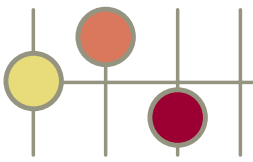

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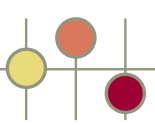

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REPORT 31

SYSTEMATIC REVIEW OF BARRIERS, MODIFIERS AND BENEFITS INVOLVED IN PARTICIPATION IN CANCER CLINICAL TRIALS

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March 2006

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ISBN 1 900640 38 4

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The Centre for Reviews and Dissemination is funded by the NHS Executive and the Health Departments of Wales and Northern Ireland. The views expressed in this publication are those of the authors and not necessarily those of the NHS Executive or the Health Departments of Wales or Northern Ireland.

Printed by York Publishing Services Ltd.

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ACKNOWLEDGEMENTS

Contributions of authors

Debra Fayter	Lead reviewer responsible for writing the protocol, study selection, data extraction, validity assessment and writing the final report.
Catriona McDaid	Involved in study selection, data extraction, validity assessment and writing the final report.
Gill Ritchie	Devised the search strategy and carried out the literature searches; wrote the search methodology sections of the report.
Lisa Mather	Provided assistance with the searches.
Alison Eastwood	Provided input at all stages, commented on various drafts of the report; overall responsibility for the report.

Source of funding

This review was produced as part of CRD's role in the National Cancer Research Network (NCRN) Co-ordinating Centre supporting the work of the National Cancer Research Institute Clinical Study Groups.

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EXECUTIVE SUMMARY

Aim

Our aim was to undertake a systematic review of the relevant literature relating to the barriers, modifiers and benefits involved in participating in randomised controlled trials of cancer therapies as perceived by health professionals and patients.

Methods

A scoping review was conducted to identify existing systematic reviews in the area of patient participation in clinical trials. Potentially relevant reviews were identified, data extracted and quality assessed. On assessment of the methodology of the existing reviews it was felt that Prescott et al[1] was sufficiently rigorous to form a basis for the early research literature (searches ended in 1996). Once the full search strategy for primary studies had been agreed a range of databases were searched from 1996. Unpublished research or research published within grey literature was sought, clinical experts were contacted and bibliographies of retrieved articles were examined. There was no restriction of study by country of origin, or language.

Studies that aimed to identify barriers to, moderators of and benefits arising from participation in randomised controlled trials in cancer from the physician or patient perspective were included. All study designs were acceptable provided relevant outcomes were reported. Included papers were assessed for methodological quality using instruments appropriate to the study design. Two reviewers were involved in the selection of studies, data extraction and quality assessment processes, with any disagreements resolved by a third reviewer. Findings are reported as a narrative summary and in tabular form with full data extraction tables and quality assessment tables included in appendices. Studies are grouped according to their perspective (healthcare professional or patient) and whether they describe recruitment to real trials or attitudes to recruitment to trials in general.

Results

A total of 12,816 references were identified from literature searches with 56 studies published in 58 papers finally selected for inclusion in the review. The included studies represented both the patients' and the health professionals' perspectives. The health professionals in these studies included doctors, nurses and Clinical Research Associates.

Several themes emerged from the research literature. From the patient perspective there were issues of treatment preference and the uncertainty patients feel about participating in trials. The role of knowledge and information was examined as was the need to time the request for trial participation more carefully. A range of sociodemographic and practical barriers to trial participation were identified alongside issues concerning the benefits of participating in trials. From the health professional perspective a range of system-related and organisational barriers were identified, barriers inherent in a trial's design and barriers connected with the attitudes of individual health professionals.

Although a range of barriers to trial participation were identified, a number of threats to the internal and external validity of the included studies limited interpretation of the evidence. In particular it was found that the issues identified in many of the studies could be, at least partially, an artefact of the research design, the methods of data collection or data analysis.

