

Participating in the United Kingdom Prospective Diabetes Study (UKPDS): a qualitative study of patients' experiences

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SUMMARY

The United Kingdom Prospective Diabetes Study (UKPDS) is one of the longest and largest clinical trials ever conducted. It explored the effects of intensive blood glucose and blood pressure control on the development of complications in patients with type 2 diabetes. Patients took part in this trial for up to 20 years and the drop-out rate was extremely low. The aim of this discussion paper is to explore patients' motivations for joining the UKPDS and for remaining in the trial, and to examine the implications of findings for good practice before, during, and after clinical trials.

A qualitative, exploratory study was undertaken, involving former UKPDS patients (n = 10) at Northampton General Hospital, England. In-depth, semi-structured interviews were undertaken and the data analysed using grounded theory approaches.

The results showed that patients were motivated to join the UKPDS because they believed this would give them the best clinical care and reduce the threat of the disease. However, all of the patients identified unanticipated benefits of trial participation, to which they attributed their strong commitment to the UKPDS. These included the reassurance provided by regular clinical examinations, the personal nature of clinical care, and the welcome discipline imposed by UKPDS professionals. Transition back to primary care at trial closure could be a lonely experience, despite follow-up being seen as competent.

Practitioners involved in recruiting patients for clinical trials should be aware that participants may be motivated by the desire for better clinical care, irrespective of randomisation consequences. Those taking back the clinical care of trial participants with chronic disease may wish to consider a 're-entry' interview, to minimise trial bereavement.

Keywords: *United Kingdom Prospective Diabetes Study (UKPDS); type 2 diabetes; clinical trial participants; qualitative research; patients' perspectives.*

Introduction

THE United Kingdom Prospective Diabetes Study (UKPDS) commenced in 1977, lasted over 20 years and involved 5102 patients in 23 centres. It was one of the largest and longest clinical trials ever conducted. Newly diagnosed patients were referred to the UKPDS by their general practitioners (GPs). The primary aim of the study was to determine the impact of intensive blood glucose control on the development of complications in patients with type 2 diabetes. This was achieved through the random allocation of patients aged between 25 and 65 years to either an intensive management policy (involving dietary advice plus sulphonylurea, insulin or metformin), or a conventional treatment policy based on dietary management.¹ In 1991 the trial was broadened to investigate the impact of intensive blood pressure control through the randomisation of consenting patients to groups receiving tight or less tight blood pressure control.² Throughout the trial, patients received all their diabetes care in UKPDS centres. Following its completion in 1997, patients' routine diabetes care was transferred to their GPs or other National Health Service (NHS) clinics.

The trial's demands were substantial, patients being required to attend study clinics at least every three to four months in order for control criteria to be monitored and/or attained. In addition, at trial entry and at intervals of three years afterwards, patients were subjected to a rigorous clinical examination, which included examination of the eyes and the autonomic and peripheral nervous systems, as well as the cardiovascular system, and assessment of renal function. To achieve the targets of glucose and blood pressure control, many patients were eventually required to take four or five different drugs for blood glucose and blood pressure management.³

Until now, attention has focused upon the importance of the UKPDS's findings for clinical practice,^{3,4} namely that improved glucose and blood pressure control reduce diabetic complications.^{4,6} However, the UKPDS was a success in another regard. Despite the demands placed on patients, attrition rates were extremely low. An estimated 2.4% of patients withdrew for reasons other than migration, ill health or death, whereas in other clinical trials, which were of significantly shorter duration, drop-out rates of between 24%⁷ and 67%⁸ are often reported. Owing to its intensive requirements and long duration, the UKPDS presents an opportunity to explore patients' underlying motives for participating and remaining in a clinical trial, and their experiences at study end, to inform future practice.

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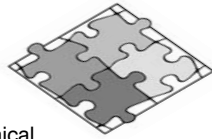
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HOW THIS FITS IN*What do we know?*

Surprisingly little is known about why individuals participate and remain in clinical trials, or what happens to them when the trial ends.

What does this paper add?

This qualitative enquiry among participants in the United Kingdom Prospective Diabetes Study (UKPDS) shows that an important reason for trial participation and loyalty is receipt of good, structured personal health care, and that loss of relationships with research staff can be a significant bereavement at the trial end. Those recruiting for trials should draw the attention of participants focused on clinical care alone to the possible harms and benefits consequent upon randomisation, and practitioners caring for those discharged from trials should consider their special needs on 're-entry' to primary care.

