P P I

Patient and Public Involvement (PPI)

GUIDE

A guide for collaboration between patients and researchers

BOOK

Japan Agency for Medical Research and Development

We published the first PPI guidebook in Japan in FY 2019.

As a digest of the guidebook written in Japanese,

we made an English version in FY 2022.

AMED, Japan Agency for Medical Research and Development

Foreword: on the publication of the Patient and Public Involvement (PPI) Handbook

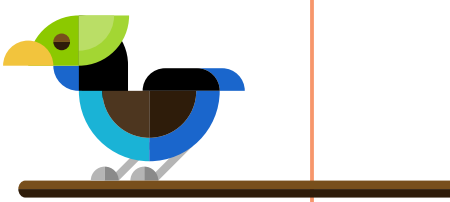
AMED (Japan Agency for Medical Research and Development) was established in 2015 and currently is in its second phase after the 5-year first phase. Among major missions for the second-phase activity established by the government, the following statement is cited. In order to guarantee research integrity and appropriate process in carrying out medical research and development, promotion on PPI (Patient and Public Involvement) should be enhanced in accordance with the concept of ELSI (Ethical, Legal and Social Issues).

In the first phase of AMED, importance of these kind of activities had already been recognized and a series of effort were made on enhancing information sharing and understanding on research ethic by citizens toward an approach to the concept of ELSI. A “Survey of Trends in Patient and the Public Involvement in Clinical Research” was initiated in 2017 in an effort to utilize perspectives from patients and the public to improve the quality of research supported by AMED. As a fruit of the survey, “Guidebook for Patient and Public Involvement” was issued in 2019, for which the English version is published herein.

As of October 1st, 2021, AMED has announced renaming our “Division of Research Integrity and Legal Affairs” into “Division of Research Integrity and Social Cocreation and Legal Affairs”. AMED will keep enhancing relations to the human society through not only with ELSI and Diversity including PPI, but also sharing efforts on Sustainable Development Goals (SDGs) which are tackling to overcome 17 problems in the current human society by 2030 with wide international collaborations under the message issued at the UN summit in 2015.

President, Japan Agency for Medical Research and Development

Yoshinao MISHIMA, PhD



Foreword: on the publication of the Patient and Public Involvement (PPI) GUIDEBOOK

The Japan Agency for Medical Research and Development (AMED), launching April 2015, aims to bring fruits of medical research and development to patients and families as soon as possible. To this end, Patient and Public Involvement (PPI) plays a crucial role. In the Summer of 2017, we started "the Survey of Trends in Patient and the Public Involvement in Clinical Research" to utilize perspectives from patients and the public for improvement of a quality of AMED-supported research and to bring us a step closer to fulfilling our mission. This guidebook was published on the basis of the surveillance coupled with a series of thoughtful discussions. In order for the guidebook to truly serve its purpose, we must continue to facilitate an understanding of the importance of PPI among all researchers engaged in medical research and development; we would also let patients and the general public aware of the rules of medical research and development and the reality of scientific verification. Progress in medicine never ends, and medical needs for patients are changing by years. This is a small but important first step to empower patient and public involvement in medical research and clinical trials.

Based on the 4 principles of bioethics: Respect for autonomy, nonmaleficence, beneficence, justice, it is crucial for all people, not only researchers and physicians, but also participants in clinical study, to understand significance of PPI. Moreover, of importance is that people in different sectors; patients, healthcare professionals, researchers, and those who have not been affected by disease yet, will continue making efforts to refine new perspectives through mutual communication and collaboration. On behalf of AMED, I would like to encourage researchers and all professionals who are engaged in supporting medical researches to read this guidebook to take the first step, wishing a wellness of all people.

President, Japan Agency for Medical Re-search and Development (as of March 2019)

Makoto SUEMATSU, MD, PhD

Foreword: on the publication of the Patient and Public Involvement (PPI) GUIDEBOOK

As a physician delivering the diagnosis and treatment of breast cancer, I have realized the importance of PPI on various occasions in clinical settings. My first message for the readers of this guidebook is that PPI in medicine and medical research, is not limited to disease awareness and patient support activities, as we would imagine from the term "patient advocacy"; in fact, it is extremely multifaceted.

When I was involved in the drug approval review process in the late 1990s, the U.S. Food and Drug Administration (FDA) had already established a system in which members of the public – who were appointed consumer representatives after receiving training – had the right to discuss and vote at various councils (advisory committees) in the review process. I was impressed that a system in which patient representatives could voice out their opinions about items subject to review at the council – in their own words – was in place. On another occasion, when I was working as a member of the International Committee of the American Society of Clinical Oncology (ASCO) in 2003, I was very excited to find out that some of the Board members of the society regularly exchanged opinions with leaders of patient organizations to obtain ideas for the society's future activities.

Later, when I presided the International Symposium on Breast Cancer in April 2010, patient organizations invited from the United States and Sweden impressed me with the importance of research advocacy and the importance of its contribution to obtain research funding. Furthermore, at a patient advocacy meeting I hosted at the National Cancer Center in May 2015, I was inspired when an executive at the UNational Cancer Institute (NCI) explained that a specialized department called the Office of Advocacy Relations (OAR) works with patients and the public in a natural way in various aspects of cancer research planning, implementation, and evaluation.

This guidebook is also designed to serve as a reference for patients and the wider public. Having witnessed the history of PPI-like activities in the United States and the multifaceted efforts being made in this field, my greatest hope is for this guidebook, which was developed under the leadership of AMED President Suematsu, is to reach every person, and for this to serve as the first step toward promoting PPI in research in Japan.

Chairperson of AMED Research Committee on Survey of Trends in Patient and the Public Involvement in Clinical Research (as of March 2019)

Yasuhiro FUJIWARA, MD, PhD

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ABOUT THE BOOK

Patient and Public Involvement: Background and Conceptualization within AMED

Japan Agency for Medical Research and Development

The Plan for Promotion of Medical Research and Development [NOTE]

(approved by the Headquarters for Healthcare Policy on July 22, 2014; partially amended on February 17, 2017)

The Plan for Promotion of Medical Research and Development states that "In conducting clinical research and trials, from the stage of planning them, it is necessary to promote the involvement of test subjects and patients, as well as actively promoting activities to raise awareness among patients and the populace as a whole regarding the significance of clinical research and trials, as well as the benefits they bring to citizens."

Based on this plan, AMED aims to bring research outcomes in the field of medicine to practical use as quickly as possible so that patients and their families are able to receive its benefits. For this aim, AMED promotes Patient and Public Involvement (PPI) in medical research and clinical trials. Ultimately our work should support each patient's life, in terms of biological existence, diary living, and lifespans.

AMED's Approach to Patient and Public Involvement (PPI)

Definition

AMED envisions a form of PPI in which researchers refer to the knowledge of patients and the public in the medical research and clinical trial processes.

Note: Patient and the Public are defined as patients, their families, former patients (survivors) and future patients..

Our Philosophy

1. Produce research results that are more useful for patients and the public
2. Promote smooth implementation of medical research and clinical trials
3. Contribute human subject protection (reduce risk)

Intended outcomes

〈For researchers〉

1. Give new perspectives and value for further advancement of research and development
2. Address patient anxiety and concerns, and facilitate understanding of medical research and clinical trials

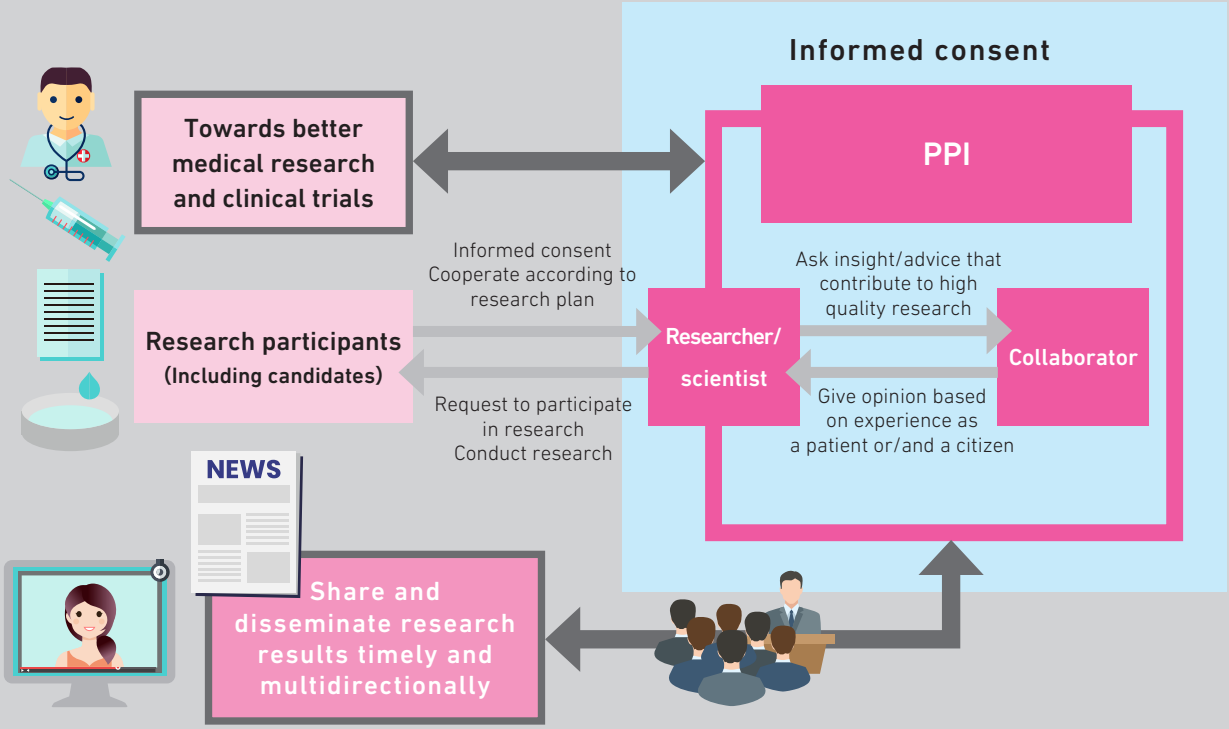
〈For patients and the public〉

1. Improve the convenience and understanding of medical research and clinical trial for research participants
2. Make medical research and clinical trials more accessible to of patients and the public and increase their interest in healthcare

