【Appendix 1】

Provisional translation

The basic approach for the Moonshot Research and Development Program

Council for Science, Technology and Innovation (CSTI)

Headquarters for Healthcare Policy

December 20, 2018

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1. Purpose of the Program

Japan is now faced with many difficult issues, such as an aging and declining population, extreme natural disasters, and global climate change. These issues should be addressed and resolved by science and technology so that we may bring a better future to our society.

Under the circumstances, to overcome these difficult challenges without being afraid of failure, the ImPACT program, a five-year research and development program, was established in 2013 as a new framework to develop the growing fields in the future.

Research and development (R&D) in the ImPACT program had high-risk/high-impact characteristics with no guarantee of success, but this R&D was also expected to have a profound impact on our industry and society once the goals were achieved. In the ImPACT program, we recruited researchers with highly ambitious research concepts and ideas, and selected excellent researchers who have challenging sprits as the Program Managers, and delegated R&D management authorities to them.

These Program Managers have crossed the boundaries of traditional

organizations and research disciplines to bring together various knowledge and ideas for high-risk/high-impact R&D activities that could not be implemented in traditional national projects. Their efforts have achieved some significant results in a very short time. On the other hand, there have been approaches that were neither daring nor original enough to meet the Program's expectations for future disruptive innovations and high-impact. In addition, concerns have been raised over the lack of participation by foreign researchers and international collaborations. These suggested that the Program needed to be improved further.

Outside Japan, the European Union, the United States, and China aim to introduce disruptive innovation by announcing their ambitions and setting their goals for resolving difficult social issues in a manner that was unthinkable in the past. These countries accelerate high-risk/high-impact R&D by a much larger scale of investment than Japan does.

Their R&D management is to seek the top researchers from all over the world, bring together their wisdom, and incorporate various ideas for business while building an open innovation platform that emphasizes speed and global aspect.

Against this background, the new Moonshot Research and Development Program ("the Program") aims to create disruptive innovations from Japan and promotes challenging R&D based on revolutionary concepts that are not simply the extension of existing technologies, i.e. moonshots.

Under the Council for Science, Technology and Innovation (CSTI) and the Headquarters for Healthcare Policy, the relevant ministries and offices will cooperate to drive the Program collectively according to the principles including the following:

a. Set ambitious goals ("Moonshot Goals") and concepts to attract people for

social issues that are difficult to tackle but will have profound impact once resolved, and aim to achieve the Moonshot Goals by bringing together wisdom from all over the world under the direction of top researchers.

b. Insights and ideas that were still in their basic research yesterday are being applied to industry and society today at an astonishing speed, and disruptive innovations are occurred in many areas. In this situation, the Program will vigorously drive highly ambitious R&D that will maximize Japan's basic research capabilities to identify and develop revolutionary research projects without fear of failure.

c. The Program will be managed in a new manner that will always be aware of developments in global R&D so that the relevant R&D activities can be optimized as a whole, with flexibility for their organizational structures and their activities to establish a world-leading R&D framework. In addition, to smoothly promote practical use of R&D results in society, the program will provide opportunities for researchers' communications with diverse people and establish a structure that enables researchers in various fields, including humanities and social sciences, to participate in R&D activities to respond to ethics, legal systems, and social issues. Furthermore, opening and closing strategies will be fully implemented to allow for future commercialization.

The National Research and Development Agencies ("the research promotion agencies") tasked with this challenging R&D initiative are the Japan Science and Technology Agency (JST), the New Energy and Industrial Technology Development Organization (NEDO), Bio-oriented Technology Research Advancement Institution / National Agriculture and Food Research Organization (BRAIN/NARO), and the Japan Agency for Medical Research and Development (AMED). Program funds have been established for these agencies.

2. Basic Program Framework

For the purpose of the Program, the Cabinet Secretariat (CAS), the Cabinet Office (CAO), the Ministry of Education, Culture, Sports, Science and Technology (MEXT), the Ministry of Health, Labour and Welfare (MHLW), the Ministry of Agriculture, Forestry and Fisheries (MAFF), and the Ministry of Economy, Trade and Industry (METI) will collaborate to promote R&D under the following framework.

(1) The CSTI and the Headquarters for Healthcare Policy each decide the Moonshot Goals, considering input from external experts. The expert members of the CSTI and under the relevant committees of the Headquarters for Healthcare Policy will offer high-level advice to effectively guide the entire Program to achieve the Moonshot Goals.

(2) Cooperating with the relevant ministries and offices and considering the advice from the expert members, the CAS and CAO implement the following:
- Coordinate the Moonshot Goal candidates[1].
- Establish an organizational structure for relevant government agencies to promote related R&D through collaboration.(establish the Strategy Council (Tentative name))
- Set guidelines for operation and evaluation of the Program that defines the process of Program Director's (PD's) appointment and Project Managers' (PMs') recruitment and selection, the procedures of middle-term/final evaluations and evaluation perspective, etc.
- Promote related R&D strategically and collectively to achieve the Moonshot Goals, based on the discussions in the Strategy Council (tentative name).

[1]The CAO coordinates the Moonshot Goals to be decided by CSTI, and the CAS coordinates the Moonshot Goals to be decided by the Headquarters for Healthcare Policy.

(3) The CAO, the MEXT, the MHLW, the MAFF, and the METI holding jurisdiction over each research promotion agency are tasked with the following:

- Formulate the R&D concept that defines areas and fields in which R&D should be promoted, cooperating with other relevant ministries to achieve the Moonshot Goals.
- Promote related R&D strategically and collectively, cooperating with the CAS or CAO to achieve the Moonshot Goal, based on the discussions in the Strategy Council (tentative name).
- Give instructions to the related research promotion agencies.

(4) Each research promotion agency implements R&D activities to achieve the Moonshot Goals by:

- Appointing PD, and recruit/select PMs.
- Establishing organizational structure for R&D activities and implement the related investigations and analysis.
- Implementing related R&D strategically and collectively, cooperating with the CAS or CAO and the relevant ministries and offices to achieve the Moonshot Goal, based on the discussions in the Strategy Council (tentative name).
- Managing the progress of R&D, including middle-term /final evaluations, and other methods.

(5) The CAS or the CAO will set detailed management policies for the Program separately if necessary, cooperating with the relevant ministries and offices.

【Appendix 2】

Provisional translation

July 17, 2020
Office of Healthcare Policy, Cabinet Secretariat
Office of Japan Agency for Medical Research and Development / Medical Data Infrastructure, Cabinet Office
Research Promotion Bureau, MEXT
Health Science Division, Minister's Secretariat, MHLW
Commerce and Service Industry Policy Group, METI

Guidelines for Operation and Evaluation of the Moonshot R&D Program

1. Program Features

○ The government presents an ambitious goal(s), Moonshot Goal(s) (hereinafter referred to as MS Goal(s)), which attracts people, and R&D concept(s) (hereinafter referred to as the concept(s)), from the perspective of looking toward a future society, and solving domestic and overseas social issues that will arise.

○ Challenging R&D concepts by being based more on bold ideas that will not just be extensions of conventional technology, and which are promoted by maximizing knowledge and ideas in the basic research phase.

○ To achieve the MS Goal(s), multiple project managers (hereinafter referred to as PMs) are, in principle, selected under respective MS Goal(s), and a program director (hereinafter referred to as the PD) is appointed to direct and supervise, in a unified manner, the program that is comprised of multiple R&D projects (hereinafter referred to as projects) that PMs promote.

○ Authority for promoting the project is granted to PMs. Flexible management is promoted under the direction of each PM, while bringing together the wisdom of researchers from all over the world.

○ The PD drafts a portfolio (the management plan that summarizes the project components (combination) and resource allocation, etc., (hereinafter referred to as portfolio) to strategically achieve the MS Goal(s), and the research promotion agency (funding agency, hereinafter referred to as FA) make a final decision on the portfolio based on this. The PMs apply diverse knowledge and ideas in the basic research phase, undertake challenging research without fear of failure, and discover and foster innovative research results.

○ While utilizing the benefits of the multiple-year funding system and repeatedly restructuring the portfolio, we implement R&D that allows for support for up to 10 years from the start of the research.

○ As well as always sharing relevant domestic and overseas R&D trends, we establish the most advanced research support system through which researchers can challenge leading-edge research through cooperation.

○ To promote the use of research data[1] generated through research activities and to support advanced research management, we pursue advanced data management, by means such as proactively utilizing the Research Data Infrastructure System (NII Research Data Cloud)[2].

○ Looking ahead to practical use of the R&D results in society in the future, we actively encourage utilization of the R&D results and examine the open and close strategy involving industry from the R&D phase.

2. Determination of the Moonshot Goal(s) and Formulation of the R&D Concept(s)

○ The Visionary Council consisting of experts was established to discuss drafted MS Goal(s), from the perspectives of looking toward a future society and solving domestic and overseas social issues that will arise.

○ The Headquarters for Healthcare Policy (hereinafter referred to as Headquarters) determine the MS Goal(s) in light of advice from the Visionary Council. When MS Goal(s) are determined, we make sure to establish a research support system to maximize ideas and knowledge from researchers.

○ Relevant ministries and offices formulate the concept(s) to achieve the MS Goal(s). Consideration is given to incorporating ideas for achieving the MS Goal(s) and international strategy perspective.

○ According to changes in the social environment and advances in science and technology, if deemed necessary, Headquarters add and/or change the MS Goal(s) after evaluating their technical feasibility and listening to domestic and overseas opinions.

3. The R&D Promotion System

[Headquarters]

○ Headquarters determine the MS Goal(s).

○ Expert Panel under the Headquarters receives a report on the progress of R&D every year from the Strategy Council (tentative name), and advises on the promotion of this entire program from a broad perspective.

[Strategy Council] (tentative name)

○ A Strategy Council (tentative name) comprised of people from industry, relevant ministries and offices, and researchers, is established to strategically promote R&D, to accelerate the practical use of the R&D results in society, and to achieve effective cooperation and coordination among the relevant ministries/offices and the relevant FAs.

○ The duties of the Strategy Council (tentative name) are listed below:

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[1]Research data means data generated in the R&D process, which is manageable in an electromagnetic form. (Source: the Cabinet Office Report, “Research data infrastructure development and international cooperation working group” October 2019)

[2]The NII Research Data Cloud is being developed for full-fledged operation during FY2020 as a research data infrastructure system to promote research data management, disclosure, and retrieval based on the Integrated Innovation Strategy 2019 (the Cabinet approval in June 2019).

1) Receive a report of progress and other matters from the relevant FAs every year in principle, and give advice and approval on the concept of project components and fund allocation, etc., from a global and comprehensive perspective to achieve the MS Goal(s).
2) Advise on the ways and means for the practical use of the R&D results in society. This involves bridging the gap between the R&D and practical use in society, collaborating with the private sector, and attracting well-timed private investment based on role-sharing at the different stages of R&D activities between the public and private sectors. Also provide support for the practical use of the R&D results in society. In addition, give advice to promote international cooperation.

○ Progress reports and the minutes of meetings of the Strategy Council (tentative name) are, in principle, disclosed to give maximum consideration to the transparency of the program's operation and accountability.

[Relevant Ministries and Offices]

○ The relevant ministries and offices formulate the concept(s) with the aim of achieving the MS Goal(s), and strategically and collectively promote related R&D, cooperating with other ministries and offices.

[FA]

○ FA is responsible for realizing the concept(s) that achieves the MS Goal(s).

○ The duties of FA are listed below:

1) Appoint a PD who is deemed qualified for each MS Goal, then manage and supervise them. One or more sub-PDs who assist the PD may be appointed, as necessary.
2) After discussions with the PD, openly recruit and select, in principle, more than one PM.
3) Determine a portfolio based on the PD`s draft.
4) Instruct the PMs to draw up a project plan under the direction of the PD.
5) Collect and analyze information on domestic and overseas R&D trends and the challenges for the practical use of the R&D results in society, with incorporating the opinions of outside experts, including researchers in humanities and social sciences.
6) Hear from the PD and PMs about the status of the project's progress, the resource allocation and the role-sharing between the public and private sectors, according to the progress of the R&D, and report the details to the Strategy Council (tentative name) every year.
7) Provide support for the management of intellectual property, international standardization, public relations, and technical trends surveys, so that the PD and PMs can properly manage these. In addition, identify a promising project (or a part of the project) in an early stage from the perspective of the practical use of its R&D results in society, and ensure that support from specialists can be acquired as necessary so that the capability to identify a project that will be practically used in society in the future can be effectively demonstrated. To gain public understanding and support, help the PD and PMs to smoothly conduct bi-directional communication activities (public dialogue on science and technology) through which they can explain to society their research activities.
8) Since crosscutting support such as ELSI (Ethical, Legal and Social Issues) /mathematical science is also important for R&D acceleration and its practical use in society, provide an opportunity for the PD and crosscutting researchers to exchange their opinions, and establish a system through which a PM can acquire the support of crosscutting researcher(s), if the PD deems it necessary, and if the PM requires it.
9) Promptly appoint a new PD when an accident occurs or a vacancy arises, or when it is deemed that the PD is not fulfilling their duties.

10) Decide the details of PDs', sub-PDs', and PMs' working conditions.
11) Construct an environment in which young researchers with bold and flexible ideas, who will define future society, can actively participate in a project.
12) The relevant FAs cooperate and share related domestic and overseas R&D trends to build the most advanced research support system.
13) To pursue advanced data management, manage a data catalogue comprised of metadata[3] submitted by PMs and researchers by utilizing system such as the Research Data Infrastructure System.

○ When performing these duties, FA strives to create an environment in which researchers can focus on research by improving the efficiency of evaluation work, as well as continue their efforts in cooperation with the relevant ministries and offices, and other research promotion organizations. Also FA utilizes advanced data management to ensure fairness of research, and engages in efforts to prevent a contractor from committing a wrongful act and misapplying research funding.

[PD]

○ The terms of the PD and sub-PD are, in principle, five years, and they may also be reappointed.

○ Any nationality is welcome to be the PD, but the PD is principally based in Japan after being appointed.

○ The duties of the PD are listed below:

1) To realize the concept(s) and achieve the MS Goal(s), strategically build a draft of portfolio, and promote R&D in a challenging and systematic way.
2) When building a draft of portfolio, in principle, combine multiple projects that take different research approaches by taking into account their R&D innovation and originality, and future economic and social ripple effects, since the chance of success (or failure) and their research results (return) will vary according to their respective research approaches, even among the research projects that aim for the same goal. For example, let's assume there is a project through which significant research results can be achieved, but with a limited chance of success, while there is another project through which a certain level of research results can be achieved with a high chance of success. In such case, funds will be allocated by comprehensively considering the chance of success and research results. In the case of a project that requires technical examination, although research results can be anticipated if successful, the project starts as its feasibility study with a small start. Thereafter the allocation of funding fluctuates according to the progress status.
3) Always understand the progress of R&D based on the portfolio, and manage and supervise in a unified manner the PMs who oversee the relevant projects while constantly reviewing the portfolio, such as allocating resources with a focus on research that is steadily progressing, and discontinuing a project if it is deemed to be unlikely to produce results.
4) Lead the portfolio review based on advice from external evaluators and the Strategy Council (tentative name).
5) Objectively evaluate the research content and lead the utilization of private funding, as well as indirectly support PM activity by pursuing the practical uses of the R&D results in the society and collaboration with the private sector, and promoting international cooperation. In addition, conduct bi-directional communication activities (public dialogue on science and technology) to explain the research activities to society.
6) Conduct other actions necessary to promote the research for which the PD is responsible.

