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Response to Hadorn et al on increasing recruitment into randomised clinical trials

The proposal by Hadorn and colleagues to increase recruitment into randomised clinical trials by changing the nature of the consent procedures has been criticised by experienced cancer specialists as being both unnecessary and wrong.[1,2]

In support of these criticisms, we think it is worth exploring further the nature of the proposed consent arrangements and the moral problems they entail. Hadorn et al are aware of the controversial moral stance in their proposals and themselves have suggested that patients, ethicists, and clinicians should examine them in detail before implementation is considered. But a number of scholars have already looked closely at ethical problems in theory and practice with post-randomisation consent (PRC). These ethical problems are so serious that we believe they make a cogent case for dropping the proposal without further consideration.

Jackson and colleagues correctly characterise the moral wrong as subordinating the right to consent to treatment to the desire to achieve recruitment targets. "For the doctor sitting with the patient the principles of honesty and respect for autonomy are paramount."[2] Furthermore, there is a strong argument, not referred to by Hadorn et al, that the lack of candour to patients in the PRC design is the *reason* for any increased recruitment, and thus it tempts clinicians into dishonesty.[3]

The proposal from Hadorn et al is to seek consent from patients who are randomised to the experimental treatment, but not from those randomised to the standard treatment (single randomised consent design). The more patients that refuse the experimental treatment, the more bias is introduced, unlike the conventional design.

Altman et al have explained the nature of the bind that the use of the PRC design puts doctors in: "By definition, they [doctors] should be participating in a trial only if they have substantial uncertainty about which treatment is best, yet they have to give information to patients in the knowledge of the treatment that the patient has already been allocated and also knowing that it is in the interests of the trial for the patient to accept that allocation."[4] The design provides subtle encouragement to investigators to provide a biased presentation of the relative merits of the treatments.

The other moral problem in the PRC design: of not telling patients who have been randomised to the control (standard treatment) arm that they are in a trial at all, is in our view given insufficient weight by Hadorn et al. They portray the issue as one of using patients' data without consent and equate it, inappropriately, with the use of routine data in observational studies.

The problem is not so much the use of data, as of not telling these patients the truth: which is that their treatment has been decided at random and, in many cases, that their treatment options have been narrowed. It is not true that "nothing has changed" for these patients. They had their treatment decided in the way it was because they were part of a clinical trial. Moreover, as Jackson et al note, there are often several versions of standard care and clinicians would be restricted in the treatment options they could

discuss. A "double randomised consent" design for PRC has been described,[3,4] in which consent is also sought from the control patients. This is clearly better, but also runs into the problems described above for the experimental arm.

The PRC design could only ever be ethical in clinical settings where there is evidence that if patients had been informed of the randomisation they would have been happy to participate. If it were really true, as Hadorn et al claim, that a major reason for lack of recruitment is unwillingness to be allocated to the control arm, they have already claimed that some patients would not be happy being in a standard care arm; thus patients would only be agreeing to standard care because they had not been properly informed.

If equipoise truly holds, and patients truly are reluctant to be randomised to the control arm, this should be met with a more concerted effort to explain the current evidence on risks and benefits of the treatments under comparison rather than withholding information. While all trial participants receive some benefits from being in the trial (such as improved quality of care and having a 50% change of getting the better treatment – which may not be the new treatment), a large part of their willingness to participate is altruism, that others may benefit from their contribution. This too is a value worth protecting.

The uses of the PRC design outside clinical settings in cluster trials tend not to raise the same moral problems. For example, a trial of screening for colorectal cancer in the UK entailed randomising households to an intervention group, who were offered a screening test, or to a control group, who were not; the control group households were not contacted and only mortality records were accessed.[7] In this case, the trial was not in the context of a doctor-patient relationship, there was no contact with the control group, and there was no temptation to provide biased information. Even so, the ethics of PRC designs in cluster trials have been subject to careful evaluation.

The newly released Ottawa Statement on the ethical design and conduct on cluster randomised trials has proposed strict conditions under which it is appropriate to dispense with consent. [5]

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