Conclusions

The methodological limitations of the primary studies identified by this review do not allow a clear interpretation of the barriers, moderators and benefits involved in trial participation as perceived by patients and health professionals. It is necessary to be cautious in stating what is and is not a barrier to trial participation. Instead it is concluded that the particular interplay of barriers, modifiers and benefits relevant to participation in cancer trials needs to be prospectively identified by trialists in the light of the themes identified in the literature. Checklists to guide this process are included in this report.

1. INTRODUCTION

1.1 Background to the project

As part of its role in the National Cancer Research Network (NCRN) Co-ordinating Centre, CRD has been supporting the National Cancer Research Institute (NCRI) Consumer Liaison Group. This report is part of a wider project investigating barriers to participation in cancer clinical trials and how these might be overcome. The three stages of the project were:

1. To undertake a systematic review of the relevant literature relating to the barriers to and benefits of participating in clinical trials in cancer as perceived by patients and health professionals.
2. To undertake a systematic review on interventions to increase participation in cancer clinical trials.
3. To ascertain whether interventions identified in part 2 could be effectively implemented on a large scale to the wider public. This phase was not conducted due to the lack of effective interventions identified in part 2.

This document forms the report for the systematic review undertaken as the first part of the project. The review was undertaken in accordance with CRD's Guidelines for Undertaking Systematic Reviews (http://www.york.ac.uk/inst/crd/report4.htm).

1.2 Participation in clinical trials

Clinical trials are an essential tool for the evaluation of medical technologies. The randomised controlled trial in particular is seen as the 'Gold Standard' for clinical research. It is crucial that sufficient numbers of participants are recruited to trials to enable high quality research to be undertaken and new and existing treatments thoroughly tested. If there are problems recruiting to a specific trial, sample size may not be achieved and the statistical power of the trial to detect an effect will be reduced. 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.[2] 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.

Although there is evidence that recruitment of children into clinical trials of cancer is generally high,[3] adult participation in clinical trials of cancer treatments is low.[2] In the UK it currently stands at 10.9% of incident cancer cases.[4] Also of concern is the low participation of ethnic minority groups in cancer trials.[5] There is clearly, then, a need to understand why both health professionals and patients may be reluctant to take part in trials of cancer treatments.

Understanding the decision to participate or decline participation in a clinical trial begins by identifying the barriers to trial participation. Once barriers are identified it may be possible to develop interventions to overcome such barriers. However the decision to participate in a trial also reflects perceived benefits of participation and it is important to identify such benefits and other aspects that might modify the decision to participate in a trial. By examining the barriers, modifiers and benefits of participating in cancer clinical trials we should be taking the first step towards increasing participation rates.

1.3 Barriers to participation

The problem of low participation in trials has been investigated from both a quantitative and qualitative point of view using a range of study designs.[6] Non-participation in clinical trials has been found to comprise several issues: patients not meeting eligibility criteria; lack of awareness of trials on the part of patients and health professionals; health professionals choosing not to offer or to enter patients for trials and patients choosing not to participate. A body of research exists that examines the benefits of and barriers to participation in trials from both the perspective of the patient and the health professional.[7]

In addition to the primary research, a number of reviews have been conducted in the broad area of participation in clinical trials.[1, 6-10] The relationship between these reviews and the existing review is discussed in section 2.2 of the Methods section.

2. METHODS

2.1 The study question

Our aim was to undertake a systematic review of the relevant literature relating to the barriers, modifiers and benefits involved in participating in RCTs of cancer therapies as perceived by health professionals and patients.

Using a systematic approach aids reflection on study methods that may distort, misrepresent or fail to pick up people's views.[11] Therefore an integral part of our review was to appraise the methods used by researchers to determine the issues involved in participating in RCTs of cancer treatments.

