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"Why don't they just tell me straight, why allocate it?" The struggle to make sense of participating in a randomised controlled trial

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Abstract

Randomised controlled trials are the acknowledged 'gold standard' method of evaluating the effectiveness of treatments, but little is known about how and why patients decide to participate in trials nor how much they understand about trial design. In this study, in-depth, semi-structured interviews were carried out with 33 middle aged and older men with lower urinary tract symptoms related to benign prostatic disease, 22 of whom had consented to participate and 11 refused to take part in a randomised trial. The trial was evaluating the effectiveness of a new technology (laser therapy) compared with standard surgery (transurethral resection of the prostate) and conservative management (monitoring without active intervention) (the *CLasP* study). Purposive sampling was used to include participants from different centres, each treatment arm, and at different stages in participation, as well as those indicated to have refused participation. Interviews explored their recall and understanding of trial information, and their reasoning about how they were allocated to a treatment. Data were analysed thematically according to the methods of constant comparison, and by examining each participant's narrative of their experiences.

Most participants recalled major aspects of trial design, including the involvement of chance, but the case studies showed that most also held other co-existing (and sometimes contradictory) views about their treatment allocation. The key to understanding their experiences was their engagement in a struggle to understand the trial in the context of their own beliefs, their recall of the study information and their actual experiences of the trial. The outcome of the struggle was the placing of trust in clinicians or the development of distrust. Non-participants made sense of their experiences in similar ways, but gave different reasons for non-participation than indicated by recruiters.

This study shows that most eligible patients, whatever their level of knowledge, will struggle to make sense of their participation in randomised trials. The provision of clearer written information or time to discuss the trial with particular individuals might be beneficial, although greater public understanding of trials is also needed.

Keywords: Randomised controlled trials; Trial participation; Patient understandings; Prostatic disease

Background

The demand for evidence about the effectiveness of treatments has led to the increasing dominance in funded health services research of the randomised controlled trial (RCT). Historically, the literature examining RCTs has tended to focus on the methodological issues that should be taken into account during design and implementation, such as blinding and placebos, ethical issues and informed consent (Pocock, 1983). Rather less research effort has concentrated on investigating the patient's perspective of participation, and studies that have been conducted have tended to

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use hypothetical scenarios to determine willingness to participate among the public, potential trial populations, specific treatment groups, or racial and ethnic groups often underrepresented in trials (Cassileth, Lusk, Miller and Hurwitz, 1982; Llewellyn-Thomas, McGreal, Thiel, Fine and Erlichman,1991; Slevin et al., 1995). Overall, such studies have found favourable attitudes towards hypothetical trial participation, but a fundamental problem with such studies is their reliance on attitudes to *hypothetical* (not real) trial participation.

Much of this literature has employed survey research methods and structured questionnaires with the aim of improving recruitment to future trials (Ross et al., 1999). Studies have identified altruism, trust in recruiting clinicians, and an expectation of personal benefit as the main motives for participation in trials (Daugherty et al., 1995; Charles, Redko, Whelan, Gafni, & Reyno, 1978). Numbers and reasons for refusals to participate appear to vary according to the type of trial and the severity of treatment (Riordan & Thomson, 1996). In a qualitative study of an HIV trial, for example, issues of confidentiality were particularly important because of fears of being identified as having a disease that assumed specific social or sexual identity (Ryan, 1995). Such barriers would not necessarily extend to other trials. In most studies, there was often an expectation that design issues would be an important reason for refusal to participate, but the evidence is somewhat mixed. In the majority of studies, only small numbers cited a dislike of being randomised or the use of a placebo or experimentation as the reason for refusal (Schwartz & Fox, 1995; Mohanna & Tunna, 1999) although in studies of women with breast cancer, objection to randomisation was given as the main reason for refusal among half of those questioned (Alderson, 1996). Other important factors for refusing to participate included inconvenience, difficulties with transport, too many clinic visits and time taken, as well as a distrust of medicine or the hospital and worries about side effects (Schwartz & Fox, 1995; Bevan, Chee, McGhee, & McInnes, 1993). Reasons for non-participation have been highlighted as an important area for further research in a recent systematic review (Ross et al., 1999).

