Do informed consent documents for cancer trials do what they should? A study of manifest and latent functions

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Abstract

Though Patient Information Leaflets (PIL) are provided to those invited to take part in medical research, they usually fall short in facilitating informed decisions about participation. We aimed to explore why there is an enduring requirement for a process that seems not to “work”, and to explain why the problems have proven resistant to correction. We analysed applications for ethical approval for 13 oncology trials, and related official guidance. We interviewed 26 patients invited to participate in the trials. Data analysis was based on the constant comparative method.

We show that PILs function latently to satisfy purposes other than their manifest function as a decision-facilitating tool. PILs are the outcome of a process of institutional scripting that is strongly shaped by the accountability demands inherent in the ethical review process. This results in the PIL being made to serve purposes both as a prospectus and as a contract.

Though PILs have value for some patients, most do not recognise these documents as operating primarily in their interests. Patients make decisions in ways that deviate from official ideals. This analysis is important in recognising that no simple technical fix is available, and in enhancing sociological understanding of the institutional role of documents.

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Introduction

Providing informed consent documents to candidates for research participation is a long-established practice, intended to satisfy legal and ethical requirements to respect participants’ autonomy and protect them from harm by supporting them in making an informed choice (Jefford and Moore, 2008; Beauchamp and Childress, 1994). In R.K. Merton’s (1968) terms, the manifest (or intended) function of Participant Information Leaflets (PILs) is to serve these requirements. Most studies of PILs to date have, unsurprisingly, focused on the extent to which participants are “informed”. Such studies have sought, for example, to determine how far people given a PIL are able to fulfil official desiderata relating to adequacy of understanding, or to determine the “readability” of PILs using various formulae. This body of work has consistently found: that research participants do not always read PILs (Sharp, 2004); that PILs are written in ways that make them hard for people to understand (Grossman et al, 1994; Cox, 2002); and that research participants generally demonstrate poor understanding of study information, especially features of study design such as randomisation (Robinson et al, 2004). These problems are usually characterized as technical ones, to be resolved by better applying principles of plain writing (Dixon-Woods, 2001). Yet exhortations to improve PILs seem to be largely in vain, judging by current studies, which, well into the 21st century, continue to report poor “readability” and understanding of studies by participants (Buccini et al, 2010; Hereu et al, 2010).

This raises interesting sociological questions both about why there is an enduring requirement (e.g. NRES, 2011) for an instrument (the PIL) that apparently fails to deliver on its manifest function, and why the problem has proven so stubborn. These are the questions we seek to answer in this paper. Drawing on an unusual dataset comprising applications by researchers for ethical approval, Research Ethics Committee (REC) correspondence, and patient interviews, we offer an examination of PILs from their development and ethical review stages through to their reception by patients. As part of our analysis, we suggest that attention to the latent functions (Merton, 1968) of the PIL helps to explain why readability and understanding challenges seem quite so remarkably resistant to correction, and why, even though they often poorly perform their manifest functions and neglect to address patients’ own priorities for communication and decision-making, the PIL remains institutionalized as an indispensible element of research practice.

Methods

This project was designed to have two parts. First, we analysed written documentation from 13 applications by triallists for REC approval to conduct 13 trials (covering Phase I, II and III trials)
in oncology. The trials (Box 1) were all being undertaken by a trials unit in a large teaching
hospital, although all were wider, multi-centre trials. The trials were purposively selected to
cover a wide range of trial characteristics, including: Phase I-III; solid tumours and
haematological; trials using novel agents, immunotherapy, surgery and cytotoxics; and
commercial/investigator-led. Second, we conducted semi-structured interviews with 26 patients
with cancer who had been invited to participate in any of these trials.

[INSERT BOX 1 HERE]

Documentation relating to applications to RECs for approval of cancer
trials

The first part of our analysis focuses on how the structure and content of the PILs in our study
was shaped both by national guidance and by exchanges between the REC and the triallists.
The REC approval process involves submission by triallists of an application using a
standardized form and accompanying documentation, including PILs. Templates for PILs and
guidance on how to prepare an appropriate submission are provided by the national research
ethics service (NRES, 2011). The REC reviews each application, and may then issue a
favourable opinion (meaning that the trial is approved without any modifications), or, much more
frequently, issue a provisional opinion, meaning that amendments or clarifications from the
triallists are required before a final opinion can be produced. A small minority of applications
receive an unfavourable opinion, which effectively means that ethical approval is denied.

