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Drivers of change that symbolize healthcare in 2040

Imagining and creating the future

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Summary

The world is moving towards the development of a new social order.

Today's information society has brought great change to our lifestyles and social structures. While people around the world are now connected through networks thanks to the spread of IoT, there are growing concerns regarding economic disparities as certain platforms drive international economic activity. Under such circumstances, we need to implement to a greater extent systems that integrate cyberspace with the real world to achieve more sustainable economic growth and solve the various social issues our current information society cannot. This, in essence, would mean creating a more human-centric society.

Looking to the medical and healthcare fields, the cost of maintaining Japan's social security has increased accompanying its transition to a super-aged society. The needs of Japan's health and medical services has diversified to include prolonging life expectancies, developing treatments for rare diseases, and shifting from cure-oriented to care-oriented treatments (maintaining good health not only in a physical sense, but also both psychologically and socially), which will require both innovation and sustainability. In addition to these social needs, we believe that Japan's social order will see large changes related to its medical and healthcare services due to future technological developments.

- Moving towards a society that allows ordinary citizens to lead healthy lives in both mind and body through the introduction of N-of-1 medical care, senolytics, and human/brain machine interfaces.
- Providing individuals with recommendations on how to prevent or treat their ailments, as well as new cyber-based lifestyle options. These options will lead to a society in which individuals can make choices in a subjective manner based on their values.
- Products, industries, and societies that have traditionally been separated will now be digitally connected with the spread of connected health and data circulation in healthcare, offering individuals the most optimal compound solutions. This will breakdown the barriers of the medical and healthcare industries, with all industries now having some sort of connection to medical and healthcare services.
- Quantifying the value of medical care and facilitating the free flow of intellectual property (IP) on the marketplace will help to visualize and share the diverse range of medical and healthcare-related values and assets that are available, with the promotion of free competition and co-creation accelerating value transformation.

In this report, we will focus on 10 factors (drivers of change) from amongst the variety of factors affecting change within the medical and healthcare fields that will drive how this social order is shaped. We will examine what kind of changes and interactions these factors will bring, as well as consider what form medical and healthcare services will take within this new social order and discuss how this will be achieved.

Furthermore, it should be noted that this report is not a prediction on what the future holds. The future is not set in stone but is something we can change through our thoughts and actions. In other words, we can imagine and create a future for ourselves. The authors of this report hope that it will arouse discussion on what sort of bright future is awaiting healthcare, as well as allow us to hold discussions with our readers and continue to make updates to the report itself.

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10 Drivers for Healthcare Transformation in 2040

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a. Outline

We extracted 10 factors that will be the key to determining how future medical and healthcare services should be in 2040. This report will treat these factors as "10 drivers of change." We can imagine a variety of futures depending on how these 10 drivers are combined. We will consider what healthcare will look like in 20 years from four broad perspectives: ordinary citizens, manufacturers, providers, and the industrial base.

[Ordinary citizens' perspective] Eternal life: Pursuing healthy life expectancies, life within cyberspace, and the wide breadth of options facing individuals

Remarkable progress has been made in the development of scientific technologies, with research that defies the laws of nature being actively conducted on topics such as genetic diseases, aging, and brain dysfunctions. In this section, we would like to examine the emergence of science on future healthcare from the perspective of ordinary citizens (Figure 1).

[Driver 1: N-of-1 medical care]

Advancements in biologics such as gene editing technologies, delivery technologies for molecular targets, and stabilization technologies for maintaining drug structures will make the fundamental treatment of extremely rare diseases a possibility. The US will have already begun clinical applications of an oligonucleotide therapeutic that will treat an individual suffering from a unique genetic disorder that only affects them. As hyper-personalized treatments continue to gain momentum, governments and academia will not stand idle. With the genes responsible for almost 3,000 rare diseases still requiring identification, there is hope that these unmet needs, which have been neglected up until now, will be resolved.

[Driver 2: Senolytics]

As the mechanisms behind aging continue to be unraveled, our notions of aging will change from that of an undeniable law of nature to instead viewing it as a life-ending disease. This nation will see both its average and healthy life expectancies prolonged, but an approximate 10 -year gap exists between these values. Shortening this gap is a major social issue within Japan's super-aged society in terms of improving quality of life and curtailing social security costs. This is where senolytics have received attention. Preventing the onset or advancement of age-related diseases such as cancer or Alzheimer's disease is expected to contribute to prolonging healthy life expectancies and curtailing increasing social security costs.

[Driver 3: Eternal life in cyberspace]

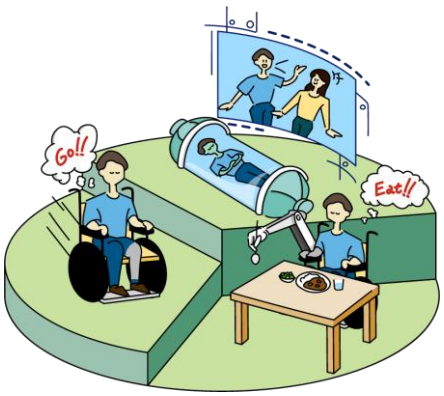
Human/brain machine interfaces (HMI/BMI) will connect our brains to machines. The emergence of deep learning will dramatically improve our accuracy in deciphering the signals within our brains, which has motivated the clinical application of HMI. Even if an individual possesses impaired motor, sensory, or language functions, HMI can reconstruct and modify these functions, resulting in an improved quality of life. Furthermore, HMI goes beyond just treatment. Through enhancements to our physical, cognitive, and perceptual capabilities, HMI will offer to us a lifestyle that overcomes human capabilities, time, and distance.
In the end, we will transfer our minds to robots or cyberspace, bequeathing to us eternal life. This option will require a variety of discussions, including a reconsideration of bioethics and the construction of new economic zones.

In this way, dramatic developments in scientific technologies will result in the development of treatments that contribute to prolonging our healthy life expectancies and curing diseases that are difficult to treat. Adding this new cyber-based lifestyle to our options will lead us to a society in which people can live to be 100 years-old and still enjoy their lives. This will bring about a big change in how ordinary citizens view both life and death.

Figure 1. Three drivers from the perspective of ordinary citizens

[Driver 1: N-of-1 medical care]

[Driver 2: Senolytics]



[Driver 3: Eternal life in cyberspace]

[Manufactures' perspective] Transforming how the pharmaceutical industry is structured: Shifting to horizontal specialization and virtual models

Pharmaceutical companies that possess vertically integrated value chains will change how their industry is structured due to declining R&D productivity in pharmaceuticals and growth in contract companies (such as CRO/CDMO). Business models will take on greater diversity, including horizontal specialization and virtual models that display flexibility in selecting and using a variety of external functions. In this section, we would like to examine how the structure of the pharmaceutical industry is transforming (Figure 2).

[Driver 4: Virtual worlds]

There is increasing hope that digitalization will help in improving R&D productivity, such as in designing in-silico pharmaceutical designs, developing digital biomarkers, and predicting the success of clinical trials. Drug discovery research that has centered on cell and animal testing as well as clinical developments that have relied on human clinical trials will undergo dramatic changes due to the modeling of biological and disease mechanisms, the democratization of RWD, and technological innovations in analysis and computational capabilities. The wide-spread adoption of modeling and simulation (M&S) in the R&D of pharmaceuticals has the potential to dramatically shorten cycle times.

This is not limited to just the R&D of pharmaceuticals. M&S is also being applied to tools that make predications on a patient's specific condition and provide recommendations on treatment. Utilizing M&S to optimize the processes found in the operations of hospitals and factories will contribute to improving the productivity of the entire industry.

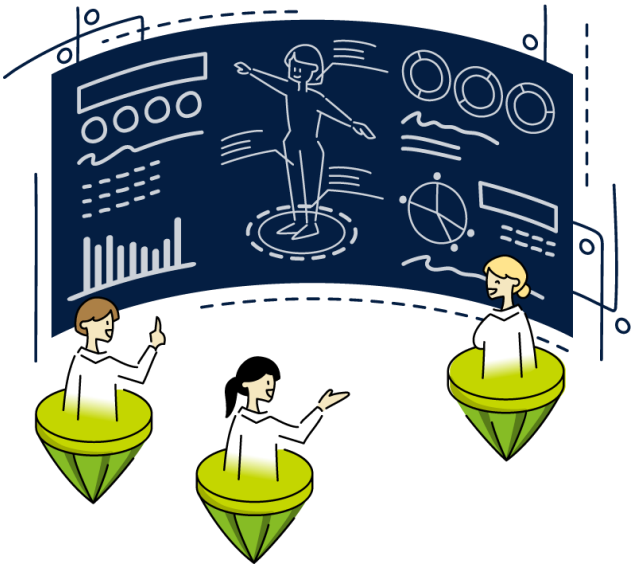
Furthermore, the metaverse will provide opportunities for a variety of players in industry, government, academia, and hospitals to form relationships and promote communication as well as expedite the development of new products/services and assist in marketing, academic conferences, and collaborative research in cyber space. We envision that these developments will contribute to the promotion of open innovation. M&S and the metaverse will be great enablers that contribute to improving the productivity of the life science industry.

[Driver 5: Virtual pharma model]

The rate at which the CRO and CDMO marketplaces have grown exceeds that of the global pharmaceutical market overall. Pharmaceutical companies are the source of at least 50% of small-molecule drugs, but biotech companies are the source of at least 50% of other pharmaceuticals (i.e., biopharmaceuticals). R&D productivity in the pharmaceutical industry is on the decline, making productivity improvements within the pharmaceutical industry essential. With the digitization of pharmaceutical R&D, competition in the pharmaceutical industry will intensify as players from other industries that possess core competencies in digital technologies enter this market.

Under such circumstances, the pharmaceutical industry will be forced to reconsider its core functions while looking to achieve sustainable growth. There is a variety of forms this could take. These companies could shift from a vertically integrated system in which the company is in possession of the entire value chain (which extends from research to manufacturing and sales) to a horizontal specialization model in which certain functions are outsourced to other companies. These companies could also shift to a virtual model in which the company only retains its core functions, while working together with international partners that are best suited to handling its other functions.

Figure 2. Three drivers from the perspective of manufacturers



[Driver 4: Virtual world]

[Driver 5: Virtual pharma model]

[Medical providers' perspective] Revamping medical care systems: Offering optimal solutions to individuals at the right place and right time

Medical and healthcare systems still face some major issues, such as growing social security costs, uneven distribution of medical resources, and an overemphasis on self-care in maintaining one's health. Circulating data and expediting the development of digital technologies will resolve these issues. Continuing to collect data from all kinds of situations as well as using AI to make accurate predictions on the onset of diseases and recommend optimal treatments will provide high quality health and medical services to all people in an equal manner (Figure 3).

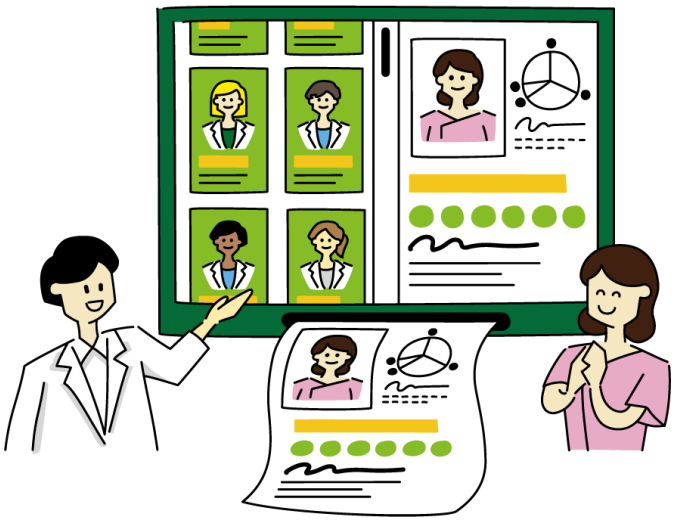
[Driver 6: AI hospital]

AI hospitals will be promoted by the Cabinet Office's Cross-ministerial Strategic Innovation Promotion Program (SIP). These hospitals will have a multitude of purposes, which will include maintaining the quality of medical services in Japan's super-aged society, curtailing increases in medical expenses, and reducing the burden placed on medical professionals. These hospitals will also be used in more diverse ways, with medical facilities seeing all of their functions being digitized and becoming their core resources. These functions include providing very accurate diagnoses, predicating the risk patients have of developing a disease, offering recommended treatments, providing digital therapeutics, managing diseases, performing remote diagnoses, and supporting operations as well as communication. Implementing AI hospitals will allow doctors to further specialize and will help in curbing the uneven distribution of medical resources and increasing social security costs.

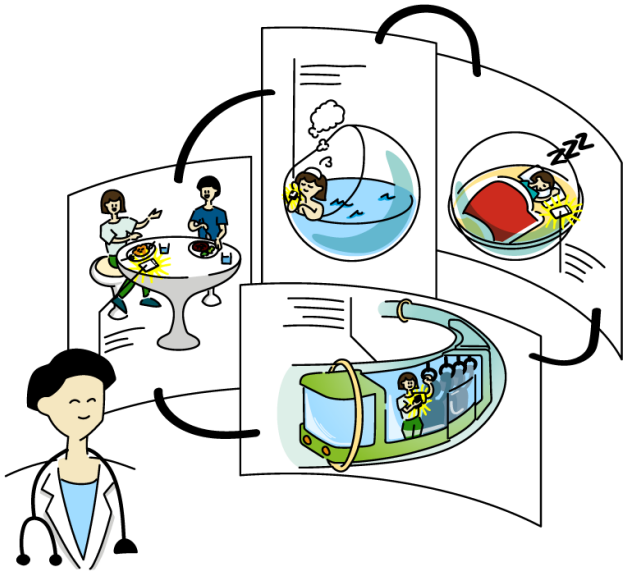
[Driver 7: Connected health]

With a focus on consumers, complex physical, mental, economic, and social issues that affect consumers will be visualized, which will result in a variety of players from the medical and healthcare fields coming together to resolve these issues in an organic manner. Future health and medical services will present individuals with optimized solutions regardless of what stage the individual may find themselves in (from maintaining health to treating an illness), leading to longer healthy life expectancies and optimized treatments. Local communities and governments will work closely together to support local residents in receiving health and medical services. Health and medical services will be integrated into society as a whole, resulting in these services having a greater impact and further reductions to social security costs.

Figure 3. Three drivers from the perspective of medical providers



[Driver 6: AI hospital]



[Driver 7: Connected health]

[Industrial base's perspective]: Accelerating value transformation: Visualizing value and circulating assets at high speeds

Various players in industry will work together to offer solutions by linking and putting into circulation various forms of data (medical, consumption, behavioral, emotional, etc.). Putting this data into circulation will quantify the value of medical and healthcare services in addition to fostering inter-industry collaboration. Furthermore, IP will be traded on digital platforms, which will accelerate open innovation.

In this section, we would like to examine how data, intellectual property, and value assessments, which are the core resources of the medical and healthcare industries, are quantified (Figure 4).

[Driver 8: Circulating healthcare data]

Medical and healthcare data will see dramatic increases, the purpose of which will be to unravel the mechanisms behind diseases and understand their symptoms in an objective and continuous manner. Consumer data that has no relation to healthcare will also be included, being integrated as personal data. Data is a source of industrial innovation and verifies what impact these efforts will have, serving as a catalyst in revitalizing industries. Furthermore, the data put into circulation will be shared with a variety of other industries outside of healthcare and will promote cooperation with the healthcare industry, helping to breakdown boundaries between healthcare and other industries. We can picture a world in which a variety of players are involved in healthcare.

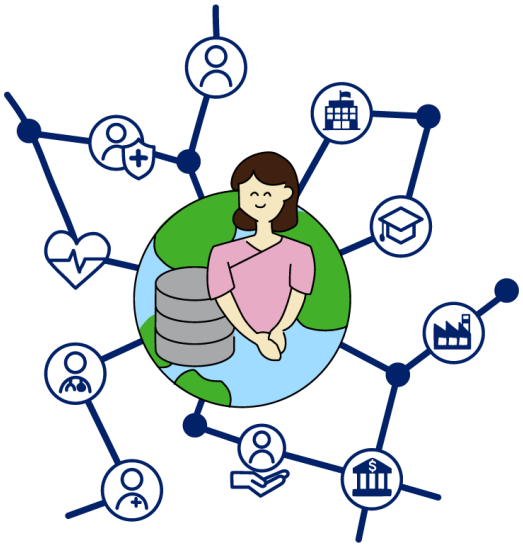
[Driver 9: Quantifying the value in medical care]

The concept of value-based healthcare (VBHC) has been advocated for a very long time. At the same time, in addition to the data circulation mentioned in the last section, progress is being made in quantifying the value of medical and healthcare services. Until now, society has seen just some of the cost benefits of pharmaceuticals. However, a multitude of value indicators for medical and healthcare services are now being defined, with products, medical practices, and even health and medical polices being scored. Quantifying these values will mean that the principles of market competition will be embedded into medical and healthcare services, which we imagine will improve value and produce more streamlined services amongst free competition.

