ADDRESSING DEMENTIA: THE ROLES PLAYED BY BUSINESSES

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SUMMARY

- Amid growing concern over the increase in people with dementia worldwide and the rise in its associated costs, drug development is not progressing as expected. An increasing emphasis has been placed on dementia risk reduction and patient-centered care.

- While the efficacy of potential therapies to reduce the risk of dementia is being tested, and early detection and diagnosis techniques are being developed, no such therapies or technologies have been established yet.

- To create a society where people can live well with dementia, it is necessary to provide seamless care and reduce the care burden through effective utilization of data. Businesses are expected to play a key role in technological development and service delivery in this area.

DEMENTIA: A GLOBAL CHALLENGE

What is dementia?
Dementia refers to a decline in cognitive function (after brain damage from any cause) that interferes with daily life.
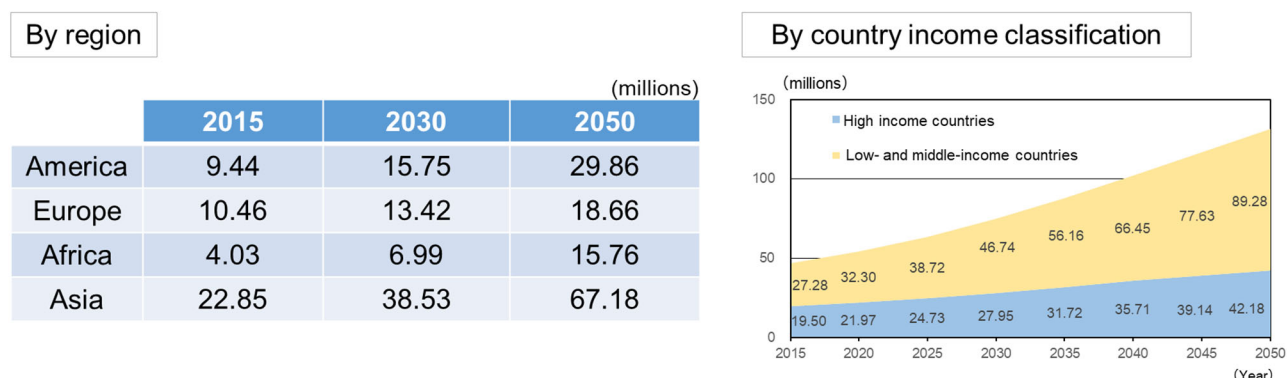
Dementia is caused by various diseases, such as Alzheimer's disease (67.6%), vascular dementia (19.5%), Lewy body dementia (4.36%) and others (including frontotemporal dementia, normal-pressure hydrocephalus, subdural hematoma, and hypothyroidism: 8.6%)[1]. Alzheimer's disease is the most common cause of dementia, but its pathogenic mechanism remains unclear.

A worldwide increase in the number of people with dementia
According to Alzheimer's Disease International (ADI), approximately 50 million people worldwide live with dementia in 2018. The number is expected to increase to 82 million by 2030 and 152 million by 2050 with a particular rise in low- and middle-income countries due to gains in life expectancy from 2015 to 2050 (Figure 1). Comparing social costs of dementia in 2010 and 2015[2] by country income level reveals that there is an increasing relative contribution of informal care costs in countries other than high-income countries, although the total costs are lower than those of high-income countries (Figure 2). The economic impact of dementia care may undermine economic growth in low- and middle-income countries.

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[1] The Health and Labor Sciences Research Grant: Comprehensive Research Project for Actions against Dementia "Prevalence of dementia in urban areas and response to life dysfunction in dementia" 2011-2012

[2] Social costs of dementia include direct medical costs paid to medical institutions, social care costs for social welfare services provided by public institutions, and information care costs for supports provided by families, friends, local residents, volunteers and others.