We obtained the written documentation accompanying the 13 cancer trial applications to seven
RECs as follows:

(i) the REC application form (13 trials), as submitted for REC review;
(ii) the “provisional” opinion letter from the REC to the researcher (12 letters, as one
received an immediate favourable opinion and therefore did not generate a provisional
opinion);
(iii) the researchers’ response to the provisional opinion letter. Eleven responses were
available for analysis as (a) the trial that received a favourable opinion on first review
required no further response and (b) the researchers’ response was not available for
another trial in which no changes to the PIL were requested;
(iv) the final favourable opinion decision letter (13 trials);
(v) the final PIL (13 trials).

We also reviewed official guidance on producing PILs. The core content of the guidance has
changed very little over time. The earliest applying to the trials that we have been able to
access was published by COREC (2004), and we have therefore referenced this throughout our
analysis. Later UK guidance (e.g. NRES, 2011) has been published by NRES (the National Research Ethics Committee and successor to COREC) and we have referenced this where appropriate.

To code text from REC letters, we drew on a structured coding frame developed in our previous projects (Angell et al, 2007). Other documents were analysed using a combination of ethnographic content analysis (Altheide, 2004) and discourse analysis (Potter, 1997). In order to provide a comparison with earlier studies, we also calculated the mean number of words and the Gunning Fog Index (a commonly used measure of “readability”) for each PIL.

Interviews with patients invited to participate in trials

Twenty-six semi-structured interviews were carried out with adult cancer patients who had been invited to participate in any of the 13 trials (Table 1). Contrary to our usual preferred practice, we refer to those interviewed as “patients” in order to avert confusion over their trial participation status.

Interviews were conducted by a non-clinical researcher (GR) who was independent of the 13 trials. Potential interviewees were identified by a hospital consultant using purposive sampling criteria designed to ensure a spread of trial types, decisions made by trial candidates, and socio-economic status. Patients were approached either by the consultant or by a trials nurse, and were asked to return a reply slip by post if willing to be contacted about an interview. Interviews were conducted within three months of the initial clinical trial approach, and took place either at the patient’s home or in a private room at the hospital. We included those who had decided to participate in a trial (“participants”), as well as patients who did not participate either because a) they declined (“decliners”) or b) they were excluded from the trial following further assessment of clinical suitability (“ineligible”). All interviews were audio-recorded and transcribed in full.

A semi-structured topic guide for the interviews was developed following a literature review and discussions within the project team. It sought patients’ views on the clarity, layout and accessibility of the written information, opportunities for discussion of the information provided, understanding of research design concepts (such as randomisation), perceived risks and benefits of trial participation, decision-making about trial participation, and general attitudes to research.

A systematic and iterative approach to analysis of the interview data based on the constant comparative method (Glaser and Strauss, 1967) was adopted. A selection of transcripts was open-coded, and key themes within the data identified through repeated close readings and review of open codes. A coding framework was developed and refined, and subsequently
applied to the full data set. Individual transcripts were compared and contrasted, and deviant cases identified and explored. QSR NVivo software was used to aid the coding, management and retrieval of data. We sought to explore analytically the shaping of the PIL in the REC review process, the multiple functions of the PIL as it goes through the process of development and use, and the meaning of the PIL to the patients as the ‘end users’ of these documents.

The interview study was given a favourable opinion by an NHS Research Ethics Committee. The analysis of the written documentation from the 13 trials was classified as service evaluation and therefore did not require REC approval.

Findings

Tracking the PIL as it moves through the ethical review process, from official guidance through to submissions to RECs, negotiations between triallists and RECs, and then on to patients as end-users, allowed analysis of the different social functions played by the PIL as it circulates between intersecting social worlds (Star and Griesemer, 1989; Clarke, 2005). The PIL is constructed, and its structure and content fixed, at the boundary between one pair of worlds (triallist and REC), and is used in those social worlds to assure conformity with standards of ethical practice, demonstrate accountability and protect against institutional risk. Yet it is delivered and consumed at the boundary between another pair (clinician and patient), where the priorities may be quite different.

