. In both China and South Korea, the fertility rate dropped below 2.0 in 1990, about the time at which South Korea crossed the threshold to becoming an upper-middle income country, whereas China was still a lower-middle income country. (Figure 8) The early decline of the fertility rate was a result of the one child policy introduced in 1979. While exceptions to this rule meant that over half of parents were allowed to have two children, it had the intended effect and fertility rates are projected to remain below

the estimated replacement rate of 2.1 for the coming decades, even though the policy was relaxed to allow for a second child.

Figure 8: Fertility rate in China 1960 to 2018



Source: World Bank (The World Bank, 2023)

POPULATION AGEING

The twin effect of a low birth rate and increasing life-expectancy means that China, currently a relatively "young" country with a share of persons aged 65 and older of 12.6% compared to 28.2% in Japan and 21.4% in Germany, is ageing rapidly. Its population aged 65 and older increased from 8.9% of the total population in 2010 to 12.6% in 2019 and 176 million people of its 1.4 billion population are now of old age (Chen et al., 2019). About a quarter of those live in the six jurisdictions that are featured in this study (Figure 9).

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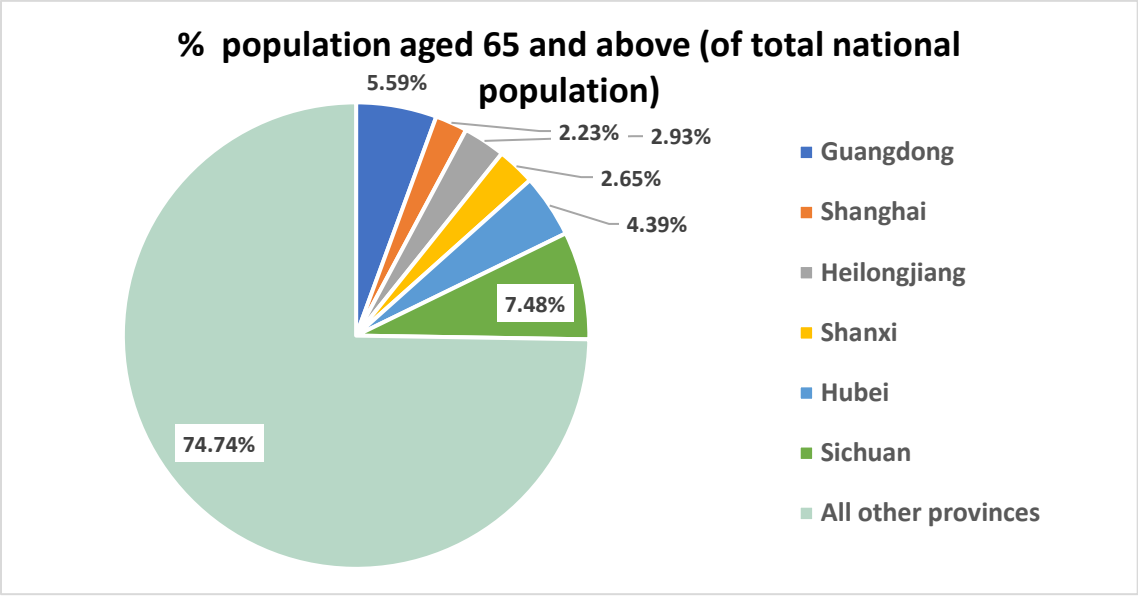
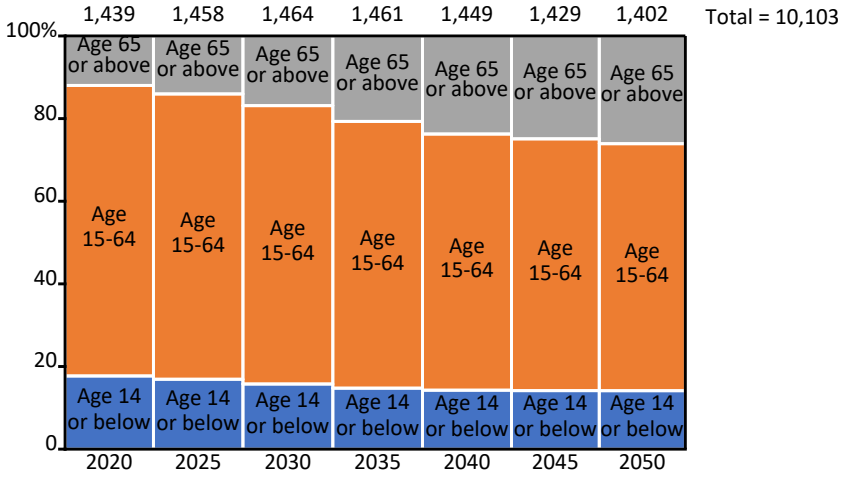
Figure 9: Share of population aged 65 and above living in the six jurisdictions featured in the study (National Bureau of Statistics of China, 2020)



Source: China Statistical Yearbook 2020 (National Bureau of Statistics of China, 2020)

The UN and the WHO define an "aged society" as an older population (aged 65 and above) accounting for 7% of the total population and a "super aged society" if for 20% of the total population. According to the World Population Prospective published by UN in 2019, China will become an "aged society" in 2025 and a "super aged society" in 2035. It is estimated that China's share of the aged population rate will increase from 11.47% to 24.71% in the next 25 years. Figure 10 shows the projected age composition for China from 2020 to 2050.

Figure 10: Fertility rate in China 1960 to 2018



Source: World Population Prospects 2019 (United Nations, 2019)

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The ageing rate differs by geography. Between 2010 and 2017, provinces in central China had the highest growth rate in the share of aging population and rural areas saw higher growth rates than urban areas (3.16% versus 2.29%) (J. Feng et al., 2020; National Bureau of Statistics of China, 2019). While historically the Eastern seaboard had the highest proportion of an elderly population, the proportion decreased in other parts of the country after 2010 (Chen et al., 2019).

MIGRATION PATTERNS

As a result of faster economic growth, the provinces on the southern and eastern seaboard have seen substantial inbound migration in the last two decades. These two regions account for almost two-thirds of in-migration in 2010 (Cao et al., 2018). The East and South Coasts received In 2010, there were around 27 million and 26 million new inhabitants to the East and South Coasts, respectively. Southwest China and Central China are the two largest migration source regions with out-migration of 12.91 million and 15.41 million individuals in 2000, 21.02 million and 29.19 million in 2010 respectively (Cao et al., 2018). With respect to individual jurisdictions, Guangdong was the dominant migration destination in 2000 and 2010, with 14.65 and 22.31 million in-migration, respectively, followed by Beijing, Shanghai and Xinjiang in 2000 and Zhejiang, Shanghai and Beijing in 2010. Sichuan is the largest migration source province in 2000 and 2010 (Cao et al., 2018). The top five jurisdictions with increases in permanent population from 2010 to

2020 were Guangdong, Zhejiang, Jiangsu, Shandong, Henan, whereas the population of six northern provinces (Gansu, Inner Mongolia, Shanxi, Liaoning, Jilin and Heilongjiang) saw reductions (Ren, 2021).

As employment prospects are the main reason for migration (Liu et al., 2014), migration rates are highest for young adults. Around 70 percent of migrants into Shanghai in 2010, for example, were between 20 and 44 years old (Chen et al., 2018). The magnitude and selectivity of the internal migration has profound implications for the population structure of provinces with large inflows and outflows in that outflow provinces experience faster ageing (Shi et al., 2020). As dementia is an ageing-related disorder, those selective migration trends mean that outflow provinces will experience a higher burden of chronic disease, while have fewer working-age adults to provide informal or formal care. For example, the 2019 dependency ratios of Liaoning, Jilin, and Heilongjiang were 1.48, 1.35, and 1.28 well below the national ratio of 2.53 (Ren, 2021).

DEMENTIA IMPACT

PREVALENCE AND INCIDENCE OF MCI AND DEMENTIA

Dementia

Many studies have investigated prevalence of and trends for dementia in China. A 2014 population-based cross-sectional study showed that the prevalence of dementia and Alzheimer's dementia among individuals aged 65 and older was 5.14% (95% CI, 4.71–5.57) and 3.21% (95% CI, 2.87–3.55), respectively (Jia et al., 2014). A 2020 study by Jia et al. (Jia, Du, et al., 2020) estimated dementia prevalence at 6.0% in adults aged 60 years and older. Another cross-sectional study of the epidemiology of mental disorders using a nationally representative sample showed that the weighted prevalence of dementia for a population aged 65 and older was 5.6% (95% CI 3.5–7.6) in 2012 (Huang et al., 2019). A meta-analysis of 96 dementia studies published in 2018 estimated the number of Chinese people aged 60 and older with dementia to be 9.48 million, which means the overall prevalence of dementia in China would be 5.3%. (Wu et al., 2018) A 2013 systematic review by Chan et al. estimated 9.19 (95% CI 5.92–12.48) million dementia cases in 2010 in individuals 65 and older (Chan et al., 2013). Their pooled estimate for the incidence of dementia in people 60 and r older was 987 cases per 1000 person-years. Prince et al. (Prince et al., 2012) estimated age and sex standardized mortality in dementia patients and reported hazard ratios of 3.02 (95% CI 2.13 – 4.28) and 3.59 (95% CI 2.47 – 5.21) for urban and rural China, respectively. Xu et al. used those data to project case burden in 2020 and 2030 of 15.07 million and 23.3 million, respectively, with prevalence increasing from 5.8 percent to 6.7 percent in individuals aged 60 and older (Xu et al., 2017). Extending their 2020 projection to the population 50 years and older yields an estimated combined prevalence of 3.13 percent.

Many studies conclude that prevalence of dementia is significantly higher in women than in men of the same age group. The prevalence ratio of women to men varies from 1.43 (1.31–1.56) to 1.65 (95% CI 1.51–1.81) for dementia and 2.37 for Alzheimer's disease (Chan et al., 2013). Prevalence of both dementia and Alzheimer's disease was about two percentage points higher in rural areas than in cities, which the authors attributed to differences in educational attainment (Jia, Du, et al., 2020).