There is a small but increasing number of studies focusing on the perspectives of actual participants in trials, asking them to describe their experiences of participation and reflections on their motives for taking part, using in-depth, semi-structured interviews (Snowdon, Garcia, & Elbourne, 1997; Appelbaum, Roth, Lidz, Benson, & Winslade, 1987). In a UK study, Snowdon et al. (1997) carried out interviews with 37 parents (21 couples) who agreed to the participation in a trial of their new-born child with acute respiratory failure. In the other, Appelbaum et al. (1987) observed the informed consent process and conducted interviews with patients immediately afterwards in four US trials of treatment for psychiatric illness.

These studies found that many trial participants did not believe that chance was involved in their treatment allocation. A third of the psychiatric patients (Appelbaum et al., 1987) and many parents (Snowdon et al., 1997) believed they had been allocated on the basis of their individual therapeutic needs. Both papers concluded that trial participants may systematically misinterpret the underlying scientific methodology and hence participate in the trial because of their belief in personalised care (Snowdon et al., 1997; Appelbaum et al., 1987). Although participants' descriptions of the trial seemed correct, further scrutiny often revealed 'distortions' of the intentions of the randomised controlled trial. Appelbaum et al. (1987) referred to this denial of random allocation as the 'therapeutic misconception' (p. 20) and suggested that patients filled such 'vacuums of knowledge' by constructing 'elaborate but entirely fictional' (p. 21) accounts of their treatment assignment. Snowdon et al. (1997) additionally concluded that most parents were 'confused' about randomisation and the methodology of the trial. A recent systematic review of informed consent similarly suggested that "patients do not always grasp what information is disclosed to them", resulting in "defects in reasoning" (Edwards et al., 1998, p. 44).

The aim of our study was to explore whether these issues were congruent with the experiences of middle aged and older men taking part or having decided not to participate in a pragmatic randomised controlled trial of treatments for a common and non-life-threatening condition—lower urinary tract symptoms related to benign prostatic disease. In particular, we sought to examine their recall of the study information and attitudes towards participation, and then their reasons for agreeing to participate in the trial or not, and their views about their ultimate treatment allocation.

Methods

The main trial

Both authors worked in a department where a range of randomised controlled trials were being undertaken. The trial chosen for this study was one that was being led by one of the authors (JD) to facilitate access to patients and study information. The trial, known as *CLasP* (the acronym relating to the treatments involved), aimed to compare the effectiveness of laser therapy (a new technology), standard surgery (transurethral resection of the prostate—TURP), and conservative management (monitoring without active intervention) in middle aged and older men with common urinary symptoms. There were three linked

trials: all three treatments were compared in men with uncomplicated lower urinary tract symptoms, and laser therapy and TURP alone were compared for men with acute or chronic retention of urine in whom immediate treatment was required (Donovan et al., 2000; Gujral et al., 2000; Chacko et al., in press).

Standard trial procedures were followed. There was a process of written informed consent, completion of questionnaires and clinical tests to establish eligibility, with treatments then allocated by clinical researchers opening consecutive opaque envelopes based on randomisation schedules generated by a researcher not involved in the study. At an early stage, patients were given an information sheet, which included details about each of the treatments and described the study in the following terms:

(a) that it was an experimental study because one of the treatments (laser therapy) was new;
(b) that the aim of the RCT design was to allow the treatments to be compared;
(c) that the treatment allocation would be by chance;
(d) that there was clinical uncertainty about which treatment was best;
(e) that the allocation would be concealed to both patient and clinician and that a clinician would open a sealed envelope to reveal the treatment allocation.

The qualitative study

Qualitative research methods were used to explore both participants' and non-participants' views, attitudes and experiences (Pope & Mays, 1995). Purposive sampling was used to ensure that individuals with a range of characteristics were included. Thus, within this study participants ($n = 22$) in the CLasP trial and men who chose not to participate for a range of reasons ($n = 11$) were interviewed.

The sample included participants from each of the two major clinical centres, in the different arms of the trial, and at different time points after randomisation. Non-participants were identified from the trial records as having refused to participate for three major reasons: they had a treatment preference, did not want to be randomised or take part in research, or did not want to undergo tests that were part of the recruitment process. One patient where no motive had been recorded was also selected.

Data were collected by semi-structured in-depth interviews (carried out by KF) using a checklist of topics to guide the discussion (Burgess, 1982; Mays & Pope, 1996). Interviews were conducted in the men's homes, audio-tape recorded and lasted from half and hour to one and a half hours. Each interview was transcribed as fully as possible. Data collection (interviews) and data analysis continued concurrently, according to the constant comparison methods of grounded theory in which data are examined for similarities and differences within themes, retaining the context of the discussion and characteristics of the individuals to aid understanding and allow interpretation and development of explanations of findings (Glaser & Strauss, 1967).

