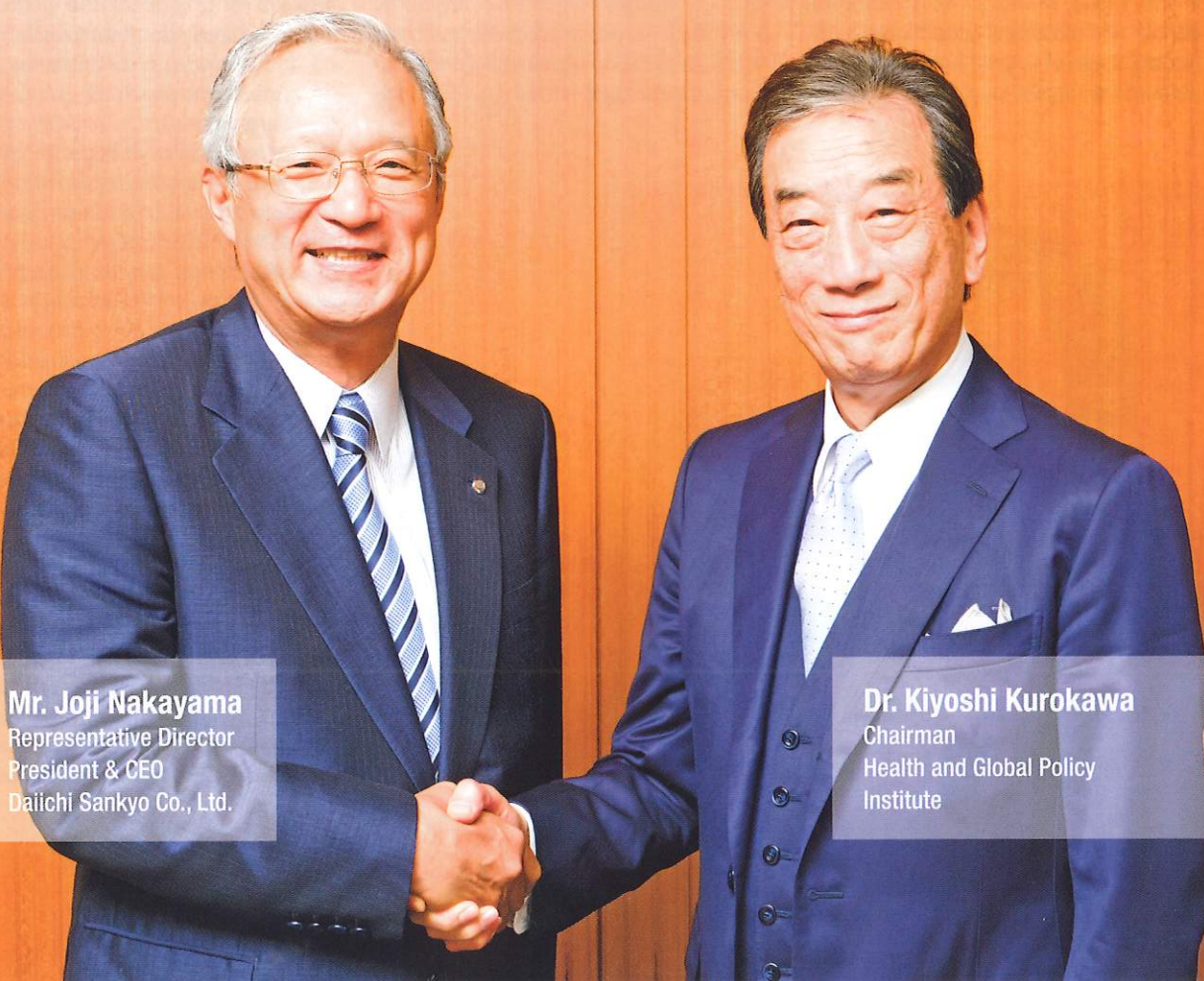


Nikkei GOODAY Daiichi Sankyo Interview

Urgent Need to Tackle Dementia: How Should The Health Sector and Big Pharma Address This Global Challenge?

In January 2015, Japan's Ministry of Health, Labour and Welfare issued a projection that the number of dementia sufferers in Japan would exceed 7 million by 2025, based on the results of a study conducted in Fukuoka Prefecture. Representing a 50% rise in just over a decade from the corresponding 2012 number of 4.62 million, this figure would mean that one in five Japanese aged 65 or more would have dementia in the next ten years. What roles are national bodies and the R&D divisions of pharmaceutical companies expected to play in combating the threat posed by dementia? In this interview, Mitsuru Miyata, Executive Leader Writer at Nikkei Business Publications, discusses this topic with Kiyoshi Kurokawa, Chairman of the Health and Global Policy Institute and Joji Nakayama, CEO of Daiichi Sankyo.