NOTE The Plan for Promotion of Medical Research and Development : This is a plan formulated by the Headquarters for Healthcare Policy, headed by the Prime Minister, in accordance with Article 18 of the Health and Medical Strategy Advancement Act (approved by the Cabinet on July 22, 2014). The plan aims to intensively and systematically drive forward research and development (R&D) measures to be taken by the government in the medical field, the improvement of the R&D environment, and the dissemination of results. In addition, in accordance with Article 19 of the law, AMED will play a central role in medical R&D that utilizes the capabilities of research institutions, and in improving the environment for such initiatives. This also applies to funding for medical R&D and improving the R&D environment undertaken at research institutions.

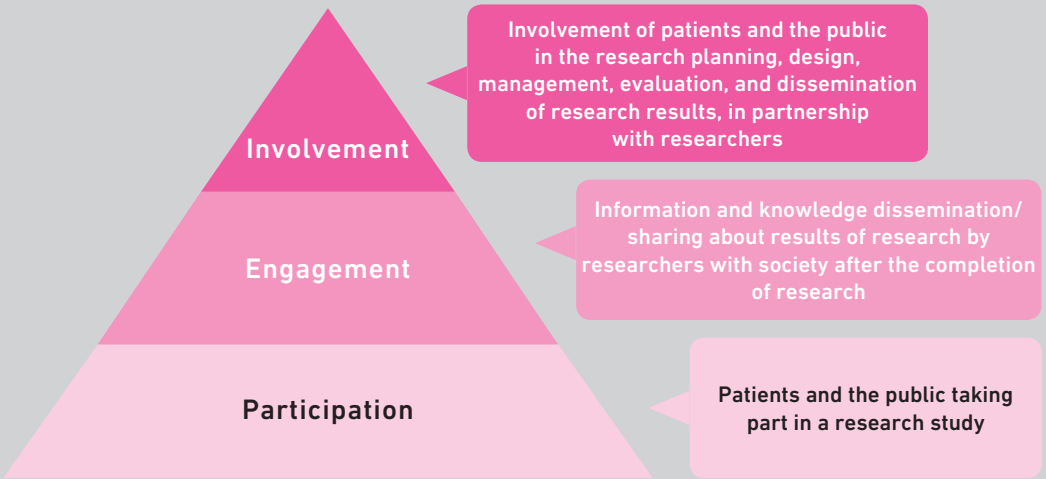
Overview of Patient and Public Involvement in AMED

PPI will improve medical research and clinical trials,
and also the dissemination of the results in a better way for society.



PPI definition in other countries

PPI definition in other countries



reference: https://www.guysandstthomasbrc.nihr.ac.uk/researchers/patient-public-involvement-advice/ppi-toolkit/what-is-patient-and-public-involvement/
(Accessed 2019.2.20)

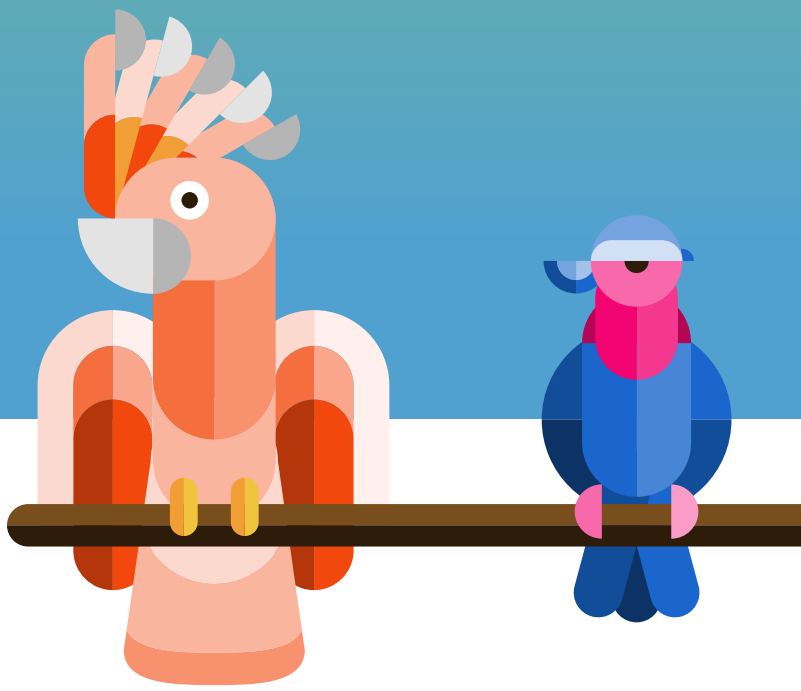
Medical Research/ Clinical Trials and Patient and Public Involvement

(PPI, Patient and Public Involvement)

Some people may believe that PPI is not quite relevant to medical research or clinical trials because they are not familiar with PPI.

However, PPI is a must for delivering better research results to society.

This chapter explains the concept of PPI and its impact.



01 Introduction

To develop new diagnoses and treatments, and to test the validity of established methods, it is necessary to carry out a variety of studies with the help from people. Research conducted with the help of people is called clinical trials, clinical research, or medical research (see ■ Figure 1), defined in detail by laws and guidelines in Japan. In this guidebook, we refer to research involving human subjects related to diseases or health "medical research and clinical trials", or "research" in short. Before discussing PPI, this chapter summarizes the significance of medical research and clinical trials.

01-1

Research differs from day-to-day clinical care

In day-to-day clinical practice, doctors generally determine appropriate treatments for the patient based on the patient's symptoms, lifestyle, and values, upon consulting the patient. When a patient's wishes are unclear, such as when the person is being urgently transported to the hospital, the priority is to save the patient's life. In this case, doctors determine the best way to treat the patient. In other words, the focus of clinical practice is to restore the health of the patients. For this purpose, the most appropriate treatment is selected. In most cases, drugs and medical devices with established safety and efficacy, and with accumulated examples of use, are employed.

On the other hand, medical research and clinical trials (referred to as "research" hereafter), sometimes involve activities that are part of day-to-day clinical practices, such as collecting blood samples or taking drugs, but the purpose is different. Research is the process of asking questions about something that has not yet been clarified, and then planning, deciding and rigorously carrying out a study to provide an answer and evidence for that answer.

Repeating these actions will yield information that will be useful for future medical care.

In other words, research places emphasis on scientific discoveries carried out for the benefit of FUTURE patients, rather than helping patients in front of you.

How, then, does research proceed?

First, the researcher has to determine the "research questions" through a process of careful consideration. For example, questions could be about what life-

Key points

❶Medical research and clinical trials differ from clinical practice.

- Clinical practice: The practice of providing optimal treatment to a patient using medical drugs and/or medical devices whose safety and efficacy have already been established in order to restore the health of patients.
- Medical research and clinical trials: The act of collecting evidence to improve disease prevention, diagnosis, and treatment/care by conducting scientific and objective data analysis to answer questions that have not yet been clarified.

❷There are more and more examples of the viewpoints of patients and the public when developing medical care guidelines and regional medical care plans, and the importance of such perspective is also being recognized in medical research and clinical trials.

style habits are associated with people who develop a particular disease in a given community; what is common in the genes and genomes of children with a disease; which existing drugs have fewer side effects; which drugs have a longer duration of effect, existing drug C or new drug candidate D?; and which is less burdensome for the patient, drug therapy or surgery?