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[3] Metadata provides explanatory information about research data, such as data name, content, administrator, location of storage, contact of administrator, and policy for closure, sharing, and disclosure of research data.

[PM]

○ All nationalities are welcome to be a PM, but PM is principally based in Japan after being appointed.

○ Allow PM to concurrently engage in other work. The time allocated for research (effort rate) is set by FA.

○ The duties of a PM are listed below:

1) Under the direction of the PD, refine a proposed project during an open call to improve it, draw up a project plan (target setting of project, preparation of R&D details and implementation schedule, establishment of an R&D system to implement the project, and formulation of a plan to allocate research funding to participating R&D institutions in the project), and strategically implement the project. Moreover, flexibly and nimbly implement project modifications and changes in direction, including practical use of some research results in society.
2) Properly manage intellectual property and information, and actively and strategically promote international cooperation.
3) Objectively evaluate the research content, seek sponsors from private enterprises if R&D is at the phase at which private funding can be used, and also try to draw on private funding. In addition, conduct bi-directional communication activities (public dialogue on science and technology) to explain the research activities to society.
4) Develop a data management plan (DMP) that defines the data to be managed, and also aggregate metadata about the data to be managed from researchers based on DMP, and submit that to FA. In addition, with system such as the Research Data Infrastructure System, store and share the data to be managed, and publish the data to the extent necessary.

4. The R&D Implementation Method

[Open Recruitment and Selection]

○ After discussions with the PD, FA openly recruits and selects, in principle, more than one PM inside and outside Japan. On this occasion, establish an evaluation system comprised of outside experts, and ask for the opinions of outside experts to recruit PMs from a comprehensive perspective. Furthermore, when establishing an evaluation system, it should be taken into consideration that the Moonshot R&D Program aims at challenging R&D concepts by being based more on bold ideas that will not just be extensions of conventional technology.

○ The following points should be taken into consideration when selecting a PM:

・They have expert knowledge and a wide human network such as relevant researchers inside and outside Japan, to promote cutting-edge research.
・They have management and leadership skills such as the ability to establish an optimal R&D system, and nimbly review the system according to the status of progress.
・Project targets and contents proposed by the PM (hereinafter referred to as proposal details) are challenging and based more on bold ideas than existing proposals, and comprise innovative proposals from which a substantial impact on future industry and society is expected.
・From the perspective of technical feasibility and practical use of its R&D results in society, appropriate scenarios (hypothesis for success) for achieving the MS Goal(s) by 2040 can be clearly explained.
・The proposals contain top-level R&D capabilities, knowledge, and ideas, regardless of whether they come from inside or outside Japan.

[Building a Portfolio/Drawing up of a Project Plan]

- ○ FA instructs the PMs to refine a proposed project during an open call to improve it and draw up a project plan under the direction of the PD.
- ○ To realize the concept(s) and achieve the MS Goal(s), the PD strategically builds a draft of portfolio.
- ○ FA determines the portfolio based on a draft of portfolio built by the PD.
- ○ FA establishes a system to check the PD and PMs do not have conflicts of interest during the course of drawing up a project plan and R&D implementation, so as to promote R&D in a fair and appropriate manner.

[R&D Implementation]

- ○ Under the direction of the PD, the PMs flexibly and nimbly promote acceleration and deceleration of individual R&D challenges in the projects according to the progress of R&D, and changes in direction, including practical use of some research results in society, with their own authority and responsibilities.
- ○ The PD and PMs always understand domestic and overseas R&D trends, and nimbly review the portfolio and projects according to the progress of R&D. In particular, they strive to understand similar R&D trends overseas, actively attract high-profile overseas researchers, and promote joint research.
- ○ The PD and PMs pursue advanced data management, such as encouraging information exchange among researchers, and data storage, sharing, and disclosure.
- ○ FA actively supports management activities of the PD and PMs, and develops an environment in which outside experts can advise the PD and PMs as required.

[Report on the Status of Progress to the Strategy Council] (tentative name)

- ○ FA reports on the status of the program's progress and other matters every year to the Strategy Council (tentative name), and improves the program (project components and fund allocation, etc.) by receiving the Council's advice and such.

[Implementation Period]

- ○ Support is available for up to 10 years from the start of the research (the start of the first project among multiple projects), while the portfolio is repeatedly reviewed.
- ○ FA reports on the results of external evaluations and self-evaluations to the Strategy Council (tentative name). After discussing with the PD, they rule on project continuation, acceleration, deceleration, modification, and termination (such as a portfolio review), based on the Council's advice.
- ○ Headquarters evaluate the status of progress of the program's R&D aimed at achieving the MS Goal(s), and the prospects of achieving the MS Goal(s) in the fifth year after the start of research, and decides whether to continue or terminate the program aimed at achieving the MS Goal(s).

5. R&D Evaluation

[Evaluation]

○ FA establishes an evaluation system comprised of outside experts, and implement external evaluations.

○ External evaluations are, in principle, implemented in the third and fifth years from the start of research. If it is decided that a program will continue for more than five years, it will then be evaluated in its eighth and tenth years. If FA finds it necessary to accelerate the evaluation period according to the project features, an appropriate schedule shall be established in advance.

○ FA implements a self-evaluation based on the evaluation criteria specified in the following section every year (other than those years in which external evaluations are implemented) and reports the results to the Strategy Council (tentative name) and the relevant ministries and offices that formulate the concept(s). They will also consult with outside experts as necessary. In that case, they will also report the details of their opinions and how they are reflected in the self-evaluation.

[Evaluation Perspectives]

External evaluation is mainly based on the following perspectives, through which FA specifies detailed evaluation criteria in cooperation with the relevant ministries and offices.

<Evaluation of the program>

・The appropriateness of the portfolio aimed at achieving the MS Goal(s)
・The status of progress of the program's R&D aimed at achieving the MS Goal(s)
・The future prospects for the program's R&D aimed at achieving the MS Goal(s)
・PD's management status (including portfolio management, direction to and supervision of PMs, flexibility and nimbleness)
・Cooperation with industry and the status of bridging the gap between the R&D and practical use in society (including the status of acquiring private funding [matching] and spin-out)
・Effective and efficient R&D promotion through international cooperation
・Challenging and innovative efforts based on bold ideas
・Effective and efficient use of research funding (including role sharing between the public and private sectors, and stage-gates)
・Bi-directional communication activities (public dialogue on science and technology)
・FA's support for PD/PM activities

<Evaluation of the project>

・The appropriateness of project targets and contents aimed at achieving the MS Goal(s)
・The status of progress toward project targets (particularly comparisons of both domestic and overseas)
・The future prospects of project targets
・The status of establishing an R&D system
・PM's project management status (including flexibility and nimbleness)
・Status of research data storage, sharing, and disclosure
・Cooperation with industry and the status of bridging the gap between the R&D and practical use in society (including the status of acquiring private funding [matching] and spin-out)
・Effective and efficient R&D promotion through international cooperation
・Challenging and innovative efforts based on bold ideas
・Effective and efficient use of research funding (including role sharing between the public and private sectors, and stage-gates)
・Bi-directional communication activities (public dialogue on science and technology)

[Handling Evaluation Results]

○ FA reports on the results of external evaluations and self-evaluations to the Strategy Council (tentative name) and relevant ministries and offices that formulate the concept(s). The results of external evaluations and self-evaluations are made public in principle.

○ FA reports on the results of external evaluations and self-evaluations to the Strategy Council (tentative name). After discussing with the PD, they rule on project continuation, acceleration, deceleration, modification, and termination (such as a portfolio review), based on the Council's advice.

○ If a project, or some part of a project, is discontinued after a review of the portfolio, FA, the PD and PMs will provide the necessary support so that the secondary research results obtained to that point can be utilized in other businesses and R&D projects, with help from the Strategy Council (tentative name).

○ FA will announce publicly how the results of external evaluations and self-evaluations were reflected in the project continuation, acceleration, deceleration, modification, and termination (such as a portfolio review).

○ FA will make a follow-up evaluation after a certain period of time has elapsed after R&D termination, and conduct a follow-up of the achievements of PMs' projects.

6. Eligible Project Costs

○ Costs necessary to promote the projects are taken care of by making withdrawals from the funds established by FA for this program.

○ Eligible project costs include the following, with details of costs determined by FA. The indirect cost ratio is 30% for universities and 10% for private enterprises (but 20% for SMEs), the ratio for others is established respectively by FA. The following R&D may include verification up to POC (Proof of Concept) as necessary.

1) Costs required to implement R&D
2) Costs required for project management

○ Costs associated with an application for intellectual property rights (hereinafter referred to as costs for intellectual property rights) may be paid as R&D expenses (direct costs) in a commissioned research contract. If it is difficult to pay the costs for intellectual property rights through direct costs, FA may pay such expenses through a contract executed separately from the commissioned research contract. Costs for intellectual property rights after project termination are borne by the R&D institution.

7. Handling Intellectual Property, etc.

○ Intellectual property rights, in principle, belong to the R&D institution that is a contractor, or a researcher belonging to the said institution, by applying Article 17 of the Industrial Technology Enhancement Act. The PMs place importance on utilizing intellectual property rights to achieve the MS Goal(s), and determine the policy for utilizing intellectual property rights. Procedural details are defined by FA.

○ In the case of the participation of a foreign R&D institution, more than 50% of the foreign R&D institution's ownership interests of the intellectual property rights obtained by carrying out the research, is compelled to belong to FA.

○ The transfer of intellectual property rights obtained by carrying out the research, and the establishment and transfer of an exclusive license, shall all require the prior approval of FA.

○ Data to be managed shall be managed by the R&D institution that is a contractor, or by researchers belonging to the said institution under their responsibilities in accordance with the data policy of each institution. The categories of storage, sharing, and disclosure of data to be managed shall be clarified based on the open and close strategy, and research data are disclosed to the extent necessary by utilizing system such as the Research Data Infrastructure System.

8. Handling Conflicts of Interest

○ Since the PD is responsible for selecting PMs and for building and managing a portfolio, the PD is not allowed to participate as a PM or as a researcher. On the other hand, it is not appropriate to judge conflicts of interest between the PD or PMs and participating R&D institutions by a one-size-fits-all criteria, if that prevents Japan from attaining top-level capabilities in R&D and diverse knowledge as a result. Therefore, FA will render proper judgment on permitting participation or not, in the light of necessity, reasonability, and appropriateness of the respective relationships, with respect to conflicts of interest between the PD and participating R&D institutions in the portfolio that the PD is responsible for building, and between the PMs and participating R&D institutions in projects that the PMs are responsible for drawing up. The results will be published as necessary. The details are defined in documents such as the application guidelines by FA.

Moonshot goal of health & medical field

●Concept of the Moonshot goal

- To satisfy the concept and standards shown in the Visionary Meeting.
  [1] Inspiring（clear objective, impact） [2] Imaginative（Reform of social system）[3] Credible（Scientific feasibility）
- To be R&D responding to future practical issues of health and medical field in Japan.
- To be R&D assuming implementation for medical and nursing care, etc.
- To be R&D not only from scientific and technical viewpoints but also from ethical, legal and social viewpoints in mind.

On the premise of [1] composite of diversified innovation with impact; [2] social and industrial reform by technology produced in the process of reaching the goal of large-scale PJ; and [3] complete project management, work by collaborating fully with the goal determined at Council for Science, Technology and Innovation through Strategy Conference (tentative name), etc.

●Social issues in the background

Necessity for prevention and living positively with disease (Extension of heathy life expectancy)
- Average life expectancy will extend further
- For the extension of healthy life expectancy, it is necessary to respond to disease, function decline, etc. as a result of life-style related disease and aging

Necessity for social participation by senior citizens (short of providers)
- Ability of senior citizens of the first half of the 70s is comparable to the latter half of the 60s of 14 years ago
- At present, senior citizens who want to work even after 70 years of age account for 80% of them

Regional disparity risk of medical and nursing care
- In 2035, one of five persons will be working in medical and nursing care field.
- While medical and nursing care demand will increase explosively in urban areas, medical and nursing care facilities will withdraw in provincial areas.

While fully collaborating with goal 1 to 3, focus on research with medical and nursing care to be the exit
Goal 1: Realization of a society in which human beings can be free from limitations of body, brain, space, and time by 2050. (PD: Norihiro Hagita)
Goal 2: Realization of ultra-early disease prediction and intervention by 2050. (PD: Gen Sofue)
Goal 3: Realization of AI robots that autonomously learn, adapt to their environment, evolve in intelligence and act alongside human beings, by 2050. (PD: Toshio Fukuda)

●Moonshot Goal

”Realization of sustainable care systems to overcome major diseases by 2040,
for enjoying one’s life with relief and release from health concerns until 100 years old”

Realization of a society where everyone can prevent diseases spontaneously in daily life
- ✓ Establish infrastructure to maintain good mental and physical health by developing technologies, in order to stay healthy and prevent the onset and aggravation of diseases by regulation of immune systems or sleep, etc., and to visualize individual physical and mental state in daily life and urge people to voluntarily take healthy maintenance actions most suitable for them by 2040.
- ✓ Develop technologies to monitor all living body trends with lower physical and mental load by 2030.

Realization of medical networks accessible for anyone from anywhere in the world
- ✓ Establish a medical network to provide the same level of medical care as a normal time regardless of region and even upon disasters and emergencies by developing diagnostic and treatment devices for simple tests and treatments at home, etc. and diagnosis- and treatment-free technologies for part of chronic diseases by 2040. In addition, develop methods for radical treatment and precision medicine for diseases such as cancer and dementia by substantially reducing the development period of drugs and medical devices, etc. through establishment of data science and evaluation systems by 2040.
- ✓ Establish a technology platform to provide quality medical and nursing care suitable for each individual appropriately even with less providers by developing compact, speedy and high-sensitivity diagnostic and treatment devices as well as technologies to further enhance doctors’ medical opinion and diagnostic capability by 2030.

Realization of drastic improvement of QoL without feeling load(realization of an inclusive society without health disparity)
- ✓ Establish a social infrastructure to enable self-reliant life at home without depending on nursing care by developing such technologies as the recovery of body function with rehabilitation without feeling load, normalization of ailing biocontrol systems, regeneration or substitution of weakened organs and so forth by 2040.
- ✓ Develop technologies to improve body function through load-reducing rehabilitation and support self-reliant life at home and to improve ailing living biocontrol systems by 2030.

* For attaining the goal, it is important to have various research approaches which cross over between basic research and practical research or between medical research and research of other field and the adoption of the latest knowledge.

Provisional translation

<Moonshot Goal #7>
"Realization of sustainable care systems to overcome major diseases by 2040, for enjoying one's life with relief and release from health concerns until 100 years old"

<Target of Moonshot Goal>

[Realization of a society where everyone can prevent diseases spontaneously in daily life]

- Establish infrastructure to maintain good mental and physical health by developing technologies, in order to stay healthy and prevent the onset and aggravation of diseases by regulation of immune systems or sleep, etc., and to visualize individual physical and mental state in daily life and urge people to voluntarily take healthy maintenance actions most suitable for them by 2040.
- Develop technologies to monitor all living body trends with lower physical and mental load by 2030.