[Driver 10: Facilitating the free flow of IP on the marketplace]

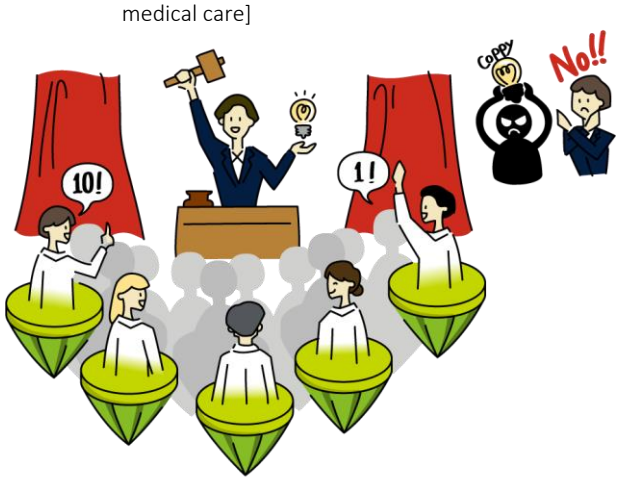
The Japan Patent Office understands that analyzing and utilizing information on IP is becoming more important and has thus begun a trial service that analyzes patent information. Patent analysis is expected to serve as a source of R&D and business strategies, such as searching for business partners, and contribute to promoting innovation. Non-fungible tokens (digital data that comes with a certificate of authenticity and proof of ownership) will promote the secure and logical transfer of patents. Furthermore, equipping open platforms used in patent transactions with AI will allow companies to search for the most suitable patents in a short period of time, which we imagine would contribute to economic development.

Figure 4. Three drivers from the perspective of the industrial base



[Driver 8: Circulation of healthcare data]

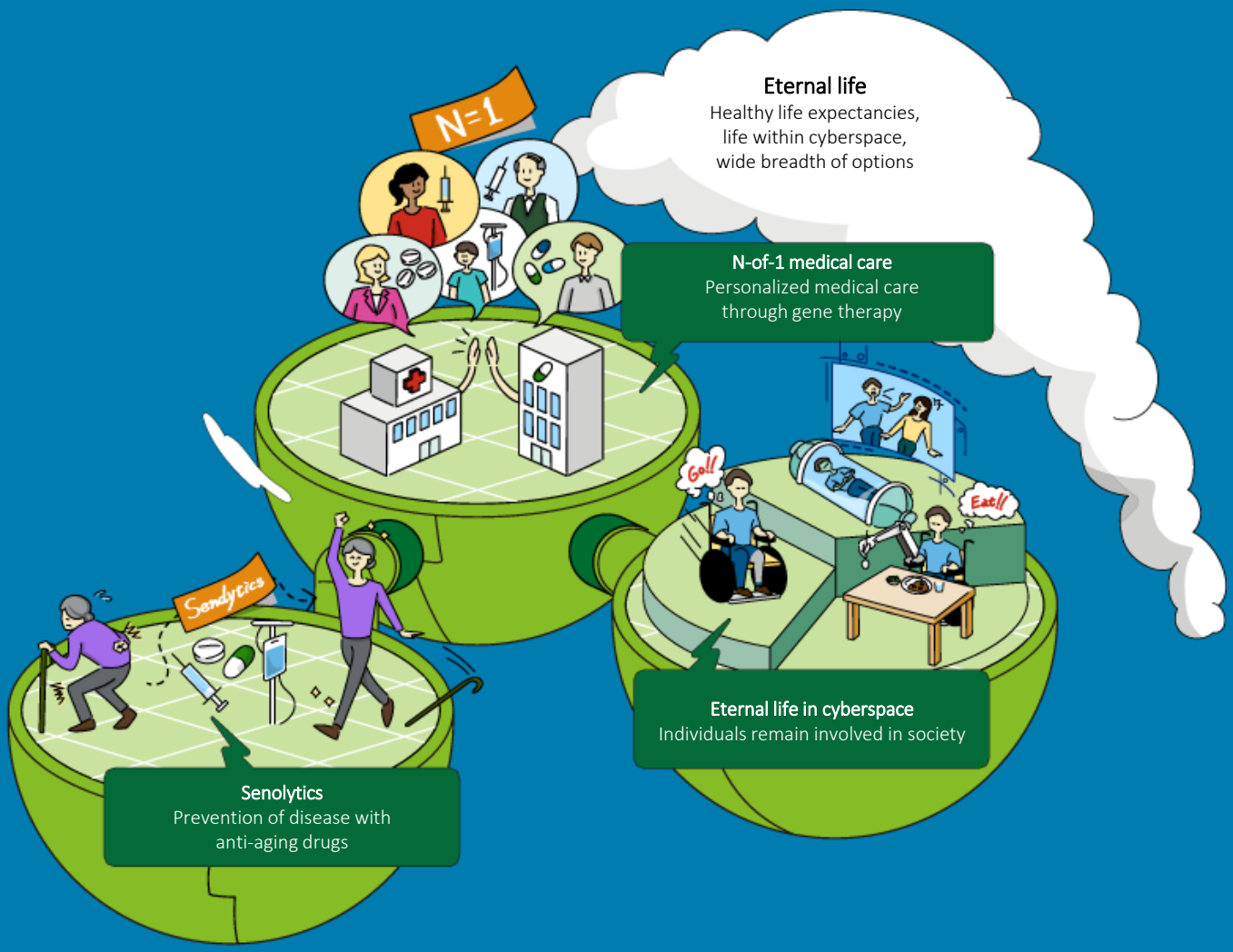
[Driver 9: Quantifying the value in medical care]



[Driver 10: Facilitating the free flow of IP on the marketplace]

What sort of healthcare will the “10 drivers of change” bring in 2040?

b. Eternal life



Challenges

Despite the medical advances made in the 21st century, people still struggle to live out healthy lives.

There are patients suffering from rare diseases, aging, and physical disabilities. In the future, it will be necessary to highlight diseases with no treatments and the difficulties consumers are faced with to present potential solutions.

[Neglected rare diseases*1-4]

Rare diseases often develop due to genetic factors and follow a chronic course, but the cause of many of these diseases have not been identified and no treatment methods have been established.
There are about 7,000 rare diseases in the world, with 350 million patients suffering from these diseases. Although 57% of rare diseases have had their causative gene identified, no adequate treatments have been developed for these diseases, with about 80% of rare diseases having no FDA-approved therapeutics.

[The gap between average and healthy life expectancies]

The proportion of elderly individuals aged 65 or above is about 30% in Japan and is about 20% in the US*5. As people age, their physical and mental functions weaken. This leads to frailty in which a marked decline in physical activity is observed, resulting in age-related diseases such as dementia. Between their healthy and average life expectancies, men have about a nine-year gap and women a twelve-year gap. From 2001 to 2016, this gap has not been filled*6. This period will result in more expense social security (medical expenses, nursing expenses, etc.), force families to care for their loved ones, and rob the elderly of their happiness.

[Physical, cerebral, spatial, and time constraints]

Individuals with some sort of physical handicap, such as being paralyzed due to an illness or accident, suffering from a sensory disorder, or having weak legs due to old age, face many inconveniences in their ordinary lives and are shut off from participating in society. In 2016, there were about 4.3 million people aged 18 or above that possessed a physical handicap, of whom 310,000 had a visual impairment, 340,000 had a hearing or speech impairment, and 2 million had a physical disability*7.
In addition, even when not faced with a physical constraint, we all live within the constraints of our abilities, as well as with spatial and time constraints. Furthermore, there are also situations in which activities must be carried out at disaster sites or a location that is hard for people to enter.

Market/technical trends

What kind of work is being done to allow consumers to live out healthy lives? We will look at some technologies that are helping to solve these challenges.

[N-of-1 medical care]

Rare diseases are becoming a big market accompanying the evolution of pharmaceutical modalities. The global market for rare disease drugs is expected to reach USD 21.7 billion in 2024 with a CAGR of 9.7%. In addition, rare disease drugs accounted for 11% of the pharmaceuticals market in 2014, but this is expected to become 18% in 2024[*8]. Based on the number of drugs in development, orphan drugs account for about 45% and 30% of new molecular entities registered under the FDA and PMDA respectively. The number of these drugs registered under the FDA has continued to rise since 2010[*9].

Oligonucleotide therapeutics can be developed in short periods of time due to being sequence dependent, possessing a clear action mechanism and design, as well as being chemically synthesized. These drugs are also suited for providing personalized care to patients with genetic diseases.

A rare pediatric disease known as Batten's disease (a type of lysosomal storage disease) has only one known patient, with no other patients having been identified to be suffering from similar variants of this disease. This patient was administered with antisense oligonucleotides (ASO), which was confirmed one and a half years after administration to reduce the frequency and duration of convulsions[*10]. As described below, initiatives aiming to develop pharmaceuticals for rare diseases have been set up in which academia and hospitals may play a leading role in developing drugs that will help make N-of-1 medical care a reality.

1. FDA-driven "IND Submissions for Individualized Antisense Oligonucleotide Drug Products: Administrative and Procedural Recommendations Guidance for Sponsor-Investigators"[*11]

(a) This initiative can offer guidance on developing oligonucleotide therapeutics for severe genetic diseases and design pharmaceuticals for very limited patient populations.

(b) This initiative will focus on companies and clinical investigators.

2. Tokyo Medical and Dental University (TMDU) will open Japan's first domestic research center that specializes in oligonucleotide therapeutics (planned for 2022) [*12]

(a) Takanori Yokota, a professor at TMDU and the chairperson of the Nucleic Acids Therapeutics Society of Japan, has stated that "Japan would be a world leader in oligonucleotide therapeutics if it were to consolidate the outstanding technologies it has developed."

(b) Ionis Pharmaceuticals and Takeda Pharmaceutical have found a way to penetrate the blood-brain barrier through their joint research. This has allowed them to develop new technologies that will make it possible to suppress genes from expressing themselves in the central nervous system through systemic administration[*13].

[Senolytics]

Aging had been understood to be an unassailable "law of nature." However, unraveling the mechanisms behind aging is changing our perceptions on aging being a pre-programed process, which is leading to the identification of targets and the development of senolytics for those targets.

According to Professor Nakanishi from the University of Tokyo, "A major factor of aging is the accumulation of senescent cells that cause chronic inflammation in organs and tissues. GLS1 is an enzyme that allows senescent cells to survive. Blocking the action of this enzyme induces cell death and eliminates senescent cells. GLS1 inhibitors eliminate senescent cells," and have been shown to be effective in disease models. In addition, there are signs that administrating GLS1 inhibitors to patients will improve type 2 diabetes, arteriosclerosis, and NASH, and may improve age-related diseases such as renal failure and COPD, as well as lifestyle-related diseases[*14].

With that being said, does this mean that using senolytics will allow us to gain eternal life in which we are free from aging? Professor Nakanishi has this to say, "Our maximum lifespans are determined by mechanisms that differ from aging and the onset of disease." The purpose of senolytics is to extend healthy life expectancies and fill the gap between average life expectancies and healthy life expectancies.

Efforts in senolytics are underway in academia, pharmaceutical companies, and the technology industry.

1. NIH[*15]

(a) The budget for the NIH National Institute on Aging has increased 2.4 times over the past six years, reaching USD 3.9 billion by 2021

2. MAYO CLINIC[*16]

(a) A small-scale study on idiopathic pulmonary fibrosis

(b) A drug for leukemia known as dasatinib and a supplement called quercetin was administered

(c) Administering these drugs nine times over the course of three weeks resulted in the subjects becoming able to walk further distances over the same time periods

3. Alphabet and AbbVie[*17]

(a) In 2013, Calico was established as a venture specializing in aging research, in which Alphabet and AbbVie invested USD 1.5 billion to promote the development of anti-aging drugs

4. Amazon[*18]

(a) Jeff Bezos has invested in Unity Biotechnology, which is a company that develops pharmaceuticals that destroy senescent cells

(b) UBX0101, a drug that treats osteoarthritis by removing senescent cells in the knee joints, is in the first phase of clinical trials

[Cyberspace]
Cyberspace is a means for us to overcome physical, spatial, and time constraints, with braintech acting as one of its underlying technologies. Braintech is a new technology that was born from the fusion of brain science and IT. The market size for this technology is expected to reach JPY 5 trillion in 2025, with Neurotech Analytics, which forecasts industry trends and conducts benchmarks for neurotech, reporting that neurotech's annual investments will grow by around 31%.

The US and Japanese governments are both establishing large-scale initiatives to unravel brain-related functions, overcome functional disorders, and develop social activities, all for the purpose of turning cyberspace into an industry.

1. US: "BRAIN Initiative" *19
This is an initiative that the Obama administration established in 2013 and is a big science project that is comparable to the "Apollo Program" and "Human Genome Project." The purpose of this research is to explore the mysteries of how the brain functions, improve how various brain dysfunctions are prevented and treated, and deepen our understanding of how humans memorize, think on, and process information.

2. Japan: "Moonshot Research and Development Program" *20
(a) This is an initiative that aims to "achieve a society in which humans are free of physical, cerebral, spatial, and time constraints by 2050." Amid the growing concerns surrounding Japan's labor shortage problem due to its declining birthrate and aging population, this country is aiming to achieve a society in which people are free of physical, cerebral, spatial, and time constraints.

Braintech is involved in the following healthcare fields, with progress being made in researching and developing solutions for each field: clinical applications of human machine interfaces (HMIs), linking our brains with AI systems to expand upon human capabilities, and achieving eternal life in cyberspace.

1. Human machine interface (HMI)
(a) HMI is a technology or device that allows people to see, taste, and experience other sensory stimulations without the use of a sensory organ. This is accomplished by reading information in the brain and sending commands to a computer that in turn directly simulates the nervous system. It is estimated that the size of the HMI market will reach USD 3.85 billion (CAGR 14.3%) in 2027 (Reportocean.com).
(b) The following chart lists three types of HMI, some of which are already seeing clinical applications*21 (Figure 5).
(c) Neuralink, which is led by Elon Musk, is developing technologies for ALS patients, having announced an implantable chip that directly reads thoughts from the brain and then outputs/communicates this information to the outside world. In the future, Neuralink aims to make this technology available to general users.

Figure 5. Types of HMI

Type of HMI	Overview	Coverage	Examples of research and clinical results
Output type	● Deciphering brain information to direct artificial limbs, computers, etc.	● Reconstruction of motor and language function ● Translation of sentences	● Text input is realized just by thinking with deep brain stimulation for ALS patients
Input type	● Taking information from sensory organs and inputting it into the brain	● Reconstruction of sensory function (Inner ear, retina, etc.)	● Implantable cochlear implant for patients with profound hearing loss ● Artificial retina for patients with amblyopia
Two-way type	● Inputting and outputting information in both the brain and sensory organs	● Treatment of psychoneurotic diseases such as epilepsy and Parkinson's	● Vagus nerve stimulation, deep brain stimulation, and responsive neurostimulation for patients with intractable epilepsy

Source: Edited by Deloitte from New medical world weekly (January 3, 2022) "BCI Connecting the Brain and AI"

2. Linking the brain with AI systems to expand human capabilities

(a) The Moonshot Project mentioned in the previous page is advocating a "cybernetic avatar life" in which anyone can participate in a variety of social activities.

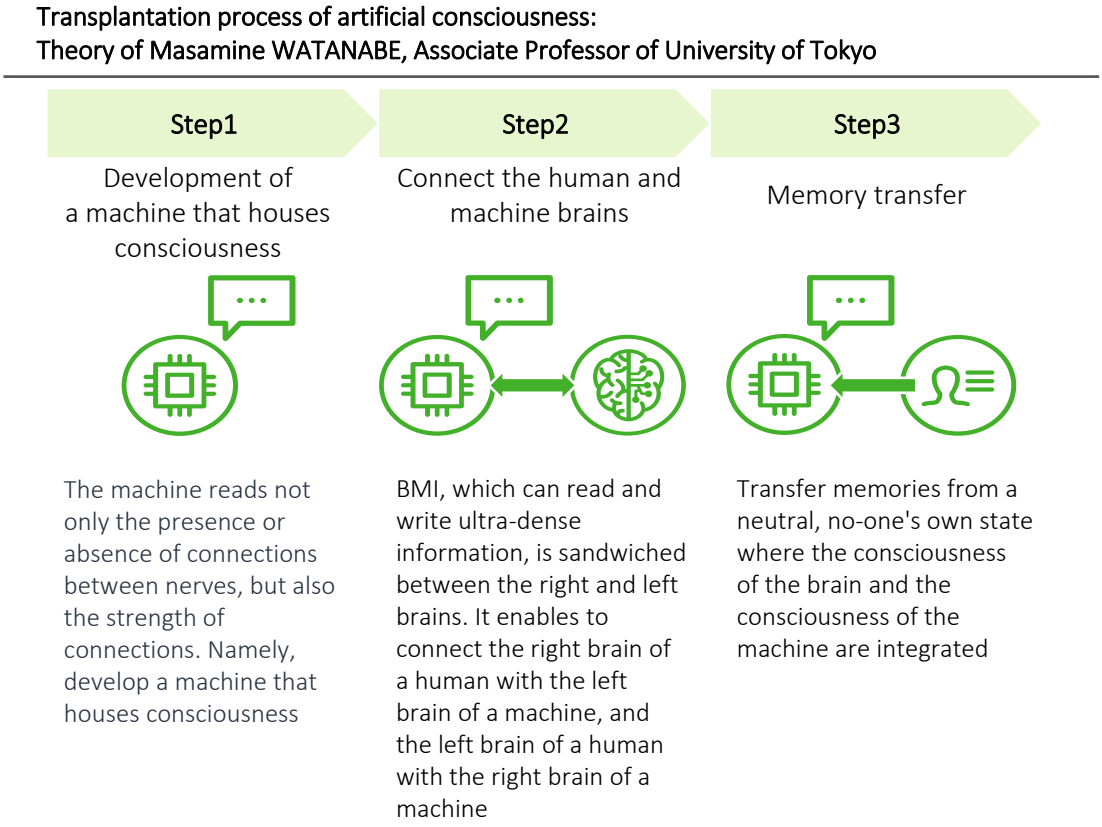
(b) In addition to developing technologies that allow anyone to expand their physical, cognitive, and perceptual capabilities to the highest levels, this project is aiming to spread a new type of lifestyle that combines robot stand-ins and virtual avatars with these technologies.