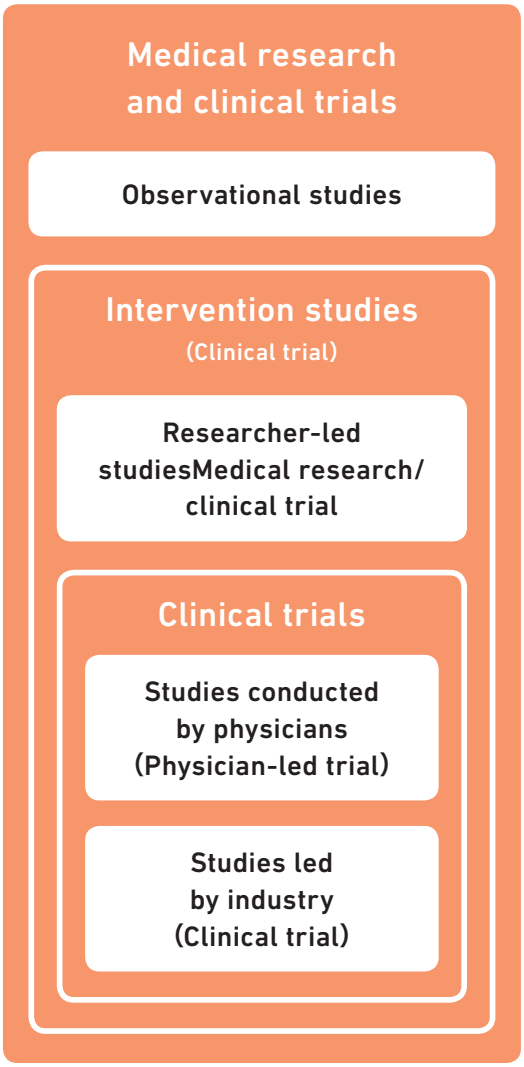
Then, researchers consider the most appropriate data for clarifying the research question, the eligibility criteria of research participants (including candidates), and a method for obtaining and evaluating the data reliably without imposing excessive burden on research participants. These considerations are summarized into a research protocol.

What, then, are the types of available research methods?

The most common type of research carried is an observational study. This is carried out through experiments in which samples of blood, urine, and skin taken from the human body are analyzed, as well as through analysis of medical records and questionnaire results. Observational studies are called as such because they are an observation of the analysis results from samples and information obtained from research participants (the people who actually take part in the research).

On the other hand, interventional studies (including clinical studies) are involving people when a candidate for new drugs or medical devices needs to be compared against conventional methods, or when it

Figure 1 Types of studies involving people



becomes necessary to test the effect of a different method using two groups of people.

In the field of pharmaceuticals, the first step of interventional studies is to verify whether a drug under development is safe in a small group of research participants. The number of participants is gradually increased, and the drug's efficacy is then assessed by methods such as comparing two randomly split groups. When those results are promising and there in a prospect of commercialization, the clinical trial is carried out with the purpose to obtain manufacturing and marketing approval from the Minister of Health, Labour and Welfare.

In interventional studies of disease prevention, people may be randomly assigned into two groups, one continuing with conventional methods and the other undertaking a new approach.

Of course, once researchers have identified the most appropriate approach, they may not be able to launch their studies immediately. Is it a feasible procedure? How will the budget be obtained? Will anyone be willing to support and participate in the research? It takes time for the researcher to consider these points and prepare a concrete framework for implementation.

01 -2

Rights and Responsibilities of Study Participants (Including Candidates)

The purpose of medical research and clinical study (referred to hereafter as "research") is to conduct rigorous and objective scientific analysis, to deepen the understanding of disease and health, and to create the basis for improving prevention, diagnosis, and treatment, all while taking caution not to impose excessive burden on research participants. Thus, researchers must understand the rights and responsibilities of research participants.

As a general rule, researchers must write a research protocol before beginning a study and obtain approval from a research ethics review committee. Before a research project begins, these committees review whether a study is scientifically significant and whether it poses undue risk or burden to the research participants. The actual name of the committee varies depending on the research or medical institution. Researchers must consult the research ethics review committee for a decision when modifying their research plans.

In addition, people who are asked to participate in research — in other words, the people who will become study subjects — are guaranteed the right to receive detailed information about research plans and to make voluntary decisions about whether to participate. Potential research participants have the right to ask any questions to researchers and receive explanation about the research in plain language. Researchers must prepare in advance to ensure that such opportunities are available.

Participating in research poses a certain level of risk and burden on the participants' physical and mental health, as well as their life. Some of these challenges may only become apparent once the study actually begins; therefore, reversing the intention to participate and opting out of the study (withdrawal of consent) is recognized as an important right for research participants. Consent may be withdrawn for any reason.

However, how to handle the research data collected before withdrawing consent depends on the research plan; hence it is necessary to give detailed explanations to research participants in advance, as well as when they request withdrawal.

As described above, it is necessary to fully convey in informed consent that research participants have various rights and will not suffer any disadvantages in exercising those rights. When a physician asks their patient to participate in a study, the

patients are often unsure whether they could ask questions and may hesitate to ask them. Patients may also worry that refusing to participate in a study or withdrawing consent at any stage may jeopardize the relationship with their physician. Therefore, the rights of research participants can never be emphasized enough. In order to protect the rights of research participants, it is desirable to conduct research with support from specialists like clinical research/clinical trial coordinators (CRC) or research coordinators.

At the same time, those who have become research participants have certain obligations, and are required to comply with instructions and respond in good faith. This could include making visits to the hospital or clinic for the specified time period, recording their daily diet and exercise, answering a questionnaire by the deadline, or taking and administering a test drug for the specified time. Furthermore, social media posts should only be published after careful consideration as some content could place the research at risk. Research participants should be aware of their role as partners for successful research, and researchers and coordinators may actively call on participants to exercise caution.

These ground rules apply to all studies. In Japan, Laws and guidelines stipulate detailed considerations and rules for each field or methodology.

01-3

Committee members from the perspective of patients and the public are needed

In the field of medical research and clinical trials (hereafter referred to as “research”), research ethics committees were the first to include non-expert voices. In addition to experts in the natural sciences, humanities, and social sciences, many research ethics review committees in Japan require the attendance of general public members to hold meetings. According to the explanation document of the Ethical Guidelines for Medical and Health Research Involving Human Subjects, “members of the general public” refers to people who are able to express objective opinions from the perspective of research participants who may not have sufficient knowledge about medical research; for example, people who are able to express objective opinions about whether the content of a consent document based on the research is generally understandable. For this reason, committee members from the general public are expected to evaluate the appropriateness of a research plan from the point of view of research participants.

In the review process at the Research Ethics Review Committee, it is important to have a “team review” of committee members with diverse areas of expertise and interest, making use of their strength. In addition, the Research Ethics Review Committee members are obliged to receive training and maintain confidentiality; training materials have also been developed for members of the general public.

However, recently in Europe and the United States, there has been a tendency to require that the direction of the research and the specific details of the plan be referred to the opinions of patients and the general public, before the research plan is submitted to the Research Ethics Review Committee. This is since there is no need to recruit research participants to start with if outcomes from the research are deemed not to be beneficial to patients and members of the public, who could ultimately become beneficiaries.

For example, in the United Kingdom, researchers are asked to explain whether they have consulted patients and the general public at various stages such as research grant application, research ethics review, and peer review, and the reasons for not involving people if they have not done so. Responses to these questions are increasingly becoming a point of consideration in those processes

Initiatives to seek opinions from patients and the public are not limited to research. For example, the goal in developing medical care guidelines for various diseases is to make them helpful and practical for patients and healthcare providers in their decision-making; thus, there is a growing movement to take into consideration the perspectives of patients and the public from the drafting phase. In addition, a policy called "Act on Promotion of Securing Comprehensive Medical Care and Long-Term Care in Local Communities (地域における医療及び介護の総合的な確保の促進に関する法律; 医療介護総合確保推進法)" - which are formulated by prefectures based on the "Act on Promotion of Comprehensive Assurance of Medical Care" - requires that the opinions of patients and residents of the area be taken into account through various methods such as town meetings and interviews.

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P P I

Patient and Public Involvement (PPI)

GUIDE BOOK

～A guide for collaboration between patients and researchers～

Japan Agency for Medical Research and Development

02 The significance of including the perspectives of patients and the public into medical research and clinical studies

Researchers are responsible for designing and properly conducting medical research and clinical studies (referred to hereafter as "research"). Therefore, patients and the general public have limited opportunities to express their views on the way research is conducted, and often, they find out about new research plans only after the details have been finalized. In other words, for patients and the public, collaboration with researchers has been 'passive' rather than 'proactive', and 'fragmented experiences' rather than an 'an ongoing journey'.

In recent years, however, the way in which research is conducted taking into account the perspectives of patients and the public have attracted international attention. This is a way of conducting research in which patients and members of the public collaborate with researchers in thinking about the research, expressing their opinions, and being involved in the decision-making process.

In this guidebook, the activities of patients and the public involved in research are referred to as Patient and Public Involvement (PPI), and our definition of PPI is referred as the knowledge of patients and the public when carrying out research.

02-1

The Significance of PPI: (1) Contribution to Research Ethics

PPI is regarded as meaningful in three ways. The first one is the significance from a research ethics point of view.

