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**Trials and tribulations: understanding motivations for clinical research
participation amongst adults with cystic fibrosis**

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Abstract

In the context of understanding motivations for clinical research participation, many authors consider issues such as informed consent and how patients perceive the research method and process. However, many investigations focus only on one method of research, most commonly the randomised controlled trial. Understanding how chronically ill members of one specific patient group respond to all requests for research participation are rare. Cystic fibrosis (CF), a genetic condition whereby those affected are used to taking a wide array of treatments and attending a specialist care centre over many years, and are generally knowledgeable about their condition, represents an ideal case for investigating how staff requests for clinical research participation are accepted or declined. Using Bloor's systems of relevance framework for risk behaviour and risk reduction, specialist CF centre patients' motivations for participation or non-participation in clinical research can be understood. The framework takes into account two sets of conceptual oppositions: habituation and calculation, constraint and volition. These oppositions represent a range along a continuum of risk behaviour rather than being absolute distinctions. Decisions to participate are influenced mainly by the patient's state of health at the time of request, the nature of the trial and the social context within which sufferers are placed. Understanding why chronically ill patients refuse some requests and yet accept others may assist researchers in designing protocols that take these factors into account and achieve the desired numbers of participants whilst protecting those in vulnerable positions.

Key words: cystic fibrosis; risk; clinical research; motivation; patient recruitment

Introduction

Many investigations of patients' responses to clinicians' requests for participation in clinical research focus on a particular aspect of the research, for example implications for participants of the research method chosen (Featherstone & Donovan, 2002; Robinson et al., 2004; Slevin et al., 1995; Snowdon, Garcia, & Elbourne, 1998) or ethical issues surrounding informed consent (e.g. Corrigan, 2003; Gammelgaard, Rossel, & Mortensen, 2004; Lynoë, Sandlund, & Dahlqvist, 1991). The rise in popularity of randomised controlled trials (RCT), whereby a new treatment is tested against existing therapy or placebo, is widely accepted by scientists as the most powerful method of gaining evidence for the efficacy of treatment (Ross et al., 1999), yet it is not the only method by which evidence of efficacy of treatment and care is gathered. If clinical research is to underpin improvements in understanding disease processes and developing treatment and care that is responsive to users' experiences, then a range of methods needs to be employed (Campbell et al., 2000) that recruit sufficient numbers yet protect those in vulnerable positions who may be overburdened by research participation (Weijer & Fuks, 1994).

In the context of participation in a particular clinical research project, participants' stated reasons for their involvement are common across diverse conditions, for example altruism amongst intravenous drug users (Fry & Dwyer, 2001) and those with cancer (Madsen et al., 2002; Snowdon et al., 1998). An opportunity to improve personal health through access to new treatments by experts has been noted in people with conditions including vascular disease (Wilcox & Schroer, 1994), acute cardiac conditions (Gammelgaard et al., 2004) and cancer (Madsen et al., 2002; Slevin et al., 1995). Reasons for subjects refusing participation or withdrawing consent after randomisation have been attributed to heavy work schedule, concern about potential risks and a change of mind (Moss et al., 2004), worry arising from uncertainty, additional demands such as procedures and appointments, and travel problems and costs (Ross et al., 1999).

Although research demonstrates that trust in doctors and the inconvenience of participation are important factors in willingness to participate in research (e.g. Ellis & Butow, 1998; Ellis, Dowsett, Butow, & Tattersall, 1999), these studies used either fixed-choice response questionnaires and/or

focused on hypothetical trials to investigate respondents' perceptions of the purpose of RCTs. Additionally, these studies of the lay public's perceptions of hospital research used some respondents who had never experienced the research process.

The research community has a duty to protect those who are vulnerable and operates with a strict adherence to codes of conduct including the Declaration of Helsinki, produced by the World Medical Association. In the UK, Research Ethics Committees serve to assess the potential risks of clinical research to both the individual and wider society. It is possible, however, that patients may have already decided whether to participate before they read literature prepared by the research team. To improve both recruitment and patients' experience of research participation, we need to understand more clearly the reasons why patients agree or refuse to participate (Ross et al., 1999) as willingness to take part in a hypothetical trial may not accurately reflect willingness to participate in an actual one (Solomon, Payer, Young, Roberts, & Butow, 2003). Currently, we have little information to guide our understanding of what factors lead patients to participate in some studies but not others. Corrigan (2003) has previously considered the social processes involved when participants in different clinical settings consent to take part in RCTs, yet many of these respondents were healthy and were paid for their participation. Reports on motivations of one specific patient group, who are dependent on on-going treatment, to requests for research participation are currently lacking.

