

VU Research Portal

Moving together towards participation

Bakker, M.

2016

document version

Publisher's PDF, also known as Version of record

[Link to publication in VU Research Portal](#)

citation for published version (APA)

Bakker, M. (2016). *Moving together towards participation: Insights into illness and care experiences of people with neuromuscular diseases*.

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal ?

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

E-mail address:

vuresearchportal.ub@vu.nl

Participating in clinical trials: participants' experiences. A qualitative study

K. SCHIPPER, M. BAKKER AND T.A. ABMA

8

UNDER SUBMISSION AT
INTERNATIONAL JOURNAL OF CLINICAL TRIALS

ABSTRACT

Background/aims: Clinical trials are widely accepted by the scientific community as the most rigorous way of evaluating interventions in health care. The success of a clinical trial depends on the participation of volunteers. The recruitment of participants is however often difficult and many trials recruit fewer participants than anticipated. It is therefore important to understand participants' perspectives on clinical trials. The aim of this article is to describe experiences and opinions of participants with a randomized controlled trial (RCT).

Methods: A qualitative study was done, interviewing 50 participants with three types of neuromuscular diseases (Amyotrophic Lateral Sclerosis: ALS, Post-Polio Syndrome: PPS & Facioscapulohumeral Muscular Dystrophy: FSHD) who participated in the FACTS-2-NMD trial. The FACTS-2-NMD study consisted of three RCT's and aimed to study the efficacy of Exercise Therapy and Cognitive Behavioural. The interviews were semi-structured and a topic list was used in order to discuss all relevant themes in the interviews. Themes that for instance were addressed included motives to participate and experiences with the trial and intervention. The process of data collection and analysis was iterative so that emerging themes could be further explored and validated over the course of the research. The interviews were analysed by two independent researchers, using inductive thematic analysis.

Results: Participants' experiences can be divided in three themes: participants' ideas about 1) the amount of control as experienced during a trial, 2) the information and communication during a clinical trial, 3) the credibility, validity and reliability of clinical trials. Participants did not always experienced sufficient control during the trial and preferred better communication. They furthermore expressed worries about the credibility, validity and reliability of clinical trials, partly as a result of their own behaviour.

Conclusion: This study gives insight in the experiences of trial participants. Participants seemed to have clear and strong ideas and experiences with the trial. Findings can be used to improve future trials and to make more patient-centred. Collaboration with patients as research partners in the RCT can help to attune the trial to patients' needs and wishes. Conducting a qualitative study along the RCT may furthermore give insights in the experiences of participants and allows researchers to modify the RCT.

Keywords: Patient; participant; inside perspectives; experiences; qualitative study; randomized controlled trial; RCT; clinical trial

BACKGROUND

Randomized Controlled Trials (RCTs) are widely accepted by the scientific community as the most rigorous way of evaluating interventions in health care (1). A RCT depends on the participation of volunteers (2) and their inclusion is the key to success. The recruitment of participants is, however, often difficult (3) and many trials recruit fewer participants than anticipated (2,4). It is therefore important to understand the dynamics of participating in a trial. However, the patients' perspectives on RCT's were not often systematically investigated and were relatively neglected (5).

Some literature already exists, for instance about the reasons why people do or do not want to participate in a RCT (5,6,7) and how participants experience randomisation (1,5). These studies describe among others personal benefits and altruistic reasons as motives to participate. They furthermore describe that participants experience randomization as only appropriate when the interventions are equally suitable and if they had no preference (5).

These studies give important insights, but there is still almost no knowledge on the general experiences of trial participants. A greater understanding of participants' views provides the potential to improve the content and management of future trials (1) and to make researchers more aware of participants' ideas and needs which can make trials more patient-centred.

The aim of this article is therefore to describe the experiences and opinions of participants of a clinical trial.

METHODS

Design

A qualitative study was conducted because qualitative studies are preferred for gaining an understanding of the experiences and opinions of people (8). Data were collected through semi-structured interviews (9) and inductively analysed (10).

Participants

Participants were selected from those who participated in the FACTS-2-NMD trial. The study consisted of three RCT's (11,12,13). The aim was to study the efficacy of Exercise Therapy and Cognitive Behavioural Therapy for reducing fatigue, improving activities and improving quality of life in patients with Amyotrophic Lateral Sclerosis (ALS), Post-Polio Syndrome (PPS) & Facioscapulohumeral Muscular Dystrophy (FSHD). Table 1 provides disease information.