Institutional scripting and the role played by the “backstage” author

The PIL is the only aspect of triallists’ communication with a potential trial candidate that the REC can directly monitor, and thus is a natural focus of attention for a body charged officially with ensuring that appropriate information is provided to patients. The PIL is also, crucially, an official record of what the REC has authorised as fulfilling the requirement that patients be given adequate information. The practical effect of these arrangements is that two of the important latent functions (Merton, 1968) of the PIL are: a) as a device for allowing scrutiny and supervision of researchers by RECs (fulfilling the duties with which they are charged; and b) as a device for enabling the REC to display its own diligence, since it has to be accountable for what it authorises. A further latent function of the PIL, for both parties, is to afford institutional protection by demonstrating that official requirements have been met. The specific form that any PIL takes is thus the result of a ritual enacted between the triallists and the REC that is “recognizable and therefore sanctioned” (Iedema and Wodak, 1999).

The final PIL for each trial is, we propose, the outcome of a “backstage” process that we term institutional scripting, which is itself strongly structured by the demands of accountability (O’Reilly et al, 2009a) implicit in the ethical review process. In Garfinkel’s terms:
Any setting organizes its activities to make its properties as an organized environment of practical activities detectable, countable, recordable, tell-a-story aboutable, analyzable – in short, accountable. (Garfinkel, 1967:33)

One of the strongest influences on the scripting process is the official guidance on how information sheets should be produced. The guidance prescribes and codifies institutionalized expectations of practice, and provides strong cues as to the legitimate claims that can be made in the PIL. Among the requirements identified by the guidance is the PIL’s role as a prospectus: to act as an invitation to participate, and provide easily understood information:

Information Sheets should be written in simple, non-technical terms and be easily understood by a lay person. Use short words, sentences and paragraphs with clear subheadings to make the text manageable, and a font size for easy reading […] The tone should be invitational and not coercive or overly persuasive. (COREC, 2004:p1)

The PIL is constructed, in official guidance, as providing the basis of the patient’s decision to take part, and thus for their ‘informed’ consent. The guidance states that the PIL should lay out explicitly what the patient can expect, including a clear statement of what it is that patients are authorizing by consenting to participate, and an explanation of what the patient will be asked to do and contribute to the research. It sets out the format the information sheet should assume, including sample questions written as though they had been posed by a prospective trial candidate (e.g. What is the purpose of the study?, What will happen to me if I take part? and What do I have to do?). It also supplies suggested or ‘suitable example’ texts for use in addressing such questions. Thus, for instance, the guidance provides a ‘suitable example’ introductory paragraph for the PIL to: explain that the reader is being invited to take part in a research study; emphasise that it is important that the reader understands what is being done and what it will involve; invite questions if anything is not clear; and suggest that the reader take time to decide. The decision-making process is thus represented as a rational, reasoned one involving detailed consideration of information.

The prospectus is not, however, the only role played by the PIL. It also functions as a contract, laying out the terms and conditions that will govern the patient’s participation, including such contractual matters as data protection procedures and details of insurance/indemnity schemes. It suggests, for example, that a statement along the following lines be included in the PIL:

E.g. ‘In the event that something does go wrong and you are harmed during the research study there are no special compensation arrangements. If you are harmed and this is due to someone’s negligence then you may have grounds for a legal action for compensation against (name) but you may have to pay your legal costs. The normal
National Health Service complaints mechanisms will still be available to you (if appropriate).’ (COREC, 2004: p7)

Three important consequences of the official guidance follow. First, the guidance orders the relationship between triallists and patients as one with contractual status: the PIL is of legal significance in forming the basis of the deal between the parties. Second, by making evaluable major areas of the triallists’ conduct, it shapes the accountability of both RECs (as the oversight agency) and triallists themselves. It thus functions latently to prescribe the social roles and identities of the parties engaged in the ethical review process and to direct attention to these evaluable areas of practice. Third, it allows the guidance to operate as a form of author. The guidance exists prior to every project, every researcher, and every REC meeting; it is the backstage of the scripting process. It structures the PIL by guiding the triallist about what to prepare and the REC about what to expect as a satisfactory demonstration of fulfilment of the official requirements.

“The hands-on” authors and the production of accountability

If the official guidance acts as a “backstage” author of the information sheet, then the individual REC and the researcher are the “hands-on” authors of the individual PIL for each trial. For the triallists, the PIL is an opportunity to display a commitment to ethical practice. For the RECs, review of the PIL allows not only an examination of the extent to which the material conforms to expectations of ethical practice, but also an opportunity to demonstrate RECs’ diligence and defence of trial participants’ interests.