Figure 1: Growth in numbers of people with dementia worldwide

By region

	2015	2030	2050
America	9.44	15.75	29.86
Europe	10.46	13.42	18.66
Africa	4.03	6.99	15.76
Asia	22.85	38.53	67.18

(millions)

By country income classification

Note: Countries are classified by the World Bank (2015)
Source: Compiled by MGSSI based on the data from World Alzheimer Report 2015 by Alzheimer's Disease International

Figure 2: Costs of dementia by country income classification (2010, 2015)

(billions of USD)

		2010		2015	
Low income countries	Direct medical cost	0.1	22.3%	0.2	20.4%
	Social care	0.1	11.5%	0.1	10.4%
	Informal care	0.3	66.2%	0.8	69.2%
Lower middle income countries	Direct medical cost	2.9	29.4%	3.7	23.9%
	Social care	1.6	16.4%	2.0	13.2%
	Informal care	5.3	54.2%	9.6	62.9%
Upper middle income countries	Direct medical cost	12.6	28.1%	19.3	22.4%
	Social care	8.3	18.6%	17.7	20.5%
	Informal care	23.9	53.3%	49.3	57.1%
High income countries	Direct medical cost	80.8	14.7%	136.0	19.0%
	Social care	245.7	44.8%	308.1	43.1%
	Informal care	222.4	40.5%	271.1	37.9%

Note: Social care: Support provided under formal systems by local governments and nursing facilities
    Informal care: Informal, non-institutionalized support by families, friends, local residents, and volunteers
Source: Compiled by MGSSI based on the data from World Alzheimer Report 2015 by Alzheimer's Disease International

Alzheimer's desease has an estimated, global societal cost of USD 1 trillion in 2018, and is expected to become a 2 trillion-dollar disease by 2030 (World Alzheimer Report 2018). There are growing converns over the increase in people with dementia and its associated costs. To address the concern, it is necessary to establish a therapy that delays the onset of symptoms (disease prevention therapy) by early detection with the aim of reducing associated costs. High-income countries need to improve the efficiency of care, whereas low- and middle-income countries need to improve their medical, nursing, and welfare systems.
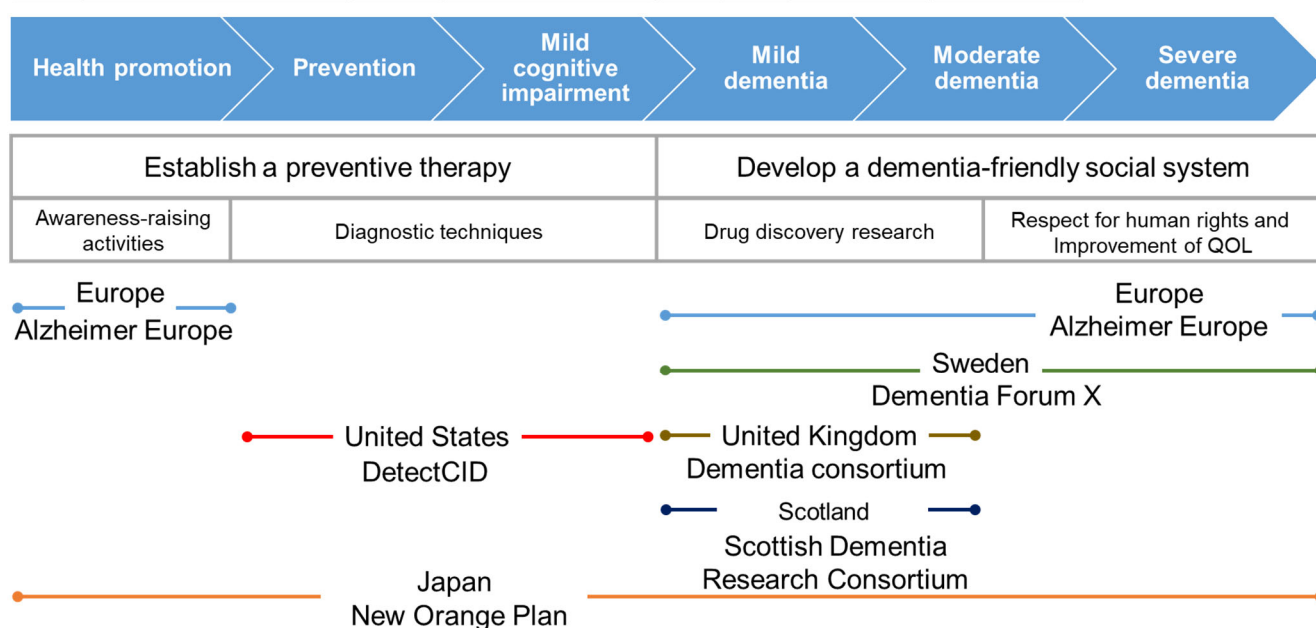
GLOBAL ACTION AGAINST DEMENTIA