The data were analysed in several ways. The men's recall of each of the five aspects of the trial (see a–e above) was assessed by KF and JD jointly and matrices were drawn up to show which men understood which aspects of trial design. Detailed descriptive accounts of emergent themes were produced by KF and checked by JD. The data were examined for patterns and themes, by contrasting and comparing accounts, noting surprising or puzzling findings for more detailed scrutiny. The data revealed a number of complex and somewhat confusing themes and so it was decided that detailed case studies would be produced for each respondent describing and charting his attitudes and experiences. These case studies were also checked by JD. Typologies were also used to examine why certain strategies were adopted by some subjects by tracing conditional paths to track the process of an event (Strauss & Corbin, 1990). The case studies illuminated the various strategies employed by each participant to explain their treatment allocation. In the light of these case studies, all the original transcripts were re-examined to check and verify the concepts and to take account of the context of the data.

The data are presented below within the major themes that emerged from the interviews with quotations to illustrate the findings and allow the reader to judge interpretations. All names and places have been changed to preserve anonymity.

Results

Thirty-three men potentially eligible for the *CLasP* trials were finally interviewed—22 participants and 11 non-participants. Men with a range of ages, from each of the clinical centres and in each of the arms of the trial were interviewed. Seven participants were interviewed within three months of being randomised, five within five months, and eight after at least six months, by which time they had completed their treatment and had been followed up. The majority of the non-participants attended clinic B and had not yet received treatment for their condition. The men were aged 54–81 years old and were predominantly retired.

A number of major themes emerged from the data, some of which appeared to be contradictory. Detailed scrutiny of these themes in the light of the individual case studies showed that the material represented a

struggle that the men engaged in to make sense of their experiences. First, the men's recall of the trial methods is presented, including both participants and non-participants together. Then the reasoning employed by the participants to explain their participation in the trial is presented. Finally, the different pathways to non-participation are described.

Recall of trial design

Participants had greater overall recall than non-participants about the design issues in the trial. About half or more of the participants recalled that the study involved experimentation, the comparison of treatments and allocation by concealment, usually by envelopes. While non-participants had lower levels of recall of most design aspects, almost all recalled the experimental nature of the trial and emphasised this aspect consistently more often than the participants. Only one participant (Mr Mott) and two non-participants (Mr Flynn and Mr Allgood), could remember none of the major design aspects, and similarly, only two men, one participant (Mr Murray) and one non-participant (Mr Becker), could recall all five.

Almost all (15) of the participants acknowledged the involvement of chance in their allocation:

> There were those three things […] and he said oh yes you've got a swollen prostate, you'll probably have to have an operation but it's a chance you might take, which one of them you take, it comes out the hat, sort of thing you know. It's out of the hat you cannot pick. [Mr Symonds: participant allocated to CM]

In contrast, only four non-participants could recall that chance was involved:

> Yes he did list for me, outline the various different methods, that's right, and explain to me that your particular case would be treated by lottery if you like, by picking up an envelope and that was to be it. [Mr Ladbroke: non-participant, a dislike of randomisation]

Twelve participants and four non-participants were aware that the trial involved the comparison of treatments:

> But the scheme itself was I think they wanted to compare, they wanted to do all three and then make a comparison of what the end results were. So after six months or whatever they are going to do it for, they assess it and I suppose the replies that I'm giving will help to decide what was going to go on in the future. [Mr Murray: participant allocated to TURP]

Overall, 13 participants and only three non-participants could recall that allocation to a treatment would be concealed:

> And of course at the same time explained that neither she or the consultant himself knew which I would get until they chose this famous envelope, one of two envelopes. [Mr Taylor: participant allocated to and preference for TURP]

> You will be allowed to pick an envelope and one will say laser and one will say surgery. Whichever you pick you'll get. [Mr Becker: non-participant refused trial tests]

Fourteen participants and only two non-participants recalled hearing that consecutive opaque envelopes were involved in the trial treatment allocation:

> They pick the—they have three envelopes or something—and they chose the envelope where they weren't going to do nothing and the specialist said that was sort of good really. [Mr Cullum: participant allocated to CM, no preference]