Triallists applying for ethical approval all included statements that highlighted their intentions to comply with the relevant guidance in relation to the PIL. These statements can be seen as a way of making visible their performance of ethical competence by conforming to the procedural norms governing the process.

The expectations and visits for the study are clearly indicated in the patient information sheet to allow the patients to consider this before entering the study. (Trial 9, REC form)

Triallists also stick very closely to the recommended script in their bid to demonstrate ethical practice and accountability; all final versions of the 13 PILs that we examined used the suggested text from their official guidance either verbatim (Trials 1, 2, 7, 8 & 10) or in a slightly modified form (Trials 3, 4, 5, 6, 9, 11, 12 & 13).

“You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you
wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.”

“Rational” understandings of participant decision-making also repeatedly surface in triallists’ descriptions of their recruitment processes in their REC application form.

The patients will return to site for the appointment with the investigator. They will be given the opportunity to ask any questions, and to go away and think about the study again if they need to. (Trial 9, REC form)

If interested in participation, the patient will be advised to read all the information on the patient information sheet carefully. […] They will be asked to review this information over a period of days before making a decision whether or not to take part. (Trial 5, REC form)

Our examination of correspondence between RECs and triallists subsequent to ethical review suggests that RECs are concerned with identifying any failure by applicants to comply with procedural standards. RECs closely supervise the production of the final draft of the PIL by negotiating with triallists through correspondence. RECs raised concerns relating to the content, format or structure of PILs in virtually all (11/12) of their provisional opinion letters. Requests for amendments often took the form of RECs referring researchers to the official guidance (the third author) or suggesting standard phrasing. Much of the attention work of RECs is thus directed towards negotiating a final version of the PIL that could be recognised as satisfying institutional demands for propriety.

The information sheets and consent forms should be separate documents and headed up as such. The standard [official] consent form should be used. (Trial 8, REC letter provisional)

It should state that the [MREC name] has reviewed and approved the study. (Trial 10, REC letter provisional)

In addition, RECs were keen to ensure that patients would not be under-informed or misled; that the PIL be written in an “accessible” way; and that the possibility of any harm or risk associated with trial participation be explicit. Thus, in all 11 trials where amendments to the PIL were requested, RECs demonstrated their concern that patients not be misled or less than fully informed about the study and identified instances where more detail, explanation or fuller disclosure of information were required. These directives were intended to ensure that the prospectus aspect of the PIL did not over-sell the trial, while also ensuring that the contractual aspects of trial participation were explicit and clear.
The Committee is concerned that the additional biopsy is understated in the participant information sheet. While the procedure only takes 30 minutes the impact on the patient is considerably longer. Please revise the participant information sheet accordingly. The Committee suggest that you consider providing an additional information sheet for the biopsy before obtaining consent to it. (Trial 2, REC letter provisional)

It was felt that the words "or get better" suggests the possibility of a complete recovery and should therefore be removed. (Trial 6, REC letter provisional)

Similarly, issues related to (perceived) lack of clarity and accessibility were raised in 10 of the 11 trials in which revisions to the PIL were requested by the REC (the exception had the way in which it conveyed complex information praised). RECs emphasized that the PIL should be written in a way that the intended participants could understand, and thus fulfil its role as a prospectus.

The Committee's main concern is with the content, tone and clarity of the patient information…The PIL, whilst attempting to give very comprehensive information, is over-complicated, poorly structured and the language is too technical. (Trial 3, REC letter provisional)

Reword control group A to “you will be treated with standard chemotherapy which includes the three drugs” (In this way the subsequent use of the term ‘standard chemotherapy’ can be clearly understood.) (Trial 9, REC letter provisional)

In 9 out of 11 letters, RECs also showed that they were concerned that the possibility of harm or disadvantage should be fully addressed. They highlighted the need for fuller information about compensation arrangements, complaints procedures, and emergency arrangements, thus emphasising the contractual purposes of the PIL.