In reflecting on the tragedy of human subject experiments conducted during World War II, countries around the world have since implemented policies that allow for studies to proceed appropriately while protecting research participants and their rights. Prior reviews of research proposals in Ethics Review Committees and informed consent constitute a major part of such efforts (see 01-2 "Rights and Responsibilities of Study Participants (Including Candidates)").

In recent years, in an effort to conduct research more appropriately, many countries are increasing-

【Section Summary】

Key points

❶PPI leads to better protection of research participants and the building of trust.

❷The lay knowledge of patients and the public gives researcher new perspective and help identify challenges that researchers are not always aware of.

❸The democratization of science has the potential to bring diversity and creativity into the research design.

❹Regulatory authorities and pharmaceutical companies, largely in Europe and the United States, are strengthening collaboration with patients and the public, aiming to improve research and development through bilateral feedback and education.

❺As a secondary outcome, PPI may reduce research costs and shorten the period of time required to recruit research participants.

ly placing value - especially from a research ethics point of view – in listening to the opinions of people who can relate to research participants at various stages of the research, beginning from the planning of research to its completion.

For example, a PPI handbook for researchers in the UK notes that patients offer researchers different perspectives because they care about things that the researchers had not thought of, and that patients can help improve the quality of research by sharing their thoughts on research methods, explanations, and consent forms.

Meanwhile in the United States, the concept of "Collaborative Partnership" has been established as a fundamental principle for conducting clinical trials in developing countries in mind. In a collaborative partnership, researchers continuously engage with relevant communities (local communities, patient and family associations, support groups, etc.) and share responsibilities as a partner, while respecting important values and culture within the community.

The latest international research ethics guidelines have also adopted the idea that it is important for communities being studied to be involved from the beginning to the end of a research project. These guidelines call on researchers, funding agencies, and government agencies to ensure that potential research participants (a person who actually participates in research) or their communities are involved in a meaningful and sustainable way from an early stage.

These international trends suggest that researchers should not only avoid conducting research that is not desired by the targeted communities, but also the need to consider research ethics after the completion of the research. Specifically, this includes how research results can benefit to society, how to return research results to research participants, and how to provide treatment after research is completed.

Thus, partnership between researchers and patients and members of the public – who can relate to research participants – is crucial for driving such measures forward.

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02-2

The Significance of PPI: (2) Lat's make use of lay knowledge

PPI also gives researchers the opportunity to make use of knowledge and wisdom from non-experts. This is because the knowledge that patients and the general public possess through their experience may give new perspective to challenges that researchers cannot overcome solely through their expertise. Such cases have been reported in several medical studies and clinical trials in the past. Results that may seem trivial to researchers can sometimes give patients and their caregivers tremendous findings or joy; for instance, only the patients truly appreciate the significance of being able to walk one meter.

The concept of utilizing wisdom from patients and the public has long been emphasized in the field of public health. This notion was clearly verbalized by the World Health Organization as the People Centered Healthcare System at its General Assembly in 2016, raising "engaging and empowering people" as one of its five core strategies. This strategy calls for people to acquire the ability and resources that allow them to make their own health decisions on their own, and to participate actively in policy-making. The reason is that people cannot easily change their behaviors even if researchers obtain scientifically validated risk information and discover secrets for maintaining health; in such cases, the research results may not be utilized. For example, when considering how to approach people in a given community to promote healthy lifestyles, nothing is more powerful than the viewpoints of people in that community.

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02-3

The Significance of PPI: (3) The Democratization of Research

PPI can also be considered as a more democratic activity.

For example, the European Commission's science and technology policy framework includes the concept of Responsible Research & Innovation (RRI). Active participation and support in democratic processes - and ultimately contribution to creating a scientifically literate society - is crucial for the development of science, technology and innovation in harmony with society. Increased involvement can lead to diverse perspectives and creativity in research projects and their results. Including an opportunity for patients and the public to communicate opinions that arise from a different standpoint from researchers, gives new value to research and makes them more accessible to people than when decisions are made by experts alone.

Japan's Science and Technology Basic Plan has mentioned the relationship between science, technology, and society since its 3rd term (fiscal years 2006 to 2010). Furthermore, the 5th term (fiscal years 2016 to 2020) recognizes that expanding on scientific activities with public participation (citizen science) will become an important foundation for open innovation. " The Plan for Promotion of Medical Research and Development " (approved on July 22, 2014, partially amended on February 17, 2017) by the Japanese Government's Headquarters for Healthcare Policy (医療分野研究開発推進計画) states that "In conducting clinical research and trials, from the stage of plan-

ning them, it is necessary to promote the involvement of test subjects and patients, as well as actively promoting activities to raise awareness among patients and the populace as a whole regarding the significance of clinical research and trials, as well as the benefits they bring to citizens."

In addition to communicating the research results to the public in an easy-to-understand manner and addressing their questions, considering the viewpoints of patients and the public when evaluating the social validity of the research plan increases the potential for achieving solutions to more socially essential issues.

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02-4

Overseas regulatory efforts

In Europe and the United States during the 2000s, regulatory authorities responsible for the review and approval of pharmaceuticals and medical devices began to communicate directly with patients and the public and strengthened efforts called "Patient Engagement". In the case of the European Medicines Agency (EMA), this was prompted by a regulatory reform in 2004 (EC No 726/2004) that required regulators to communicate with patient and consumer representatives. Meanwhile, the Food and Drug Administration (FDA) began working on a rebuilding of trust in the aftermath of extreme patient and family protests. In 2016, the EMA and FDA began sharing information about collaboration with patients and the public.

Through the "the Survey of Trends in Patient and the Public Involvement in Clinical Research (臨床研究等における患者・市民参画に関する動向調査)", we confirmed that efforts by regulatory authorities - which initially seemed to be a series of trial and error - are now leading to concrete measures. The involvement of patients and the public has been progressing in a variety of ways, such as public hearings for taking patient opinions into consideration in research development and reviews; better methods for utilizing data from PRO (Patient Reported Outcome) assessments, which are completed by clinical study participants, in reviews; providing skill development and training for patients and the public; and checking the readability of official documents in advance.

In response to these regulatory actions, pharmaceutical companies are also making efforts to use input from patients in clinical trials and drug development; this is referred to as "Patient Centricity". Pharmaceutical companies in Japan have started with activities such as checking the readability of written explanations and consent forms, and sharing study results with clinical trial participants.

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02-5

Various cases in Japan

Although “patient and public involvement (PPI)" has not been a familiar term in Japan, many collaborative activities with patients and the public, which are essentially similar to PPI, have been undertaken in the past. However, since there has been no systematic effort to accumulate case studies, the number of documented cases is limited.

For example, with regards to the development of innovative medicine, there are records of patients and the public expressing their opinions on a clinical trial plan on regenerative treatment for people with spinal cord injuries, and on a clinical trial plan using iPS cells for retinitis pigmentosa.

What outcomes can we expect from successful PPI? As a familiar example, opinions from patients and the general public can be helpful for preparing explanation and consent documents and for deciding how to carry out the informed consent process, which in turn leads to a more understandable and patient-friendly decision-making process. In addition, PPI could contribute to a shorter recruitment period for research participants (a person who actually participates in research), or a reduction in withdrawal of consent or study dropouts.

In addition, revising research plans based on the opinions of patients and the public before the beginning of a study can reduce the likelihood of major objections being raised after a study begins. Modifying the research plan into one that patients and the public want, and one that researchers are also satisfied with, may reduce the cost of conducting research.

PPI tends not to be successful when there is an absence of a common goal or a lack of clear rules for collaboration. For example, research teams established as part of Japan’s rare disease policy measures have fostered a cooperative relationship with patient organizations over many years. In some cases, however, the collaborations were not successful when the direction of the lead researcher did not match the goal of the patient organization’s activities. In particular, in several cases, the lack of feedback on the study results after participation in the study led to dissatisfaction among the patients. Please refer to the section "What happened to that research we collaborated on?" on page 31 for comments from patients, citizens, and researchers. In a breast cancer trial, patients and researchers had very different views, and both sides’ statements and views were published.

In going forward, it is important to promote objective reflection, including appropriate methodologies, quantitative evaluation methods, and publication of unsuccessful cases.

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P P I

Patient and Public Involvement (PPI)

GUIDE BOOK

～A guide for collaboration between patients and researchers～

Japan Agency for Medical Research and Development

03 Basics of PPI

Having described the philosophy and background of PPI, some may be wondering what it takes to achieve it. Let's give a little more concrete examples and push for PPI. Here are four basic points of PPI.

03-1

PPI is a forum for dialogue between researchers, patients and the public

PPI is different from petitioning researchers from patient and family associations. It is also different from the physician-patient relationship in clinical practices.

In PPI settings, we seek opinions from patients, families, former patients (survivors), and future patients of a disease, and promote dialogue in order to further advance research on a disease. It can be done in person or through written communication.

PPI can easily be confused with activities such as recruiting subjects to participate in a study or public relations activities about research progress and results.

PPI is not a place to recruit research participants (a person who actually participates in research) for research. PPI refers to having patients get involved with and provide input to researchers at every possible opportunity, from the idea stage to final evaluation. This should be distinguished from participation in a specific research program (participation). Careful attention should be paid when discussing specific research plans that will be conducted in the course of dialogue with patients and the public.

