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**ORIGINAL ARTICLE**

# Experiences of randomization: Interviews with patients and clinicians in the SPCG-IV trial*

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**Abstract**

*Objective*. Recruitment of both patients and clinicians to randomized trials is difficult. Low participation carries the risk of terminating studies early and making them invalid owing to insufficient statistical power. This study investigated patients' and clinicians' experiences of randomization with the aim of facilitating trial participation in the future. *Material and methods*. This was a qualitative study using content analysis. Patients offered to participate in a randomized trial and randomizing clinicians were interviewed. Five participants, four non-participants and five randomizing clinicians were interviewed, 2–8 years from randomization. *Results*. Clinicians used strategies in interaction with the patients to facilitate decision making. Patients' attitudes differed and experiences of relatives or friends were often stated as reasons for treatment preferences. Patients described that letting chance decide treatment was a difficult barrier to overcome for randomization. The clinicians used a number of different strategies perceived to make randomization more acceptable to their patients. The clinicians' own motivation for randomizing patients for trials depended on the medical relevance of the study question and the clinicians' major obstacle was to maintain equipoise over time. Regular meetings with the study group helped to maintain equipoise and motivation. *Conclusions*. To establish a good platform for randomization the clinician needs to know about the patient's treatment preferences and the patient's attitude concerning the role of the clinician to facilitate decision making. The strategies used by the clinicians were perceived as helpful and could be tested in an intervention study.

**Key Words:** *prostate cancer, interview, randomized, content analyzis*

## Introduction

The randomized controlled trial is widely accepted as the preferable research method for minimizing confounding variables when comparing treatments. However, recruitment of both patients and randomizing clinicians is difficult, with the risk of terminating studies early making them invalid owing to insufficient statistical power [1,2].

Patients' unwillingness to let chance decide treatment [3], patients' concern about information and consent [4] as well as a preference for a particular treatment have all been found to be obstacles [5,6] to recruitment into clinical trials. Among doctors, worry about an impaired patient–doctor relationship, reluctance to recruit severely ill patients, feelings of personal responsibility if the allocated treatment fails and loss of clinical autonomy have all been suggested as impeding factors [7–10]. Information about how successful trialists overcome recruitment difficulties is limited, however [8].

Men with localized prostate cancer, who at the time of diagnosis were invited to be randomized in the fourth Scandinavian Prostate Cancer Group study (SPCG-4) [11], were interviewed for this study. Clinicians who had randomized for the trial were also interviewed. The aim was to understand attitudes to the randomization process among patients

*Fourth Scandinavian Prostate Cancer Group study.

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and clinicians in the hope of rendering the process more acceptable for these stakeholders in future.

## Material and methods

*Source population and study sample*

To investigate whether radical prostatectomy was beneficial compared with watchful waiting, 695 men, diagnosed with early prostate cancer between 1989 and 1999, were randomized to either watchful waiting or radical prostatectomy in the SPCG-4 study in Sweden, Finland and Iceland [11]. In Sweden, 15 clinicians randomized patients at 11 centres. The centres varied from county hospitals to university hospitals and enrolled two to 182 patients each.

In 2000, after approval from the regional ethics committees, nine patients (five participants and four non-participants) and five randomizing clinicians in Sweden were selected for interviews. The patients were selected from the population of men asked to participate in the SPCG-4 study at two major Swedish randomization centres between 1992 and 1998, with variation concerning age, time since diagnosis, treatment received and participation or not in the SPCG-4 study (Table I). The clinicians were selected to obtain variation in relation to number of recruited patients and hospital size.

*The interview*

The interviews were conducted by one of the authors (AC), a cancer specialist nurse with psychotherapy training. She used a semi-structured checklist (Table II). The patients chose the setting for the interview: at their hospital, work or home. All clinicians were interviewed at work. The interviews were audiotaped, lasted for 40–80 min and were transcribed verbatim.

*Analysis*

The interviews were analysed using content analysis [12,13]. The principal author listened to the tapes, read the transcriptions several times, picked statements that corresponded to the study's purpose, grouped statements that concerned the same issues in categories and labelled them. Thereafter, the statements were compared in terms of similarities and differences. Two of the other authors also read all the interviews and confirmed the results.