The participant information sheet should clearly explain that participants should be advised not only to inform their insurance company but to consult with the company before entering the study to ensure that their participation would not adversely affect their medical insurance. (Trial 5, REC letter provisional)

The correspondence from triallists in response to such comments from RECs shows how both parties in effect co-produce the final version of the PIL. This version embodies assumptions about the ideal reader of the information sheet and the expectations of accountability implicit in the process. Consistent with the hierarchical ordering of relationships between RECs and researchers implied by ethical review (Dixon-Woods et al, 2007; O’Reilly et al, 2009b), full or partial researcher compliance with REC requests for
PIL changes was demonstrated in all 11 of the response letters. We counted 110 separate instances across the letters that signalled compliance.

REC: In section 9 of the participant information sheet the words 'toxicities' and 'limited value' could be considered coercive; please remove or rephrase.
Researcher: The sentence containing these words has been removed at the Committee's suggestion. (Trial 2, Researcher response)

REC: Please use the standard wording for the review of the application by a research ethics committee.
Researcher: Done.
REC: Please include in the PIL details of who to contact in the event of a reaction.
Researcher: Done. (Trial 12, Researcher response)

By demonstrating compliance, researchers could display trustworthiness and commitment to ethical principles. Non-compliance, by contrast, had the potential to cast triallists as uncooperative and lead RECs to question their ethical soundness. So it is perhaps not surprising that examples of researcher non-compliance, or no response to the REC’s concern, were rare. We found only 10 instances, occurring in five letters. They were accompanied by careful justification – for example by invoking the official guidance as a legitimizing authority for the proposed course.

REC: Subjects should be informed that should they decide not to participate or withdraw from the study their current or future care will not be affected.
Researcher: The standard [official] wording was used in the section entitled, “Do I have to take part?” to inform subjects of this, therefore no changes to the text have been made. (Trial 4, Researcher response)

End product of institutional scripting

Our analysis suggests that the end product of these negotiations – the final, approved PIL – is the outcome of a process of institutional scripting driven by the needs of each party to satisfy not only their ethical responsibilities, but also their accountability requirements: the REC to perform a duty of surveillance, and researchers to get approval by demonstrating trustworthiness and compliance. One striking consequence was the remarkable degree of homogeneity displayed by the 13 information sheets in our sample: they all looked very similar. Though the trials themselves were often very different in terms of study design and type of intervention, and ranged across all three phases of trials (Box 1), all PILs provided extensive description of the research study, all included standard phrases, and all included sections on:
why patients were selected

voluntary nature of participation

detailed information about the intervention and what participation in the trial would involve

detailed information about risks, benefits and possible side effects

arrangements in the event of harm occurring to research participants

contact details for the study team

The information sheets were also typically long, with a mean word count of 4,562 (range 2,644 to 6,799). Despite the emphasis in the official guidance and in the REC correspondence on accessibility and clarity, all would all be ranked difficult to read using standard readability formula, with a mean Gunning Fog index of 12.92 (range 11.09 to 14.07), somewhat above the reading level of an 18 year old school-leaver and well above the level of 8 thought to make texts more universally accessible. Part of the explanation for the “hard to read” quality of the texts seems to lie in their dual status as both a prospectus and a contract. The language used in the PILs was highly mitigated, tending to emphasise far more the possible risks of trial participation and including little detail of possible benefits.

What are the possible disadvantages and risks of participating?
It is possible that you may develop antibodies against [drug a], since it is a foreign protein to your immune system. This is possible with any similar treatment of this nature. This means that your body may become allergic to [drug a] and the allergy may extend to other monoclonal antibody treatment. Such an allergy might mean that you are not able to receive [drug a] or other similar antibodies in the future, or it might limit their effectiveness which might affect your future cancer treatment. [...] 

What are the possible benefits of participating?
There is no guaranteed benefit of participating in this study. ...Researchers do not know if the treatment works in first line therapy as it has only been shown to work in second line therapy in combination with [drug b] for colorectal cancer. (Trial 4, final PIL)

Patients as end users of the PIL

While the PIL is co-produced between REC and researcher in the context of the institutionalized ethical review process, it is delivered in a very different space: at the interface between clinician and patient, and consumed in the patient’s own social world. The PIL is scripted to support the
principles of ‘good’ decision-making as defined by official guidance. Some of the 26 patients we
interviewed did offer descriptions of a decision-making process that seemed consistent with the
ideal implied by the official guidance, and nine patients (four trial participants, two decliners,
three ineligible) reported that the PIL had played a significant and valuable role in this. For
these patients, the PIL seemed to provide information they required to make a decision, and/or
it stimulated questions to have answered before making a decision.