3. Eternal life in cyberspace

(a) Allowing the brain to interface with machines through HMIs would in all likelihood allow us to continue to live in perpetuity through the machines connected to our brains even if, in the worst-case scenario, we were to lose the function of our bodies or brains.

(b) According to Associate Professor Watanabe from the University of Tokyo, artificial conscious is an extension of existing technologies and is something we can hope to achieve within the next 20 years[*22] (Figure 6).

Figure 6. Process for transplanting artificial conscious



Source: Edited by Deloitte from HBR "Aiming for transplantation of human consciousness in 20 years and society with consciousness in a few years"
https://www.dhbr.net/articles/-/6268、https://dot.asahi.com/aera/2020072100020.html?page=1

What the world will look like in 2040

A life expectancy of 100 years = healthy life expectancy and life within cyberspace: Consumers will be faced with even more choices

Scientific technologies have made remarkable progress, with what we used to see in science fiction becoming a reality.
By 2040, there will be less people who are worried about their health, and more people will continue to participate in society after reaching the age of 100 (our life expectancies will be equal to our healthy life expectancies). The same will be true for people who have some sort of physical disability due to an accident or illness, as these individuals will be able to overcome their physical constraints and participate in society through the virtual world.
Furthermore, this future will achieve a form of well-being that incorporates the hobbies and diverse lifestyles of consumers, while also resolving social and healthcare issues.

1. N-of-1 medical care: Semi-custom medical services based on drug discovery technology platforms

[The world we will have achieved]

Patients with rare diseases will be discovered/diagnosed early on. If we use genome analysis to identify the causative genes of a disease, we can decide upon a product concept using a drug discovery platform as a base, then promptly implement a treatment.

[The value chain for N-of-1 medical care]

The value chain for delivering orphan drugs will undergo a transformation.
(1) Identifying patients
The rare diseases we can detect at an early stage are mainly those that occur during infancy and for which early intervention is important.
In addition, registries for patients with undiagnosed diseases, such as the UDP (Undiagnosed Disease Program) in the US or the IRUD (Initiative on Rare and Undiagnosed Diseases) will be implemented by AMED in Japan, are being expanded upon.
(2) Developing N-of-1 therapeutics
Patients with rare diseases will have the causative genes of their diseases identified through genomic testing and will thus make a smooth transition to more definitive diagnoses. To develop semi-custom therapeutics, we will examine how to treat the cause of a disease based on its mechanisms and then select an optimal combination from a variety of modalities, such as oligonucleotide therapeutics, gene therapy, and cell therapy, from which the therapeutic's concept will be designed.
(3) N-of-1 clinical trials
The use of in-silico experiments and organoids to reproduce disease mechanisms will help to establish safe and efficient testing, clinical trial methodologies, and approval processes.
(4) Manufacturing/distribution
CDMOs as well as biotech and pharmaceutical companies that excel in manufacturing high value-added products will manufacture orphan drugs. A limited set of wholesalers will distribute each product. Information on the whereabouts of patients scattered throughout the country will be collected, which means working together with wholesalers will be important when conducting clinical trials or post-marketing surveillance. In addition, we believe some manufacturers will attempt to form direct contracts with medical institutions to shorten vein-to-vein lead times.
(5) Post-marketing surveillance (PMS)
PMS will become even more important in testing for safety, with clinical trials that target small patient populations becoming the primary focus. Progress will be made in constructing a registry that covers a range of rare diseases that will allow companies to follow-up with patients scattered throughout the country over the long-term.

[The role of pharmaceutical companies in developing N-of-1 treatments]

What is the role of pharmaceutical companies in offering orphan drugs within the pharmaceutical value chain? Existing pharmaceutical companies will likely target rare diseases with relatively large patient populations that can be expected to generate a certain number of sales, even amongst rare diseases. A family of rare diseases that can be approached using the same technological base may be identified and used as a single market to offer drugs and treatments that cover a variety of rare diseases. It is here that pharmaceutical companies, medical institutions, and academia can work together to improve productivity within the entire value chain.

2. Senolytics: Making our life expectancies equal our healthy life expectancies

[Preventing the functional decline and diseases that accompany aging]

With the emergence of senolytics, the world in 2040 will shift its focus from treating illnesses to preventing them. In other words, a senolytic will be administered to prevent age-related diseases when a biomarker indicating the progression of aging exceeds its threshold.

Doing this will reduce the number of people that develop frailty and age-related chronic diseases such as cancer or dementia. Our life expectancies will come to equal our healthy life expectancies, giving us the freedom to enjoy our lives to the very end and the choice of ending them in the comfort of our homes.

[Resolving social issues]

The spread of senolytics can be expected to reduce medical expenses, alleviate the care burden borne by society, and increase the working population.

In addition, raising the working age in response to the declining working population due to falling birthrates and an aging population will increase the working population and alleviate the financial burden from certain social security costs such as pensions.

3. Cyberspace: Liberation from physical constraints with the "mind" at its core

[Allowing individuals with physical disabilities to participate in social activities]

The practical application of human machine interfaces (HMIs) will allow people to overcome their physical and bodily constraints and thus participate in daily life and social activities. For example, an individual that has lost the free use of their limbs due to an accident or illness will still be able to perform actions (writing, walking, etc.) using their mind through the help of support equipment if the individual imagines said action in their brain. Even individuals with impaired sensory organs that intake external stimuli, such as sight or hearing, will be able to restore their sight or hearing within their brains and feel these sensations.

Removing the physical constraints placed on individuals with physical disabilities will allow them to enjoy daily life or participate in social activities such as work. In addition to improving the patient's QOL, this will also alleviate the burden placed on the families caring for these patients.

[Achieving well-being for all consumers]

HMIs are not just limited to the above-mentioned therapeutic applications and replacing devices that support certain bodily functions.

Connecting peoples' minds with robot stand-ins (physical alter-egos) and virtual avatars (virtual alter-egos in cyberspace) will create another version of themselves that can perform various activities in both the physical and virtual worlds.

<Experiencing life through a robot stand-in>

(1) Activities in areas hazardous to humans

Dispatching stand-in robots in situations that could be hazardous for humans and result in secondary disasters, such as an earthquake, fire, or accidents at sea or in the mountains, will allow for smooth rescue operations.

(2) Expanding skilled workforces

Producing copies of stand-in robots that possess abilities equal to or greater than one's own will make it possible to acquire a highly skilled workforce in a short period of time and improve labor productivity.

(3) Experiencing the world through another version of oneself

When faced with spatial or time constraints (such as not having the time to travel abroad or wanting to avoid becoming fatigued from a long trip), individuals can connect their minds to stand-in robots installed in tourist spots around the world. Doing so will let them enjoy these locations vicariously through a variety of sensory experiences, such as feeling the wind on one's skin, taking in different smells, and breathing in the air.

(4) Using avatars to protect one's healthy life expectancy

It will become possible to inject nano avatars into one's body and use these avatars to protect oneself from or treat diseases.

<Experiencing life through a virtual avatar >

(5) Interacting with people in cyberspace

Having a virtual avatar act as one's alter ego in cyberspace will allow people to overcome their spatial/time constraints and meet a variety of people.

[Transferring one's conscious to attain eternal life]

Those praying for immortality might be able to live forever by integrating their conscious within a machine while still alive, and then transferring said conscious to a machine post-mortem. For those who have unfinished business in this world (for example, someone who could not see their children grow up due to becoming ill at a young age), this will allow them to speak with their families, check up on them, as well as touch and feel them through an interface despite their cyber minds existing in cyberspace. This will allow them to live virtual lives while experiencing their children's growth within their brains.

Experts in various fields such as science, business, politics, and art will be able to persist in their activities and contribute to scientific and economic developments. Those who choose to exist in cyberspace will contribute to the formation of a new economic sphere post-mortem.

What merits discussion in implementing these changes

The world of 2040 will present challenges that must be resolved.

[N-of-1 medical care]
The following challenges must be discussed for our societies to implement N-of-1 medical care

1. Streamlining the entire value chain: How do we streamline all of the processes involved in the value chain, from basic research to offering patients medicine?
We need to drastically improve the efficiency of our value chains in order to implement N-of-1 medical care into our societies.
(1) Working together to unravel the mechanisms behind diseases
An international team that included institutions such as the US National Human Genome Research Institute announced that it had managed to decode 8% of the heterochromatin regions that had in the past been considered difficult to decode. In addition to understanding the cause of rare diseases and developing treatments, the US has plans to help advance discoveries on diseases and health conditions related to the human genome. In the pharmaceutical industry, AbbVie, Biogen, Pfizer, and others have collaborated on analyzing the exome sequence to build the world's largest database that links how mutations in protein-encoding genes affect health and diseases.
(2) Co-creating R&D platforms
The FDA's Bespoke Gene Therapy Consortium (BGTC) includes the NIH, 10 pharmaceutical companies, and five NPOs. This organization is aiming to optimize the development of gene therapies by building a shared R&D platform that will include technologies such as standardized gene delivery technologies.
(3) Creating networks for clinical research
The Rare Disease Clinical Research Network (RDCRN) in the US is promoting clinical research aimed at developing treatments. The RDCRN is a consortium of university hospitals, research institutes, and hospitals, with seven national research institutions involved in its operations and more than 5,000 registrants.
(4) Strengthening drug repositioning
The therapeutic uses developed and recognized in orphan drugs have also been confirmed to be effective against other diseases, creating a positive feedback loop that has improved the value of these pharmaceuticals.

2. Approval systems: How should ultra-personalized medicine be positioned within Japan's national strategy?
Japan's Ministry of Health, Labour and Welfare has established the "Designation System for Orphan Drugs, Orphan Medical Devices, and Orphan Regenerative Medical Products."

The US also has a similar support system. However, this system also includes drugs, devices, and regenerative medical products "with fewer than 200,000 patients or that face difficulties in recovering their development costs within the US." Companies under this system are also given exclusive sales rights to their products for seven years after receiving approval, as well as preferential tax treatment. As a result, more drugs to combat rare diseases are being developed under this system than in Japan.

3. Drug prices and the scope of social security: How should Japan set its drug prices and the scope covered by its universal health insurance?
At present, developing N-of-1 medical care is extremely expensive.
N-of-1 medical care will be covered in Japan due to it having universal health insurance and having developed high-cost medical care systems. However, measures will need to be taken to curtail social security costs. To do so, the cost of developing and providing N-of-1 treatments needs to be reduced through optimizations to the entire value chain that provides such treatments and strengthening support offered in receiving approval. On the other hand, Japan also needs to ensure that valuable drugs are rewarded with high prices based on the concept of value-based healthcare (VBHC).

[Senolytics]
The following points should be discussed regarding the spreading of senolytics.

1. Drug prices and coverage of social security: What should be done about the coverage of Japan's universal health insurance and its drug prices?
Under the current Japanese medical insurance system, medical care administered for preventative purposes is, in principle, not reimbursed except in certain areas, such as vaccines against infectious diseases.
In 2019, a medical device was reimbursed for "preventative purposes" in Japan for the first time. This device was an incision management system that is dedicated to preventing surgical site infections (SSIs). By supporting the quick recovery of patients and preventing reoperations as well as additional medical expenses, this machine helps to reduce the burden placed on medical facilities. Looking at this example, we can consider the following three options.
(1) Not covered by insurance (maintain current coverage): The cost of preventative medicine is not covered by insurance and is instead borne by the individual.
(2) Reimbursement is adjusted based on risk (similar to current pharmaceutical rules): Reimbursement is given if it is proven that the effects of the pharmaceutical reduce the risk of developing a disease and that patients who develop said disease will suffer more complications. Furthermore, we need to consider whether out-of-pocket payments should be changed from that of ordinary treatments.
(3) Reimbursement based on individual effects: Taken from the idea of VBHC, reimbursement will be given on a case-by-case basis only when the pharmaceutical has the effect of reducing the risk of developing a disease.

2. Touchpoints within the patient journey: How will targets be identified and who will be prescribing senolytics and in what manner?
Examinations that use objective indicators will be important in detecting aging during its early stages. In addition, it also needs to be determined whether regular hospitals can perform diagnoses or provide prescriptions, or if a high level of specialized knowledge is required to perform these actions.

3. Service operators: What should life science companies consider before entering this market?
In developing their preventative medicine businesses, pharmaceutical companies are anticipating a multitude of scenarios, with the topic of how to organize their R&D portfolios, or in other words, how to make proper investments into senolytics, serving as a major point of discussion.
Outside of their portfolios, pharmaceutical companies should also consider the following points of discussion.
(1) Shortening development periods: Longer follow-ups may be required to demonstrate the protective effects of these pharmaceuticals. How can development periods be shortened through the development of surrogate endpoints and use of in-silico simulations?
(2) Refining business feasibility evaluations: How should companies evaluate the target size of their senolytics, taking into account whether target patients will be receptive to these drugs, as well as drug prices and the possibility that these drugs may be covered under insurance?
(3) Building supply chains: Where should patients undergo diagnosis and receive prescriptions?
(4) Creating rules and shaping public opinion: What should be done to create new rules for the approval and medical insurance systems, as well as to gain public support?

[Eternal life within cyberspace]
If ever presented with the choice to live forever in cyberspace, how society will form a consensus on how to view life and death and the ethics behind such a choice will merit discussion

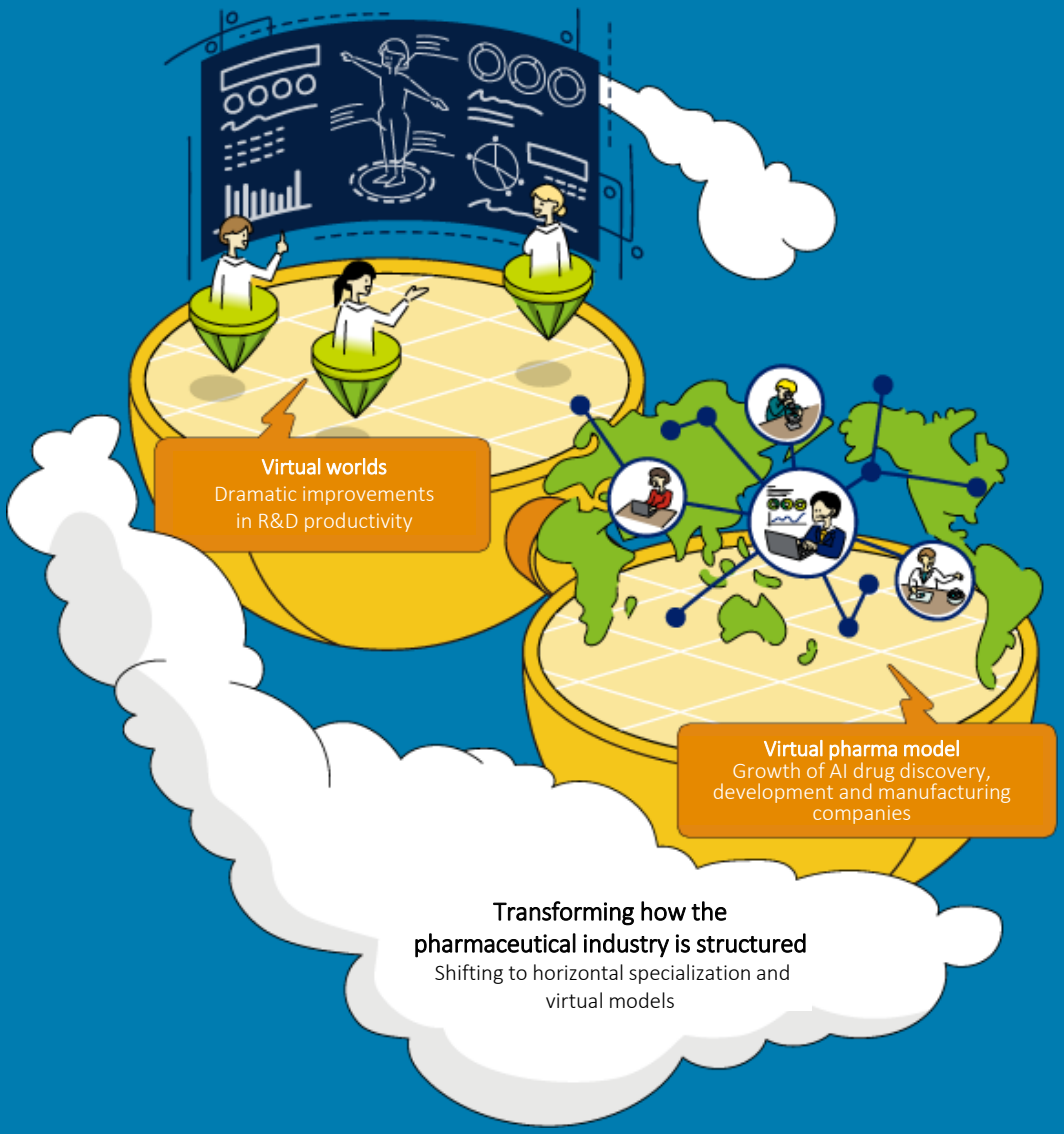
1. Should everyone seek out eternal life? Who will make the decision to transfer someone's mind to cyberspace?
Associate Professor Watanabe of the University of Tokyo has stated that the combined cost of the surgical operations not covered under insurance plus the servers should add up to about the cost of one car[*23]. However, should everyone that can afford to pay these fees seek out eternal life?

