RESEARCH ETHICS

Attitudes towards clinical research among cancer trial participants and non-participants: an interview study using a Grounded Theory approach

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The attitudes of women patients with cancer were explored when they were invited to participate in one of three randomised trials that included chemotherapy at two university centres and a satellite centre. Fourteen patients participating in and 15 patients declining trials were interviewed. Analysis was based on the constant comparative method. Most patients voiced positive attitudes towards clinical research, believing that trials are necessary for further medical development, and most spontaneously argued that participation is a moral obligation. Most trial decliners, however, described a radical change in focus as they faced the actual personal choice. Almost no one got an impression of clinical equipoise between treatments in the trials, and most patients expressed discomfort with randomisation. A patient's choice to participate was mainly determined by whether the primary focus was on treatment effect or on adverse effects. Both knowledge about and feelings towards trials originated mostly from the media, although paradoxically the media were largely seen as untrustworthy. Mistrust was shown towards the pharmaceutical industry, and although most patients originally trusted that doctors primarily pursued the interest of patients, they did not trust the adequacy of doctors or industry in maintaining self-regulation. Thus, public control measures were judged to be essential.

key aspects of the trial poorly. Featherstone and Donovan¹¹ showed that adult men both participating in and declining trials were engaged in a personal struggle to make sense of trial experiences, often resulting in lay explanations of key trial concepts.⁹ The development of such lay explanations is portrayed elsewhere as well.¹⁰ Seemingly, an expectation of being treated based on needs, even in a clinical trial, is a common misinterpretation among patients who often, in addition, emphasise the importance of trusting doctors.^{4 5 9–12 14}

Our study is part of a complex of questionnaire and interview studies with an intended "gradient of seriousness" in condition, including the healthy background population, non-cancerous outpatients,³ patients with inflammatory bowel disease participating in trials⁴ and patients with cancer (both men and women) associated with choices related to trials with a severe risk of serious adverse effects.⁵

We carried out in-depth qualitative research interviews among women patients with cancer either accepting (trial participants) or declining (trial decliners) participation in one of the three randomised clinical trials including chemotherapy. All interviewees had previously participated in questionnaire studies.⁵ Our objective was to explore a broader description and understanding of the meanings assigned to patients' lived experiences during their treatment courses within or outside a trial setting. The results on patients' attitudes to different trial aspects are reported here, whereas findings with reference to patients' choice strategies, decision-related experiences, actions, and findings on male patients with cancer are reported in other papers. Still, a summary of some results is given, as they are important for interpreting some of the findings in our study.

MATERIALS AND METHODS

We interviewed patients with premenopausal breast cancer invited to participate in one of two non-blinded randomised studies (Danish Breast Cancer Cooperative Group (DBCG) protocols 89b and 89d) and patients with advanced ovarian cancer also invited to participate in a non-blinded randomised trial.

Abbreviations: CEF, cyclophosphamide/epirubicine/fluorouracil; CMF, cyclophosphamide/methotrexate/fluorouracil; DBCG, Danish Breast Cancer Cooperative Group; TEC, paclitaxele/epirubicine/carboplatine

Attitudes towards clinical research are, in general, positive both among the public and patients.^{1–6} Most studies—the majority based on questionnaires—have merely explored hypothetical questions about imaginary trials,^{2 3 7} whereas studies exploring actual experiences with clinical trials have been relatively rare.^{4 5 8} Whether findings from hypothetical studies are directly comparable to real-life scenarios is questionable. Recently, an increasing number of studies have been published using a qualitative research methodology.^{9–12} Such studies have the capacity to explore the unexpected, explain the multiplicities of phenomena and unveil detailed narratives of lived experiences to a different extent than questionnaire-based studies.¹³

The comprehension among the public and patients of the nature and procedures of clinical research is probably relatively inadequate.^{9–11 14 15} Snowdon *et al*¹⁰ showed that parents of critically ill babies randomised in a clinical trial understood

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Box 1 Key questions or topics in the interview guide used in interviewing participants in randomised breast cancer trials (protocols Danish Breast Cancer Cooperative Group (DBCG) 89b and DBCG 89d) and in a randomised trial of advanced ovarian cancer