**Method**

A comprehensive literature search was undertaken using MEDLINE and the Web of Science, which identified many studies that have explored attitudes towards clinical trial participation, but these had limited relevance to this study. None had examined patients' views of participating in a trial of comparable duration to the UKPDS. Many used hypothetical trial scenarios, which are not directly relevant to actual participation in real trials.⁹⁻¹⁰ The majority used questionnaires, which typically restrict responses within a predetermined framework, and only give a poor indication of what responders actually consider to be the most salient issues.¹⁰

A qualitative design was then chosen, as this research was necessarily exploratory. This allowed themes to be identified and tested during the study, rather than simply assessing those formulated before data collection.¹¹ An interview topic guide was designed in which participants were invited to talk about their experiences; for example, why they had agreed to join the trial, what they had anticipated their participation would mean to themselves and others, whether they had wanted to withdraw, and how they had felt when the trial ended. This approach allowed participants to raise issues that they perceived as salient, thereby minimising the possibility of their responses being framed by any preconceived notions held by the research team.

Further flexibility was achieved through an emergent design informed by grounded theory research.¹² Data collection and analysis occurred concurrently, and systematic efforts were made to check and refine developing categories of data. Analysis continued after data collection, when individual transcripts were repeatedly re-examined and cross-compared using manual, iterative methods.

Recruitment and interviews

Patients were recruited from Northampton General Hospital, one of the UKPDS participating centres. All patients scheduled to attend an annual post-study monitoring appointment between August and September 2000 were sent information about the study together with an invitation to be interviewed

by an independent researcher. Patients were informed that participation was strictly voluntary and that all information shared would be treated in confidence.

All interviews were conducted immediately after patients' post-study monitoring appointments. Written (witnessed) consent was obtained prior to the interview. Patients were also asked to provide information that included their age, (previous) occupation, and year of recruitment to the UKPDS. Interviews lasted between 25 and 50 minutes, they were audiotaped and then professionally transcribed.

Results

All patients who were approached ($n = 10$) consented to take part (Table 1). The issues that they raised were strikingly homogenous. Several themes emerged repeatedly within and between transcripts, indicating that theme saturation had occurred in some areas.¹²⁻¹³

Why did patients agree to participate in the UKPDS?

'And I said, "well, as long as you look after me, I will help you."' [Female 3.]

'I joined because I thought I'd get better treatment, rather than necessarily because I'd be helping other people.' [Female 2.]

Despite the long period of time since patients joined the UKPDS, all but one claimed to remember the factors that had led them to agree to become trial participants. These patients described their decision as being very straightforward and as having been influenced by the broader historical context. There was a general perception that at the time they were invited to take part their GPs did not have the necessary training and resources to provide specialist diabetes care in their own practices. Several patients also described how their confidence in their GPs had been undermined by their failure to diagnose their diabetes immediately when they first presented with symptoms. Consequently, patients welcomed the opportunity to join the UKPDS because they believed this would enable them to receive 'the most up-to-date, state-of-the-art care' (Male 5) from professionals with a specialist expertise in diabetes:

'Everybody, I think, who decided to come here, recognised how well up they were on the programmes at the time, you know. They seemed to know a lot, so I was happy to be under them.' [Male 2.]

Although a few patients also suggested that altruism had been a consideration, this did not feature prominently in the interviews.

Costs and benefits of participation***Practical problems***

Patients described a number of practical problems that they had not fully anticipated when they consented to take part in the UKPDS. To enable fasting blood samples to be taken,

Table 1. Characteristics of participating patients.

	Age in years (mean = 68)	Social class ^a	Number of years in the UKPDS
Male 1	62	IV/V	10
Male 2	69	IIIM	14
Male 3	78	IV/V	15
Male 4	74	IV/V	16
Male 5	65	IV/V	17
Male 6	64	IV/V	13
Female 1	76	IV/V	14
Female 2	52	IV/V	12
Female 3	71	IV/V	16
Female 4	73	IV/V	11

^aSocial class was assessed using the Registrar General's social class method.

patients had to attend early morning appointments. Therefore, they had to travel to appointments in rush hour traffic, a particular problem for those who lived far from the hospital. A number described the frustrations of being unable to find a car parking space on their arrival. The long duration of the clinic appointments (sometimes lasting the whole morning) also created difficulties, especially for those in full-time employment.

The clinical examination and peace of mind

Patients spoke of their experiences of receiving regular, comprehensive clinical tests in uniformly positive ways. Far from being seen as an intrusive, albeit necessary part of trial participation, patients regarded the clinical examinations as constituting a major benefit. Several likened the clinical examinations to a regular 'MOT' (an annual Ministry of Transport roadworthiness test for road vehicles in Great Britain). The opportunity to receive regular clinical monitoring had provided the peace of mind of knowing that they were healthy or, if a secondary complication had emerged, that it would have been identified and acted upon immediately:

'And you had all these different tests and things done on your heart and everything, and you knew that you were, you know, everything was alright sort of thing.' [Female 1.]

