Modified informed consent procedure: consent to postponed information

Han Boter, Johannes J M van Delden, Rob J de Haan and Gabriël J E Rinkel

BMJ 2003;327;284-285
doi:10.1136/bmj.327.7409.284

Modified informed consent procedure: consent to postponed information

Han Boter, Johannes J M van Delden, Rob J de Haan, Gabriël J E Rinkel, for the Home Evaluation of Stroke Induced Aid Study Group

How do you obtain a valid assessment of subjective outcomes in a trial in which the participants cannot be blinded to the intervention? Bias is inevitable from unblinded patients, but trials that have not told patients about treatment in all arms have been heavily criticised. Asking participants to consent to postponed information could be a solution

Department of Neurology, Rudolf Magnus Institute of Neuroscience, University Medical Centre Utrecht, PO Box 85500, 3508 GA Utrecht, Netherlands

Han Boter
junior researcher

Gabriël J E Rinkel
professor of neurology

Julius Centre for Health Sciences and Primary Care, University Medical Centre Utrecht

Johannes J M van Delden
professor of medical ethics

Department of Clinical Epidemiology and Biostatistics, Academic Medical Centre, PO Box 22660, 1100 DD Amsterdam, Netherlands

Rob J de Haan
professor of clinical epidemiology

Correspondence to:
H Boter
h.boter@azu.nl

BMJ 2003;327:284–6

Members of the steering committee are listed on bmj.com

The most powerful tool for studying the effectiveness of a medical treatment is a randomised controlled clinical trial with blinded assessment of outcomes. However, blinding is not always possible—for example, in a trial comparing a surgical intervention with non-surgical treatment or the effectiveness of supplemental care compared with conventional care. Blinding needs special attention in such studies in order to prevent bias. When outcomes are assessed by doctors, it is often easy for the assessment to be done by doctors other than those who performed the procedure. However, when studies measure patients' assessment of outcomes, blinding is much more complicated or even impossible.

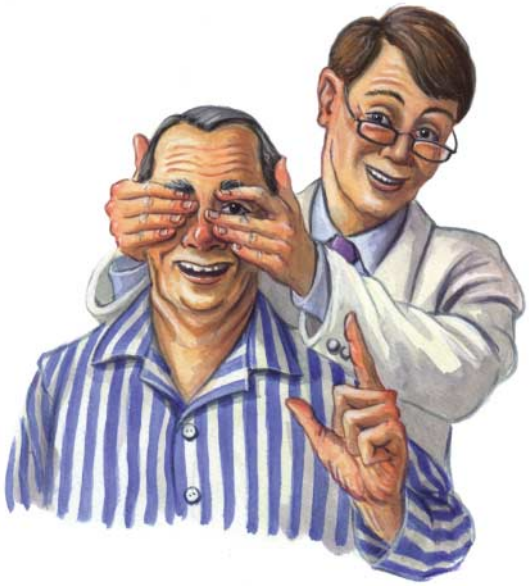
Dealing with unblinded participants

Unblinded patients who assess outcomes after being informed about the different treatment options during recruitment might bias the results of a study. The likelihood of bias increases when patients have a preference for one of the treatment options. For example, patients may have been told during recruitment that the new or supplemental strategy has been developed because the current strategy has disadvantages. The best way to obtain valid assessments in such studies remains unclear.

Intense debate was generated when researchers tried to mask patients in a trial on the effectiveness of additional care from a stroke family care worker by keeping them ignorant of the treatment options.[1–10] The researchers used a "two-stage randomised consent design,"[11 12] in which they sought patients' consent for follow up but not for randomisation. Patients were randomised after they gave consent. The researchers then sought additional consent from patients randomised to non-standard treatment but not from patients randomised to receive standard care.[1 11]

Modified informed consent procedure

We developed a modified consent procedure for a trial on the effectiveness of an outreach nursing care programme for patients who returned home after being admitted for a stroke. Because many stroke patients experience reductions in quality of life or are dissatisfied with the care received after discharge from hospital,[13 14] we intended using self reported quality of life and satisfaction with care as primary outcomes. However, we were concerned that unblinded patients could lead to biased results. Firstly, patients in the control group might be dissatisfied because they knew that other patients were receiving outreach care. Secondly, patients who received outreach care might make a more favourable assessment out of loyalty to the programme's staff. We therefore asked patients' consent to follow up and to postpone information on the study until the end of the follow up (six months after discharge).[10 15]



PETER GRAY

The box shows the oral and written information that study nurses gave to eligible patients before discharge. Additionally, patients were given telephone numbers for one of the authors (HB) and the treating neurologist, in case they had questions or complaints about the study.

Patients who gave consent were randomised. Those in the intervention strategy were then informed about the outreach care programme and asked to participate but were not told that the study was assessing the effectiveness of the programme. Patients who were randomised to the control strategy received no further information at that time. After six months, we sent a letter with the postponed information to all recruited patients who were known to be alive at follow up. It contained the postponed information on the additional research question, the randomisation, the reasons why we did not inform the patient about the additional question and the randomisation during recruitment, and telephone numbers of HB and the treating neurologist. We wrote this letter in close cooperation with the patient service office and the ethics committee of one of the university hospitals and paid special attention to its clarity.