Table 1: Short description of diseases

Disease	Description
ALS	<p>ALS is a fatal progressive neurodegenerative disorder affecting motor neurons in the spinal cord, brainstem, and motor cortex. Patients are afflicted by progressive wasting and weakness of limb, bulbar, and respiratory muscles, and die on average within 3 years after symptom onset, usually because of respiratory failure. Besides physical limitations, cognitive function deficits in a frontotemporal pattern may be apparent, including impaired frontal executive abilities in up to 50% of patients (14).</p> <p>The median age of onset of ALS is 55 years. The incidence of ALS is between 1.5 and 2.5 per 100,000 person-years of follow-up in industrialized countries and life-time risk of ALS is estimated to be between 1/600 and 1/2000 which makes it the most common motor neuron disease. ALS is familial in 5% of cases (14).</p> <p>The grave prognosis of ALS can have a severe psychological impact on patients and their social environment. The majority of patients report not only physical but also existential problems. Depressive symptoms and hopelessness are more common in patients with ALS than in the general population (14).</p>
FSHD	<p>FSHD is the third most common inherited neuromuscular disorder.</p> <p>The disease primarily affects the facial muscles, the muscles of the shoulder girdle and various leg muscles, while pelvic and trunk muscles are eventually affected as well. The pattern of muscle weakness is often asymmetrical, and the rate and extent of progression may vary considerably with sudden periods of unexplained rapid disease progression. In a small percentage of the patients, even respiratory insufficiency may occur. FSHD may eventually lead to serious disabilities of speech, swallowing, reaching, standing and walking, even in early adulthood. Twenty percent of the patients become wheelchair bound. Fatigue is a common problem among patients (13). It is an autosomal dominant slowly progressive myopathy with a variable age of onset, mostly in the second or third decade of life. Its yearly incidence rate is approximately 1:20.000 (13).</p>
PPS	<p>Poliomyelitis anterior acuta is an acute viral disease that attacks the anterior horn cells of the spinal cord and the motor neurons of the lower brain stem resulting in flaccid paresis or paralysis. Usually there is partial and sometimes complete recovery from the self-terminating disease. However, many people with a history of poliomyelitis report late onset neuromuscular symptoms and a decline in functional abilities. These late symptoms are referred to as Postpoliomyelitis Syndrome (PPS) and include new or increased muscle weakness, abnormal muscle fatigability, generalized fatigue, muscle atrophy, muscle and joint pain, muscle cramps and cold intolerance (12). The prevalence of PPS has been reported from 15% to 80% of all patients with previous paralytic polio depending on the criteria applied and population studied (12).</p>

The sampling was purposeful as we were selecting a rich variety of participants in terms of age, gender, disease, type and location of intervention (14). Patients, allocated to one of the interventions, were asked by the RCT coordinators to participate in this study. After giving consent they were called by the researchers. During this phone call, participants got further information about the study and were asked to participate in an interview.

Data collection

For this study, semi-structured interviews were held with 50 participants. The interviews had an open nature and aimed to cover various aspects of the participants experiences with the trial and interventions. Themes that were formulated in a topic guide and

addressed in the interviews included motives to participate, expectations of and experiences with the intervention and trial, and experienced effects of the intervention. The topics were broad in order not to restrict participants and to gather information about themes participants addressed.

The process of data collection and analysis was iterative so that emerging themes could be further explored and validated over the course of the research (15). No new information emerged after 50 interviews which suggested data saturation (16). The interviews were conducted by trained interviewers who took general quality criteria for interviewing into account (17). The interviews lasted about 60 minutes and were, after participants' consent, audio-recorded and transcribed.

Data analysis

The interviews were analysed using inductive thematic analysis (18). The transcripts were read and re-read and coded by the research team during as well as after data collection. While reading the transcripts, phrases considering trial experiences were coded. New codes in the transcripts were added to the list of codes. All transcripts, including the ones that were already coded, were re-read and coded with use of the new code list. Codes and coded segments were compared and grouped as main and subcategories. The different categories of the researchers were compared and discussed in the research team until consensus was reached. This was done to increase dependability by preventing interpretations caused by the background of the individual researchers. Relevant themes were agreed upon, and, for each theme, the most suitable quotes were selected. A mix of computerized (MAXqda) and manual techniques was used to facilitate data analysis.