In addition, it is recommended that the progress and results of research be explained to the general public in an easy-to-understand manner, and that not only one-sided explanations and lectures but also interactive efforts be made.

It's true that taking the form of symposia and science cafes can lead to lively Q & A from participants. However, the implication of PPI is that research should be conducted together with patients and the public, and it must be clearly distinguished from activities that seek understanding by explaining research content and research results. Of course, research and activities to raise awareness of the results must be carried out steadily, and these are also inseparable from PPI. It is also expected that the quality of PPI will improve as a result of increased awareness of research.

【Section Summary】

Key points

❶PPI is a forum for dialogue between researchers, patients and the public. It is neither a place to recruit research participants nor a place to enlighten and publicize research.

❷Ask patients and the public to give objective opinions.

❸Conflict of interest management and confidentiality issues are important for PPI.

❹If it is determined that there is no need for PPI, explain the reason for the decision.

03-2

Engage patients and the public to speak up objectively

The human resources required for PPI are patients with the disease covered by the research plan, those who have experienced the disease in the past (survivors), their families, and caregivers. They need to be interested in research and have an understanding of the significance and role of PPI.

When conducting research on healthy people, people living in the area or working at the research site may be candidates. Furthermore, depending on the purpose and content of the PPI, there are cases where even people who have no relation to the disease can respond while imagining the position of the research subject (including the candidates).

However, whatever their position, it is important that the people who participate in PPI make an effort to understand what the research is about and what the researchers want to solve together, and that they are willing to ask questions about what they do not understand. Furthermore, PPI requires people who can explain to the researcher what they can tell from their own experience, and what they cannot tell from their own experience. Researchers should not spare the efforts of searching for and selecting such people.

PPI does not require the involvement of patient and family associations or citizens' groups. Therefore, it is not necessary to have executives or members of patient and family associations or civic groups as collaborative members. At Cancer Research UK, for example, freshness is important and there are no extended tenure rules, to ensure that the people involved in PPI are not always the same. In addition, the "Patient and Citizen Panel" of the National Cancer Center in Japan accepts applications considering the diversity of patients.

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03-3

Conflict of Interest Management and Confidentiality

A conflict of interests (COI) is a situation where the same person has obligations to do more than one thing, which may lead to a conflict of mutual interest. For example, a researcher who is funded by a pharmaceutical company has an obligation to report the results of a clinical study to the company in good faith and to protect the research participants (a person who actually participates in research). However, if a researcher receives excessive funding or remuneration from the same company, or owns stock in that company, there is a risk that the researcher will

focus on producing data that is favorable to the company, neglecting to protect the research participants or analyzing the data in a sloppy manner.

Data and articles published by researchers with serious COI cannot be trusted and can damage society. For this reason, researchers are required to disclose to their institutions, the research funding, their positions as board members of companies, and their stock holdings before conducting research. By doing so, they are managed by research institutions so as not to fall into the "worrisome COI." In recent years, there have been many opportunities for pharmaceutical companies to provide funds to patient and family associations, and the status of the funding has been disclosed.

Under these circumstances, it is necessary to have the general public, who cooperate with PPI, declare the status of economic transactions and social roles and manage them. Patients and the public who have certain inters in pharmaceutical companies or other organisations from the perspective of COI management should not be involved in PPI and should be asked to withdraw.

In addition, research projects also contain a wealth of confidential research and personal information. Especially in the early stages of research, there are a lot of confidential details that must not be revealed to competitors. Therefore, researchers must also impose confidentiality on those who collaborate in PPI.

Although some patients and the public may be unfamiliar with COI statements and confidentiality pledges, these commitments are important to become partner of researchers.

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03-4

If your research is going to run without PPI, make sure the researchers can explain why

If researchers decide that PPI cannot or should not be carried out, they should be able to explain why.

For some diseases, it may be difficult to get input from patients and the public. For example, if the disease is very rare or if the disease is so mild and common, it may be difficult to find someone willing to help. Instead, it is meaningful to guess the feelings of the research subjects (include candidates) by referring to literature. This is because the purpose of PPI is to make researchers to think about and use their minds and imaginations about people who are greatly affected by the research project. In some cases such as basic experiments, researchers may determine that PPI is not necessary at this time. These researchers' decisions need to be respected.

In other countries, there have been an increasing number of cases in which plans and practices related to PPI are included in the application forms of Research Ethics Review Committees and research grant applications. In these situations, it is considered rather harmful to implement PPI that has lost substance. For this reason, it is often replaced by a statement of reasons for not implementing PPI.

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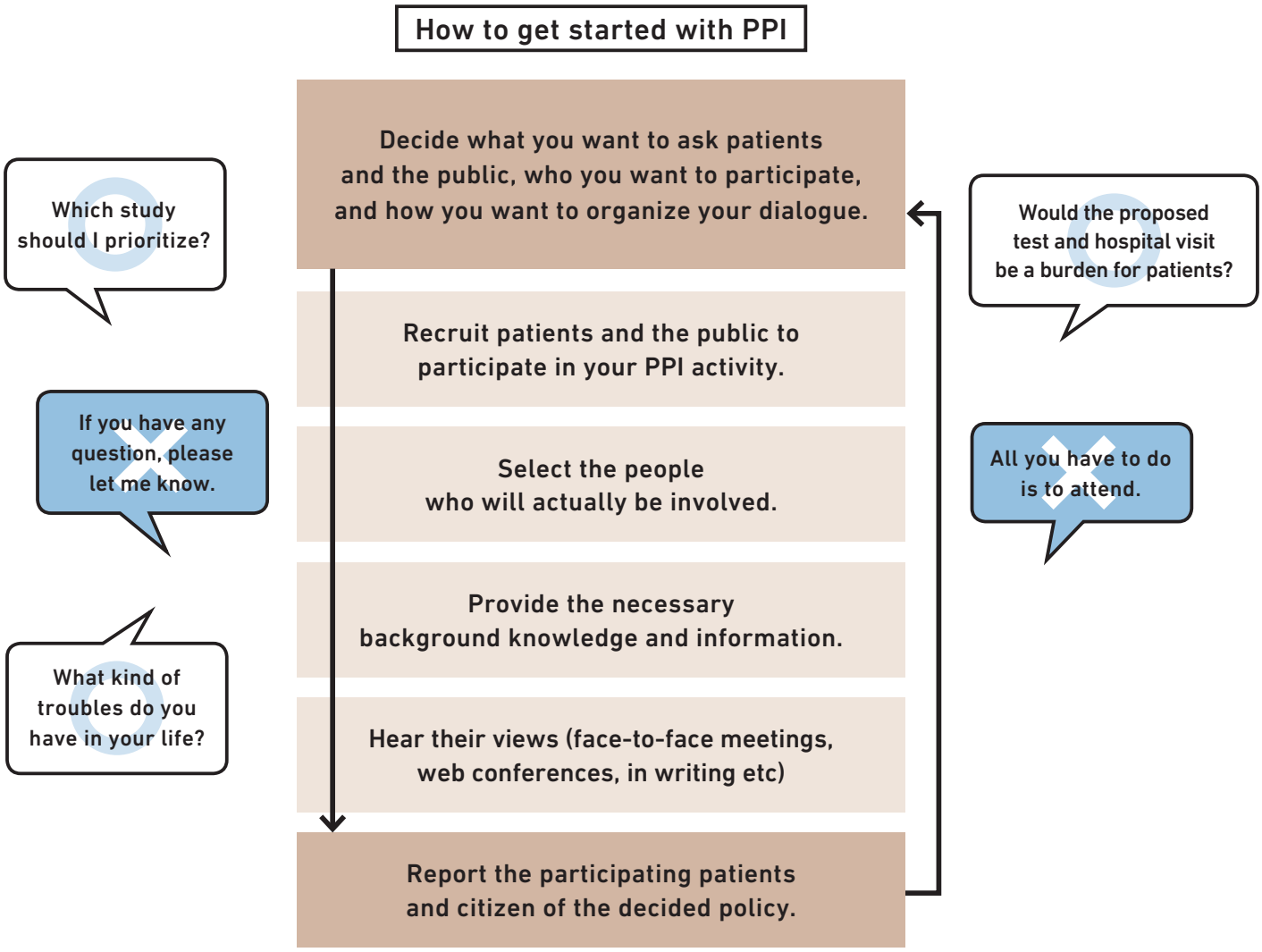
KEY POINT

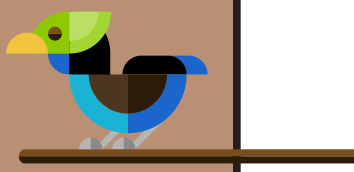
Key point

How to get started with Patient and Public Involvement (PPI)

Asking simple and/or small questions is a great way to engage patients and the public. The key to success is to clarify your goals (i.e. what insight to get from patients and the public) before asking for their views.



