

# Increasing patient participation in cancer trials

Identifying barriers to patient participation in cancer trials, and evaluating the interventions aimed at increasing participation: systematic reviews of the evidence

- Clinical trials are an essential tool for the evaluation of medical technologies. Sufficient numbers of trial participants are needed to ensure valid results. Low participation rates may delay the potential introduction of new treatments and more detailed evaluation of existing ones.
- The research literature fails to identify in a clear, reliable and consistent way the barriers involved in trial participation. However, themes can be identified.
- Questions based on the themes could provide trialists with a starting point for identifying potential barriers to participation.
- Trialists could include patients and health professionals when identifying potential barriers to participation.
- Few interventions were shown to improve participation in trials.
- There is a clear need for further research into the range of interventions that might increase participation. Such research should take into account a number of important methodological issues.

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## Background

Clinical trials are an essential tool for the evaluation of medical technologies. It is crucial that sufficient numbers of participants are recruited to trials to ensure valid results. Difficulties in recruitment to a trial may limit the statistical power of the trial to detect a treatment effect. Additionally, the external validity of the trial will be threatened as the sample may be less representative of the population in which the treatment might be used. At worst the trial may not recruit sufficient numbers of participants to proceed. Low participation rates may thus delay the potential introduction of new treatments and more detailed evaluation of existing ones.

In 2000, the NHS Cancer Plan set the target of doubling the total proportion of cancer patients entering clinical trials within three years.<sup>1</sup> This target was met by 2004, when almost 11% of people with newly diagnosed cancer participated in trials.<sup>2</sup> However, this remains a small proportion of all cancer patients. Of 333 randomised controlled trials (RCTs) conducted in the UK between 1971 and 2000, one fifth recruited at least 75% of the planned sample, just over one half did not reach the planned sample size, while one fifth recruited less than 25% of the planned number of patients.<sup>3</sup>

There is clearly a need to understand why both health professionals and patients may be reluctant to take part in trials of cancer treatments, and also to assess the effectiveness of strategies to overcome barriers to trial participation.

### Nature of the evidence

This short report is based on two systematic reviews funded by the National Cancer Research Network (NCRN). The first reviewed the literature relating to the barriers, modifiers and benefits involved in participating in RCTs of cancer therapies as perceived by health professionals and patients.<sup>4</sup> The second reviewed the evidence on the effectiveness of any interventions to increase cancer patient participation in RCTs.<sup>5</sup> Details of the methodologies used can be found in the full reports.

### Barriers to participation

**Findings:** The issues identified were around time constraints, availability of resources, the importance of the research question, patient preference for a particular treatment (or no

treatment), worry about uncertainty of trials, concerns about information and consent, and the clinician acting as a barrier to patient participation.

These findings support those of a previous review,<sup>6</sup> however, this review<sup>4</sup> also highlights the limitations of the research literature in identifying in a clear, reliable and consistent way the barriers to trial participation. A major concern is that the predictors of trial participation could be partially an artefact of what has been studied and how the data have been collected or analysed.

The listing of barriers to participation in cancer trials belies the complexity of the issue. From the existing evidence it is not possible to say that all the potential barriers to participation have been identified. Nor is it possible to say to what extent each of those that have been identified affect participation or how they interact. In individual trials the barriers vary in importance and are likely to interact in unique ways.

**Recommendations:** It is necessary to be cautious in stating what is and is not a barrier to trial participation. Boxes 1 and 2 contain questions addressing the themes identified in the literature. Trialists could, as a starting point, ask themselves these questions in order to identify barriers that might apply in their given setting.

### Interventions to improve participation

**Findings:** The second review<sup>5</sup> found that overall there is not a strong evidence-base for interventions that increase cancer patient participation in trials. A small body of research was found, of which six studies were considered potentially relevant to the UK setting.

A good quality RCT, conducted in the UK found that nurses and urologists were equally effective in recruiting men with prostate cancer to a treatment trial.<sup>7</sup> Based on a cost minimisation analysis, recruitment by nurses was more cost-effective.