2. The divide between cyberspace and the real world
Once people are able to live in cyberspace, some people may voluntarily choose to end their lives in the real world and live only in cyberspace. There is the possibility that these people will lose the ability to give shape to their minds and bodies in the real world, as well as interact with other people, something we have taken for granted up until now. If these two worlds exist in parallel and become divided from each other, the real world may eventually disappear.

3. Who will decide when to end someone's life, and who will be the one to pull the plug?
How long will people continue to live after their minds are transferred to cyberspace? Will their lives end if these people can no longer pay for server maintenance? Do we need to decide under what conditions people can choose to end their lives? A compelling argument could be made for those that have lost the function of their bodies. However, the ability to choose when to end one's life might become a burden for some.

What sort of healthcare will the “10 drivers of change” bring in 2040?

c. Changes to how the pharmaceutical industry is structured



Challenges

An urgent task facing companies is to increase productivity across the entire value chain while continuing to create innovative drugs in order to adapt to turbulent changes and achieve sustainable growth

In the pharmaceutical business, only a handful of products can go to market despite spending huge amounts on R&D, making it necessary to manage R&D expenditures and sales, as well as increase the productivity of such activities. However, the productivity of R&D activities has continued to fall. Companies will be faced with the urgent task of improving the productivity of their R&D activities and their entire value chains while continuing to create innovative pharmaceuticals in order to adapt to changes in the turbulent pharmaceutical and healthcare industries as well as to continue to achieve growth.

[Declining productivity in the pharmaceutical industry]

1. Declining productivity in the R&D of pharmaceuticals

According to a survey conducted by Deloitte from 2010 to 2021[*24], R&D productivity reached 7.2% in 2014, but has since continued to decline, falling to 1.5% in 2019. Productivity then improved to 2.7% in 2020 and 7.0% in 2021. This decline in productivity can be broken down into three factors: (1) decreased sales per pipeline, (2) extended cycle times, and (3) increased development costs.

(1) Decreased sales per pipeline
Peak revenue projections per asset continued their downward trend from 2013 to 2019, dropping to USD 360 million in 2019. Advances in personalized medicine are thought to be a factor.
(2) Extended cycle times
The average cycle time for assets in the later stages of their development has continued to grow, reaching 7.14 years in 2020, which is the longest cycle time seen in the past seven years. The reasons for these extended cycle times are thought to come from the fact that companies need more time to recruit patients due to intensifying competition, especially in oncology, and that more trials now require long-term follow-ups.
(3) Increased development costs
The average amount spent on R&D to develop and market a compound has continued to increase from 2013 to 2019, with an average of USD 2.431 billion spent on R&D in 2019. This is an increase of USD 1.135 billion and USD 22 million compared to what was spent in 2013 and 2018 respectively. Declining development success rates are thought to be behind these increases. Factors contributing to this decline in development success rates include a lack of promising pipelines that would put new pharmaceuticals on the market and unreliable clinical predictions.

2. Declining productivity across the entire value chain of the pharmaceutical industry

Pharmaceutical companies have seen declining productivity in not only R&D, as discussed in the previous paragraph, but also throughout their entire value chain. 27 domestically owned pharmaceutical companies had operating margins of about 20% in 2006. This fell to 11% in 2014, recovered slightly after 2017, and then reaching about 14% in 2019[*25].

Market/technical trends

What can we assume will help to resolve the issue of diminishing productivity in the pharmaceutical industry at a fundamental level?

We can assume that innovative approaches will be employed both in terms of cutting-edge technologies and corporate governance.

[Virtual worlds]
Typical examples of virtual technologies include modeling & simulation (M&S) as well as the metaverse. The former identifies drug discovery targets within a virtual environment and analyzes the pharmacokinetics and biological reactions of drugs in past basic research or clinical trials conducted in the real world. These activities are conducted with the intent of improving R&D productivity.

1. Modeling & simulation (M&S)
Technologies involved with M&S include (1) MID3 and (2) digital twins.
(1) MID3[*26]
MID3 is an abbreviation for model-informed drug discovery and development. This process serves as a quantitative framework for drug discovery that centers around knowledge and predictions gained from integrated models and simulations on drugs and their effects as well as pathologic physiology. The following eight benefits can be gained from using this framework.
(a) Identify drug discovery targets using in-silico models and unravel their mechanisms
(b) Select compounds and propose dosages/regiments
(c) Optimize study designs
(d) Optimize dosages by building ADME prediction models
(e) Predict early clinical outcomes by building risk-benefit prediction models
(f) Select in-silico dosages and rules as well as indications
(g) Understand the value and differentiators of new pharmaceuticals
(h) Select and expand patient populations

Using MID3 in this fashion can greatly contribute to improving the efficiency of pharmaceutical R&D. A study by Pfizer showed that using MID3 could reduce annual development budgets by USD 100 million and improve success rates in the later stages of development. In addition, Merck and MSD have reported that using this process can result in savings of USD 500 million in decision-making costs.

(2) Digital twin
A digital twin is a technology that reproduces various data collected from the real world on a computer, creating something similar to that of a twin. The global market size for this technology is projected to exceed USD 60 billion in 2027[*27].
Three areas in which digital twins are being applied are as follows.
(a) Applications for human
Constructing a virtual patient (replica) based on individual patient data will make it possible to precisely understand a patient's condition, unravel the mechanisms behind their disease, predict how each patient's condition will progress, and decide what kind of treatment would be best.
For example, as a part of its "bio-digital twin" initiative, NTT has announced a project that will help prevent and treat illnesses in the most effective and safe manner, as well as support patients in empowering themselves in unique ways. To achieve this objective, NTT aims to build general anatomical models of organs and relationships between them, then add physiological and behavioral information to these models to individualize them so that it becomes possible to predict (and understand) how a patient's organs will behave in the future.
(b) Applications for products/solutions
Integrating product profiles with patient replicas will allow optimal treatments to be selected for each patient. In addition, this will make it possible to use replicas to predict the future condition of medical devices based on the product's operating conditions, as well as find maintenance targets and optimal timings, allowing for improvements to maintenance efficiency.
(c) Applications for factory and medical institution operations
Modeling corporate organizations as well as hospital and factory operations can contribute to optimizing resource allocations, streamlining operations, improving customer and employee experiences, and improving product quality. For example, as a part of its "digital enterprise" concept, Siemens is advocating that all of its product life cycle processes be digitized and that support be given to providing efficient and innovative products/services to promote the three areas of "products," "manufacturing processes," and "performance."

2. The metaverse

The metaverse is a portmanteau that combines "meta" with "universe," and is a virtual world where an unspecified number of participants can act freely in a virtual space through the internet. The global market size for the metaverse is expected to reach more than USD 800 billion in 2028[*28].

Looking at the current state of the metaverse, virtual spaces are being built in entertainment and consumer industries, which includes SNS platforms, online games, live music events, and VR shopping malls.

The metaverse could find applications in the following three areas of medical and healthcare services.

(a) Open innovation

In the area of open innovation, the metaverse is anticipated to help in matching experts from across the world and promoting cooperation that overcomes time and geographical constraints, such as finding new drug candidates and research/manufacturing platform technologies, inheriting development licenses, and finding places to conduct joint research and proof-of-concept demonstrations.

(b) Customer communities

The metaverse will be a community place in which three parties will gather: life science/healthcare companies, medical professionals, and patients. As a result, this will allow companies and patients to search for new needs and exchange information on new proof-of-concept services, leading to customers playing a direct role in the product development of new services. In addition, medical professionals and patients will share their experiences and exchange opinions between themselves, helping to stimulate communication between all parties.

(c) Living space for consumers

The metaverse will create new places that will allow not just able-bodied individuals, but also those with physical constraints stemming from illness or aging to pursue new activities and find self-fulfillment, forming new customer touchpoints and economic spheres.

[Virtual pharma model]

Many pharmaceutical companies are forming vertically integrated business models that have ownership over the entire value chain, which includes everything from R&D to sales. The virtual pharma model is a business model in which companies identify their core functions based on their own core competencies and market position. These companies then allocate functions that fall outside of their core competencies to various other players, allowing for companies to make flexible changes to their partner companies.

(1) Creating new pharmaceuticals

In terms of which companies serve as the originators of new pharmaceuticals, pharmaceutical companies account for more than 50% of small-molecule drugs, but biotech companies account for more than 50% of biopharmaceuticals, which is expected to increase in the future. Partnering with biotech companies will become increasingly important for pharmaceutical companies.

(2) Developing and manufacturing pharmaceuticals

CROs, which are in charge of development operations, and CDMOs, which are in charge of pharmaceutical manufacturing, have seen growth rates of 8.5% and 6.5% respectively, exceeding the growth of the prescription drug market. As seen in the growth of CROs and CDMOs, the outsourcing market is expected to grow accompanying the increasing number of clinical trials being conducted and biopharmaceuticals on market. CROs and CDMOs are already playing a role in the value chain of pharmaceutical companies in-lieu of subcontractors.

(3) New players in the market

Players from other industries that incorporate digital technologies into their core competencies are making in-roads into the pharmaceutical market due to the digitization of R&D functions, such as AI-based drug discovery.

What the world will look like in 2040

Shift to horizontal specialization and virtual models due to changes in how the pharmaceutical industry is structured

Sales per product are expected to decline as advancements are made in precision medicine, making it inevitable that drastic improvements will be made to the productivity of R&D activities and the entire value chain. For this reason, companies will need to transform their business models and corporate governance by virtualizing their operations and reorganizing their value chains. In doing so, what will the world look like in 2040?

1. Virtual worlds: Improving productivity in the real world based on predications made in the virtual world

[Shaping what the metaverse will look like in the field of healthcare]

In 2040, the metaverse will be applied to the healthcare field, in which various industry players, academia, government, patients, and consumers will gather within its virtual spaces and conduct the following activities.

(1) Product lifecycle management that involves multiple stakeholders

At present, academic conferences, consortiums, and communities are being formed in various fields, such as health and medical services, R&D, and data. This will result in the formation of multidimensional spaces in which people with different attributes and groups working towards different objectives can interact with each other. In such a virtual space, a flexible ecosystem will be formed amongst a wide range of players within the processes used to develop new drugs and digital health products and the subsequent product life cycle.

Academic conferences, research seminars, and more casual exchanges amongst peers will take place to share the latest technical information, individual experiences, and knowledge. In addition, this will allow for more useful exchanges of information to occur that contribute to the integrated value of medical services.

Furthermore, the metaverse will become a place to conduct proof-of-concept demonstrations for developing new products/services and developing products with user involvement, which includes understanding user needs, manufacturing prototypes, and receiving feedback based on user impressions.

(2) Ecosystem in which consumers help each other

Even patients whose actions are limited in the real world will be able to act freely and interact with others in the metaverse. The metaverse will allow these patients to discuss information on disease treatments or their own experiences to help encourage others, participate together in entertainment events, relieve their anxiety, and maintain or improve their motivation.

(3) Creating an environment that is more open to regulatory change

Until now, opportunities for people of diverse backgrounds to participate in discussions on regulatory reform were limited. At present, more attention is being paid to the increasing influence that consumers wield due to the spread of SNS. However, the metaverse has the hidden potential to be used as a forum for open discussion between individuals of diverse attributes in industry, government, academia, and the private sector. The metaverse will allow information to be shared to eliminate information disparities as well as enable constructive and open discussion. Some examples of this will include diversifying how people express their opinions (through conversation, chat, etc.) and allowing for opinions to be analyzed in real time.

[Using M&S to improve productivity]

1) Applications for R&D

In 2040, the utilization of healthcare information and data, such as databases that contain articles, drug discovery targets, as well as compounds, genomics, clinical information, and PHR will be encouraged, and advanced analysis technologies that use large volumes of data will be developed. These developments will connect and expand upon models for particles, cells, organs, and each region of the body, as well as improve the accuracy of simulations related to disease mechanisms and drug actions in humans. Using these simulations throughout the R&D process has the hidden potential to dramatically improve R&D productivity.

(1) High speed R&D cycles
This will expedite the drug discovery process, allowing for the series of processes that include the identification of drug discovery targets, design and optimization of compounds, and formulation to be analyzed and simulated in a continuous manner.
(2) Reducing the number of conventional clinical trials and improving success rates
This will identify optimal target diseases, dosage/administration, and concomitant drug/regimen for a pharmaceutical's mechanism of action and predict if the pharmaceutical is effective and safe.
(3) Streamlining decision-making processes
In addition to improving how accurately we can analyze the likelihood of a clinical trial succeeding, this will also improve how accurately we can analyze target patient populations, which will improve the accuracy of decisions made relating to non-clinical and clinical practices, or whether to engage in post-market indication expansion.
(4) Customizing drug development
A custom-made drug development model in which drugs are developed based on the identification of causative genes in patients with rare diseases at medical institutions will become feasible.

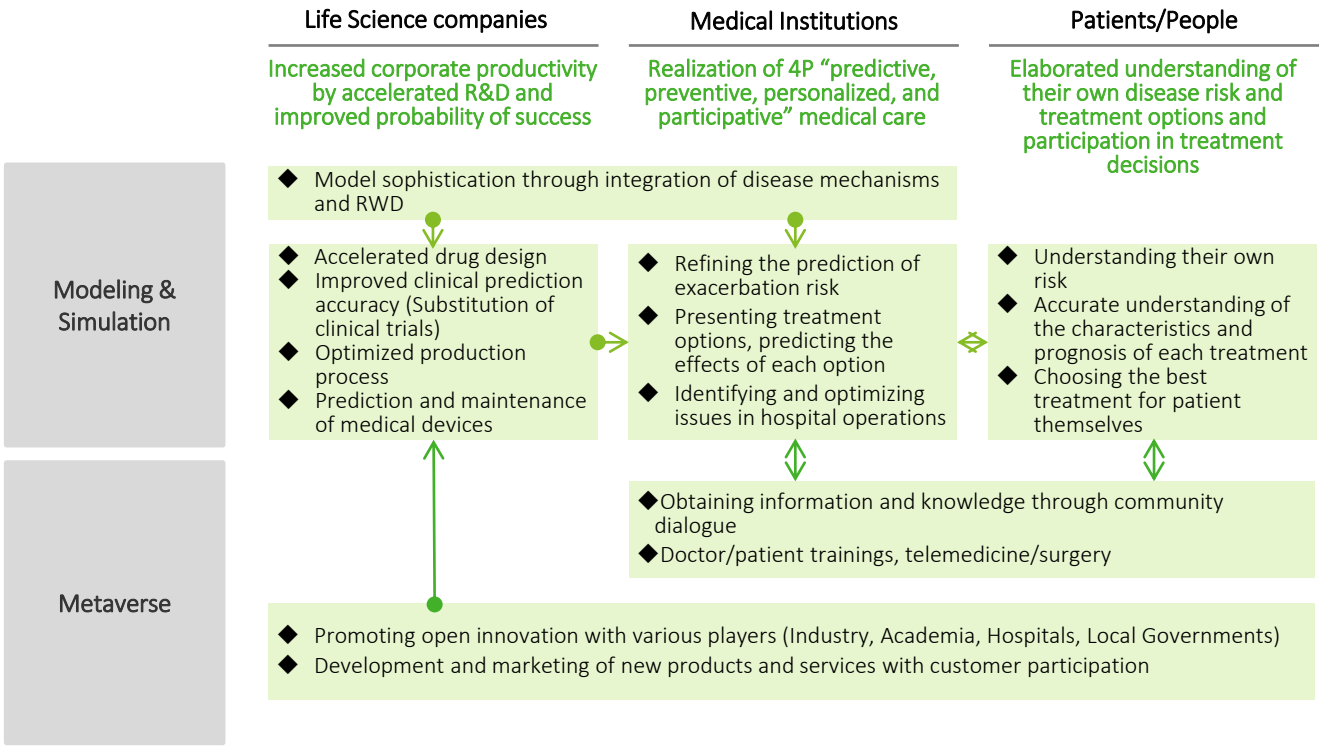
2) Applications for operations

Modeling is not limited to humans, but also has applications in product/solution maintenance, as well as hospital and factory operations. When introducing a new product or operating process, using a virtual model to analyze changes in the patient, operations, or product itself will make it possible to verify beforehand what effect these changes will have and what issues may arise.