## Results

All patients and clinicians who were asked to participate agreed and were interviewed.

*Patients (Table III)*

*Treatment preference.* Patients' attitudes varied from having no set treatment preference at all to having a strong preference. Those with no set preference had limited or no previous knowledge of prostate cancer. Those with a strong treatment preference commonly had previous contact with prostate cancer through friends or relatives. The experience was of particular importance for patients who knew somebody who had died of prostate cancer.

*Decision making.* The patients had different attitudes towards decision making. Some patients saw it as the doctor's responsibility to make any medical decision. When confronted by the lack of evidence for a rational choice between treatment modalities some would persist and ask what choice their doctor would prefer for himself or his own relatives if caught in the same situation. Others found it impossible to let chance decide their treatment or were reluctant to let someone else decide; they wanted to be responsible for their own decision.

*Attitudes towards research.* The patients' attitude ranged from research being very important to a sceptical view that doctors used patients as guinea-pigs for the doctors' own benefit. Some patients considered it an obvious choice to participate in research since they felt it to be a way to help others.

Table I. Patient characteristics.

| Patient | Born | Family | Diagnosis | Treatment | Participant |
|---|---|---|---|---|---|
| 1 | 1937 | Partner, children | 1995 | WW | Yes |
| 2 | 1938 | Married, child | 1995 | WW | Yes |
| 3 | 1921 | Married, child | 1992 | RP | Yes |
| 4 | 1940 | Married, children | 1995 | RP | Yes |
| 5 | 1929 | Married, children | 1995 | RP | Yes |
| 6 | 1926 | Married, children | 1996 | WW | No |
| 7 | 1929 | Partner, children | 1993 | WW | No |
| 8 | 1927 | Partner, children | 1998 | RP | No |
| 9 | 1930 | Partner, no children | 1997 | RP | No |

WW = watchful waiting; RP = radical prostatectomy.

Table II. Interview guides.

| |
|---|
| *Interview guide, patients* |
| *Socioeconomic circumstances*: |
| *Diagnosis of prostate cancer*: When and how were you informed about your cancer? What were you told about prognosis and treatment options? |
| *The randomized trial*: When, by whom and what were you told about the trial? Did you want more/less information? If you could choose, how would you have liked to be informed? |
| *The choice to participate*: Why were you selected for the study? Why did you decide to participate/not participate? What was your doctor's opinion of the trial – did he/she have an opinion on whether you ought to participate? Did you know what would happen if you turned the trial down? |
| *Treatment*: Which treatment did you think best? Which treatment did you receive/how was this decided? What do you know about other possible treatments? Did your knowledge make a difference for your decision to participate/not participate in the trial? |
| *Participation in the trial*: What is your experience of participating (participants)? Would you participate if asked today? Would you ask for more/less information? How would you advise someone else if asked to participate? Advantages/disadvantages of being a participant? |
| *General*: What has been your family's/friends' reaction to the trial? How does the disease affect your life? |
| *Interview guide, clinicians* |
| *Background*: For how long have you worked as a medical doctor/urology specialist/in this workplace? |
| *The randomized trial*: Why did your clinic decide to contribute to SPCG-4? Which of the treatment options in the trial are considered standard therapy at your clinic? Your own treatment preference? |
| *Information to patients on prostate cancer*: What do you tell new patients about prostate cancer – areas you cover – information on the disease – survival rates – treatment options – other? Something you try not to mention? What do patients ask? |
| *The trial*: How do you inform patients about the trial – research in general – randomization? How/when do you perform randomization? Any information about the trial you try not to mention? |
| *Patients' comprehension*: How do you think your patients perceive and understand your information on: prostate cancer, treatment options, research and trials, randomization? |
| Why do you think patients chose to participate in/abstain from trials? |
| *Doctor's significance*: As the doctor in charge of your patient's care, how essential do you think you are to them/do you think they perceive you to be for their care? Does/how does your attitude to the various treatment options/the trial influence your patients' choice of treatment/ participation status? How do you think you are perceived by your patients? |
| *An ideal situation*: In an ideal situation: how would you choose to inform patients on prostate cancer/treatment options/research? How would you inform next of kin? What do you like to accomplish with your information? |
| *Working as a medical doctor, development over time*: What were your views on your own role as a doctor/the patient–doctor relationship and information giving to patients when you started out in the profession? Have your views changed? Why? How? |

Others were positive in a more general way, thinking of research in general being important, but being vaguer about their own contribution.