Amid these developments, a variety of actions against dementia are being taken in many countries and regions worldwide (Figure 3). In particular, the UK has been implementing government-led initiatives against dementia from early on. In the UK, many reports on elderly people with dementia have been issued since 2000. The reports, along with estimates of epidemiological and economic costs, raised public criticism against the government's policy on dementia, which led to the launch of "Living well with dementia: A National Dementia

Strategy" in February 2009. In 2013, the UK hosted the first G8 dementia summit where leading nations committed to developing a cure or treatment for dementia by 2025. Since then, discussions on neurodegenerative disease including dementia have been held globally in close coordination. The UK is leading efforts to reduce the risk of dementia by developing preventive strategies, and the National Institute for Health and Care Excellence (NICE) published a clinical guideline on dementia. Indeed, the US established an evidence-based guideline in reference to the UK standards.

Fig. 3. Dementia initiatives in major countries and regions

Country/Region	Initiative/Organization	Purpose	Organizer and Partners
Europe	**Alzheimer Europe**	Promote a rights-based approach to dementia, support dementia research and strengthen the European dementia movement	Alzheimer's associations, NGOs (42 organizations in 37 countries) across Europe
Sweden	Dementia Forum X	Identify the challenges associated with dementia, establish action plans and collaborate with hospitals and nursing care facilities	**Organized by Forum for Elderly Care** Universities, government agencies, NPOs, foundations, care facilities, medical equipment, pharmaceutical, and housing companies
United Kingdom	Dementia consortium	Support for early-stage drug discovery: Provide academic researchers with the funding, expertise and project management resources to capitalize on new emerging drug targets	Alzheimer's Research UK and pharmaceutical companies (Private charity partnership)
(UK) Scotland	Scottish Dementia Research Consortium	Help develop dementia research by promoting collaboration and the sharing of new ideas	Dementia researchers, policy makers, and people with dementia across Scotland
United States	DetectCID	Improve the quality of patient evaluations for detecting cognitive impairment in everyday clinical settings	**Organized by the University of California, San Francisco** Albert Einstein College of Medicine, Northwestern University
Japan	New Orange Plan	Raise awareness and promote understanding of dementia, provide healthcare and long-term care services in a timely and appropriate manner as the stages of dementia progress, reinforce measures for younger onset dementia, support those looking after people with dementia, create age and dementia-friendly community, Promote research and development (IROOP™, Orange Platform) and disseminate the results, Prioritize the standpoint of persons with dementia and their families	**Organized by Ministry of Health, Labour and Welfare** Government agencies, medical institutions, nursing facilities, and community health centers

● Scope of activities covered by the major countries and regions (above) at each stage of dementia

Health promotion	Prevention	Mild cognitive impairment	Mild dementia	Moderate dementia	Severe dementia

Establish a preventive therapy		Develop a dementia-friendly social system	
Awareness-raising activities	Diagnostic techniques	Drug discovery research	Respect for human rights and Improvement of QOL

Europe
Alzheimer Europe

Europe
Alzheimer Europe

Sweden
Dementia Forum X

United States
DetectCID

United Kingdom
Dementia consortium

Scotland
Scottish Dementia
Research Consortium

Japan
New Orange Plan

Source: Compiled by MGSSI based on information from each organization's website

In Japan, which has entered a "super-aging" society sooner than other countries, the prevalence of dementia is 2.33%, much higher than the OECD average of 1.48% (OECD: Halth at a Glance 2017). The Comprehensive Strategy to Accelerate Dementia Measures, known as "New Orange Plan," formulated in 2015, emphasized

