

## The rights of patients in research

### *Patients must come first in research*

See pp 1279, 1305, 1313, 1315, 1318, 1338, 1341

Clinical trials cannot be done without patients, and the whole purpose of conducting trials is to benefit patients. These two indisputable statements should mean that patients should be at the front of researchers' minds when they design, conduct, and report medical research. But they rarely are. Too often patients are forgotten in the complex business of conducting research. We argue that patients should help to decide which research is conducted, help to plan the research and interpret the data, and hear the results before anybody else.

The patients certainly seemed to have been forgotten in the notorious case of the "trial" of the complementary treatment offered to women with breast cancer by the Bristol Cancer Help Centre.<sup>1</sup> The women who had willingly participated in the research knew nothing of the results until they heard on the television news on the evening of 5 September 1990 that those of them who had been to the centre were twice as likely to die and three times as likely to relapse as women who had not been to the centre.

As far as the women were concerned, the study was still in progress and they had received only four of the five annual questionnaires they were expecting to be asked to complete as part of the five year study. Nobody had sought their permission to publish interim results, and no one had written to thank them for their cooperation (as recommended by the Royal College of Physicians<sup>2</sup>) or to communicate even in broad outline the conclusions of the study. Instead, the results were published in the *Lancet* (dated 8 September) and released prematurely to the media with a fanfare of publicity. (The *BMJ* contributed by publishing a news story entitled "Death from complementary medicine."<sup>3</sup>) The result was desolation for the women and financial disaster for the Bristol Cancer Help Centre.

But, as most readers of the *BMJ* will know, the study was fundamentally flawed. The women who chose to pay for visits to Bristol in addition to NHS treatment were, as a group, more ill than the controls they were compared with (as might well have been expected). Two months after the paper was published a letter in the *Lancet* from one of the sponsors—the Imperial Cancer Research Fund—acknowledged this point.<sup>4</sup> But by this time huge damage had been done, and the women in the trial had become "activists"—the first patients to challenge the results of a trial in which they had participated. They made a complaint to the Charity Commission about the conduct of the two charities that had funded the study, and their complaint was upheld.<sup>5,6</sup> The commission

then went on to recommend guidelines on the responsibilities of charities funding medical research.<sup>7</sup> Controversy still surrounds the trial (p 1341),<sup>8,8a</sup> and a television programme in the series *Taking Liberties* to be broadcast on 23 May will make further accusations about its handling (see a review on p 1338).<sup>9</sup>

But, as women with breast cancer know better than most, disasters can lead to opportunities and a chance to make major advances. The Bristol study focused thinking on how patients can best be involved in research, and two papers in this week's *BMJ* take up the theme.<sup>10,11</sup> Iain Chalmers, director of the UK Cochrane Centre, argues that "greater lay involvement in health research would help to promote reliable, relevant research of importance to patients and those caring for them" (p 1315).<sup>10</sup> And Sandra Oliver, an antenatal teacher from the National Childbirth Trust, describes how "consumer groups are well placed to bridge the gap between the public and researchers by explaining research issues to a wide audience, by presenting the needs and views of health service users to the research community, and by suggesting how members of the public may be approached for their views directly" (p 1318).<sup>11</sup>

### **Patients should help to set the research agenda**

The first way that patients and the public can be involved in research is by helping to set the research agenda, and in Britain the NHS research and development programme is committed to trying to reflect the concerns of consumers throughout its work.<sup>12</sup> The concerns of patients are not the same as those of researchers.<sup>13</sup> For instance, women with breast cancer want more research on quality of life, environmental and psychosocial issues, and the optimum dose of radiotherapy to control the tumour but cause minimal damage to healthy tissues. And the first choice for research by members of the National Childbirth Trust was research into effective communication and support to meet individual needs.<sup>11</sup> As well as making clear their preferences patients may, as Chalmers describes, suggest highly productive lines of research not considered by researchers<sup>10</sup>: it was the mother of a young woman with vaginal adenocarcinoma who put forward the idea that it might have been caused by diethylstilboestrol; and the mother of a child with trisomy 18 was the first to hypothesise that a low maternal serum  $\alpha$  fetoprotein concentration might be a marker for the abnormality.

Secondly, patients must—almost by definition—be the best people to advise on the outcomes to be studied. Too much research is concerned with midpoints of dubious relation to outcomes that really matter to patients—like quality of life and mortality.

Thirdly, patients can, by commenting on the design of the study, increase the chances that patients will be willing to cooperate with and complete the research. They might also reduce the prevalence of unnecessary research. Would patients, for instance, agree to be included in a study of a new drug against a placebo when the important question is whether the new drug is any better than existing treatments? This question is explored further in the following editorial by David Henry and Suzanne Hill (p 1279)<sup>14</sup> and in the paper by P P Koopmans (p 1305).<sup>15</sup> Greater involvement of patients in the planning of trials might also reduce the chances of trials being expensively halted—as happened in the United States with a large National Institutes of Health trial of tamoxifen to prevent breast cancer after the National Women's Health Network discovered that the trial's organisers had been associated with irregular research.<sup>16</sup> The organisers were accused in Congress of delaying publication of results showing that tamoxifen is associated with endometrial cancer.<sup>16</sup> A similar trial in Britain has also proved controversial, and the Medical Research Council is no longer supporting it because of concerns about the toxicity of tamoxifen. If women with long experience of tamoxifen's side effects had been consulted the trial might have been designed differently or, more probably, might never have started.

Fourthly, patients are in a much better position than researchers to assess the quality of consent that is to be sought for a piece of research. Are the risks and benefits adequately described from the patients' point of view? Is the information sufficiently clear?