*The randomization process.* The patients' recollection of the doctor's information about the disease did not differ much. They all remembered the different treatment possibilities. However, the variation between the patients' memories about the randomization process was from no memories at all to a vivid recollection of the information received many years ago. Some patients remembered they had agreed to participate in a study, but no details about the

Table III. Quotations from patients.

| |
|---|
| *About treatment preference* |
| "I didn't know anything . . . you have to trust the doctor who's taking care of you." (Patient 1) |
| "I had a neighbour who was suffering terribly before he died, so for me it wasn't difficult to opt for surgery." (Patient 8) |
| *About decision making* |
| "Well since I didn't know anything I pretty much told him it was up to him to decide. After all he knows more than I do." (Patient 2) |
| "In the end I can only trust my own judgement." (Patient 8) |
| *About research* |
| "If it can make it easier for somebody in the future, count me in." (Patient 4) |
| "It might seem a bit contradictory to not agree to participate . . . If everybody declined to participate there would be no research." (Patient 6) |
| *About the randomized trial* |
| "They just asked me if I wanted to participate. However I don't recall much about it since I did not spend much time thinking about it." (Patient 1) |
| "There were some guys in Stockholm who were supposed to make the decision. I didn't like that. They had one group that would get surgery and one group that did not." (Patient 8) |

randomization process or the study design. When presented with the written study information they had initially received, the majority recognized it.

*Clinicians (Table IV)*

*Decision making.* Clinicians' attitudes varied from the position that ultimately the patient is, and should be, left to make his own decision, to the view that in a fundamental way the doctor always, depending on how he or she chooses to inform the patient, influences and steers the patient's choice. Some clinicians felt that the patient had to make the decision to participate or not in the study, to take personal responsibility for the future outcome and not blame anybody else if the outcome was unfavourable.

*Strategies.* The clinicians used individual strategies to increase the patients' acceptance of randomization. The trial was mentioned early on to patients to accustom them to the study. Sometimes a second clinician were present at the consultation for discussion on treatment options in the hope of helping the patient to feel more confident and open to consider randomization. This routine was also thought to support the randomizing clinician. Some clinicians used extra consultations, away from stressful surroundings with the aim of giving the patient, and often his spouse, additional time for reflection. Careful wording when describing the randomization process was thought to decrease the risk for misunderstanding. Words with associations to gambling, such as "lottery", were thought to imply winners and consequently also losers. Some doctors took care to individualize the information, based on the patient's preformed opinion, to lead the patient in the direction of equipoise. Informing patients about the study's potential implications for future patients was thought to increase patients' awareness of their own contribution. The clinicians did not remind included patients of the randomization procedure, in the hope of reducing feelings of randomness. Instead, they actively strengthened their patient's trust in the allocated therapy.

*Attitudes towards research.* The attitudes ranged from clinical studies being extremely important to clinical studies being a routine part of the job. However, all clinicians felt that the research question had to be relevant, the time consumed had to be reasonable and the paperwork must be kept to a minimum. One aspect of research projects was that every patient gave an opportunity to learn more for the future if they were included in studies. All stressed that the principal issue was always the individual patient and his well-being.

*Equipoise.* The SPCG-4 study was open for inclusion over a period of 10 years, and during this time diagnostic procedures and treatments changed. Several clinicians expressed difficulty in maintaining equipoise, whether initially having had a preference for surgery or watchful waiting or having been neutral. Some thought it increasingly difficult to randomize younger patients since they suspected that those were the ones that may benefit most from surgery. One strategy that facilitated the preservation of equipoise was the regular meetings with the SPCG-4 study group, where the development of the trial and new knowledge on prostate cancer were discussed. These meetings also served as a motivation booster for the attendees.

