

Perspectives of non-specialists on the potential to serve as ethics committee members

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Abstract

Objective: In Japan, under the new Clinical Trials Act pertaining to investigator-initiated clinical trials that came into effect on 1 April 2018, review boards should review proposed clinical trials while considering written opinions from specialists. Additionally, involvement of non-specialists is mandatory, and attention is being placed on their effective contributions. This study was performed to determine representative key issues with which to promote these contributions.

Methods: This qualitative study was conducted in 2018 using a focus group interview of six non-specialists regarding perspectives on clinical research itself and research ethics committees.

Results: For perspectives on clinical research itself, 33 codes were established and sorted into 2 categories and 6 subcategories relating to ambivalence toward clinical research. For perspectives on research ethics committees, 54 codes were established and sorted into 3 categories and 10 subcategories relating to the theme “knowledge and an environment that promotes non-specialist members’ participation.” One notable result was the willingness of participants to obtain details about a study should they be selected.

Conclusions: The results suggest that detailed explanation of a particular study would encourage non-specialist members to participate in a clinical research review committee. Education aimed at non-specialist participation should therefore be considered in future studies.

Keywords

Ethics committee, non-specialists, members, perspectives, Japan, clinical research

Date received: 17 August 2018; accepted: 18 December 2018

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Background

It is now widely acknowledged that reviews by an independent ethics committee are essential for biomedical research involving human subjects. Since establishment of the first ethics committee for reviewing investigator-initiated biomedical research at Tokushima University in 1982, ethics committees have been set up in various institutions of Japan without a national directive. These ethics committees operate under governmental ethics guidelines such as the Ethical Guidelines for Clinical Studies, which were established in 2003.¹ In 2013, a scandal involving several clinical trials of the antihypertensive drug valsartan made headlines in Japan and worldwide.^{2,3} Data related to the blockbuster antihypertensive drug were manipulated in several multi-institutional clinical trials, and exposure of this manipulation resulted in the retraction of published papers. No applicable laws regarding these types of clinical trials existed, and Japanese regulations pertaining to clinical trials had to be completely revised. Governmental ethics guidelines have since been strengthened for quality assurance, and new regulations regarding investigator-initiated clinical trials came into effect on 1 April 2018.

The new Japanese Clinical Trials Act⁴ includes several regulations aimed at clinical trials that are performed to evaluate the efficacy and safety of drugs, medical devices, and cellular and tissue-based products. For example, certification from the Ministry of Health, Labour and Welfare is now mandatory for review committees that review such clinical trials. The composition and procedures of committees certified by the Ministry of Health, Labour and Welfare (certified clinical trial review boards) are strictly specified in the new act and related ministerial ordinances.

Notably, certified clinical trial review boards require certain documentation, including written opinions from specialists. Specialists include individuals specialized in a particular disease, clinical pharmacologists, biostatisticians, and specialists in specific areas such as medical devices. Such specialists are selected from outside the review board. If a board member happens to be a specialist in the stipulated area, then that member can provide the written opinion. The board itself is composed of individuals with expert knowledge and experience in clinical trials as well as experts in the areas of law and bioethics. Board experts review clinical trials from their own viewpoint, and their written opinions reflect the perspectives of specialists in a stipulated area. Review board participation by non-specialists is also mandatory. In addition to the role of specialists, attention is being placed on non-specialists' effective contributions to review boards.

The role of ethics committee members outside the institution (non-affiliated members) and/or members whose primary concerns are non-scientific (non-scientist members) have also been discussed and emphasized.⁵⁻¹⁰ Non-affiliated members are often referred to as community members.⁹ In the present study, the term "non-specialists" refers to those who have no involvement with clinical research. Certified clinical trial review board members (including those providing written opinions) who are specialists, such as physicians, specialists in law and/or bioethics, clinical pharmacologists, and biostatisticians, are excluded from the category of "non-specialists." This study focused on the perspectives of these non-specialists. The purpose of the present study was not to establish or verify new theory based on covering analysis of large-scale samples but to identify representative key issues with which to promote the contribution of non-specialists to review boards.

Methods

Study and ethical approval

This cross-sectional qualitative study was conducted after obtaining approval by the Ethics Committee of Tokushima University Hospital (#3096). The study was performed according to the consolidated criteria for reporting qualitative research (COREQ) 32-item checklist.¹¹

Research team and reflexivity

Personal characteristics. The focus group interview was facilitated by a member of the Clinical Trial Center for Developmental Therapeutics (CTCDT) of Tokushima University Hospital in attendance with other researchers. The member was a female PhD who had experience in qualitative research and had an interest and roles in the promotion of the clinical study environment, including ethics committees.

