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Original Paper

Attitudes of Patients to Randomised Clinical Trials of Cancer Therapy

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The aim of this study was to test an instrument which might be useful for doctors in explaining the randomisation procedure to an individual patient. The sample comprised 323 patients with cancer attending for out-patient appointments and/or chemotherapy treatment in two major cancer centres in the U.K. 315 patients completed a self-report questionnaire—The Attitudes to Randomised Trials Questionnaire (ARTQ). The results show that the majority of subjects 287 (91.1%) believe that patients should be asked to take part in medical research, but only 242 (76.8%) would be prepared to take part in a study comparing two treatments. If treatment was randomised, only 141 (44.8%) would agree to participate. When given further information about the randomisation procedure, 119 (68.4%) of the 174 (55.2%) who initially said 'no' to randomisation or who were unsure, would change their minds and take part in a trial. The ARTQ discriminated between three categories of patient with the following prevailing attitudes: (a) those who seem comfortable with the concept of randomisation; (b) those with some concerns, who with fuller explanation are prepared to consider randomisation; and (c) those firmly against randomisation and participation in trials whatever information is provided. Prior knowledge of patients' attitudes might assist communication about trials and encourage more doctors to approach eligible patients.

Key words: clinical trials, randomisation, patients' attitudes
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INTRODUCTION

ALTHOUGH LARGE numbers of patients are eligible to participate, accrual in clinical trials of cancer therapy is very low [1]. This impedes the introduction and evaluation of new treatments. Recruitment difficulties arise from, and are exacerbated by, a variety of issues, which include the changing pressures on delivery of healthcare [2], concern about ethical and medico-legal issues [3], and attitudes of both patients [4, 5] and doctors [6–8]. Patients may decline entry into randomised clinical trials because of uncertainty about personal benefit [5], concerns as to whether or not the best available treatment would be given (although it has been shown that trial participation leads to better outcomes [9]) and overestimation of the likely therapeutic benefits of standard therapy [10]. Poor understanding about the value of clinical trials specifically, and experiments in medicine in general, produces suspicion and confusion among the general population [11, 12].

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Considerable ignorance exists about the meaning of randomisation. Many patients are worried about the process, preferring the doctor, whom they trust, to make treatment decisions rather than leaving them to a computer and the play of chance [13]. One study reported that 63% of patients refused entry into a trial because of their aversion to randomisation [5]. Even if a patient does agree to participate in a clinical trial, there is evidence that this consent is not always as informed or educated as it ought to be [14]. Many patients do not even recall that they are receiving experimental treatment [15–17].

There is evidence that most patients are generally altruistic and are willing participants in clinical trials if they are approached. Slevin and colleagues [18] reported that the most important aspects of trial participation, as ranked by patients, were: the likelihood of being treated by a doctor with a specialist interest in cancer, having progress closely monitored and contributing to research knowledge that benefits humanity. When patients were asked if they would take part in a research trial 42% said that they would, 10% said that they would not and 48% were uncertain. This study did not examine the specific question of randomisation.

There has been little study of the differing needs of patients for information, either in its amount or content. Patients can suffer from too much being said, as well as too little [19, 20]. Whatever a trial protocol may suggest, it is clear that many doctors make intuitive decisions about the disclosure of different sorts of information to individual patients about prognosis and therapeutic benefits expected from different treatment arms. They argue that adapting the information giving is done in the patient's best interests [21]. Despite the importance of the topic and the contentious debates in the literature [22, 23], this whole area is not well-informed by empirical studies. A more rational basis for determining how much and what sort of information needs to be given to *an individual patient* who is eligible for entry into a clinical trial is required [24] and cancer patients' preferences for different sorts of information have been published [25, 26].