"coexistence" to help dementia sufferers live their daily lives comfortably and with hope. On June 18, 2019, the government adopted a comprehensive package of measures for dealing with dementia, whose two key concepts are "coexistence" and "prevention." In addition to research and development for dementia prevention, diagnosis and treatment, the package includes training for medical professionals to better respond to dementia patients; training for "Dementia Supporters" who aid people with dementia and their families in communities and workplaces; and development of the so-called "Dementia Care Pathway[3]" by municipalities. Since methods to prevent dementia have yet to be established, "prevention" is defined as "delaying the onset of dementia" or "slowing down the progression of dementia."

To create a society where people with dementia and their families can live in comfort, it is necessary to improve both physical aspects, such as housing, and human aspects, such as shopping and meal support, community activities and monitoring services. This cannot be covered by a single company or organization, and requires collaboration between private and public sectors. Meanwhile, new players from various industries are developing services to reduce the risks stemming from dementia in an aging society. Under these developments, dementia ecosystems led by NGOs and companies have been established in Japan (Figure 4). Legislation related to dementia, such as the Next Generation Medical Infrastructure Act, is progressing, and a data management system for tracking health and medical history is being established. Medical data sharing is expected to reduce the care burden by reducing medical examination costs and improving the efficiency of nursing care.

Figure 4: Dementia ecosystems in Japan

Ecosystem	Leading organization	Activities
Co-Creation Hub for a Dementia-Friendly Future	**Health and Global Policy Institute, Keio University, etc.**	Share the experience and wisdom of people, develop support systems for social engagement and employment, provide recommend policies, develop and evaluate services for people with dementia. Partners: patients, companies, municipalities, and citizens
SOMPO Dementia Support Program	**SOMPO Holdings, Inc.**	Develop and offer dementia insurance products, provide nursing care services, conduct various kinds of research (in cooperation with National Center for Geriatrics and Gerontology), awareness raising and support activities. Partners: companies, insurance, research institutions, organizations
Eisai Dementia Ecosystem	**Eisai Co., Ltd.**	Develop new products and services, including provision of services for the prediction and prevention of dementia, and collaborative development of a safe driving system for the elderly. Developing AI to assess cognitive function and predict cognitive decline. Partners: companies, insurance
Joint research on neurodegenerative diseases and dementia	**Juntendo University**	Promote initiatives that lead to the prevention, early detection, progression of neurodegenerative diseases and dementia, and maintenance of living standards. AI technology from IBM Japan is applied in the initiatives. Partners: universities, companies, banks, insurance

Source: Compiled by MGSSI based on information from each organization's website

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[3] Dementia Care Pathway describes the process of medical and nursing services that a person with dementia may receive from early diagnosis to end-of-life care. It is prepared by approximately 60% of all municipalities in Japan.

CHALLENGES IN ADDRESSING DEMENTIA

Integrated dementia care and ecosystem facilitated by data sharing

Each ecosystem for dementia being established in Japan has its own uniqueness and exists independently. However, since the symptoms of dementia are progressive over a long period of time, it is desirable to provide appropriate and seamless care through continuous monitoring from an early stage with no symptoms in order to delay the onset of dementia and to prevent dementia from getting worse. In providing high-quality medical care that respects the wishes and lifestyles of each patient from the early stages to later stages, such as "I want to enjoy eating rather than caring about dietary habits causing lifestyle diseases", "I want to relieve pain from bed sores rather than aiming for complete recovery" and "I want to choose the best end-of life care for me", it is desirable to build a platform where data can be shared between medical and nursing professionals and the families of dementia patients (Figure 5). Under the common goal of creating a society where people with dementia and their families can live in comfort, it is expected that patient information, including their wishes and lifestyles, will be managed and shared by municipalities, medical institutions, welfare organizations, and service providers without being lost during the handover process, and coorporation between the ecosystems will be promoted.