COLUMN



COLUMN 1

Initiatives to making research participants the key players in research

Kaori Muto, The Institute of Medical Science, The University of Tokyo

Patient-reported outcomes (PRO), as an opportunity for research participants to become important data providers, are common than ever.

According to the FDA guidance*, PRO is “any report of the status of a patient’s health condition that comes directly from the patient, without interpretation of the patient’s response by a clinician or anyone else.” Typical examples are records of pain and sleep. Evaluation scales should be accurate and reliable to be robust withstand subsequent rigorous evaluations. Japanese versions of an internationally standardized scales are sometimes used.

Other initiatives to note are Participant-Centric Initiatives (PCI). Enabled by ICT (Information and communication technology) transformation, user-friendly research infrastructures make it easier for people to express their willingness to participate in research and to complete questionnaires online, most functioning as a disease registry. The purpose of PCIs are (1) to record patients' medical history and daily life in advance so that medical research and clinical trials can start smoothly in the future, and (2) to record patients' daily lives so that researchers can be interested in them in the future.

In some cases, it is inconvenient and cumbersome for research participants to provide data that meet the standards required by researchers. To provide participants a better environment to submit high-quality data with less burdens, it is essential that the views of patients and the public are heard from the planning stage of research.

* Guidance for Industry Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. the Food and Drug Administration. 2009.

COLUMN 2

Importance of research advocacy

Naomi Sakurai, Japan Federation of Cancer Patient Groups

I first came across the word “research advocate” in 2009 when I attended a lobbying training program sponsored by the National Breast Cancer Coalition, and I learned the importance of evidence-based patient advocacy.

At the program, I found about the Research Advocate Training Program “Project LEAD®” and applied for it immediately. The program provided me a week of clinical study training with patient advocacy leaders from 24 countries.

The training included online lectures from The Johns Hopkins Bloomberg School of Public Health, followed by a face-to-face lecture, where we learned about the significance and protocols of clinical study, PICO, medical safety, medical ethics, how to read statistics, and how to search and structure the medical articles, and the role of patients.

In Europe and the United States, from the viewpoint of maintaining and improving HTA (Health Technology Assessment) and the quality of life of patients, patients are involved in clinical study from the protocol planning stage to provide their perspective. To this goal, scientific education programs for patients are actively held at academic conferences and patient associations.

Clinical study are the future and hope of patients and their families.Patients are expected to express their perspective not only as a personal experience but also as a representative of their diseases, disabilities, age, or gender. In terms of both human resources and funding, “research advocates” play an important role in progressing and improving clinical study. Also, it is important to develop patients and public as “citizen scientists”.

COLUMN 3

Drug Development with patients (Initiatives of Pharmaceutical Companies)

Kazuhiko Kamiyama, The Japan Pharmaceutical Manufacturers Association

As awareness of patient-centered healthcare grows, Japanese pharmaceutical companies are beginning to make use of patient' voice in drug development. This is an initiative in which patients and companies work together as partners, and it is believed that patients' voices will lead to the creation of new perspectives and values in the medical field.

Specific examples include the formulation of a clinical study design that reduces the burden on patients, the preparation of easy-to-understand explanations and written informed consent forms, the provision of results to study participants in plain language, the obtention of feedback from study participants after the completion of clinical study to utilize future development, and the release of study information in Japanese on a public and centralized website.

For patients, this approach not only contributes to society based on their own experience, but also has the potential to expand opportunities for faster use of better drugs through more realistic clinical study.

We also want to know the experiences and thoughts of many patients about their diseases, treatments, and medicines, so that we can deliver better medicines to patients by making use of their voices.

COLUMN 4

Aiming to be a citizen who expresses meaningful opinions

Ikuko Yamaguchi, Consumer Organization for Medicine & Law (COML), an authorized non-profit organization

Having changed from the days when medical professionals took all the initiative, the need for patients and medical professionals to collaborate is being challenged. As a result, there is a growing tendency for local and national government agencies, and medical institutions to incorporate the opinions of patients and citizens.

This movement is now spreading to a variety of fields. For example, hospitals that provide highly advanced medical care are required to establish a medical safety audit committee that include those who receive medical care, and ethical review committees for clinical trials and clinical research are required to have general members in attendance. In addition, it is now recommended that clinical practice guidelines, mainly developed by academic societies, incorporate the opinions of the general public from the drafting stage.

This is a movement that is finally starting to realize what is essentially a matter of course: to place importance on the viewpoint of users who may not be noticed from the perspective of experts.

I think it is important for us to make efforts to express our opinions calmly and objectively so that people can see the significance of PPI.

COLUMN 5

Promotion of Patient Public Involvement by Pharmaceuticals and Medical Devices Agency

Yasuhiro Fujiwara, Pharmaceuticals and Medical Devices Agency

PMDA created a “Patient Centiricity Working Group” in May of 2019. After discussion with various stakeholders in the span of 2 years, “Guidance on Patient Participation” by Pharmaceuticals and Medical Devices Agency was issued in September of 2021.

The basic concept of this guidance is to firstly, embody PMDA's philosophy of “Patient First” by actively collecting patient voices, and secondly, to deepen the understanding of patients regarding PMDA operations and pharmaceutical administration by striving to “enhance the information provision for patients” so that information can be collected more effectively.

In order to collect the voices of patients, in addition to information gathering through existing systems such as review meetings for unapproved drugs/off-label use drugs with high medical need, we will push forward (1) holding study sessions and opinion exchange meetings with patient advocacy groups, and (2) the participation of patients in conferences held by PMDA. Based on these voices, we will also work on development using the patient reported outcome (PRO) as an evaluation index.

As information provision for patients, we will provide (1) basic information on pharmaceutical affairs, and (2) safety information, that the general public can understand through the PMDA website (which will be improved for easier use), SNS, and participation in and/or holdings of various events. We will also evaluate the effects of the provision of the information. Please look forward to it in the near future.

Voice of patients, public and researchers

Reference: "the Survey of Trends in Patient and the Public Involvement in Clinical Research"

1 What is the significance of collaboration among clinical researchers, patients and the public?

Voices of Japanese researchers

- Patients have a first experience of the issues surrounding their disease, and they sometimes have views and opinions that researchers and medical professionals would never be able to recognize; their perspectives are highly thought-provoking.【A cancer researcher】
- We think it is important to consider the opinions of patients and their families, because, at times, there are motivational differences between what researchers regard as a priority and what patients are having problems with.【A researcher of an incurable disease (Nan-Byo)】

Voices of Japanese patients and the public

- We believe medicine develops from direct interaction with patients, not from past lectures or literature in medicine. While medical research serves as the foundation for protecting the lives of patients, efforts to make such specialized information visually accessible is just as important, and steps should be taken to seek the understanding and cooperation of the public. This is because it is essential to change the awareness and behavior of the public who are the end-users of healthcare, in order to change medical care.【The Association of Cancer Patients and Families】
- When promoting medical research, we have a genuine interest in learning more about it, simply because we are patients or a part of their family. We believe that communicating our thoughts in the form of an opinion exchange from both sides could give rise to new perspectives, or the discovery of new insight.【A patient and family association of incurable disease (Nan-Byo)】

2 What do you keep in mind for better collaboration?

Voices of Japanese researchers

- We held a symposium to hear opinions about drug development for pediatric cancer. However, it seemed difficult for patients and families to express their views, and only a few actually shared their opinions. We felt that a platform for the exchange of opinions was necessary. Next time, we will hold study meetings in advance to help exchange opinions.【A cancer researcher】
- We need to be collaborative relationships, not in a doctor/patient relationship.【A researcher of incurable disease (Nan-Byo)】
- When providing information to patients, it may lead to unexpected understanding and impressions, and we consider it necessary to devise ways to provide information.【A researcher of incurable disease (Nan-Byo)】

Voices of Japanese patients and public

- When communicating patients' point of view on research, be careful not to speak out only from our own subjective point of view. Provide a concise and accurate answer. Don't complain or get off track.【The Association of Cancer Patients and Families】

- It is important for patients to understand what researchers are doing and what they are aiming for. That also motivates the patient. It is also important that the patient's personal information is not leaked.【The Association of Cancer Patients and Families】
- When communicating opinions from the patient's perspective to researchers who are conducting research, I try to speak with a feeling of "I want to support the researchers.【A patient and family association of incurable disease (Nan-Byo)】

3 A little worried at times

Voices of Japanese researchers

- We often receive opinions that are not feasible, from those who seem not have sufficient expertise.【A cancer researcher】
- To what extent can we share our true feelings about research design with patients who participate in our PPI? Will we hurt them?【A cancer researcher】
- Ideally, we would like to have voices of patients who are "excellent" opinion leaders with broad perspectives, who can speak out the direction of the patient's overall opinion. The problem here is that we do not know to what extent a patient's opinion reflects the overall patients community. In order to ensure that this is not the opinion of some patients with loud voices, I think more surveys should be conducted on patients, and I feel that we need to establish an infrastructure for such research.【A cancer researcher】
- I think it is important to listen to the opinions of patients when conducting research, but sometimes it becomes a personal patient counseling meeting.【A researcher of incurable disease (Nan-Byo)】
- When I was invited to give a lecture at a patient and family meeting, some people complained about the time taken for basic research because they had a strong desire for a therapeutic drug. Although this is understandable considering their difficult situation, I think it's important to prevent the research from being biased by patients' opinions.【A researcher of incurable disease (Nan-Byo)】

4 What patients and the public can do?

Voices of Japanese patients and the public

- I find it very frustrating to find that a system designed for the benefit of patients is very far from being a good one. I believe that many opportunities for everyone in the respective field of healthcare to listen to the opinions of patients, bereaved families, and those involved in patient support activities will deepen mutual understanding and make it easier to use.
- I believe that I can make use of my experience as a recipient of healthcare to express my opinion, for example, on the wording of "Explanation and consent form for patients" in clinical research, how to explain it, and the support system, which will lead to improvements. The risks and benefits from the subject's perspective can be communicated to the researcher. More detailed consideration can be given to the subjects. The research can be widely disseminated to the public.
- We can convey the feelings of patients and their families that are beyond the researcher's consideration (anxiety, expectation, hope, etc.).