Rigor

To enhance credibility, all participants received an interpretation of their interview to check the accuracy of the interviewer's interpretation (15). Besides, different investigators were involved in the analysis process (19). The investigators arrived at the same conclusions, which heightened our confidence in the findings (20). Different procedures, such as using quotes, have a positive influence on the transferability of the findings presented in this article. Qualitative research aims for theoretical generalization, and there is reason to assume that the themes and patterns presented here are applicable to a broader group of trial participants (8).

RESULTS

50 interviews were held with participants with FSHD (n=23), PPS (n=17) and ALS (n=10) who participated in one of the interventions (ET or CBT). The interviews gave insight in how participants experienced the trial and the analysis lead to the identification of the themes that will be described one by one.

Having control and influence

Participants mentioned diverse reasons to participate in the trial. Some mentioned personal benefits as motive to participate:

'I say yes to every study. I have still some hope that something will work for me.'(ALS)

Others mentioned altruistic reasons. By participating they had the hope to get a solution for the next generation(s):

'I'm not going to recover or improve. I have to learn to live with it, but I can help other people. Maybe there will be a treatment for them in the future.'(FSHD)

Participants with an inherited disease mostly participated, because they wanted to do something for their own children who have or might have the same disease:

'We have 3 children and they have 50% chance of having the same disease. It will take years before this study may give results. That will be too late for me but not for my children!' (FSHD)

Others mentioned a moral duty to participate:

'If you want to use health care, you also should make that possible. I want my physician to help me, so I have to participated in (his) studies.'(PPS)

Besides personal benefits and altruistic reasons, guilt and making sense of the disease were mentioned as drive to participate:

"Participating gives me a sense of usefulness. It makes the disease less useless.' (ALS)

'It is my duty to do this. It's a consequence of our decision to get children. I will go on, even if I will collapse. My daughter also asked me: "grandma did not participate in any research. Please can you do that for me?' (FSHD)

The motives seemed to influence the degree in which participants wanted to have influence on the randomisation and preferences for a certain treatment. It seems that those who participated for personal benefits wanted to have more influence:

'I definitely had a preference, I was not enthusiastic about the psychological treatment.' (FSDH)

'I would be very disappointed if he would end up in the control group.'(FSDH)

Many participants were disappointed about the fact that neither they or the researcher could influence the outcome of the randomisation. Participants would have preferred to choose for an intervention instead of being randomly allocated to a group:

'I asked the researcher explicitly: "do I or you have influence on the outcome[of the randomisation]?" but that wasn't the case.' (FSDH)

Participants also had problems with the fact that they could not decide whether they wanted an individual or group intervention while they had strong preferences as can be seen in table 2.

Table 2: quotes regarding advantages and disadvantages of group interventions

Theme	Advantages	Disadvantages
Contact with fellow sufferers	'The contact with other patients was nice but also confronting. Their story was mine and the other way around. The recognition was pleasant.' (PPS) 'You may learn from each other.' (FSDH) 'You are in the same situation, we could talk about difficult themes like euthanasia and we could make jokes about the disease.' (ALS)	'I'm not someone who is going to talk about each other's suffering and problems.' (ALS) 'Brrrr.....Some people are only complaining.' (FSDH) 'If your problems aren't severe enough...you aren't part of the group.' (PPS)
Confrontation with restriction of other patients	'Seeing the things that other people weren't able to do anymore, made me realise how lucky I am with the things I still can do. That was quite motivating for me.' (FSDH)	'It's very confronting to see how the disease may progress.' (FSDH) 'I don't want to meet people with PPS. It's too confronting for me.' (PPS)
Distraction and attention	'I was able to chat with others. It gave me distraction. It was nice to be in a group because I like to be together with other people.' (FSDH)	'I don't want to be distracted.' (FSDH) 'You will receive less attention in a group.....I think it is better to do it individual.' (PPS)



Other feelings of having less control had to do with the planning of the treatment sessions. Some participants had the feeling that they had to adapt their agenda to those of the professionals instead of the other way around. They did not experience much influence:

'I had to train three times a week. I was surprised by the fact that professionals presume that you have plenty of time. The training was only possible on some days, but they did not take my possibilities and preferences into account.' (ALS)