Eleven participants and almost all (9) of the non-participants knew that the trial was an experimental study of some sort, involving 'guinea pigs':

> It was ideal, no problem, no problem. They have got to have these experiments and this sort of thing and I was quite prepared you know, they've got to learn somewhere, somewhere along the line you know. [Mr Daw: participant allocated to CM]

> Well all they were doing at that moment in time, they were doing so many with surgery and so many with laser and they were using people like guinea pigs too. [Mr Becker: non-participant refused trial tests]

Knowledge of clinical uncertainty was at a much lower level with only six participants and four non-participants indicating an understanding of this:

> Well … no because as they say, when they spoke about the two operations they explained to me then that the results should be the same all things being equal. Fair enough if that's the way. [Mr Taylor: participant allocated to TURP]

> I think I would have thought well either have it cut out or have it lasered out. It wouldn't make no odds as long as it does the job. Yeah, I mean I wouldn't have, I don't think I would have minded either way there. [Mr Young: non-participant travel,]

Levels of recall were examined in relation to various patient characteristics, but, other than participation, no clear patterns were apparent. For example, the eight men who could recall four or more of the trial concepts had been allocated to a range of

treatments, represented both trial centres and had been interviewed between three and eight months after randomisation or 'refusal'. Age and time after randomisation appeared to have little influence on these men's recall and understanding of trial information. The influence of social class was also examined. It is often stated that obtaining informed consent to participate in a trial from poorly educated patients is a 'sham' (Editorial, BMJ, 1995). However, the eight 'middle class' men had varying levels of recall and understanding of these five elements, ranging from the highest (Mr Murray) to one of the lowest (Mr Bullock).

Participants: the struggle to make sense of participation

Whilst the majority of participants had a good or partial recall of the major aspects of trial design and methods, many indicated in their interviews that they had difficulties understanding the terminology and coming to terms with the concepts inherent in the trial design. The case studies of each man showed that all were involved in what was, essentially, a struggle to make sense of their participation. Table 1 outlines the major explanations given by the men to describe their understanding of how they wanted to be, or thought they had been, allocated to a treatment. Their views appeared to arise from two main sources: their expectations about the way they thought they ought to be treated and their actual experiences of participating in the trial. These factors were closely linked to the presence of fatalism and trust or distrust of the study and clinical staff, which in turn fed back into a confirmation or undermining of what they understood about trial design. There appeared to be no consistent relationship between the level of recall of trial elements and the presence of alternative and fluctuating views—in most men, these were coexistent.

Individualised treatment

Just over half of the participants (12) indicated that they had expected to receive treatment based on their diagnosis and an assessment of their specific needs by a clinician or practical issues, in the way that they perceived normal clinical practice to occur. Their experience of completing several questionnaires and various clinical tests and examinations within the trial helped to reinforce this belief:

> Well I think it was based on the tests that they gave me and it was one of the types. I think this was for a scan on my bladder to see if it was empty and everything and [the recruiting clinician] came back and she says to us reading the notes and everything and what had happened up to then as regards

Table 1
Alternative 'non-randomised' explanations of treatment allocation

The five elements of the RCT	Participant	Rationing	Individualised allocation	Fate/destiny	Trust	Distrust
5	Mr Murray			✓	✓	
5	Mr Taylor					✓
5	Mr Pierce	✓	✓	✓		
5	Mr Houghton		✓		✓	✓
5	Mr Hall	✓	✓	✓		✓
5	Mr Daw			✓		
4	Mr Cooper			✓		
4	Mr Booth			✓		✓
4	Mr Flint			✓		✓
4	Mr Cullum		✓		✓	
3	Mr Bowler	✓		✓	✓	
3	Mr Formby		✓	✓	✓	
3	Mr Symonds	✓	✓			✓
2	Mr Jamison		✓		✓	✓
2	Mr Grange		✓	✓		✓
2	Mr Stone			✓	✓	✓
2	Mr Brown		✓	✓	✓	
2	Mr Mills		✓			✓
2	Mr Watson		✓		✓	
1	Mr Webster			✓		
1	Mr Bullock	✓	✓		✓	✓
0	Mr Mott					
		5	12	13	10	11

my case, in their opinion as well the middle operation was the best option they thought. [Mr Watson: participant allocated to TURP]