In the context of intravenous drug use, Fry and Dwyer (2001) have called for examination of the suitability of various theoretical frameworks to explain research respondents' motivations for participation, and the relative weight respondents place upon these motivations. One approach to conceptualise motivations in the context of clinical research participation in a defined patient group is to look more widely at theories of risk perception and risk management. Much has been written in the sociological literature about management of risk in late modernity at both a societal and individual level. Beck's 'Risk Society' (1992) and Giddens' 'Modernity and Self Identity' (1991) present theoretical approaches to dealing with risk on a macro-level. In considering risk behaviour and risk management on a micro-level, Bloor sought to specify a conceptual scheme that 'provides a heuristic framework for the description of various diversities of risk practices and risk reduction' (1995, p. 27). Bloor's work

draws on Schutz's (1970) 'system of relevances' in developing a phenomenological approach to understanding risk management. Here, the conceptual focus is on the immediate situation and considers a wide range of influences on circumstances, including strategic relationships, orientations brought to the situation, automatic activity and rational weighing of risks and benefits.

Bloor's approach for explaining risk behaviour is to use a theoretical scheme of 'intrinsic' and 'imposed' relevances whereby topics become problematic either by self-selection or by the actions of others. In doing so, Bloor takes into account two sets of conceptual oppositions in his framework; habituation and calculation, constraint and volition. These oppositions represent a range along a continuum of risk behaviour rather than being absolute distinctions. A routinisation (habituation) of risk behaviour arising from the recurrence of certain situations can become an established and 'taken for granted' aspect of daily life, so that some moments, once 'fateful', whereby careful consideration of the costs and benefits of actions must occur, become no longer so. The calculative end of the continuum may be akin to Giddens' (1991) 'fateful moment' where the risk decision taken may have far-reaching consequences for present and future time. The individual would consciously identify these situations as a 'risk' and the costs and benefits of each path of action would therefore be carefully considered.

In Bloor's second set of conceptual oppositions, constraint and volition, constraint may be absolute or only partially restrictive. Here Bloor considers structural and normative constraints; for example, which actions are permissible in the situation and which actions are preferable to the individual. The conception of risk taking as a volitional act, Bloor argues, is inappropriate where the risk situation involves more than one individual and where the risk is not taken from free choice.

Cystic fibrosis (CF), the UK's most common autosomal recessive genetic disease with an incidence of 1:2415 births (Dodge et al., 1997), represents an excellent opportunity to examine research participation within a defined patient group. The major symptoms of CF arise from abnormal sticky secretions in the respiratory and digestive tracts, the most common symptom being lung damage from recurring chest infections. Current routine treatment for CF is palliative, not curative, and so aims to maintain health by treating the symptoms of the disease as they occur. The mainstays of a wide array

of daily therapies are chest physiotherapy, regular courses of antibiotics and pancreatic enzymes, with patients attending specialist centres for paediatric and adult care reported to achieve a better clinical outcome (Mahadeva et al., 1998). Survival age has steadily increased from under one year in the late 1930s (Anderson, 1938) to 31.5 years currently (Dodge et al., 1997), as the disease is better understood and treatment and care are developed. Adults are generally knowledgeable about their disease and treatment and most have well-established relationships with healthcare staff. As more is known about CF and more patients survive into adulthood, new treatments and service models become necessary. Perhaps the most evident example of this is the identification of the 'CF gene' in 1989 (Rommens et al., 1989), which paved the way for trials to investigate the safety and tolerability of gene replacement therapy (GRT) in patients with CF (Moss et al., 2004), although adults living with CF currently are unlikely to receive this as a licenced treatment.

This paper presents perceptions and management of the risks of participating in clinical research amongst a group of adults with CF attending a specialist centre for the disease in the UK. Giddens' work is used together with Bloor's framework to understand further the risk perception and management strategies of these adults with CF who have been asked to participate in, or are currently engaged in RCTs and other hospital research. The paper presents the analyses of patients' interview data in terms of Bloor's four categories, habituation and calculation, volition and constraint, to form a typology of risk management.

Method

Thirty-one adults with CF aged between 18 and 40 years were interviewed as part of a larger study of living with the disease. Seventeen were female and 14 male. Nineteen respondents (61%) had passed the predicted survival age of 27.6 years for this cohort when interviewed (FitzSimmons, 1993). All participants attended a specialist CF centre for their treatment and care and were regularly asked to consider participating in research that staff were conducting.

Letters were sent to 183 clinic patients living in one geographical area and 47 patients agreed to participate (16 opted to complete a health questionnaire only). Participants were interviewed in their

own homes for between 1 and 1.5 h on average, with the aid of an interview topic guide. Besides exploring respondents' perceptions of the risks of participating in clinical research, the interview aimed to cover issues such as the health and quality of life of those with CF (Lowton & Gabe, 2003), and the perceived risks and benefits of other current and future potential treatments and care (Lowton, 2003). Confidentiality was assured for all participants, and assurance given that all interview material would be made anonymous by using pseudonyms in any reports. Approval was obtained from the hospital ethics committee.

Analysis

Interviews were tape-recorded and fully transcribed. Transcripts were coded using the ATLAS-ti software programme for qualitative data. Codes were attached to a segment of text such as a word, phrase, sentence or paragraph. These codes were then grouped into categories, providing the conceptual foundations for analysis as described by Dey (1993). The majority of conceptual categories had started to be developed over the course of interviews and were subsequently developed analytically with conceptual relations being established (Strauss, 1987).