Is modified consent ethical?

The ethical acceptability of our modified procedure for informed consent can be questioned. At least three arguments have been raised against modifications of this kind.[1 4 16] The first is that by not providing patients with full information during recruitment we are not treating them with respect. The ethical basis for informed consent is not that informing patients enables them to make informed decisions about participation in the study. Instead, the basis for informed consent is the respect that we owe them as moral actors, irrespective of how they evaluate being informed or the information as such. A second argument holds that a modified procedure might evoke negative responses in patients, leading to a decreased willingness to participate in future research. A third, closely linked criticism is that it may reduce patients' trust in their doctors.

However, questions can also be raised about using costly services that have not been evaluated appropriately. In some instances unbiased evidence can be gathered only by using modified procedures for informed consent. We think that, on balance, there can be good reasons for using such a modified procedure. We also feel that our modified procedure exceeds the two stage randomised consent design used previously.[1] Our participants knew that they were not fully informed during recruitment and gave their consent. Admittedly this is not the same as being fully informed, but by giving patients a choice we took them seriously as moral actors. Additionally, all enrolled patients, including non-respondents, who survived until follow up were eventually informed about the intervention and the randomisation.

Although conventional informed consent procedure should be the first choice, our modified procedure with postponed information deserves consideration when subjective outcomes are used as the primary outcome measurements, the outcome assessors cannot be blinded, the additional treatment entails no risk, and the intervention seems attractive to patients.

Information given to patients during recruitment

- We are studying patients' needs six months after discharge and their satisfaction with services received after discharge
- We cannot inform you about an additional research question since that would affect the results
- You will be informed about this question after assessment of the outcome
- This additional research question entails no risk
- The ethics committee approved this study

Summary points

Blinding of patients in trials that use self reported assessment of outcomes is crucial but can be difficult in some circumstances

The ethics of blinding patients by asking consent to follow up but not to randomisation have been intensely debated

An alternative is to ask consent to follow up and postponed information

Although patients know that they will be fully informed after follow up, some people may still believe that the procedure does not treat patients with enough respect

We thank A Algra, J van Gijn, and L J Kappelle for their comments on a previous version of this manuscript.

Contributors and sources: HB is a nurse researcher with experience in healthcare research. JJMvD is a nursing home physician and medical ethicist. RJdeH has expertise in clinimetrics. GJER has experience in stroke research. All authors were involved in the development of the informed consent procedure.

Funding: The trial was supported by an established clinical investigator grant from the Netherlands Heart Foundation to G J E Rinkel (grant D98.014), by a grant from the Netherlands Heart Foundation and the Netherlands Organisation for Scientific Research (940-32-014), and by a grant from the University Medical Centre Utrecht.

Competing interests: None declared.

1 Dennis M, O'Rourke S, Slattery J, Staniforth T, Warlow C. Evaluation of a stroke family care worker: results of a randomised controlled trial [with commentaries by Dennis M and McLean S]. *BMJ* 1997;314:1071-7.
2 Correspondence. Informed consent. *BMJ* 1997;315:247-54.
3 Correspondence. Informed consent in medical research. *BMJ* 1997;314:1477-83.
4 Doyal L. Informed consent in medical research. Journals should not publish research to which patients have not given fully informed consent—with three exceptions. *BMJ* 1997;314:1107-11.
5 Doyal L, Tobias JS, Warnock M, Power L, Goodare H. Informed consent in medical research. *BMJ* 1998;316:1000-5.
6 Smith R. Informed consent: the intricacies. *BMJ* 1997;314:1059-60.
7 Smith R. Informed consent: edging forwards (and backwards). *BMJ* 1998;316:949-51.
8 Tobias JS. BMJ's present policy (sometimes approving research in which patients have not given fully informed consent) is wholly correct. *BMJ* 1997;314:1111-4.
9 Informed consent [letters]. *BMJ* 1998;317:947-9.
10 Clement S. Full information about trials might be given retrospectively to participants [letter]. *BMJ* 1999;318:736.
11 Rodgers H, Soutter J, Kaiser W, Pearson P, Dobson R, Skilbeck C, et al. Early supported hospital discharge following acute stroke: pilot study results. *Clin Rehabil* 1997;11:280-7.
12 Stott DJ, Langhorne P, Rodgers H. Informed consent. Two stage randomisation and consent would overcome many problems [letter]. *BMJ* 1997;315:253.
13 Wyller TB, Sveen U, Sodring KM, Pettersen AM, Bautz Holter E. Subjective well-being one year after stroke. *Clin Rehabil* 1997;11:139-45.
14 Pound P, Gompertz P, Ebrahim S. Patients' satisfaction with stroke services. *Clin Rehabil* 1994;8:7-17.
15 de Craen AJ. "Informed consent" en prerandomisatie [Informed consent and prerandomization]. *Ned Tijdschr Geneeskd* 2000;144:1301-3.
16 Lambert MF, Wood J. Incorporating patient preferences into randomized trials. *J Clin Epidemiol* 2000;53:163-6.