But I thought they would probably they're only picking ones that are retired for doing that [conservative management]. I can't see them having fellas who are going to work because they wouldn't be able to do it. [Mr Symonds: participant allocated to CM and preferred active treatment]

Rationing

Five participants thought that the study involved the rationing of treatments. Mr Bullock implied that the rationale for allocating him to a treatment was because a patient was needed to fill the quota for the laser treatment at the time he attended the clinic:

Well I think I was slightly cynical about it, I didn't really believe it. I thought that they, you know that...I really thought that they were just going to divide people up. I thought it was a bit of a con. [Mr Bullock: participant allocated to and preferred laser]

These participants thought that randomisation was being used by the clinicians/the NHS as a way of rationing scarce resources. This was believed to be related to waiting list size, the limited availability of one of the treatments or cost (laser required a shorter hospital stay and conservative management effectively no additional costs at all). Such beliefs were often based on these patients' experience of receiving treatment. Within this trial, laser patients were grouped together to use the laser machine in one surgical session. Hence patients receiving either laser or TURP tended only to see other patients receiving the same treatment as themselves:

Whether or not there is a chance of you getting a treatment in there I don't know. But I asked others afterwards and they all said the same, they all said the same as me. I never got any chance of getting laser. Cos I says to her, can I have the laser. [Mr Symonds: participant allocated to CM and preferred active treatment]

Fate and destiny

Almost two-thirds of the participants described in detail their belief that fate or destiny played a role in their (randomised) treatment allocation. These beliefs were particularly strong when patients obtained the treatment they had apparently preferred:

I was convinced from the start that I was going to have a laser operation. I felt that that was what was going to be the result. I don't think the envelopes would've mattered. [Mr Grange: participant allocated to and preferred laser]

I preferred the one that I got, so I must have been lucky. I wasn't too keen on this laser idea of having the tube through the stomach into the bladder. [Mr Cooper: participant allocated to and preferred TURP]

Trust and the development of distrust

Trust in the clinician involved in the trial or doctors in general was apparent in many of the accounts. Typically, this trust was expressed in terms of the doctor being an expert:

It didn't worry me too much. I thought they know what they're doing like, you know, so I sort of I'm in their hands like sort of thing, that's the attitude I took, they know more about it than what I know about it like you know. [Mr Cullum: participant allocated to CM]

The laser one he said was more of an experimental one, how would I feel about it. I said whatever you think is best, you know. I mean I'm a layman, I don't know what goes on so I've got to leave it to them. [Mr Stone: participant allocated to laser]

The trust in doctors extended to trust in the trial itself:

You know I'm quite prepared to accept the fact that these guys have to learn their profession the same as everyone else. [Mr Houghton: participant allocated to and preferred laser]

However, for 11 of these participants, their experiences led to the development of distrust. For some, difficulties in making sense of randomisation led to cynicism:

You know, you'll know for a fact that they're giving you the choice of picking one but you're saying to yourself, no matter which one you pick, you're not getting onto the other one. […] Yes, I think that, I don't know mind. But I think it's obviously they decide on what, what they've found out on examining you I think they decide which is going to be best for you. That's only to keep you happy I think. [Mr Symonds: participant allocated to CM]

> Well I think I was slightly cynical about it, I didn't really believe it. I thought that they, you know that…I really thought that they were just going to divide people up. I thought it was a bit of a con. [Mr Bullock: participant allocated to laser]

For Mr Mills, distrust developed because he was unable to accept that randomisation could be a sensible alternative to receiving treatment according to clinical need. He wanted the doctors to tell him what treatment would be most suitable for him, and perceived the trial to be 'a trick':

> They still let you do the three card trick and they just carry it on because from the very first start it's written in the pamphlets they give you. That's one of the things they'll do. You've got your three choices[…] but I think it would be even better if they were to tell you that they prefer, that you're going to get. Because after all with, it's going to be the first time for everybody, you don't have this thing done twice. So therefore, after all if they tell you you still don't know what it's going to be so it makes no difference… [Mr Mills: participant allocated to CM]

For the majority of those who expressed distrust, this could be tempered by a successful outcome. For example, in contrast to Mr Symonds above, where the failure to obtain his preference led to distrust, the fact that Mr Grange received his preferred treatment seems to have outweighed any suspicion of how this actually occurred:

> I was convinced from the start that I was going to have a laser operation. I felt that that was what was going to be the result. I don't think the envelopes would've mattered. [Mr Grange: participant allocated to and preferred laser]