Results

Before the results of analysis are presented, the research needs to be set in context. At the time of interviews, GRT trials had recently begun at the centre. Other research carried out around the time of patients' interviews included investigating the effects of the disease on the body, for example magnetic resonance imaging (MRI) to explore CF-related liver disease, the development of laboratory tests to enable doctors' prediction of CF-related diabetes and the estimation of the degree of osteoporosis in adults.

All participants stated that they had been asked to participate in at least one research project other than the current one. Although the majority of clinical research patients spoke about did not involve their taking new substances, there was still the consideration of undergoing medical procedures (e.g. scans or blood tests) that were not part of their routine medical care and were likely to cause a degree of social disruption. During their interviews most patients spoke of RCTs and other clinical research participation (for example the development of new diagnostic tests or understanding of physiological

and psychosocial processes) together. Many patients were unclear about the methods and/or aim of the research that they had participated in, as the following quotation illustrates:

KL: Do you worry about the risks to yourself [when taking part in research]?

Keith: Yeah, I mean [pauses]. I say I do choose the things that I get involved with carefully, but I remember one where they made me slightly radioactive for a couple of days! [laughs].

KL: What was that one?

Keith: I forget now. It was something to do with a scan, they had to, I can't remember what it was for, it was years ago now, it was something to do with liver, and I had to inhale this [searches for word] not iodine, an ionised formula, something like that, and then I had to lie rigid on a bed for two hours not moving an inch, and I do remember actually thinking 'God, what have I let myself in for?' when I did that [laughing].

For this reason, it is not possible to provide precise details of the number and type of research studies in which patients had participated.

All adults stated that they placed a basic level of trust in the specialist centre to deliver their routine treatment and care, although as they got older and more expert in managing their condition their care became managed more as a partnership between themselves and staff members:

Something I realised as I got older, I have to kind of [understand] that people are fallible and you've got to present all the facts to people and not just to blindly accept what anybody says. In other words I've got my part to play in it as well, you know I've got to look after myself, I've got to make sure I tell the doctors or whatever how I've been, particularly if I haven't been as well. And let's say I go and they

say, "Have you ever had this drug before?" And I say, "Yeah, I responded well to that." So I'm trusting them to give me that but at the same time I'm kind of using my own judgment, I'm remembering how that affected me. So, oh yeah, I absolutely trust their decision but realise that I've got a part to play in that as well. (Jack, 35)

It is therefore against the backdrop of working towards a cure for CF, trust in the specialist centre, and being an active participant in the management and treatment of CF, yet being unable to recall precisely the nature and purpose of all research studies that they had participated in, that patients' perceptions and management of the risks of clinical research are presented.

Risk and Habituation

Any rounded explanation of risk management needs to take into account the routine nature of some risk behaviour (Bloor, 1995). It is possible that these CF patients' long experience of treatment and care at the centre, with requests for their participation in clinical trials, has resulted in an 'ease' in being involved in research. Two main factors were influential in adults' decision to habitually accept some requests for their research participation; the type of research project in which patients were being asked to take part and their trust in the specialist centre and its staff.

Type of research project

The type of research that patients perceived as a habitual risk would not involve the testing of new drugs in a RCT. Requests for a blood sample for subsequent investigation in projects that appeared to enable staff to better understand and treat CF were more likely to be seen by patients as not only a routine, but often a very frequent, request from doctors at the centre:

A few weeks ago I was up there [at the specialist centre] and two doctors came up to me [to request participation] on the same day, which is sort of showing you something. (Clare, 38)

Wider social considerations, for example taking time off work or needing to delay trying to start a family in order to participate in the research, would not usually need to be taken into account by

patients in these instances. Adults' participation in this type of research was normally limited to a short amount of time that would otherwise be spent waiting to see hospital staff, or easily fitted into necessary routine investigations. In this case, the risks of participation were not given any thought, as Rose, 27, explained in the context of being asked to give blood for non-RCT research:

KL: Have you had bloods taken for research?

Rose: Oh there was one lot of bloods [that] was taken. Not the last visit, the visit before I think. I don't even know how it was asked for, actually. All I remember them saying is, 'Oh, put it in the green envelope and leave it with someone. When you have your bloods taken get an extra one done.'

KL: Can you remember what that was for?

Rose: No, it just said it was going to some other place in the hospital, extension something or other. That's all I remember seeing on the envelope. I don't know, I didn't take too much notice. As far as I was concerned, they could have my blood; I wasn't worried about it.

As Giddens (1991) proposes, certain actions exist that are immersed in an individual's habit of daily living, here in Rose's 'habit' of giving frequent blood samples, which for people who are in relatively good health, pose little physical risk other than slight discomfort and bruising. Giddens suggests that an individual may follow a pre-established pattern of behaviour, with his or her management of risks being linked to a trust in the medical profession in general. This means that people will not stop to assess the consequences of each new risk separately, but will assess the overall 'package' of risks that are inherent in maintaining their chosen lifestyle. Here the package would include participating in research as part of routine hospital appointments as the individual who wishes to achieve their overall lifestyle plan (i.e. to maintain good health) sees this risk-taking as acceptable, by causing minimal or no damage to their own current health and permitting possible future benefits of new treatments.