2.2 Previous systematic reviews

A scoping review was conducted to identify existing systematic reviews in the area of patient participation in clinical trials. An initial search for systematic reviews was carried out on the following databases: Cochrane Database of Systematic Reviews (CDSR), Cochrane Database of Methodology, Database of Abstracts of Reviews of Effects (DARE), Health Technology Assessment Database (HTA), National Coordinating Centre for Health Technology Assessment Database, TRIP Database Plus and the Ongoing Reviews Database (see Appendix 1 for details of the search strategy).

Four potentially relevant reviews were identified.[1,6,7,9] One review was concerned with interventions to encourage participation in trials and was found to be most relevant to the second part of the NCRN project.[9] The remaining reviews [1,6,7] were data extracted and quality assessed. Cox et al[6] was considered to be a non-systematic literature review. A comparison was made between the systematic reviews of Ward[7] and Prescott et al[1]. Differences in their inclusion criteria and search strategies were assessed. Review authors were contacted to obtain more information on the reviews, to check for any possible updates and to learn of any other reviews that might be in existence. Replies indicated that none of the reviews were currently being updated and no other significant reviews were identified. Whilst searching for primary studies for this review two further literature reviews were identified.[8,10]

On assessment of the methodology of the existing reviews it was felt that Prescott et al[1] was sufficiently rigorous to form a basis for the early research literature (searches ended in 1996). This Health Technology Assessment (HTA) systematic review explored a range of factors that limit the quality, number and progress of RCTs most of which were beyond the scope of our review. However it included the identification of barriers to participation in trials from both a patient and health professional viewpoint. In this review the barriers identified from the health professional viewpoint were: time constraints, lack of staff and training, worry about the impact on the doctor-patient relationship, concern for patients, loss of professional autonomy, difficulty with the consent procedure, lack of rewards and recognition and an insufficiently interesting research question. From the patients' perspective barriers were the additional demands of being involved in a trial, patient preference for a particular treatment (or no treatment), worry about uncertainty of treatment or trials, as well as concerns about information and consent. The review identified the clinician as a barrier to patient participation in several ways: by the protocol causing problems with recruitment (incompatibility with normal practice), clinician concerns about information provision to patients, and the clinician influencing the patient's decision not to join a trial. However the review was not restricted to cancer patients. In our review we were particularly interested to ascertain whether we would find similar barriers to participation in cancer trials and whether the barriers identified would have changed since the Prescott et al review.[1]

2.3 Search strategy

The search strategies of the existing reviews identified were examined to determine their relevance to the current review. After consideration, Medical Subject Headings (MeSH) indexing terms and keywords were used from two reviews[1,6] but the strategy was developed independently (see Appendix 2).

The search strategy proved problematic and initial searches retrieved high numbers of irrelevant records (for example any study making a passing reference to the enrolment of patients in a trial). The strategy was adapted several times, the results examined by the review team, and decisions made about which search terms to exclude and which should remain.

Once the full search strategy had been agreed the following medical and social science databases were searched: MEDLINE, EMBASE, CINAHL, PsycINFO, ISI Science Citation Index, ISI Social Science Citation Index, Sociological Abstracts, and ASSIA. In addition unpublished research or research published within grey literature was sought by searching the following resources: SIGLE (System for Information on Grey Literature in Europe) and HMIC (Health Management Information Consortium).

All searches were conducted from 1996 following the previous HTA review.[1] There was no restriction of study by country of origin, or language. Attempts to identify further studies were made by contacting clinical experts and examining the bibliographies of all retrieved articles. The results of the searches were transferred into Endnote 5 bibliographic management software and de-duplicated.

2.4 Inclusion and exclusion criteria

Studies that aimed to identify barriers to, moderators of and benefits arising from participation in RCTs in cancer were included. Included participants were adults or children with a diagnosis of cancer of any site and stage. Studies that included cancer patients in addition to other patient groups were included if data were reported separately. Those aimed at the general population discussing hypothetical participation in trials were excluded. Studies relating to barriers to, modifiers of or benefits of health professional involvement in clinical trials were included. Studies that examined participation solely in Phase I and II cancer trials were excluded. However where studies included randomised trials in addition to earlier phase studies these were included but highlighted as such. Studies that discussed interventions to address barriers or benefits were to be assessed in the second part of the project.