- We believe that we can contribute to the realization of more meaningful research by expressing our opinions based on the thoughts of patients and the public about participating in treatment and research. We also hope to find a way to resolve the gap in awareness between healthcare providers and patients/public regarding clinical trials (confusion between study and treatment, etc.).

- PPI may lead to research from the viewpoint of the research participants, and in a form that is close to them.

- When patients with the same disease talk to each other, they may share physical discomfort or symptoms. Since it is not yet medically clear whether these kinds of things are resulting from the disease, we believe that PPI will give influence future medical advancement.

- I have two thoughts about my contribution. The first is to convey my gratitude to researchers by saying, “Thank you” and to express my support in words or some other form (other than money or goods). Second, even if a researcher’s research is delayed or returned to the starting point, it is necessary to accurately convey our status and thoughts, without being caught up in the implicit codes of conduct in the medical research community. I believe that will in the long run make each research highly reliable and valid. I believe that this will eventually be returned to us as accurate disease information, QOL scales, and treatment development.

5 What happened to that research we collaborated on?

Voices of incurable disease (Nan-Byo) patients and their families in Japan

- Although we try to cooperate with requests from researchers as much as possible, we regret that feedback on the results is rare.
- Regular reports on the results and progress of the research after specimen donation will encourage future activities to recruit specimen donors.
- We had given comments on the way a questionnaire survey was written, but it is not clear whether this has led to improvements in the research design.
- Even if we provide the information to researchers, there is no report on how it was used in research.
- The patient side is willing to actively cooperate with researchers, but it becomes difficult for us to cooperate if researchers do not give us progress reports. We need a relationship of trust.

6 We don’t even have a chance to interact with researchers.

Voices of incurable disease (Nan-Byo) patients and their families

- As far as I know, there are no researchers who specialize in my disease in Japan. Because it is a disease with few opportunities, we try to respond sincerely, quickly, and without fail to not miss out on the few opportunities that may lead to researchers and research.
- Although I am acquainted with the professors conducting the research, I have not met them in person or exchanged emails with them, so I do not receive any information about what kind of research is being conducted at present or the progress. I’d like some information.

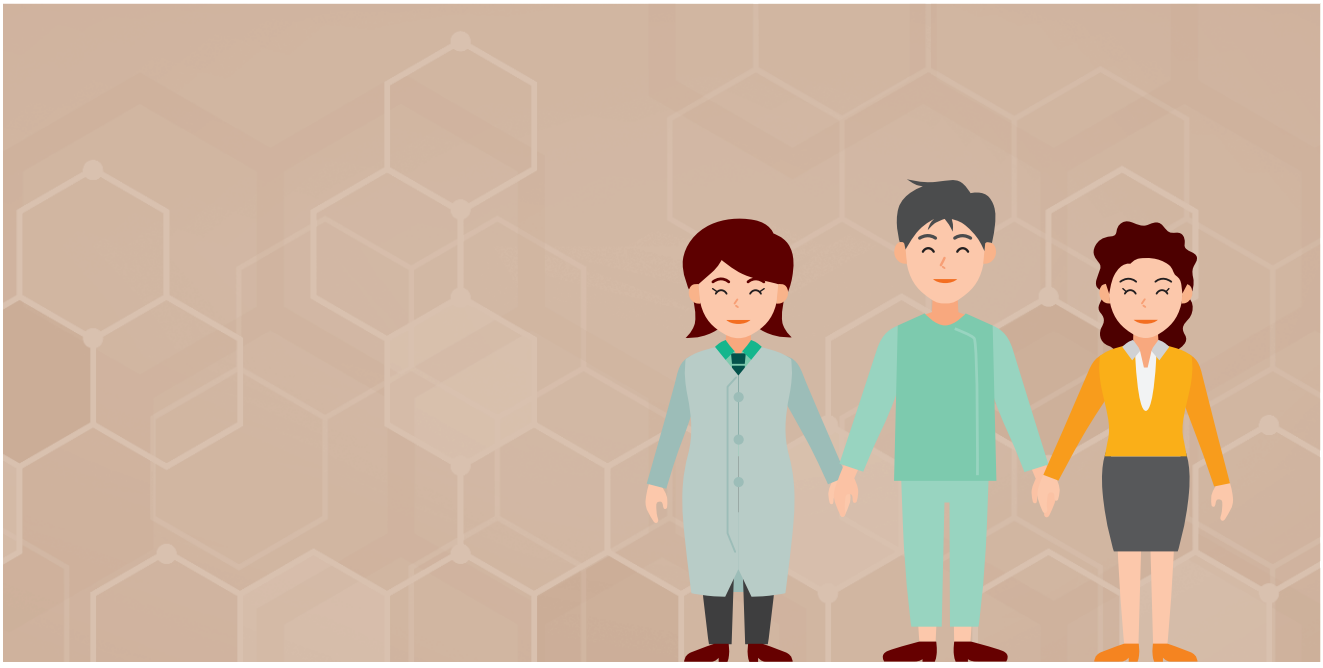
7 Let's create a system for better collaboration.

Voices of Japanese researchers

- In some cases, results may be undesirable from the patient's point of view. It cannot be ruled out that too close a relationship between a researcher and a patient could lead to some bias in the publication of results, fearing that the relationship might collapse. I feel the need to draw up "Guidelines for establishing appropriate patient-researcher relationships." 【A cancer researcher】
- I think it would be good if there were opportunities where researchers who do not actually treat the patients under study to communicate with them. 【A researcher of incurable disease (Nan-Byo)】

Voices of Japanese patients and the public

- I think it is very important to convey opinions from the patient's point of view. However, first of all, I think it is important for patients to have knowledge and insight to convey their opinions , and if they are asked to do so, to make efforts to be able to fully understand them. Isn't it necessary to train patients to be able to do that? 【The Association of Cancer Patients and Families】
- I think some people can find a sense of self-affirmation, a place, and the value of living by realizing what they can do, for example, helping others. I hope we can create a better system and relationship for patients, researchers, and future patients. I think there is a strategy to improve the image such as "Patient cooperation is of great value for future medical progress! 【The Association of Cancer Patients and Families】
- Because patients want information about the progress of research that leads to new treatments, when new treatments will be available, and who will receive new treatments, it would be helpful to have a professional intermediary to provide information and opportunities to ask questions to researchers about these on a regular basis, and to have a contact relationship for these purposes. 【A patient and family association of incurable disease (Nan-Byo)】



PPI 10 Tips for Researchers

1	**PPI Fundamentals**	**Patients and the public should be considered to be research partners** PPI is a forum for dialogue, not a petition, with patients and the public to improve research. In addition, when you talk with someone you normally see as your patient, that persons not your patient but your research partner in PPI settings and you are not their doctor but a "research partner" in the context.
2	**PPI Fundamentals**	**PPI is not an occasion to recruit research participants nor to report research results for the public** PPI means involving patients and the public at every possible opportunity from the stage of deciding the content of research theme to the final evaluation of the research. It is different from participating in a study (ex. human subject, or respondents of questionnaire). It must also be clearly distinguished from public relationship activities such as communicating research content and results to general public.
3	**PPI Fundamentals**	**Work with patients and the public who can give an objective opinion** The requirements for patient and public involvement will vary depending on the research project and the purpose of the involvement, but it is advisable to involve people who can tell researchers what they can say from their own experience and what they cannot say from their own experience. Participants do not necessarily have to be executives or members of patient and/or family associations or civil society organizations to be able to give an objective opinion.
4	**PPI Fundamentals**	**If you decide not to involve patient and the public, explain the reason** If you determine that you cannot/should not involve patients/the public, explain why. In particular, it is detrimental to patients and the public if researchers engage in formal dialogue without a sense of collaboration. Instead, refer to the literature and make assumptions about the feelings of the research subjects.
5	**Preliminary steps**	**Set specific objectives for your PPI in your research plan.** Be specific about the reasons why you are conducting PPI at this stage of your research and what you would like to ask people involved. It is also important to make sure that the people involved understand the objectives of the PPI project.

