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Reshaping consent so we might improve participant choice (III) – How is the research participant's understanding currently checked and how might we improve this process?

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Abstract

Valid consent requires the potential research participant understands the information provided. We examined current practice in 50 proposed Clinical Trials of Investigational Medicinal Products to determine how this understanding is checked. The majority of the proposals ($n = 44$) indicated confirmation of understanding would take place during an interactive conversation between the researcher and potential participant, containing questions to assess and establish understanding. Yet up until now, research design and review have not focussed upon this, concentrating more on written material. We propose ways this interactive conversation can be documented, and the process of checking understanding improved.

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Introduction and methods

Anyone agreeing to join a research study must understand the information they are given if their consent is to be legally and ethically valid. Consequently, the confirmation of understanding is recognised as a requisite for informed consent. The World Medical Association's Declaration of Helsinki (World Medical Association, 2013) requires the researcher ensures the participant has understood the information (para 24). A similar requirement is in the EU Clinical trials - Regulation (2014):

> *5. In the interview referred to in point (c) of paragraph 2, it shall be verified that the subject has understood the information.*

The United Kingdom's Health Research Authority (HRA) review processes have seemingly come into line with this judgement. Question H7: '*How will it be assured that potential participants (or their legal representative) have understood the information, and that consent is informed?'* has been added to the application form that must be completed when seeking research ethics committee (REC) ethical approval for a proposal to conduct a Clinical Trial of an Investigational Medicinal Product (CTIMP) in the UK.

To examine current practice, we undertook content analysis of the answers to this question in 50 consecutive applications to conduct a CTIMP submitted to a UK Research Ethics Committee (REC) between 2021 and 2023, and the associated informed consent forms (ICFs). Trials from all phases (i.e. phases I to IV) were included, except those that planned to recruit adults who lacked capacity (and therefore could not consent for themselves). When children were to be included, we analysed the provision for seeking consent from their parents or legal guardians. The letters were analysed as to determine:

i. who would be ensuring the participant understood the information provided;
ii. how understanding would be determined; and
iii. the role of written material in this process.

Author HD performed the initial analysis which authors SK and AL then reviewed and confirmed. As consent would be recorded by the participants' signatures on an ICF, HD performed a content analysis of these documents to ascertain:

i. Whether this sought confirmation of understanding from the participant by a signature;
ii. Aspects of the process that were confirmed (e.g. voluntariness, the ability to withdraw, whether a conversation had taken place); and
iii. Other specific aspects of the study (e.g. data handling, risks and benefits of participation etc).

Results

The responsibility for confirming understanding was allocated to a member of the research team in virtually all applications ($n=47$ out of 50). Twenty-six then expanded on the experience and training of those who would be undertaking this:

> *The investigational sites selected are experienced research sites at which the study staff are experienced and have a good understanding of the ethical principles underpinning informed consent. . ..and of the ethical principles underpinning informed consent.*

Seven described codes that would be followed:

> *At screening, a one-on-one interview with the physician or nurse will be conducted in accordance with ICH/GCP guidelines.*

Forty-four indicated confirmation of understanding would take place during a conversation between the potential participant and the researcher. Of these, 15 indicated the researcher would ask questions of the possible participant to check understanding:

> *Once the patient decides to be a participant in this study, the study team will ensure that the participant has demonstrated a clear understanding of the information provided during the informed consent process by asking the potential participant questions and having an open conversation.*

In 39 applications, it was stated that the conversation would be supported by written material, a participant information sheet (PIS), or ICF (these terms were used inconsistently). These written materials would serve three possible functions:

- providing information

> *The trial information provided to potential participants is written in understandable/lay language. The information will be provided in a considerate manner by the trial team according to each potential participant's needs.*

- supporting further discussion

Potential participants will be encouraged to take away the trial material to read and discuss with others. The trial team will provide the potential participant with the Main PIS/CF and a Summary information sheet.

- checking understanding

A consent point has been added to the Participant Information Sheet & Informed Consent Form to state 'I confirm that I have read and understand the participant information sheet for the above study. I have had the opportunity to consider the information, ask questions and I am satisfied with the explanations provided.

The 50 ICFs were checklists with between 6 and 20 items. Nearly all started with statements that potential participants were asked to confirm that they:

- understood the information provided (42)
- understood their consent was voluntary (49)
- understood they could withdraw at any time (48)

and that they had:

- the opportunity to ask questions (48)
- adequate time to consider the information (47)
- received a participant information sheet (45)

Otherwise, the most common items concerned data protection. This was in all ICFs (146 items in total) but other issues which might be deemed of likely importance for the potential participant were infrequently cited as:

- the alternatives to joining the study ($n=3$)
- that the project was a research study with consequent uncertainty ($n=2$)
- details of the possible benefits ($n=8$)
- details of the possible harms ($n=8$)

In specific cases:

- 15 studies involved a placebo. This was mentioned in six of the ICFs.
- 23 studies involved a comparison in which treatments would be allocated randomly and not chosen by the patient or doctor. This was mentioned in three of the ICF.
- 25 studies involved giving different treatment doses (dose escalation studies). This was mentioned in only two of the ICFs.