All study designs were acceptable with the exception of expert opinion, letters containing no outcome data and editorials and discussion papers reporting no outcomes. No language or cultural restrictions were applied but barriers to participation that might only apply to a given cultural context were highlighted as such.

2.5 Study selection

The titles and, where available, abstracts of articles were scanned for relevance independently by two reviewers according to the criteria described above. Discrepancies between reviewers were resolved through discussion and, where necessary, by consultation with a third reviewer. Full papers of identified studies were then assessed for relevance in the same way.

2.6 Data extraction

Data extraction was piloted to determine the level of detail required and to ensure consistency. Full data extraction was performed by one reviewer and checked by a second reviewer. Discrepancies between reviewers were resolved through discussion and, where necessary, by consultation with a third reviewer. Where a study was reported in abstract or letter-form only, data extraction was completed as far as possible. Data extraction was carried out using MS Access.

2.7 Validity assessment

Included papers were assessed for methodological quality using instruments appropriate to the study design. Surveys (and chart reviews that included some form of patient or health professional survey) were assessed using Crombie's checklist[12] (see Appendix 3). Qualitative studies were assessed using the CASP tool[13] (see Appendix 4). Chart reviews with no element of survey and reports of specific trials were assessed, where possible, based on their design, methods of data collection, analysis and interpretation. Validity assessment was performed by

one reviewer and checked by a second reviewer. Discrepancies between reviewers were resolved through discussion and, where necessary, by consultation with a third reviewer.

2.8 Analysis and synthesis

Findings are reported as a narrative summary and in tabular form with full data extraction tables and quality assessment tables included in appendices. Studies were grouped according to their perspective (health professional or patient) and according to whether they described recruitment to a real trial or described attitudes to cancer trials in general.

3. RESULTS

3.1 Overview of included and excluded studies

A total of 12,816 references were identified from literature searches. All references were screened by two reviewers and 289 full papers were ordered for further consideration (including 13 identified from checking the references of identified studies). A total of 56 studies published in 58 papers were selected for inclusion in the review (see Figure 1).