Treatment preferences

The type of treatment received by the men appeared to have some influence on their views. It is important to bear in mind that these are preferences described *after* the process of randomisation and it is not possible to know whether these preferences were present earlier. The preferences expressed by the men suggested that half were randomised to the treatment they suggested they had preferred (see above). Eight participants, however, appeared to have been randomised to a treatment that was not their original or rationalised preference. Interestingly, the majority of this group appeared to be satisfied with their allocation, perhaps because they received one of the active treatments (laser or TURP). Five men (Mr Formby, Mr Mills, Mr Symonds, Mr Daw and Mr Jamison) preferred TURP or laser, but had been allocated to conservative management. They had been assured that they would receive active treatment (TURP) once they had completed the trial.

However, a few participants found their allocation to conservative management difficult to accept. Despite being able to recall the involvement of chance in their allocation, these participants also wanted and expected 'treatment'. Conservative management was interpreted as exclusion from treatment and this was upsetting for these patients:

> You know at the moment, as I said like, the problem with this water trouble is you know four or five times every night and it's a bit annoying you know. I can go to the toilet, come downstairs and within a matter of minutes I've got to rush back upstairs. Well I think something ought to be done about it. […] I naturally thought that they were going to do something about it but as I said I had no tablets or nothing for it, so that's all I can tell you. [Mr Jamison: participant allocated to CM but preferred active treatment]

Non-participants: pathways to refusal

Although reasons for refusal were written by recruiting clinicians in the patients' notes, it quickly became apparent in the interviews that patients often gave very different explanations of their 'refusal'. In the interviews, five were able to cite clear and particular reasons for non-participation. However, there was less clarity among the remaining 'refusers', with three indicating that they had treatment preferences but thought they were participants in the trial, and three who could not recall the trial or being asked to take part. Each of these groups is considered below.

Active refusers

The non-participants who appeared to have made an active decision not to take part in the trial (Mr Young, Mr Ladbroke, Mr Frost, Mr Gibbon and Mr Williams) had a good recall of the trial in terms of experimentation, but low levels of recall of the other design aspects. All expressed a clear treatment preference, the majority wanting TURP because they believed this to be the standard and most effective treatment:

> Well I think me being me, if the TURPs is the standard one then I'm quite happy thank you because that's been proven with everyone else. Having said that I appreciate someones got to do, you've got to have someone for research. But me

worrying, no thank you, [Mr Gibbon: non-participant treatment preference]

The decision not to participate was made by Mr Young because he perceived no direction from the clinician about the trial:

When he said 'well its entirely up to you' he didn't seem to want to make any decisions or choices for me and so I said well I thought the easiest option, the thing is to go for the operation because I've been told about it before.[Mr Young: non-participant travel]

Mr Gibbon, however, felt he had been directed away from the trial because of his uncertainty:

I wasn't expecting this to be honest. I thought it was 'here take these pills you'll be OK', …I think my face must have changed and then [the recruiting clinician] said I don't think this is for you, I don't think it's in your best interest for you to, and I agreed. [Mr Gibbon: non-participant treatment preference]

Mr Ladbroke believed the clinician tried to force him into the trial:

I said give us the pills, I thought I'll have the pills thank you very much! (Laughs)[…] He was definitely, yes he gave me the impression, perhaps wrongly, that he was er having trouble getting anyone submitting themselves to the trial (laughs). [Mr Ladbroke: non-participant a dislike of randomisation]

It is interesting that the perception of different direction from the clinician could lead to eventual non-participation. It also appears that some of these non-participants were eased away from the trial by clinicians.

'*Inactive*' *refusers*

Three patients with high levels of recall of trial design issues were confused that they had been labelled 'refusers'. All had indicated that they would have been willing to accept trial participation, but there were also hints in their accounts that they had expressed treatment preferences which might have led to the clinicians deciding that they had refused:

He went on to say to me would I be interested in a laser job? I said that would suit me fine. So he went, he left the room and went out, spoke to someone, came back in and said 'well it appears that it's not bad enough for a laser job' So I said well OK. So then he surprised me again and said 'now I can still put you down for an operation' So I said 'well, OK'

In the notes it stated that you would prefer the operation...