- Try to describe your general attitude towards clinical trials.
- How do you feel about friends or close relatives participating in a clinical trial?
- Do you have any criticisms towards trials?
- Do you think it necessary to study new treatments using scientific methods before they are implemented in clinical practice? Why?
- Try to describe the trial you were asked to participate in (both trial participants and—decliners asked). If not spontaneously described, the interviewer asked specifically about knowledge of and attitude towards the purpose of the trial, allocation method, chances/risks of getting a specific treatment option, differences in adverse effects, coverage of trial costs etc.
- From where do you think your attitude towards and knowledge about medical research including clinical trials originates?
- What do you think of the information on the issue of clinical trials from the media?
- What do you know about how clinical trials are financed?
- How do you feel about the pharmaceutical companies financing a substantial part of clinical research?
- Did it have an impact on your decision to participate in the trial, that we in Denmark have a legally based public system of research ethics committees, which controls that clinical trials are conducted in accordance with accepted ethical principles? What do you think about public control of medical research? Why?
- Did your experiences in connection with your actual trial participation/treatment outside the trial change your general attitude toward clinical trials?
- What motives do you think doctors have for planning and conducting medical research?
- Try to describe and evaluate the information you received. Supplementary questions explored experiences with and attitudes towards both the written and the oral part of the information given before the patients' choice of whether to participate and regarding the information received during the treatment course (adequacy, amount (too much/too little), form, expectations etc.).
- Were your questions during your treatment course (either within or outside the trial setting) answered sufficiently? Try to describe this further (if answered with Yes/No).
- Try to describe your experiences with the medical staff. Supplementary questions (if not mentioned spontaneously) dealt with the perception of staff knowledge, the ability of staff members to support the patient (emotionally and physically), feelings of safety, trust etc.
- Try to describe the way you made your decision about accepting/declining to participate in the trial.
- Try to describe the reason(s) why you chose to accept/declined to participate in the clinical trial.
- What expectations did you have of the treatment you got? Supplementary questions dealt with the expectations the patient had of the treatment she did not get.
- You (and others among family and friends) have probably already benefited – and will presumably in the future – from treatment results of previous clinical trials. Do you feel that this creates an element of obligation to participate in a trial? (only trial participants asked)

Patients with breast cancer, who were oestrogen-receptor positive, were eligible in the 89b study comparing chemotherapy (cyclophosphamide/methotrexate/fluorouracil (CMF), every third week, nine treatments in all) with ovarian radiation (given daily, five treatments). Receptor-negative patients with breast cancer could participate in the 89d study comparing two chemotherapies (CMF v a combination of cyclophosphamide/epirubicine/fluorouracil (CEF), both given every third week, nine treatments in all). Finally, the patients with ovarian cancer were randomised in a study comparing two regimens of chemotherapy (TC: paclitaxele/carboplatine; TEC: paclitaxele/epirubicine/carboplatine, both given every 3rd week, six to nine treatments in all). In all three multicentre trials, the experimental treatment was only available within the trial. The results of these trials (now completed) are still unpublished. Patients were interviewed after the completion of treatment. None of the authors—not being oncologists and not working within clinical oncology—participated in any stage of the patients' treatment or care.

The clinical studies were conducted in Denmark at the oncological departments at Herlev University Hospital, Herlev, Odense University Hospital, Odense, and Sonderborg Hospital, Sonderborg, Denmark, during 1998–2001. Consent to be interviewed was obtained from patients agreeing to participate in a questionnaire study exploring attitudes towards and experiences of clinical trials.⁵ After completing treatment, a new consent was obtained. The study fulfilled the demands of Danish law and the Helsinki Declaration IV, and was approved by the relevant regional research ethics committee (registration no KA 95059). During approval, the committee expressed ethical concerns about the interviewing of patients without a treatment response, and we were not allowed to conduct such interviews.

Sampling

All patients eligible to participate in the clinical cancer trials were also eligible to participate in a questionnaire study, and only six of the approached patients in our entire complex of questionnaire studies declined to participate.^{4,5} Patients who agreed to complete the questionnaires were asked whether we could contact them at the end of the treatment to set up an interview. None declined. After the completion of trial or treatment, the potential interviewees were contacted by telephone, a new oral consent was obtained and an appointment was made to conduct the interview. We initially planned to continue recruiting for the interviews until we reached about 30 interviewees, based on our experience from previous studies.