Partially because of the above-mentioned migration trends, the prevalence of dementia varies across geographical areas. The prevalence in West and North China was estimated at 5.5% compared to 5.2% and 4.8% in Central and South China, respective (Wu et al., 2018). A 2020 study (Jia, Du, et al., 2020) indicates that prevalence in western China is significantly higher than other parts of China. (Figure 11)

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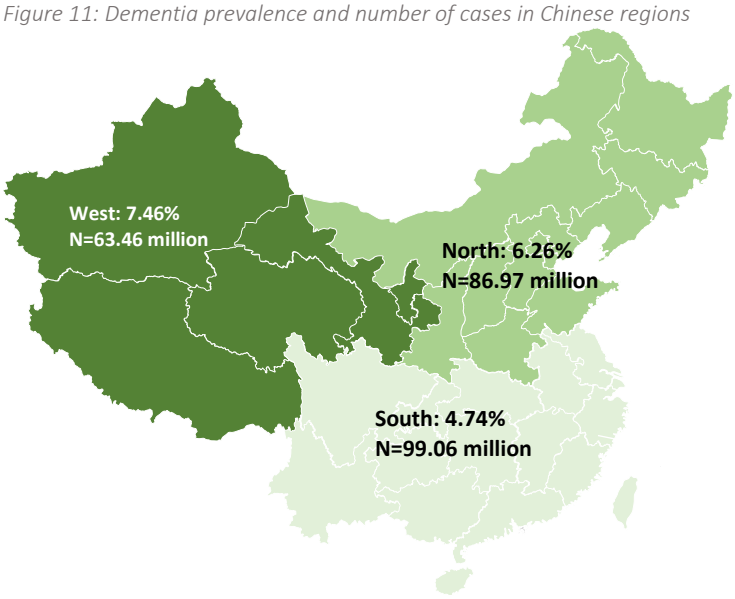
Figure 11: Dementia prevalence and number of cases in Chinese regions



MCI

We used a meta-analysis by Nie and colleagues (Nie et al., 2011) and a systematic review by Chan et al. (Chan et al., 2013) to estimate prevalence of MCI in different age brackets nationally and by the six jurisdictions (Table 2). These estimates of a pooled prevalence of 6.98 percent in individuals aged 50 years and older are consistent with those from a global meta-analysis (Petersen et al., 2018). The overall estimated number of MCI cases was 32 million, similar to a recent estimate by Jia et al. of 39 million (Jia, Du, et al., 2020). We were unable to identify robust data for the incidence of MCI in China and are using previously published data from a global meta-analysis by Gilles et al. (Gillis et al., 2019)

Table 2: Estimated MCI prevalence among individuals aged 50 and older by age bracket in China

Age bracket	MCI prevalence	GuangDong	HeiLongJiang	HuBei	ShaanXi	ShangHai	SiChuan	National
50-54	3.38%	257,826	158,955	194,668	122,378	94,867	218,017	4,172,454
55-59	4.48%	241,919	147,302	202,884	112,664	94,774	314,835	4,423,574
60-64	5.94%	238,039	141,253	215,215	109,673	88,378	334,167	4,604,340
65-69	7.88%	305,755	162,872	271,281	132,236	93,875	464,764	5,843,002
70-74	10.44%	274,869	140,335	205,543	112,747	75,245	346,533	4,692,748
75-79	13.85%	234,378	93,218	163,835	89,738	87,122	249,353	3,676,429
80-84	18.36%	190,956	62,075	109,862	60,891	64,808	208,988	2,970,908
85+	24.34%	230,847	61,285	112,324	51,155	102,031	206,651	2,540,289
Number of cases		1,974,589	967,296	1,475,611	,481	701,100	2,343,309	32,923,744
Average prevalence		7.25%	6.43%	6.84%	6.63%	7.21%	7.30%	6.98%

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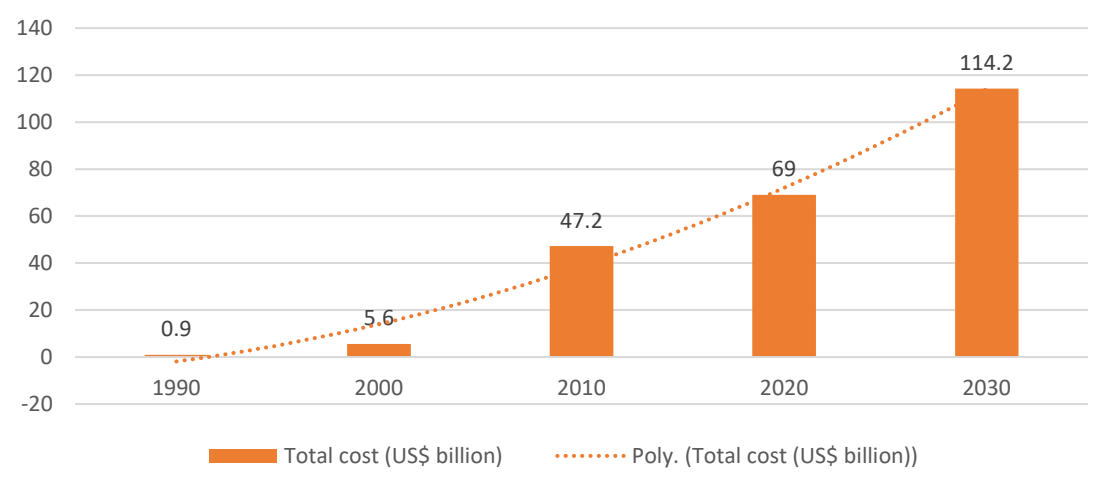
ECONOMIC IMPACT

A prevalence-based study published in 2017 estimates that the total annual cost of dementia increased from 0.9 billion dollars in 1990 to 47.2 billion dollars in 2010 and will reach 114.2 billion dollars by 2030 (Xu et al., 2017). Informal care is the largest contributor to overall dementia cost and accounted for 94.4% in 1990, 92.9% in 2010 and will reach 81.3% by 2030, which is comparable to findings from a recent systematic review (Schaller et al., 2015) but higher than the 60% reported for low- and middle-income countries by the World Health Organization. Another study pegged the contribution of productivity losses for family caregivers at 70 percent (Clay et al., 2019). The second largest contributor to cost in 2010 was nursing home care with 12.8 percent, whereas hospital and outpatient care as well as the valuation of lost disability-adjusted life-years played a minor role (Xu et al., 2017). The authors also predicted continuously steep increases in overall cost through 2030 (Figure 12) by when China will account for 10 percent of the global economic burden of dementia.

Figure 12: Estimated overall annual cost of dementia in China (Xu et al. 2017)



DEMENTIA PLANNING

There is no specific national dementia plan in China as of this report. Instead, plans for dementia care have historically been part of plans for overall long-term care as well as mental healthcare, both of which have continued to evolve rapidly in recent years.

Under the 12th 5-year plan (2011-2015), China instituted a three-tier care framework for all forms of long-term care (including dementia), which focused on making home care the default with community care as a support and institutional care as a supplement following a 90-7-3 breakdown (Wang et al., 2018). Alongside this, recognizing the increasing healthcare needs of older adults in long-term care, China has also promoted the growth of integrated care models - yi-yang-jie-he— in the form of partnerships between medical and long-term care facilities; the addition of long-term care to medical facilities, and more community-based medical services (Z. Feng et al., 2020).

A more urgent focus on dementia and the needs of older adults more generally is evident in the most recent comprehensive national healthcare strategy laid out in the Healthy China 2030 Blueprint, which includes the goal of curbing the growth rate of dementia among people 65 years and older by 2030. Improved capacity for dementia care at all levels is a core element of a planned national system for providing care to older adults, to be overseen by the Department of Aging Health (Health, 2019).

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Key dementia-related goals and strategies in the Healthy China 2030 (C. P. s. G. o. t. P. s. R. o. China, 2016; S. C. o. t. P. s. R. o. China, 2016) Blueprint and (National Health Commission, 2021) other related plans and directives include the following:

Strategy 1: Expand access to high-quality geriatric care; Lead agency: National Development and Reform Commission

- Geriatric departments to be set up in at least 50% of general hospitals above Tier 2 by 2022 and 90% in 2030 (National Health Commission, 2021), with increase in the number of beds
- All long-term care facilities to provide an appropriate basic range of medical services by 2022 and to continue to improve until 2030 (National Health Commission, 2021)
- Institutions of higher learning and vocational colleges to set up geriatrics-related majors or courses, focusing on geriatrics, rehabilitation, nursing, nutrition, psychology, and social work, and accelerate the adoption of modern geriatrics training, with geriatrics, rehabilitation, and nursing included as priority areas in the national health personnel training plan (Ministry of Education Clinical Medicine Professional Certification Working Committee, 2022)
- Establishment of a long-term care financing system, which includes privately-provided long-term care insurance
- Expansion of long-term care manpower and beds
- Geriatric-related research and development to be led by Ministry of Science and Technology, which will promote new geriatric research centers as well as partnerships with medical research enterprises, to encourage technological innovation in this sector

Strategy 2: Expand dementia care at all levels of the healthcare system; Lead Agency: Chinese Center for Disease Control and Prevention

- Basic Alzheimer's disease training to be carried out by psychiatrists, neurologists, and geriatricians in general hospitals at county level
- Procurement of dementia drugs to be allowed in primary care facilities in order to increase access to care. (National Bureau of Disease Control and Prevention, 2020)

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Strategy 3: Expand access to community-based care for the elderly; Lead Agencies: National Development and Reform Commission, the Ministry of Finance, and the State Administration of Traditional Chinese Medicine

- Door-to-door home-based eldercare services to be provided by primary care institutions
- Strengthening of community management, including provision of daily care and psychological support services
- Early screening, early intervention and health guidance for neurodegenerative diseases such as Alzheimer's disease to be instituted (Commission, 2019)

Dementia is also a major priority under the first and second (current) National Mental Health Work Plan (2002-2010) led by the National Health Commission (formerly the National Health and Family Planning Commission) (S. C. o. t. P. s. R. o. China, 2016) in collaboration with a range of other government agencies. The plan generally aims to develop integrated services, train mental health specialists, improve

rehabilitation services and community and family-based supports, promote social awareness and mitigate social stigma. A key target of the workplan is to develop the capacity to professionally treat all mental health conditions at the county-level, including having at least one general psychiatry clinic in at least one qualified general hospital in each county by 2020 (National Health and Family Planning Commission, 2015).

In conjunction with these plans, over the course of the 13th Five Year Plan, the Chinese government has supported a series of pilot projects focused on mental health for older adults as well as home and community-based long-term care services (Development, 2017), funded by a dedicated public welfare fund of 1 billion yuan per year (5 billion RMB in 5 years) (General Office of the State Council, 2013).

