

THE IMPORTANCE OF PATIENT INVOLVEMENT IN CLINICAL TRIALS

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The best known role for patients in clinical trials is that of research subject. In this article I want to address the other roles patients (can) have in clinical trials. They can be involved as information providers, advisors, reviewers, co-researchers and even as the driving force behind the research. In fact, in many countries, the involvement of patients is becoming a requirement to obtain funding.

The new European Union Clinical Trials Regulation (CTR) No. 536/2014 will come into effect in 2018 and will drive patient involvement in clinical trial design. It dictates that in a study protocol researchers must describe “*where patients were involved in the design of the clinical trial, and a description of their involvement*”.

Currently, the level of patient involvement differs immensely between different clinical trials and there are no standards on best practice for patient involvement. In my opinion, patients should be involved from the very start as equal partners, although others are hesitant and want to keep the patients at arm's length. The ways in which a patient can be involved in a trial are illustrated in figure 1, where the balance in exchange of information is indicated by the size of the arrows (from unequal relationships to more equal, such as co-creation with patients as members of the research team).

Patients add urgency and relevance by making sure that the relevant questions are asked and addressed in the clinical trial. They bring the patients' needs to the

table, not just as text on a piece of paper, but as lived experience. By involving patients in clinical trials you add the unique vision and experiences of the people that are the end users of the results of your trial. Patients have a unique perspective based on their collective experience and knowledge of their disease(s), and this knowledge is complementary to the knowledge of physicians, researchers and clinicians. The future in clinical trials and pharmaceutical research and development lies in the involvement of patients and researchers as equal partners in setting research priorities and in developing, designing, planning, and conducting the research, as well as in the dissemination and communication of the results.

INVOLVING PATIENTS IN CLINICAL TRIALS

This article is based on my experience as a patient advocate in many projects. I was involved in all the projects mentioned below.

Before the clinical trial: setting research agendas

As Chalmers wrote in 2009, involving patients before a study and identifying research that is relevant to both clinicians and patients can prevent a lot of waste. By setting research priorities together gaps can be identified and areas in which the

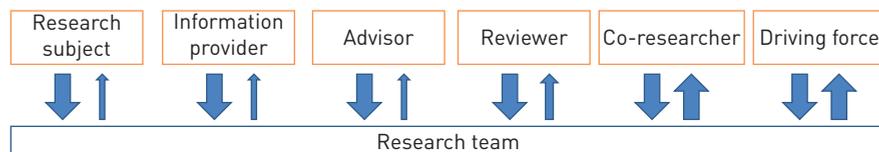


FIGURE 1. The various roles of the patient in clinical trials. The balance in exchange of information is indicated by the size of the arrows.

results of research might have the most benefit can be established, such that the unmet needs of patients can become a research priority. A good way of doing this is to involve clinicians, doctors, researchers and patients together in the setting of research agendas and this is now seen in more and more disease areas. A recent good example of this is the European Asthma Research and Innovation Partnership (EARIP) project where the patient advisory group (PAG) was involved from the beginning in identifying key gaps in asthma knowledge and the development of a research agenda. Patients' input was key in setting priorities and research strategies for the coming years.

The Dutch Lung Foundation started such a process in 2004 by setting the asthma and COPD research agenda with patients and the process was repeated in 2009 and expanded to other lung diseases. On the broader themes there was significant overlap between the priorities of the patients and those of the researchers/clinicians; however, challenging perspectives and issues were revealed when considering the details. It was found that in the topics that patients found important, but which were perceived as less important by researchers, the chances were higher that researchers would not develop proposals on the subject. Just setting the agenda together does not mean that researchers will address the high priority topics of patients. A good example of this is the subject of fatigue, which was added to the research agenda in 2009. Very little research was done on the subject and, in 2016 when new research agenda meetings were organised by the Netherlands Respiratory Society (NRS), patients again mentioned fatigue as one of their priorities. This time the researchers listened and organised a meeting on "Fatigue in Chronic Diseases" with a broader perspective than just lung diseases.

We can conclude from this that it is not always enough to just include patients, the process requires listening, mutual learning and mutual respect to develop a research agenda that will lead to research proposals that fit the priorities set by patients and researchers together.