No that's not correct at all, I accepted what was offered to me. I was prepared to accept anything that was offered to me. [Mr Maynard: non-participant treatment preference]

He did say that all three methods really are quite OK and they are quite happy with all three methods but er you know what suits some may not necessarily suit someone else. So the impression I got was that it would be as a result of talking to me about it before it was decided. [Mr Maynard: non-participant treatment preference]

Well I self-allocated to the watch and wait. Of course they did mention the main side effects, well of course the main side effects is that you can become sterile […]But that's the position with me, watching and waiting, sort of putting it off I suppose, I don't know. [Mr McCarthy: non-participant treatment preference]

No recall of being asked to participate in the CLasP trial

Three patients (Mr Flynn, Mr Allgood and Mr Frame) stated in the interview that they could not recall the trial or being asked to participate. Two of these had extremely low levels of recall of trial design issues (Mr Flynn and Mr Allgood), but Mr Frame (an aeronautical engineer) had very high levels of recall and indicated a strong willingness to participate:

I don't remember being asked at all [to take part in the trial]. Now he may have said these things but I certainly don't remember. The reason I would have responded in the way that I would have agreed for trials was because all my life at British Aerospace I was involved with engineering which involved a great deal of testing and I know the benefits of going through stringent testing and weighing this method against that method, length of times, temperatures and all sorts of things like that so had he asked me I would have approved. [Mr Frame: non-participant no reason given]

All three believed that they had been directed by the clinician towards one treatment:

He said that I think it would be best if you didn't go in for it, so I left it like that. Now I've got to go again in September. [Mr Flynn: non-participant treatment preference]

So I said I'd like it done with the laser beam. So when I went down again I seen Mr — and he said 'you wanted it done with the laser beam didn't you' and I said yes. Well he said you can count that out. He said if I do you with a laser beam he said it would damage

your kidneys […] so he said 'what we've got to do is we got to take the tissue out and that's what they done. [Mr Allgood: non-participant a dislike of randomisation]

They seemed to say that your condition is not so bad as to need surgery, therefore we recommend you have tablets and that's really how it was presented to me. […] and of course would be a lot cheaper over the period of time, although it would take longer to effect, I was quite happy with that. [Mr Frame: non-participant no reason given]

Discussion

This study shows that it is possible to engage trial participants and non-participants in discussions about their attitudes towards a trial, their allocated treatment, and the method of allocation. Previous studies have suggested that trial participants are confused about randomisation and give distorted accounts (Snowdon et al., 1997; Appelbaum et al., 1987). The men in this study acknowledged that randomisation was confusing and difficult, and many formed alternative accounts to explain the treatment allocation. Superficially, these accounts appeared contradictory and suggest confusion, but seen in the context of the men's experiences of some of the trial procedures and their struggle to understand the difficult concepts inherent in trial design, these accounts were rational and reasonable.

There were a number of factors that contributed to the men's struggle to understand. It was clear that most of these men were able to recall and understand aspects of trial design, including randomisation. Such recall did not, however, mean that such concepts made sense or were believable. Allocation according to randomisation appeared to some to be very haphazard (as is the lay definition of the word (Feathersone & Donovan, 1998)). It was difficult for these men to believe that such a haphazard procedure was reasonable, particularly when they had completed so many questionnaires about their symptoms and undergone clinical tests, some of which were very invasive. The men reasoned that the data from the questionnaires and clinical tests must be useful, not just for research purposes, but also for clinicians to make individualised treatment decisions—hence the unacceptability of randomisation.

Participants adopted several approaches to making sense of the trial. Some became distrustful because of assumptions about the existence of rationing, others put their trust in their clinician and their beliefs about fate and destiny, while others just keep struggling with the perceived inconsistencies. Thus, in attempting to make sense of their participation, men produced narratives which on one hand described their understanding of elements of randomisation, but on the other hand challenged aspects of trial design based on, for example, their desire to trust clinicians to make treatment allocations based on individual clinical characteristics, or distrust relating to fears about rationing. Both the participants and non-participants tried to make sense of their experiences using similar rationalisations.

The evidence from this study suggests that non-participation may be something of a lottery. While it was reasonably clear that some of those labelled 'refusers' had expressed strong treatment preferences and thus were rightly considered non-participants, there were others who appeared to want to participate. There were hints in some of their accounts that they had expressed preferences, but some were surprised and concerned that they had been labelled as non-participants. It would seem that the role of the clinician recruiter was absolutely crucial in eliciting such preferences and deciding who should participate. Our focus was on patient perceptions and so we did not have access to what was actually said by recruiters, and this is an area that urgently requires further research. It is interesting that the non-participants were much more aware and concerned than participants about the 'experimental' nature of the study and their perception that they might be used as 'guinea pigs' might be an important factor in refusing to participate.