Participants at last mentioned a lack of control regarding the transition to regular care after the RCT intervention:

'The transition can be better. I think the intervention stops too promptly. Of course you are aware that there will be an end and you should do something yourself, but I think that the organisation should also arrange a transition to regular care. They must do everything reasonably possible to provide care afterwards.' (ALS)

Information and communication

Getting adequate information seemed to be a important theme for participants. They were in general positive about the information they received in advance about the trial. They received enough information during the appointment in which they also signed the informed consent:

'It was totally clear and they took all the time you needed [to explain things].' (PPS)

After the intake and signing of the informed consent, some things went however wrong in the communication. This gave participants a sense of being a number or not taken seriously:

'I received a standard letter: you have the Chronic Fatigue Syndrome and you are going to receive a treatment for that. But it don't have that! I have FSHD. I was really angry about that! (FSHD)

'The information in the letters we received was incompatible. Sometimes you were not allowed to drink coffee the day before the appointment and in other letters you were not allowed to drink anything on the day of the appointment. I think this is an example of unnecessary sloppiness. It doesn't lead to feelings of trust.' (ALS)

In the beginning patients were, after the intake with the researcher, by email informed about inclusion or exclusion decisions. This was not appreciated:

'I received an email from the doctor.....I am not allowed to join since I am not tired

enough. It hurts me. How can a questionnaire [One of the inclusion factors in the trials was a certain score on the CIS-fatigue questionnaire. This questionnaire measures the experienced fatigue. Patients were excluded if their score was below the cut-off score] say something about my tiredness? I think they should not communicate by mail about the exclusion. Furthermore they should not say: you are not tired enough. Patients feel the tiredness, but it isn't bad enough.'(PPS)

The communication about the questionnaires that needed to be filled in was sometimes not sufficient. Some participants missed some explanation about the content and character of the questionnaires. The lack of information sometimes led to frustration and anger:

'Don't repeat the question that often. It made me feel irritated.' (FSHD)

'The questions irritated me and my son, enormously! 'I would commit suicide if I had the possibility' is outrageous! My son has thrown away everything and he will never participate in a study from this hospital again. (...) Whose ideas are these questions? Are they from a researcher who doesn't have a clue about the possible effects of these questions?' (FSHD)

The lack of communication about the individual trial results was, at last, sometimes disappointing for participants:

'It's a pity that I haven't heard anything about the final measurements but I was just another patient for him [the psychologist]. I think it's more important for me than it is for him. He had promised me to give me the results, but I haven't heard anything.'(PPS)

'It would have been nice if I had heard my own progression. Why isn't that possible?' (FSHD)

Validity, reliability and credibility

Participants expressed doubts about the credibility, validity and reliability of the trial. The first reason, responsible for their doubts is the fact that participants did not always fill in the questionnaires honestly:

'There was a question: are you able to walk for 10 minutes without any help. I can't, but I really wanted to participate, so I said 'yes'. (FSHD)

Another doubt influencing the credibility, validity and reliability had to do with the blinding:

'The researcher isn't allowed to know what intervention I'm doing. But he is

walking through the waiting room if the training is about to start... so it's not that difficult for him to know what I'm doing. And one day I wasn't able to come to the training so I called the hospital to inform them and the blinded researcher answered my phone call... '(PPS)

The doubts also arose due to the way participants filled in the questionnaires themselves:

'You are going to respond faster and less secure because of the repeated questions. You want to get rid of the package and you are doing it routinely without actually thinking about the answers.' (FSDH)

Participants were, furthermore, wondering whether the questionnaires were a good representation of the reality because they were not always secure or honest while filling in the questionnaires:

'I think that I'm not completely honest in a questionnaire. I think I was a too positive.' (PPS).

'I'm just filling in something. The questions are only a snapshot. I think if I had filled it in 14 days ago, it would have given a completely different picture of me.' (PPS)

Participants were also worried about possible reduced validity because of potential risk of misinterpretations of the questions:

'I said NO in response to the question: "Do you go for a walk?". I think they will interpret this as not being able to walk, but I simply don't have enough time to go for a walk!' (FSDH)

DISCUSSION

This study has focussed on the motives of participants to be involved in clinical trials and their experiences with and opinions on trials in order to gain insights that may improve future trials.