While results of these pilots are still not known, key projects that have been implemented or launched include

- Mental health assessments at home for elderly people aged 65 and above in project cities
- Training of family members and caregivers of patients diagnosed with Alzheimer's disease by community doctors to increase the intervention rate and improve the quality of life.
- Public awareness campaigns via community-based social-marketing techniques, leveraging both traditional culture and new digital platforms such as local dramas, folk songs, WeChat, Weibo, and mobile media to provide evidence-based education on Alzheimer's disease.
- Establishment of a social mutual-assistance-based insurance system in 15 pilot cities for long-term care (Department of Health Insurance, 2016)

THE CASE FOR WORLD-CLASS MEMORY CARE IN CHINA

As we have shown, the confluence of rapid ageing and epidemiologic transition to chronic disease means that dementia will have a substantial impact on China, not just from a health but also from an economic growth perspective because of its effect on consumer spending and the workforce.

With 36 percent, China has a savings rate that is thrice as high or more than that of OECD countries (Figure 13) and several studies (Hancock, 2021; Woetzel et al., 2009) have suggested that reducing it to increase consumption would stimulate economic growth. Protection for long-term care needs is an important contributor to this high rate: İmrohoroğlu and Zhao (İmrohoroğlu & Zhao, 2018) estimated that the savings rate could be seven percentage points lower if China had comprehensive long-term care insurance.

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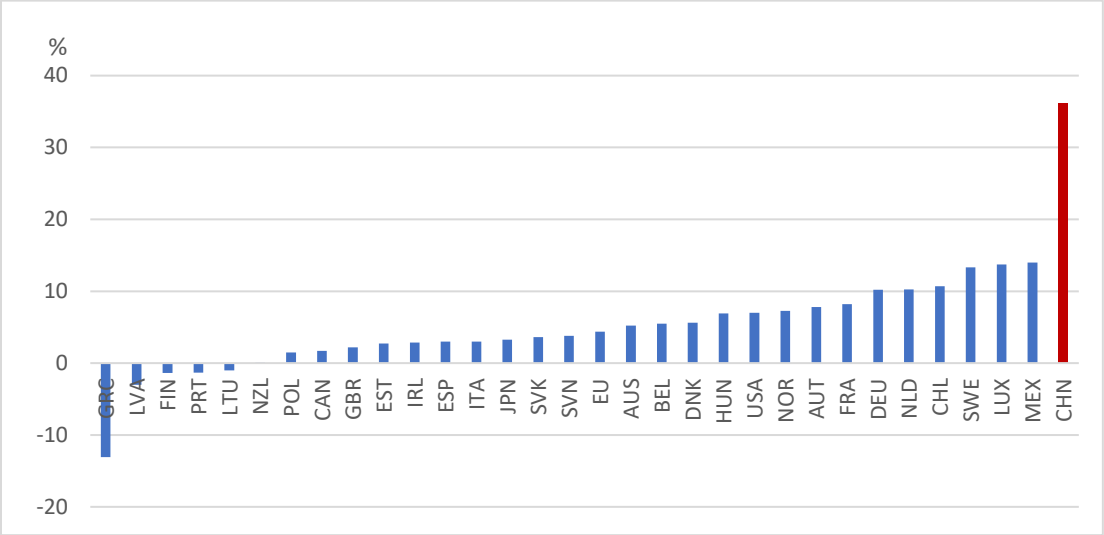
Figure 13: Household savings, % of household disposable income, China and 37 OECD Countries (2016)



In addition, China relies heavily on family caregivers for long-term care, which are typically women. An increasing burden of dementia might further reduce female labor market participation, which according to World Bank estimates, has already fallen from 73 percent in 1990 to 61 percent in 2019 (The World Bank, 2023). Accelerating this trend is problematic because China's working age population has started shrinking in 2012 and is projected to fall by about a quarter by 2050 (World Economic Forum, 2016). Further, the above-mentioned migration patterns make it less likely for adult children to live close to their parents. Thus, financing and provision of world class memory care will be important for China to maintain its fast economic growth. This report takes stock of the status quo and points to opportunities for future development.

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PATIENT JOURNEY TOWARDS A DMT

SCREENING FOR MCI

Like other countries, China does not have a population-based screening program for cognitive decline at the national level. However, the National Health Commission, which is the government agency that would introduce new screening programs, launched a pilot program in 2019 (National Health Commission, 2021). Under this program, primary healthcare facilities in 1,600 pilot urban communities (50 in each province) and 320 rural communities (10 in each province) across the country invite its (Department of Family Planning and Family Development, 2017) residents over age 65 to undergo free MMSE based systematic cognitive assessments and to achieve a screening rate of at least 80% (Division of Aging and Health, 2019b).

CASE FINDING

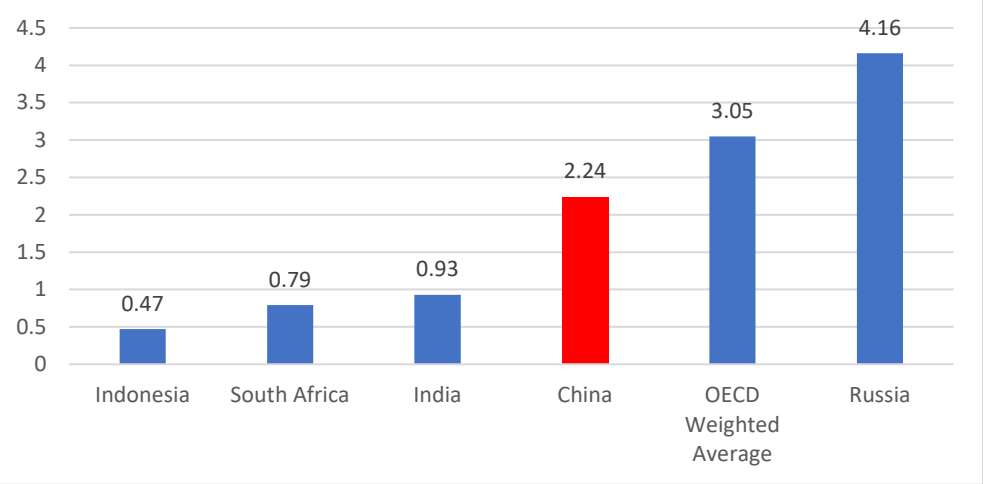
As pointed out above, China does not have a strong primary care tradition (Li, Krumholz, et al., 2020), and cognitive decline is most commonly detected based on subjective memory complaints rather than during routine wellness assessments. We were told that those concerns often emerge when children visit during national holidays and urge their parents to get evaluated. Given a widespread perception that cognitive and behavioral changes are a normal sign of ageing – a survey of caregivers suggested that

about half share that perception (Zhang et al., 2004) -, a diagnosis is often sought at advanced stages of the disease (Libo Sun, 2014). According to a 2017 meta-analysis, over 90% of dementia cases remain undiagnosed in China (Lang et al., 2017).

In urban areas, patients typically go straight to hospital-based neurology clinics[2], as referrals are not needed, whereas in rural areas the primary point of contact tends to be the local community health center or village doctor. Hospital-based clinics typically conduct a structured assessment with anamneses and cognitive testing, followed by a complete evaluation if cognitive decline is confirmed. In contrast, rural providers rarely have access to local clinicians trained in formal assessment of cognitive decline and tend to recommend traditional Chinese medicines rather than referrals to urban centers for further evaluation because of travel distances and concerns about cost (Quail et al., 2020).

In both settings, office visit slots tend to be readily available either on a walk-in basis or by making an appointment (Ying et al., 2020), as China has increased the number of physicians to almost 3 per 1,000 population in recent years (Figure 14).

Figure 14: Physicians per 1000 population



Source: OECD Health Statistics (OECD, 2023)

According to expert input, wait times rarely exceed a week unless a patient insists to be seen by a department head. Visits are covered by insurance, albeit with high co-payments as explained above, and rates differ by the seniority of the physician. Provider payment is regarded as adequate, but visits tend to be quite short, with about 15 minutes for an initial consultation and 5 minutes for a follow-up. Patients may request longer office visits in exchange for higher rates.

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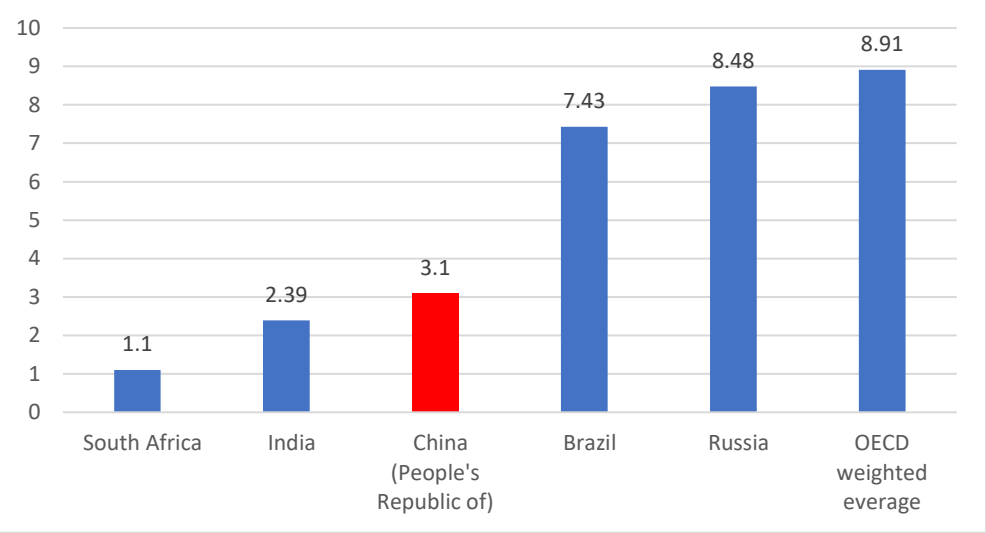
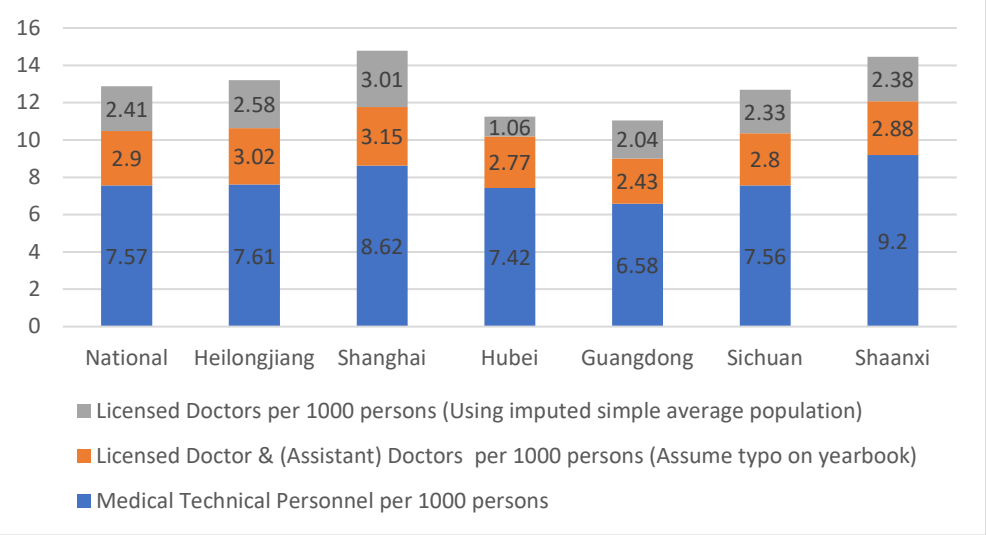
[2] Psychiatrists are less commonly sought out because of concerns about stigma. (Sun 2014)