Fig. 5. Seamless care for dementia
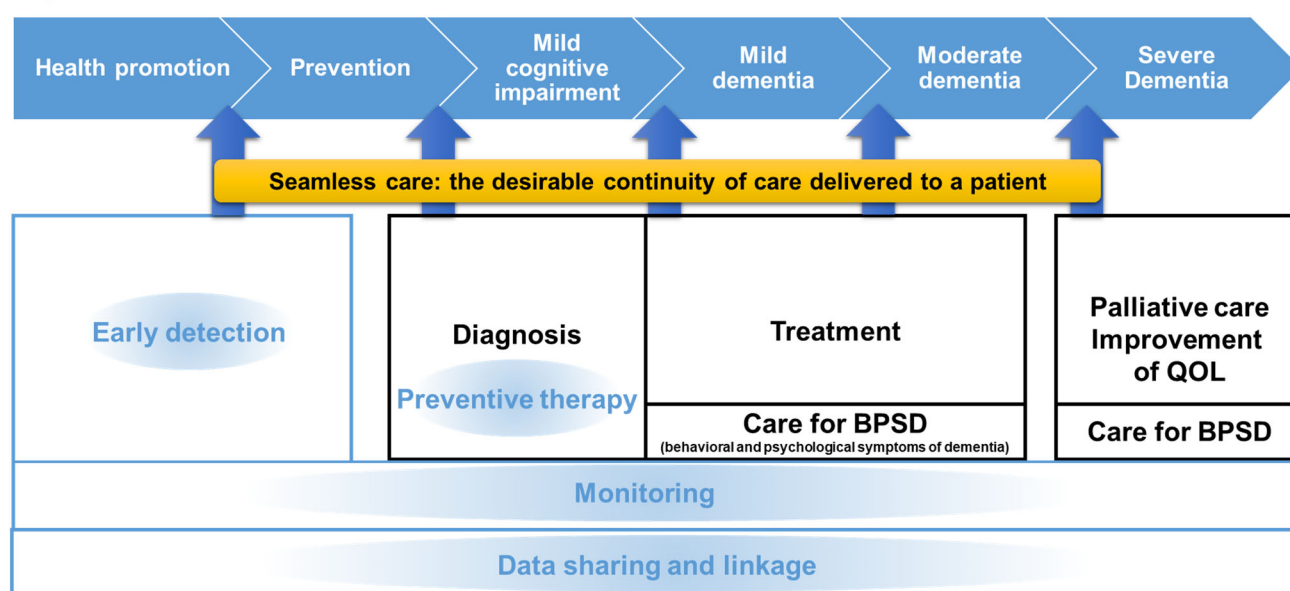
Note: Early detection, preventive therapy, monitoring, and data sharing and linkage are areas where development is expected to occur in the future. It is expected that seamless care (preemptive medicine) through each stage will be established.
Source: Compiled by MGSSI

Challenges in preemptive medicine: 1) A better understanding of MCI leads to a higher diagnostic rate

According to experts, while the word "dementia" is widely recognized, Mild Cognitive Impairment (MCI) is "misunderstood" as a precursor of Alzheimer's disease. MCI is not dementia, although its causes include neurodegenerative diseases such as Alzheimer's disease, dementia with Lewy bodies, as well as neurosurgical diseases such as chronic subdural hematoma, normal pressure hydrocephalus, vascular disorders, and psychoneurotic disorders such as depression and epilepsy (Katsuyoshi Mizukami, Psychiatria et neurologia Japonica, 111(1), 26-30, 2009). The transition rate from MCI to dementia is 5-15% per year. Although MCI constitutes a high risk group for dementia, symtoms of MCI caused by diseases other than neurodegenerative diseases can be improved with early treatment.