Another interesting area for further research is in patient preferences. While some work has been done in this area (Silverman & Altman, 1996; McPherson, 1994) this study suggests that patients may agree to randomisation even when they have a preferred treatment. The outcome of the randomisation may then have an impact on their satisfaction with the study and, potentially, their outcome. What we cannot tell in this study is whether the treatment preferences expressed by these men were held a priori, or whether they developed once treatment had been assigned. Further work is required.

Much of the literature has concluded that providing better or more information will resolve difficulties inherent in the recruitment process. However, research examining informed consent has found that even when trials adhere to strict informed consent procedures and ensure that 'simple language' is used, this does not guarantee that subjects will fully understand the implications of participation and that they may still have unrealistic treatment expectations (Harth & Thong, 1995). It is true that clearer information in this trial would have been beneficial, particularly about the use of envelopes in the allocation procedure, but it is also clear that this would not necessarily provide a solution. The patient information in this study was well received and largely accurately recalled, but patients still struggled with the concepts underlying the design and developed competing accounts to make sense of their experiences.

It has been suggested that potential trial participants should be informed specifically about the components of research that constitute a change from the standard doctor–patient relationship—randomisation and blinding, plus any additional clinical examinations and therapies (Editorial, BMJ, 1995). Edwards et al. (1998) similarly conclude that abstract concepts such as randomisation should receive particular attention, "since it is the conceptual scientific basis of trials rather than details of the treatments themselves which patients find hard to grasp" (p. 53). It is also important that participants understand clinical equipoise and thus have realistic expectations of the benefits of trial participation. Clinicians are known to have difficulty in expressing uncertainty, and perhaps it should be some other member of the research team that could be involved in explaining and discussing the rationale for the trial. It is not clear who might be suitable for this role (nurses? lay advocates?) and this may also only provide a partial solution. Having the chance to discuss these issues before making the decision to participate may or may not help patients make sense of the trial. It may also lead to lower rather than higher levels of participation in trials—this remains to be established.

There is some evidence from this study that the men's views may have had some impact on their outcome following treatment. Some found the difficulty of reconciling their views difficult and upsetting. In some cases, patients became very cynical and some began to doubt the veracity of the trial, considering it to be part of some elaborate 'con trick' or resource-saving scheme. These findings have implications for trial design and for trialists as such beliefs may affect the internal and external validity of a trial.

It is important to consider the potential limitations to this study. It has included only men, and only relatively small numbers involved in this trial. Also, interviews were conducted after these men had been asked to participate, and so we do not know how their views changed during the recruitment process or how their preferences for particular treatments might have changed. There are, however, a number of themes from this study that find echoes in previous research, particularly conducted by Snowdon et al. (1997) and Appelbaum et al. (1987) about the difficulties participants have in understanding randomisation. This study extends this work by showing that participants engage in an ongoing struggle to understand the methods of the trial and the process by which they are allocated treatment. It will be important for further research to investigate whether this struggle is found more widely in other trials and other patient groups. Another very useful avenue for further research would be to examine the struggle in the context of participants' beliefs before their involvement in the trial.

This study used qualitative research methods to explore the experience of participation in a trial. If a structured questionnaire had been used to assess recall and understanding, it is likely that the majority of these participants would have been shown to be aware that they were taking part in a trial and to have understood some or most of the basic aspects of the design. There was some evidence of confusion about key concepts, as has been found in previous studies, but we have shown that these men tried to make sense of their involvement in the trial rationally and sensibly in relation to their own beliefs, their recall of the study information, and their actual experiences. As they engaged in the struggle, some found peace of mind in their trust of the clinicians, others became very cynical about the study, and the remainder continued to struggle. One conclusion might be that more information should be provided for potential participants—such as clearer written information or time to discuss the issues with particular individuals. Such interventions require further research, but the findings from this study suggest that most participants (and non-participants), whatever their level of knowledge, will struggle to make sense of the need for randomised trials. Perhaps the greatest need is for more open debate about trials amongst trialists, recruiting clinicians and the public.

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