The reluctance of clinicians to enter eligible patients into clinical trials may be a more limiting factor than patient reluctance to participate [8, 27, 28]. Barriers include practice constraints within the system of healthcare delivery [2], but inadequate training in communication skills contributes to difficulties when explaining randomisation. Giving complex information and obtaining informed consent were acknowledged by 178 senior oncologists attending communication skills courses to be their primary problem areas [29]. Some doctors perceive conflicts between the role of clinician and scientist [7, 8] and many express anxiety about the impact that the necessary disclosure of uncertainty might have on the doctor–patient relationship [6, 8, 27]. In a recently published survey of cancer clinicians' attitudes to clinical trials, a wide range of factors that influenced the willingness of doctors to approach eligible patients were identified. Doctors have idiosyncratic criteria, not only for disclosure of information, but also for deciding who they should approach about trial entry [8].

The present study was carried out to determine the attitudes of cancer patients to the concept of randomisation, and to ascertain whether, for those patients expressing unease, their attitude would be modified after further explanation. The longer term aim was to develop an instrument which might subsequently be useful for doctors in explaining randomisation to an individual patient.

MATERIALS AND METHODS

Questionnaire

The seven-item Attitudes to Randomised Trials Questionnaire (ARTQ) was constructed by three of the authors using information from the literature and comments made by colleagues and patients about their attitudes to trials and randomisation. When we were satisfied that the ARTQ was as brief as possible and had sufficient face validity to measure the concepts of interest, that is a positive or negative inclination toward (a) medical research in general, (b) a personal willingness to be involved in research and (c) research involving randomisation, we distributed it to approximately 50 people with and without cancer. People were asked to make comments about any confusing wording or terminology and the instrument was slightly modified before being piloted on a further sample of approximately 50 patients in oncology outpatient clinics at University College Hospitals, London to check its comprehensibility, ease of administration and acceptability to patients. The final version of the questionnaire used is shown in Table 1.

In this paper, we report the results of a survey of a different sample of 323 patients with cancer. The aim was to determine prevailing attitudes to randomisation in clinical trials with the intention of incorporating this information into a future intervention trial to encourage more clinicians to approach eligible patients and to increase satisfaction of both patients and clinicians with the consultation.

Sample

The questionnaire was given to a consecutive sample of 323 patients with cancer attending clinics at two major cancer centres, University College Hospitals and the Royal Marsden. An information leaflet informed patients that they were being asked to help with the development of a questionnaire to be used in a future study about doctor–patient communication. 315 patients completed the ARTQ, unassisted. 6 patients refused to participate and 2 patients were unable to complete questionnaires due to poor eyesight. 100 (31.7%) patients had previous experience of having been in a trial, 194 (61.6%) were trial naive; information about the trial experience of 21 (6.7%) was unavailable. The range of cancer sites of patients is shown in Table 2 and the age and sex distribution in Table 3. These patients represent a broad cross-section of unselected patients attending several clinics in the two centres. The distribution of cancers was somewhat unusual, with an excess of bone and testicular cancer, reflecting the specialised nature of some of the clinics. This also meant that a large number of patients were less than 45 years of age. The sample comprised patients who had relapsed and those who had not. Some were attending for their first appointment at an oncology clinic, others for routine follow-up visits and prechemotherapy consultations. It was not necessary for patients to be eligible for trial entry themselves when approached to take part in the study. The data collected were analysed using a standard SPSS package.

RESULTS

The responses to Questions 1–3 of those patients who were known to have had previous trial experience (100), those who were known to be trial naive (194), and for the total group (315), are shown in Figure 1. Overall, 287 (91.1%) patients said yes to the question 'Do you think that patients should be asked to take part in medical research?', 8 (2.5%) said no and 20 (6.3%) did not know (Figure 1).

Patients were given the information 'Suppose that you were asked to take part in a research study comparing two treatments, both of which were suitable for your illness' and were then asked 'Would you be prepared to take part in a study comparing different treatments?', 242 (76.8%) said that they would, 26 (8.3%) said no and 47 (14.9%) did not know (Figure 1b).