### No excuse for double standards

Generally, medical researchers and ethics committees have been willing to accept a much poorer quality of consent when patients are undergoing what might be called routine treatment than when they are participating in trials. An example was research published in the *BMJ* in 1988 that purported to show that treatment with buserelin, an agonist of luteinising hormone releasing hormone, and human menopausal gonadotrophin was more effective than conventional treatment in stimulating oocyte production and achieving pregnancy in women undergoing in vitro fertilisation.<sup>17</sup> Patients were not randomly allocated to the two different treatments: 77 women had the new treatment and 328 the old. The authors say in the paper that "After formal discussion with this hospital's drug committee and informal discussion with its ethics committee, it was decided that the usage we report was merely an extension of the drug's regular use and that formal ethical approval was not necessary as our study was not a randomised trial."<sup>17</sup>

Chalmers and Silverman have argued that these double standards are inexcusable and that those who promote the view that "the interests of patients involved in casual, poorly controlled experiments are less in need of formal protection must be called to account."<sup>18</sup> Informed patients consulted about the buserelin trial might well have argued against the trial being conducted at all because the results are really uninterpretable.

The fifth benefit that patients can bring to research is help with publicity to encourage recruitment. Sixthly, they may insist on the publication of research that has been undertaken on patients. John Pearn argues on p 1313 that publication of research is an ethical imperative.<sup>19</sup> At the moment too

much research, much of it undertaken with patients, is not published because the results are boring or do not fit the marketing strategy of the sponsors.

Finally, patients may be able to counter problems of the results of research not being put into practice.<sup>20</sup> Doctors might be slow to pick up on the results of important research, but patients alerted to results by active organisations are likely to pay much closer attention and to prompt their doctors to implementation.

One thing that may be important for achieving the full cooperation of patients in designing, conducting, reporting, and implementing the results of research may be to ensure that they are the first people to hear the results. Editors of medical journals have been one force preventing this happening because of their fear of results leaking out and appearing in the mass media before they appear in journals.<sup>21</sup>

### Early warning

But there is a precedent for announcing the results first to the participants of research. This is a tradition in occupational health research, and the *BMJ* and some other journals have reached an agreement with authors, employers, and trade unions that the results of research on the risks of working in nuclear establishments will be presented first to the workforce. This gives those people directly affected by the research (on, for instance, the chances of their children developing leukaemia) an opportunity to question those who have conducted the research. This is far better than hearing on the television news that your child has a greatly increased chance of developing leukaemia. The meeting between researchers and workers usually takes place early in the week of publication, and a similar model could be followed for the results of other research.

Both researchers and patients stand to benefit from well conducted research, particularly clinical trials, and they must not waste valuable energies fighting each other over such trials' design, conduct, and reporting. Ultimately, they have the same interests and must work together with mutual respect.

HEATHER GOODARE

Horsham,  
West Sussex RH13 6DF

RICHARD SMITH  
Editor

*BMJ*,  
London WC1H 9JR

Heather Goodare was a participant in the Bristol Cancer Help Centre study and has been active in the campaign to challenge its results.

- 1 Bagenal FS, Easton DF, Harris E, Chilvers CED, McElwain TJ. Survival of patients with breast cancer attending Bristol Cancer Help Centre. *Lancet* 1990;336:606-10.
- 2 Royal College of Physicians. *Research involving patients*. London: RCP, 1990.
- 3 Richards T. Death from complementary medicine. *BMJ* 1990;301:510-1.
- 4 Bodmer W. Bristol Cancer Help Centre. *Lancet* 1990;336:1188.
- 5 Charity Commission. *Findings of inquiry under section 8 Charities Act 1993. 1. Cancer Research Campaign. 2. Imperial Cancer Research Fund*. London: Charity Commission, 1994.
- 6 Smith R. Charity Commission censures British cancer charities. *BMJ* 1994;308:155-6.
- 7 Charity Commission. *Principles governing the funding of medical research by charities*. London: Charity Commission, 1994.
- 8 Hodgkinson L, Metcalfe J. *The Bristol experience*. London: Vermilion, 1995.
- 8a Brewin T. The Bristol experience. *BMJ* 1995;310:1341.
- 9 Martyn C. Medicine and the media. *BMJ* 1995;310:1338.
- 10 Chalmers I. What do I want from health researchers and researchers when I am a patient? *BMJ* 1995;310:1315-8.
- 11 Oliver SR. How can health service users contribute to the NHS R&D programme? *BMJ* 1995;310:1318-20.
- 12 Peckham M. Research and development for the National Health Service. *Lancet* 1991;338:367-71.
- 13 Breast cancer: clearing trails in the forest without losing our way. *Lancet* 1994;343:1049.
- 14 Henry D, Hill S. Comparing treatments. *BMJ* 1995;310:1279.
- 15 Koopmans PP. Registration of drugs for treating cancer and HIV infection: a plea to carry out phase 3 trials before admission to the market. *BMJ* 1995;310:1305-6.
- 16 Horton R. Errors admitted over falsified US cancer data. *Lancet* 1994;343:1029.
- 17 Rutherford AJ, Subak-Sharpe RJ, Dawson KJ, Margara RA, Franks S, Winston RML. Improvement of in vitro fertilisation after treatment with buserelin, an agonist of luteinising hormone releasing hormone. *BMJ* 1988;296:1765-8.
- 18 Chalmers I, Silverman WA. Professional and public double standards on clinical experimentation. *Control Clin Trials* 1987;8:388-91.
- 19 Pearn J. Publication: an ethical imperative. *BMJ* 1995;310:1313-5.
- 20 Haines A, Jones R. Implementing the results of research. *BMJ* 1994;308:1488-92.
- 21 Lowry S, Smith J. Duplicate publication. *BMJ* 1992;304:999-1000.