Figure 15: Number of registered nurses per 1,000 population (2019)



Source: OECD Health Statistics (OECD, 2023)

Figure 16: Clinicians per 1,000 population nationally and in the selected six jurisdictions (2020)



Source: China Statistical Yearbook 2019 (National Bureau of Statistics of China, 2019)

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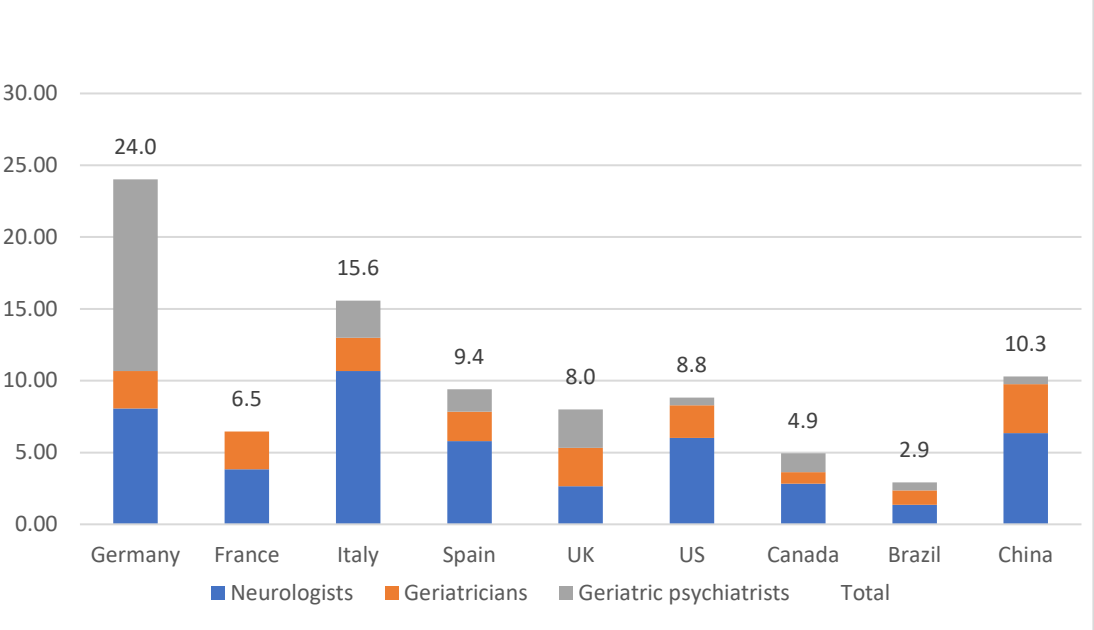
COGNITIVE TESTING

The dementia specialist workforce in China predominately consists of neurologists focusing on memory care. A smaller proportion of psychiatrists practices geriatric psychiatry, which includes dementia care but usually with a focus on managing neuropsychiatric symptoms, like agitation and hallucinations. While geriatrics has yet to emerge as a specialty, larger hospitals tend to have a geriatrics department that is staffed by multidisciplinary teams.

In China, a formally designated dementia specialist is defined as having a qualification as an associate chief physician or above, with clinical practice experience treating cognitive disorders over the past 5 years, more than 1 year of learning experience in the dementia center of a major national academic hospital, and the ability to independently diagnose dementia. Doctors who do not fulfil these criteria but

still engage in dementia treatment are referred to as dementia doctors (Jia, Quan, et al., 2020). Based on expert input, 56% of the 13,270 psychiatrists, 85% of the 107,545 neurologists and 66% of the 74,454 geriatricians, who were licensed to practice in China in 2023, would be considered appropriately trained in evaluation of cognitive impairment for an estimated total of 147,985 dementia doctors, which we will consider the AD specialist for this analysis, or 10.28 specialists per 100,000 population compared to a G7 2019 average of 11.27 (Figure 17).

Figure 17: Number of dementia specialists per 100,000 capita in China compared to other countries



Source: (Mattke, Ullrich, & Wang, 2020)

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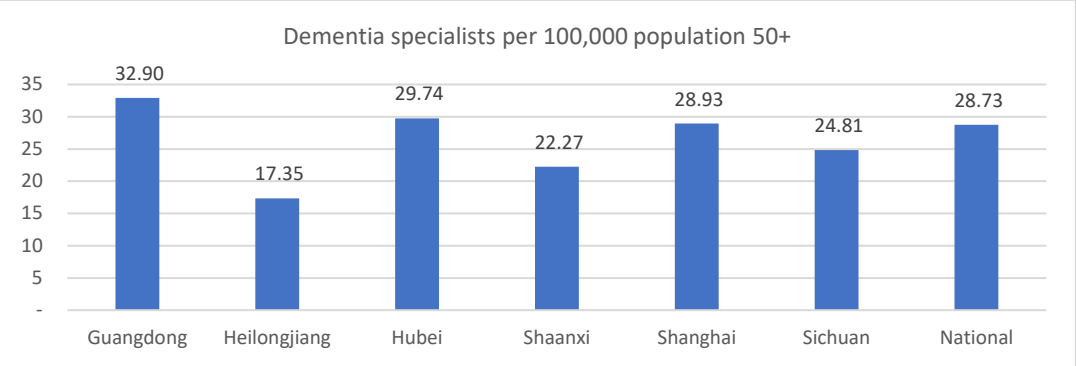
There are marked differences in dementia specialist density by province as Figure 18 shows. We express counts in per 100,000 aged 50 and older, the age at which identification for an AD treatment would start, to account for the substantial differences in age structure across provinces. Wealthy jurisdictions, like Guangdong, Hubei and Shanghai, have numbers over the national average, whereas Heilongjiang, the province with the lowest GDP per capital, lies far below the average.

Figure 18: Number of dementia specialists per 100,000 capita 50+ nationally and by selected province



Source: Authors' estimate based on expert input

Patients with suspected cognitive decline based on a brief test may seek further evaluation in memory centers, which are typically only found in academic Tier 3 hospitals (Jia et al., 2016). These centers are typically led by neurologists who are trained in the Chinese guidelines for diagnosis and management of cognitive impairment and dementia (Jia et al., 2011). Few Tier 1 and 2 hospitals have memory clinics and evaluation of cognitive decline in those mostly lies in the hands of internists, who have limited formal training in memory care, which leads to higher rates of missed or incorrect diagnoses (Jia et al., 2016). While non-academic Tier 3 facilities typically have neurology departments, they usually lack specialized memory clinics (Jia, Quan, et al., 2020).

> *"Because of staff shortage, we mainly rely on students to administer cognitive tests. Normally, there should be training on such scales, but no national and authoritative unit to evaluate these matters. In addition, we need to digitize these scales. There is still a lot of room for improvement."*
>
> Neurologist, Heilongjiang

As formal memory centers have only been launched relatively recently, capacity is limited and experts voiced concern about capabilities as well. Only about 10% of the Tier 3 hospitals have them, and data from the Neurology Branch of the Chinese Medical Doctor Association suggest that China has 2,340 Tier 3 hospitals with 96,000 neurologists and but only around 2,000 active formally certified dementia specialists (Jia, Quan, et al., 2020), compared to our expert estimate of 77,701 neurologists with sufficient training to offer evaluation of cognitive impairment. Memory centers are usually large-scale operations with substantial task shifting. The specialist will see a patient briefly and order a range of tests, which are carried out by other clinicians, for example technicians to perform comprehensive neurocognitive testing, and then meet again with the patient to discuss a care plan.

Neurocognitive testing and specialist evaluations are covered by health insurance with the customary copayments. The streamlined operation of a memory center makes the practice financially attractive for dementia specialists, since they are seeing large numbers of patients, reportedly around 50 per day, for consultations of 5 to 15 minutes. Patients prefer to be admitted for evaluation of cognitive decline, as insurance coverage is more generous for inpatient care, but competing demands for hospital beds in Tier 3 facilities often precludes this option.

While formal data on wait times are lacking, the low number of memory clinics and dementia doctors in neurology, psychiatry, or geriatric departments and hospitals represents a major problem. In 2018, the government approved plans for the Cognitive Disorders Committee of the Neurology Branch of the Chinese Medical Doctor Association to establish a program that would train dementia specialists at dementia centers in national academic hospitals and to mitigate the shortage of dementia doctors in China (Jia, Quan, et al., 2020).

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BIOMARKER TESTING

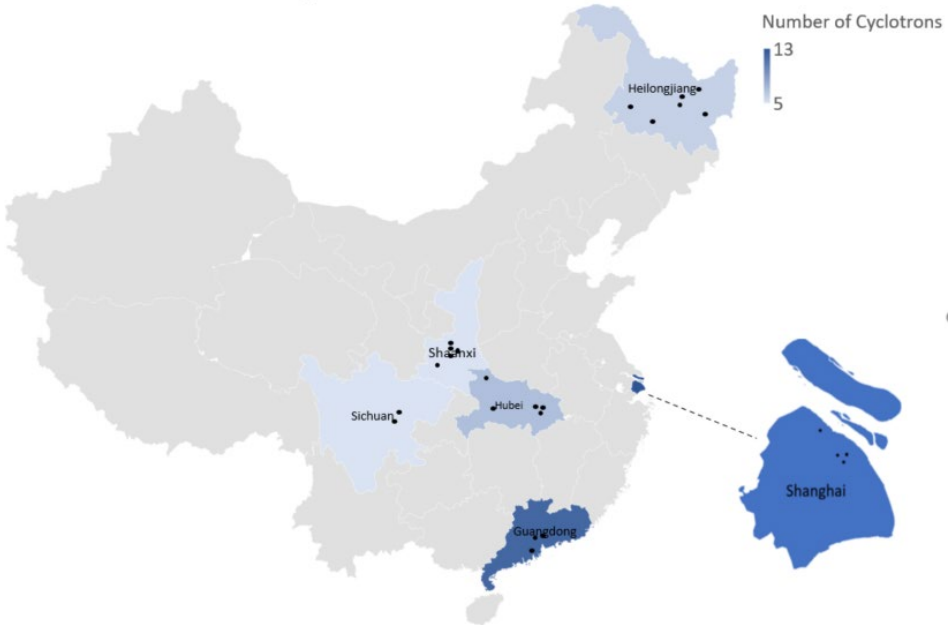
While formal data on wait times are lacking, the low number of memory clinics and dementia doctors in neurology, psychiatry, or geriatric departments and hospitals represents a major problem. In 2018, the government approved plans for the Cognitive Disorders Committee of the Neurology Branch of the Chinese Medical Doctor Association to establish a program that would train dementia specialists at dementia centers in national academic hospitals and to mitigate the shortage of dementia doctors in China (Jia, Quan, et al., 2020).