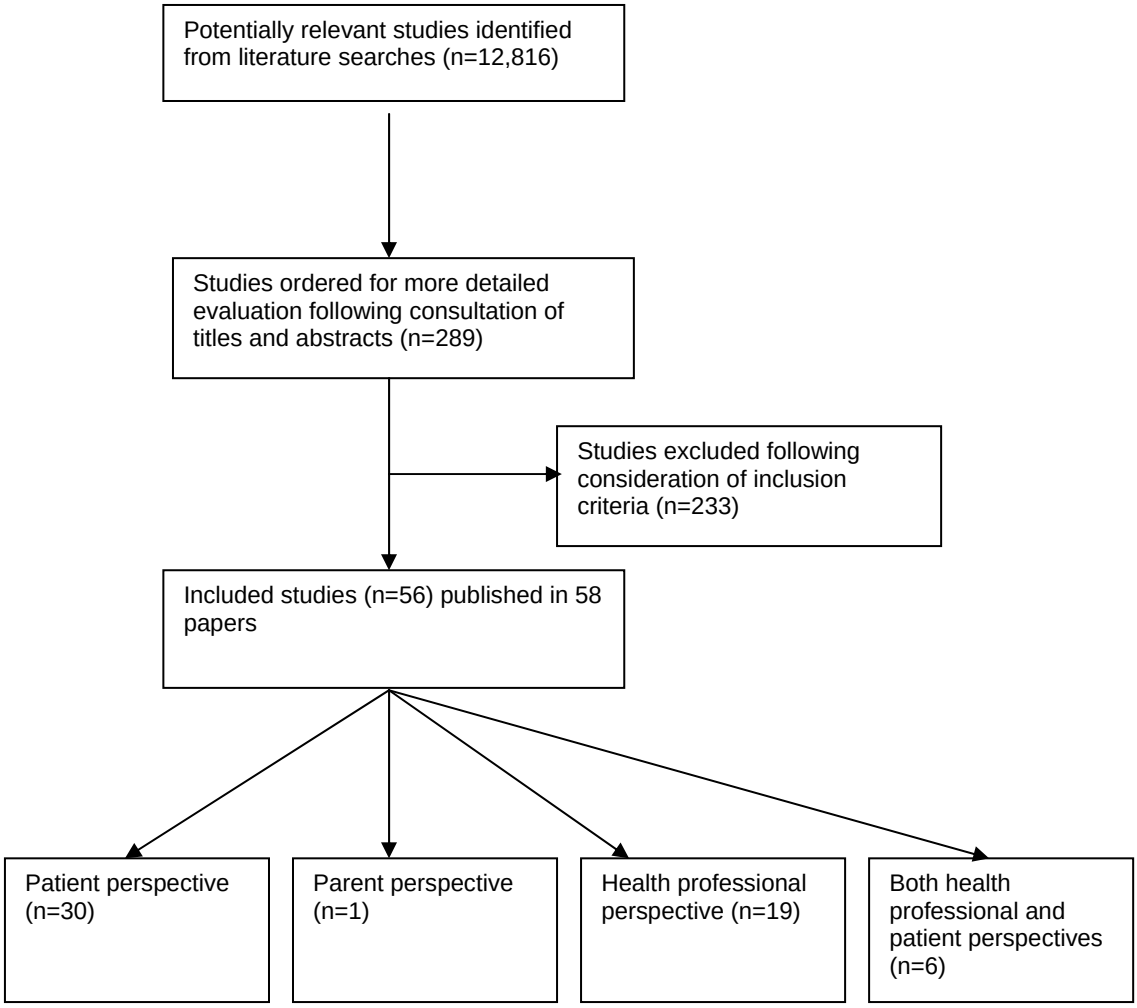

Figure 1

As can be seen from the figure, both the views of the patient and health professional are represented in the literature. The health professionals in these studies were doctors, nurses and Clinical Research Associates. The literature is international. Fourteen studies were conducted in the UK, six elsewhere in Europe, four in Australia, four in Canada, one was multinational and 27 were conducted in the US. Where findings may be culturally specific this has been highlighted.

Some studies were conducted only with patients with a given cancer type, such as breast cancer or prostate cancer, whilst others were conducted in patients with a variety of diagnoses. Stages of cancer differed between studies. Where these issues may have impacted on results we have noted this.

Studies were of varying types and included trial reports, observational studies, chart reviews, surveys and qualitative studies. Studies were quality assessed according to study type where possible. Four studies could not be quality assessed as they were too briefly presented in letter or abstract form.[14-17]

Included studies examined a range of benefits of trial participation as perceived by the patient. These included such concepts as 'to benefit oneself and others', 'to find a cure', 'to further research' and 'to have the latest (and best) treatment' (not an exhaustive list). A range of modifiers to trial participation, including both sociodemographic and clinical aspects, has been explored including: age, race, educational level, cancer site and stage, perception of the health professional and previous participation in trials. A range of barriers which might actively discourage participation in a trial are examined including: the uncertainty involved in trials, treatment allocation and randomisation, treatment preference, clinical equipoise and practical barriers such as transport, cost and time.

Although a range of barriers to trial participation were identified, a number of threats to the internal and external validity of the included studies limited interpretation of the evidence. Such limiting factors are described in more detail within the following sections.

The results section of this report synthesises the themes identified in the included studies. Full details of all 56 studies, including quality assessments, are presented in Appendices 5 and 6. Those studies that were only available in letter or abstract form have been extracted as far as possible.