Next, patients were told 'Usually the only scientific way to compare one treatment with another is for the choice between the two to be made randomly, rather like tossing a coin', then asked 'Would you take part in a study where treatment was chosen at random?'. 141 (44.8%) would agree, 92 (29.2%) would not and 82 (26%) did not know (Figure 1c).

There were no statistically significant differences between the responses of men and women, nor between the different age groups. However, more of the patients without previous clinical trial experience (i.e. 72/194) would not agree to participate in a randomised trial ($\chi^2 = 18.8$, df = 2, $P = 0.00008$); Table 4).

Table 1. *The Attitudes to Randomised Trials Questionnaire (ARTQ)*

Patient Attitudes to Trials Questionnaire

CONFIDENTIAL ID.....

Please tick one of the boxes

(1) Do you think that patients should be asked to take part in medical research? Yes ☐ No ☐ Do Not Know ☐

Suppose that you were asked to take part in a research study comparing two treatments, both of which were suitable for your illness.

(2) Would you be prepared to take part in a study comparing different treatments? Yes ☐ No ☐ Do Not Know ☐

Usually the only scientific way to compare one treatment with another is for the choice between the two to be made randomly, rather like tossing a coin.

(3) Would you be prepared to take part in a study where treatment was chosen at random? Yes ☐ No ☐ Do Not Know ☐

.....

CONFIDENTIAL ID.....

You answered "No" or "Do not know" to Question 3, so we would now like to ask you a bit more about this. (Please tick one of the boxes)
In a randomised study a choice would be made between two treatments, either of which would be suitable for you. Your doctor and experts in the field do not know for sure if one treatment is better than the other, or if they are both the same, that's why they want to do the study.

(4) Would knowing that encourage you to take part? Yes ☐ No ☐ Do Not Know ☐

In a random choice study, if the treatment you were receiving did not suit you for any reason you could always leave the study. Your doctor would then give you whatever other treatment might be appropriate for you.

(5) Would that encourage you to take part? Yes ☐ No ☐ Do Not Know ☐

Before you agreed to enter a random choice study the doctor would tell you all about the two treatments being compared, before you were allocated one or the other.

(6) Would that encourage you to take part? Yes ☐ No ☐ Do Not Know ☐

If you knew that the following were taken into account
(a) that either treatment was completely suitable;
(b) that you could leave the study if the treatment did not suit you;
(c) that there is plenty of information before the random choice was made;

(7) Would all these things together mean that you would change your mind and agree to take part? Yes ☐ No ☐ Do Not Know ☐

We would like to know if there is any other information you would like to have before making a decision on whether to take part in a study.

.....

.....

Thank you very much for your help

Table 2. *Summary of patients by cancer site* (n = 315)

Site	n (%)
Bone	29 (9.2)
Breast	70 (22.2)
Cervix	12 (3.8)
Colorectal	10 (3.2)
Lung	15 (4.8)
Haematological	17 (5.4)
Ovary	12 (3.8)
Prostate	61 (19.4)
Testicular	66 (21.0)
Other	23 (7.3)

Table 3. *Summary of patients by age group and sex (*n = 307, 8 *missing cases)*

Age group (years)	Male n (%)	Female n (%)
< 25	15 (8.6)	4 (3.0)
25–44	63 (36.0)	26 (19.7)
45–64	36 (20.6)	72 (54.5)
> 65	61 (34.9)	30 (22.7)

Questions 4–7 were completed by most of the 174 patients who answered either 'no' or 'do not know' to Question 3 (Table 5). When given the information that 'The random choice would be made between two treatments, either of which would be suitable for your case. Your doctor and experts in the field don't know for sure if one treatment is better than the other, or if they are both the same, that's why they want to do the study', 115 (66%) of the previous dissenters and those not sure said they would now feel encouraged to take part. Knowledge that 'In a random choice study if the treatment you were receiving did not suit you for any reason you could always leave the study. Your doctor would then give you whatever other treatment might be appropriate for you' would encourage 125 (73.1%) to participate.