This article adds knowledge by describing participants' ideas about 1) the amount of control as experienced during a trial, 2) the information and communication during a clinical trial, 3) the credibility, validity and reliability of clinical trials. These findings are, as far as we can conclude, not described in the literature yet.

Regarding the first finding can be concluded that the motives of participants seem to influence the amount of control participants want to have. Just as in other studies

we have found that participants want to be involved because of altruistic reasons or for personal benefits (5-7). Our study adds first of all knowledge by stressing the fact that participants also may participate in order to make sense of their disease or as a result of guilt. It seems that those who participated for personal benefits wanted to have more influence than those who participated for altruistic reasons. This might be a quite logical and not very problematic. Participants, however, experienced only a small amount of control. They would have preferred more influence on the outcome of the randomisation, the character of the intervention, the planning of the treatment sessions and the transition to normal care after the intervention. Participants do not only prefer more control, they also would like to be better informed about the trial, questionnaires, blinding and randomization.

Patients are normally informed about clinical trials and they are giving their permission since having consent is a must for participation in clinical trials and research projects (21). The concept of consent arises from the ethical principle of patient autonomy and basic human rights (21) and the informed consent of participants is ethically and legally required for most research involving human subjects (22). As defined in U.S. regulations governing research with human subjects, informed consent to research includes some obligatory elements as described in table 3 (23).

Table 3: obligatory elements of informed consent (23)

1)	a statement that the study involves research
2)	an explanation of the purposes of the research
3)	the expected duration of the subjects' participation
4)	a description of the procedures to be followed
5)	identification of any procedures which are experimental
6)	a description of any reasonably foreseeable risks or discomforts to the subject
7)	a description of any benefits to the subject or to others which may reasonably be expected from the research
8)	a disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject
9)	a statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained
10)	for research involving more than minimal risk, an explanation as to whether any compensation, and an explanation as to whether any medical treatments are available, if injury occurs and, if so, what they consist of, or where further information may be obtained
11)	an explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject
12)	a statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits, to which the subject is otherwise entitled



Participants in the described trials were in an information letter informed about the obligatory aspects. Specific attention was given to the measurements (using repeated questionnaires which will take about 1.5 hour each time), the process of randomization and the usefulness of randomization. The questions as raised by participants in our study are however more profound or beyond the scope of the informed consent. Participants wanted for instance to know how the researchers were going to analyse and interpret the questionnaires and they also would have preferred a more detailed explanation of the content of the questionnaires. These elements were not covered by the information letter since researchers wanted to prevent an overkill of information (24-26). Researchers could not know that participants wanted to receive such profound knowledge. Solutions should be found to solve this information needs of participants, without overwhelming them with information.

Our study did not focus on the actual understanding of the information letter/informed consent but it is well known that trial participants failure to understand or remember information about randomisation and equipoise, despite the provision of clear and readable trial information leaflets (27). Our study is in our opinion the first study that gives insight in possible questions of participants (about blinding, the content and analysis of questionnaires, reliability and validity), next to the received information. Communication and better information before, during and after the trial may enlarge the amount of control as experienced by participants and may also increase the understanding of participants which may prevent frustration or irritation or even drop-outs.

Adequate communication may also positively influence the ideas participants have about the credibility, validity and reliability of clinical trials. This study is the first study that describes the potential negative or wrong ideas of participants about credibility, validity and reliability which might influence their willingness to participate and their belief in the results of clinical trials.

It might thus be important to give participants as much as control as possible, to communicate adequately and to influence their ideas about credibility, validity and reliability in order to increase the willingness of volunteers to participate, to increase the satisfaction of participants and to prevent drop-outs.

Giving participants control, among others by giving adequate information is important, especially because patients with a chronic disease often experience a lack of control over their disease (28). Studies have shown that, at some point in the course of a chronic illness, patients experience powerlessness (28). This can be described as 'the inability to have agency in one's own life' or a 'perceived lack of personal or internal control of certain events or in certain situations' (28). Powerlessness may be a real loss of power or a perceived loss of power. For some persons the feelings of powerlessness may be short lived, whereas for others, they are persistent. Powerlessness is influenced by the

natural history of the illness itself. It is variable and does not conform to a predictable course of events. The uncertainty if a chronic illness, the exacerbation of symptoms, deterioration despite treatments, can all contribute to powerlessness. Powerlessness furthermore occurs when an individual is controlled by the environment rather than the individual controlling the environment. Researchers are not able to change the course of the illness but they may give patients more control over their environment, by giving them more control in clinical trials (28).