Relationship with participants. Neither the facilitator nor other researchers had a relationship with the participants prior to study commencement. The participants had no knowledge about the facilitator prior to this study.

Study design

Theoretical framework. The theoretical framework of the present study was based on content analysis.¹²

Participant selection. We focused on the issue of “non-specialists” in clinical studies, and purposive sampling was applied. The inclusion criteria were no present and/or previous work experience related to clinical research, no present and/or previous experience as a member of review boards, and status as a healthy adult. Physicians, specialists in law and/or bioethics, clinical pharmacologists, and biostatisticians were

excluded from the study. We first tried to recruit volunteers among employees of Tokushima University for feasibility. Considering the inclusion criteria, the staff members of Tokushima University Hospital were not approached. The participants were approached by email, and the researchers explained the study in a face-to-face meeting. Six participants were enrolled in the present study after obtaining written informed consent. No individuals who received an explanation of the present study refused to participate, and no individuals ended their participation or withdrew from the study.

Setting. The data were collected in a room of the CTCDT of Tokushima University Hospital. No persons other than the participants and researchers were present at the data collection.

All six participants were female; three were in their thirties, and three were in their forties. Three were engaged in secretarial work, two were engaged in technical work for *in vitro* experiments, and one was engaged in both. One participant involved in technical work in *in vitro* experiments was a clinical nutritionist.

Data collection. We used a focus group interview to collect the data because this technique is reportedly superior to individual interviews.^{13,14} To respect group dynamics, the facilitator was aided by only a simple interview guide (Table 1) constructed for this study based on findings in the literature. An important goal of the present study was to include participants who were not members of any review board. The participants were encouraged to express their own views on potentially serving as a member of a research ethics committee. No repeated interviews were carried out. No audio or visual recording was used to collect the data, but field notes were made during and/or after the focus group

Table 1. Focus group interview guide.

1. Perspectives on clinical research itself
(1) What are your views on clinical research and registration trials in general?
(2) Do you know of anyone who has participated in clinical research or registration trials?
(3) Have you heard of research misconduct and, if so, what do you think about it?
2. Perspectives on research ethics committees
(1) What do you think about research ethics committees?
(2) How would you feel if you were invited to become a member of a research ethics committee?

interview. The focus group interview was performed in March 2018 and lasted approximately 1 hour.

The transcripts were not returned to the participants for comment and/or correction.

Analysis and findings

Data analysis. The transcripts were analyzed and segments were extracted in accordance with the research aim regarding perspectives on clinical research and research ethics committees. These segments were coded by the facilitator from the CTCDT with consensus among the other five researchers. Codes with a similar context were then sorted into categories and subcategories and finally into broad overarching themes. The reliability of the coding was repeatedly examined until agreement was reached. When no new themes were obtained after repeated analysis, we considered that data saturation had been reached within the sample. The themes were not identified in advance but were derived from the data. No software was used to manage the data. The participants did not provide feedback on the findings.

Reporting. In addition to clearly presenting the identified themes, we included

representative participant quotations as helping aids to illustrate the identified themes. We included quotations from different participants to add transparency and trustworthiness to the findings and interpretations of the data.

Results

Ambivalence toward clinical research

For the participants' perspectives on clinical research itself, 33 codes were established and sorted into 2 categories and 6 subcategories. The two categories were "unfamiliar with clinical research but consider it useful" and "negative impression of clinical research." These two categories were sorted into an overall theme of "ambivalence toward clinical research" (Table 2).

The first category, "unfamiliar with clinical research but consider it useful," was further divided into four subcategories: "difficulty distinguishing between registration trials and clinical research" (9 codes), "feeling that differences exist between clinical research and registration trials" (4 codes), "favorable impression of clinical research" (4 codes), and "unfamiliar with research misconduct" (4 codes). The subcategory "difficulty distinguishing between registration trials and clinical research" included the code "no experience with registration trials and lack of awareness of the practical role of clinical research." Meanwhile, under the subcategory "feeling that differences exist between clinical research and registration trials," several remarks suggested that the participants believe that clinical research has a wider scope than registration trials. In the positive subcategory, one participant showed willingness to participate in clinical research, while in the "unfamiliar with research misconduct" subcategory, one remark suggested that research misconduct is not evident in clinical research.

Table 2. Summary of themes, categories, and subcategories revealed through the focus group interview.