Both CSF and PET tests for the Alzheimer's pathology are approved in China but only CSF tests are covered by insurance. With a charge of around 7,000 to 10,000 RMB for a PET scan (Chen et al., 2017), few patients opt to pay for the test out-of-pocket and only 2.7% of all scans were conducted for neurological disorders in 2015. For those who do, capacity to conduct PET scans is readily available in urban locations. China has a density of PET scanners comparable to other middle-income countries and close to that of the U.K. (Figure 20) and a higher density in wealthy jurisdictions like Shanghai and Guangdong (Figure 21). With around 2,000 scans per device conducted annually compared to 3,280 in the U.K., substantial excess capacity should exist.

> *"Patients` acceptance of lumbar puncture is relatively low because it is invasive and you must be hospitalized. A PET scan is 78,000 yuan compared to 5,600 yuan for an MRI. Only if the PET price reaches acceptable levels, biomarker testing will pick up. And we are looking forward to the plasma biomarkers entering the clinic. "*
>
> Geriatrician, Sichuan

Overall, biomarker testing is not commonly performed, as patients are fearful of undergoing lumbar puncture and reluctant to pay for the high cost of a PET scan (Ren et al., 2022). Locally developed a blood-based test for the Alzheimer's pathology are available in China but not recommended by guidelines nor routinely used (Ren et al., 2022), and a blood test based on proteomic profiling has been developed at the Hong Kong University of Science and Technology (Jiang et al., 2022).

Figure 19: Location of Cyclotrons used for Radionuclide Production



Source: IAEA (International Atomic Energy Agency, 2023)

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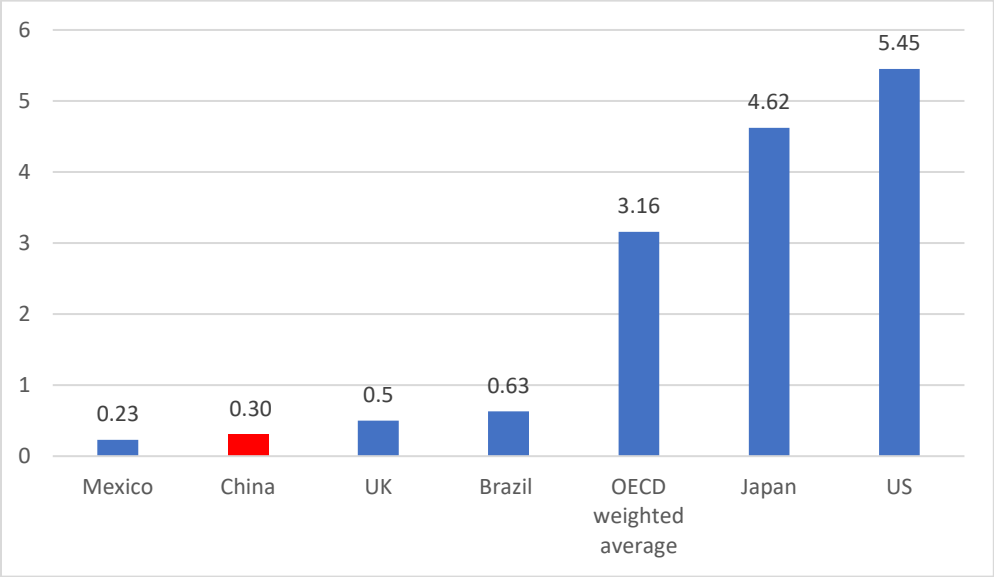
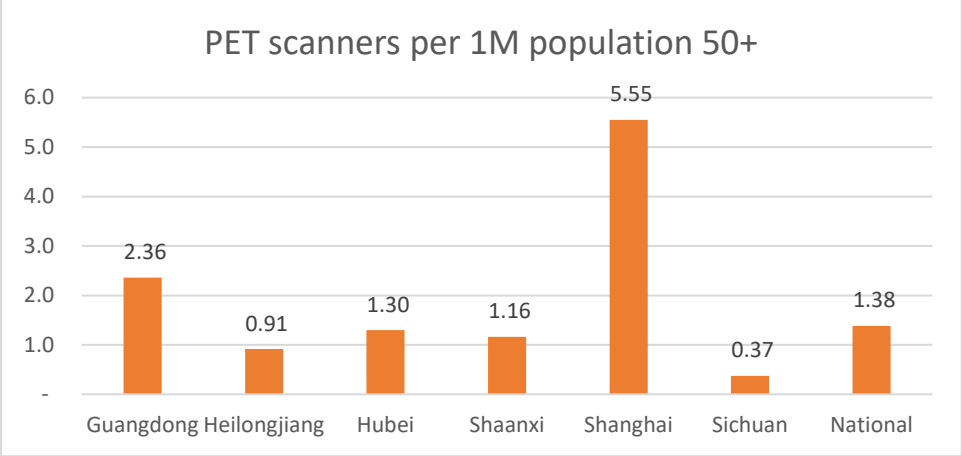
Figure 20: Density of PET Scanners (devices per 1 million population) in 2019



Source: OECD Health Statistics (OECD, 2023) ,China : https://www.qianzhan.com/analyst/detail/220/200103-780afa88.html

Figure 21: PET scanners per 1 million population 50+ nationally and in the six selected jurisdictions



Source: Chinese Society of Nuclear Medicine (Chinese Society of Nuclear Medicine, 2018)

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TREATMENT DECISION

Patients seen in memory centers often go through a complete evaluation during one clinic visit or inpatient admission that includes neurocognitive testing, structural imaging and other tests, and see their physicians to discuss the diagnosis and treatment plan. The China Food and Drug Administration is the regulator that decides whether a medical product meets the requirements for market registration and the TCM Administrative Bureau is responsible for the management of traditional Chinese medicines (World Health Organization. Regional Office for the Western Pacific, 2015). The decision on inclusion in their positive list is based on a health technology assessment.

To be either fully or partially reimbursed at the national level, new drugs need to be included on the National Reimbursement Drug List (NRDL). Historically, China required new drugs to have been on the

market for over two years of clinical use, meaning that new therapies introduced to China relied on out-of-pocket demand for a significant initial period. Nomination to the NRDL is not manufacturer-led, but has historically been determined by government-led stakeholder committees consisting of clinicians and medical experts. Candidate drugs then undergo clinical and pharmacoeconomic review by technical expert groups before a final stage of price negotiations between manufacturers and the three insurance schemes.

In recent years, this process has been consolidated under a single body, the State Medical Insurance Administration (SMIA), streamlining the process of updating the NRDL every two years. In addition to this, individual provinces have their own provincial drug reimbursement lists, which take reference from the NRDL, but to which new drugs may be added independently in a similar process of nomination, review and negotiation (and which may pre-date inclusion on the NRDL). As a result, reimbursement and levels of copayment for new therapies can vary across provinces.

Recent years have seen moves to enable access to innovative medicines, including drugs developed outside China. Since 2018, China has accepted clinical trial data from other countries and established a so-called special channel to expedite technical review of new drugs approved and marketed in the U.S., EU, or Japan in the past 10 years. China's latest 2019 NRDL update resulted in the successful listing of 52 non-Chinese patent medicines.

At the beginning of November 2019, a Chinese-developed original drug, GV-971, received conditional approval for treatment of mild to moderate Alzheimer's disease from the National Medical Products Administration (Martins et al., 2020).

TREATMENT DELIVERY

At the beginning of November 2019, a Chinese-developed original drug, GV-971, received conditional approval for treatment of mild to moderate Alzheimer's disease from the National Medical Products Administration (Martins et al., 2020).

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> "Infusion treatment is highly scalable in hospitals. It often requires as little as folding chairs and infusion poles."
> Geriatric Psychiatrist, Shanghai

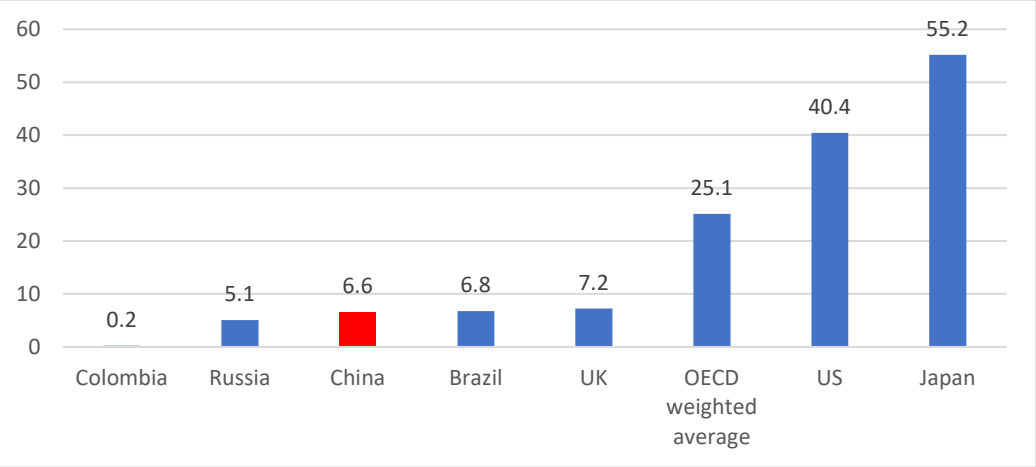
We were unable to identify data on current or future capacity to deliver infusion treatments. However, expert opinion suggests that hospital-based infusion centers are large-scale operations and could easily be scaled up for the delivery of a disease-modifying Alzheimer's treatment.