Since MCI is often misunderstood as a precursor of Alzheimer's disease, potential patients often hesitate to see a doctor for fear of being dianosed with dementia. As the symptoms of dementia progress, patients become less aware of their desease, which delays diagnosis and treatment. At present, there is no drug for suppressing the progression of Alzheimer's disease, and no specific therapy for delaying the onset has been established,

which makes it difficult to promote esarly diagnosis of MCI, including Alzheimer's disease. However, It is necessary to raise the awareness of the significance of dianosing MCI and establishing medical and preventive therapies for MCI in order to reduce the risk of developing dementia. Recently, lifestyle-related diseases have been reported as risk factors for dementia, and non-pharmacological therapies have been reported to reduce the risk of progression to dementia. It is increasingly recognized that the treatment, management, and non-pharmacological therapy of lifestyle diseases are important for patients with MCI evolving to neurodegenerative diseases such as Alzheimer's disease and Lewy body dementia. The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER study) shows that interventions such as management of lifestyle diseases, dietary advice, exercise guidance, cognitive training, and communication for people diagnosed with MCI can reduce the risk of onset. These nonpharmacologic, lifestyle interventions are expected to provide additional evidence for preventive health strategies.

Challenges in preemprive medicine: 2) Drug development for MCI
To develop a drug for Alzheimer's disease, antibodoies to amyloid β and tau or inhibitors against aggregations of amyloid β and tau, which are two hallmark proteins in Alzheimer's disease, have been studied, but the progress is slower than expected. There is no drug for suppressing the progression, and no pathogenic mechanism has yet to be clarified.

The failure of clinical trials has led to a shift in the perception that interventions should be initiated before the onset of dementia, rather than targeting patients with Alzheimer's disease. The A4 trial (Anti-Amyloid Treatment in Asymptomatic Alzheimer's Disease), an international clinical study being held in the US, Canada, Japan and Australia, identifies the risk of developing Alzheimer's disease for clinically normal older individuals and provides preventive interventions to those at high risk. This trial is testing the efficacy of solanezumab, an antibody targeting Amyloid-β developed by Eli Lilly (US) and the results are expected to be available in 2022. The clinical trial of BAN2401, another antibody targeting Amyloid-β developed by Eisai (Japan) and Biogen (US), in patients with early Alzheimer's disease is also getting attention. In these trials, ealy detection and diagnostic techniques are expected to identifiy a high risk group of dementia and improve cost-efficiency and efficacy evaluation. Research and development are ongoing.

Palliative care to improve the quality of life for people with severe dementia
An increasing emphasis has been placed on patient-centered care that respects the wishes and lifestyles of each individual, but it is still not enough. In recent years, startups Aikomi (Japan) and Dthera Sciences (US) have been developing individualized care services to alleviate behavioral and psychological symptoms of dementia (BPSD) with the aim of improving the quality of life for patients and their families. The companies use deep learning and artificial intelligence (AI) to optimize their services (Figure 6). Aikomi acts on the visual, auditory and olfactory senses of care receivers, using tablet PCs, speakers, and aromators, respectively, and analyzes the data obtained by these actions with machine learning and original algorithms to provide individually optimized non-pharmacotherapies and reflects them in their activities. Dthera Sciences is developing a digital therapeutic that delivers reminiscence therapy to patients with Alzheimer's disease via a tablet PC. The device will use AI to automatically optimize the therapy based on various forms of biofeedback from the patient. In August 2018, the US Food and Drug Administration (FDA) has granted Breakthrough Device designation to the development-stage product. Hammerton Court, the UK dementia care unit, works within a philosophy of "person-centred care." Person-centred care is based on the idea that a patient with dementia should feel understood, respected and treated as an individual. Instead of prescribing drugs to patients who are violent or unable to sleep, carers should listen to the patients and their families, understand their memories and reasons behind, let them do what they want, watch and provide assistance if needed. For example, patients who panic when using an elevator may have a fear of beling enclosed in a small space because they have a trauma from being locked in a closet when they were young. Carers should learn their stories from their families and avoid using an elevator in such a case. In another case, when patients are comfortable sitting on the floor, carers should let them be rather than forcing them to sit on a chair. Person-centred care has been successful in improving the condition of patients with severe dementia, and its personalized approach is considered promising for patients with severe symptoms.

While it may be difficult to curb the increasing prevalence of dementia for the time being, various actions should be taken immediately, such as establishing clinical evidence of non-pharmacological preventive therapies and early diagnosis techniques, developing an inclusive social system through a close coordination between ecosystems, and improving the readiness of medical and nursing facilities, as well as the whole of society, to accept the increasing number of patients.