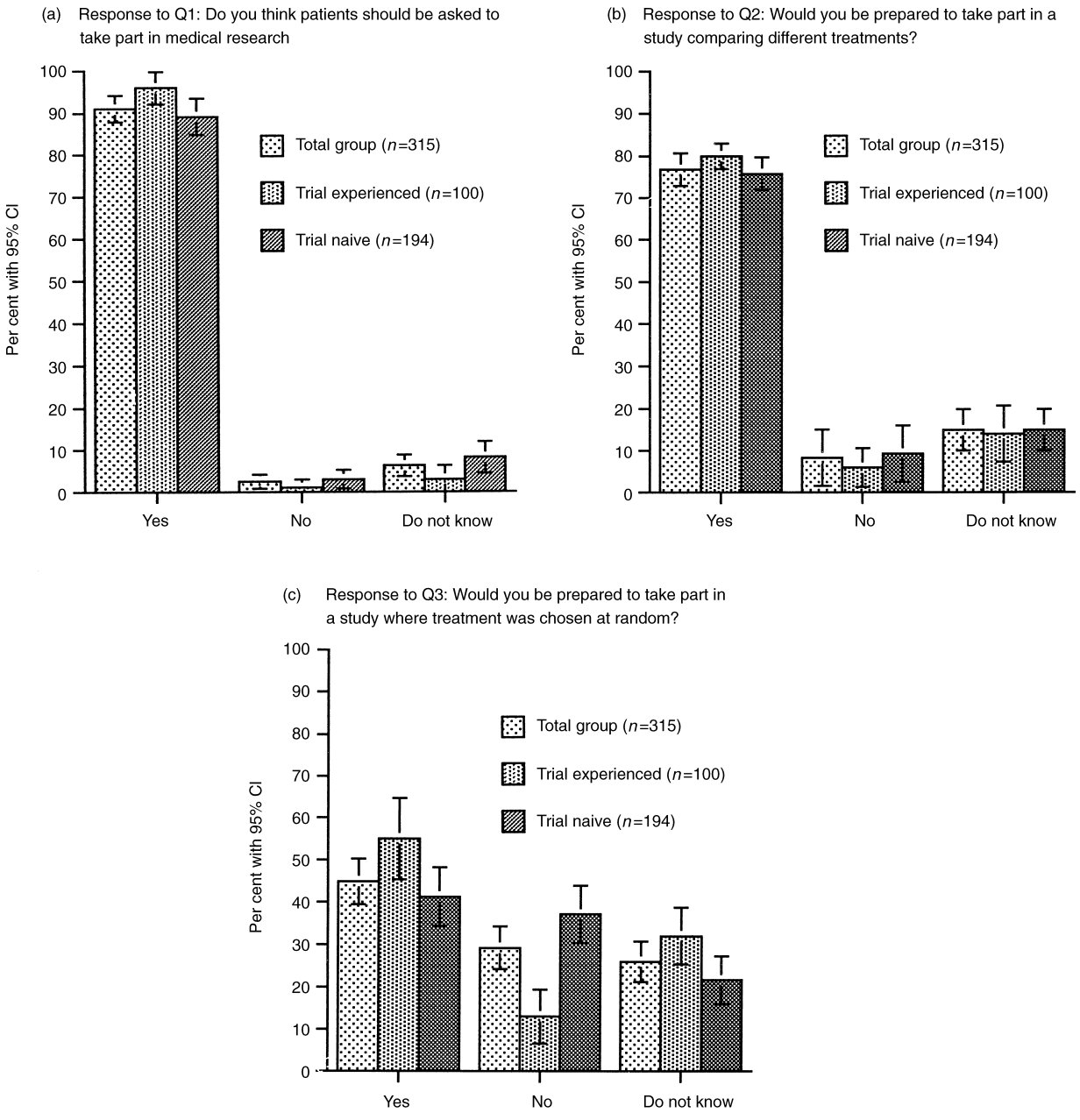

Figure 1. The responses of patients to (a) Question 1, (b) Question 2 and (c) Question 3 of the Attitudes to Randomised Trials Questionnaire (ARTQ).