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Dementia is the next major target after lifestyle diseases and cancer

Miyata Why is tackling dementia an urgent issue for Japan and the rest of the world?

Kurokawa It is only in the last 50–60 years that increasing numbers of humans have come to live as long as we typically do now. The 20th century saw all manner of breakthroughs in scientific research, among which were startling advances in public health, medical and pharmaceutical sciences. Longer life is one of the benefits of that progress.

The data show about a quarter of Japan's current population of about 120 million is aged over 65. We have more than 10 million people aged 80 or more, and at least 60,000 centenarians. Japanese life expectancy is the highest in the world and a healthy life span is increasing.

The question is what health issues are posed by population aging. Starting in the 1980s, in Japan we focused on cancer and lifestyle related diseases affecting those of middle age, who represented the largest part of our popula-

tion. Now that we have found ways of overcoming cancer and these lifestyle related diseases, the next major target is dementia.

We are now making steady advances in early detection and treatment of cancer, but the diagnosis and treatment of dementia—in particular, Alzheimer's Disease, which accounts for half of dementia cases—is still a difficult area.

Nakayama Japan is in the vanguard of super-aged societies. As such, I believe we now need to consider how to develop social structures from the perspectives of the dementia sufferers and their family members, and how to prevent this disease. Our efforts in this area could have global significance.

Current prescription drugs aim to slow disease progression Drugs now in development to aid recovery of cognitive functions

Miyata How much progress has been made in developing drugs and other therapeutic approaches to treat Al-

zheimer's?

Nakayama We have a good overall idea of the nature of Alzheimer's, but we have not yet elucidated all of the primary disease mechanisms. As Professor Kurokawa said, it is still difficult to diagnose the condition or to gauge the degree of disease progression. A number of assessment scales are in use, but I think it will take a little longer before we work out exactly what is going on.

On the face of it, there is no clear relationship between drug development and degree of disease progression with Alzheimer's, but a better understanding of how the disease progresses is essential to make it easier to judge drug efficacy and to determine the best direction for future drug development.

At the moment we see Alzheimer's therapeutic approaches as falling into two categories. The first involves preventing any reduction in neurotransmitters so that neural transmission of information is unimpeded. In the second, the aim is to protect the neurons to support information transmission related to memory. In both cases, early drug treatment should help to alleviate disease progression.

The next challenge is the recovery of cognitive function. We see this as an issue that we must address as a pharmaceutical manufacturer for the benefit of society. High-priced antibody drugs will not do the job in this case: we need to develop reasonably priced drugs in a form that people can take easily. We are hopeful that we can solve the related issues somehow in the near future.

Kurokawa We are certainly looking to the biotech and pharmaceutical industries, because it would be of little significance if a medicine could not be used by many people.

Miyata You said that assessing disease progression remains problematic. What advances have been made in the early detection and diagnosis of dementia?

Nakayama There are some approaches that measure serum antibody

levels, but the principal diagnostic methods in use today are CT or MRI scans to gauge cerebral atrophy and bleeding reduction.

Miyata Is it not the case, though, that the disease would have progressed substantially if it were possible to see atrophy of brain tissue on a CT or MRI scan?

Kurokawa What we do know about Alzheimer's is that it is the accumulation of beta-amyloid(A β) or tau proteins in neuronal tissue that is responsible for blocking the transmission of information. Scientists are looking at the possibilities of diagnostic uses of A β deposits, tau proteins, in body fluids and also molecular imaging.

A huge amount of progress has been made in the science, but now the question is how to confirm the disease using biomarkers as indicators of pathology and clinical manifestations, and then how to design the appropriate clinical trials.

Miyata I understand Daiichi Sankyo is conducting joint research with the University of California at San Francisco on the beta-amyloid hypothesis?

Nakayama Our research is focusing on degenerative changes in proteins.

Miyata That sounds like a novel approach. I also understand there is disagreement at the fundamental research level, with some arguing that beta-amyloid deposits are not necessarily consistent with the loss of cognitive ability? Basic research tends to fluctuate.

Kurokawa I think it is fair to say that we do not yet have all the answers.

Nakayama Scientists naturally would like to elucidate all of the mechanisms at work within the human body, but medicine must operate differently. And even once research has progressed, how to create an effective drug is a totally different question.

Developing drugs is often likened to mining for gold, in that you do not know what you will find until you start digging. However, there is the huge reward of discovering a drug if we can dig skillfully in the right place, so to

speak.

More scientific evidence needed to develop better prevention

Miyata So if treatment of dementia still presents difficulties at this stage, are there any ways of preventing the disease to alleviate the burden on society?

Kurokawa One approach could be to analyze past medical data on dementia sufferers to look for any common background factors. I think this is one area where we could deploy big data analytics.

The problem is that it is taking too long to design and develop clinical trials in this area. Rather than focusing excessively on sourcing data on people in Japan, it might be better if we could find suitable data sets to study from around the world.