[Realization of medical networks accessible for anyone from anywhere in the world]

- Establish a medical network to provide the same level of medical care as a normal time regardless of region and even upon disasters and emergencies by developing diagnostic and treatment devices for simple tests and treatments at home, etc. and diagnosis- and treatment-free technologies for part of chronic diseases by 2040. In addition, develop methods for radical treatment and precision medicine for diseases such as cancer and dementia by substantially reducing the development period of drugs and medical devices, etc. through establishment of data science and evaluation systems by 2040.
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[Realization of drastic improvement of QoL without feeling load (realization of an inclusive society without health disparity)]

- Establish a social infrastructure to enable self-reliant life at home without depending on nursing care by developing such technologies as the recovery of body function with rehabilitation without feeling load, normalization of ailing biocontrol systems, regeneration or substitution of weakened organs and so forth by 2040.
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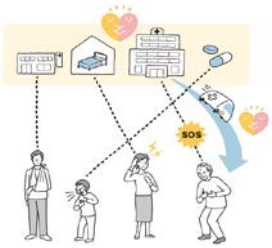
rehabilitation and support self-reliant life at home and to improve ailing living biocontrol systems by 2030.

* For attaining the goal, it is important to have various research approaches which cross over between basic research and practical research or between medical research and research of other fields and the adoption of the latest knowledge.

-----[Reference]-----



[Reference]

<Related Area and Vision>

Area : "Leveraging the Aging Society (Turning the aging society into the innovative and sustainable society by harnessing diversity through techno-social transformation)"

Vision : Society without health concerns: everyone can enjoy life until 100 years old (achievement of well - aging)

<Background of the goal setting>

- In light of the fact that average life expectancy will continue to grow and the population of 100 years or older will reach 300,000 in 2040, it is necessary to have environments where anyone can enjoy life at any age without health concerns by improving the healthy life expectancy.
- Response to life-style related diseases and diseases due to aging which account most of the diseases have become an issue and initiatives need to be taken for the prevention of life-style related diseases and coexisting with aging and diseases.
- The present preventive healthcare and health promotion have difficulty regarding to behavior change and it is rather hard to persuade indifferent persons who account for 70%.
- While life-style related diseases and the like are easier to control thanks to the progress of medical care and IoT technologies, individual issues which are hard to detect like psychosomatic disorders have become obvious.
- Also, toward 2040, it is assumed that shortage of manpower due to declining

population and withdrawal of medical and nursing care facilities will become serious problem in provincial areas and access to medical and nursing care will also become more difficult. On the other hand, demand for medical and nursing care will increase explosively in urban areas due to population concentration and there will be increased concern of supply being short. Amid the probability as high as 70% for Nankai Trough Earthquake or Tokyo metropolitan earthquake to occur within 30 years to come, it is imperative to re-establish the access to medical care at the time of disaster.

- In recent years, there are many senior citizens who still want to work, resulting in the increase of their labor-force participation ratio, which is changing the image of the elderly. On the other hand, there are also people who cannot cope in mind and body with the change of life stage due to declined QoL by aging and may lose a purpose in life and give up participation in society. There is increasing necessity for establishing social systems enabling them to participate.

<Society which the Moonshot aims for>

- Each and every one can live a healthy life of one's own accord, predicting the future health conditions, and at the same time, mechanisms to lead to health are embedded in every line of daily life.
- Regardless of the skill levels and number of medical and nursing caregivers, secure and quality medical and nursing care can be provided and accessed no matter where one lives and even upon disaster or emergencies.
- Even when faced with various changes in life stage with ailing mind and body function, each and every person can be empowered by technologies and social infrastructure without falling ill, and then their capabilities are unlocked.

Provisional translation

[Moonshot Goal #7]

R&D Concept of ”Realization of sustainable care systems to overcome major diseases by 2040, for enjoying one’s life with relief and release from health concerns until 100 years old”

July, 2020
Cabinet Office, Government of Japan
Ministry of Education, Culture, Sports, Science and Technology (MEXT)
Ministry of Health, Labour and Welfare (MHLW)
Ministry of Economy, Trade and Industry (METI)

1. Moonshot Goal

With the Japan Agency for Medical Research and Development (AMED) as a research promotor, the Cabinet Office, MEXT, MHLW and METI will promote R&D for attaining the following Moonshot Goal (Decision by Headquarters for Healthcare Policy dated [month day], 2020).

<Moonshot Goal>

”Realization of sustainable care systems to overcome major diseases by 2040, for enjoying one’s life with relief and release from health concerns until 100 years old”

[Realization of a society where everyone can prevent diseases spontaneously in daily life]

- Establish infrastructure to maintain good mental and physical health by developing technologies, in order to stay healthy and prevent the onset and aggravation of diseases by regulation of immune systems or sleep, etc., and to visualize individual physical and mental state in daily life and urge people to voluntarily take healthy maintenance actions most suitable for them by 2040.
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[Realization of medical networks accessible for anyone from anywhere in the world]

- Establish a medical network to provide the same level of medical care as a normal time regardless of region and even upon disasters and emergencies by developing diagnostic and treatment devices for simple tests and treatments at home, etc. and diagnosis- and treatment-free technologies for part of chronic diseases by 2040. In addition, develop methods for radical treatment and precision medicine for diseases such as cancer and dementia by substantially reducing the development period of drugs and medical devices, etc. through establishment of data science and evaluation systems by 2040.
- Establish a technology platform to provide quality medical and nursing care suitable for each individual appropriately even with less providers by developing compact, speedy and high-sensitivity diagnostic and treatment devices as well as technologies to further enhance doctors’ medical opinion and diagnostic capability by 2030.

[Realization of drastic improvement of QoL without feeling load (realization of an inclusive society without health disparity)]

- Establish a social infrastructure to enable self-reliant life at home without depending on nursing care by developing such technologies as the recovery of body function with rehabilitation without feeling load, normalization of ailing biocontrol systems, regeneration or substitution of weakened organs and so forth by 2040.
- Develop technologies to improve body function through load-reducing rehabilitation and support self-reliant life at home and to improve ailing living biocontrol systems by 2030.

2. Direction of research and development

Based on expert hearings and study at expert panel of healthcare policy, the direction of research and development at this point in time is as follows.

(1) Social and healthcare issues in the background

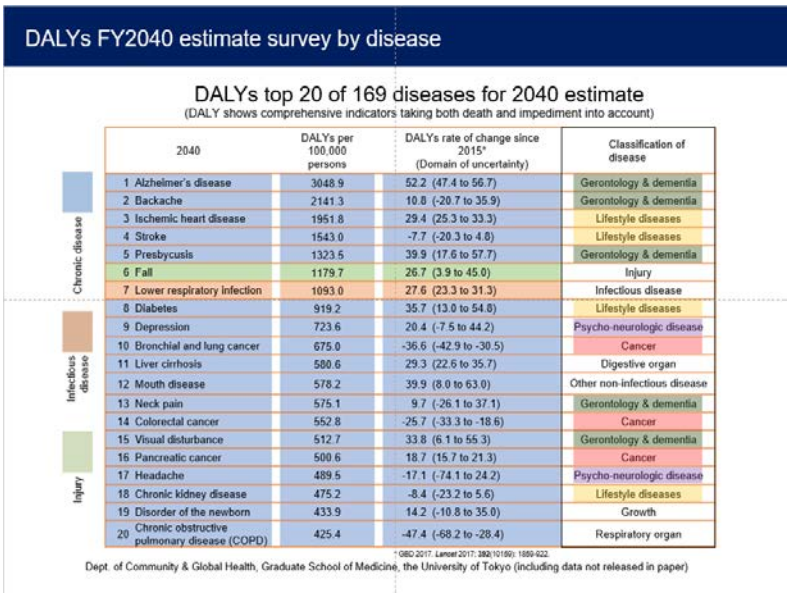
In Japan, the population of 100 years and older is expected to be 300,000 or more in 2040. The research by U.S. and other countries also said, “In Japan, a half of the population born in 2007 will live longer than 107 years.” The arrival of 100 years of life is thus around the corner ahead of other countries of the world.

Not only the average life expectancy but healthy life expectancy has also extended steadily to 72.14 years for men and 74.79 years for women in 2016. While the difference between healthy life expectancy and average life expectancy, that is, unhealthy period with limitations to daily life due to health reasons like diseases has been reduced by about 0.3 years for both men and women during the period from 2010 to 2016, it is still close to 10 years and efforts for further reduction are desired.

In view of Japan’s structure of diseases, not only single-target type diseases such as infectious diseases and genetic diseases but multiple-factor diseases like so-called life-style related diseases and age-related diseases are giving significant impact on the people and this tendency is expected to continue in the future.

In order to further extend healthy life expectancy amid ongoing growth of average life expectancy, in the face of responding to those diseases, the importance of prevention increases in addition to diagnosis and treatment and it is desired to live with the least restrictions to a daily life even if affected with a disease, that is to take measures for living positively with diseases to go hand in hand.

Fig.1. DALYs FY2040 estimate survey by disease

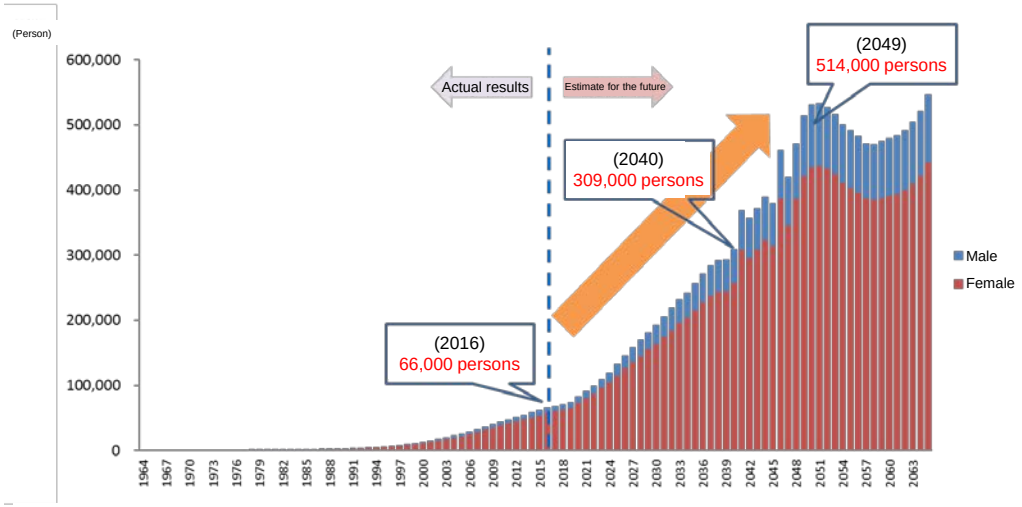


	2040	DALYs per 100,000 persons	DALYs rate of change since 2015* (Domain of uncertainty)	Classification of disease
1	Alzheimer's disease	3048.9	52.2 (47.4 to 56.7)	Gerontology & dementia
2	Backache	2141.3	10.8 (-20.7 to 35.9)	Gerontology & dementia
3	Ischemic heart disease	1951.8	29.4 (25.3 to 33.3)	Lifestyle diseases
4	Stroke	1543.0	-7.7 (-20.3 to 4.8)	Lifestyle diseases
5	Presbycusis	1323.5	39.9 (17.6 to 57.7)	Gerontology & dementia
6	Fall	1179.7	26.7 (3.9 to 45.0)	Injury
7	Lower respiratory infection	1093.0	27.6 (23.3 to 31.3)	Infectious disease
8	Diabetes	919.2	35.7 (13.0 to 54.8)	Lifestyle diseases
9	Depression	723.6	20.4 (-7.5 to 44.2)	Psycho-neurologic disease
10	Bronchial and lung cancer	675.0	-36.6 (-42.9 to -30.5)	Cancer
11	Liver cirrhosis	580.6	29.3 (22.6 to 35.7)	Digestive organ
12	Mouth disease	578.2	39.9 (8.0 to 63.0)	Other non-infectious disease
13	Neck pain	575.1	9.7 (-26.1 to 37.1)	Gerontology & dementia
14	Colorectal cancer	552.8	-25.7 (-33.3 to -18.6)	Cancer
15	Visual disturbance	512.7	33.8 (6.1 to 55.3)	Gerontology & dementia
16	Pancreatic cancer	500.6	18.7 (15.7 to 21.3)	Cancer
17	Headache	489.5	-17.1 (-74.1 to 24.2)	Psycho-neurologic disease
18	Chronic kidney disease	475.2	-8.4 (-23.2 to 5.6)	Lifestyle diseases
19	Disorder of the newborn	433.9	14.2 (-10.8 to 35.0)	Growth
20	Chronic obstructive pulmonary disease (COPD)	425.4	-47.4 (-68.2 to -28.4)	Respiratory organ

* GBD 2017. Lancet 2017; 392(10159): 1859-922.

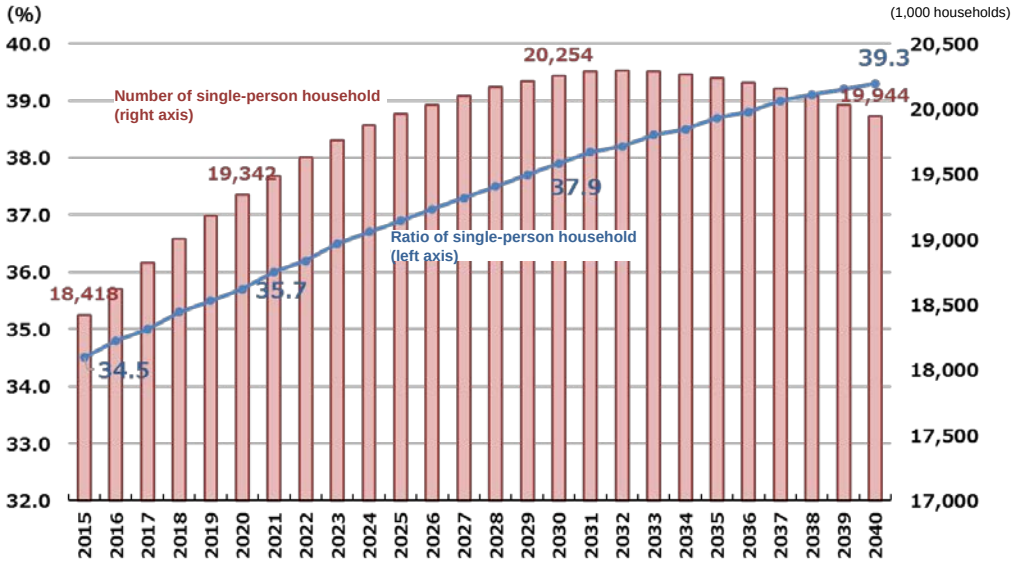
As a result of declining birthrate and aging population, three major metropolitan areas which enjoyed the population bonus now enter a rapid aging situation. Particularly in Tokyo, the ratio of increase in hospital and nursing care needs is the highest nationwide, threatening the outflow of medical and nursing care providers from a locality. In provincial areas, on the other hand, the declining population advances “a sponge effect of provincial cities” and lower density of DID (densely inhabited district), making it difficult particularly for hilly and mountainous areas to maintain a village function. Fund outflow as a result of service transfusion from Tokyo will also become the norm.