We chose to begin our initial interview analysis including only women with breast cancer. During the early analysis, we observed that the number and perceived experience of doctors at check-up appointments were important. This was already noted in preceding questionnaire studies including patients with and without cancer,^{4,5} and we therefore decided to include patients with ovarian cancer also from a questionnaire/interview study at the oncological satellite centre at Sonderborg Hospital in the analysis. This small centre had only two oncologists attached, in contrast with the university hospitals where a larger number of doctors treated the patients. Although a substantial number of patients overall declined to participate in the ovarian cancer trial, all those approached in Sonderborg declining participation during our sampling period (four patients) had a lack of treatment response. As our primary reason for including women with ovarian cancer was the low number of oncologists attached, we were forced to include only trial participants. We thus used both consecutive and theoretical sampling methods.

The interviews

We used an interview guide containing a semistructured list of topics (eg, see box 1). The audiotaped interviews, each lasting 45–90 min, were carried out in the patient's home and later transcribed verbatim by a professional agency (Akademisk Afskrivnings Anstalt, Copenhagen) and saved as single text files that were subsequently transferred to the computer program The Ethnograph V.5.07 (Qualis Research Associates, <http://www.QualisResearch.com>) for analysis. All interviews were conducted by SMM.

Data analysis

The version of the inductive constant comparative method described by Strauss and Corbin (Grounded Theory)¹⁶ was used. The initial open text coding included examining each interview, breaking the transcript down into individual units of meaning, and labelling them to identify categories and concepts. Next, evolving concepts were regrouped to form more abstract categories important to the overall studied phenomenon. Categories were systematically sorted, compared and contrasted, yielding increasingly complex and inclusive themes until saturated. This analytical process was non-linear in nature, with the analyst going back and forth between the different stages of coding while constantly reviewing memos and diagrams. The emerging themes were integrated and refined to identify a central one able to link most categories and form an explanatory whole. Finally, the findings were compared with the original tapes, ensuring that untranscribed features (eg, tone of voice, pauses, etc) did not contradict the transcribed text. Detailed records of the analytical process were kept in the form of extensive memo writing and construction of diagrams. All interviews were analysed together with the goal of developing the most comprehensive account of the data-set.

To maximise theoretical sensitivity and rigour, all authors contributed to the analysis independently. SMM fully analysed all interviews. SH carried out full open coding in five randomly chosen interviews and the codings were compared, showing almost complete agreement, the main differences being about the exact start or end of a given segment. A few new themes were found and subsequently coded. All authors participated in discussions through the analysis.

Illustrative narratives from interviews are given to make it possible for readers to judge interpretations. Pseudonyms are followed by patient characteristics, including disease, status in trial (participant/decliner) and treatment allocation. Owing to space limitations, the surrounding context is not described in detail.

RESULTS

Participants

Only patients with a treatment response were contacted (breast cancer: 9/11 trial participants, 18/21 trial decliners; ovarian cancer: 5/5 trial participants, 0/4 trial decliners). Three patients (all breast cancer trial decliners) contacted by telephone did not want to be interviewed when contacted. Twenty four women with premenopausal breast cancer (9 trial participants and 15 trial decliners) and five patients with advanced ovarian cancer (trial participants) were interviewed. Table 1 shows the patients' ages, treatment received and treatment centres.

The core category—the balancing of options

All patients described a relatively active, deliberate and careful balancing of options, weighing personal advantages and chances against possible disadvantages and risks as the central process of their decision making. The focus was clearly the patients' own best interests—that is, personal maximised safety, confidence and trust. The features of this process are described in detail in another paper (unpublished).

Perceived lack of clinical equipoise

The consensus state of uncertainty among clinicians at the start of a trial that no convincing justifications exist for supposing any patient advantaged or disadvantaged if allocated to one treatment arm rather than to another has been labelled clinical equipoise. However, almost all patients got the impression that treatment options in the trials were not in clinical equipoise and therefore developed a definite treatment preference.

Trial participants and decliners, however, in general considered different factors as deciding. In their weighing up of opportunities the eventual trial participants concentrated on possible differences in treatment effect, where the experimental treatment option was seen as superior. By contrast, almost all trial decliners focused on the adverse effects and risks related to the investigational treatment option. All patients, however, considered both issues in their personal balancing of options. Details of these courses of action are given in another paper (unpublished).

Attitudes towards clinical research

Both trial participants and decliners expressed very positive attitudes towards clinical research in general not only in response to direct questions but also spontaneously throughout the interviews. Clinical trials were seen as pivotal for further development, and no patient saw trials as unnecessary.