'When I was on the study, I knew I was healthy. If something was wrong, I'm sure the X-rays and everything would have picked it up, if something was up.' [Male 1.]

'Also, you're — how can I put it? You felt happy because the tests that you've had made you feel that you wouldn't have had them if you didn't come to the centre. You wouldn't have had an MOT every three or four months. It does give you a lovely cushion to know that, whatever, they are going to pick something up, even if it's not diabetic related, which I found very good.' [Female 2.]

The importance patients attached to regular diabetic check-ups becomes particularly meaningful when the concerns raised in other parts of their interviews are taken into account. Many voiced fears of the future, stemming from their experiences of witnessing unpleasant and distressing

diabetic complications in others:

'I've seen a mate lose his leg, he had to have it cut off. That put the fear into me, you know? That could happen to me as well.' [Male 3.]

'I mean I've had one of my friends, he died. He went blind and just gave up and died, and he was only 40-odd. And my brother, you know, he died of it too. So, I've had a bit of heartache.' [Male 6.]

Indeed, several used a 'time bomb' metaphor to describe their current state, thereby drawing attention to an omnipresent concern of dying in an unpleasant and dramatic way. Such concerns are often shared by patients with other life-threatening diseases, such as cancer and coronary heart disease, for whom the opportunity to receive regular medical check-ups is, likewise, a welcome aspect of trial participation.¹⁴⁻¹⁵

Being a 'special patient'

Many patients also believed that they received a more personal form of care as a consequence of trial participation. In their opinion, this was made possible by high levels of staff continuity, and by the fact that UKPDS staff did not appear to have to operate within the same tight time constraints as GPs and other medical practitioners. Several patients likened the UKPDS clinics to a 'safe haven' or a pseudo-surrogate family. They described how the clinics provided a safe space in which to share concerns with professionals who had time to listen, and in whom they had developed trust over many years. This experience was particularly valued by those who felt unable to share their worries with their families and/or did not wish to burden their seemingly over-stretched GPs:

'Everyone seemed so kind type of thing. And I'll always remember that part of it, you know. They made you feel like a member of a family ... they've been my shoulder to cry on.' [Male 4.]

'Because they took time ... they spent time with you. You felt like you were being looked after: you're not a number, you're a person. And sometimes you do feel that you're perhaps just a number.' [Female 4.]

'Basically, you sit in the doctor's [general practice surgery] and you can wait for ages. He's a bit late, he hasn't got time. It's not his fault. He's got too many patients.' [Female 1.]

Several patients discussed the notion of reciprocity. The fact that they had given their time and commitment to the trial, in their opinion, had given them the *right* to ask staff for practical and emotional support. Importantly, these patients alluded to the possibility that they would not have raised concerns or sought advice so promptly had they been under their own GPs for their diabetes care at the time.

Discipline

In order to achieve the trial's targets, UKPDS staff had to adopt a directive approach with patients. All patients indicated that they had appreciated this approach:

'Whereas here [the UKPDS clinic], they would say, "you should do so-and-so", or whatever, there, on the whole, I have to tell them if I want to know something, or if I am not happy with things. So, yes, I miss the discipline ... If you've got a problem, you tell her [the specialist diabetes nurse in the general practice clinic], rather than she says, "I think you should do so-and-so or you should see so and so".' [Female 2.]

'I'm not criticising doctors, the local GPs or anything like that, because they haven't got time to devote purely to diabetes. But the problem is that it puts a lot more onus onto the individual, i.e. myself, to control it much better, do the checks and everything else.' [Male 1.]

Several of them drew attention to the complex nature of the disease management process. This, combined with their fears of developing complications, had led them to value the input of UKPDS professionals who could 'do the thinking, planning and worrying for [them]' (Female 1).

Patients' preference for a passive role in treatment decision making was also indicated in another key finding. Despite the results of the UKPDS being made available to them (they were all sent a letter informing them of the findings), none had attempted to find out which arms of the trial they had been in.

Trial closure: the loss of the safety net

Unsurprisingly, patients were disappointed when the UKPDS ended. Reactions to the news of the trial closure were described as follows: 'It was a bit of a blow'; 'In a way I suppose I was a bit anxious'; 'I felt as though I was losing friends here'.

In practice, the effects of coming out of the trial had not been as traumatic as patients had anticipated. Most were attending annual appointments at their general practice clinics, some with their doctors, others with a diabetes specialist nurse. They all rated the knowledge and competence of these professionals highly, thereby adding resonance to Murphy *et al's* finding that modern general practice constitutes a welcome environment for routine diabetes care.¹⁶ Nonetheless, a sense of loss and isolation was still apparent. Several patients described feeling alone with their diabetes, an experience brought about by having less structured and frequent contact with medical professionals:

'I think they [GPs] seem to tend to, you know forget you, if you don't come. If you know what I mean, and you let yourself go.' [Male 6.]