A list of excluded studies is available from the authors. Briefly, of the 233 considered studies, reasons for exclusion were as follows (not mutually exclusive): did not discuss barriers or benefits of participating in cancer clinical trials (144), were not undertaken with cancer patients (151) or did not report barriers to participating in RCTs (149).

3.2 Patient perspective

Thirty-seven studies provided usable data on participation in trials from a patient's perspective. Thirty studies investigated a patient's decision to participate in a real trial or trials [14-16,18-44] whilst seven studies examined attitudes to trials in general.[45-51] As the seven studies represent hypothetical scenarios and may not reflect a patient's decision when faced with a real trial these studies are grouped separately.

3.2.1 Studies investigating accrual to real trials

3.2.1.1 Study characteristics

As can be noted from Table 1, a wide range of study designs have been used to address the issue of trial participation. Where stated, chart reviews ranged in size from 152 to 6906 participants and surveys had between 88 and 276 participants. A small number of qualitative studies, a case-control study and two trial reports also contributed to the literature. The majority of studies included both those who had accepted and those who had refused participation in a trial. Studies either focused on the general barriers to recruitment associated with a particular trial, on a particular issue such as health professional communication or on general barriers to recruitment at a particular cancer centre or location.

Ten studies investigated barriers to participation in trials of breast cancer treatments.[15,18,19,24,29,34,37,39,41,42] Other cancer sites included prostate cancer, melanoma, lung cancer, gynaecological cancers, patients with various diagnoses and palliative care. One study considered the views of parents whose children had cancer.[44] Two studies specifically considered the recruitment of patients from ethnic minorities but neither was conducted in the UK.[18,25]