Most of the patients specifically stated that a major part of both their knowledge about and attitudes towards trials originated from the media. However, the media were judged to be untrustworthy in general and as promoting disproportionately negative views of clinical trials. A continuum of beliefs concerning the media was, however, expressed across the interviews. The trial decliner patient 18 in several statements stated her strong—explicitly named as media-derived—distrust of both doctors and pharmaceutical companies, although still believing trials necessary for development. These views were the main reason for her refusal to participate in the trial. To illustrate some of her distrust, she said,

... the doctors are all in the pocket of the medical industry. That's how I feel ... It probably comes from television and the other media You keep up with things from the media, and you think about different things you've heard, and that leads you to say NO. [patient 18 (breast cancer, trial decliner, CMF)]

But other patients expressed much less confidence in the media coverage of trials and an increasing confidence in doctors. The trial decliner patient 22 exemplifies another extreme. She had an almost unlimited faith in the doctors and trials, and in addition found the media debate in general had no importance for personal attitudes or choices. She said,

... maybe it has some importance for some, but certainly not for me ... but sure, I keep an eye on the debate, but I wouldn't say it has had any effect on me ... But I think, in the moment, where you face that you have to make a decision yourself ... if it was something forceful you'd heard, then maybe—but I don't think so. I would listen a lot to those I think know about it. I would listen to what the doctors said [patient 22 (breast cancer, trial decliner, CMF)]

Yet, the large majority of both trial participants and decliners ascribed a major significance to the media related to both general attitudes to trials and to specific choices of whether to be randomised in one.

Most patients in all groups expressed doubts about industrial financing of trials owing to worries about industry placing

Table 1 Ages and treatment allocation of interviewed patients in randomised breast cancer trials (protocols Danish Breast Cancer Cooperative Group (DBCG) 89b and DBCG 89d) and in a randomised trial of advanced ovarian cancer

Patients	Age (years)	Treatment allocation in randomised cancer trials					
		Breast cancer				Ovarian cancer	
		DBCG 89b-trial		DBCG 89d-trial		TC/TEC-trial	
		CMF	CEF	CMF	Ovarian radiation	TC	TEC
Patients participating in trial							
Patient 1*	51				X		
Patient 2*	58		X				
Patient 3*	45		X				
Patient 4*	48		X				
Patient 5*	51		X				
Patient 6*	50	X					
Patient 7*	51	X					
Patient 8†	48	X					
Patient 9†	54		X				
Patients declining trial							
Patient 10*	51			X			
Patient 11*	49				X		
Patient 12*	44				X		
Patient 13*	49				X		
Patient 14*	43				X		
Patient 15*	38				X		
Patient 16*	50			X	X		
Patient 17*	45	X					
Patient 18*	62	X					
Patient 19*	50	X					
Patient 20*	51	X					
Patient 21*	51	X					
Patient 22*	44	X					
Patient 23*	43	X					
Patient 24*	41	X					
Ovarian cancer							
Patient 25‡	49						X
Patient 26‡	50						X
Patient 27‡	58						X
Patient 28‡	51					X	
Patient 29‡	58					X	

CEF, chemotherapy with cyclophosphamide/epirubicine/floururacile; CMF, chemotherapy with cyclophosphamide/methotrexate/floururacile; DBCG, Danish Breast Cancer Cooperative Group; DBCG 89b, randomised therapeutic trial, eligible patients with premenopausal breast cancer who were oestrogen-receptor positive; DBCG 89d, randomised therapeutic trial, eligible patients with premenopausal breast cancer who were oestrogen-receptor negative; TC, chemotherapy with paclitaxele/carboplatine; TEC, chemotherapy with paclitaxele/epirubicine/carboplatine.

Patients with breast cancer: trial participants (median age 51 years); trial decliners (median age 49 years). Patients with advanced ovarian cancer: trial participants (median age 51 years).

*Patients treated at the oncological department at Herlev University Hospital.

†Patients treated at the oncological department at Odense University Hospital.

‡Patients treated at the oncological department at Soenderborg Hospital.

commercial motives before the interests of patients. They, however, in general accepted the collaboration between doctors, hospitals and the pharmaceutical industry as a necessity, as financing the necessary trials solely by governmental resources was deemed to be unrealistic.