MONITORING

Monitoring a patient in treatment for the Alzheimer's pathology requires regular office visits to track cognitive state and other symptoms as well as repeated MRI scans to detect ARIA. These services would be covered by insurance with the usual copayments. China has a relatively high and growing capacity for imaging devices, as hospitals are allowed to charge higher fees for imaging but need to offer basic care below cost, even though devices tend to be located in urban hospitals. According to 2013 data reported by He and coworkers, China had about a third of the CT scanners per capita and a tenth of the MRI scanners per capita as the OECD unweighted average, albeit highly concentrated in urban centers, and capacity grew by about 10-20% annually (He et al., 2018). The authors also explained that a Certificate of Need Policy and reweighting of fee for imaging versus basic care services were introduced to reduce the growth in equipment and resulting costs. More recent data (Figure 22) show that China installed about a third of the OECD average PET capacity per capita in 2018, making scans readily accessible in urban

centers. With about 1,000 RMB per scan, the test is considered reasonably affordable and also profitable for hospitals.

Figure 22: Number of MRI scanners per 1 million population in China compared to other countries in 2019



Source: OECD Health Statistics (OECD, 2023) (Li, 2020)

CAPACITY PROJECTIONS

As mentioned above, we use a simulation model to project wait times during the diagnostic process that would identify patients eligible for a disease-modifying AD treatment, which has been described in detail in previous publications (Mattke & Hanson, 2022; Mattke, Ullrich, & Wang, 2020). It simulates the journey of patients seeking evaluation for subjective memory complaints or as part of a wellness exam in primary care with two interacting layers between 2023 and 2043. The first layer captures one of four true health states: cognitively normal, MCI due to AD, MCI due to other causes, and dementia using age and sex specific estimates for incidence and prevalence of MCI and dementia. The second layer captures a patient's journey through different evaluation stages: initial evaluation by a primary care clinician, neurocognitive testing and comprehensive evaluation by a dementia specialist, biomarker testing with Positron Emission Tomography (PET) scanning or cerebrospinal fluid (CSF) testing to confirm the presence of the Alzheimer's pathology and infusion delivery of the treatment. Dementia specialist evaluations and biomarker testing are capacity constrained, and patients progress from cognitively normal to MCI and from MCI to dementia in the resulting wait times. We use the following assumptions based on expert input on how patients progress through the different steps of their journey in our base case scenario:

- When a treatment becomes available, 20% of Chinese 50 years and older, who have never had a cognitive evaluation, would visit a hospital-based memory clinic for a cognitive evaluation each year. As we explain below, the absence of a robust primary care system and lack of need for referrals causes most Chinese to seek specialty care directly.
  - Each subsequent year, 10% of those who previously tested negative for cognitive impairment would return for another evaluation.
- The clinic would identify those with manifest dementia, i.e., a disease stage in which the treatment would no longer be effective, those without impairment and those with obvious explanation for cognitive impairment (depression, prior stroke, etc.) and order confirmatory biomarker testing in the remaining 80%.

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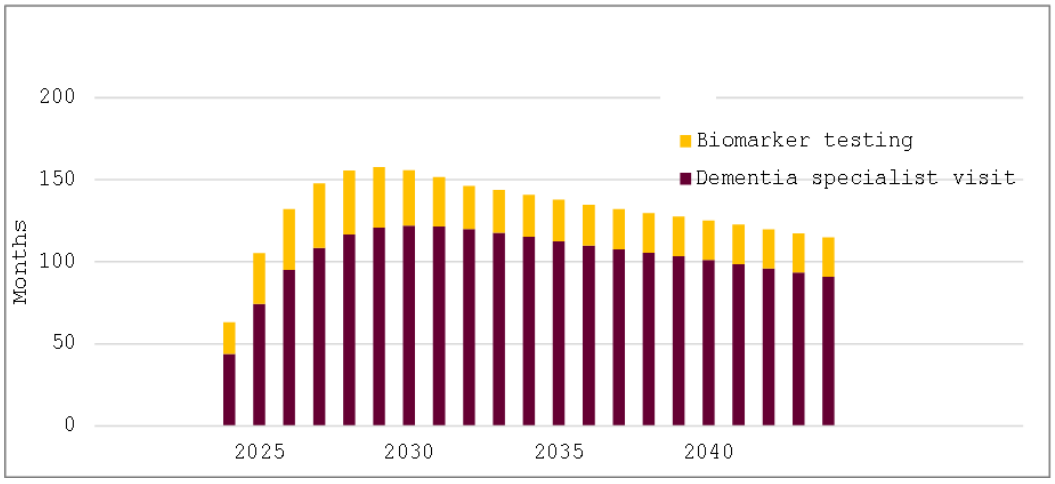
- 63% of biomarker tests would be based on CSF examination and 37% based on a PET scan.
- 55% are estimated be amyloid-positive based on data from the IDEAS study (Rabinovici & Carrillo, 2019).
- 80% would have a confirmed treatment indication after full diagnostic evaluation, as specialists might determine a different etiology to be mainly responsible for cognitive impairment or a different life-limiting disease to make a clinical benefit unlikely.

At each step, patients can be found to not have MCI due to AD based on test results and exit the queue for that year. We explored two alternative scenarios. In the first, individuals would first see a primary care clinician and only be referred to a clinic if a brief cognitive test suggested mild cognitive impairment. In the second a blood test for the AD pathology with sensitivity of 0.89 and specificity of 0.73 would be conducted to decide on the need for confirmatory biomarker testing. Parameters for sensitivity and specificity of those tests and their sources are documented in a previous publication (Mattke, Cho, et al., 2020).

NATIONAL PROJECTION

In our base case scenario, which represents current practice in China, where use of primary care clinicians as gatekeepers remains uncommon and referrals to specialty care not required, wait times would peak at 155 months in 2028 and remain over 100 months largely because of wait times for specialist appointments (Figure 23).

Figure 23: Wait times for Alzheimer's disease testing and treatment in China - base case scenario



Using a model of specialist referral based on cognitive testing in primary care, wait times would peak at 90 months in 2028 and later remain at 50-60 months. Confirmatory biomarker testing in specialist clinics would become the rate-limiting constraint. (Figure 24)

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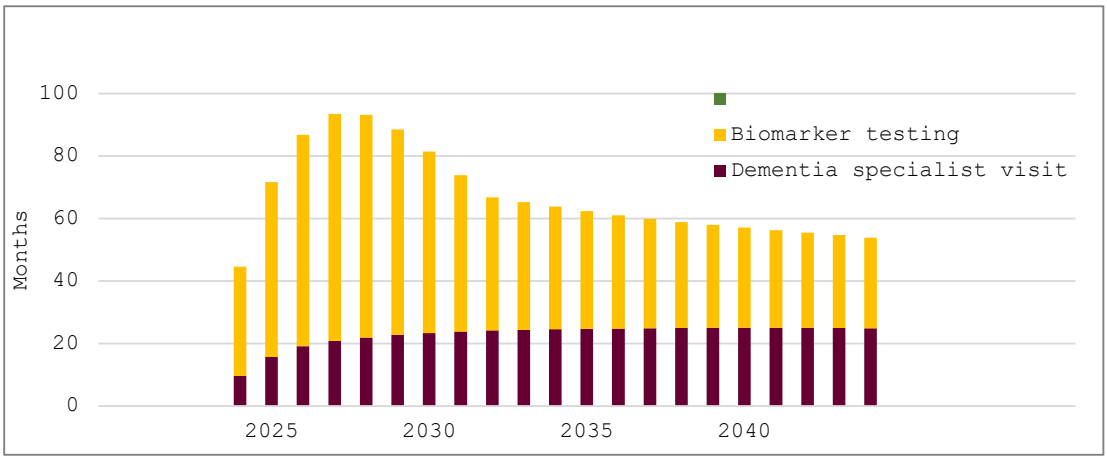
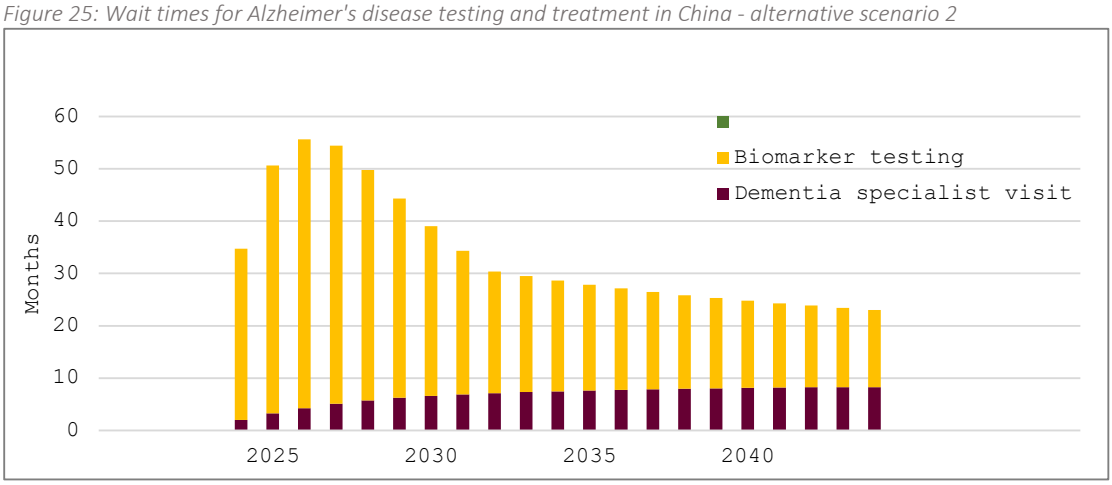
Figure 24: Wait times for Alzheimer's disease testing and treatment in China - alternative scenario 1



If the initial triage in primary care combined a brief cognitive test with a blood test for the AD pathology, peak wait times would fall to 55 months and to about two years later, still because of wait times for confirmatory biomarker testing (Figure 25).