Only two studies indicated there would be a record of this conversation, and none described or referred to a structure or tools for this conversation. Only one referred

to a test that would be used to provide objective confirmation of understanding. This was a complex neurosurgical trial involving intracerebral transplantation of stem cells obtained from human foetal tissue:

> *Potential participants understanding of the trial is assessed prior to completing the informed consent . . . . If the potential participant's responses to these questions do not demonstrate appropriate understanding of the trial, they will be unable to sign the consent form at that time and further meetings with the participant will take place to ensure the trial is fully understood.*

Discussion

Our results demonstrate that current practice is for the potential participant's understanding to be confirmed through a dialogue between the researcher and participant, and then confirmed in writing when the ICF is signed. These findings are hardly surprising, but they emphasise the importance of this conversation reported in earlier publications (Anderson et al., 2017; Flory and Emanuel, 2004; Fons-Martinez et al., 2021; Glaser et al., 2020; i-CONSENT Consortium, 2021; Jefford et al., 2005; Joffe et al., 2001;Kass et al., 2015; Nishimura et al., 2013; Taylor et al., 2021) and, taking this further, show that this conversation has a specific purpose in checking understanding in current practice.

The conversation

Despite its importance, the content and form of the dialogue is largely left to the discretion of individual recruiters (Wade et al., 2023), while the initial REC review pays more attention to the supporting paperwork. A recent survey of UK REC chairs has shown that, while they universally recognised the importance of the conversation, reported that between 1/3 and 1/2 of their RECs did not consider this in their deliberations (HRA, unpublished data). Consequently, the importance of conversation in the consent processes goes unguided and undocumented. In adopting this position RECs may have fallen victim to the McNamara Fallacy by making the 'measurable' elements in the documents (PIS and ICF) important, as opposed to working out how to make the important conversation measurable (and then judging it) (McNamara Fallacy. 2023). If, therefore, RECs are to judge this process and avoid this fallacy, there needs to be a documented description of this conversation, as there is for the PIS. We have recently published a proposal for an Information and Decision Aid (IDA) as a template for this consent discussion (Davies, 2023; Davies et al., 2023), which we would propose could provide such a record.

On its own, we recognise this would not necessarily improve understanding. Interactive conversational techniques are needed. One possible method would be 'TEACHBACK', a widely supported technique (National Institute of Clinical Excellence (NICE), 2021) in which the researcher describes the study and then

assesses the potential participant's understanding by asking them to repeat what they understood, repeating this cycle as many times as necessary if some aspects were unclear (Seely et al., 2022). This has evidential support in surgical consent (Glaser et al., 2020). Talevski et al. also found this to be an effective tool but added the important point that those using the technique needed training and support (Talevski et al., 2020). The IDA, again, could be such a supporting tool.

The informed consent form

Applicants indicated that understanding would be confirmed and documented when the potential participant signed the ICF, yet content analysis of the understanding showed it to be at a 'high level', confirming only that the potential participant had understood the information provided, their participation would be voluntary, and that they could withdraw at any time. Otherwise, this was focussed on issues primarily of interest to the research team (data and sample usage) rather than on points which would seem to be of importance to those thinking of joining a study. Alternatives options, the uncertainty of a research study, or detail of either benefits or harms were infrequently cited and, when relevant, the possibility of being on a placebo, treatment allocation, or changes of dosing within a protocol were similarly rarely mentioned in the ICF. The question, 'Has the participant understood these points of the study?' is clearly left unanswered. We propose that this could be remedied if an IDA and ICF were aligned and used together to document consent. This would also move to a more individualised consent process, in tune with the participant's concerns and understanding.

A further criticism of the current processes is that understanding is subjectively confirmed either by the researcher or participant, both of which have been criticised as being subject to bias and error (MacQueen et al. ,2014; Mordel v Royal Berkshire NHS Trust, 2019; Pietrzykowski and Smilowska, 2021; Talevski et al., 2020). If we are to be more confident that the potential participant has indeed understood what they have been told, objective confirmation will be needed. Only one study, a complex neurosurgical trial, included objective such an assessment of understanding in which potential participants would need to pass a 'test' to confirm check they had understood the proposal before they could sign the ICF. Possible tests have been used and evaluated (Buccini et al., 2009; Lindegger et al., 2006) but there is no consensus as to when such objective tests should be employed. Bambery et al. argue for such testing in Human Infection Challenge Studies, which is research clearly of greater than minimal risk (Bambery et al., 2016), and this was required of human SARS-CoV-2 infection challenge studies conducted in the UK (Davies and Oxford, 2022):

> *understanding would be checked by a consent quiz before signed consent was taken using an itemised informed consent form, matched to the introductory 'key facts'.*

Summary, strengths and weaknesses

We have explored how research teams propose to assess potential participants' understanding. Our results demonstrate the central importance of the consent conversation in this process. We do recognise that such data carries the disadvantage that answers to such a question on an application form may not be complete. However, this was real-world data, indicating what will happen in reality. More detailed, resource intensive, interrogation and data collection would be needed to meet this criticism.

We have referred to the IDA recently reported, but we recognise more work is needed to test possible implementation and provide guidance on how such a tool can help evaluate the conversation and the understanding achieved.

When considering objective assessment of understanding, more work is also needed to develop a consensus. Challenges remain as there is no consensus as to when such objective assessment would be required, which test should be used, what aspect of a CTIMP should be tested, and what would be deemed a 'pass mark'.

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Supplemental Material

Supplemental material for this article is available online.

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