3) Applications for clinical practices at hospitals

Modeling extends to actual clinical practice. Digital twins can be used to create a virtual replica of an individual patient's body, making it possible to predict what risk this patient has of contracting a disease/experiencing a recurrence, as well as how effective a drug may be and what side effects an individual patient may experience. Showing this information to patients receiving medical care will allow them to accurately understand what their treatments will entail and their prospects for recovery, as well as choose of their own volition optimal preventative measures and treatments. This will make it possible to implement the 4P (Predictable, Preventable, Personalized, Participative) medical approach, which will be ideal for patients.
From the perspective of medical institutions, this will result in higher quality and more efficient operations, which includes the process of making a diagnosis, selecting a treatment, and providing said treatment. Doctors will go over with their patients what method of treatment is being proposed to them based on simulations performed on human models and will then fill out a prescription. In addition to making the medical examination process more efficient, this will also reduce inconsistencies in treatment quality due to a doctor's specialties and ability (Figure 7).

Figure 7. How virtual spaces will look in 2040



2. Virtual pharma model: Building value chains with the help of experts across the world

In 2040, we will not only have models in which pharmaceutical companies maintain vertically integrated value chains. Models that use horizontal specialization to build value chains in collaboration with experts across the world to offer pharmaceuticals and solutions will also emerge, in addition to virtual models in which some functions are retained in-house while many others are performed in collaboration with external partners to allow for partners to be changed in a flexible manner. Until now, pharmaceutical companies have introduced pipelines and outsourced business functions (variable costs) through open innovation and partnerships. In the future, there will likely be a dynamic shift to retain only core functions in-house and separate the rest of the value chain from the company.

Pharmaceutical companies in 2040 will have several business models to select from.

(1) Vertically integrated model

A conventional self-sustaining model in which companies retain control of the entire pharmaceutical value chain. Innovative technologies will be made both in-house and imported from external sources, and the entire value chain will be digitized to improve productivity and aim to improve the company's overall corporate value.

(2) Drug discovery model

A business model centered on design capabilities that integrate disease biology and drug discovery technologies into product concepts, as well as drug discovery processes that take these concepts and uses them to quickly formulate and derive new drug candidates.

(3) Disease model

A business model centered on the ability to form customer networks that originate from the development phase and persist onto sales by consolidating knowledge on specific diseases and franchising pipelines. This model aims to offer total care to patients through the formation of disease ecosystems and intends to acquire medium- to long-term data and provide digital health products. The value chain in this model can either be in-house or virtual, and will be selected according to the disease, modality, or regional characteristics.

(4) Business platform model

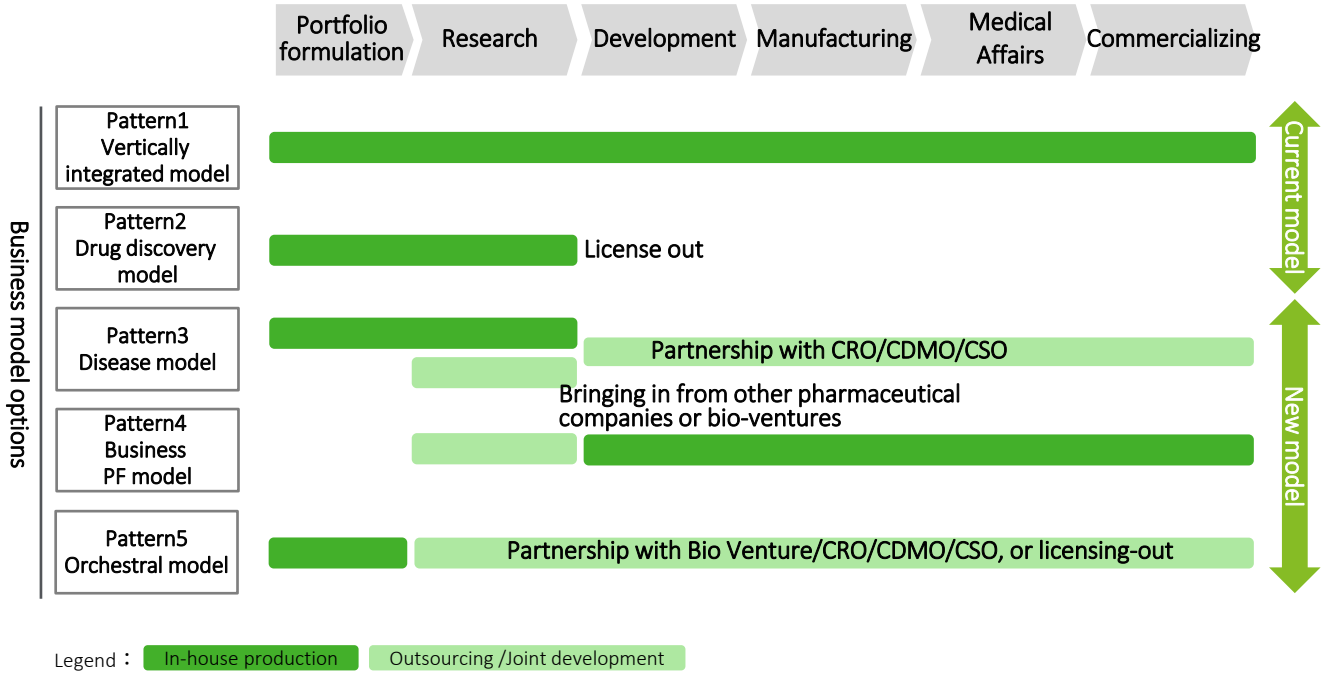
A business model centered on de facto operations that maintain large-scale workforce structures for the development, manufacturing, and sales functions, and work in close contact with medical institutions. Unlike existing outsourcing models, this model is consistent in how it works from the strategy to execution phases and functions as a platform within the target region. There is also the potential for CROs and CDMOs to elevate to this type of business model.

(5) Orchestra model

A model that only considers product licenses to be assets and minimizes the value chain. This model is centered on value chain virtualization in which companies search for the optimal partners to make up a flexible value chain for each disease, modality, and region. You could say that this model is an extension of the capital venture model. In addition to understanding what unmet needs exist, the core competencies of this model are its ability to search for and assess partners, commercialize products, and manage risk.

The emergence of this orchestra business model will reduce the barriers to entry for startup companies and other industries that lack the development know-how and financial resources in the pharmaceutical market, as well as allow companies to create high-value products in an efficient manner. On the other hand, pharmaceutical companies, which are the traditional players in this market, will be posed with the challenge of finding a position that allows them to remain competitive (Figure 8).

Figure 8. Virtual pharma business model options



What merits discussion in implementing these changes

[Virtual worlds]

1. Investing in and deciding whether to implement new technologies

What merits discussion in regard to MID3 and digital twins is determining when to judge whether these technologies have a practical application within the target disease area and R&D processes as well as to what extent these technologies should be implemented. We imagine that the technological progress in each disease area will differ, which includes technologies that provide entire industries secure access to highly confidential information spread across several companies and research institutes, methodologies that model disease mechanisms based on a variety of information sources, IT platforms that analyze complex and dynamic biological mechanisms at high speeds, and methodologies that review simulation results in an efficient manner.

Companies that can make huge investments may be able to build their own systems, but we can assume that there are companies that are unable to cover such costs through their own investment reserves. Under such circumstances, industry, government, and academia will need to work together to develop common industrial platforms as a part of the government policies seen in various countries to promote industry.

2. Reforming regulations based on a benefit-risk balance

Methods for evaluating pharmaceuticals and rules for using approval systems will need to be established. In MID3, the FDA is leading efforts to introduce a pilot program and is examining what rules to implement. However, manufacturers will also need to work with authorities to formulate rules in a constructive manner. What merits discussion here is to what extent these models have been validated, how accurate the derived simulation results are, and how much human clinical trials can be reduced or avoided as a result.

The medical system will need to build an appropriate system that can evaluate the reimbursement price of pharmaceuticals, what benefit these pharmaceuticals have for patients, and what unknown risks will arise if clinical trials are not conducted.

3. Finding acceptance at clinical centers

Modeling & simulation (M&S) is also being considered for clinical use at medical institutions. This will allow doctors who are trying to apply treatments to their immediate patients to predict the effectiveness and safety of those treatments and to then use those results to select treatments. Programs for predicting the severity of a disease have already been developed in Japan and overseas, and as the accuracy of such predictive programs improve, discussions will center around clarifying how to judge the willingness of doctors to accept these programs and the scope of their responsibilities.

【Virtual pharma model】

1. Redefining the core function of pharmaceutical companies

Among the many existing functions that a company possesses, such as research, development, manufacturing, medical affairs, and sales, companies will need to redefine which functions should remain in-house or be outsourced as a source of their competitiveness. Until now, pharmaceutical companies have been inconsistent in which functions remain in-house and which functions are outsourced. This holds especially true for operational functions. However, these companies will need to consider frameworks that look beyond their operational functions as this industry looks for ways to dramatically improve productivity.

2. Finding a balance between retaining functions in-house and outsourcing (risk management)

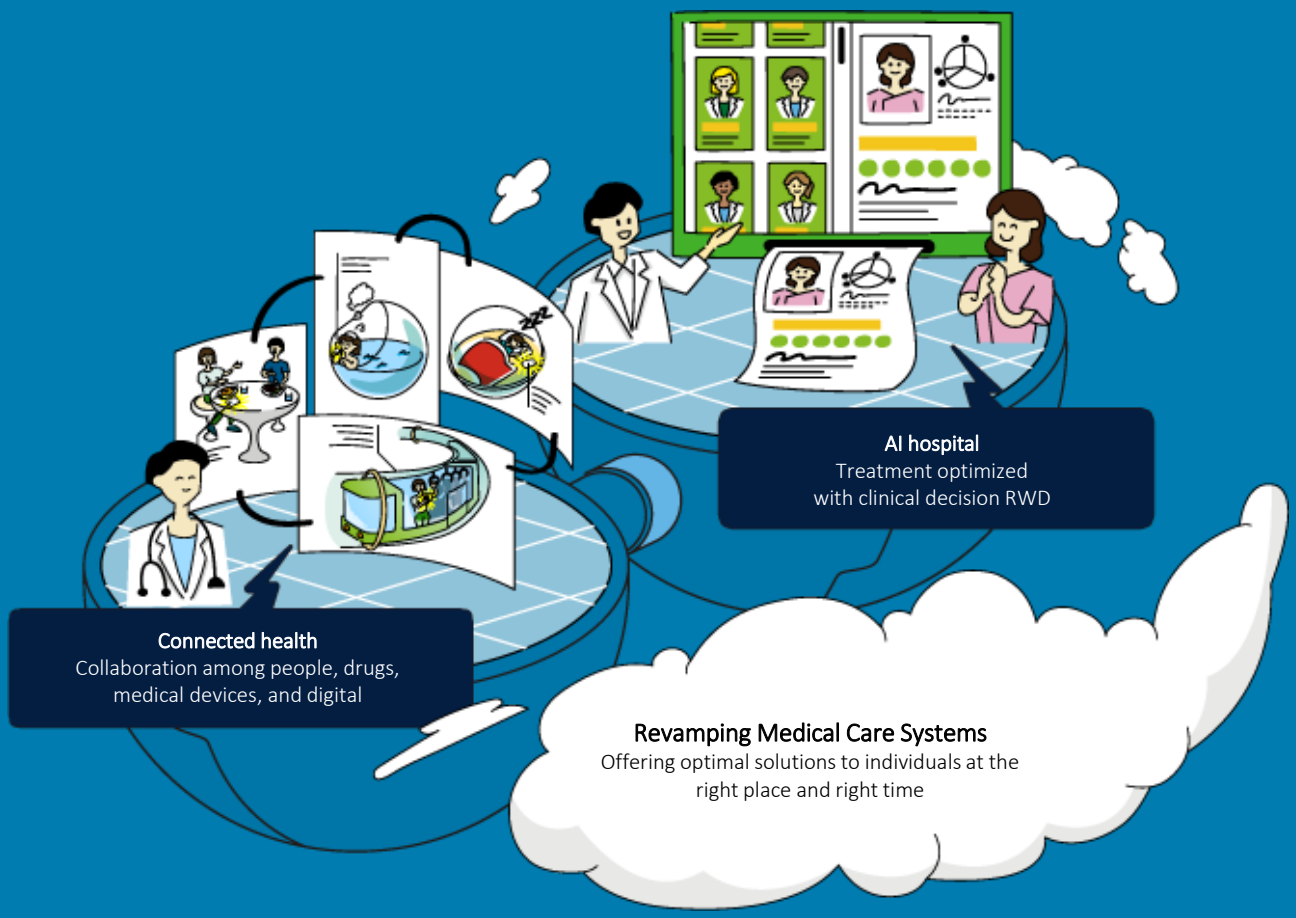
What merits discussion is whether companies should retain their core functions but outsource all non-core functions or continue to retain a certain number of these functions. While it will be possible for companies to put together models in which individual functions are operated in collaboration with partner companies, these companies will need to consider what workload their partners can accept and the maturity of their functions. The expectation is that the digitization of entire operations will gradually reduce their dependence on humans, but careful judgement will be required as companies will need to offer a stable supply of pharmaceuticals and safety information as a continued part of their social responsibilities.

3. Restructuring corporate systems

We will need to reexamine/restructure the kind of workforce systems pharmaceutical companies should possess. Virtualization will not just become a possibility at the individual function level, but also within said functions. There are already some companies that are managing their best workforces as virtual organizations on a global scale. However, location-based restrictions will disappear if operations continue to undergo further digitization. How to combine functions, people, and digital technologies on a global scale will be a point of discussion in building these systems.

What sort of healthcare will the “10 drivers of change” bring in 2040?

d. Revamping medical care provision systems



Challenges

There is an urgent need to drastically reduce social security costs, which could include preventing chronic diseases that require huge medical and nursing costs and shifting to VBHC

Japan's medical provision systems are facing serious challenges.
From a public financing perspective, the gap between social security costs and the income from insurance premiums has exceeded JPY 50 trillion, with the fiscal deficit for social security costs having already reached its limit[*29].
Measures will need to be taken to control social security costs, which includes a shift to preventing chronic diseases such as dementia and diabetes, which require large medical and nursing expenses the more acute symptoms become, as well as a transition to VBHC.
From a patient's perspective, elderly patients in rural areas continue to be cut off from receiving adequate medical care. This is due to the age-related decline in their bodily functions and the so-called "North-South" problem, in which patients can only receive advanced medical care, such as cell and gene therapy, at core hospitals located in central Tokyo. Furthermore, under current medical provision systems, consumers have to make efforts to look after themselves to prevent illnesses or take action during the pre-symptomatic stage prior to diagnosis, meaning that health and medical services are unable to intervene in an effective manner.

[Uneven distribution of medical resources]

1 Barriers to accessing medical care

The general belief is that emerging countries are faced with challenges in providing access to medical care. However, even in Japan, 70% of patients with chronic diseases feel that they are not given sufficient access to medical resources[*30], and it has been reported that this largely diverges from the understanding of medical professionals.
Causes for this include a lack of ability in rural areas to accommodate patients due to a shortage of doctors, difficulties in balancing work and hospital visitations, and difficulties in visiting hospitals due to aging. More recently, the spread of COVID-19 has served to aggravate this issue of accessing medical care.

2. North-South problem for medical care

While innovative treatments have emerged, such treatments often require a high degree of expertise and do not guarantee that all patients will equally benefit from such treatments.
For example, facilities that provide innovative cancer gene therapies are limited to university hospitals, and cancer gene panel testing is available only at specific cancer centers. Patients can only receive the latest treatments from specialized medical institutions in metropolitan areas that possess advanced technologies.
Against this backdrop, a serious medical gap is emerging between the residents of urban and rural areas.

[Growing social security costs]

1. Increase in chronic diseases

With populations in developed countries continuing to age, we will see more patients with chronic diseases that require long-term treatment. For example, compared to 2010, the number of patients that have experienced a cerebral infarction or are suffering from ischemic heart disease is expected to increase 1.5 times and 1.3 times, respectively, in Japan by 2030[*31].
It is well known that chronic diseases generate huge social costs. As an example, it is estimated that dementia costs Japan JPY 14.5 trillion on an annual basis, which includes medical, nursing, and care costs[*32].
The fear is that such age-related changes to disease structures will lead to even more increases in social security costs.

2. Increasingly expensive medical care

Various modalities have emerged due to rapid evolutions in technology. Pharmaceuticals that make full use of these advanced biotechnologies will result in treatments that cost tens to hundreds of millions of Japanese yen per person on an annual basis due to the effectiveness of these drugs and the complexity of the manufacturing processes involved with producing these pharmaceuticals, which could have an impact on Japan's public medical insurance.
In the United States, which stands at the forefront of developing innovative pharmaceuticals, the cost of medical care per patient is continuing to increase on a year-by-year basis, which, in addition to changing disease structures, is yet another factor contributing to growing social security costs.