Table 1

Study, Country	Trial / issues being evaluated	Study design
Brown (2000)[18] US	Differences between African-American and Caucasian women in terms of trial participation	Survey of 196 patients with breast cancer including both trial participants and non-participants.
Camerini(1999)[19] Italy	Prevention of contralateral breast cancer through fenretinide (4-HPR)	Chart review of 4030 patients
Cook (2002)[20] UK	Cross-over trial of interventions for oral dryness in palliative care patients	Unclear
Diener-West (2001)[21] US	Radiotherapy versus standard enucleation in patients with melanoma	Chart review of 6906 patients
Fleissig (2001)[22] UK	Intervention to improve communication about randomised trials	Survey of 265 patients (72% women). Inc. both trial participants and non-participants.
Grant (2000)[23] US	The relationship between the physician's communicative behaviour and accrual to trials	Survey of 130 patients. Included trial participants and non-participants.
Hietanen (2000)[24] Finland	Endocrine in patients with breast cancer	Survey of 261 trial participants
Holcombe (1998)[25] US	Experience of the enrolment of black Americans at the Louisiana State University Medical Center	Chart review of an unstated number of patients
Huizinga (1999)[26] Netherlands	The decision-making process involved in trial participation	Qualitative study of 14 patients (13 trial participants and one non-participant)
Jenkins (1999)[27] UK	Doctor-patient communication in the discussion on trial participation	Observational study of 82 patients (both trial participants and non-participants)
Jenkins (2000)[28] UK	Differences in attitudes between those who accepted and those who refused trial participation	Survey of 204 patients (55% breast cancer patients) including both trial participants and non-participants
Kemeny (2003)[29] US and Jamaica	The willingness of older patients to participate in trials and reasons for decisions in younger and older patients	Survey of 154 patients with breast cancer. Included both trial participants and non-participants.
Klabunde (1999)[30] US	Factors influencing trial participation with specific reference to insurance coverage	Chart review of 573 patients with mixed cancer diagnoses (40% breast cancer) including both trial participants and non-participants
Lara (2001)[31] US	Characteristics of patients who participate compared with those who do not.	Survey of 276 patients (cancer sites unspecified) including both trial participants and non-participants
Madsen (2002)[32] Denmark	Comparison of attitudes between trial participants and trial non-participants	Survey of 88 patients with breast cancer, Duke C type colon cancer or disseminated colorectal cancer including both trial participants and non-participants
Mannel (2003)[33] US	The impact of individual physicians on trial enrolment	Chart review of 248 patients with untreated endometrial, cervical or ovarian cancer
Maslin-Prothero (2000)[34] UK	British Association of Surgical Oncology Trial (BASO II) investigating radiotherapy after surgery for breast cancer of low aggressive potential	Qualitative study of 28 women (21 trial participants, 7 non-participants)
Mills (2003)[35] UK	ProtecT study evaluating treatments for localised prostate cancer	Qualitative study of 21 men (10 trial participants, 11 non-participants)
Moritz (2002)[36] Canada	Examined the accrual process to trials and investigated differences between those who accepted and those who refused participation	Chart review (359 patients) and survey (29 patients) of those approached to take part in a trial. Included both those who accepted and those who declined trial participation
Motzer (1997)[37] US	Family Home Visitation programme	Trial report of 96 families who refused participation in the programme
Richardson (1998)[38] US	Support groups or imagery groups	Chart review of 158 patients
Ringberg (2000)[39] Sweden	Breast conserving therapy with or without radiotherapy	Chart review of 331 patients
Sinnott (2002)[14] UK	Amitriptyline and sodium valproate for patients with cancer-related neuropathic pain	Chart review of 152 patients
Spiro(2000)[40] UK	Chemotherapy as an adjunct to surgery, radiotherapy or best supportive care	Chart review of 6906 patients
Stevens (2004)[41] UK	Reasons for declining participation in trials of adjuvant cancer therapy	Qualitative study of 22 trial non-participants.
Tripathy (1998)[15] US	Barriers to participation in trials (general)	Survey with unknown number of breast cancer patients. Patient trial participation status is unclear
Twelves (1998) [42] UK	Factors influencing entry of women with invasive breast cancer into clinical trials in Scotland. Focused on demographic and physician-related barriers	Chart review of 4688 patients with breast cancer
Westcombe (2003)[43] UK	Aromatherapy massage	Trial report
Wiley (1999)[44] US	Attitudes towards randomisation and demographic and clinical characteristics as predictors of trial participation	Case control study of 192 parents of children with various cancer diagnoses. Included both trial participants and non-participants.
Wilt (2003)[16] US	Prostate cancer Intervention versus Observation Trial (PIVOT)	Chart review of 4279 patients

3.2.1.2 Threats to validity of the evidence

Three studies could not be assessed as they were too briefly presented in abstract or letter form.[14-16] An assessment of the quality of the remaining studies revealed several threats to the validity of the evidence.

Many of the studies were vulnerable to selection bias in that patients were not necessarily representative of the populations from which they were drawn. In most cases poor reporting of recruitment methods made it difficult to ascertain whether a study was free of selection bias but two studies showed a clear potential for selection bias.[36,40]

Many of the studies were based on surveys of patients. However methods of survey design and details of any piloting were not always reported fully.[28,29,31,32,36] This raises the possibility that the issues identified in several of the studies could be at least partially an artefact of what the authors chose to investigate rather than a reflection of those surveyed.

Further problems were identified with data collection procedures. These included researchers asking respondents for just one reason for trial participation or refusal[19,38,39] and only documenting patient reasons for refusal from those who offered a response rather than asking the whole sample.[40] Another problem was not giving respondents the opportunity to make additional comments, thus losing potentially valuable data.[23,28,31] Poor or limited reporting of methods of data collection and analysis made it difficult to assess the introduction of bias into these procedures in many studies.

3.2.1.3 Results

Treatment preference and uncertainty

Treatment preference (either for or against a specific treatment arm) emerged as an issue in several studies[16,22,27,29,31,36-40,43] and was often a reason to decline entry to a randomised trial where the desired treatment might not be obtained.