During the clinical trial: involving patients in all stages

Another example of the advantages to be gained by involving patients in the design stage of the study is seen in the Unbiased BIOmarkers in PREDiction of Respiratory Disease Outcomes (U-BIOPRED) project. The researchers were interested in studying people with severe, difficult to control asthma. They planned to include a group of patients with severe uncontrolled asthma in the study and ask them, when their asthma was stable, to stop taking their medication for research purposes. Fortunately, in the early stages of the research application process, the researchers organised a focus group with patients with severe uncontrolled asthma. When the researchers explained the research method they were proposing the group of patients was appalled. The response from the patients was that when they finally had one of their rare moments of stability, no way were they going to stop taking their medication. The risk of an exacerbation would be too high and the chances were very high that the patients would rapidly become too sick to participate in the study. As such, even if you could enrol enough patients, the dropout rate would likely be very high. This led to a redesign of the study such that patients with severe uncontrolled asthma could safely be included and could remain included.

During a study patients can identify acceptable comparators, relevant outcomes

and acceptable risks *versus* potential benefits from the patients' perspective, as well as help researchers in identifying relevant target populations.

In the U-BIOPRED project, members of the patient input platform (PIP) became involved in the various "work packages". This led to improved procedures and information on various processes, for example bronchoscopy and exposing patients to rhinovirus, which helped recruit patients and keep them involved. Patient input also led to a reduction in the number of questionnaires the research subjects needed to answer (including only the information that was really necessary) and the number of study visits was reduced, with more procedures being carried out in one visit. In the paediatric study, hospital visits were made shorter to better fit with the time young patients could tolerate, making the life of the patients and their carers easier. In another study, the PIP advised on making the lay informed consent information available not only on paper but also on the internet, in a spoken-word format, in order to make it accessible to people with low literacy skills.

After the clinical trial: informing and disseminating results

At the end of the study, members of the U-BIOPRED PIP worked together with the researchers on preparing lay summaries of the studies/articles to be reported. In addition, members of the PIP were involved in presenting results from the study, both in writing and at conferences.

GUIDANCE ON INVOLVING PATIENTS IN CLINICAL RESEARCH

The experience of working with the PIP in the U-BIOPRED project led to the publication of an Innovative Medicines Initiative (IMI) practical guide on how to involve patients in all healthcare research. The advice is consistent with what is written above: involve patients early, provide coordination for patient involvement and involve patients in



FIGURE 2. Presenting on patient empowerment at the European Respiratory Society (ERS) Presidential Summit.

all aspects of the project. At the end, patients can help you gain visibility for the project and its results. The role of patients and how they may be empowered to contribute has also been a topic in meetings of the European Respiratory Society (ERS) (figure 2). In the European Patients Academy on Therapeutic Innovation (EUPATI), involving patients in clinical trials is seen as just one step in the process. Patients are trained to become part of the whole process of medicine development (figure 3), from developing the strategic framework in research and discovery to the moment the drug is taken off the market at the end of its post-approval lifecycle.

FINAL THOUGHTS

When patients and researchers work together they gain respect for each



FIGURE 3. Sharing U-BIOPRED good practice with other patients at the European Patients Academy on Therapeutic Innovation (EUPATI).

other's perspective and knowledge, and, by exchanging views in open discussion, a fruitful cooperation can be achieved. It is a two-way street where all the parties involved go through a learning process. Training and information for both patients and researchers will help this process forward. It requires a change in both attitude and culture. In the different projects I was involved in I noticed a big difference in the level and the extent of patient involvement depending on the attitude of the project leader. In all process change the project leader has a key role to play. He/she is the person who needs to advocate and support any change and influencing his/her attitude towards patient involvement is often the best way to achieve a fruitful cooperation that leads to a better project.

Though good research on the benefits of patient involvement is still rare, a number of studies have been performed. Several of these are included in the recommended reading list and will lead you to more information. As in all aspects of clinical research, patient involvement should become part of the evaluation process which will help us learn from good practice. By sharing experiences we can increase the quality of patient involvement in research. In addition, lay persons such as patients or patients' organisations should be involved in the assessment of applications to conduct clinical trials. The ability to organise the involvement of ethics committees and many other requirements of trial design will conceivably be easier to achieve if

patients are involved from the very first in selecting and designing a trial.

CONFLICT OF INTEREST

None declared.

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