Figure 6: Early detection and diagnosis of dementia and development of technologies to improve QOL
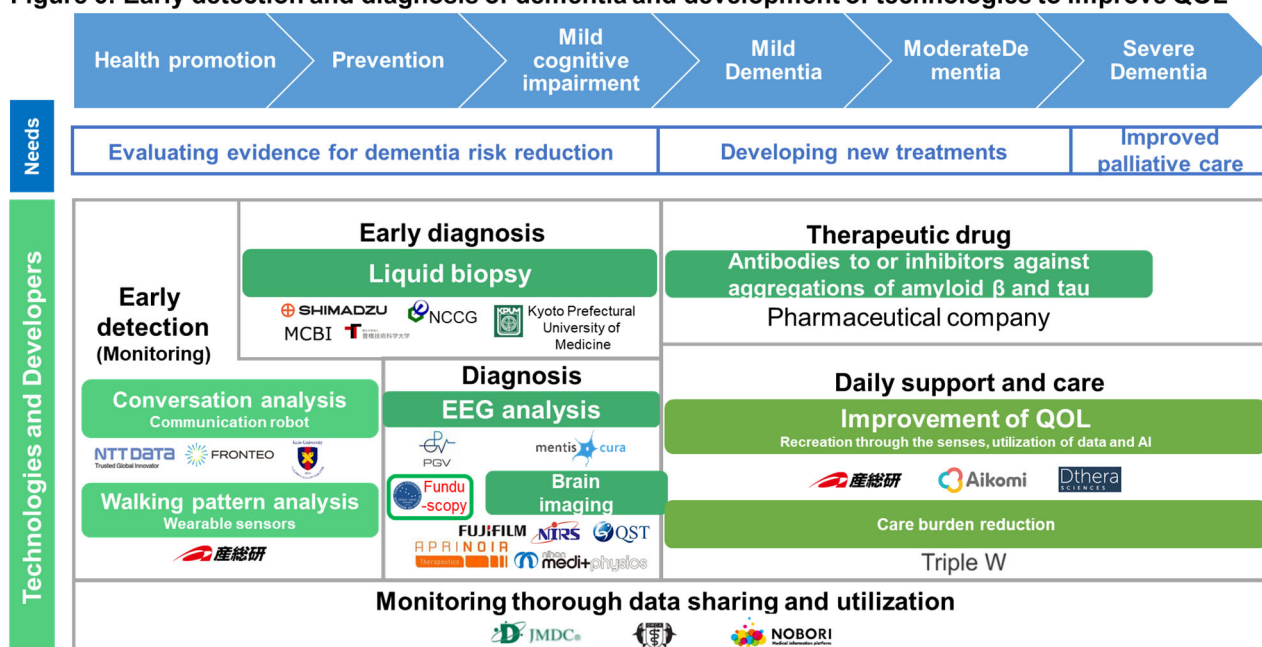
Note: Early detection technologies involve communication robots, walking tests, and liquid biopsy. Diagnostic techniques include brain imaging, EEG analysis, cerebral blood flow analysis, and funduscopy.
Source: Compiled by MGSSI

Future Prospects

Dementia drug development and clinical evidence of therapies that decrease its progression

Although drug development in dementia is facing many challenges, the research and development of new therapies such as gene therapy and electric and magnetic seizure therapy, in addition to drug trials targeting amyloid β and tau are progressing. There are high hopes for protein engineering focusing on amyloid β and tau aggregation, research into the links between gut microbiota and dementia risk, research on anti-aging, longevity and omix analysis, as well as the development of new drugs and therapies using AI and machine learning. In developing these drugs, it is necessary to establish a therapy for decreasing the risk of dementia with clinical evidence.