Awareness that 'Before randomisation the doctor would tell you all about the two treatments being compared before you were allocated one or the other' would encourage 132 (76.3%) to take part.

Patients were then asked if the knowledge that (a) either treatment was completely suitable, (b) that they could leave the study if the treatment did not suit and (c) plenty of information would be given about both treatments before the random choice was made, would make them change their minds and take part in a trial. 119 (68.8%) of the previous dissenters and those uncertain would change their minds.

In conclusion, 260/315 (82.5%) patients would agree to take part in a randomised clinical trial, 21/315 (6.6%) were uncertain and 33/315 (10.5%) would not participate, whatever information was provided. In contrast to Questions 1–3, there were no apparent differences in responses to Questions 4–7 between those patients with previous trial experience and those without. It is recognised, however, that the numbers are too small in these subgroup analyses and confidence intervals too wide for adequate statistics and satisfactory conclusions to be drawn.

DISCUSSION

Our results show that of the total population of 315 patients, 141 (44.8%) would agree to take part in a randomised trial, 92 (29.2%) would not and 82 (26%) were uncertain. When further explanation about the implication of the trial was given in the form of three statements to the 174 patients who refused or did not know, 119 (68.4%) changed their minds and agreed and 55 (31.6%) would not or

Table 4. *Contingency table showing responses to Question* 3, *according to previous trial experience (*21 *missing cases)*

Responses	Trial experienced ($n = 100$)	Trial naïve ($n = 194$)
Yes	55 (55%)	80 (41.2%)
No	13 (13%)	72 (37.1%)
Do not know	32 (32%)	42 (21.6%)

remained uncertain. Thus, of the total population, 260 (82.5%) would agree to take part in a randomised clinical trial, 21 (6.6%) were unsure and 33 (10.5%) would not participate whatever information was provided.

Although the population is not completely typical of cancer in general, we have no reason to suppose that these findings would not be generalisable to other populations of patients, at least in the U.K. Previous trial participation appeared to influence willingness to participate in further randomised trials. The difference was not great, and may reflect greater familiarity with and less concern about the concept of randomisation. It is of course unclear how much information the previously trial experienced had been given. Nor is it known whether or not those who had been involved in a trial before, but who now said 'no' to Question 3, would be reluctant to participate because of a bad experience or because they had never understood the experimental nature of their previous treatment.

The ARTQ, therefore, discriminated between three categories of patients: (a) those who appear comfortable with the general concept of randomisation; (b) those who are worried initially, but do not have fixed views and after a fuller explanation seem prepared to consider randomisation; (c) those who are firmly against participation in randomised trials whatever information is given. The ARTQ does not have a score as such, but is a useful tool that allows the clinician to see at a glance where the patients' primary areas of difficulty may lie. This might prove to be useful information, if known in advance. Patients who were entirely comfortable with randomisation would be identified and the doctor could move on to explanations more specific to the trial. They would also know which patients were unlikely to accept trial entry whatever information was given. Indeed it might be considered as unethical to attempt to dissuade such patients from a clearly expressed refusal to randomisation. Other patients will require particular, and more specific, details and explanations and the doctor would be able to devote more time to these areas. Some randomised trials, especially those with a major difference in policy, are difficult to explain to patients independent of the issue of randomisation. The ARTQ will not help with this aspect, but may nonetheless assist a difficult discussion by clarifying whether the patient has problems with the concept of accepting experimental therapy in general or of randomisation in particular.