Patients' trust in the specialist centre and its staff

Although most patients stated that they trusted the specialist centre in the management of routine treatment, trust in the hospital and its staff was a pertinent issue in patients' perception of the risks of research participation. In addition to considering the type of research involved in habituated risk, the awareness of being a 'special patient' at the specialist centre, through prompt access to clinical staff and treatment, was influential amongst patients. Part of the centre's role was therefore perceived by adults as not to expose 'special patients' to unnecessary harm through routine treatment or through hospital research:

I think the [centre staff] are very sensible in what they offer. And if they feel that it is time for you to change a drug, they will suggest it. They know what drugs are there, they are at the cutting edge of everything...they know what they're doing, so there's no point in worrying about it. (Mark, 38)

Giddens suggests that 'an individual might feel that governments, scientists or other technical specialists can be trusted to take the appropriate steps to counter them [dangers].' (1991, p. 131). In this context, with the doctors performing both treatment and research, the centre could therefore do their patients no harm, demonstrating how patients might implicitly accept the scientific (doctors') perception of the risk of medical research in this instance. In addition, the notion of a basic trust in the hospital was also present in patients' thoughts of hospital research; that is, doctors could be trusted in the development of new drugs that would one day become routine:

I don't think people put themselves through seven years of medicine training to get it wrong, basically. I've got full faith in the medicines that I'm given and the research that's done on the new medicines that come out of that [research]. (Keith, 26)

Therefore, a background of trust in the centre and indeed patients' thoughts of the necessity of research meant that some patients based their decision to participate in the hospital's research projects on their trust in the centre and its staff, with doctors' roles as researcher or clinician no longer clearly differentiated (Taylor, 1992). In this situation, Brewin's (1997) and Featherstone and Donovan's

(2002) notion that consent to participate is based on trust rather than information given about the research is pertinent.

However, there was one patient in the current study who stated that she had decided not to participate in a non-RCT research project and had based her decision partly on her distrust of the junior doctor asking for her permission. This suggests that once trust in a relationship has been lost, a previous willingness to participate in hospital research that has been based on trust in staff is also lost:

One [doctor] I really wanted to help. He was doing a diabetic one [research study], a Chinese chap and he was really nice and non-pushy, and I almost wanted to do it because of his attitude, but the other one [doctor] I didn't like. [Later] The other one was [doing] things up your nose and stuff and I really don't like the doctor anyway, so I just thought, "Oh, no, nothing about that [study] attracts me to wanting to do it." (Clare, 35)

Indeed, Ellis et al. (1999) note in their study of oncology outpatients responses to a hypothetical RCT that the strongest reason stated to consider participation in RCTs was a favourable perception of the doctor. Robinson (1999) argues that who is doing the asking may be a more important consideration for the patient than what the study actually involves; Wilcox and Schroer (1994) suggest that it is the doctor who is patients' primary motivator for entry to RCTs. As many studies have found, provision of information regarding participation in research is provided in a social context in which trust is crucial (Mark & Spiro, 1990). This suggests that although an element of trust must be present to underpin habituation, an element of habituation (i.e. being treated by the same doctor over a long period of time) may enhance the development of this trust. In this context, many of these adults appeared to let centre staff become the risk assessors and managers on their behalf, due mainly to trust established over a long period of time, questioning, and knowledge seeking.

In summary, being repeatedly asked to give samples of blood or participate in other physiologically based research and having trust in the staff and hospital illustrate the habituated nature of some risk

management by adults with CF. Boundaries were blurred when considering the role of many research staff, as much of the research at the centre was undertaken by clinical staff who were also responsible for patients' routine treatment and care. However, there were times when patients felt that they were unable to participate when approached by researchers because of various constraints. These constraints were a common explanation amongst patients for refusal to take part in research.

Risk and constraint

In the context of how relevances (i.e. habituation and constraint, volition and calculation) may be socially constructed, Bloor has suggested that 'constraint may be absolute or only partially restrictive'. However, Bloor considers constraints only in the social sense, for example what actions are allowable in the situation and which are preferable to the individual. In the present group of patients, the notion of constraint was identified as being due to social constraints by patients, for example obligations to the family or to employers, and constraints perceived by patients to be set by the centre, but also due to health constraints such as increasing age and/or failing health.