Meanwhile, as mentioned above, it is suggested that treatment of lifestyle diseases is effective in reducing the progression of dementia. It is important to provide guidance about the prevention of lifestyle diseases and appropriate treatment in MCI stages. Despite some negative reports, many studies support the effects of exercise (aerobic exercise) and cognitive stimulation in MCI patients, and engaging in a program combining both. The establishment of clinical evidence of highly reproducible therapies for MCI while verifying the efficacy of these non-pharmacotherapies is of great social significance. Since preventive health care is not covered by the national health insurance scheme in Japan, it is difficult to monetize the business with only consumer spending. It is expected that non-pharmacotherapies for MCI will be set at a low cost. Therefore, the key is how to structurize the huge amount of data obtained to multiply profits through secondary use of data and other means.

Technology development in the field of dementia care

In the field of early detection, remote medical care using IT and wearable devices and the development of solutions for early detection and monitoring of diseases are active mainly in the US, and many startups have been founded. In Japan, NTT Data Kansai is leading the development of a dementia diagnosis support sytem through daily conversations with its communication robot, aiming for commercialization in 2020. A group led by Keio University is developing a sytem for evaluating the severity of dementia based on conversations with

docutors using KIBIT, the AI engine of FRONTEO (Japan). The group is planning to begin clinical trials in 2019 in order to obtain regulatory approval for medical devices after completing a prototype. The National Institute of Advanced Industrial Science and Technology has been developing early detection techniques through monitoring walking patterns and speed. In the field of elderly care, excretion care is one of the most demanding tasks for carers because it can affect the patient's self esteem. Depending on the stage of dementia, it may be difficult for the patient to recognize the need to urinate or defecate. A toilet timing predicting device known as D-Free developed by Triple W Japan has been used as a tool to reduce the burden on patients and carers. Going forward, there are high hopes for the development of sensing and monitoring technologies in this field.

The roles played by businesses in building a society where people can live well with dementia
In each stage of dementia (early detection, onset risk reduction, disease management, daily support, monitoring, etc.), there are many roles that businesses can play in offering systems and services to meet the needs of people with dementia and their families and improve their quality of life. These include daily necessities designed to help people with dementia; daily support services such as shopping; nutritionally balanced meal services; excretion predictors; lifestyle proposal and support services to reduce the risk of developing dementia; lifestyle disease management services that can be shared with families and health care professionals; and comfortable housing and communities for people with dementia. Governments around the world are launching the Social Impact Bond4 to foster more cross-sector collaboration with the voluntary and the private sectors to tackle complex social problems, and some projects have been implemented in Japan as well. In June 2019, the Ministry of Economy, Trade and Industry launched a new one-stop support centre named "Healthcare Innovation Hub (InnoHub)" to help startups create innovation and establish a startup ecosystem in the field of healthcare and life sciences. These government initiatives encourage private companies to tackle dementia, which is a pressing social challenge.

While dementia events hosted by public organizations, such as the Dementia Cafe5, are increasingly held, an MCI awareness-raising event called "Smile Garden" is held by 3H Medi Solution (Japan), a contract development company in the pharmaceutical and healthcare industy, for its customers. The company, in collaboration with its partner, Tokyo Center Clinic, is working on the development of early detection techniques and establishment of clinical evidence of preventive therapies. There are high hopes for both physical and virtual community services, as well as medical data sharing systems, as these are areas where not only pharmaceutical companies, but also other inudstry players who are aiming to develop products and services that meet the needs of dementia sufferers and ther families can demonstrate their concepts.

In this aging world, anyone can develop dementia. Businesses should play a key role in developing and providing inclusive services for people with dementia regardless of the stage they are in. This will help meet the needs of dementia suffers and their families and lead to the creation of a dementia-friendly society. If Japan can build a society where people can live well with dementia, the successful model can be transferred to other aging countries with appropriate adjustments, and will be of great social significance as a solution to the global health challenge of dementia.

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4 Social Impact Bond, a public-private partnership, is an outcomes-based contracting that leverages private capital to address social issues.

5 In Dementia Cafe, people with dementia, their families, local residents, and nursing and welfare specialists can gather for information exchange, consultation, and activities to prevent and improve symptoms of dementia. The concept started as an Alzheimer Cafe in the Netherlands in 1997, and it has begun to spread in Japan in 2012. It is mainly hosted by nursing facilities and their operators, or community health centers.