[Overemphasis on self-care]

There is a lot of talk about preventing the onset and reducing the severity of chronic diseases, which has led to various systems being established to encourage companies and insurance associations to intervene. However, in their current state these systems are not functioning well.
The fundamental factors behind this dysfunction include (1) lack of literacy, (2) lack of judgment criteria, and (3) underdeveloped infrastructure.
(1) Lack of literacy
Consumers, without having received the appropriate information, do not possess the literacy to determine what information is correct amongst the deluge of information on health and medical services.
(2) Lack of judgement criteria
There is a lack of evidence regarding many existing health and disease prevention initiatives, as well as a lack of indicators to discern which solutions are of good quality.
(3) Underdeveloped infrastructure
Communities and social infrastructure that focus on promoting health in order to prevent disease are underdeveloped and do not make it clear what parties should be consulted on health matters. In addition, various medical societies are advocating the importance of shared decision making when it comes to treatments, but patients are presented with few opportunities to select doctors and treatment plans that align with their values. Although the level of treatment an individual can receive for an illness has improved dramatically, these same individuals will be forced to search on their own for a solution to the mental/social issues (such as feeling anxiety towards their illness/treatment as well as struggling to continue working while leading a normal life) that accompany their illness.

Market/technical trends

Core technologies that will revamp medical care provision systems: AI hospitals and connected health

Digital health products such as telemedicine will be involved in revamping medical care provision systems. The global market for these major products is expected to experience rapid growth at a CAGR of about 19%, reaching approximately JPY 100 trillion in 2025[*33].
In this section, we would like to look at some examples regarding AI hospitals and connected health, which are likely to serve as core technologies in revamping medical care provision systems.

1. AI hospital: Babylon Health

Babylon Health is a company that provides AI-equipped online medical care systems, enabling its users to receive the necessary medical services in one stop, with AI doctors acting as the core of these services. When a user reports their symptoms via a chatbot, an AI will diagnose their condition, determine whether it is necessary to seek medical attention, and even make an appointment for an online medical examination or, if necessary, a visit to a medical institution.
The NHS has certified Babylon Health's AI hospital service as an alternative to a GP and has 2.3 million users in the UK (with 5.6 million users across the globe).
In the UK, all individuals must first see a designated GP, except in the case of an emergency. GPs have a large number of patients, which results in many cases in which patients cannot secure an appointment until several weeks later. This service, which can offer immediate online consultations, has been launched amidst these troubling circumstances and has been able to attract a certain number of patients.
What makes this business special is that as it continues to acquire huge volumes of data from an increasing number of users, the quality of its services will improve (accuracy of AI-based diagnosis), leading to the acquisition of more users. Babylon Health is expanding its business through this value-enhancement cycle.

Furthermore, there is a high need for businesses that offer digital replacements for human-based medical care, such as AI hospitals, in developing countries where medical care provision systems are inadequate. Babylon Health is currently planning to expand its business in Africa.
For example, in Rwanda, Babylon Health is partnering with the Ministry of Health to work with local medical services in spreading their services. Patients first receive an initial diagnosis through an app using AI, and if the problem cannot be resolved, a nurse will respond. If the problem is too difficult and still cannot be resolved, a doctor will respond using telemedicine.
As a result of this service, only 17% of users ultimately required treatment at a hospital, with 83% of patients able to figure out remotely what treatment to receive.

2. Connected health: Livongo Health

Livongo Health offers corporate employees with comprehensive lifestyle disease prevention programs that cover diabetes, hypertension, mental illness, and more.
In addition to providing devices to employees, using AI to analyze the data provided from said employees, analyzing the data and successful behavior of people similar to those employees, and then offering advice, a professional coach will call employees to follow up if the data that was measured greatly exceeds its proper value.
Furthermore, Livongo Health provides its users health knowledge and online communities that best suit them and supports them in exchanging information that will be useful in changing their behavior.
Demonstrating the effectiveness of this program has resulted in HbA1C levels, a standard indicator used to diagnose diabetes, to fall by 0.8 points, blood pressure values to decrease by 10mmHg, body weights to decrease by 7.3%, and mental illness to improve among 55% of patients. In addition, a study of two large clients found that this program had succeeded in reducing the cost per patient by USD 996 per year.
As a result, Livongo Health has seen its sales and number of users double or triple each year and has thus found success in obtaining a very large number of users (4.5 million users as of 2020).
An example of this is when Livongo Health signed a large-scale contract with GEHA (Government Employees Health Insurance Association), which resulted in them acquiring 2 million new users.
Furthermore, Livongo Health was acquired by Teladoc Health in 2020, enhancing their collaborative work on telemedicine.
In addition to preventing diseases and promoting health, integrating connected health with AI hospitals in this way is expected to make medical services even more efficient as it can contribute to preventing the onset and advancement of diseases by offering medical treatments.

What the world will look like in 2040

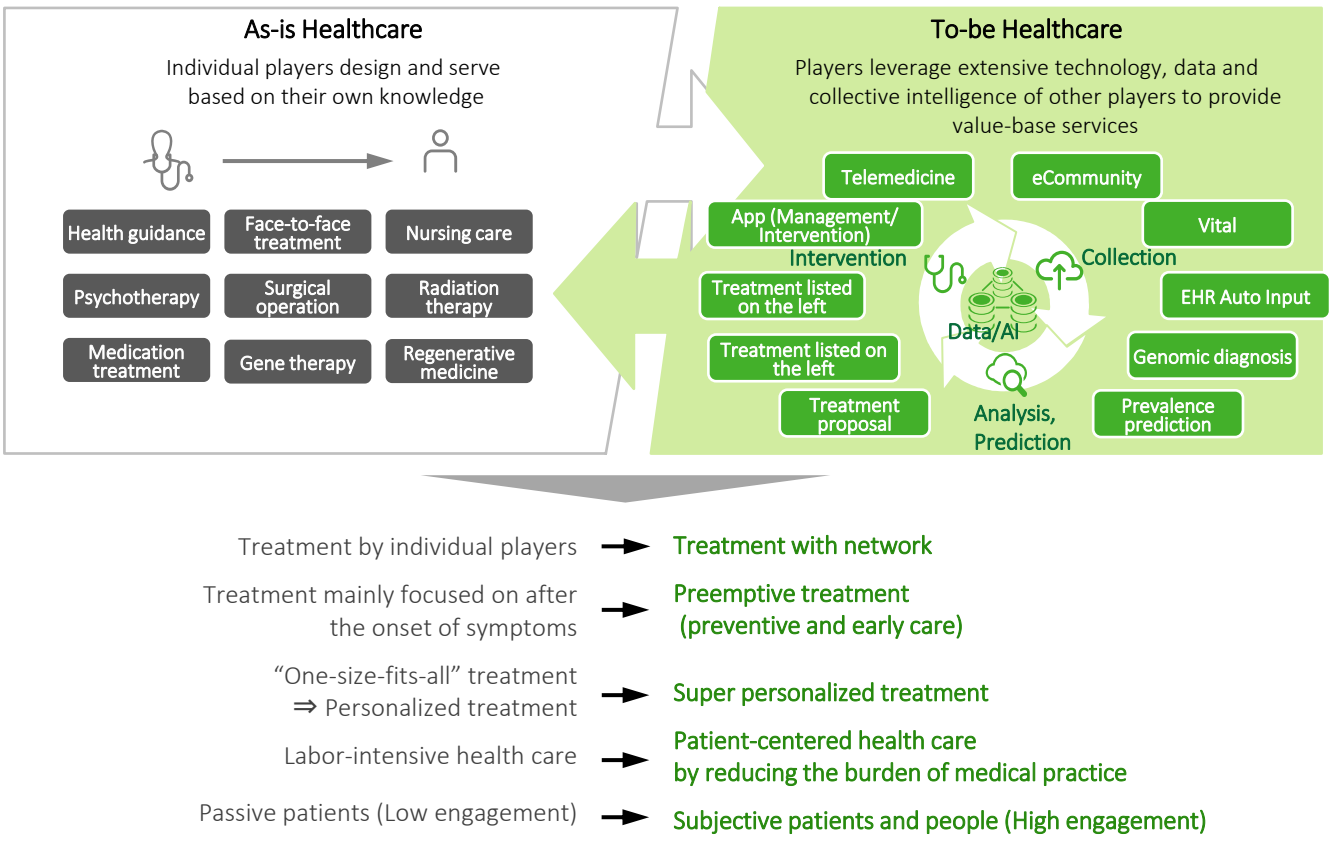
Medical care provision systems will be revamped to provide individuals with the most optimal care at the right place and right time

In 2040, AI hospitals and connected health will play a central role, with PHR data, which is gathered at all times from the variety of situations experienced during a consumer's life journey, and AI making it possible to predict the onset of diseases with high levels of accuracy, and thus allowing hospitals to intervene with immediate and optimal health and medical services.

1. AI hospital: Providing all patients with the most optimal medical care

Medical facilities and hospital departments will be offered cloud-based AIs that have undergone sophisticated training based on the characteristics of the residents in each medical zone. This will allow residents in both urban and rural areas to select the latest and most appropriate treatments.
In addition, this AI will analyze in real-time medical data gathered from patients to determine whether the medical treatment provided was truly effective as well as whether the outcome was cost-effective and will then provide this feedback to medical professionals. This will allow for modifications to be made to medical services that will help optimize them. This will also contribute to the efficiency of medical operations. Improvements such as the initial triage of patients, automation of medical records, and support in receiving informed consent, are expected to reduce the medical burden placed on medical professionals, mainly doctors (Figure 9).

Figure 9. The kind of future medical care that data and AI will bring about



2. Connected health: Visualizing individual health conditions and supporting health promotion

Information on all life scenes that have occurred since an individual's birth is accumulated as a part of their history and can be viewed at any time. This is not just limited to health and medical information, such as examinations or treatment history, but could potentially also include vital signs, purchase information, behavioral history, and information on financial transactions. This information will serve as a foundation for individuals learning on their own what signs indicate deteriorating health, how to understand their health conditions, how to identify underlying causes, and how to find the optimal balance in their health investments.

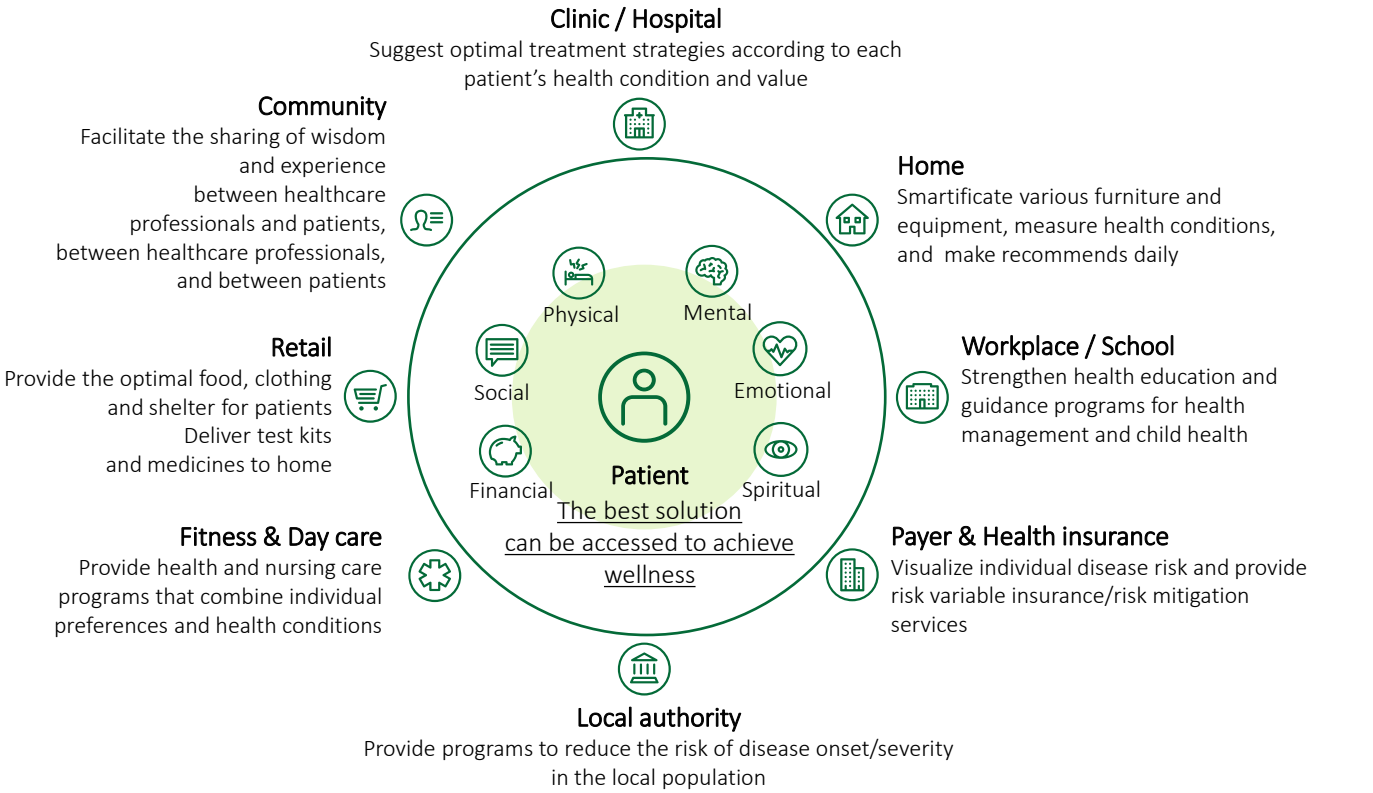
In addition, an AI will analyze data gathered at all times from various situations, which has been made possible with the spread of certain technologies such as wearable devices, implantable devices, and smart houses. This AI will provide individuals with highly accurate predictions on the onset/advancement of diseases, as well as options that allow for immediate and optimal interventions to take place. This will eliminate problems associated with medical care access and ensure that medical facilities always intervene with the most optimal medical treatments. Furthermore, prior, effective intervention is expected to prevent the onset and advancement of chronic diseases, curb increases in social security costs, extend healthy life expectancies, and contribute to the well-being of an individual throughout their life.

In addition to the digital and data-focused solutions mentioned in the prior section, local communities will offer care services that integrate topics such as health, medical care, insurance, nursing care, and entertainment in an organic manner. Furthermore, providing living spaces in which housing, transportation infrastructure, and entire cities contribute to promoting health and treatments will result in societies that on a whole supports what healthcare is offered to its consumers.

Monitoring health and medical outcomes will allow each local government to contribute to correcting biased outcomes, improving cost-effectiveness, and supporting the vitality of consumers.

Connected health differs from the idea of maintaining and promoting one's health, which places an emphasis on consumers helping themselves, in that it offers options that are tailored to individuals looking to support themselves. We believe that finding a synergy between mutual and public assistance will assist in forming new health and medical systems (social orders) that are focused on helping people in the truest sense (Figure 10).

Figure 10. The significance of connected health



What merits discussion in implementing these changes

1. AI hospital

We believe that the following three points will serve as hurdles in implementing AI hospitals.

(1) Addressing the increasing diversity found in doctor's specialties

In the process of upgrading medical systems, which could include incorporating AI into medical treatments, providing feedback on medical treatments through data analysis, and collaborating with a variety of healthcare players, what functions will be needed to provide medical care will dramatically change. Doctors, who play a central role in medical care, will be required to play new roles (the following eight types) in addition to their traditional roles.

- Complex care manager/Care integrator: A playing manager who brings together a wide variety of medical professionals
- Digital consultant: Devising optimal diagnosis and treatment methods by making full use of advanced technologies
- Analytic consultant: Providing insights for upgrading/streamlining medical professional teams
- Proceduralist: Designing medical operations and building mature medical environments
- Data and informatics specialist: Interpreting diverse data and providing optimal solutions to groups and individuals
- Researcher: Integrating and interpreting diverse information sources to provide optimal solutions to groups and individuals
- Executive: Conceptualizing future healthcare ecosystems and presenting paths to achieving them
- Educator: Providing education on new clinical models based on their academic knowledge

Securing human resources capable of fulfilling the above roles will be a challenge. For this reason, radical human resource development plans will be needed that include revisions to education curriculum, with a focus on medical schools.

(2) Building regional medical systems that implement recommended treatments derived from algorithms

When AI algorithms are put into clinical use, the AI may make a request to conduct tests needed to make definitive diagnoses that differ from the doctor's opinion. There may also be situations in which the AI encourages the use of advanced treatment methods or high-level collaboration between multiple departments, all of which will put pressure on medical facilities to meet such requests. Because individual medical institutions are limited in their functions, it will be necessary to develop an advanced regional medical cooperation system that can offer these functions.

(3) Giving doctors the discretion to address evolving algorithms

It is unlikely that AI will have the final decision-making power to diagnose or treat patients, but as algorithms become more accurate, differences in opinion between doctors and AI will become more noticeable. It will be more important to develop a decision-making process that assists in determining, for example, how to deal with these differences in opinion and come to conclusions that are agreeable to both the patient and the doctor.