Theme	Category	Subcategory
Ambivalence toward clinical research	Unfamiliar with clinical research but consider it useful	Difficulty distinguishing between registration trials and clinical research Feeling that differences exist between clinical research and registration trials Favorable impression of clinical research Unfamiliar with research misconduct
	Negative impression of clinical research	Negative image of clinical research arising from its “trial” nature Apprehension over the unreliability of clinical research
Importance of knowledge and an environment that promotes participation of non-specialist members	Need for knowledge to serve on a research ethics committee	Willingness to obtain adequate information about a study Difficulty participating without a full understanding of the role of the review committee Difficulty of commenting without having an adequate understanding of each study
	Need for an environment that promotes participation	Importance of scheduling and creating an atmosphere that encourages participation Willingness to participate in a non-specialist area Willingness to participate if interested in a particular study Willingness to participate after discussion with family members
	Lack of awareness of the role of ethics committees	Belief that an ethics committee aims to guarantee ethical standards Difficulty relating the ethics committee to clinical research Belief that an ethics committee guarantees the safety of clinical research

Under the category “negative impression of clinical research,” two subcategories were revealed: “negative image of clinical research arising from its ‘trial’ nature” (7 codes) and “apprehension over the unreliability of clinical research” (5 codes). In the first subcategory, clinical research was considered to involve trial subjects putting themselves at risk for medicine, while in the second subcategory, comments revealed concern over the conduct of clinical research without applicable regulations.

Knowledge and an environment that promotes participation of non-specialist members

For the participants’ perspectives on research ethics committees, 54 codes were established

and sorted into 3 categories and 10 subcategories. The three categories were “need for knowledge to serve on a research ethics committee,” “need for an environment that promotes participation,” and “lack of awareness of the role of ethics committees.” These three categories were sorted into the theme “knowledge and an environment that promotes participation of non-specialist members” (Table 2).

The category “need for knowledge” comprised three subcategories: “willingness to obtain adequate information about a study” (7 codes), “difficulty participating without a full understanding of the role of the review committee” (7 codes), and “difficulty of commenting without having an adequate understanding of each study” (7 codes). The subcategory “willingness to

obtain adequate information” included several codes indicating a willingness to learn about a study as well as an understanding of the personal and societal benefits. One remark also indicated anxiety over being able to understand each study without sufficient knowledge of technical terms and practical procedures.

In the subcategory “difficulty participating without having a full understanding of the role of the review committee,” several comments indicated that the participants would regret joining an ethics committee if they were not confident that they could contribute to its activities. In the subcategory “difficulty providing comments,” several remarks showed concerns over providing comments in the presence of numerous specialists in clinical research.

The category “need for an environment that promotes participation” was divided into four subcategories: “importance of scheduling and creating an atmosphere that encourages participation” (13 codes), “willingness to participate in a non-specialist area” (3 codes), “willingness to participate if interested in a particular study” (2 codes), and “willingness to participate after discussion with family members” (2 codes). In the first subcategory, contrasting remarks were revealed. Some participants favored participation via Internet-based discussion, while others favored participation in person with many members present. Another comment suggested the importance of detailed explanations of each study for promoting participation of potential committee members. In the subcategory “willingness to participate in a non-specialist area,” participation without specialist knowledge in clinical research was favored. Meanwhile, in the subcategory “willingness to participate if interested,” the participants’ remarks revealed that willingness does not necessarily depend on the level of interest in clinical research as a whole but more on the level of

interest in a particular study. In the subcategory “willingness to participate after discussion with family members,” the participants tended to regard the opinions of their family as important.

The category “lack of awareness of the role of ethics committees” comprised three subcategories: “belief that an ethics committee aims to guarantee ethical treatment of human subjects” (5 codes), “difficulty relating the ethics committee to clinical research” (5 codes), and “belief that an ethics committee guarantees the safety of clinical research” (3 codes). In the subcategory “belief that an ethics committee aims to guarantee ethical treatment of human subjects,” participants indicated the belief that ethics committees review each study from the viewpoint of human ethics to avoid disadvantaging the study participants. In the subcategory “difficulty relating the ethics committee to clinical research,” one participant indicated that she was unaware of the role of ethics committees when participation in clinical research was suggested to a member of her family. Finally, in the subcategory “belief that an ethics committee guarantees the safety of clinical research,” several comments indicated a perception of the reliability of ethics committees in guaranteeing safety.