Although very positive in attitudes towards clinical research, a large proportion of trial decliners articulated a situational change as they faced a personal choice of whether to participate in a clinical trial. At this point many of them assumed a more critical and cautious approach, eventually leading to a refusal of personal participation. Nonetheless, all still maintained both their positive attitude towards clinical trials and their acceptance of a necessity of trials. Statements from patient 11 illustrate some of these:

I see—using my common sense—the necessity of the trial, because that's the way you get things developed, get new knowledge and so forth, but in the situation, when it's yourself standing in it ... It became entirely different for me ... It was a shocking experience to realise that now it was personal and I couldn't participate. I was shocked that I

couldn't contribute in helping others ... I would very much have liked to do that, but I wasn't capable of it ... I felt like a piece in a jigsaw ... they were going to draw lots about whether I should have the best or the second best treatment ... to compare and find out who survives and who dies ... you see black and white only ... For me it was about life and death also if you put it sharply ... due to that, I wanted to choose myself. No drawing of lots should decide what should happen with my life ... [patient 11 (breast cancer, trial decliner, ovarian radiation)]

Relative necessity of trials

Although clinical trials were accepted as necessary, a widespread attitude among most was that some scenarios weakened the demand for testing (ie, where knowledge or experience of an obvious effect of “the new” existed, or the expected risk was small, or in situations of desperate illness).

Patients wished to improve their situation in a broad sense. They ranked this consideration higher than the perceived desire from the medical establishment for hard statistical knowledge.

This way of thinking about the nature of medical science was widely expressed across interviews in all groups, including statements that trials largely concentrated on “hard statistics” instead of “the patient as a human being”. Such views were expressed by most participants and decliners. A participant argued,

... if I’m made an object, the chance of them taking a risk on my behalf is greater, and the more I’m considered a whole person and a human being, namely subject, the less I perceive the risk of being exposed to something irresponsible ... I was observant to which relation I had to those people who recommended the trial [patient 3 (breast cancer, trial participant, CEF)]

Randomisation—unease with letting chance decide

All but two patients knew they were free either to accept randomisation or to decline and receive conventional treatment outside the trial setting.

The trial decliner, patient 21, had a clear negative attitude towards the principle of “drawing lots between treatments”, and was truly surprised and a little shocked during the interview on realising that the trial was randomised. She declined to participate in the trial almost entirely due to uncertainty related to the new treatment and the risk of experiencing graver adverse effects in connection with it. She said,

... I just couldn’t cope with getting such poison inside me ... The thought was almost worse than the surgery I just went through ... if you must participate in a trial it has to be voluntarily so you know what you’re doing. I want to know concretely how it works and what the result will be ... [patient 21 (breast cancer, trial decliner, CMF)]

The other patient (patient 29) who did not realise that treatment in the trial was distributed by chance in fact participated in the trial. She had almost complete confidence in the doctors, and felt no need for explanations. Before the interview she did not in detail comprehend what the trial was about, and had without hesitation accepted what she was offered, including trial participation. When she was told during the interview about the random distribution between treatments, she was almost indifferent:

... I trusted the doctor. He told me, that the chemo was especially suited to my cancer, how much I should have, and how much I could tolerate and so on. I trusted them firmly, and I still do [patient 29 (ovarian cancer, trial participant, paclitaxele/carboplatine)]

In addition, two patients believed that they had some influence in the choice of treatment despite clearly recognising the allocation of treatments by chance (patient 1 (breast cancer, trial participant, ovarian radiation) and patient 27 (ovarian cancer, trial participant, treated with paclitaxele/epirubicine/carboplatine)).

A general discomfort with the randomisation in itself was articulated across interviews. Most patients, however, accepted the procedure, although many did not understand the reason for it. To illustrate a patient said,

... in that moment I thought it peculiar, that when you are going to have something, that it will be decided by a

drawing of lots. They spoke highly about that chemo I got. However, they can just give it to me. Why must I be put in a pool, [of patients] and then toss a coin about it? ... I just think that the drawing of lots is strange. Why can’t they just give you the one they think is the most effective? I did not understand ... [patient 2 (breast cancer, trial participant, CEF)]

A few patients thought that the randomisation was used as a way of rationing scarce resources. Yet, the major problem for most patients in relation to randomisation was that they did not get the impression of true equipoise between treatments.