Some patients, who had doubts initially about trial participation, took the opportunity to write further questions and concerns on their questionnaires, providing the clinician potentially with additional opportunities to tailor information giving appropriately to the individual. Ethicists might argue that all patients should always receive the same information, but in practice this rarely happens [30]. We stress that we are not advocating the withholding of information about randomisation, or refusing to provide patients with sufficient information leaflets or access to further discussion; we simply hope that we are providing, via the ARTQ, a more logical basis for identifying patients for whom different levels of information may be desired.

Previous work has demonstrated that the Patient Preference for Information Questionnaire discriminates quickly and easily the amount of information patients require about their cancer and its treatment in general [25, 26]. The efficacy and utility of this instrument, together with the ARTQ, in helping doctors feel more comfortable about approaching eligible patients and in improving patient satisfaction with the consultation when trials are discussed, should now be compared with the standard methods of discussion in order to determine its usefulness.

Table 5. *Responses* n *(%) to Questions* 4–7 *by patients* (n = 174) *who said no or who were uncertain to question* 3

Question	Yes	No	Do not know
Question 4 In a randomised study a choice would be made between two treatments, either of which would be suitable for you. Your doctor and experts in the field do not know for sure if one treatment is better than the other, or if they are both the same, that's why they want to do the study. Would knowing that encourage you to take part?*	115 (66.9)	26 (15.1)	31 (18)
Question 5 In a random choice study, if the treatment you were receiving did not suit you for any reason you could always leave the study. Your doctor would then give you whatever other treatment might be appropriate for you. Would knowing that encourage you to take part?†	125 (73.1)	27 (15.8)	19 (11.1)
Question 6 Before you agreed to enter a random choice study the doctor would tell you all about the two treatments being compared, before being allocated to one or other. Would knowing that encourage you to take part?‡	132 (76.3)	23 (13.3)	18 (10.4)
Question 7 If you knew that the following were taken into account: (a) that either treatment was completely suitable; (b) that you could leave the study if the treatment did not suit you; (c) that there is plenty of information before the random choice is made Would all these things together mean that you would change your mind and agree to take part?‡	119 (68.8)	33 (19.1)	21 (12.1)

*2 patients omitted; †3 patients omitted; ‡1 patient omitted.