It’s very detailed, which is what you need really. And I took it away and spent a couple of
hours reading it, underlining things. This is a copy of the original one I got. Underlining
things I don’t understand and then I went back, I asked them questions about the pieces
I’d highlighted. (Patient 10, Trial 10, participant)

When it came to actually reading the fine print it was a lot, a lot more complicated and
there was a lot more involved and it made my decision easier really because here was so
much involved in it, I just didn’t want to be [in it]. (Patient 16, Trial 13, decliner)

The value of the PIL as a decision-making tool was, however, limited for most patients by its
length and complexity. Although eight patients found the PIL accessible, the majority (18 of the
26 patients interviewed, including two trial participants, three decliners, three ineligible) found it
too detailed or difficult to understand. For many, this was because the contractual functions of
the PIL - especially completeness of information - overwhelmed the intention that it be easy to
read.

There was a lot of jargon that didn’t really necessarily need to be in there, I don’t
think. I think that there was a lot of information that sort of baffled you. (Patient 19,
Trial 8, ineligible)

I did read it all, but I mean obviously the medical terms didn’t mean anything, you
know what I mean? On there where they quoted different, well they state what your
chemo is, blah, blah, blah, you understand what I mean? I read it and I know I am
having that but to me it doesn’t, I don’t understand what all the figures and that are
about, but only a medical person really would, wouldn’t they? (Patient 24, Trial 5,
participant)

For most patients, in addition to failing in their manifest function of ensuring that patients were
fully informed, PILs also often failed their manifest function of facilitating decision-making.
Fourteen patients (13 trial participants, one decliner), reported that the PIL had not played a
significant role in their decision. These patients described making their decision in ways that
diverged from the official ‘ideal’. Some patients had already made the decision about trial
participation before even receiving the PIL. Four patients (three offered Phase 1 trials, and one
offered a Phase 2 trial) specifically framed declining to participate as simply not an option: the
chance to participate was not something they were going to turn down. For them, the PIL was redundant.

Whether I’d got the information or whether I hadn’t I would still have said yes. I think you have got to give yourself a chance. (Patient 21, Trial 1, participant)

[Doctor] says “I think we have got one (a trial) here that you might be alright with” and I just said “well put me down for it” and he said “well you haven’t read the information yet” (laughs) and I said “well put me down for it”. (Patient 15, Trial 12, participant)

For the majority, decisions about participation, rather than being fully reasoned or based on a rational evaluation of options (Dixon-Woods and Tarrant, 2009), were made in a relational context. Verbal discussion with members of the clinical team, and trusting relationships established with those clinicians, tended to be far more significant in the decision-making process than was the PIL, which was only one of a wider range of resources on which patients drew.

Q. Do you think it played an important part in your decision? The written information?
A. Well part of it, but mostly it was what the doctor and the nurse said. (Patient 1, Trial 4, participant)

Q. Did the written information play a role in your making a decision about the trial or not?
A. No, because I had made it up so firmly. I mean it was that or perhaps another drug or nothing. [Doctor] said, you know, ‘this is the best, this is the best chance I can offer you’. Well I just trusted that to be true. (Patient 11, Trial 7, participant)

Patients did, nonetheless, acknowledge that the PIL had a role in the ritual of recruitment to a trial, and recognised the accountability expectations it imposed on patients as parties to the process.

She gave it [the PIL] to me during the consultation, asked me to go home with it, think about it and come back on the Tuesday. So I went home, I have got to be honest, I never read it, because I had made my mind up hadn’t I? So then when I went back I realised she might ask me some questions so I quickly read it in the waiting room. I thought “you dummy, she is going to ask” and she did. (Patient 23, Trial 9, participant)
The PIL also performed a latent function as a marker of the credibility of the researchers, institutions, and funders involved in a trial. In this sense, it functioned well as a prospectus. Nine patients (8 participants, 1 decliner) suggested that they used the PIL to discern trustworthiness and honesty/integrity, and that this contributed to their decision-making.