Practically all the trial participants wanted to get the new experimental treatment, irrespective of possible graver adverse effects. They strongly expressed unease and discontent with not just “getting it” and having to accept a drawing of lots (ie, randomisation), and some of them even considered the procedure unethical due to the perceived lack of clinical equipoise. Patient 5 (breast cancer, trial participant, CEF) argued,

... deep inside I believed the new treatment being better, and now I accepted to participate in a drawing of lots. I was not certain of winning the draw, if you understand? If I had got the standard treatment I maybe would have felt... it’s not as good as the one I’ve got. I think it’s wrong ...

Trial decliners on the contrary, although also considering the investigational treatment to be superior in effect, stated strongly that they did not want to take the risk of getting this due to graver adverse effects. To illustrate, a trial decliner said,

... I primarily didn’t want to participate in this trial because I felt there was a health risk for me, and I didn’t dare say YES ... I was convinced that the new treatment was better ... I have always been convinced that I would say YES to trial participation, but I was scared of this heart-problem (authors bracket: a possible cardiologic adverse effect of epirubicine) and thought “I can’t do this” [patient 20 (breast cancer, trial decliner, CMF)]

In fact, only a few patients clearly stated a positive attitude towards the allocation of treatment by chance. Still, even these patients argued that a prerequisite for their positive position was that the treatments compared were in clinical equipoise.

Trial participation as a moral imperative

Although focusing on their own best interests, most acknowledged the importance of helping others (future patients, doctors, science, etc). Most patients stated that these thoughts had real significance in the actual choice, although many also described them as a subsequent rationalisation.

All trial participants were explicitly asked whether trial participation was a moral obligation considering that earlier generations of trial participants have made the treatments of today possible. Two thirds of the patients stated that trial participation possessed elements of a moral imperative not only when they were answering the specific question, but also spontaneously in other parts of the interview. A patient said,

It’s no good if everybody says NO. That was also a part of why I said YES. You in a way have got to participate. [patient 8 (breast cancer, trial participant, CMF)]

Owing to ethical considerations, patients who had declined trial participation were not asked about moral obligations. Nevertheless, 10 of the 15 patients spontaneously argued that trial participation is a moral obligation, although a change in focus occurred for most of these patients. Their main priority was their own best interests, and the importance of altruistic thoughts for others was weakened. Statements from a patient illustrate this:

I had a guilty conscience keeping in mind that, if we all said NO, we never would get any further, and would never find out if anything were better. But again, I didn't feel so sick that I should bear all these side effects. That's why I said NO. I had a bad conscience, although the doctor said that I shouldn't [patient 22 (breast cancer, trial decliner, CMF)]

Public and the internal control—both necessary

Several patients across groups reasoned that control with trials had two important sides—namely, both internal control among doctors, researchers and industry (ie, self-regulation, codes of ethics, etc) and public control (ie, research ethics committees, health authorities, etc).

Several patients saw internal control as more important than public control, but only a minority of patients trusted it to be adequate. Mainly due to this scepticism about internal control, all patients emphasised that public control should be obligatory. The scepticism regarding the adequacy of doctors' internal control was most strongly articulated by trial decliners, who at the same time were relatively confident in the public control system. Still, both groups expressed serious doubts about the ability of doctors and researchers to maintain self-regulation. These doubts were strongly related to beliefs about influence from the pharmaceutical industries. Yet, the efficacy of public control of trials in Denmark was fundamentally trusted. Trial decliners, however, most vigorously argued for its necessity. Patient 3 argued,

... I believe the main part of control with trials and research lies within the profession itself, and I trust that very much ... I feel that there is an appropriate level of control – not necessarily external control, but internal from the medical community itself – the balance between the two is important... [patient 3 (breast cancer, trial participant, CEF)]

Motives of doctors and researchers

A position held by almost all patients, albeit most strongly by decliners, was that doctors primarily had altruistic motives in doing medical research. Nevertheless, several patients had suspicions about doctors placing advances in personal career, and other personal advantages including economic advantages or the interests of the pharmaceutical industry before the interests of patients.

Only three patients explicitly stated that doctors' considerations about personal career did not have any effect on their motives at all. The remaining patients reasoned that such motives were important for most doctors, although most believed that career issues had only a minor role in the complex of doctors' motives. Altruism was still named as the main consideration.

DISCUSSION

This study reports both trial-participating and -declining female cancer patients expressing very positive attitudes towards clinical trials. Public control measures were, however, argued to be important as the internal control among doctors and

pharmaceutical industry was doubted. Almost all patients experienced a lack of clinical equipoise between treatment options in the trial in which they were asked to participate, and this was very important for choices related to participation.