'But they don't ring you, you know. You know, the GPs. You've got to ring them. It's true, isn't it?' [Female 3.]

Indeed, the majority volunteered that they would have no

hesitations joining another clinical trial as long as it provided the same contact with professionals as they had received during the UKPDS.

Discussion

Summary of main findings

Patients were motivated to join the UKPDS because they believed this would enable them to receive the best clinical care. However, all of them identified unanticipated benefits of trial participation, which they used to explain why they had remained in the trial despite its intensive demands. Key elements relating to retention included the personal nature of care offered and the reassurance associated with regular monitoring and directive advice from respected experts. Patients experienced a sense of bereavement at trial closure, despite follow-up being seen as competent.

Strengths and limitations of the study

In-depth interviews provided an effective means of capturing patients' perspectives without drawing on a framework predetermined by professional perspectives. While the sample size is small, the homogeneity of the participants' responses suggests the occurrence of theme saturation. It was therefore deemed justifiable to report the findings despite this limitation. The participants were all patients who had completed the study, but the perspectives of those who dropped out would also have been valuable in assessing trial generalisability. The results may be applicable only to those who enjoy frequent surveillance and intensive clinical support. We also acknowledge the limitations of working in only one centre, and with participants entering a trial a quarter of a century ago. Nonetheless, we believe these findings can still inform current debates, especially since the participants' demographic characteristics are roughly representative of those who take part in clinical trials — a willingness to participate in clinical trials is associated with being older, less educated, and from a lower socioeconomic group.¹⁷

Implications for clinical and research practice

The finding that patients entered the trial because they believed this would enable them to receive better clinical care concurs with Edwards *et al's* observation that self-interest is a more common reason for trial participation than altruism.¹⁰ While patients theoretically have nothing to gain personally from involving themselves in clinical trials, apart from a possible short-term 'trial effect';¹⁸⁻¹⁹ the participants spoke of real and long-lasting practical and emotional benefits of involvement. These overshadowed the trial itself so much that none spoke of the arm of the trial to which they had been randomised, despite clear results favouring one arm having been published.¹⁻² Practitioners involved in recruiting for clinical trials should be aware of this, and ensure that patients also reflect on the potential harms and benefits of the interventions themselves.

It is well established that logistical factors, such as ease of access to services, can have a major influence on patients' preferences for services and the likelihood of their attending appointments.^{16,20} Despite considerable logistical difficulties, UKPDS participants rarely dropped out of the trial. This sug-

gests that the benefits of trial participation outweighed the costs. Importantly, many of the benefits identified by patients had not been anticipated when they agreed to join the trial. These issues should be addressed in the conduct of future trials.

While preferences for directive care stand in opposition to the developing ethos within biomedicine that patients want, and should be actively encouraged, to take an active role in medical decision making,²¹ the demographic characteristics of the participants must be borne in mind. As some commentators have observed, older patients, especially those from lower socioeconomic groups, often prefer a more directive style than their younger counterparts.²²⁻²³

The need for a balance between a counselling and directive approach in the management of chronic disease is argued across the literature.^{22,24} Coulter, for example, has highlighted the importance of finding ways of offering involvement that do not place an unwanted burden on sick people, and older people in particular, who may not wish to adopt an active role in decision making.²² Interestingly, trial involvement gave some of the participants a more assertive voice, their commitment to the trial empowering them to ask staff for practical and emotional support which they felt the NHS was otherwise too hard pressed to offer.

Since participants value the clinical environment of a well-run trial so highly, researchers and clinicians have a responsibility to remember the level of trust placed in them by trial participants, and regularly question the presence of equipoise that may underlie the advice offered to different groups.

The finding that patients experienced bereavement on trial closure should inform the transitional care of such patients. Trial participants often have an 'exit interview' with trial clinicians, but how often do primary care professionals offer them a 're-entry' interview? The National Service Framework for Diabetes will recommend that outcomes are better where all patients are informed of local services and are regularly called for clinical monitoring and review.²⁵⁻²⁷ Our findings indicate that trial participants returning to practice care should perhaps be treated like new patients in this respect.

The development of research governance in clinical practice will demand that those leading or collaborating in trials should ensure that issues of informed consent and ethical approval are systematically addressed. The voices of the participants from one of the largest, longest clinical trials raise important questions about the extent to which perceived current clinical benefits and trust in experts should sway informed consent and continuing trial participation, and how best to manage these perceptions at trial closure.

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