(Accepted 19 May 2003)

Commentary: an imperfect compromise

Martin Dennis

Department of Clinical Neurosciences, University of Edinburgh, Western General Hospital, Edinburgh EH4 2XU

Martin Dennis *professor of stroke medicine*

msd@skull.dcn.ed.ac.uk

Boter and colleagues have proposed a compromise to obtaining fully informed consent before enrolment for randomised trials that have primary outcomes based on a subjective measure, which makes blinding impossible and bias likely. This compromise aims to involve the patient and show them as much respect as possible. As with all compromises it is imperfect. From the trialists' point of view it still has several drawbacks compared with obtaining consent only for follow up.

Telling patients that there is a secret additional research question is likely to reduce the proportion of patients who agree to participate and thus the generalisability of the trial's results. The number of patients who refused to participate in the study, and their characteristics compared with participants, would indicate the size of this problem.

The wording of the patient information is bound to raise curiosity about the nature of the additional questions. Some participants may make the link between the intervention they receive and the questions asked at follow up. This would introduce an unknown amount of bias, although it is likely to be small.

The reassurance given to patients that the "additional question entails no risk" is potentially misleading. Firstly, if the intervention improves outcome then those in the control group will have a risk of a worse outcome. This statement could therefore be used only when the patient would have access to the intervention only within the trial and where the control arm would receive normal care. Also, in our trial, those allocated a stroke family care worker judged themselves more helpless than controls at follow up. We have subsequently shown that helplessness in these stroke patients was associated with poorer long term survival, even after we adjusted for important prognostic factors.[1] No treatment should be assumed to be free of adverse effects. Perhaps the reassurance should read that there are no likely adverse effects.

No doubt the ethicists, who focus mainly on the rights of the individual, will see this compromise as unacceptable. They do not have to struggle with the everyday double standards applied to consent procedures in research compared with those in routine care and audit. We have no universally accepted solution to the clinical trialists' dilemma that to provide treatments of proved benefit to many future patients (and to avoid putting them at risk) we may sometimes have to compromise the rights of current patients to be fully informed in advance about treatment options and research methods.

Of course, we shouldn't have to rely on what the ethicists or the trialists think. Surely, we should involve potential participants in the design of the consent procedure. We should ask the patients who were enrolled in this study for their views. Did they feel, once they had been informed, that they had been treated with respect? Was the approach taken in this case acceptable to them?

Competing interests: None declared.

1 Lewis SC, Dennis MS, O'Rourke SJ, Sharpe M. Negative attitudes among short-term stroke survivors predict worse long-term survival. *Stroke* 2001;32:1640-5.

A memorable patient

Compartment syndrome

The 6 year old boy arrived in the night with a painful and swollen elbow after a fall. His supracondylar fracture was manipulated, the subsequent x ray films looked excellent, and he was discharged. He returned two days later with severe pain and a blistered, swollen forearm. The diagnosis of compartment syndrome crossed my mind, but my registrar soon ruled it out. He said, "Swelling is quite common in this fracture. The child's pulses are palpable, and sensations are fine. Send him home." Being a beginner, I did not have enough clinical knowledge and experience to challenge the decision. Who would challenge his senior, anyway? Hence the child was discharged the second time with a follow up appointment in the clinic after two days.

This patient's subsequent visit was the most devastating experience of my professional life. He was reviewed in the clinic by my professor (who eventually turned out to be the architect of my future orthopaedic career). As luck would have it, the senior registrar was on annual leave that day—good for him, bad for me. The puffy forearm had all the signs of a well established compartment syndrome (and a "neglected" one), with no movement, pulses, or sensations. My professor was furious. His words burnt my ears like molten lead. I stood before him like a culprit in a witness box with my hands tied behind my back. There were no pauses and no opportunities for explanations. In those few minutes of constant fire, I saw my clinical career collapsing like a house made of playing cards. I was almost in tears, and I felt guilty, worthless, and incompetent.

The subsequent decompression was obviously unsuccessful, and the child developed Volkmann's ischaemic contracture.

I knew this stigma would remain with me forever. And so it did. The story was told over and over again to each new group of undergraduate and postgraduate students. It was referred to as "Dr Anwar's case." My boss always emphasised the importance of early identification of this condition. Interestingly, my registrar would always nod his head in agreement like a true disciple without sensing the red hot rage in my chest.

Ten years later, when I visited my professor in India, I tried to clear my name by explaining things to him again. He replied: "My boy, what happens when you see a child with a supracondylar fracture of the humerus now? You remember me, you remember that child, and you remember compartment syndrome. That is what it was all about." I will never forget those golden words that were so true and meaningful.

Rahij Anwar *clinical fellow in trauma and orthopaedics, Maidstone Hospital, Kent*
rahijanwar@hotmail.com