The following ten tips summarize the essence of Patient and Public Involvement (PPI, Patient and Public Involvement) . We encourage all researchers to take this into account when conducting PPI.

6	Preliminary steps	**Prepare an appropriate application form for patient and the public** Before recruiting PPI participants, it is important to decide what experience and knowledge you are looking for, the format and location of the event, honoraria, travel expenses, conflict of interest management, confidentiality issues, etc., and to be ready to explain them. We recommend that you create a "application guide (p.37)" to help you prepare for this.
7	Preliminary steps	**Provide sufficient information** Patient and the public are less knowledgeable about research than researchers. Depending on the purpose of your PPI, you should provide them with enough background knowledge to enable them to interact with the researchers. If possible, you should also give them in advance the documents you plan to use on the day.
8	Practice	**Make sure you create a comfortable environment** For face-to-face meetings, we recommend that the venue is a rented meeting room or a coffee shop rather than the researcher's own institution, and that everyone dress casually so that patients and the public can relax. In addition, reasonable consideration should be taken to ensure that breaks are taken and that multipurpose toilets are available. In some cases, it is advisable to be flexible, for example, by holding videoconferencing or hearing opinions in writing.
9	Practice	**For fruitful PPI, let's all share the rules** PPI requires that researchers and patients and the public are willing to listen and understand each other. It is a good idea to set up and share rules such as not using the terms "professor" or "doctor", other names that may emphasize the difference in position, not discussing personal symptoms or treatment if it's outside of the PPI. If you don't know, a rule such as "I don't know" may be effective.
10	Post-Practice	**Communicate the results of the PPI to people involved** After each PPI, let the people involved know what you, as researchers have learned from them. It is up to the researchers to decide whether to incorporate the feedback their received into the scientific validity of the research. It is advisable to inform the participating people (patients and public) of your decision, the reasons for it, and how the research plan has changed.

PPI 10 Tips
for Patients and the Public

1	Basics of PPI	**PPI participants should be aware that they are research partners** PPI is a place to have a dialogue between researchers, and their PPI partners (patients and the public) to promote research better. It is not a place for patients and/or patient organization to convey petitions to researchers. Also, when you communicate with a person you see as your doctor in your PPI activities, the person is not an your “primary care physician” but a “researcher” and you are not a “patient” but a “research partner.”
2	Basics of PPI	**Distinguish PPI from participating in research as research subjects and/or listening to reports on research results** PPI means engaging researchers during each research at every possible opportunities from the stage of considering the content of the research to the final evaluation. It is different from participating in a study (participation). It must be clearly distinguished from opportunities to hear about research content and results.
3	Basics of PPI	**Be objective when you participate in PPI** Determine what you can say from your own experience and what you don’t understand from your own experience and give your opinion to the researcher. You do not necessarily need to be an executive or members of a patient/family association or a civil organization, as long as you give your opinion objectively.
4	Basics of PPI	**Not all studies involve patients and the public** In some cases, researchers may decide that they cannot or do not need to engage with patients and the public. For example, they are some diseases that may be difficult to obtain input from patients and the public. Instead, researchers are encouraged to deduce the feelings/values/opinions of their target community by referring to the literature.
5	Preliminary steps	**Make sure you understand the purpose of the PPI event** Before participating in PPI, make sure you understand the reason for conducting the PPI, and what researchers want to ask the PPI participants. If you are unsure of the purpose of the event, you may ask your contact person.

Based on the 10 PPI tips for researchers, we created 10 tips for patients and the public. We encourage researchers to share this information to PPI participants.

6	Preliminary steps	**Make sure you are provided with sufficient information** If you are applying for an open application, the experience, knowledge required, honoraria, and travel expenses should be indicated in the application guidelines. Also check the need for conflict of interest declaration and confidentiality commitments. You should also provide enough back ground knowledge to be able to interact with communicate researchers effectively. If possible, ask to be given materials the researchers plan to use on the day in advance so that you can understand the contents.
7	Preliminary steps	**Make sure you have a comfortable environment** In a face-to-face meeting, make sure that the environment is conducive to relaxation for patients and the public. If reasonable considerations such as ensuring breaks and checking for multipurpose toilets are insufficient, don't hesitate to ask researchers to improve. The same is true if you request video conference or written comments. If you feel that the environment is not comfortable for you, you may decline to participate.
8	Practice	**Be sure to value both your opinion and the opinion of others** It is worthwhile for researchers to learn from your experiences as patients and public. Please don't be nervous to come and share your experiences and opinions. That said, other people's opinions are just as valuable as yours. Be respectful of what others have to say, and try to listen carefully.
9	Practice	**Let's share the rules with everyone to ensure a fruitful PPI** In PPI, it is desirable that all participants, both researchers and PPI participants, feel comfortable to expressing their opinions to each other. To this end, set and share rules beforehand, such as not using terms such as "professor" or "doctor," not discussing personal symptoms or treatments, and saying "I don't know" if you don't know.
10	Post-Practice	**Ask the researchers to tell you the results of the PPI** It is desirable to share your impressions/thoughts with each other after the PPI event. In addition, after PPI, researchers should decide whether to reflect the opinions expressed in the PPI by comparing them with scientific validity. Ask the researcher to inform you of the results and reasons for the decision, and how the research plan has changed.

Patient and the public application guide template (assuming an opinion exchange meeting)

1 Name of the activity

■First, let's decide the title. As there is no specific designation for patients and the public, institutions and research groups can decide on one, such as "patient and citizen panels" or "patient and the public advisers".

Title example 1: Recruitment of patients and the public who give advice to researchers concerned with XXX*
Title example 2: Recruitment of people who can cooperate with PPI in research of XXX*

*Please add names of the target disease of your research.

2 Knowledge and experience required of participants

■Identify the requirements for participation and engage the appropriate people. For example, you might want to include the following:
・Gender
・Age
・Relationship to the disease (e.g., Patient/Patient's Family/Caregiver)

Other necessary knowledge and experience (e.g., knowledge about medical research and clinical trials).

3 Background of the study

■You also briefly introduce the research institutions and research groups. Be sure to write what you expect from patients and the public, that is, the purpose of PPI.

■Some of the things you should include in this section are:
・Name of your university, or your research institution
・Introduction of your research groups
・Research funding sources
・What kind of impact do you expect to have PPI in your research (Purpose of your PPI)?

4 What we would like to ask of patients and the public

■Be explicit about what patients and the public are expected to do. For example, this could include:
In what position do you want them to express their opinions (e.g., could you tell us if our research plan is burdensome for a patient involved in the disease?)

・Declaration of conflicts of interest
・A pledge of confidentiality
・Constraint time (If it is held at a specific venue, please specify that you will ask participants to come to the venue).

Based on this guidebook, the following is a list of items that should be clearly specified when recruiting patients and the public.
Please modify the items according to your own purpose. You can also use this table as a checklist for advance preparation.

5 Outline of your PPI event

■ Specify the scale, procedures, and support for participants. You may want to provide the following information:
・Number of people
・Location
・Rough timetable for the day (outline of the PPI meetings, if any such as time schedule of the day)
・Whether online/remote participation is possible (e.g., performing a video conference)
・Information on parking lots for wheelchairs, multipurpose restrooms, day-care centers, etc.

6 Cost burden and rewards

■ Be sure to specify whether the actual expenses will be borne by patients and the public participating to the PPI event and whether they are compensated or remunerated. It is desirable that researchers bear the actual costs. Refrain from setting a high amount as remuneration, and if you can't provide a remuneration, try not to impose an excessive burden on participants.

■ This section should clearly state the following information:
・Whether any actual costs are to be borne (examples of actual expenses: transportation, accommodation, parking, cost of a caretaker or daycare center to be requested on the day).
・Description of the actual payment process.
・Availability of remuneration. Amount of remuneration

7 Schedule

■ Let people know the schedule before and after the opinion exchange meeting. Do not forget to provide feedback to patients and the public and report on the research results. In general, it is up to the researchers to decide whether or not to reflect the opinions received in their research based on scientific validity. Not reflecting is not wrong, so give feedback honestly.

■ This section should cover, for example, the following:
・Period of application
・Period of implementation of PPI
・Timing of feedback on how or not the opinions obtained were reflected in the research
・Timing of reporting the research results after the research period is over

8 Contact information

■ Specify the period and method of application and provide a contact point for inquiries. It is advisable to designate a contact person within the research group to deal with such inquiries.
The following information should be clearly stated:
・Period of application
・Application method
・Contact details
・Name of person in charge

PPI GUIDE BOOK

Patient and Public Involvement (PPI)

～A guide for collaboration between patients and researchers～

Japan Agency for Medical Research and Development

〈 Acknowledgments 〉

We would like to express our sincere appreciation to all those who have cooperated with "the Survey of Trends in Patient and the Public Involvement in Clinical Research" and to all the researchers, patients, and citizens who have expressed their opinions regarding the draft of this guidebook.

Patient and Public Involvement (PPI) Guidebook

A guide for collaboration between patients and researchers

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〈Special thanks for cooperation in hearings and case studies〉

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