Discussion

In terms of the overall perspective of clinical research itself, we identified the theme “ambivalence toward clinical research.” Even when participants were employees of Tokushima University, our study indicated a lack of experience in registration trials and a lack of awareness of the practical role of clinical research. Moreover, the study also revealed a negative image of clinical research, such as the concept of clinical research involving trial subjects putting themselves at risk for medicine and concern over the conduct of clinical research

without applicable regulations. Klitzman⁸ suggested that affiliated review board members not only have different backgrounds, training, and approaches toward reviews but may also have inherent conflicts of interests. Meanwhile, Kuyare et al.¹⁰ found no differences in the responses of affiliated and non-affiliated members in terms of the perceptions and experiences of board members, similar to the findings of Allison et al.⁷ Although one subcategory suggested a favorable impression of clinical research, the participants viewed themselves as non-specialists in clinical research and individuals with no vested interest in the success or failure of the study.

The importance of training opportunities tailored to non-specialist participation was also emphasized; however, such training has yet to be established. In 2003, Sengupta and Lo⁵ reported the results of a study of 32 non-scientist and non-affiliated ethics committee members, revealing that 72% received written documents for training while only 22% received formal training, and 47% identified the lack of education and training as a problem. The desire for formalized training on documents such as the Belmont Report and the Code of Federal Regulations Title 21 was particularly noteworthy. Setoyama¹⁵ reported the results of a survey of non-affiliated members of Japanese ethics committees, revealing that only some were provided introductory training such as the distribution of documents (guidance, guidelines, manuals, and brochures) and given an explanation of the purpose, role, and review procedures of the ethics committee. These findings emphasize the need for an increase in basic training with development of modules including those available online.¹⁰

The participants in the present study also suggested further possibilities in education, revealing a willingness to obtain detailed information about a study and to understand its personal and societal benefits. Concern over the ability to understand

each study without adequate knowledge of technical terms and practical procedures was also indicated. Moreover, the participants' responses suggested the possibility that detailed explanation of each study itself promotes member candidates' participation.

It is often mentioned that non-scientist and non-affiliated ethics committee members can better reflect the concerns and viewpoints of research participants than can specialist board members. For example, Lidz et al.⁹ revealed that community members in the United States try to remain naïve to the study and see themselves as having a particular kind of expertise; that is, as a person whose expertise comes from a lack of specialized knowledge. Additionally, in a study of Indian board members, Kuyare et al.¹⁰ suggested that being experienced may actually be counterproductive to the role of non-specialist members as participant/community representatives. That is, the more experience they gain, the more knowledgeable they become and therefore the less able they are to represent the community. Meanwhile, Mhaskar et al.¹⁶ reported that review board members, even those who are not community members, tend to have poor knowledge of research study design; however, non-community members aside, this can in fact benefit community members.

These findings suggest that to pursue a role as a non-specialist board member, candidates should understand the study protocol in as much detail as required of the study participants without additional specialized or experienced knowledge of clinical research. By doing so, the contribution of non-specialists can be promoted.

Although detailed consent forms are essential when obtaining informed consent in interventional clinical trials, investigators must also provide a face-to-face explanation to the study participants. As part of a review committee, non-specialist members should carefully read study-related documents,

including informed consent forms, and should seek further explanations from investigators where necessary. However, non-specialist members are often reluctant to do so in environments with many specialists. It may be advisable to develop a system in which an investigator carries out the informed consent procedure with non-specialist committee members before a study is reviewed. Alternatively, an administrative member of the review board committee with some knowledge of medicine could briefly explain the study objectives. This would help to increase non-specialist members' overall understanding of the particular study, thereby encouraging their active participation.

Attempts to increase awareness of clinical research among the general public are important for promoting clinical research. If non-specialist board members are recruited from the general public and obtain in-depth knowledge of clinical trials from the viewpoint of the study participants, this could help to increase awareness of clinical research within the general public. This would also help to promote public involvement,¹⁷ an important element of clinical research.

The main limitation of the present study is that it was conducted by purposive sampling in participants affiliated with same university as researchers. Nevertheless, the present study revealed that the participants not only had perspectives in support of clinical research but also had ambivalence toward clinical research. Under these conditions, we were able to capture the theme of knowledge and an environment that promotes participation of non-specialist members; the importance of receiving a detailed explanation of a particular study was also suggested. Further studies are warranted to examine whether these findings can be applied to present review board members. Interventions such as education that aims to provide a detailed explanation of a

particular study to these members may result in promotion of their contributions to review board activities.

Datasets

The datasets used in the current study are available from the corresponding author on reasonable request.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Funding

This research was supported by Grants-in Aid (JP171k1803042j0001 and JP181k1803045j0001) from the Japan Agency for Medical Research and Development (AMED).

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