Social Constraints

It might be suggested that patients may rate their social concerns as 'trivial' when compared to treatment priorities, suggesting that patients may ignore the social risks in favour of any potential health benefits arising from participation in drug development. However, adults with CF found consideration of their social concerns to be essential when being approached to participate in research. Social concerns most commonly identified by this group of patients were obligations to their families and employers. Although some research was of a short duration, for example that carried out at the outpatients clinic as described above, other projects took months to complete and often involved frequent visits to the hospital. These projects were set against a background of at least three-monthly routine outpatient's visits for most patients. The constraint imposed by employment meant that those patients who were fit enough for paid work did not feel able to take time off from their job, especially if that time had to be 'saved' for when they were unable to work through anticipated future periods of acute illness such as chest infections. Therefore, many patients in paid work felt that although their employment stopped them from being involved in longer-term research, projects that could be fitted in

to a day that had already been taken off from work for the outpatients appointment were acceptable. Indeed, the inconvenience of extra visits to the clinic has previously been cited as a major negative factor in patients' participation in research (Henzlova, Blackburn, Bradley, & Rogers, 1994).

I mean there was a study they [the specialist centre staff] were going to do on, oh blimey, what was it? It took a couple of weeks to do, all to do with going for either urine or blood tests and, I can't remember. There was a thing up your nose, wasn't there? I did that, didn't I? It was all to do with gene therapy, it was, there was some tests on that, and I just, I mean, when I'm at work, I just couldn't do it. I've got too much of a demanding job, and they wanted me up there. It took I think about a month to do. The first week you went up three times in a week, the second week you went up twice, you know, and you were up there sort of for four hours at a time and I just couldn't do that. So there was just no choice. (Nicholas, 37)

Although Nicholas could not remember precisely what the research involved, his decision appeared to be based initially on the social constraint rather than the risks to health that GRT research could potentially involve. Involving partners or the wider family in decisions to participate in clinical research was a point that was made by many patients, especially those who had or were contemplating having children. Those who were trying for a child or considering undergoing fertility treatment frequently decided against participation in research at that time due to the unknown risks it could present to the foetus; in this instance social and health risks were considered together.

Health Constraints

The knowledge of already having outlived the survival age predicted for CF patients as a group and the likelihood of declining health state with increasing age was a significant health constraint on patients in their late twenties. The thought that something might 'go wrong' through participation in research projects and lead to damaging the health that they considered to be currently good and were so carefully controlling was enough to stop patients from participating:

That [participation in research] is my one big fear, that I have got this far [after liver transplantation] and I feel that I have never been so well in all the years that I, you know, and that is my one big fear. That something would go wrong, it wouldn't be right for me, and I would end up in worse health than I am now. (Anna, 31)

Modification of risk management over time appeared to be linked very closely to perceived health state. At some point in their illness trajectory, most likely when their health was controllable through the use of routine treatments, these patients started to filter out requests for help in research to exclude those that may be not only harmful to their health but also have no immediate health gain. Older patients (those in their late twenties and above) tended to say that now they were older they were 'more careful', only participating in research that they thought would not put their current health at risk. They were less likely therefore to participate in RCTs, preferring to participate in psycho-social research.

Partial health constraint was also apparent, in most cases through the possible local damage to the body that some research could inflict. At the time of her interview, Tina was awaiting a repeat lung transplant as she was chronically rejecting her first transplant. When asked if she always took part in clinical research of any kind she answered that she did not, as her 'vein' was invaluable in necessary, routine treatment:

I mean I do say no, I have lots of problems with my veins, so if they want to take lots of blood and put me in for trials that involves having blood, I have said no now because I've only got one vein left and it's really precious! [laughing] (Tina, 26)

Tina's perception of the risks of having blood taken are very different to those of the medical perception of slight bruising or discomfort, and Rose's habituated response to having bloods taken discussed above. For Tina, the implications of damage to a vein that she relied on to receive treatment for her declining health meant that the risk was too big to take.

Risk and Calculation

So far it has been shown that in some instances patients will participate in research without seeming to consciously weigh up the costs and benefits, yet in other cases social and health constraints play a large part in the decision to accept or decline research requests. In some situations patients have to calculate much more closely the costs and benefits of their actions. Calculation in risk behaviour involves a conscious deliberation of the costs and benefits of different courses of action (Bloor, 1995). Patients asked by the hospital to participate in RCTs that were testing new drugs such as Pulmozyme®, a nebulised drug used to improve lung function that was licensed for use in CF in 1994, appeared to use a carefully calculated approach to decision-making and risk management, as did those who had been approached to take part in GRT research. Here the risks to health were calculated much more frequently than social risks, although it was acknowledged that social benefits, for example being able to play sports with children or being able to work, would arise from any health benefits that arose. The factors that appeared to influence patients' careful calculation of the risks of their participation were the type of research patients were asked to participate in; the role of information in patients' decision-making; and the notion of participation in drug development as 'necessary' or 'unnecessary' for maintaining their health.

The role of information

A variety of sources were used by patients for information on medication and care, the CF Trust newsletters, other patients and the centre being the most common sources. Information about ongoing hospital research generally and its outcome, however, was much more difficult for patients to access:

But I find they [staff] don't tell you enough, it would be nice if they could say, "Oh, this is what's going to happen". I mean I don't know whether they know but if they said, "Oh, this drug's going to come out soon"...they seem very hush-hush. (Zara, 25)

Unless they had been approached by the hospital to take part in a particular piece of research, patients stated that they were not well informed about possible future treatments that were being investigated, especially noticeable in the number of patients who asked the researcher about the

progress of GRT research at the centre. As Featherstone states, 'the provision of information occurs within a social context, with trust and the quality of the doctor patient relationship important' (2003, p. 646). In the case of participation in drug development, patients also found out details from other patients who were already enrolled on the trials:

Mark: If they're [research drugs] unsafe you very quickly hear on the grapevine that there's a trial going round that you shouldn't do.