A drug from a reputable drug company, been used by reputable hospitals, in this case it was [name] and [name] and [name], the drug company. You know that they are good, good sized operations where it is likely that, you know, they wouldn't be doing the trial unless there was the likelihood of success. (Patient 7, Trial 11, participant)

I went home and read it and if I didn't want to take part I, well it says on here, I'd still get the same treatment. It wasn't bribery. (Patient 24, Trial 5, participant)

Although the focus of ethical review is on the role of the PIL in informed consent, many (13) patients described using it long after the decision to participate had been made. They referred back to it as an ‘instruction manual’ throughout their participation; some even reported its being of most use after the trial had started rather than beforehand.

Well it didn’t mean anything when I read it [before the trial] but now it does. I mean oxyplatin is if you put your hands in cold water and you get tingles. So when you want anything out of the fridge or freezer you put your gloves on. So I’ve got a little pair of gloves on the radiator. It makes more sense now. (Later in the same interview) I’ve kept mine [PIL], I don’t know whether other patients keep them or bin them, but I’ve kept it and I’ve gone back to it as I say at least ten times. (Patient 4, Trial 5, participant)

The PIL as a formal contract

The contractual function of the PIL was explicitly recognized by many patients: 18 saw their trial participation as meaning that they were entering into a contractual arrangement with the researchers, and acknowledged the PIL as the basis of this.

I’d got to read it because then I’d put pen to paper that I’d go on it. Well it were no use if I hadn’t read it and then signed it. I knew exactly what it entailed and at any given time I could draw out or they could. (Patient 24, Trial 5, participant)

Patients did not, however, necessarily see this function of the PIL as for their benefit. Consistent with previous studies in the area of consent to treatment (Akkad et al, 2006), six patients (3 participants, 1 decliner, 2 ineligible) suggested that the PIL primarily served institutional interests, by protecting researchers and medical staff, rather than those of patients.
Well obviously they are just covering their backs. They're covering, you know, it's a medical covering document for them. It's not to help the patient understand things really. (Patient 8, Trial 5, participant)

I think you can go too deeply into it, I think that (the PIL) goes a little bit too far. I know nowadays you are in a blame society and things like that where people have got to cover their backsides, but it goes into too many side effects, too much information. (Patient 16, Trial 13, declined)

Discussion

Our analysis suggests that patient information leaflets (PILs) for obtaining informed consent to cancer trials may engage only weakly with how patients actually make decisions about trial participation and with their priorities for their recruitment process. This finding is consistent with decades of research showing that PILs usually disappoint in delivering on their aims. PILs are not unique in continuing to be used even though they may not “work”: as Merton (1968) notes, many social practices persist even though their manifest purpose is clearly not achieved. The puzzle is why PILs persist as an indispensable element of the process of recruitment to clinical trials, and why they take a form that often frustrates the very purpose for which they are intended. Our analysis helps to unravel this puzzle by identifying that informed consent documents in the current system of ethical review function latently to satisfy purposes other than their manifest function as a decision-facilitating tool.

The form taken by PILs is strongly shaped by institutional assumptions about how patients should make their decisions, by official instructions about how patients should be invited to be participants in research, by collective understanding of the PIL as imbued with contractual status, and by the latent role of the PIL as a device for the parties involved in its production to demonstrate their accountability. PILs carry a large burden in relation to accountability because they are the only part of the informed consent procedure that the REC can directly scrutinise. The PIL functions within ethical review arrangements as an aspect of performance, in the sense of being directly observable and evaluable in relation to explicit criteria.

The role of crafting a PIL is assigned to the triallists, but is supervised and in effect co-produced by the REC, with official guidance acting as a form of third author. RECs’ motivations to protect the interests of patients are clearly evident in their letters, and they frequently intervene to ensure that documents are truthful and accessible. However, both RECs and triallists are bound by formal criteria specifying what qualifies as ethical conduct and by a need to show that risks have been identified and managed. The PIL is thus the outcome of a process of institutional scripting structured by the accountability demands inherent in the ethical review process, and the final, approved version of the PIL functions latently as what Langdon Winner (1986) describes as “a way of settling an issue in the affairs of a particular community”. Thus, though
the manifest function of the PIL is to satisfy needs in the social world of the patient, it is in reality shaped by its latent function to satisfy needs in the worlds of triallists and RECs.