Many solutions can be mentioned in order to give patients more control. Some solutions have been described in the area of the research design. Researchers may for instance consider the use of the 'patient preference option' which allows patients without strong preferences to be randomized while those with strong preferences are given their choice (29). Making a trial more attuned to the needs and wishes of patients can also be reached by including a patient research partner in the research team (30-33). Patient research partners are patients or relatives with experiential knowledge who participate as equal members in the research team. They are involved in all research activities and decisions are made by researchers and patient research partners together (30). Patient participation in research is becoming more and more accepted and has several advantages like making research more patient-centred. By including patients as equal team members, research becomes more patient-centred since fellow sufferers have a better insight in the needs, wishes and thoughts of other patients (31-33) which improves communication and increases the amount of control of patients (30). Patient participation remains however still unusual in clinical trials. Patient participation, by adding patients as partners in a research team, may nevertheless improve several elements of the research process like choosing the questionnaires (which prevents over-burdening or frustration), choosing the design of the trial, developing the content of the intervention, adequate communication about exclusion decisions and making an adequate information letter (with for instance patient friendly information about the questionnaires, the confronting nature of some questions, why they are repeated, how they will be analysed, why studies are blinded).

Conducting a qualitative study along with the RCT, as we did, can at last give insights in the experiences of participants and allows researchers to adapt small things during the RCT which results in improvements of the RCT and possible reduced drop-out rates.



ACKNOWLEDGEMENTS

We wish to acknowledge the willingness of those who participated in this study. We also want to thank the funders, namely the Prinses Beatrix Fonds (The Dutch Public Fund for Neuromuscular and Movement Disorders) and the Netherlands Organization for Health Research and Development (ID: ZonMW 89000003) for their financial support.

CONFLICT OF INTEREST

The authors do not have any conflict(s) of interest.