Fig.2. Annual changes of people aged 100 years and older



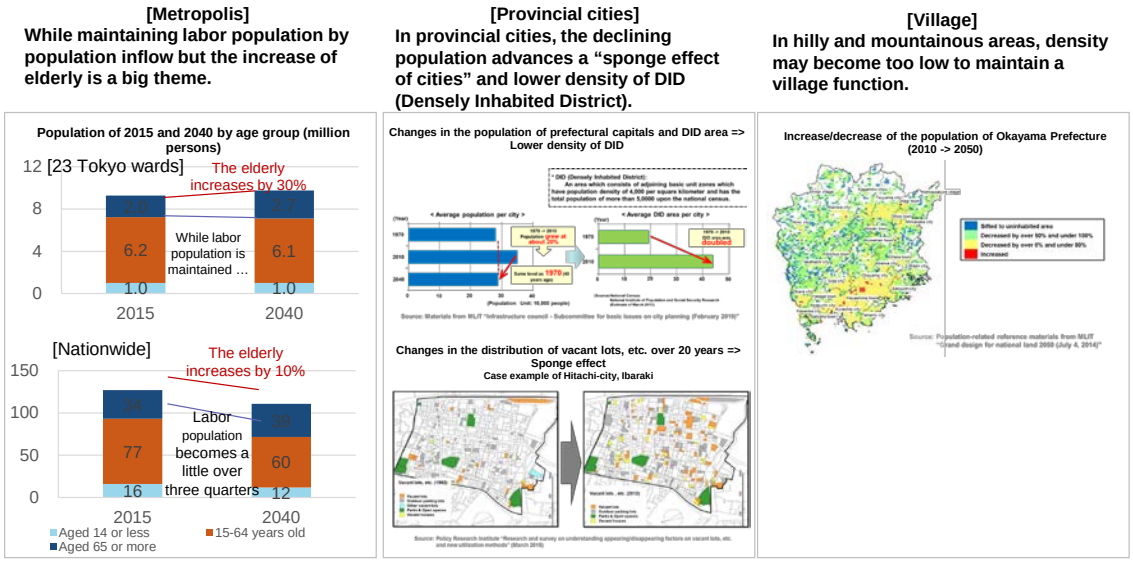
(Source) Ministry of Health, Labour and Welfare “Annual changes of people aged 100 years and older by gender” National Institute of Population and Social Security Research “Estimated future population of Japan” (Estimate of April 2017)

Fig.3. Changes in the ratio and number of single-person household



(Source) National Institute of Population and Social Security Research "Future estimated number of households of Japan (National total): Prepared by estimate of 2018

Fig.4. Medical issues of urban and provincial areas

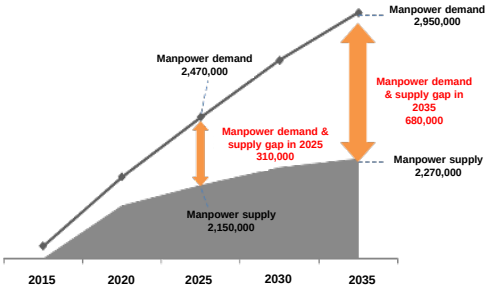


(Source) National Institute of Population and Social Security Research "Estimated future population of Japan" (Estimate of 2017), Prepared based on the summary of primary and secondary reports of Ministry of Internal Affairs and Communications, Regional Governments Strategy 2040 Initiative Study Group

Under such circumstances, while medical and nursing care demand increases explosively in urban areas, the withdrawal of hospitals and nursing homes is highly likely in provincial areas. Particularly for nursing care, the demand will increase year after year as the number

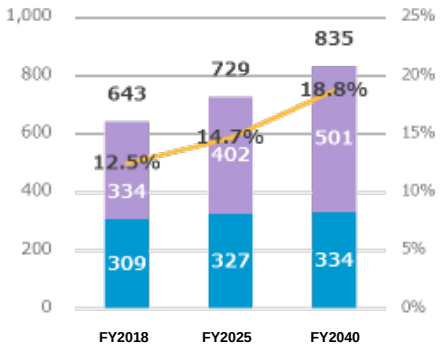
of the elderly increases and the total population of those dependent on care will hit 10 million in 2035. Consequently, the labor shortage in the nursing care industry will amount to 680,000 people and to fill the gap, one out of five workers needs to engage in medical and nursing care industry in 2040.

Fig.5. Changes in manpower demand & supply gap of nursing care industry



(Source) Made from the data 4-1 of the 6th Council on Fiscal and Economic Policy of 2018

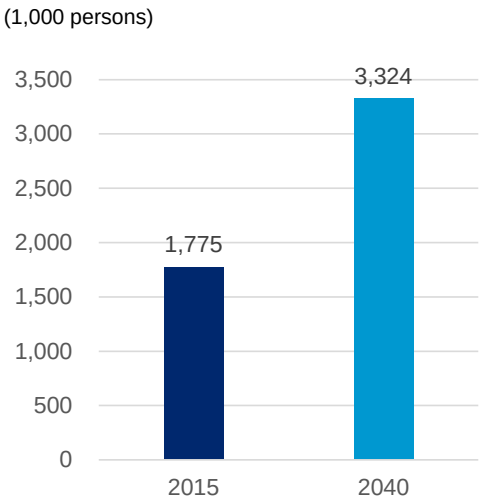
Fig.6. Changes in the number of medical and nursing care staff



(Source) Made from the data 4-1 of the 6th Council on Fiscal and Economic Policy of 2018

In addition, responding to the labor shortage in Japan, the number of foreign residents is expected to increase and 17.75 million foreign residents as of 2015 are estimated to increase to 33.24 million in 2040. In provincial areas, the growth rate of the number of foreign residents already exceeds 10%. With the increase of population movement from overseas, the provision of medical systems to meet diverse environments is required in order to cope with the difficulties such as conversing in Japanese.

Fig.7. Estimated population of foreign residents in Japan



(Source) Made from National Institute of Population and Social Security Research "Estimated future population of Japan" (Estimate of 2017)

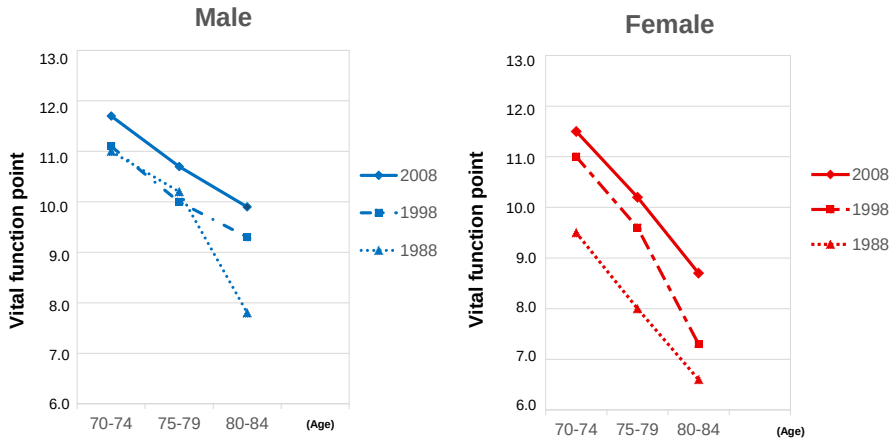
Fig.8. Changes in the number of foreign residents by prefecture

Prefecture	Growth rate by the end of 2018
Kagoshima	15.9%
Shimane	15.3%
Kumamoto	14.7%
Miyazaki	14.5%
Hokkaido	13.9%
Okinawa	13.7%
Aomori	13.0%
Saga	12.1%
Ishikawa	11.4%
Shiga	10.2%

(Source) Immigration Control Bureau of the Ministry of Justice "Number of foreign residents in Japan as of the end of June 2019 (Quick estimation)"

Furthermore, in recent years, there are many senior citizens who still want to work, resulting in the increase of their labor-force participation ratio and subsequent needs for establishing social systems enabling them to participate. For example, according to the survey by the Japan Gerontological Society and the Japan Geriatrics Society, for the current senior citizens, the appearance of the change in physical and psychological functions due to the aging process is delayed by 5 to 10 years compared to 10 to 20 years ago, showing a rejuvenation phenomenon. Under such circumstances, senior citizens who want to work even after 70 years of age account for 80% of them.

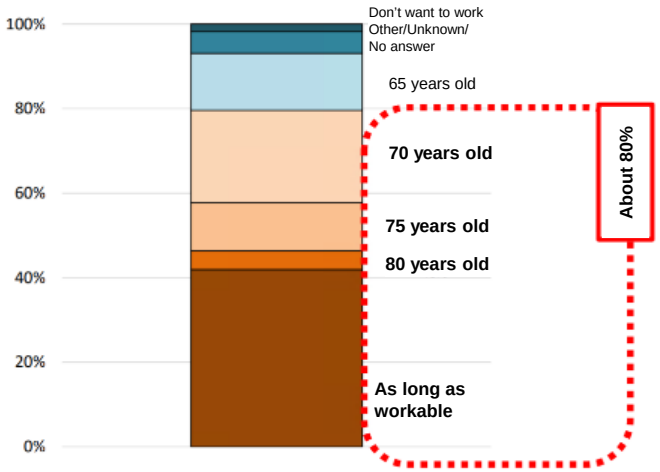
Fig.9. Vital function difference in periods



(Source) Quoted/revised from "Working group report on the study of definition of senior citizens" of the Japan Gerontological Society and the Japan Geriatrics Society

Fig.10. Age group of senior citizens who want to work

- Senior citizens who want to work even after 70 years of age account for 80% of them



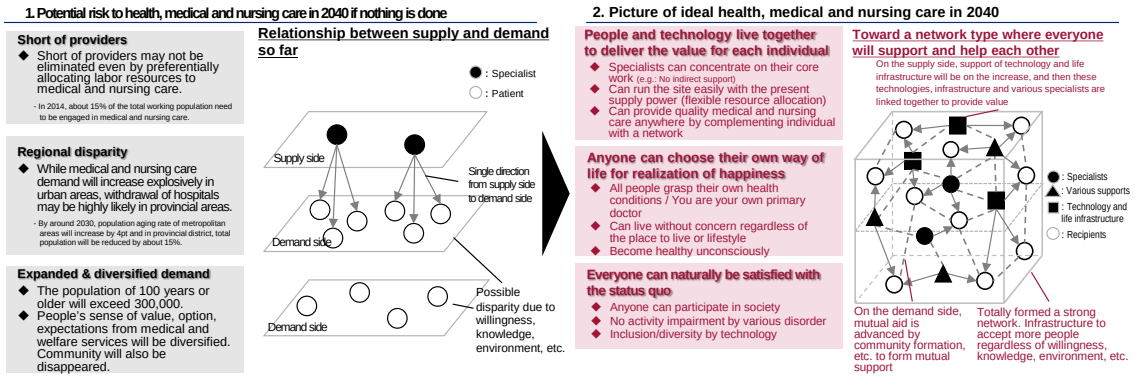
(Source) Future Innovation Working Group Interim Summary data (prepared based on the data of Ministry of Education, Culture, Sports, Science and Technology and the Cabinet Office

(2) Field/area to be promoted with challenging research and development

Under such circumstances, the environment is sought where people can enjoy life and play an active part in society without health concerns at any age. On the other hand, there is concern about the lack of provider for medical and nursing care systems to support such environment. To maintain such systems, it is important to have medical network systems under which anyone can be a provider and help each other rather than dividing duties between supply side (doctors, nurses, etc.) and demand side (patients and persons requiring nursing care).

It is therefore important to [1] prevent diseases spontaneously in the course of a daily life; [2] establish medical networks accessible to necessary medical care from any place; and [3] realize a society in which QoL can be drastically improved without feeling the load even under a decline of physical and mental function. The field and area to cover these, such as technologies to prevent the onset and aggravation of disease, technologies to measure and predict biological information and promote behavior change, technologies to simplify and automate diagnosis and treatment, establishment of an infrastructure for research and development using data science, technologies to complement and enhance body function and remedy disorder and so on shall be challenged for research and development.

Fig.11. Picture of ideal health, medical care and nursing care

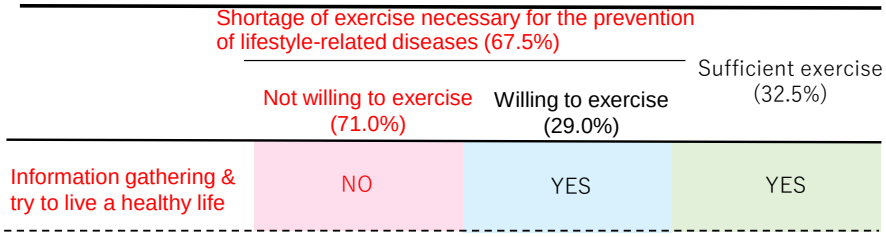


(Source) Future Innovation WG "Message from Future Innovation WG: Realizing the next generation care where people and advanced technology live together to support individual way of life" March 2019

[Realization of a society where everyone can prevent diseases spontaneously in daily life]

There was an opinion that the past preventive measures have so far reached only those who have relatively high health literacy and interest in health and the approaches to those who have low health literacy and low interest in being healthy has been insufficient. In fact, this no-interest population may account for as much as 70% and, with new information gathering on health being almost none, it is considered that their behavior change can hardly be expected.

Fig.12. Interest in health



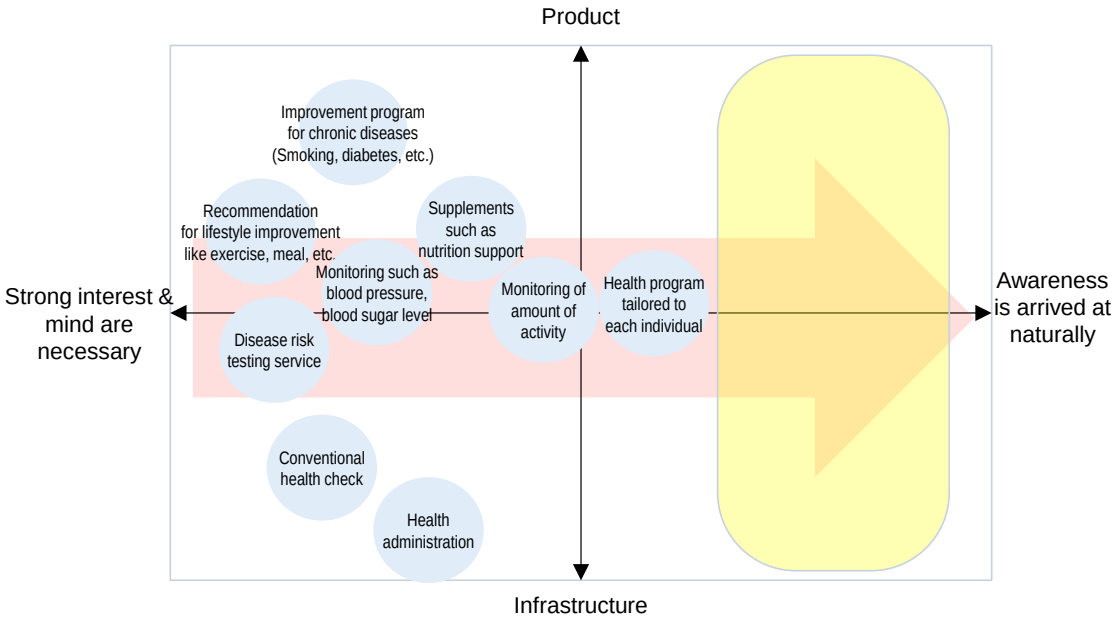
FY2010 University of Tsukuba, Kuno Laboratory (1,914 effective answers)

(Source) Shinya Kuno, University of Tsukuba, Graduate School of Comprehensive Human Sciences "Health points for behavior change project including unconcerned group for healthcare" October 28, 2015 (partly modified)

Therefore, efforts will be made for the development of technology to voluntarily make decisions or change behavior while forecasting future health conditions of each and every one and to have mechanisms embedded to lead to health in every line of daily life.

The importance of exercise, nutrition, sleep, etc. is also pointed out for health maintenance. Focus will also be on the research and development of health maintenance and prevention of onset and aggravation of diseases based on the understanding of the mechanism affecting the homeostasis of biological functions such as immunity and sleep.