1. Ward LC, Fielding JWL, Dunn JA, Kelly KA. The selection of cases for randomised trials: a registry survey of concurrent trial and non-trial patients. *Br J Cancer* 1992, **66**, 943–950.
2. Smyth, JF, Mossman J, Hall R, *et al.* Conducting clinical research in the new NHS. *Br Med J* 1994, **309**, 457–461.
3. Collins R, Doll R, Peto R. Ethics of clinical trials. In Williams C, ed. *Introducing New Treatments for Cancer. Practical, Ethical and Legal Problems*. Chichester, John Wiley & Sons, 1992.
4. Wingerson D, Sullivan M, Dager S, Flick S, Dunner D, Roy-Byrne P. Personality traits and early discontinuation from clinical trials in anxious patients. *J Clin Psychopharmacol* 1993, **13**, 194–197.
5. Llewellyn-Thomas HA, McGreal MJ, Theil EC, Fine S, Erlichman C. Patients' willingness to enter clinical trials: measuring the association with perceived benefit and preference for decision participation. *Social Sci Med* 1991, **32**, 35–42.
6. Taylor KM, Kelner MJ. Interpreting physician participation in randomised clinical trials: the Physician Orientation Profile. *J Health Soc Behav* 1987, **28**, 389–400.
7. Taylor KM, Feldstein ML, Skeel RT, Pandya KJ, Ng P, Carbone PP. Fundamental dilemmas of the randomised clinical trial process: results of the 1,737 Eastern cooperative oncology group investigators. *J Clin Oncol* 1994, **12**, 1796–1805.
8. Fallowfield LJ, Ratcliffe D, Souhami RL. Clinicians attitudes to clinical trials of cancer therapy. *Euro J Cancer* 1997, **33**, 2221–2229.
9. Van Dongen JA, van de Velde CJ. The benefits of participation in clinical trials. *Eur J Surg Oncol* 1996, **22**, 561–562.
10. Sheldon JM, Fetting JH, Siminoff LA. Offering the option of randomised clinical trials to cancer patients who overestimate their prognoses with standard therapies. *Cancer-Invest* 1993, **11**, 57–62.
11. Raphael A. How doctors' secret trials abused me. *Observer*, London, 1988.
12. Toynbee P. Random clinical trials are one of life's biggest gambles. *BMA News Review* 12 March 1997, 50.
13. Gotay CC. Accrual to cancer clinical trials: directions from the research literature. *Social Sci Med* 1991, **33**, 569–577.
14. Montgomery C, Lydon A, Lloyd K. Patients may not understand enough to give their informed consent. *Br Med J* 1997, **314**, 1482.
15. Sutherland HJ, Lockwood GA, Till J. Are we getting informed consent from patients with cancer. *J R Soc Med* 1990, **83**, 439–443.
16. Penman DT, Holland JC, Bahna GF, Morrow G, Schmale AH, Derogatis LR. Informed consent for investigational chemotherapy: patients and physicians' perceptions. *J Clin Oncol* 1984, **2**, 849–855.
17. Mackillop WJ, Stewart WE, Ginsburg AD, Stewart SS. Cancer patients' perceptions of their disease and its treatment. *Br J Cancer* 1988, **58**, 355–358.
18. Slevin M, Mossman J, Bowling A, *et al.* Volunteers or victims: patients' views of randomised cancer clinical trials. *Br J Cancer* 1995, **71**, 1270–1274.
19. Simes RJ, Tattersall HHN, Coates AS, Raghavan D, Solomon HJ, Smartt H. Randomised comparison of procedures for obtaining informed consent in clinical trials of treatment for cancer. *Br Med J* 1986, **293**, 1065–1068.
20. Tobias JS, Souhami RL. Fully informed consent can be needlessly cruel. *Br Med J* 1993, **307**, 1199–2001.
21. Lynoe N, Sandlund M, Jacobsson L. Clinical cancer research—some aspects on doctors' attitudes to informing participants. *Acta Oncol* 1996, **35**, 749–754.
22. Doyal L. Informed consent in medical research—a response to recent correspondence. *Br Med J* 1998, **316**, 1000–1001.
23. Tobias JS. Informed consent in medical research. Changing the BMJ's position on informed consent would be counterproductive. *Br Med J* 1998, **316**, 1001–1002.
24. Baum M, Houghton J. Confirmed dissent and informed consent. *Eur J Cancer* 1993, **29A**, 295–296.
25. Fallowfield LJ, Ford S, Lewis S. No news is not good news: information preferences of patients with cancer. *Psycho-Oncol* 1995, **4**, 197–202.
26. Meredith C, Symonds P, Webster L, *et al.* Information needs of cancer patients in the West of Scotland. *Br Med J* 1996, **313**, 724–726.
27. Mackillop WE, Palmer MJ, O'Sullivan B, Ward GK, Steele IR, Dotsikas G. Clinical trials in cancer: the role of surrogate patients in defining what constitutes an ethically acceptable clinical experiment. *Br J Cancer* 1989, **59**, 388–395.
28. Tannock IF. The recruitment of patients into clinical trials. *Br J Cancer* 1995, **71**, 1134–1135.
29. Fallowfield LJ, Lipkin M, Hall A. Teaching senior oncologists communication skills: results from phase 1 of a comprehensive longitudinal program in the UK. *J Clin Oncol* 1998, **16**, 1961–1968.
30. Williams CJ, Zwitter M. Informed consent in European multicentre randomised clinical trials—are patients really informed? *Eur J Cancer* 1994, **30A**, 907–1000.

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