For example, the University of Michigan is gathering relevant health data on virtually the entire US population. In Japan there is a need for an open environment suitable for the analysis of such data. Another approach might be

to analyze the medical and treatment histories of currently diagnosed dementia sufferers in Japan incorporating the clinical trial data owned by pharmaceutical companies.

Miyata The results of the Hisayama Study, a cohort study conducted by Kyushu University in Hisayama, a town in Kyushu, clearly point to the incidence of Alzheimer's increasing as Japanese society continues to age.

Nakayama We do not yet have a good understanding of the individual mechanisms involved, but different strands of research are pointing to a heightened correlation between Alzheimer's and other conditions such as cardiovascular disease or diabetes.

Miyata So if you can achieve control over diabetes just by walking more, could this also be a potential way of preventing Alzheimer's? Orange County in California is undertaking a prevention program along such lines to study potential ways of controlling blood pressure, blood sugar levels, diet and exercise.

Nakayama My feeling is that little information on Alzheimer's is getting out to the public, who remain ill-informed in



relation to ways of preventing and dealing with the disease. People do not know the correct facts about the condition, in my view.

Miyata I think more information is starting to be released. There is a range of information available concerning the prevention of dementia, but I think what we would like is more relevant scientific evidence.

Nakayama That is something we would certainly like to see as well.

Miyata Recently a new tool has been developed for keeping track of what medicines people have taken. I believe that sort of approach might be ideal for sufferers of dementia. What do you think about making use of information technology here?

Nakayama We are certainly interested, and this is an approach that we are studying. The critical point in this case is the form in which drugs are administered.

Patch formulations are often used with dementia sufferers so that family members can visibly confirm medication is being taken. In the future, however, we might want to try delivering drugs using different formulations or methods.

An issue for the whole of society requiring a global response

Miyata Countries worldwide are improving in terms of sanitation, hygiene, nutrition and access to medical care. While there will be some variation, we can expect the life expectancy of the global population to continue rising.

China, for example, is aging quite fast, and dementia is becoming a social issue. And not just in China, either.

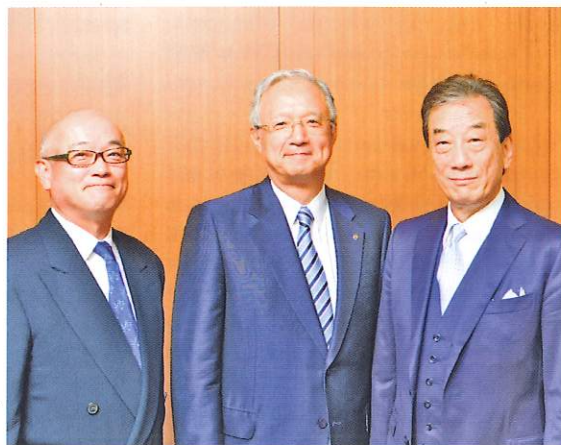
Nakayama Rising numbers of dementia sufferers will inevitably be a problem in developing countries as well. The situation is likely to become quite wretched if the issue is neglected, with the cost to society climbing dramatically unless governments adopt effective policies.

Miyata In Japan, we hear of senior

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citizens wandering off or going missing. Families or society will need to offer help when people can no longer take care of themselves. One way or another, the issue of dementia will draw on society's resources. In that sense, I would argue that it poses a different problem than other diseases. What sort of stance are countries outside Japan adopting?

Kurokawa Many countries have only just begun formulating policies in this area. When we look at the developed countries where aging has happened in a similar way to Japan, we see that in the UK, for example, there is a growing sense of crisis, despite the pride in its public-funded National Health Service.

The British government used the opportunity of hosting the G8 Leaders' Summit at the Lough Erne Resort in Northern Ireland in 2013 to highlight the problem of rapidly rising numbers of dementia sufferers, which is only forecast to get worse. Other countries with public-funded health systems are also starting to wonder how their societies will afford the costs of treating dementia amid progressive aging.

Miyata The government policies adopted in Japan to date will not adequately address the problem. Do you think there is a case for creating a new decision-making body to tackle the issue based on broad participation from different stakeholder groups?

Kurokawa The problem is that public

sector budgets in this area may not be increasing. One way might be to start planning social infrastructure now based on where we would like our society to be in coming decades. Another approach could be to devise business models to boost quality of life for carers. Just cutting budgets is not a solution.

Nakayama I think we need to approach our medical and care systems in a more holistic way that is consistent with society as a whole. It is important that we take a step back and decide what sort of care we want to provide overall, and at what stage of disease nursing care should be required. At the same time, we must respect the feelings and consider the happiness of the individual patient.

My feeling is that dementia is an area where pharmaceutical companies need to work with more groups than just physicians. I think we need to be looking at sharing more information with care workers and family members in the future if we are to address this issue successfully.

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