2. Connected health

The following four points will serve as hurdles in implementing connected health.

(1) Guaranteeing data reliability and continuity

Connected health is based on a system that reliably gathers user data at all times. For this purpose, data must be collected with the cooperation of various companies to ensure that not just devices but also all usage scenarios are covered. These usage scenarios will include house builders and automobile manufacturers. Standardizing not only EHR but also PHR will be essential for data integration.

(2) Building systems for evaluating health indicators and recommended treatments

In order to develop the various intervention solutions that will form connected health, indicators will need to be built to prove their utility. What will be extremely important is how to evaluate the utility and feasibility of the indicators themselves, as well as how to implement said indicators in society.

Furthermore, controls will be needed to make improvements to the various solutions that are based on these indicators and to withdraw certain solutions that fall below certain levels from the marketplace.

(3) Compensation and responsibility

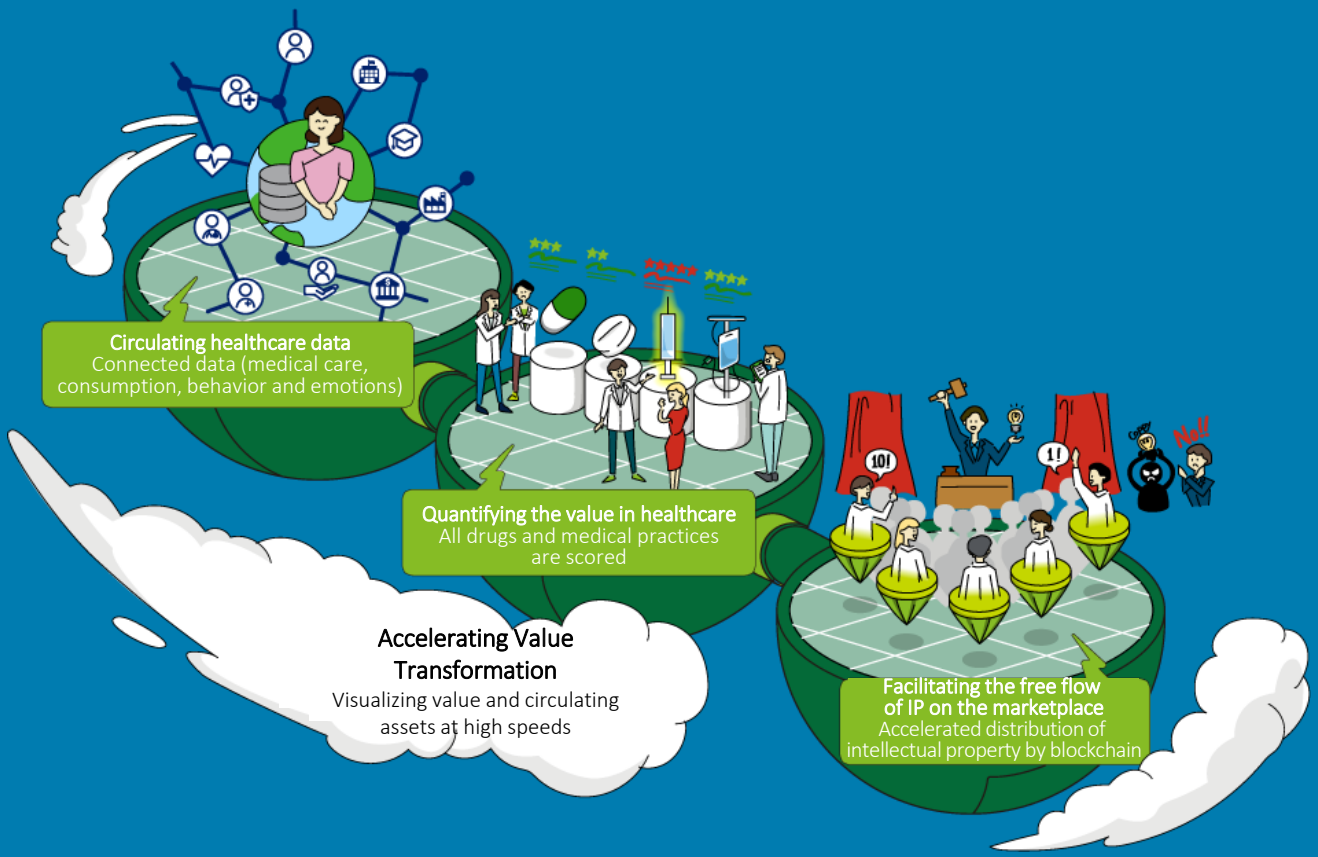
Connected health will present recommended treatments that best suit an individual consumer, but it should not be assumed that a positive outcome is completely guaranteed. Furthermore, when working closely on multiple solutions, it may be difficult to determine where responsibility lies. Assuming such a situation does develop, what will be needed is to set rules regarding compensation as well as the responsibility of individual users and service providers, which will serve as a basis for maintaining a healthy social order.

(4) Cybersecurity

Unifying various sets of data will improve the value of said data. Historical precedence has made it clear that evolutions in technology are accompanied by negative effects, meaning that it is inevitable that cyberattacks will become more intense. As various players connect to each other and expand their networks, there will be a continued need to address how to protect highly sensitive health and medical data in a secure manner.

What sort of healthcare will the “10 drivers of change” bring in 2040?

e. Accelerating value transformation



Challenges

The concept of healthcare is shifting from health to well-being; What is being sought is holistic solutions to the various pains that consumers experience during their entire life journey

The concept of healthcare will shift from health to well-being as we move towards 2040. For this reason, holistic solutions to the various pains (challenges faced by consumers and patients) that each consumer experiences during their entire life journey are being sought out. However, our current healthcare systems are only able to cover a portion of this entire pain.
This is due to deficiencies in the following areas: (1) constructing large-scale/diverse data sets, (2) developing environments to distribute IP and basic research, and (3) defining medical value indicators.

[Lack of large-scale/diverse data]

1. Delays in integrating medical databases

Learning data is essential for developing innovative healthcare products and services. In Japan, substantial progress has yet to be made in developing environments that can make use of medical data, with industry, government, and academia accumulating data for their own individual purposes. At present, the only data in use is data on medical insurance claims and small-scale EHRs. On the other hand, companies overseas, such as private insurance companies, are not just integrating and utilizing the EHRs of tens of millions of people but are also combining and utilizing this data with other types of data, such as genetic and insurance claims data.
As a result, the West has taken the lead in terms of the quality and quantity of data being used in areas such as disease mechanism research and pharmaceutical development, which is one of the hurdles that Japan must overcome to create its first set of innovative healthcare products and services. In addition, Japan is lagging behind in developing AIs that support complex medical decisions and make predications based on a patient's PHR due to a lack of learning data, resulting in the development of such AI being focused overseas.

[Hoarding of intellectual property and research]

1. Underutilized research

Life science companies will need to integrate the results from a variety of advanced research topics such as AI and IoT into the development of innovative pharmaceuticals, the digital transformation of value chains, and the development of digital health products.
The main method for achieving this is through open innovation. However, currently only 47% of companies in Japan practice open innovation. This is much lower than Europe and the US, where 78% of companies practice open innovation. In particular, the practice of outbound open innovation, which is when a company allows its IP to be used by external parties, has yet to gain widespread acceptance[*34].
As a result, startup companies in Japan are not leading the development of pharmaceuticals and digital health products such as advanced medical AIs, which require large amounts of resources to develop. Instead, what is mainly seen is either large companies developing products with a limited set of uses, or universities undertaking small-scale development projects. In contrast, overseas it is common to see spinout companies form based on research conducted by large companies. This has resulted in various digital health products being developed based on research that was not being utilized by larger companies and has continued to offer patients a multitude of value.

[Limited approaches for demonstrating the value of products and services]

Value-based healthcare (VBHC) is "an idea that emphasizes patient treatment outcomes and allocates medical resources and costs in an optimal manner, taking into account patient preferences and values." In introducing VBHC, a mechanism needs to be established to standardize outcome indicators, such as treatment results, and cost indicators, such as investment resources, for health and medical related products and medical practices, as well as to share this information with industry, government, academia, and the private sector. However, the following major issues still exist.

1. Lack of standardization in indicators of value

What is the most appropriate indicator of value will differ depending on the stage of the individual's life journey and disease. These indicators will also differ depending on their purpose, which could include evaluating products such as pharmaceuticals or medical practices. However, the lack of common indicators is a major issue in promoting VBHC. Medical societies are publishing clinical guidelines for various diseases, but with an increasing number of diseases making use of common indicators in their diagnosis and treatment, we believe that an urgent task facing the relevant medical societies is working together to build a set of common indicators that can be implemented as nominal clinical and real-world data.

2. Demonstrating medical value places too much emphasis on clinical trials

Clinical trials for receiving drug approval are based on prospective comparative studies. The resultant low cost-effectiveness from re-collecting data on existing treatments and the burden placed on patients involved in placebo treatments have long been issues.
Similar to pharmaceuticals, there is currently too much emphasis placed on clinical research outcomes in proving the medical value of digital health products, which has led to low cost-effectiveness. As a result, startup companies are reluctant to develop digital health products with high added value.

Market/technical trends

Developing technologies for circulating data and content

[Market trends]

In order to resolve the aforementioned issues, the government is taking the lead in promoting various policies, some of which include integrating EHR/PHR data standards and developing environments for obtaining patient consent.

In Japan's medical data market, it is estimated that medical big data analytics will reach JPY 642.2 billion in 2032[*35]. Although the utilization of such data has been gradual in its spread, it is assumed that there will be an increasing need for such medical data. An emerging example of this is how the Ministry of Health, Labour and Welfare (MHLW), in light of increasing opportunities to introduce VBHC, is proposing as a part of "Heath Care 2035" that the technologies of healthcare providers and the benefits of their medical products (i.e., medical technologies) be evaluated in consideration of the value these products and services could offer to patients and that these evaluations be incorporated into medical fee points. Another example of this is how the Japan Council for Quality Health Care (JCQHC) has established a consortium with organizations such as the MHLW, various hospital groups, and medical associations as a part of its project to develop systems for improving the quality of medical care and has begun preparing a guide for developing and maintaining medical quality indicators to help standardize such indicators.

In regard to analyzing and utilizing information on IP, the Japan Patent Office is taking the lead in introducing on a trial basis a service for analyzing patent information based on the idea that patents are a source of corporate R&D strategies and business strategies, such as searching for business partners, and contribute to promoting innovation.

[Technical trends]

In this section, we will discuss how Japan is building the necessary platforms to develop innovative healthcare products and services.

1. Integrating data standards

Currently, both EHR and PHR standards are being developed to encourage the utilization of data. In order to unify the EHR standards used amongst the various manufactures and medical institutions, the government is leading efforts to integrate this data by combining the conventional SSMIX and HL7 FHIR standards[*36]. Furthermore, six overseas companies, which include Microsoft, Google, and Amazon, announced in a joint statement in August 2018 their adoption of FHIR[*37]. In the future, more outside cooperation on EMR/EHR is expected under these standards.

On the other hand, the General Incorporated Association PHR Council is holding discussions on PHR standardization. In 2021, this same organization published its recommendations on creating guidelines for PHR services in the private business sector[*38], in which discussions on standardizing information on health checkups and collaborating via Mynaportal (a portal site for Japan's individual number holders operated by the government) are mentioned as the first initiative.

2. Data utilization platforms

To develop environments in which private businesses can more easily use medical information, the government is currently taking the lead in developing laws and regulations that allow these companies to acquire medical checkup information and detailed information on medical fees through Mynaportal if the consent of the party in question is obtained.

Prior to this, information on health checkups from 2020 and beyond could be viewed through the Mynaportal starting from October 21, 2021.

In addition, the Next Generation Medical Infrastructure Act, which allows medical information to be collected without the consent of the party in question, came into effect in 2018. Two companies, NTT and ICI, are conducting their operations having received certification under this law.

If such utilization platforms are enhanced, this will make it possible to collect a variety of information that is linked to EHRs.

3. Non-fungible token (NFT)

A non-fungible token is a mechanism that issues a digital asset with metadata, such as the asset's creator or owner, linked to a unique ID that cannot be replicated. The transaction data for these assets are managed via blockchains. At present, this technology is finding use in online transactions involving digital content such as digital art, product designs, and in-game characters/avatars. With counterfeited goods and pirated copies causing more and more serious damage, the non-fungible nature of NFTs is attracting attention as a means of guaranteeing the security of all online transactions.

In trading IP and research as digital content on the marketplace, the authenticity of such content will be important. If a pirated copy were to be purchased and used, the purchasing company would be at risk of litigation, making it difficult for active trading to take place. In the life science industry, where growth is driven through the handling of IP, NFTs will be an important element in forming future markets that facilitate the free flow of IP, serving as a tool for determining the authenticity of such content.

What the world will look like in 2040

Value transformation will accelerate; Value will be visualized and assets will circulate at high speeds

As we move towards 2040, the core value of healthcare will shift from health to well-being. For this reason, it will be important to both verify the effectiveness of healthcare policies aimed at maintaining sustainable social security costs and to promote innovations that will resolve the various pains that individual consumers encounter throughout their life journey in a holistic manner.

1. Circulating healthcare data

Data will be one of the important social resources in achieving the above. Circulating large and diverse data sets will allow all players (industry, government, academia, and individual consumers) to benefit. On the other hand, this will require a system that respects the individual and maintains fairness throughout the entire industry.
In this kind of world, the following three results would be achieved.

(1) Rapid growth in data types and sizes

In order to eliminate the pain a patient experiences throughout their life journey, healthcare companies will need to analyze not only conventional medical data, but also behavioral and vital data that exists outside of hospitals, as well as data that can be used to understand the patient's inner self, such as their personal preferences and values. In addition to medical data such as disease names and test values, omics information such as genes or proteins will be integrated to better understand biological systems and diseases mechanisms. This will result in a dramatic increase in the amount of information that can be handled. Furthermore, the spread of digital devices will allow healthcare companies to collect more objective data on patients found outside of hospitals in addition to the above-mentioned medical information, as well as health checkup and prescription information to be integrated using government-developed data utilization platforms. On top of this, useful consumer data will be gathered in addition to healthcare data as a result of different industries working together.

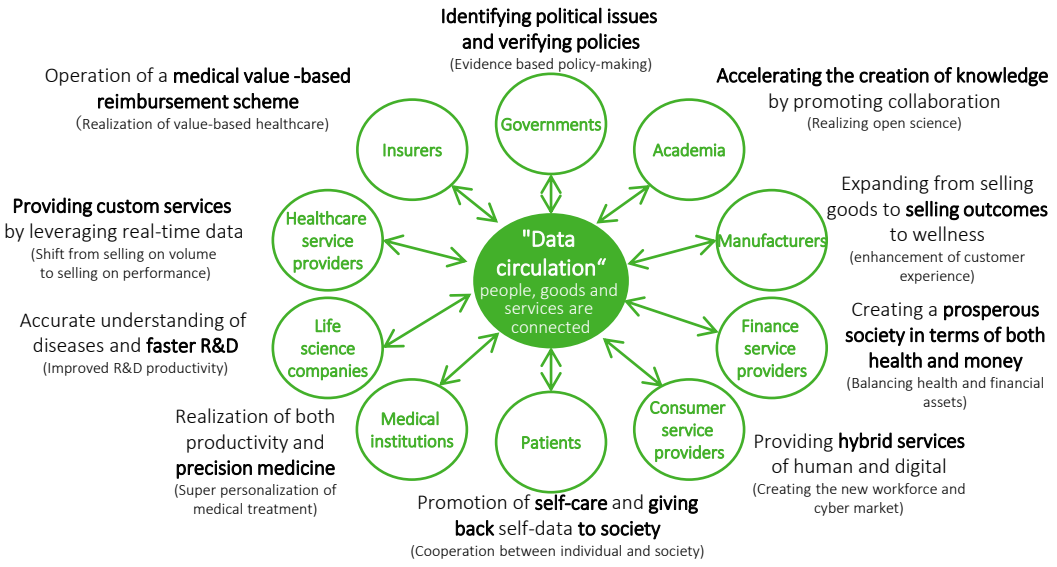
(2) Democratizing data

Due to the backlash platform businesses have faced from collecting customer data in secret and amassing vast amounts of wealth, Japan will also see rigorous debate concerning data ownership. As there are more opportunities to consolidate and handle data on more diverse healthcare topics such as genomes, medical care, and lifelogs, decisions on how this data is utilized will be left up to the individual given the high sensitivity of said data. In addition, since data is also a public good, it will be essential to develop laws and regulations that allow for free access to data without waiting for an individual's consent when said information could be utilized to benefit the public.
Under these circumstances, healthcare companies will be required to play a role in creating new value that contributes to improving consumer convenience. These companies can fulfill this role by making use of this diverse data on healthcare to expand the value of their own businesses with the consent of patients and offer this data in the form of data hubs to various external companies, medical workplaces, and patients themselves.
The aforementioned data hubs will play an elevated role in coordinating with local municipalities and serving as information banks. Local municipalities and private companies will combine the data in their possession to conduct activities that contribute to the health and medical services offered to individual data donors. Providing anonymously processed data from individuals that have consented to their data being provided to third parties to various companies in the form of information banks and then returning the profits obtained from these transactions as compensation to those individuals will help to circulate data and value. Utilizing this kind of data will make it possible for companies to create advanced healthcare services.