Figure 25: Wait times for Alzheimer's disease testing and treatment in China - alternative scenario 2



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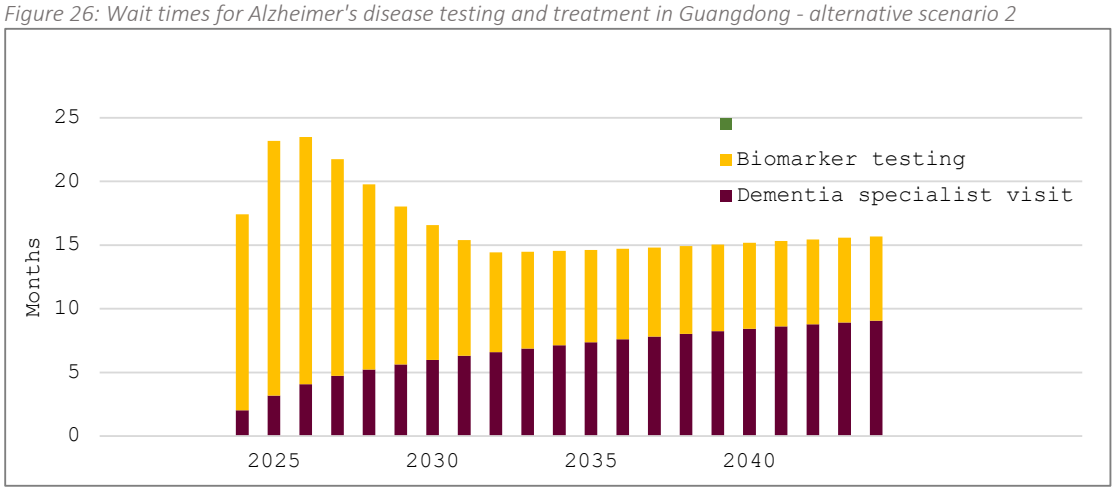
PROJECTIONS BY PROVINCE

We used provincial data to show the effect of differences in diagnostic capacity on wait times. We compare our third scenario, i.e., triage with a cognitive test in primary care and availability of an AD blood test.

Guangdong

As expected from the comparatively high capacity, wait times in Guangdong are projected to be about half the national average Figure 26.

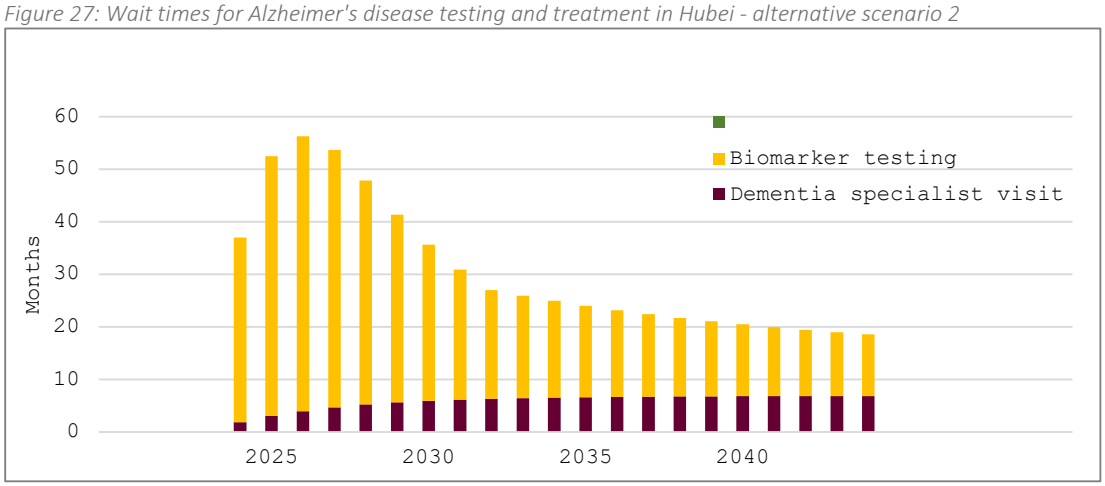
Figure 26: Wait times for Alzheimer's disease testing and treatment in Guangdong - alternative scenario 2



Hubei

Hubei, also a wealthy province with diagnostic capacity above the national average, is estimated to have initial peak wait times in line with national projections, but wait times drop considerably faster (Figure 27).

Figure 27: Wait times for Alzheimer's disease testing and treatment in Hubei - alternative scenario 2



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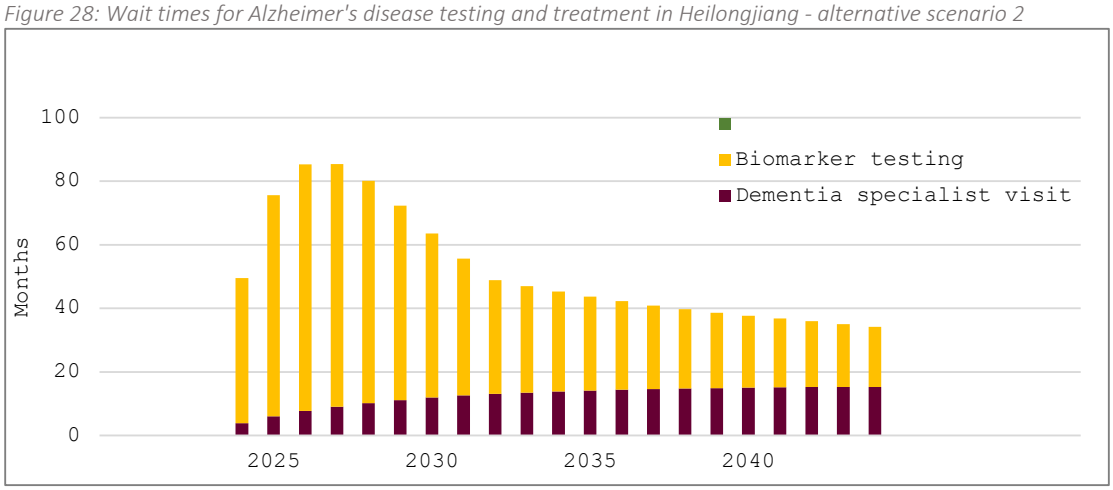
Heilongjiang

In contrast, Heilongjiang, the province with the lowest GDP per capita in our sample and limited diagnostic capacity, would have peak wait times of over 80 months compared to a national estimate of 55 months, and wait times over three years over the course of the simulation compared to a national estimate of two years (Figure 28).

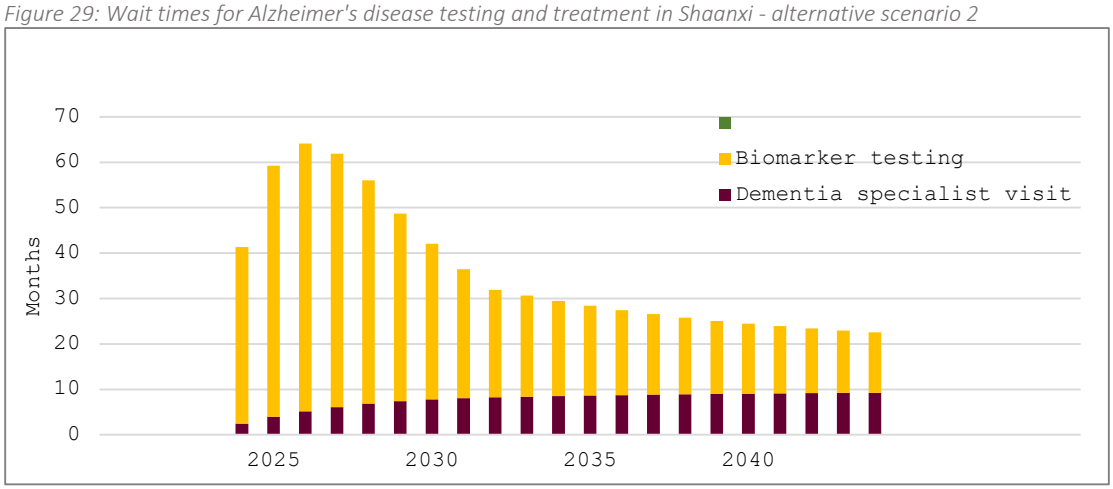
Figure 28: Wait times for Alzheimer's disease testing and treatment in Heilongjiang - alternative scenario 2



Shaanxi

Projections for Shaanxi show a pattern similar to the national estimates with slightly higher peak wait times (Figure 29).

Figure 29: Wait times for Alzheimer's disease testing and treatment in Shaanxi - alternative scenario 2



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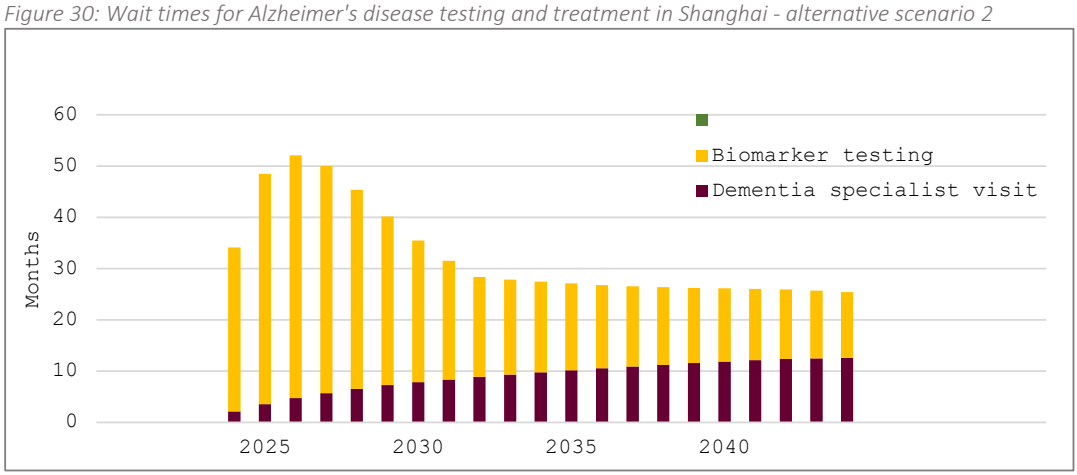
Shanghai

While Shanghai has considerably higher numbers of specialists and imaging devices per capita than the national average, it also has the most rapidly ageing population in China, leading to wait times projections similar to the national average (Figure 30). As detailed below, these shortcomings are seen as a policy problem and being addressed accordingly.

Figure 30: Wait times for Alzheimer's disease testing and treatment in Shanghai - alternative scenario 2



Shanghai : Government strategies for expansion of capacity

A large city with the most rapidly ageing population in China, Shanghai represents some of the forward looking, comprehensive government planning efforts related to dementia. Strategies to improve access to and the quality of health and community care for older adults with (Ren et al., 2022) cognitive impairment are featured in the 'Shanghai Implementation Plan for Developing Elderly Care Services (2019–2022)' and the 'Notice on Strengthening Care Services for the Elderly with Cognitive Impairment in Older Adults Care Services'. The most recent 'Fourteenth Five-Year Plan for the Development of Civil Affairs in Shanghai', released in August 2022 also emphasized the critical position of management and care services for older adults with cognitive impairment as well as the prioritization of projects aimed at older adults and cognitive impairment-friendly communities. Ren et al. (Ren et al., 2022) report that since 2018, 26 medical institutions in Shanghai have opened memory clinics, including 11 comprehensive tertiary hospitals, 8 mental health specialty institutions and 7 primary community health service centers, and that since 2020, the city has built 4999 beds to facilitate dementia care, with a plan to have 8000 available by 2022.