Fig.13. Direction to be focused on for realizing a society where prevention is a matter of course in daily life

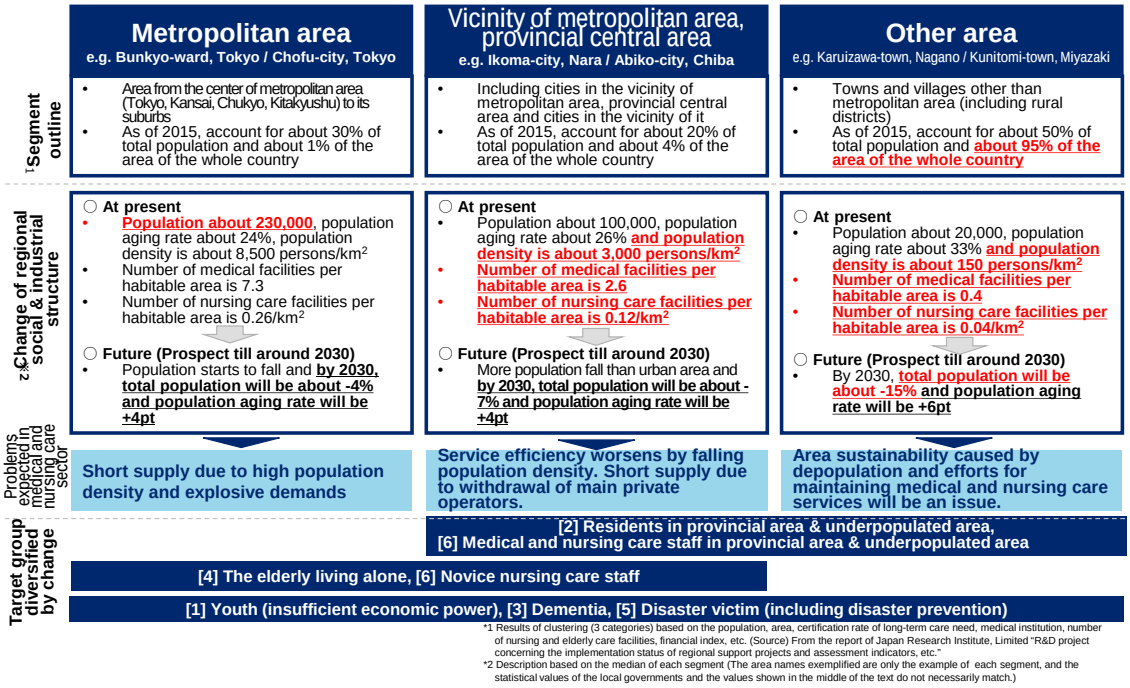


(Source) METI commissioned project "Investigation project on the future priorities in health, medical and welfare sectors in 2040" expert panel data

[Realization of medical networks accessible for anyone from anywhere in the world]

In around 2040, population density will increase in metropolitan areas where medical and nursing care demand will be explosively increase. In provincial areas, on the other hand, deteriorating efficiency of medical and nursing care service and insufficiency of supply by the withdrawal of private operators due to declining population density are envisaged.

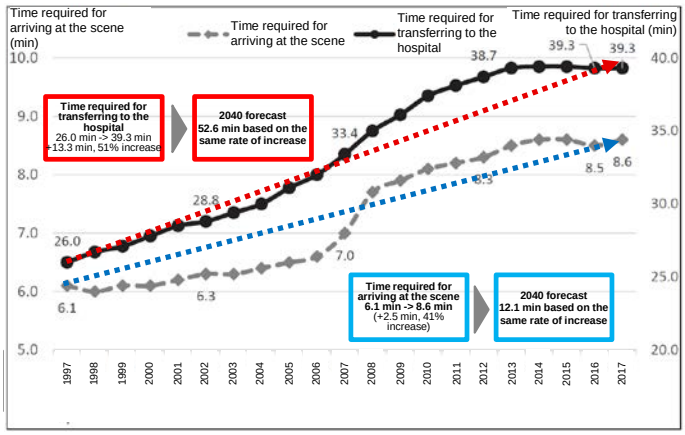
Fig.14. Changes in social structure by regional segment and suggestions



(Source) METI commissioned project "Investigation project on the future priorities in health, medical and welfare sectors in 2040" expert panel data

Under the circumstances, it has become more important than ever to secure access to medical care centering on provincial areas in light of already increased time required for transferring to the hospital for critical care. It is also pointed out that, due to the shortage of specialist medical teams and insufficient emergency response, there is significant regional disparity in the death rate of acute diseases, leading to higher death rate in provincial areas.

Fig.15. Relation between time required for transferring to the hospital and aggravation of disease



(Note) Due to the effects of the Great East Japan Earthquake, compiled by excluding the data of Kamaishi Otsuchi District Administrative Affairs Union Fire Department and Rikuzentakada-city Fire Department Headquarters for 2010 and 2011.

Elapsed time for over 50% death rate (guideline)

Symptom	Time
Cardiac arrest	3 to 5 min
* Time required for arriving at the scene as of 2017	8.6 min
Respiratory arrest	About 10 min
Copious bleeding	About 30 min
* Time required for transferring to the hospital as of 2017	39.3 min

(Source) Fire and Disaster Management Agency “Present situation of lifesaving and rescue, 2018 version”, Hokkaido Kushiro General Subprefectural Bureau website “Your first aid - Six minutes to save a life”

Fig.16. Regional disparity of death rate

(Source) Fire and Disaster Management Agency “Present situation of lifesaving and rescue, 2018 version”, Hokkaido Kushiro General Subprefectural Bureau website “Your first aid - Six minutes to save a life”

It has also become more important to secure medical care access particularly at the time of disasters as shown by the higher death rate in patients undergoing dialysis for diabetes in the Great East Japan Earthquake due to damages caused to medical institutions. Amid the probability as high as 70% for Nankai Trough Earthquake or Tokyo metropolitan earthquake to occur within 30 years to come, reinforcement of medical care access upon such disasters is also imperative. It is also assumed that a new infectious disease may spread, and securing medical access upon the occurrence of a pandemic will be required.

Table 1. Ratio of patients who need to visit hospitals regularly

		Disease name	Ratio in outpatients
Problematic diseases	1	Hypertension	15.2%
	2	Diabetes	7.3%
	3	Dental disease	6.5%
	4	Unknown	6.4%
	5	Low back pain	6.3%
	6	Other	4.7%
	7	Eye trouble	4.1%
	8	Hyperlipidemia	3.8%
	9	Depression, other mental diseases	3.1%
	10	Joint disease	2.7%

(Source) MHLW “2016 National Livelihood Survey”

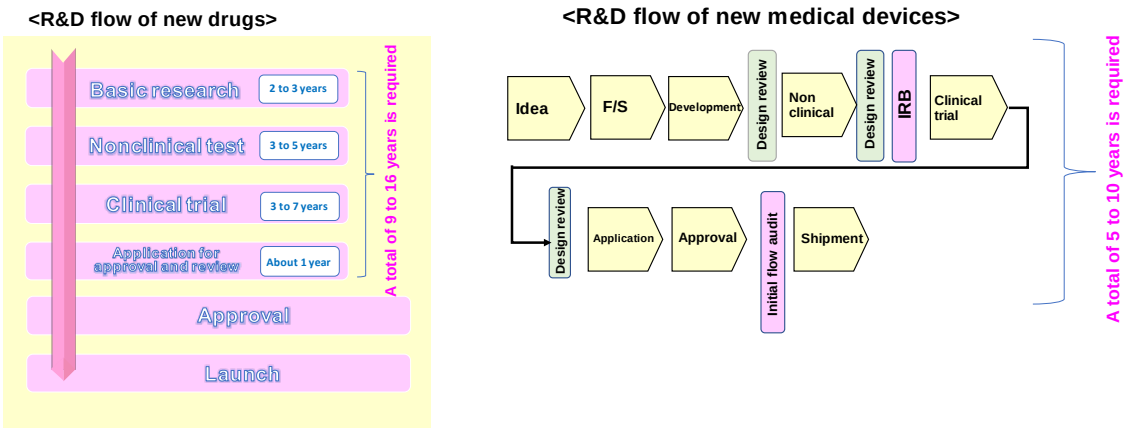
Table 2. Comparison of death rate of dialysis patients in the three Tohoku prefectures

	Total number of deaths			Rough death rate		
	2010	2011	Up year-on-year	2010	2011	Up year-on-year
Iwate	317	334	3.5%	11.0%	11.5%	0.5%
Miyagi	459	524	16.2%	9.6%	10.8%	1.2%
Fukushima	441	494	15.3%	9.6%	10.9%	1.3%
Average of three Tohoku prefectures	1,217	1,352	12.4%	9.9%	11.0%	1.1%
Average of four Shikoku prefectures	1,120	1,166	4.1%	10.3%	10.5%	0.2%
National average	28,882	30,743	6.4%	9.8%	10.2%	0.4%

(Source) The Japanese Society for Dialysis Therapy “Academic study report on the Great East Japan Earthquake – Proposal for dialysis medical development upon disasters”

In terms of an access to drugs and medical devices, the state of being already approved for use in overseas while use is not approved yet in Japan, or so-called “drug lag” and “device lag”, is being improved by the initiatives taken so far. In the meantime, there has been little change in the fact that drugs and medical devices still take a long time from the research stage to their market launch and their success rate is not so high, either. Drugs take 9 to 16 years and medical devices (particularly those of which safety and effectiveness need to be evaluated carefully) take 5 to 10 years of R&D period. It is anticipated to accelerate each stage of R&D and achieve higher accuracy to streamline each process for the reduction of the R&D period and promote regulatory science at the same time, thereby improving access to innovative drugs and medical devices.

Fig.17. R&D period for drugs and medical devices

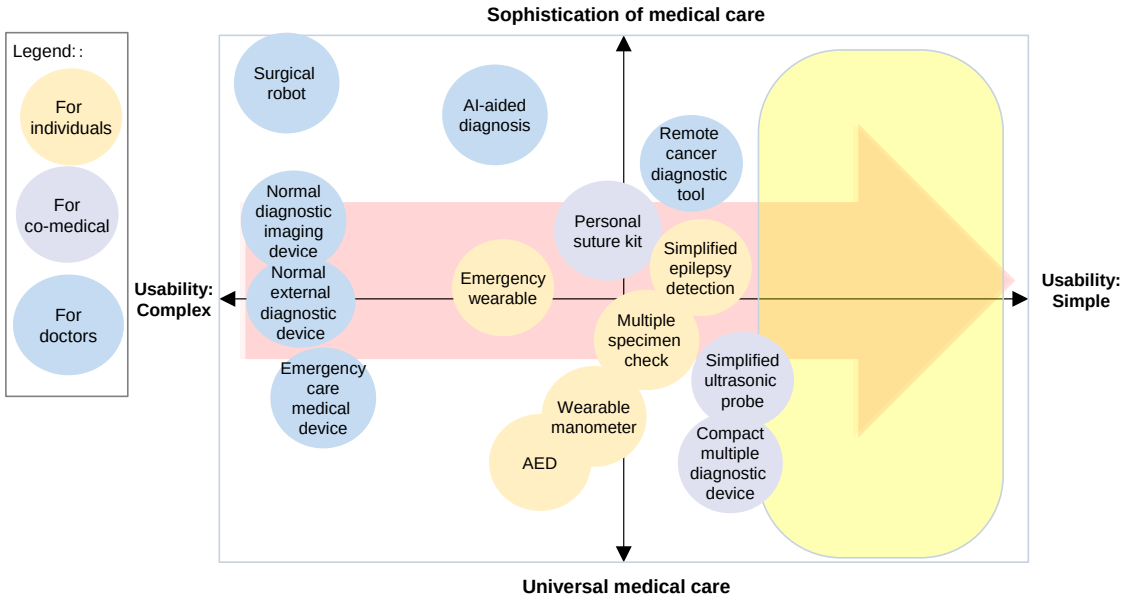


Source: Website of the Japan Pharmaceutical Manufacturers Association

Source: Medical Engineering Technology Industrial Strategy Consortium & The Japan Federation of Medical Devices Association "Medical Devices Regulatory Science Handbook"

In light of those social issues, efforts will be made to significantly reduce development period for drugs and medical devices and develop methods for radical treatment and precision medicine for major diseases. At the same time, exert efforts to realize technologies to provide high-quality medical and nursing care for anyone regardless of the skills of medical and nursing care staff and to establish infrastructure accessible to necessary medical and nursing care regardless of where one lives and even at the time of disaster or emergency.

Fig. 18. Direction of emphasis for realizing medical networks accessible to necessary medical care from anywhere in the world

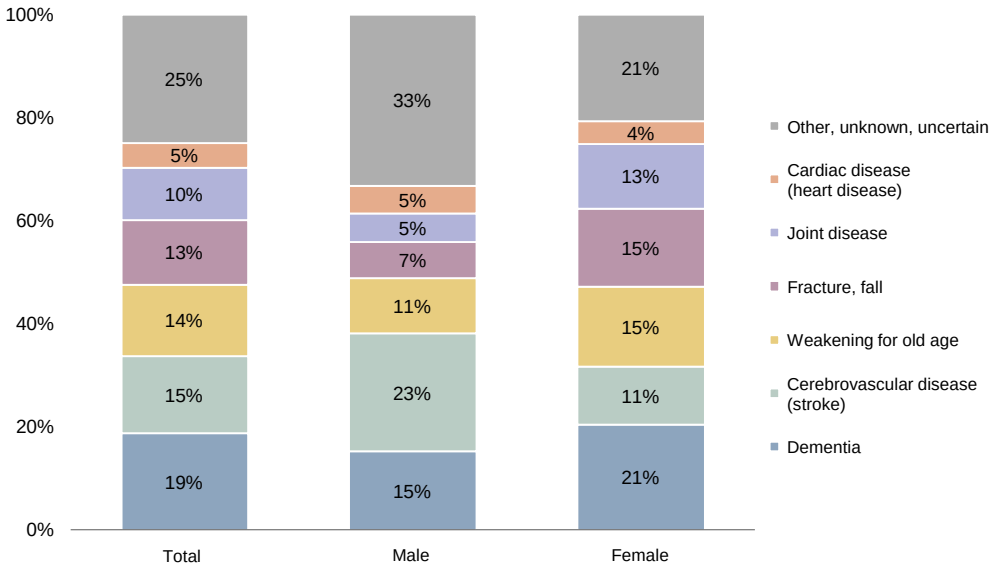


(Source) METI commissioned project “Investigation project on the future priorities in health, medical and welfare sectors in 2040” expert panel data

[Realization of drastic improvement of QoL without feeling load (realization of an inclusive society without health disparity)]

The three of dementia, cerebrovascular disease and weakening due to old age account about half of the reason for becoming care-requiring conditions and it is imperative that the measures have to be taken for these diseases.