(3) Accessing data for the public's benefit

Although ownership of medical data belongs to the individual, there are cases in which this medical data is used for the public's benefit, such as during emergency responses to pandemics or earthquakes, as well as in clinical research that is being conducted to overcome intractable diseases. In addition, data utilization by the Japanese government will be essential in prolonging healthy life expectancies and improving the happiness of consumers while curbing increasing social medical expenses in Japan's super-aged society.
Under these circumstances, it is likely that the government will have free access to personal medical data.
In the future, governments will inevitably be required to hold themselves accountable to consumers on how their taxes are used within the medical field based on data. Consumers will likely demand that the effectiveness of healthcare policies be published and third-party evaluations be conducted on their cost effectiveness (Figure 11).

Figure 11. The significance of circulating healthcare data



2. Facilitating the free flow of IP on the marketplace

Intellectual property (IP) is a source of corporate R&D and business strategies such as searching for business partners. In 2040, IP will be traded online and IPs that have been hoarded by companies will come into active circulation, accelerating open innovation.

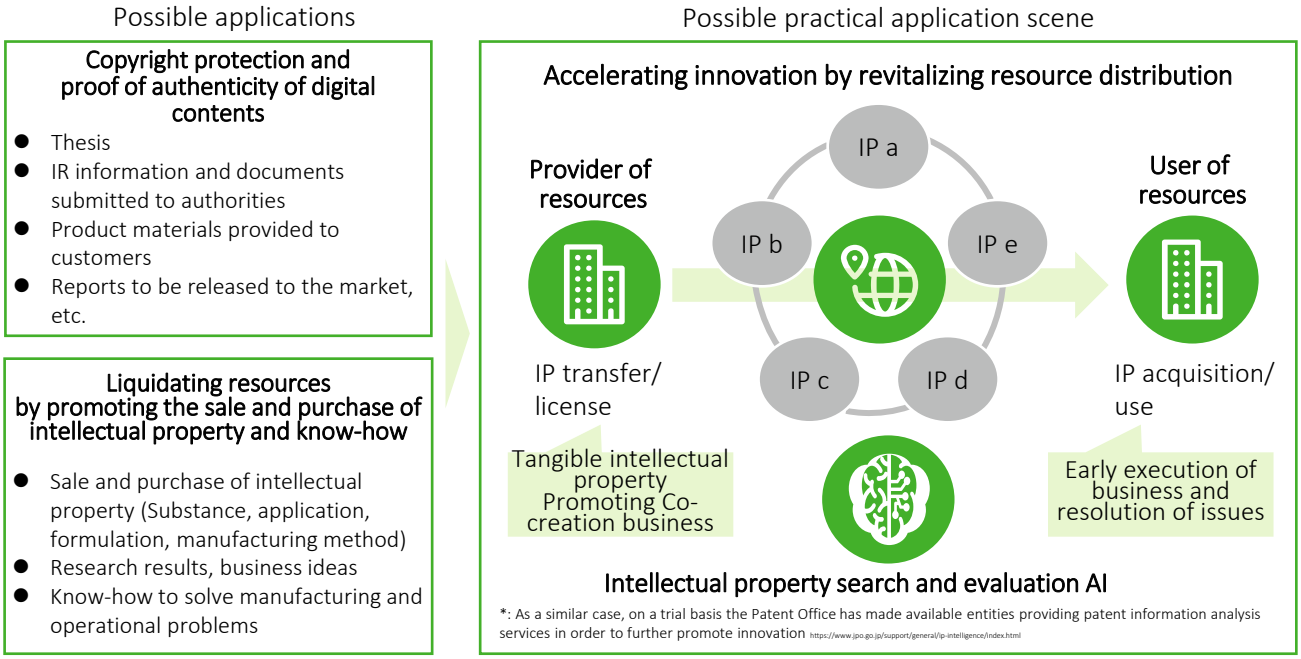
(1) Utilizing non-fungible tokens (NFTs)

Because digital content is easily copied, there is a need to protect the copyright of such content and prove its authenticity in order to facilitate the sound and active trading of IP and know-how on the market. In 2040, NFTs using blockchain technology will be used to prove the authenticity of digital content such as IP and know-how, which will then be traded on the marketplace. In addition to IP and research, various tangible and intangible assets, which include algorithms such as AI and collected medical data, will be traded, having had their authenticity verified using NFTs.

(2) Establishing asset trading platforms*[39]

An online market will be formed to actively trade such digital content. Companies will place IP and digital assets that have little use within their company on the marketplace. Companies that have an interest in said content will then purchase them in real time. These platforms will come equipped with algorithms that will evaluate the value of intangible assets and find buyers for said assets. This will make it possible to sell IP and digital assets to appropriate buyers at appropriate prices (Figure 12).

Figure 12. The potential of facilitating the free flow of IPs from the life science industry on the marketplace



3. Quantifying the value in medical care

The value in medical care is quantified for the purpose of promoting innovation in healthcare and ensuring sustainability in medical finance, with healthcare policies, products, and services evolving based on this value.

(1) Implementing evidence-based policy making

It would be fair to state that finding a balance in improving the quality of healthcare and controlling its costs are the most important topics for governments and insurers. The number of topics that should be evaluated will increase, which will include measures for prolonging healthy life expectancies, preventing the progression of diseases, offering palliative care, and developing medical services as well as innovative diagnostic/treatment methods. With various countries advocating the importance of evidence-based policy making, it will become essential to analyze the value in medical care to verify the effectiveness of healthcare policies.

(2) Evaluating medical providers to democratize medical care

Individual patients struggle to determine which doctors from which medical institutions should examine them, with the medical information disparity that exists between patients and medical facilities having been a long-standing issue that needs correction. Analyzing medical data such as EHRs or receipts and highlighting the medical outcomes of medical providers will make it possible to understand the quality of the medical care being provided by these medical institutions and their medical staff, which will encourage consumers to choose medical institutions and doctors on their own. This quantification will translate to the principles of market competition being incorporated into medicine and healthcare, with free competition contributing to improvements in value and streamlining of solutions.

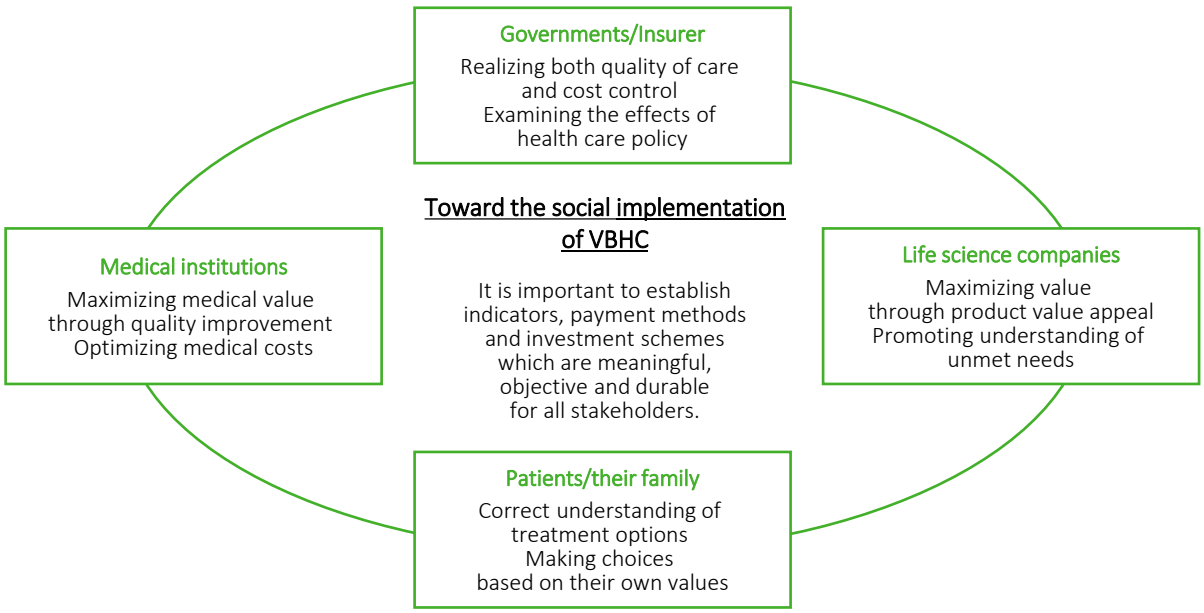
(3) Quantifying patient centricity: Assessing value that is based on patients and consumers

The spread of digital health products such as PHR and IoT has made it possible to measure and evaluate a patient's QOL that takes into account their mental and social aspects, as well as quantify the value in medical care using objective indicators such as QALY analysis.

(4) Understanding unmet needs and streamlining solutions for assessing value

Quantifying the value in medical care has significant benefits for various private companies operating in the life science and healthcare industries. Quantifying this value will make it possible to visualize how effective preventive measures and treatment methods are at that point in time, as well as to what extent problems exist. Private companies conduct multiple, repeated surveys extending from the R&D to the commercialization stage in order to grasp the needs of the market. Qualifying medical value is expected to improve the productivity of such activities. In addition to making it easier to obtain clinical outcomes that represent true value, being able to evaluate a diverse range of values will result in more practical measurements of cost-effectiveness. Startup companies will also begin to work more than ever on developing healthcare services intended for use in clinical settings. Insurance reimbursements will also become available for products that have proven to be cost-effective, which will increase the use of digital health products in clinical settings (Figure 13).

Figure 13. The significance of value-based healthcare



What merits discussion in implementing these changes

1. Circulating healthcare data

The following three points are hurdles to achieving a society in which a diverse range of healthcare data is circulated amongst various players in industry, government, and academia.

(1) Proliferation of data platform providers

Various companies are working to collect medical data with the aim of becoming data platform providers. A high-level overview of each company's strategy shows that these companies are all fixated on similar business models, with there being no clear differentiating factor between their strategies.

As a result, small-scale data platform providers possessing similar sets of data may become prolific, creating an inefficient market. In order to increase the value of data, it will be necessary to create large databases that gather as much data as possible. Based on the fact that data is a public good, as well as the sensitivity associated with healthcare data, building a model in which data is shared and circulated amongst a variety of companies and institutions will be necessary to avoid an unfair competitive environment in which data is collected by only a few private companies.

(2) The need for data quality assurance

As more flow data such as PHR becomes available, quality assurance will become essential, and above all, ensuring that data is accurate per medical standards will be important. For example, clinical guidelines for hypertension, diabetes, and COPD also mention the clinical uses of PHR. However, all of these guidelines assume that medical devices such as blood pressure monitors or pulse oximeters are in use. Ensuring that data is accurate per medical standards will be essential if the goal is to utilize this data in a clinical setting.

In addition, taking into account how PHR data flows, ensuring data continuity and providing robust authentication processes as well as data checks will be essential.

(3) Guaranteeing the basic human rights of individuals

More data will become available that can be used to profile individuals, such as personal genome data, medical data, and personal preferences that can be understood from the individual's purchase and search histories. Doing this, however, risks limiting an individual's rights and evaluating said individual without their consent. For this reason, social rules should be formulated so that specific groups are not placed at a disadvantage.

2. Quantifying the value of medical care and facilitating the free flow of IP on the marketplace

The following points will be hurdles in quantifying the value in medical care and achieving the free flow of IP on the marketplace.

(1) Stakeholder resistance to VBHC and building new medical care provision systems

With the medical fee system shifting from a more conventional "fee for service" model to a VBHC model, how to maintain equality in medical institutions and quality in healthcare will be up for debate due to the impact this change could have on the income-expenditure models of medical institutions, especially medical clinics. For this reason, medical fee adjustments should be allowed, similar to MIPS (Merit-Based Incentive Payment System) in the US, to incentivize doctors to participate in the new reimbursement program when transitioning to VBHC. This will be necessary to both reduce medical costs and improve the quality of healthcare.

In addition, there is a need to control patient behavior in an appropriate manner outside of medical facilities in order to maximize the impact of treatments. To this end, organizations such as medical institutions, pharmacies, insurers, and local municipalities should remain in close communication with each other while sharing patient information and building systems that can offer the best medical care.

(2) Addressing the risk of counterfeit products that could arise from circulating IP on the marketplace

If it becomes easier to search for IPs on platforms, then we must also consider the risk that more counterfeit products based on these IPs will find their way onto the marketplace. Additional measures will be required to counter this risk. This could include publishing products that ultimately benefit more from being in circulation on the marketplace or publishing products in which patent infringement can be discovered in the final product.

Discussing social orders related to healthcare systems in 2040 and challenges of healthcare transformation

Discussing social orders related to healthcare systems in 2040 and challenges of healthcare transformation

So far, we have discussed current issues, market/technical trends, what the world will look like in 2040, and what merits discussion in implementing these changes from the following four perspectives based on drivers of change: "eternal life," "transforming how the pharmaceutical industry is structured," "revamping medical care provision systems," and "accelerating value transformation." While Japan's super-aged society is increasing social security costs, its healthcare needs are becoming more diverse, which includes prolonging healthy life expectancies, developing treatments for rare diseases, and shifting from cure-oriented to care-oriented treatments. To fulfill these needs, both innovation and sustainability will be required.
In addition to these social demands, we expect that Japan's social order in relation to its medical and healthcare services will see significant changes due to future technological developments. We anticipate that three major social orders will emerge.

A happy, long-lived society

With more consumers wanting to live out their lives in a state of good health, both physically and mentally, we are working towards a society that can fulfill those demands.

Life design society

Individuals will be offered choices in recommended prevention methods and treatments, as well as choices in new cyber-based lifestyles. These choices will lead to a society in which individuals can make independent choices according to their own values.

Inter-industry co-creation society

Digital technologies will connect products, industries, societies, and people that have up until now been isolated from each other to develop and provide the most appropriate solutions to individuals. This will, as a result, breakdown the barriers of the medical and healthcare industries, with all industries now having some sort of connection to medical and healthcare services. Visualizing and sharing the diverse values and assets associated with medical and healthcare services as well as encouraging free competition and co-creation will accelerate value transformation.

As these changes to Japan's social order come closer to becoming a reality, major players in healthcare will face new challenges. We will list what points we believe merit more discussion ("What merits discussion regarding healthcare in 2040"), which includes those that require major overhauls to their ideas and mechanisms, having been established over the years by existing industry players (Figure 14).
For example, N-of-1 medical care and senolytics fall outside of the scope of Japan's current universal health insurance scheme, which means we must consider in terms of social security how such treatments should be handled. In addition, virtual pharma will, as a concept, impart great changes to the vertically integrated business model that pharmaceutical companies have continued to use for many years.
When adopting new technologies, history teaches us that we must deal with both the positive and negative aspects such technologies bring with them. However, in adopting AI hospitals and connected health, we must consider how humans and AI can properly coexist. We must also consider both how we can reduce the risks and disadvantages posed to users in circulating data and facilitating the flow of IP.
However, the drivers of change and social orders cited in this report are rooted in the principle that healthcare should strive to help consumers in their pursuit of happiness and health, something which the authors of this report believe that future healthcare is sure to accomplish.

Figure 14. What merits discussion regarding healthcare in 2040

	Governments	Hospitals/ Healthcare providers	Life science companies
Eternal life	**Redesigning self-help and public assistance** Social security system responding to longevity, N = 1 health care and happiness	**Redesigning the health care system** Diversification of value offerings such as preventive interventions and therapeutic drug creation	**Reorganizing R&D strategy** Reassessment of unmet needs with a bird's-eye view of life journey
Transforming how the pharmaceutical industry is structured	**Japanese industrial model** A competitive industry model that creates innovation around the world	**Integration and division of labor with life sciences** New collaborations to create innovative treatments and increase industry productivity	**Sustainable business models** Establishing a new model to survive in the increasingly competitive environment
Revamping Medical Care Systems	**Innovation and safety** Managing both enjoying digital innovation and ensuring medical safety	**Co-existence healthcare with AI** Development of a new medical system in which humans and AI coexist	**Participation in health care initiatives** Concept of total disease care and the company's positioning in the market
Accelerating Value Transformation	**Privacy and industrial development** Overcoming trade-offs between supply-and-demand parties in data circulation	**Democratization of health care** Implementation of a patient-centric and free competition model	**Accelerating Innovation** Identification of areas of competition and co-creation

In conclusion

In this report, we focused on 10 factors (drivers of change) from amongst the variety of factors affecting change within the medical and healthcare fields that will drive how Japan's social order is shaped.
In doing so, we examined what changes and interactions each driver would bring about, considered what form medical and healthcare services would take in this new social order, and what merits discussion in implementing these changes.

This report is not a prediction of what the future holds for this world. The future is not set in stone but is something we can change through our thoughts and actions. In other words, we can imagine and create a future for ourselves.
The authors of this report hope that it will arouse discussion on what sort of bright future is awaiting healthcare, as well as allow us to hold discussions with our readers and continue to make updates to the report itself.

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