One consequence is that The PIL has dual roles as prospectus (providing information that the patient might want to know before making the decision to take part), and as a contract (setting out full terms and conditions, information about risks and liability). Our analysis of interviews shows that the PIL was far more salient to patients as a contract than as a prospectus.

Provision of the PIL was not, however, an empty ritual; the routine enacted by being given the PIL was recognisable to patients as a sanctioned one, consistent with more generalised norms of governing quasi-legal transactions. For most (though not all) patients, the main role that the PILs played was in providing a license or warrant for the trial (signalling that the researchers came from credible institutions), and demonstrating that they were entering into a contract. But it was also understood by many patients that this was not a routine that necessarily operated in their interests – rather, it was perceived to be there to serve the interests of institutions.

The sense that the PIL was not really there for their benefit was reinforced by the end-products of the institutional scripting of PILs through the ethical review process. The PILs approved by RECs were long and complex, and relatively homogeneous even for different trials. The standardised format and content was not a good reflection of what most patients actually value and prefer; most found it difficult to use the PIL as a source of information. The length and complexity of the documents was an important challenge to patients’ ability to engage in a fully rational, reasoned process of decision-making. But it is important to stress that even if PILs were easier to understand, it is not at all clear that they would play the role of supporting rational decision-making for which they are intended. Patients often describe making their decisions about participation in ways that do not concur with official ideals of ‘good’ decision-making (Dixon-Woods and Tarrant, 2009). For many patients, the most significant sources of information are precisely those to which RECs have no access under the current system of ethical review (e.g. discussions with clinical team and/or researchers, talking to family and friends, beliefs about the value of clinical trials). Some patients have made their decision before they even get the PIL. Thus, though for some patients the PIL did indeed deliver valued information and function to support decision-making, for many it did not perform this role.

Conclusions

Our findings are confined to cancer trials, and our study design does not permit generalisation to other kinds of trials where the issues may be quite distinct. Nonetheless, our data suggest that in the cancer trials context at least, PILs continue to be used even though they do not properly serve the functions for which they are intended. The suitability of the PIL as a tool to support informed decision-making - or at least to signal more respect for patients’ real priorities - might be improved if the prospectus and contract elements could be separated out. Rather
than being based on standard templates, the design of the prospectus element of the PIL might be informed by a set of principles outlining good practice, and by involving patients more closely in the design and testing of PILs. Every trial is different, and in designing the PIL triallists should aim to produce a version that covers the particular issues that are important to patients who may be approached about recruitment to that particular trial.

Our research suggests that supporting patients in their decisions about trial participation requires more than just a re-think of the structure and format of the PIL, and instead may involve a more fundamental restructuring of how institutionalised practices of “ethics” function in contemporary research. The ideal of the rational patient diverges considerably from the reality of how most patients make decisions, and many patients make their decisions in ways which are at odds with official ideals about ‘good’ decision making. Patients understand the role of the PIL in the recruitment ritual, but often place little weight on the information it provides, instead relying heavily on their trust in the person recruiting them, and the informal discussions about the trial with their doctor or nurse. We need to consider how staff recruiting patient to trials can enable patients to make decisions consistent with their values and preferences, especially when patients want to rely on trust rather than being fully informed.

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References


National Research Ethics Service. (20011) Information sheets and consent forms: guidance for researchers and reviewers.


Box 1: Details of the 13 trials

Phase I trials aim to determine the safety, pharmacokinetics and pharmacodynamics, and maximum tolerated dose of a drug. There were four Phase I trials in our sample:

- Trial 1, non-specified advanced cancer
- Trial 7, non-specified advanced cancer
- Trial 11, non-specified advanced cancer
- Trial 12, non-Hodgkins lymphoma

Phase II trials aim to assess whether the drug is effective against cancer, and to identify responding tumour types and appropriate administration schedules. There were three Phase II trials in our sample:

- Trial 2, neuroendocrine tumours
- Trial 9, oesophageal / gastric cancer
- Trial 10, pancreatic cancer

Phase III trials aim to compare the new treatment with standard therapy. There were six Phase III trials in our sample:

- Trial 3, lung cancer
- Trial 4, colon / colorectal carcinoma
- Trial 5, colon / colorectal carcinoma
- Trial 6, melanoma
- Trial 8, oesophageal / gastric cancer
- Trial 13, oesophageal / gastric cancer
Table 1: Details of the 26 interview participants

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