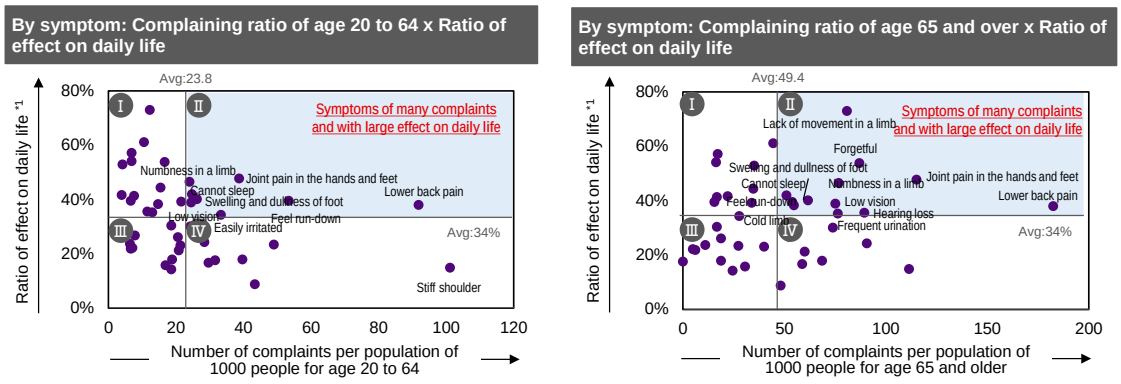
Fig.19. Care-requiring factors for 65 years or older by sex



(Source) Made from MHLW “FY2016 National Livelihood Survey”

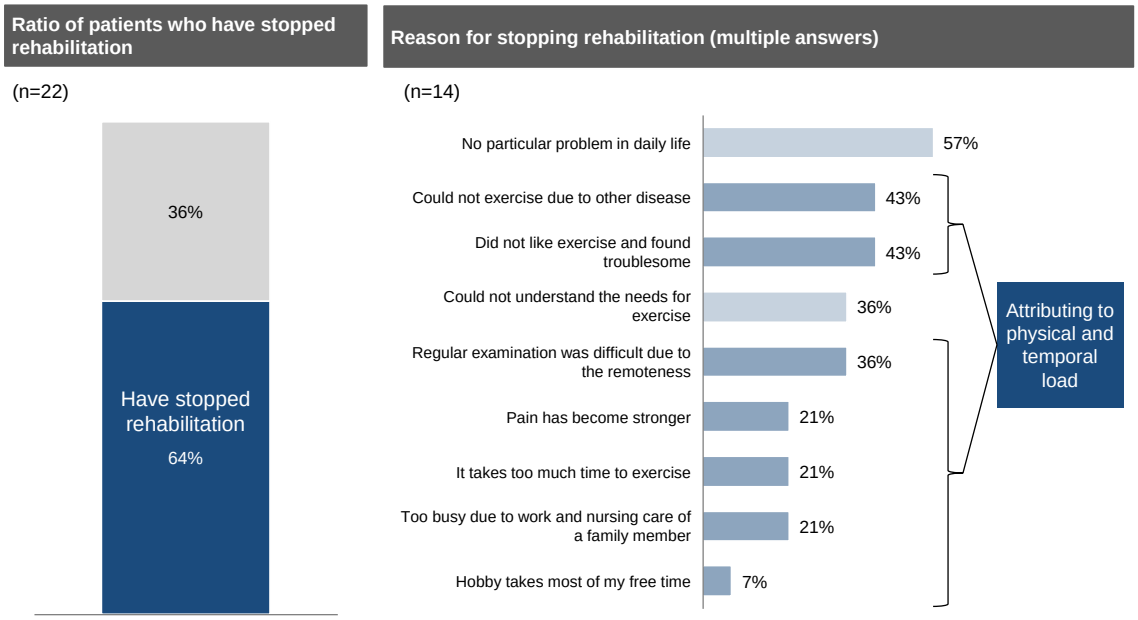
On the other hand, there are many who appeal a pain or visual and auditory sense disorder in the working generation between 20 and 64 years of age and, as a symptom to affect a daily life, backache and joint pain in the hands and feet are listed. In addition, upon becoming 65 years or older, symptoms like feeling listless and sleeplessness are added. Therefore, reducing factors of QoL are considered not only by a simple disease but by symptoms of physical disorder. Besides, there are many who give up rehabilitation for remedying such disorder for reasons of its difficulty, pain and lack of effects.

Fig.20. Relationship between complaining ratio by symptom and effect on daily life by generation



(Source) Made from MHLW “FY2016 National Livelihood Survey”

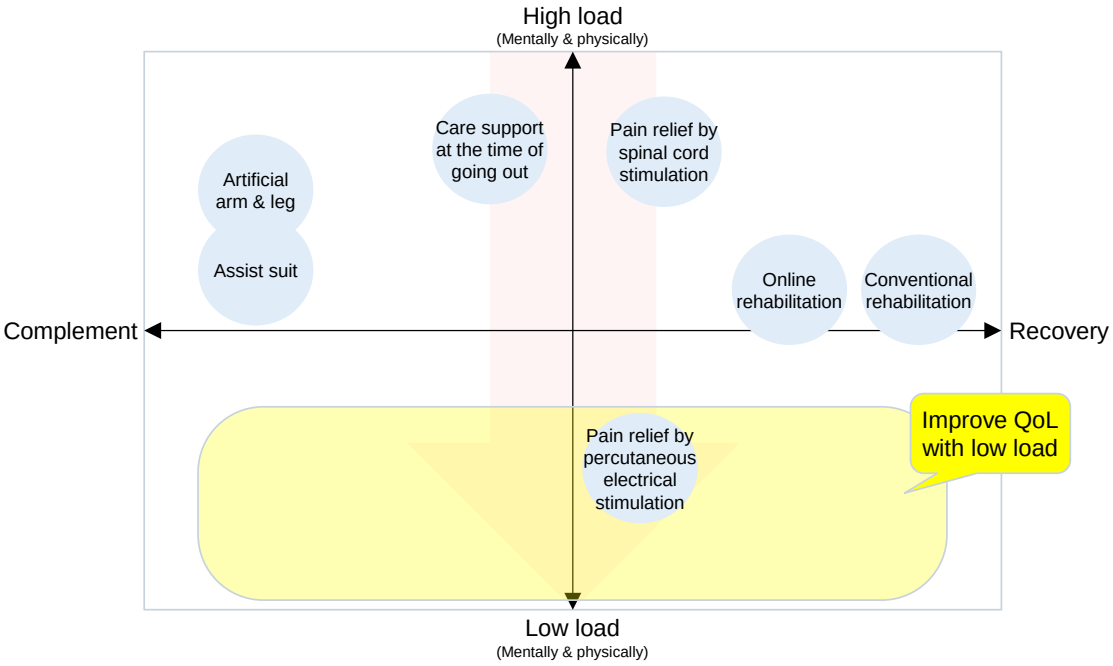
Fig.21. With/without suspending rehabilitation and its reason



(Source) Made from Ken-ikukai Group research case example “Present situation and issues of outpatient rehabilitation”

Therefore, technologies will be developed to expand and complement physical functions, leading to the drastic improvement of QoL with reduced load, independent life at home without relying on nursing care and for everyone to enjoy life until 100 years old.

Fig. 22. Direction of emphasis for realizing drastic improvement of QoL without feeling load



(Source) Data of expert panel, “Investigation project on the future priorities in health, medical and welfare sectors in 2040”

(3) Research subject for attaining the goal

In the Moonshot Research and Development Program, establish the field and area of challenging research and development, and promote challenging research and development to contribute to “Realization of sustainable care systems to overcome major diseases by 2040, for enjoying one’s life with relief and release from health concerns until 100 years old.” In addition, in order to adopt the most efficient and effective means, research the latest scientific trends and put them to good use in promoting the research and development.

Specifically, the following R&D will be promoted.

[Realization of a society where everyone can prevent diseases spontaneously in daily life]

Research and development to collect and analyze mental and physical data accurately to promote behavior change based on individual characteristics and research and development for the prevention of the onset and aggravation of diseases based on the understanding of biological function such as immunity, sleep, etc. are envisaged.

[Realization of medical networks accessible for anyone from anywhere in the world]

Research and development for elimination of medical blank even at the time of emergency and disaster to drastically reduce the death rate and aftereffect and, at the same time, R&D to eliminate problem of medical and nursing care provider shortage and R&D leading to substantial reduction of development period for drugs, medical devices, etc. are envisaged.

[Realization of drastic improvement of QoL without feeling load (realization of an inclusive society without health disparity)]

In addition to enabling independent life by maintaining and improving health conditions, R&D is envisaged to maintain QoL by complementing the physical and mental functions even upon the occurrence of disorder.

In order to attain the goal, various research approaches will become important such as the fusion between basic research and practical research, fusion between medical research and research of other field as well as adoption of the latest knowledge, data sharing and utilization. The R&D will be promoted toward the attainment of goal by adopting various knowledge and ideas and evaluating them at each stage gate.

In addition, with a view to smooth social implementation of research results, study a structure in which researchers of various fields can participate on the changes in social systems at home and abroad, and ethical, legislative and social issues.

(4) Direction of research and development toward attainment of Goal

○ 2030

[Realization of a society where everyone can prevent diseases spontaneously in daily life]

Develop technologies to monitor all living body trends with lower physical and mental load.

[Realization of medical networks accessible for anyone from anywhere in the world]

Establish a technology platform to provide quality medical and nursing care suitable for each individual appropriately even with less providers by developing compact, speedy and high-sensitivity diagnostic and treatment devices as well as technologies to further enhance doctors' medical opinion and diagnostic capability.

[Realization of drastic improvement of QoL without feeling load (realization of an inclusive society without health disparity)]

Develop technologies to improve body function through load-reducing rehabilitation and support self-reliant life at home and to improve ailing living biocontrol systems.

○ 2040

[Realization of a society where everyone can prevent diseases spontaneously in daily life]

Establish infrastructure to maintain good mental and physical health by developing technologies, in order to stay healthy and prevent the onset and aggravation of diseases by regulation of immune systems or sleep, etc., to visualize individual physical and mental state in daily life and urge people to voluntarily take healthy maintenance actions most suitable for them.

[Realization of medical networks accessible for anyone from anywhere in the world]

Establish a medical network to provide the same level of medical care as a normal time regardless of region and even upon disasters and emergencies by developing diagnostic and

treatment devices for simple tests and treatments at home, etc. and diagnosis- and treatment-free technologies for part of chronic diseases by 2040. In addition, develop methods for radical treatment and precision medicine for diseases such as cancer and dementia by substantially reducing the development period of drugs and medical devices, etc. through establishment of data science and evaluation systems.

[Realization of drastic improvement of QoL without feeling load (realization of an inclusive society without health disparity)]

Establish a social infrastructure to enable self-reliant life at home without depending on nursing care by developing such technologies as the recovery of body function with rehabilitation without feeling load, normalization of ailing biocontrol systems, regeneration or substitution of weakened organs and so forth.

In order to realize sustainable care systems to overcome major diseases by 2040, for enjoying one's life with relief and release from health concerns until 100 years old, after establishing technologies to prevent the onset and aggravation of diseases, technologies to measure and predict biological information and promote behavior change, technologies to simplify and automate diagnosis and treatment, establishment of an infrastructure for research and development using data science, technologies to complement and enhance body function and remedy disorder and so on, it is necessary to sophisticate technologies so that the implementation scene can be expanded from specific environments to a daily life and general medical and nursing care fields. To this end, the target at the time of 2030 will be the goal to the practical stage under basic technologies and specific environments.

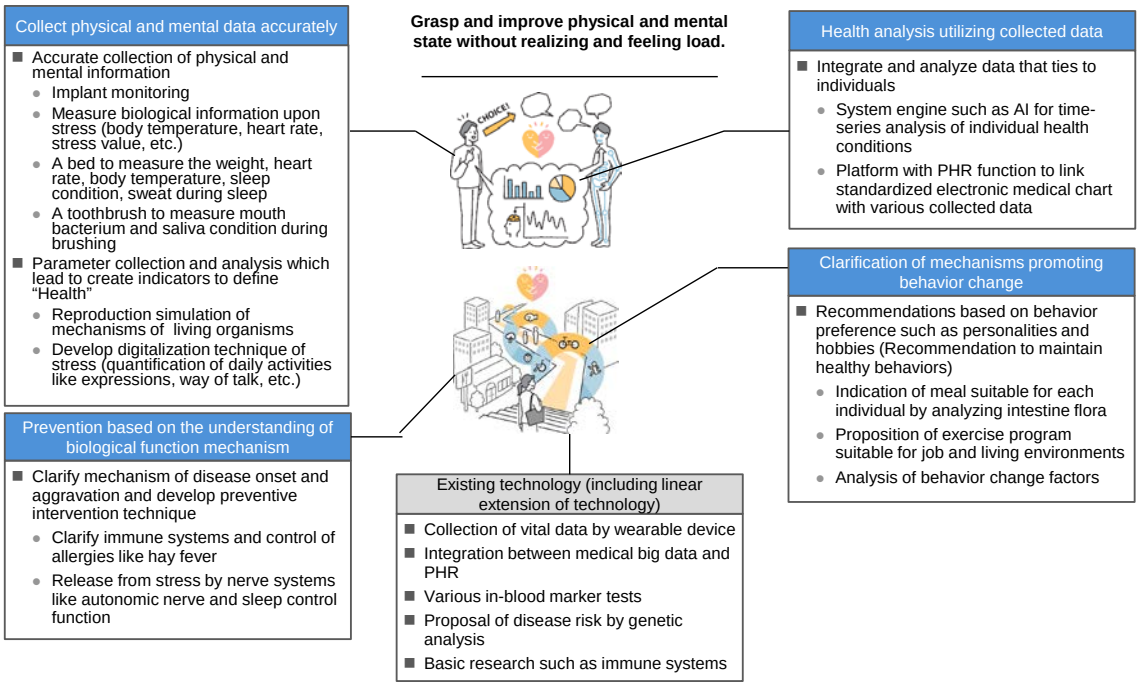
<Reference: Analysis for the attainment of goal>

The analysis based on the hearings of experts is summarized as follows.

(1) Structure of field and technology groups concerning the Goal

Technology groups for each target are shown in the following figure. Under this Goal, research and develop necessary technology component and it is also necessary to integrate and use/utilize them, for which challenging research and development are required.