In a qualitative study directed at the same trial, there was evidence of increasing participation rates following amendments to the nature and emphasis of the information given to patients.<sup>8</sup> This was an uncontrolled study, and therefore the influence of other factors on the recruitment rates cannot be excluded.



The remaining four studies investigated the following interventions:

- a two-stage process for seeking parental consent for their child's participation in a leukaemia trial compared to the standard approach;<sup>9</sup>
- a written consent document designed to be easy to read compared with the standard consent form;<sup>10</sup>
- providing doctors with information on patients' individual information needs and attitudes to trials prior to seeking consent compared with the doctor not having this information;<sup>11</sup>
- a multi-component, system level intervention (including education and information elements) compared with no intervention.<sup>12</sup>

There was no evidence that any of the interventions investigated led to an increase in cancer patient participation in clinical trials. Equally, the evidence was not of sufficient quality to be able to conclude that these interventions were not effective.

Overall the studies had a range of methodological weaknesses, a reflection of the many practical barriers to assessing the effectiveness of interventions to increase trial participation.

**Recommendations:** There is a clear need for further research assessing interventions aimed at increasing patient participation in cancer trials. Wherever feasible, RCTs should be the method of choice to minimise the risk of selection bias.

The interventions in this field are effectively complex interventions and would benefit from being treated as such.<sup>13,14</sup> This could include use of qualitative as well as quantitative methods and piloting to define the intervention. Similar methods could be used to assess whether the intervention is being used in the appropriate context in terms of the barriers to patient participation in the trial/s being considered. One of the included studies effectively used such an approach to investigate the barriers to patient participation specific to the cancer trials.<sup>8</sup> Examples of such approaches are available in other areas of research.<sup>15,16</sup>

When designing studies to assess interventions to increase participation in cancer trials, consideration needs to be given to

### *Box 1: Patient perspective - key questions*

- What role might any patient treatment preference play?
- What key information needs to be given to enable patients to feel more comfortable with the uncertainties involved in the trial and the concept of clinical equipoise?
- How might information overload be avoided?
- How might the timing of the request to participate in the trial be sensitively addressed?
- How might practical barriers such as cost to patients, transport and time commitments be addressed?
- How might the benefits of the trial be explained to patients?

### *Box 2: Health professional perspective - key questions*

- What infrastructure is needed to run the trial effectively and what system-related barriers might arise?
- What extra workload and time commitment will be demanded of the various health professionals involved?
- How difficult will the trial be to explain to patients and how much time will be needed for informed consent interviews?
- What special difficulties might arise in identifying suitable patients and in accruing certain groups e.g. older people, ethnic minorities?
- Will there be competition for patients from other trials?
- How restricted are the eligibility criteria?
- How easy will it be for physicians to comply with the trial protocol?
- Does the trial design reflect standard practice?
- How might individual physicians view the trial in terms of its scientific merit and more specifically its design?
- What are likely to be the views of all the health professionals involved in the trial?
- Might individual equipoise be a problem?

generalisability to different ethnic and social groups.

## **Implications for trialists**

The first review highlighted issues related to participation from the patient's perspective and that of the health professional. A beneficial way forward could be for trialists to include both



these groups when identifying potential barriers to participation. The questions listed in boxes 1 and 2 could provide a framework for such discussions.

## Implications for research

High quality research is required to identify potential barriers to patient participation in trials and to understand the individual and combined effect of these barriers. Interventions to overcome barriers also need to be developed and high quality research undertaken to assess their effectiveness.

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This short report is based on two systematic reviews commissioned by the National Cancer Research Network (NCRN). The first reviewed the literature relating to the barriers, modifiers and benefits involved in participating in RCTs of cancer therapies as perceived by health professionals and patients. The second reviewed the evidence on the effectiveness of any interventions to increase cancer patient participation in RCTs. The systematic reviews are published in full in CRD reports 31 and 32. These can be downloaded free of charge from the CRD website at: [www.york.ac.uk/inst/crd/crdpublications.htm](http://www.york.ac.uk/inst/crd/crdpublications.htm). For more information about obtaining copies of the full reports contact the CRD publications office ([crd-pub@york.ac.uk](mailto:crd-pub@york.ac.uk)).



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