REFERENCES

1. Snowdon C, Garcia J, Elbourne D. Making sense of randomization; responses of parents of critically ill babies to random allocation of treatment in a clinical trial. *Soc Sci Med* 1997; 45(9): 1337-55.
2. McCann SK, Campbell MK, Entwistle VA. Reasons for participating in randomised controlled trials: conditional altruism and considerations for self. *Trials*. 2010; 11: 31. doi: 10.1186/1745-6215-11-31.
3. Dickson S, Logan J, Hagen S et al Reflecting on the methodological challenges of recruiting to a United Kingdom-wide, multi-centre, randomised controlled trial in gynaecology outpatient settings. *Trials* 2013;14: 389. doi: 10.1186/1745-6215-14-389.
4. Festen H, Schipper K, de Vries SO et al. Parents' perceptions on offspring risk and prevention of anxiety and depression: A Qualitative Study. *BMC Psychol* 2014; 2:17. doi:10.1186/2050-7283-2-17.
5. Jackson CJ, Dixin-Woods M, Eborall H et al. Women's views and experiences of a patient preference trial in surgery: a qualitative study of the CARPET1 trial. *Clin Trials*. 2010 ; 7(6): 696-704. doi: 10.1177/1740774510381286.
6. Berger AM, Neumark DE, Chamberlain J. Enhancing recruitment and retention in randomized clinical trials of cancer symptom management. *Oncol Nurs Forum* 2007 Mar;34(2):E17-22.
7. Edwards SJ¹, Lilford RJ, Hewison J. The ethics of randomised controlled trials from the perspectives of patients, the public, and healthcare professionals. *Brit Med J* 1998; 317 (7167): 1209-12.
8. Mathieu E, Barratt A, Carter SM et al. Internet trials: participant experiences and perspectives. *BMC Med Res Methodol* 2012; 12:162. doi: 10.1186/1471-2288-12-162.
9. Lincoln YS, Guba EG. *Naturalistic inquiry*. Beverly Hills: Sage Publications, 1985.
10. Kvale S. *Interviews. An Introduction to Qualitative Research Interviewing*. London: Sage Publications, 1996.
11. Elo S, Kyngäs H. The qualitative content analysis process. *J Adv Nurs* 2008;62:107-15.
12. Koopman FS, Beelen A, Gerrits KH et al. Exercise therapy and cognitive behavioural therapy to improve fatigue, daily activity performance and quality of life in postpoliomyelitis syndrome: the protocol of the FACTS-2-PPS trial. *BMC Neurol* 2010; Jan 18;10:8. doi: 10.1186/1471-2377-10-8.
13. Voet NB, Bleijenberg G, Padberg GW et al. Effect of aerobic exercise training and cognitive behavioural therapy on reduction of chronic fatigue in patients with facioscapulohumeral dystrophy: protocol of the FACTS-2-FSHD trial. *BMC Neurol* 2010 Jun 30;10:56. doi: 10.1186/1471-2377-10-56.
14. van Groenestijn AC, van de Port IG, Schröder CD et al. Effects of aerobic exercise therapy and cognitive behavioural therapy on functioning and quality of life in amyotrophic lateral sclerosis: protocol of the FACTS-2-ALS trial. *BMC Neurol* 2011 Jun 14;11:70. doi: 10.1186/1471-2377-11-70.
15. Denzin NK, Lincoln YS. *Handbook of qualitative research*. Thousand oaks: CA Sage, 200
16. Mays N, Pope C. Qualitative research in health care. Assessing quality in qualitative research. *Brit Med J* 2000;320:50-2.
17. Meadows ML, Morse JM. Constructing evidence within the qualitative project. In: Morse M, Swanson JM, Kuzel AJ (eds) *The nature of qualitative evidence*. Thousand Oaks: Sage Publications, 2001.
18. Rubin HJ, Rubin IS. *Qualitative interviewing: the art of hearing data*. Third Edition ed. London: Sage Publications; 2012.
19. Braun V, Clarke V. Using thematic analysis in psychology. *Qual Res Psychol* 2006;3(2):77-101.
20. Mays N, Pope C. Qualitative research: rigour and qualitative research. *Brit Med J* 1995;311(109).
21. *Medical Ethics Manual*. World Medical Association, Inc. 2005. p. 105. Available from: <http://www.wma.net/>
21. Joffe S, Cook EF, Cleary PD et al. Quality of Informed Consent: a New Measure of Understanding Among Research Subjects. *J Natl Cancer Inst* 2001; 93 (2): 139-147.
22. <http://www.hhs.gov/ohrp/policy/consentckls.html>
23. Susman EJ, Dorn LD, Fletcher JC. Participation in biomedical research: The consent process as viewed by children, adolescents, young adults, and physicians. *J Pediatr* 1992; 121(4): 547-552
24. Synnot A, Ryan R, Pictor M et al. Audio-visual presentation of information for informed consent for participation in clinical trials. *Cochrane Database Syst Rev* 2014; 5: CD003717. doi: 10.1002/14651858.CD003717.pub3.
25. Vaz M, Vaz M, Srinivasan K. Listening to the voices of the general public in India on Biomedical research-an exploratory study. *Indian J Med Ethics* 2015;12(2): 68-77.
26. Robinson EJ¹, Kerr CE, Stevens AJ et al. Lay public's understanding of equipoise and randomisation in randomised controlled trials. *Health Technol Assess* 2005; 9(8):1-192, iii-iv.
27. Lubkin I, Larsen P. *Chronic illness: impact and intervention*. Burlington: Jones & Barret Learning, 2006.



28. Arenstein M, Treweek S, Gagnier JJ et al. Pragmatic Trials in Healthcare (Practihc) group. Improving the reporting of pragmatic trials: an extension of the CONSORT statement. *Brit Med J* 2008; 337: a2390. doi:10.1136/bmj.a2390.
29. De Wit M. *Patient participation in rheumatology research. A four level responsive evaluation.* Thesis VU Amsterdam 2013.
30. Schipper K. *Patient participation and knowledge.* Thesis VU Amsterdam 2012.
31. Schipper K, Abma TA, van Zadelhoff E et al. What does it mean to be a patient research partner? An ethnodrama. *Qual Inq* 2010; 16:501–510.
32. Nierse, C., Schipper, K., van de Griendt J et al. Collaboration and co-ownership in research. Dynamics and dialogues between patient research partners and professional researchers in a research team. *Health Expect* 2011, doi: 10.1111/j.1369-7625.2011.00661.