Fig. 23. Research and development example of each target



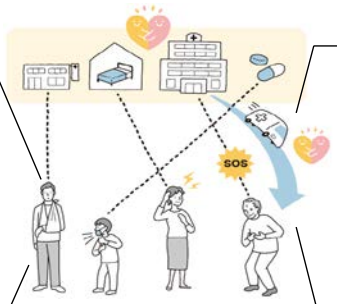
Technology to avoid medical blank even at the time of disasters and emergencies

- Technology for automation of diagnosis and treatment
  - Remote living body scanning technology (scanner by invisible electromagnetic wave, etc.)
  - Technology to enable remote 3D technology (reproduction of sense of touch and smell)
  - Reproduction of sense of touch (ICPF actuator, etc.)
- Diagnosis- and treatment-free technology for bio intervention
  - Technology relating to complete implant type device
  - Medicine automatic sustained release technology by the feedback from biopsy
  - Ultra-small nanorobot related technology (wireless charging for nanorobot in the body, technology for self-propelled mobility in the body)

Technology for much shorter development period of drugs and medical devices

- Utilize data science and establish evaluation system
  - Soonest establishment of drastic disease treatment method by super efficient development of drugs and medical devices using AI.
  - Digital/real phantom

Medical care accessible for anyone from anywhere



Existing technology (including linear extension of technology)

- System of diagnosis from body inside (capsule endoscope)
- Medical image analysis of specific disease by AI
- In silico screening
- Compact multi remote diagnostic device
- Technology to detect cancer cell in the blood
- Compact ultrasonic probe
- Insulin pump

Technology to drastically reduce death rate and aftereffect upon emergencies

- Simple test/treatment device to realize the standard of care
  - Multi & compact type device for primary treatment of emergency care
  - Ultra-small image diagnostic device (e.g.: Flexible ultrasonic grid array sensor)
  - Personalized pill dispenser
- Technology for automation of diagnosis and treatment (repeat)
  - Remote living organisms scanning technology (scanner by invisible electromagnetic wave, etc.)
  - Technology to enable remote 3D technology (reproduction of sense of touch and smell)

Efficient medical and nursing care costs, solution to short provider problem

- Technology to further enhance medical opinion, diagnostic capability of doctors
  - AI complete auto diagnostic technology (AI for doctor's medical opinion and diagnostic capability with case reports as teaching data, support of language, etc.)
  - Link and integrate big data analysis with medical care information
- Proper and efficient guidance to hospitals and pharmacies
  - Sensing technology for auxiliary diagnosis at home
  - Systematization of hospital network

Maintain and improve health conditions to enable independent life

- Technology to maintain the muscle mass and bone density even at an old age
  - Efficient muscle recovery technique in daily life using electric stimulation, etc.
  - Sensing technology to assist physical exertion suitable for individual to the minimum possible and maintain the state
  - Urban design to urge exercise in a lifestyle
- Technology to restore physical function lost by cerebrovascular disease, etc. to the original state
  - Reprogramming of cranial nerve system
  - Neuro-rehabilitation

Technology to reduce load of caregiver and person requiring care

- Companion robot technology to casually support daily life of those of dementia and requiring care
  - Auto driving technology for robot devices and robots moving a short distance at low speed
  - AI-utilized voice & sound recognition and speaker identification technologies which are better than human performance in natural environments
- Technologies of avatar cyborg suits, etc. to realize care, nursing & rehabilitation, test, diagnosis, etc.
  - Technology for avatar sophistication by analysis of action data and conversion to AI (realizing multi-function AI robot)
  - Technology for collecting the vitals characteristics of the elderly and enabling signals to be conveyed to the body

Realizing drastic improvement of QoL without feeling the load

Existing technology (including linear extension of technology)

- Dialogue: Minimum communication by BCI
- Mind and body function: Powered suit
- Movement: Movement by personal mobility
- Hearing: Super high-performance hearing aid
- Basic research and clinical application of regeneration medicine

If disorder occurs, complement mind and body function to maintain QoL

- Technology to complement the decline of physical function
  - Artificial arm and leg for free movement by connecting with nerve
  - Robot and AI to assist living and enable people to enjoy home life till the terminal phase
- Technology to normalize the disordered biocontrol system
  - Nerve reprogramming technology
  - Technology to eliminate nervous system disorder and pain by giving noninvasive external stimulation (electromagnetic stimulation, voice, etc.)
  - Watching the elderly by remote sensor, etc.
- Technology to revive or substitute organs, etc., of weakened function

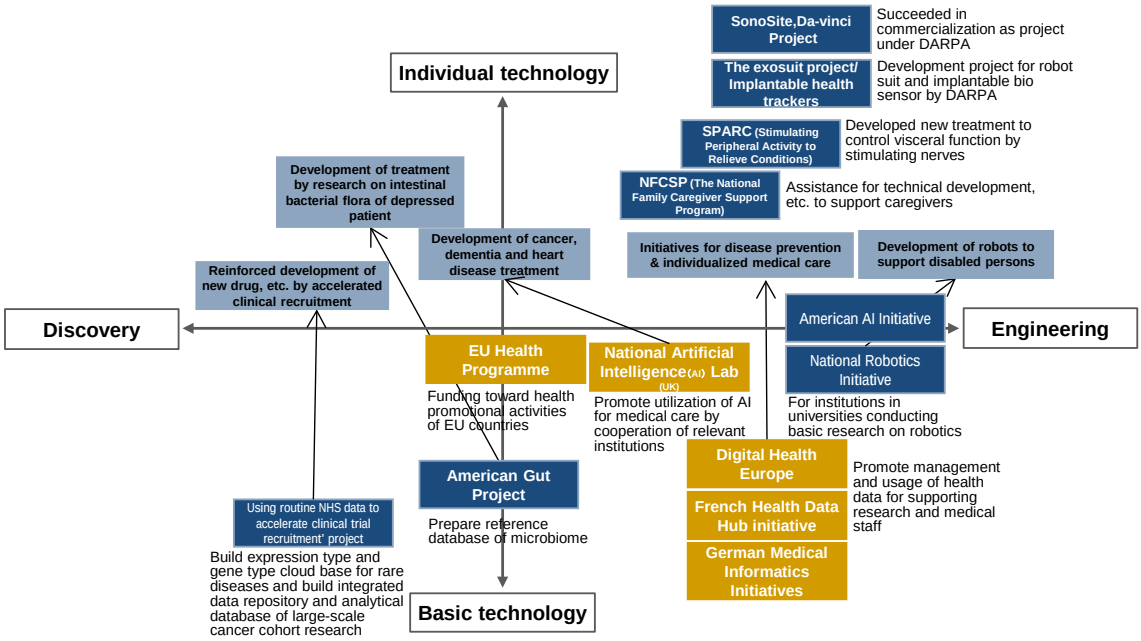
(Source) METI commissioned project "Investigation project on the future priorities in health, medical and welfare sectors in 2040" expert panel data, partially revised

(2) Trends of related research and development

[1] Moonshot-type research and development in the world health and medical fields

The following exists as research and development similar to the Moonshot R&D Program in the world health and medical fields.

Fig. 24. Moonshot-type R&D in the world health and medical fields



(Source) METI commissioned project “Investigation project on the future priorities in health, medical and welfare sectors in 2040” expert panel data

[2] U.S. major project “Precision Medicine Initiative”

This is the new and bold research initiatives to revolutionize the advancement of health and treatment of disorder announced by President Obama in his State of the Union address of 2015 and long-term research activities involving the National Institute of Health (NIH) and other multiple research centers.

Aiming to develop a new patient-led research model for possible promotion of biomedical discoveries and provide clinicians with new tools, knowledge and therapies for the selection of the best therapy for each patient, the U.S. research cohort comprising one million volunteers or more was created. All of Us Research Hub was launched as a research base where data management is underway. The U.S. Congress has approved US$1.455 billion for 10 years from 2016.

Table 3. Data available for researchers of All of Us

Data available for researchers of All of Us	
Data source	**Details**
Present information	
Health survey	The first survey includes sociodemographic characteristics, overall health, lifestyle and information on the use of substances, and subsequent module covers individual and family medical history and access to medical care.
Body measurement	Prior protocol measurement includes blood pressure, heat rate, weight, BMI, hip and waist size.
Living body sample	Blood and urine samples are tested on DNA, RNA, cfDNA, serum and blood plasma. If blood sample cannot be obtained, saliva sample is used.
Electronic health record	The first capture of structured data includes invoice code, medical history, test results, vital sign, and records from medical provider organization. In the pilot research, Sync for Science and other data collection by health data aggregator are tested.
Digital health information	Data can be captured from compatible devices owned by participant like Fitbit. Interaction is being studied between pilot research of other device and health app.
Future information	
Health survey	Additional module including the survey on the factor determining the social action of health is under development.
Bioassay	Pilot research of genotyping and total genomic sequence will be started by the beginning of 2020. Additional pilot test of bioassay is planned.
Medical bill invoicing data	A system to use invoicing data such as invoice code and medication data is under development.
Geographical space and environmental data	These types of data include geographical space linkage to measurement values such as meteorology, air quality, pollutant data level, and census data. Assay of exposure and measurement of sensor base are being studied.
Other information	Voluntary donation of data from social network (Twitter feed, etc.) and additional living body sample collection are being studied.

(Source) The NEW ENGLAND JOURNAL of MEDICINE 'The "All of Us" Research Program'

[3] U.S. major project "Cancer Moonshot"

Cancer Moonshot (current Cancer Breakthroughs 2020) is a large national project announced in January 2016 for the purpose of the prevention, early detection and improvement of treatment of cancer. This is an initiative with the National Cancer Institute (NCI) playing a major role under direct control of the National Institute of Health (NIH) and the U.S. government approved fund provision to the Cancer Moonshot for US$1.8 billion in seven years from 2016, which is to be appropriated to NCI in each financial year over seven years.

Specifically, the Blue Ribbon Panel (BRP) established as a working group of the National Cancer Advisory Board (NCAB), a specialist group appointed by the President, reported ten innovative recommendations in order to achieve ambitious target of the Cancer Moonshot whereby the progress equivalent to ten years in the prevention, diagnosis and treatment of cancer would be made in five years and research implementation team was launched in acknowledgement of it. In addition, jointly with 11 major bio pharmaceutical companies, Partnership for Accelerating Cancer Therapies (PACT), a cooperative research by the public and private sectors, was established under the budget of US$215 million for five years, and then initiatives with unified effort of public and private sector took place.

Table 4. Budget by category for fiscal 2018 in Cancer Moonshot

<Budget by category for fiscal 2018>

Research category	Budget (USD)
Network for direct engagement with patients	864,531
Translational science network of immunotherapy for cancer	67,643,470
Identification of therapeutic target to overcome refractoriness to cancer therapy	4,005,166
Building national cancer data eco system	9,557,020
Fusion cancer protein in childhood cancer	37,358,770
Research for minimizing debilitating side effects of cancer therapy	32,162,876
Prevention and early detection: Implementation of approach based on evidence	32,547,322
Retrospective analysis of living body sample from patients who received standard therapy	8,370,414
Preparation of human tumor atlas	74,246,242
Development of new cancer technologies	38,356,361
Total	**305,112,172**

(Source) NIH National Cancer Institute

[4] U.S. major project “Development of Da-Vinci, a surgery supporting robot”

In the latter half of the 1980s, for the realization of a remote surgery of soldiers in a battle field, the U.S. Army requested SRI International to develop it, which was an organization developing various element technologies used for remote robots at that time as a project under DARPA (Defense Advanced Research Projects Agency).

Under the supervision of DARPA, with the investment for about JPY300 million per month since 1995, Intuitive Surgical Inc. has developed a world most practical surgery supporting robot whereby a doctor operates by remote-controlling a robot arm looking at the 3D image obtained by an endoscope. It was commercialized in 1999 by Intuitive Surgical Inc., a venture capital company established in Silicon Valley, and received FDA certification in 2000.

(3) Strength of Japan and overseas trends

Table 5 shows comparison of the present situation and trends between Japan and other major countries. According to the reports, etc. from the Center for Research and Development Strategy, Japan Science and Technology Agency (JST-CRDS), the main trends of relevant research and technology fields are as follows.

In the field of immunological science, Japan shows strength in biochemically and molecular

biological mechanism research but falls behind others in the next generation immunological basic research such as immune informatics and immunity engineering. According to the 2016 survey by Thomson Reuters, Japan's immunology is ranked 5th in the world in the citation rates for theses, which is the highest in all Japanese biological sciences area and at the same rate as materials science and chemistry. Contribution of immunology in Japanese science is still high but trends are on the decrease when considering the departure of the youth from immunology and the lack of fund. In the field of development, there is no Japanese seeds-derived biopharmaceuticals that follows Actemra and Nivolumab. The Japan's original seeds of new type treatment technologies such as CAR-T and TCR-T are extremely limited and the fact is that overseas technologies are gradually making inroads into Japan and clinical trials are being started. To break through this situation, it is imperative that the basic research in Japan is revitalized.

In the field of time science (biological clock), Japan is a front runner in the world in basic study such as the discovery and molecular mechanism of suprachiasmatic nucleus (SCN), discovery of mammal clock gene "Per" and 24-hour formation mechanism at the level of clock proteins and leading the world of basic study of RNA-autonomous circadian clock protein. Furthermore, search and identification of sleep and arousal substances are at the world top level and leading the world in the achievement of the discovery of Orexin and elucidation of neural mechanism. As for development, Takeda Pharmaceutical launched melatonin receptor agonist which acts on intracerebral clock centrum as a sleep inducer.

In the field of gerontology, as institutions professing in aging research in Japan, there are National Center for Geriatrics and Gerontology, Tokyo Metropolitan Institute of Gerontology, and Institute of Development, Aging and Cancer, Tohoku University but are mostly for disease research and their scales are not sufficient. For high social needs and necessity for government support, dementia-related R&D are underway by multiple companies in collaboration with national institutes, universities, etc. but the research system is still far from being sufficient when compared to the U.S. and Europe including uncertainty of the research support. In anti-aging medical care as a whole, activities of domestic companies are predominantly low as compared to Europe and America.

With regards to the field of healthcare IoT, Japan is promoting R&D of devices, materials and measurement technologies in the world-leading medical measurement field mainly by universities and public research institutions. The R&D are underway at universities and companies on minimally invasive diagnostic devices using interstitial fluid for biological sample, bio-device using noninvasive biological gas, and power supply, sensor and material for wearable devices. In addition, it draws high attention as exemplified by the presentation of medical diagnostic devices by large and midsize companies of Japan and there are many who are studying new entry.

In the field of measurement data analysis, while basic study is active in Japan on medical image processing, etc., there is restrictions on the data to be handled and shortage of absolute number of participating researchers. Various measures have been taken in Japan for the strengthening and acceleration, but we are far from being advantageous in light of many countries of the world investing a huge sum of fund and vigorously promoting their research. However, it has become an essential domain in promoting every field of science

and we need to take initiatives strategically.

In the field of regenerative medicine, Japan has so far reported many world-leading important study reports including establishment of human iPS cell, large scale culture of ES cell, and establishment of organoid. Furthermore, in recent years, the development is accelerating for clinical researches and clinical trials and Japan is trailing only U.S. in the number of clinical trials using pluripotent stem cell. Japan implemented the first clinical research by transplanting autologous iPS cell, thus leading the world in the application of iPS cell. On the other hand, Japan trails in regenerative medicine using other cell strain and not depending on cell therapy and so forth.

In the field of diagnostic drug and biomarker, expectations are high on liquid biopsy in the diagnosis area but Japan, with insufficient study results on human, got a late start compared to other countries. Japan has successful cases of new drug to be among the top five in the world but the examination guidelines for new diagnostic drug is much different from those of Europe and America, resulting in insignificant number of successful cases. The small domestic market is also a problem.

In the field of life-style related disease, Japan has strength in kidney disease research with remarkable achievements leading the world in hypoxia, fibrosis and regeneration research, and basic research leading to the clarification of a patient condition of COPD and NASH with achievements equal to those of Europe and the U.S. However, leading those excellent basic research results to clinical trial and actual application requires a huge amount of fund and it is therefore difficult to develop independently in Japan.

In the field of psychiatric and neurological disorders, milestone researches have been made in the basic neuroscience ahead of the world such as development of fMRI and PET ligand for intracerebral molecule and basic researches for neural circuit visualization of marmoset and protein visualization in the neurodegenerative process, influencing the trends of psychiatric disorder research. Also, Japan exerts efforts in their application to neuro rehabilitation in therapies for neurodegeneration disease and development of near-infrared spectroscopy expected for use as a wearable device, showing a progress close to the U.S. in the decoding technologies in motion and perception systems and application to BMI.

In the field of generic robotics, extensive researches including the development of soft actuator, research on flexible electronics, development of flexible high polymer material along with a treatment system combining high-intensity focused ultrasound with a robot are underway and development of a healthcare device such as a rehabilitation robot, wearable device, etc., applying them is very popular. Amid various surgical robots already commercialized or nearing their commercialization in many countries, the movement of Japan is a bit slow. The world trends of research and technology in medical and healthcare sector is in a process of its center of gravity being shifted from “Medical treatment” to “Prevention” and its subject from “Across-the-board” to “Individualization” and the future direction of study will be toward “individual medical care” and “predictive medical care” of a whole nation participation type.