It is encouraging and relevant that most patients expressed positive attitudes towards clinical research and that almost all acknowledged that clinical trials are of paramount importance for further progress. This position was articulated as a response to direct questions and was voiced spontaneously across interviews. The centrality of positive attitudes is further strengthened as even trial decliners maintained these attitudes. The reality and credibility of these positive findings is reinforced by being in agreement with the results of the bulk of other studies, including our own questionnaire studies.¹⁻⁶

Studies investigating reasons for acceptance of trial participation are relatively few, but in general both non-altruistic and altruistic motives are found to be important.^{3-5 7 17} In this context, it is important that our own previous findings of rejection of trial participation as a moral obligation were not confirmed here. In contrast, two thirds of patients argued unprompted that trial participation had elements of a moral imperative. Thus, it could seem to be appealing to consider trial participation a moral obligation. Still, the long history of human rights abuse makes it imperative that trial participation should be voluntary and not be seen as a duty. The finding further emphasises the importance of supplementing questionnaire studies with qualitative methods, reflecting a more comprehensive exploration of the patients' perspective¹² (triangulation). Helping others had an important meaning to these patients, although for most, other factors became more important for their actual choice. The patients were in general not "egocentric in attitudes". Yet, they were "egocentric in decisions" due to the major personal implications of the choices, which, on the other hand, had only minor implications for future patients.

An important part of the unease related to the randomisation felt by most was the strong expectation of receiving treatment and care based on individual therapeutic needs. This "therapeutic misconception" and discomfort with randomisation¹⁴ was widespread across interviews and has also been shown by others.⁹⁻¹¹ It is very important that almost no one perceived the treatment options in the trials as being in actual equipoise, and that in the end a patient's choosing or not of trial participation was mainly determined by whether the primary focus was on treatment effect or on adverse effects. In this context, it is fully understandable that the idea of treatments being allocated by chance troubled most patients in their anxious pursuit of hope, confidence and trust in a life-threatening situation.

One of the fundamental ethical justifications of randomised clinical trials is the existence of genuine clinical equipoise. However, whether true clinical equipoise exists is not necessarily straightforward to define, and the acceptability of studies with larger disparity in effects and adverse effects between interventions is not clear cut.^{15 18-21} Whether a patient experiences equipoise is an individual judgement depending on numerous factors. Such patient-directed estimates are almost bound to deviate from perceptions held by the doctors, and there will be many instances where the patient cannot be persuaded about the existence of equipoise. Given a lack of equipoise, the patient most likely will decline to participate in randomisation unless trial participation is the only way to get the treatment perceived by the patient to be the best. Problems in dealing with randomisation procedures have also been shown in other studies.^{3-5 7 9-11 15 18 22-24}

In the concrete situation of choice, a large number of issues became important for the patient and the very positive attitudes towards trials apparently only had relatively limited

importance. This has also been indicated in other studies.^{1 17 25 26} Another noteworthy result is that if the potential participants believed that patients were not in focus as "whole human beings", the confidence and trust in the doctor was lost or at least reduced, and criticism resulted.

Although most patients had an a priori confidence in doctors pursuing altruism in doing medical research, they did not trust the adequacy of the internal control among doctors, researchers and industry. Owing to this scepticism, all patients judged that public control measures with trials should be obligatory. The importance of the existence of public research ethics committees for patients' attitudes and choices were also shown in previous studies.³⁻⁵ That a clinical study has been reviewed and approved by an independent ethics committee apparently gives Danish patients a sense of security and increases willingness to participate. Public control of clinical trials in the European Union is increasing dramatically with the recent implementation of full-scale GCP rules relating to all therapeutic research on human beings. We can hope that this will also increase accrual of patients to trials, although studies have indicated that there are increasing recruitment problems with increasingly complex logistics.^{1 26 27}

Some limitations to the study must be considered. Our findings may not reflect the perceptions of patients with a poor outcome, as we were prohibited from interviewing such patients. These patients may be more negative towards clinical research than the patients interviewed in this study. In addition, interviews were carried out after the completion of treatment courses lasting approximately 6 months. Thus, it is unknown whether the views argued here are identical to those present at earlier time points. Likewise, it is unknown whether men with cancer would hold the same views as the women in this study. Future studies should include patients at earlier time points as well as men and those with poor treatment outcome.

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