Table IV. Quotations from clinicians.

| |
|---|
| *About equipoise* |
| "Unconsciously you get influenced during the years passing." |
| "I have tried to be active and participate in all meetings with the study group and steering committee, for different reasons, but the most important was to maintain my interest and motivation for the study and become updated on the current discussion." |
| *About decision making* |
| "It is always the doctor who makes the decision depending on how he informs the patient." |
| "If the patient makes the decision he's more content and cannot blame anybody else . . . but it can also be harder to have decided something that turned out badly." |
| *About research* |
| "A study that is accepted on all levels and is really important and where the hospital has agreed to partake . . . than your own opinion is subordinate." |
| "I think that in order to learn more we need to do trials, otherwise we might do the wrong things for 50 years without knowing it." |
| *About strategies* |
| "In this situation it's important to make them understand that the alternatives are equivalent and if a patient preferred surgery I stressed the risks with surgery. The point is to get the patient neutral, not until then is he fully informed and at the same level as current knowledge." |
| "We were usually two urologists who informed about the disease and the study and evaluated the tumour stage. We perceived it helpful and I think the patients experienced it as something positive that they were so well taken care of". |

## Discussion

Both patients' and clinicians' perspectives were investigated in a trial on a malignant disease. The randomized study had a no-treatment group and was open for a long period. This study found similar barriers to randomization as others [1–10] but, of potential value for the development of clinical praxis, one central finding was that clinicians used strategies in interaction with the patients to overcome the patients' preformed attitudes as barriers to participate in the study. These strategies essentially evolved around building a trusting patient–doctor relationship, and facilitate decision making.

Difficulties in delivering effective information and obtaining full informed consent have been reported to be problems [8]and this trial was no exception. There was a spectrum from study participants with vague or no memories of randomization, to non-participants with vivid recollections of the study. However, this range of experiences cannot be fully explained by a lack of information, since all patients remembered all treatment options well. One hypothesis is that patients who did not want to participate remembered being asked since they had to make two memorable active decisions: first, not to participate, and then which treatment to choose. The patients who agreed to participate only had to make one, tentatively more passive decision, namely to agree to the doctor's suggestion. It is also possible that the fading memory of randomization is a function of time, or that it reflects an adaptation to the uncertainty of which treatment choice might have been the best. Furthermore, the interviews with the doctors revealed that, in order to help the patient feel secure after randomization, the clinicians did not remind him of the chance factor during follow-up visits.

The study has several limitations. It is exploratory in its nature and the findings are hypothesis generating and do not allow direct clinical inference. The small sample means that even if the interviewer perceived saturation, it cannot be excluded that several more interviews may have led to more or different hypotheses. Furthermore, the sample does not allow a dissection of whether the lack of memory of the randomization is a function of time or a coping strategy. The authors had intended to select patients from different socioeconomic and educational backgrounds, but the medical records used to select patients did not contain such information; however, they otherwise achieved a variation in patients' and clinicians' background and a varying time perspective which is informative regarding both short- and long-term adaptation and reflection over the patient and the clinician perspective. Content analysis is appropriate in small studies, but does not allow a deeper analytical approach. Strengths of the study are that, to minimize bias, the interviewer was independent of the randomized trial or any urology clinic. The main author who performed the analysis is a urologist involved in the SPCG-4 study.

Several hypotheses raised from the data could be tested in clinical research. To understand patients' attitudes and to establish a common ground for decision making the doctor needs to explore key elements of an individual patient's needs. The doctor needs to know about the patient's treatment preferences and whether these are built on personal experience of the disease. The doctor needs to be informed of the patient's expectations of the doctor in the decision-making process; for example, does the patient perceive the doctor as an absolute authority or rather as a consultant? Further, doctors may gain from understanding patients' personal views of research. Several of the strategies used by the clinicians, such as the use of a joint consultation, can be tested to learn whether patients in general find them helpful. It is likely that some of these strategies worked well, since the randomizing clinicians succeeded in including many patients into a very difficult trial. This hypothesis is supported by the findings of Donovan et al. [14], that small changes in patient information and presentation substantially increased patient acceptance and recruitment to a trial.

Although many of the barriers to randomization could be overcome by patients and clinicians, two major difficulties remained. The results indicate that for patients an important barrier was unwillingness to let chance decide, and for clinicians it appears that the major obstacle was maintaining equipoise over time in a field with rapidly changing treatment traditions. However, regular contact with the SPCG-4 study group was an important motivating factor for clinicians that helped them to remain impartial and to discuss and evaluate the clinical relevance of novel findings.

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