When the trends of papers are further reviewed by modalities (technology and technique), among modalities of increasing the number of papers and popularity of researches, Japan is increasing the number of papers particularly in the field of “Wearable device,” “Microbiome,”

“Rehabilitation,” and so on. (Source: Web of Science and PubMed of Clarivate Analytics)

Table 5. International comparison of relevant research and technology area

Country, Region	Phase	Immune science		Time science (biological clock)		gerontology		Healthcare IoT (Bio measurement, sensor, wearable)		Measurement data analysis (AI)		Diagnostic agent & Biomarker (liquid biopsy)		Regeneration medicine		Lifestyle related disease		Psychiatric and neurological disorder		Robot basic technology	
		Present	Trend	Present	Trend	Present	Trend	Present	Trend	Present	Trend	Present	Trend	Present	Trend	Present	Trend	Present	Trend	Present	Trend
Japan	Basic research	○	↘	◎	↗	○	→	○	→	○	→	○	↗	◎	→	◎	→	◎	↗	○	→
	Practical research	○	→	○	→	○	→	○	↗	△	↘	○	↗	◎	↗	○	↘	◎	→	○	→
U.S.	Basic research	◎	↗	◎	↗	◎	↗	◎	↗	◎	↗	◎	→	◎	↗	◎	→	◎	↗	◎	↗
	Practical research	◎	↗	◎	↗	◎	↗	◎	↗	◎	↗	◎	↗	◎	↗	◎	→	◎	↗	◎	→
Europe	Basic research	◎	→	◎	↗	◎	→	◎	→	○	↗	○	→	○	↗	◎	→	◎	→	○	→
	Practical research	◎	↗	○	↗	◎	→	◎	→	○	↗	◎	↗	◎	↗	◎	→	◎	→	○	→
China	Basic research	◎	↗	○	↗	△	↗	○	↗	◎	↗	○	↗	○	↗	○	↗	○	↗	△	→
	Practical research	○	↗	×	↗	△	↗	○	↗	◎	↗	○	↗	○	↗	○	↗	△	→	△	→

(Source) Overview report of JST CRDS research & development Life science & clinical medicine field (2019)
Nanotechnology & material field (2019)

(Note 1) Phase Basic research phase: Base study level at universities, national laboratories, etc.
Practical research & development phase: Technical development level(including prototype development), Mass production technology level

(Note 2) Present * This is not relative assessment based on the present situation of Japan but absolute assessment.
◎: Notable activities and results are seen compared to other countries ○: Activities and results to some extent are seen
△: Notable activities and results are not seen compared to other countries X: Activities and results worthy of special mention are not seen

(Note 3) Trend ↗: Upward trend →: Keeping the status quo ↘: Downward trend

(Source) Center for Research and Development Strategy, Japan Science and Technology Agency (Overview report of research and development) Life science & clinical medicine field (2019)

Fig. 25. Direction of future healthcare research

Healthcare (Prevention, diagnosis, human measurement)

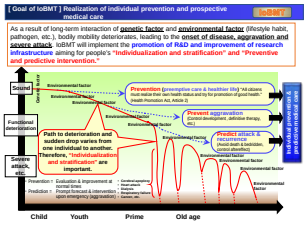
Center of gravity of healthcare is in a process of shifting from “Medical treatment” to “Prevention” and from “Across-the-board” to “Individualization”
1. Gene panel test
2. Liquid biopsy (gene, extracellular particle, protein, metabolism, cell)
3. Microbiome, virome
4. Image analysis, diagnosis
5. Real world data (HER, PHR (wearables like smartphone, watch, etc.)

Genome diagnosis & test	■ In November 2017, FDA approved FoundationOne CDx™ of Foundation Medicine Inc. (FMI) for the first time as a test to provide comprehensive genetic analysis profiling information of solid carcinoma. ■ In Japan, in December 2018, SYSMEX Corporation obtained approval for “OncoGuide™ NCC Oncopanel System” developed jointly with National Cancer Center. ■ FDA Foundation Medicine the direct-to-customer type test kit of 23andMe (U.S.-based company), which checks gene relating to various cancers (March 2018). It sells anonymous data for several million people to companies, research institutions, etc.
Liquid gas biopsy : Cost is significantly lower than the conventional test and results can be obtained in several minutes after submission of sample	■ In 2016, FDA approved Roche liquid biopsy kit for the detection of EGFR gene mutation in ctDNA of lung cancer patient. ■ In 2019, Anpac Bio reported that, through joint research with worldwide hospitals over 140,000 cases, its CDA (Cancer + Differentiation + Analysis) liquid biopsy diagnosis could detect over 20 types of initial stage cancer at the sensitivity and specificity of 80 to 90%. ■ U.K. Owlstone Medical developed a diagnostic device and diagnostic kit for breath VOC. Clinical tests on lung cancer and asthma are underway. ■ Also in Japan, NEDO and AMED “Development of measurement technology infrastructure of micro RNA in body fluid”, JST-CREST “Extracellular particle,” etc.
Microbiome	■ Clinical tests are underway centering around venture capitals. ■ AMED project “Microbiota,” etc.
Image analysis and diagnosis	■ In February 2018, FDA approved AI analysis software of computer tomography (CT) capable of informing medical provider of the possibility of apoplexy. ■ In April 2018, FDA approved a device using AI to detect diabetic retinopathy developed by IDX (U.S.-based company) as a medical device for the first time. ■ In 2018, Google announced image recognition AI “capable of detecting metastatic breast cancer with 90% accuracy” and “capable of discriminating major two types of lung cancer with 97% accuracy,” etc. ■ Researchers of UCSF announced that AI can predict onset of Alzheimer's disease earlier by 6 years from the cerebral PET test images. ■ In April 2019, FDA started to study new regulatory framework regarding necessary approval method before the launch of medical devices using AI (How to grasp and control learning and updating by AI). ■ Also in Japan, as achievement of SHOWA University and AMED, AI endoscope image diagnosis support software was approved (December 2018).
Real World Data (RWD)	■ Abbott, Dexcom, Empatica, Medtronic, Zoll, etc. provide wearable devices approved by FDA. ■ In 2017, FDA approved Abbott “FreeStyle Libre” flash glucose monitoring system. It is also covered by insurance in Japan. ■ In 2019, AliveCo's KardiaMobile was approved by FDA for the first time as a personal electrocardiogram device capable of detecting not only atrial fibrillation but also bradycardia of slow pulse and tachycardia of heart rate increase.

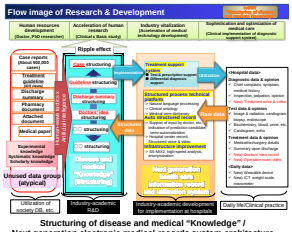
- **FDA (U.S. Food and Drug Administration) started Digital Health Innovation Action Plan in July 2017 in order to establish a system to appropriately evaluate innovations using digital technologies.**
- **For the pilot program, 9 companies were joined in, including Apple (U.S.), Fitbit (U.S.), Johnson & Johnson (U.S), Roche (Swiss), Samsung Electronics (Korea), Verily (Google, U.S.), etc.**
- **In preventive and predictive diagnosis, PaaS (Product as a Service) type business model is expected to pick up stream.**
- **Healthcare industry on the scale of 3.5 trillion dollars in U.S. alone will provide a good business opportunity for GAFA. Other industry groups are making inroads into the global healthcare business.**

Apple	■ In 2015, Apple started providing researchers and developers with the software framework “ResearchKit” designed for medical research investigation. In Japan, NTT DoCoMo developed an app for diabetes jointly with the University of Tokyo. It is utilized also at Juntendo University for multiple disease researches including hay fever. ■ Jointly with Stanford University, recruited 400,000 persons in less than one year for Apple Watch heart health survey and shared medical information. ■ FDA approves Apple's ECG App (an app for electrocardiogram) for Apple Watch 4 (September 2018). ■ As many as 100 CHS related hospitals (one of the largest U.S. healthcare service providers) support health record function of iOS device. Patients can have access to EHR information via multiple providers. ■ In March 2018, established own medical institution, AC Wellness.
Google	■ In U.K., DeepMind Health (Google) has been implemented by national hospitals operated by National Health Service (NHS) since 2016 and provided for members of hospitals who monitor the condition of patients in order to develop an app, “Streams.” ■ Since 2017, at Verily Life Sciences, with Duke University and Stanford University, Google Baseline Project has been implemented (to collect data such as heart rate, electrodermal activity, exercise habits obtained by various sensors through a smartwatch). ■ In 2018, NIH STRIDES (Science and Technology Research Infrastructure for Discovery, Experimentation, and Sustainability) initiative started. The purpose is for biomedicine researchers to have access to large scale biomedicine using Google cloud, thereby reducing economic and technical barriers to computing.
Amazon	■ In January 2018, Berkshire Hathaway, Amazon and JPMorgan Chase jointly announced the launch of Haven, new medical care system business. Using big data and virtual technology, try to take measures for chronic diseases of own employees (as many as one million persons) and reduce medical costs and at the same time, try to expand this system to other companies. Berkshire Hathaway increased their stake in Teva, a major generic drug company of Israel. ■ Amazon purchased the startup internet drugstore PillPack.
Ping An Insurance Group	■ The world largest insurance company. It built an Internet medical care service platform for the first time in the world. ■ Family doctor service, consumer healthcare, online shopping, health maintenance service, etc. are expanded digitally.

Future direction of research - IoBMT (Integration of Bio-Medical Things) -
Through strategical revitalization of “Human Research” x “Data Research”, R&D and infrastructure improvement to accelerate the realization of 1) “Structuring and integration of knowledge” on life science, engineering and medical science, and 2) Popular-participation-type “Individual prevention and prospective medical care (precision medicine)” and “Appropriate medical resource distribution”



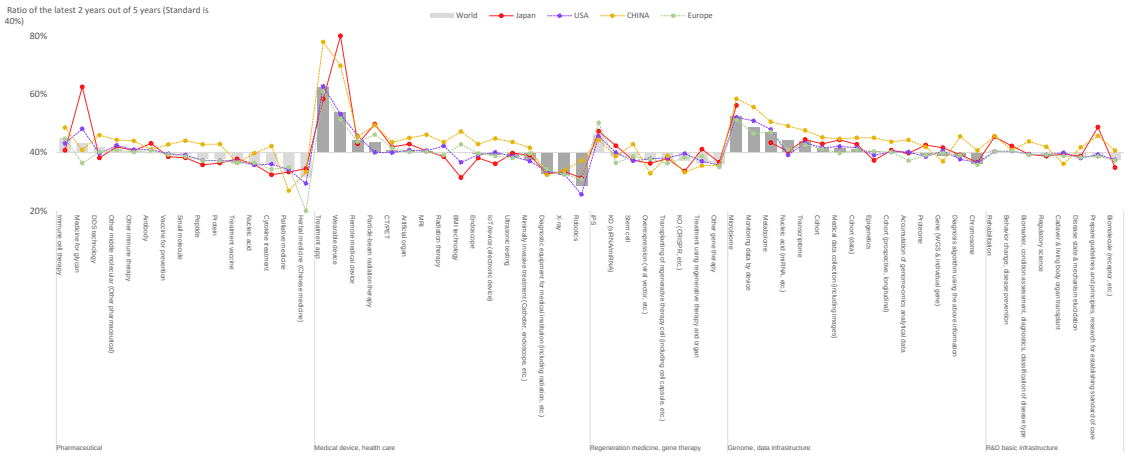
Social image targeted by IoBMT



Structuring of disease and medical “Knowledge” / Next generation electronic medical records system architecture

(Source) Center for Research and Development Strategy, Japan Science and Technology Agency (Overview report of research and development) Life science & clinical medicine field (2019)

Fig. 26. Survey of distribution of papers (Ratio of 2016-2017 to 2013-2017)



(Source) Cabinet Secretariat, Office of Healthcare Policy, The 19th Healthcare Promotion Expert Panel, Reference Data 5 "The Next Generation Medical R&D Promotion Program"

Supplementary Information from the PD

PD: Dr. Toshio Hirano
(President of the National Institutes for Quantum and Radiological Science and Technology)

1. Open call and selection policies, and related matters

(1) Open call and selection policies

- Please propose an adventurous and challenging scenario for achieving the following goal: Realization of sustainable care systems to overcome major diseases by 2040, for enjoying one's life with relief and release from health concerns until 100 years old.
- Achieving this goal will require an approach encompassing multidisciplinary perspectives and up-to-date knowledge, including a fusion of basic research and research targeting practical applications and a fusion of medical research and research in other fields. Your proposal must be based on innovative and groundbreaking concepts, as opposed to efforts targeting incremental progress. Although it is not always necessary to implement it by 2030, the halfway point. However, your proposal must ultimately demonstrate the feasibility of practical social implementation and adaptation, with ethical, legal, and social implications (ELSI) and related social issues in mind.

(2) The nature of the proposals

The Moonshot goal of health & medical field as determined by the government have three targets or subsidiary goals. The prime emphasis will fall on the viewpoints described below, in addition to the moonshot goals determined by the government and R&D concept established by the corresponding ministries.

- Achieving a society characterized by health and longevity will require medical care that maintains QoL and goes well beyond mere treatment of disease. Medical care includes treatment, prevention, rehabilitation, and daily life post-treatment. We believe QOL is the key aspect of such medical care and post-treatment life.
- Another goal is to overcome major diseases. In a society characterized by health and longevity, major diseases such as cancer and brain and cardiovascular diseases will be regarded as lifestyle conditions attributable to genetic factors and to lifestyle factors since infancy, such as diet, exercise and sleeping, and aging (i.e., the life course). The keyword or

concept here appears to be chronic inflammation. Aging and obesity are intimately related with uncontrolled chronic inflammation, which in turn give rise to major disease, including diabetes, arteriosclerosis, dementia, and cancer. Aging itself may be regarded as the result of uncontrolled inflammation. Crucial perspectives in achieving a society characterized by health and longevity will include controlling inflammation and controlling immunity and sleeping. We seek innovative perspectives that address the problem of lifestyle diseases while maintaining QoL and the problem of controlling the homeostatic mechanisms that cease to function effectively with age.

- Subsidiary Goals 1 through 3 are interlinked. Quantum life science, molecular biology, basic and clinical medicine, medical networks, data science, and the development of medical devices incorporating innovative technologies, all individually and/or cooperatively offer the potential to achieve effective control of the homeostatic systems that cease to function effectively with age and various lifestyle conditions. For Subsidiary Goal 3, we welcome R&D not just in the sphere of rehabilitation and regenerative medicine, but innovative QoL-based treatments. In addition to innovative proposals within the framework of a single subsidiary goal, we very much welcome proposals that address more than one subsidiary goal and proposals with strong links to or implications for other subsidiary goals. In sum, we are seeking adventurous, groundbreaking proposals.

2. R&D promotion policies

(1) Portfolio management

The relationships between multiple R&D projects will be managed as parts of a portfolio. Thus, the program will entail both cooperation and competition among PMs. Consequently, you will specify a scenario and the milestones to be achieved in years 3, 5, and 10 from the time of PM selection based on the scenario, then reappraise your proposal and budget plans to a reasonable extent based on consultations with the PD and other personnel.

(2) Industry/academia/government partnerships

We expect results that will contribute to and have material consequences for society and industry. However, this does not mean that such results must be achieved by 2030. We recommend against an excessive focus on applications at the start, as this is likely to discourage the bold, innovative outlook needed to achieve paradigm-shifting discoveries. It is important to regard failures as stepping stones to progress. At the same time, you will be expected to keep in mind at all times the potential for actual social implementation and to explore seriously, at each

milestone, the potential for industry/academia/government partnerships, translation of research results with an eye toward future social implementation, and the pursuit of such potential where possible.

(3) International collaboration

As set forth in the Application Guidelines, the proposals are expected to represent a combination of leading R&D capabilities, knowledge, and ideas, whether from Japan or abroad.
Therefore, ideally, you will monitor R&D activities both at home and abroad and, where necessary, be willing to pursue R&D in partnership with overseas institutions (universities, government or nonprofit organizations, academic societies, and companies).