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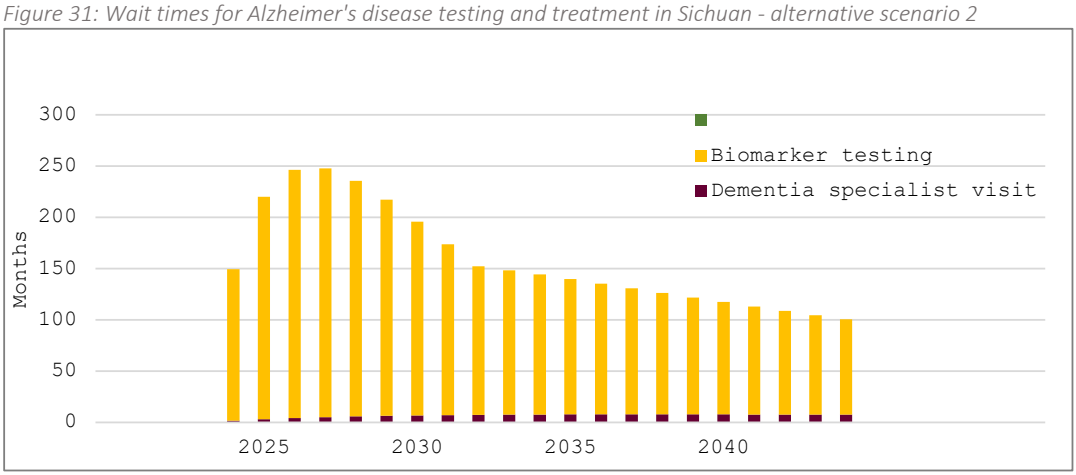
Sichuan

With a number of PET scanners per capita only about a quarter of the national average, predicted wait times for confirmatory biomarker testing in Sichuan are extremely long. (Figure 31) An interviewee confirmed that Sichuan has limited access to PET scanners with only two hospitals in the province being licensed to operate them as of 2021.

Figure 31: Wait times for Alzheimer's disease testing and treatment in Sichuan - alternative scenario 2



SUMMARY

Our findings suggest that China's healthcare system is ill-prepared to provide timely access to an Alzheimer's treatment, with predicted wait times of about two years and a growing number of people on wait lists, even in our "best case" scenario. To our knowledge, this is the only the second such analysis conducted in a middle-income country after Brazil (Mattke et al., 2022), whereas several have been published on high-income nations. The results resemble what has been found in those earlier studies. For example, an analysis of the U.S. healthcare system (Mattke & Hanson, 2022) predicted wait times of over 50 months based on established diagnostic technology and about one year with use of a blood test for the AD pathology. The aforementioned study of Brazil predicted average wait times of over two years even with the use of a blood test (Mattke et al., 2022). However, while those and other studies had found the scarcity of AD specialists to be the main constraint, it is capacity for confirmatory biomarker testing in China, a bottleneck that is considerably easier to address by installing PET scanners and expanding use of CSF testing than that of training highly specialized physicians. To illustrate, China has about as many AD specialists per capita as Japan, a G7 country with about three times the share of population aged 65 and older (30% versus 13%)(The World Bank, 2023).

Our findings also lay bare two structural challenges of the Chinese healthcare system. The first is the immaturity of primary care, highly unusual for a developing economy and even more so for one that had made great strides in expanding basic medical services earlier, such as dramatic improvements in maternal and child health (Guo & Huang, 2019). The current hospital-based pathway is very efficient at getting to a formal diagnosis of cognitive impairment and its etiology, often within a day or two and with readily available appointments. It is less well-equipped to provide longitudinal care for those complex patients, as they might see different physicians at each visit and visit durations are short. Further, the current model is operating near capacity and would not be able to handle the projected influx of cases without triage in primary care, if a disease-modifying treatment became available.

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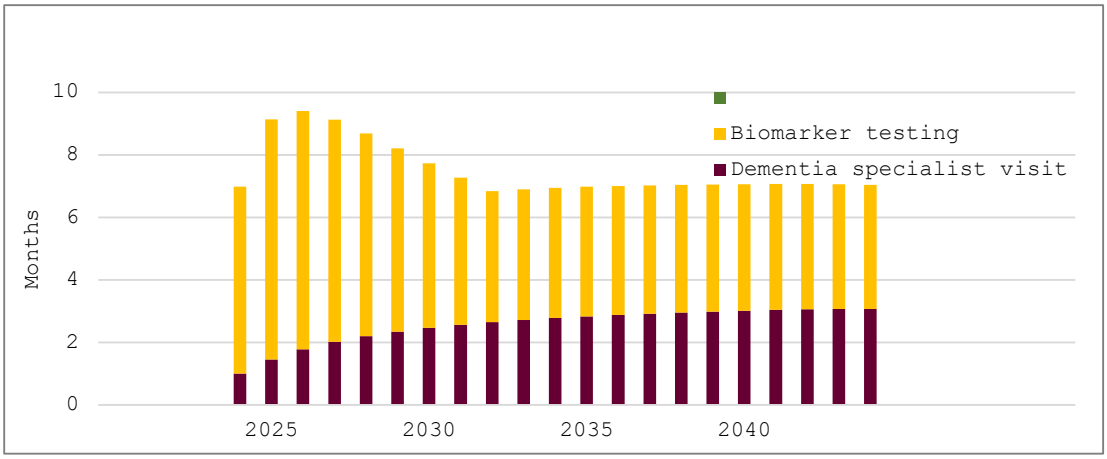
> *"70% of the rural population needs medical resources, but only has 30% of the medical resources; the urban population only accounts for 30%, but has 70% of the medical resources. The state should adopt preferential policies to increase the training and services of grass-roots general medical personnel."*
>
> Neurologist, Heilongjiang

The second structural challenge is the urban-rural divide. Our simulation results reflect the average wait times for the country, but we also learned that rural areas largely lack access to any type of specialty care, and substantial cost-sharing requirements might deny many of access to diagnosis and treatment.

Conversely, access to a timely AD diagnosis is likely to be much easier for urban residents than what our predictions suggest. As an illustration, we applied the existing diagnostic capacity only to the 63% of the population that lives in urban areas (Figure 32) and find that wait times would never exceed ten months. While this result reflects an oversimplification, because it ignores differences in age structure and life expectancy between urban and rural residents, migration and partial access for rural residents, they suggest that capacity would be sufficient for the urban population under this scenario.

Figure 32: Wait times for Alzheimer's disease testing and treatment in China - alternative scenario 2 – capacity only available to urban residents



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Several demographic and societal trends make timely access to an AD treatment particularly important for China. It is one of the world's fastest ageing countries and, unlike many high-income countries, has yet to start aggressive management of cardiovascular risk factors (Li, Wu, et al., 2020). This combination means that it will not have a similar benefit of declining age-specific incidence of dementia (Wolters et al., 2020) but experience the full brunt of this ageing-related disease. The changing demography with an increased dependency ratio also threatens the viability of the traditional social care model that relies heavily on children and grandchildren as caregivers. In addition, internal migration and high workforce participation of women reduces the availability of family caregivers. With a shrinking population, a growing burden of dementia and the resulting care dependency

> *"As we become an ageing society, the incidence of MCI will increase, and we must strengthen health education for patients. That is, diseases enter from the mouth, and many diseases are caused by eating. As MCI is related to diabetes, hypertension, and coronary heart disease, if we control these diseases a little, will it be better for MCI? This aspect needs to be strengthened."*
>
> Geriatrician, Shanghai

without a concomitant expansion and subsidization of the formal social care sector could become a drag on economic growth, if more women were to leave the workforce to care for their elders.

Lastly, limited safety nets are one reason for the very high household savings rate in China, which at 36% (Shikha Jha, 2009) is thrice the OECD average, as consumers need to be prepared for unexpected and expected life events, such as severe chronic illness. For example, İmrohoroğlu and Zhao (İmrohoroğlu & Zhao, 2018) estimated that the savings rate could be seven percentage points lower if China had comprehensive long-term care insurance, and a treatment to reduce dementia risk could have a similar effect. The growing dementia burden, if left unchecked, might therefore deprive the economy from both labor and capital, an important consideration now that economic growth has stalled.

While dementia care is clearly a policy priority in China, as evidenced by the above-mentioned plans and pilots, preventing dementia has received less attention. Tackling preventable causes (Livingston et al., 2020), such as smoking, diabetes and hypertension (Livingston et al., 2020; Rosenberg et al., 2019), which will also reduce the incidence of other noncommunicable diseases, and providing access to a disease-modifying treatment AD as for the most common cause of dementia should therefore become an area of focus. And neither of those two objectives can be reached without addressing the two structural challenges of China's healthcare system. Management of risk factors and triaging for diagnostic evaluation of suspected cognitive impairment requires a robust primary care system, and novel care models, such as virtual (Rhoads et al., 2021) and mobile clinics (Pond et al., 2021), are needed to project specialist knowledge into rural areas.

LIMITATIONS

This study is not without limitation. First and foremost, a simulation does not constitute direct evidence and only time will tell whether the predictions were accurate. The projections for capacity rely on historic trends and those for care seeking behavior on expert input and both may have to be revised. Assumptions for care-seeking behavior rely on expert input and may be incorrect. Our estimate for amyloid positivity was derived from a study of elderly U.S. patients and the rate might be higher in younger patients and those from different origin. However, with around 90% of MCI patients being 65 years of age or older, the error introduced is likely to be small. We represent a highly stylized patient journey in the model and acknowledge that real-world pathways are likely to vary. Given the uncertainty in our assumptions, we want to stress that the analysis is meant to illustrate the magnitude of the challenge and point to opportunities to reduce wait times rather than to generate a precise point estimate.

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CONCLUSIONS

The twin challenge of rapid ageing and growing burden of risk factors leaves China's health system and also its economy exposed to the impact of rising rates of dementia prevalence. This threat could and should become a catalyst to confront two the major weaknesses of an overly episodic care model and lack of access to specialist care in rural areas. Building a robust primary care system with equitable geographic coverage would be an important step.

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