KL: What's the grapevine? The other patients?

Mark: Ah, just the grapevine.

KL: No, you've got to tell me! [Laughing]

Mark: [Laughing] You just hear. You do hear. It can be something overheard, it can be from a nurse, it can be from a doctor, it can be from other patients, it can be anything. You just, you do hear.

KL: You pick up bits here and there?

Mark: Yup. But also, I mean that doesn't mean to say you should necessarily not do it, you should listen first. And on the odd occasion that those sort of things would come along, I've always listened first, to see whether everything I'd heard was rubbish, or not.

Beck (1992) argues that today's increased risk consciousness comes in part from the greater relative importance of relevant news and reportage in the mass media, and it is this perception that makes people feel at risk. Some patients experienced this 'risk consciousness' from the CF Trust News

magazine, which influenced their decision to participate. For example, Catherine, aged 40, stated that she found out from the CF News that Pulmozyme® had already been granted a licence in America, and this played a significant part in her decision to participate in a British RCT as she then believed the new drug to be safe:

It was an easy decision because most of the research and everything else had been done, and it had already been licensed in America at that stage. So I thought, "Well, it's got to be alright, hasn't it?" (Catherine, 40)

As Catherine's quotation also shows, for some patients information regarding the stage of the RCT was also an important consideration. Clinical trials in their earlier phases were seen as possessing more risk than those that had been running for longer.

'Necessary' and 'unnecessary research participation'

For most patients, the necessity of scientists developing drugs to become part of their future routine treatment in order to improve or maintain health was a significant consideration in their decision to participate in research. This consideration strongly depended on patients' perception of their current and/or future health state. Calculation of the costs and benefits of participation in research projects tended to focus on the potential benefit to the patient of taking unlicensed drugs in their attempt to improve his or her failing health. Some patients stated that as their health became poorer their motivation for participation was to take part in a trial that was a 'safe bet' (for example the Pulmozyme® trials) in an attempt to improve or maintain their health.

Perhaps peculiarly to this group of patients, some individuals whose health could not be maintained by their current routine treatment would initiate contact with those at the centre who were conducting the trial to ask if they could participate, sometimes asking more than once. This again was particularly true of the Pulmozyme® trial. One respondent stated that he managed to be recruited onto the trial just months before he had his heart-lung transplant:

Cause I wanted to get on the Dnase [Pulmozyme®] trial so, 'cause you heard about, you heard about how good it was. I'd been fighting to get on that. Anyway I was either too ill or too well, each time it came up and that, so, er, but I eventually got on it, sort of for like one of the later trials.' (Oscar, 26)

By the very nature of drug development, patient volunteers are studied in the assessment of new drug therapy, from which they may or may not gain any direct or immediate health benefits. For those patients who perceived their health to be well controlled with current therapy, the observation of their participation in some research projects was that they were unnecessary to maintain their current health. Perceptions of current and anticipated future health state were used to calculate the 'necessity' of their participation in the research:

But drug, drug trials [pauses]. Again this is probably a bit dodgy to say but I take the attitude that when I'm a bit, if and when I get a lot worse then I'd probably be more open to trying new things. At the moment my quality of life and all the rest of it I regard as being sufficiently high that I don't want to jeopardise what I've got. I'm not sort of, "Oh my God, I'm really ill, I'll try anything". That period is a long way off for me. And that's, I mean I know it's not necessarily the right way but there's, you know, it's important to me to keep as well as possible, and I'm not going to mess that up. (Emma, 33)

In considering centre requests for participation in Pulmozyme® or GRT research, the substances under investigation were unlike anything patients had previously taken. Patients stated that they were therefore unable to compare the new substance against existing therapy. Furthermore, if patients saw the substance as unnecessary to maintain current good health they were freer to consider the risks of their participation, most notably the possible side effects of substances:

I think it's [GRT research] the one, one of the things I'd really want to know a lot about. And I think the side effect things would be much more in my mind with that than anything else that I'd ever been asked to do. I would certainly consider it [the request] very carefully. (Catherine, 40)

During their calculation of personal risk, patients stated that they were conscious of the possible benefits to others that would arise from their participation in such trials. However, in this decision-making, the potential benefits to others were perceived as secondary to the risks to the individual, and a bonus if they did then decide to participate. In some cases, the potential cost to the self outweighed any possible benefit to others, making the denial of possible benefit to fellow patients a difficult decision for patients to reach. Two patients who had refused to take part in drug development expressed feelings of selfishness and guilt; in Mike's case below, this was due to his reluctance to undergo a general anaesthetic as part of GRT research:

I was in two minds about it 'cause I said to [Senior nurse] when I was due to go on it, this was back in January, that I saw these guys up on the ward where their friend had sort of given up on life, if you like, and I said to [Senior nurse] I felt sort of quite guilty really, there's somebody like me, quite fit and healthy, probably, you know, a good candidate for a gene therapy trial, to refuse it and then you know, possibly affect somebody's chances in the future of being healthier than they are. (Mike, 33)

Of note, the risk was not always perceived to be in the trial substance itself (for example genetic material used in GRT trials), but rather in procedures surrounding the gathering of data (for example, undergoing a general anaesthetic so that researchers could obtain biopsies):

I think if the gene therapy trial had been similar [just nebulising a solution, seen as without risk] I'd have probably taken part in that. It was just the fact you know they, the going under the general anaesthetic and things like that I was a bit concerned about so that was probably the main reason I refused that one. (Mike, 33)

As Barofsky and Sugarbaker (1979) note, patients' refusal to participate in some research can be attributable to attitudes of aversion towards particular aspects of treatment.

In summary, calculation of risk occurred most often when a hospital request was made to participate in drug development or participate in GRT research. Drug development projects were seen by patients as necessary or unnecessary depending on patients' current health state and the efficacy of their routine treatment to maintain it. Here benefits and risks to the self were carefully considered and, especially in the context of GRT, often outweighed thoughts of benefit to others.

Risk and Volition

Bloor argues that the conception of risk taking as a volitional act is inappropriate where the risk situation involves more than one individual and where the risk is not taken from free choice. However, in the context of research undertaken by adults with CF, it is possible to consider volitional risk-taking when more than one individual is involved, although this may not hold true for other patient groups or indeed others with CF who never participate in research. Here, a favourable comparison of personal health to others with CF, and gratitude to those involved with CF and its treatment were identified as influential factors in the decision-making process.

Seventeen patients explicitly stated that their motivation for participation in some research projects was to 'help others'. More specifically, an additional seven patients stated that they wished to 'give back' to others as a form of repayment for the treatment and care that they themselves had received.

Many patients stated that they were in better health or experienced 'milder' disease than most of the other patients with CF that they saw at the centre. A perception of being 'lucky' with the state of their health to the present time was common amongst these patients (Lowton & Gabe, 2003); luck being set against a background of a firm positive attitude towards living with CF. This sense of being lucky with their health and fitter than most others was a consideration when 'giving back' to fellow patients.

People with CF closely defined the 'others' that might benefit from their participation in hospital research. The specialist centre was a recipient named by the majority of patients, and in these instances the patient was 'giving back' to the hospital and staff for the care already received:

I suppose it tends to give a little back, doesn't it? ... I think to myself, "Well, it is right that I get all the benefits that other people are helping to give me, without trying to give something back?" (Nicholas, 37)

Other beneficiaries of 'giving back' were fellow patients, usually perceived as being in worse health than themselves, who may benefit from the research results and past patients (those now dead) who had taken part in trials for drugs from which the patient was currently benefiting, for which participants paid their dues in recognition of what these people had effectively done for them. Future patients (children and those not yet born with CF) were also identified as those who would benefit from the treatments of the future, which the patients of today were helping to develop through their participation. No other beneficiaries of 'giving back', such as society in general or patients with other chronic disease, were named by any CF patient. This is in contrast to Gerhardt's (1996) work, where patients felt they were to 'give back' to society in general after their kidney transplant by achieving as much of a return to 'normality' as they could manage, in an attempt to show that they were worthy of the transplanted kidney.

Although consideration of the risks to self of research involvement came before consideration of potential benefits to others for the majority of patients, in cases where the focus of participation for the patient was on helping others, the benefits to self were secondary to the potential benefits to others. For some patients their advancing age or declining health state did not hinder their desire to help others through their participation in any kind of clinical research, as one respondent who was crippled with arthritis, noted:

But I have always been like that. Any research that comes along, I've always been there. I've always liked to think, well, that's going to help somebody else, not worried about meself so much, you know. I'm like that, I mean if it's going to help somebody else coming along, little infants, sort of thing, yeah, great stuff, all the better for them. No worries. (Brian, 32)

'Giving back' through participation was always spoken about in beneficial terms; not one patient considered that their taking part in clinical research might help to produce a drug that may have harmful long-term effects that would affect others taking it too. This may be partly explained by the patients' positive attitude to the disease and their refusal to think of long-term negative effects of drugs. However, it must be noted that these interviews took place before the death in September 1999 of the GRT research participant Jesse Gelsinger from Arizona, who suffered from ornithine transcarbamylase deficiency (OTC), an inherited liver complaint (Campbell, 1999); this may have a bearing on the data.

No patient here expressed that they ought to participate in research to ensure their good care in the future, or to be seen as a 'good patient'. However, Graham, aged 40, who at the time of his interview was considering assessment for lung transplant, stated that he had believed that his taking part in research at the centre was mandatory:

KL: Why did you do trials in the past?

Graham: Because I always thought it was necessary. I thought it was expected of you. Until somebody said, 'You don't have to do them.' So, fair enough, [he stopped participating].

KL: It was never explained to you that you didn't have to do them?

Graham: No, not really. No-one twisted your arm. I saw a doctor there and he was always getting me to do trials and I always used to say yes. And when he went the trials went away.'

Graham's quotation illustrates the unequal power relationship between Graham and the specialist centre staff that resulted in Graham's felt obligation. Research Governance for Health and Social Care (2001) states that researchers must stress to the patient that he or she is under no obligation to participate, something that did not appear to have happened in this case.

Discussion

Patients were discriminate in deciding which research projects they participated in, despite often being unable to recall precisely the nature, aims and methods of research studies, highlighting the importance of contextual factors in risk management. In the present study, there were many common factors that influenced patients' decision to participate in research and clinical trials. Increasing age, failing health, and social considerations such as family and work pressures influenced patients to constrain their risk-taking behaviours, similar to previous findings (Moss et al., 2004; Ross et al., 1999). Habituated risk behaviour did not only occur through a repetition of circumstances but also through a basic trust in those requesting the patients' participation; this may be particularly relevant to patients with chronic illness. Knowledge of their health state, current and future potential therapy, the stage of the trial and procedures surrounding it appeared to be all-important considerations in calculating the risks of taking part in research. A sense of obligation to past, current and patients and the hospital underpinned many patients' motivations to participate.

The paper has considered data from patients who had actually participated in previous research projects. It is likely that patients attending a specialist centre would be asked more often than those attending a local hospital to be asked to participate in research programmes. However, this study did not include the patients who never participated in research or who filtered out projects of a psychosocial nature; in this respect the findings are biased towards those who did participate in clinical research to some extent. We do not know whether those who decide never to participate in clinical research are likely to consider the risks of participation more carefully, or indeed whether there is a group who consistently refuse every request. Certainly at the time of the interviews there was a great deal of optimism for genetic treatments generally in the mass media (Henderson, 1998) and this may have had an influence on patients' views of participation in research. An established patient 'grapevine', ease of interacting with staff, networking with other patients and understanding of the stages of clinical trials suggests a highly knowledgeable and medicalised group, and as such findings may not be generalisable to others with chronic illness, although parallels may be drawn with some sections of the community living with HIV/AIDS.

As Grinyer (1995) has found, risk perceptions are multi-dimensional, people managing different agendas that may conflict with official ones. Doctors as investigators have a duty to protect patients both from harm and undue risk (Weijer & Fuks, 1994). However, it was noted in the current study that the role of modification of risk in selecting projects for participation was actively undertaken by patients themselves, for instance in choosing to only participate in RCTs that were in their later stages or relying on mediated information in deciding to take part.

Most previous work has considered factors for consent or refusal in context of one clinical trial; however, patients with chronic conditions are likely to be exposed to many requests over their lifetime and may not always be consistent participators or refusers. Reasons for participation and non-participation found here are broadly similar to those that others have found; self interest (knowledge or to improve or stabilise health), altruistic reasons (Fry & Dwyer, 2001; Madsen et al., 2002), and for the health benefits of taking new drugs (Gammelgaard et al., 2004; Madsen et al., 2002; Wilcox & Schroer, 1994). The motivation to participate in order to be treated by experts (Gammelgaard et al., 2004) was not found, most likely because patients were already attending a specialist centre.

Most previous work on patients' participation in research has focused on RCTs; here the inclusion of all types of hospital research has meant that patients' motivations could be contextualised and analysed more fully using Bloor's (1995) framework for understanding risk perception and management. Although specific reasons are important to understand why patients choose to participate in research, looking more widely at social and health constraints may be more beneficial to researchers when planning successful research protocols. However, Bloor does not emphasise issues of power and trust in risk management; it has been shown here that these are important factors to consider patients participating in hospital research at a specialist centre.

Declining to participate may be the most common reason for non-participation in clinical trials (Gross, Mallory, Heiat, & Krumholz, 2002), yet the reasons for non-participations are complex. Bloor asserts that risk-taking may follow less from learned orientations, i.e. Douglas's (1982) use of the group/grid approach to risk, than from strategic relationships in risk situations. Although the relevances may be oppositions in theory, here they are not considered oppositionally in practice. Rather they are

dependent on the social and health contexts of the research programme and the structure and power relations surrounding the research projects. These findings lend support to Fry and Dwyer's argument against uni-dimensional constructs of participant motivation; that 'research participants may be motivated by a diverse number of benefits to both themselves and others' (2001, p. 1323).

Patients' social context is a very important, yet often neglected, consideration in planning and executing research. By focusing on patients' perspectives of decisions to participate, rather than clinical researchers' perspectives, a better understanding of the influences on patients' decisions to participate or decline participation in clinical research can be gained. This is required so that research programmes can be designed to recruit patients who are constrained by social commitments such as employment or family responsibilities in order to increase response and lower attrition rates, whilst protecting those that are vulnerable to such requests.

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