The uncertainty and experimental nature of trials was found to be a problem for patients.[15,26,27,29-31,36,44] Although there was some evidence that patients understood the importance of cancer trials[34] patients experienced problems with the concept of clinical equipoise.[27] In a small UK study of men with prostate cancer it was found that the concepts of 'chance' and 'comparison' were similarly understood by those who accepted randomisation. Almost all study participants understood the concept of clinical equipoise but nearly all did not find equipoise acceptable.[35] The uncertainty of taking part in a trial might create additional problems or worries,[37] lead to potential loss of control and evoke fears about confidentiality.[15] Patients were concerned about uncertain side effects and uncertain outcome[15,19,29,30,36,41] and the possibility of unnecessary tests.[36]

Knowledge and information

The role of knowledge about trials in the participation decision was examined in the included studies. A small, but in-depth, UK study of breast cancer patients refusing to participate in a trial of cancer therapy found that problems in understanding trial information as well as unfamiliarity with research might lead to information overload and consequent trial refusal.[41] Study respondents commented that more information but presented in a variety of ways and at different times might encourage participation. In addition to the timing and presentation of information, other studies considered the nature of information required. Two studies found that specifically knowing that you could leave the trial at any time and knowing that either treatment would be suitable made a patient more likely to participate.[28,36]

Timing the request for trial participation

An issue that arose in a more limited way in the literature was that of timing of the approach to participate in a trial. It was suggested that patients were being asked to participate in trials often at a time when they are feeling vulnerable, perhaps shortly after diagnosis. In two studies patients felt that participating in clinical trials would add to their anxiety especially if approached soon after diagnosis.[34,41]

Sociodemographic modifiers
A range of sociodemographic modifiers was investigated in the studies included in this review. The evidence regarding older age (with various definitions) as a modifier of trial participation was inconsistent. Some studies found no effect of older age[22,28,29] but another (focused on breast cancer patients in Scotland) found older patients less likely to participate.[42] There was some evidence to suggest that older patients might be less frequently offered a trial.[29]

Where investigated, in the majority of studies potential modifiers such as race, marital status, gender and education level did not tend to affect the participation decision.[16, 22,28,30,31]

Practical barriers
Practical difficulties emerged as (sometimes minor) barriers in several studies. These included work and childcare,[38] problems with transportation and travel,[19,34,38,43] time,[15,34,37,38] length of the trial,[19] distance from the clinic,[31] and costs.[15, 30]

Other modifiers
The health professional as a modifier for trial participation was noted in several studies. This included the patient's perception of the health professional or the recommendations made by the health professional,[15,23] the role of the physician as a primary investigator,[33] and the case load of the surgeon.[42]

In several studies, family members were found to influence patients against trial participation.[15,16,19,37,40]

Benefits
Where investigated, benefits of trial participation, as perceived by patients, were both self-motivated and 'altruistic'. These included expectation of health improvement,[26,29] wanting to have the latest treatment,[29,32] wanting to have the best treatment available,[26,29,36] and to receive closer monitoring.[32]

There were motivations of finding a cure for cancer,[29] benefiting other people in the future,[24,26,27,32,36] gaining personal satisfaction[24] and helping with the doctor's research.[36]

3.2.2 Attitudes to recruitment to trials
In seven studies the trial participation decision was hypothetical in that patients were being surveyed about their attitudes to trials rather than being asked to participate in an actual trial. Such trials may have limited external validity as they may not reflect the barriers involved in real trial participation decisions. The seven attitudinal studies are described briefly below.

3.2.2.1 Study characteristics
As can be noted from Table 2, studies assessing attitudes to trial participation have mainly used a survey design. Surveys had between 60 and 545 participants. One qualitative study based on focus groups also contributed to the literature. One study combined data on intended and actual participation decisions and is thus treated as an attitudinal study.[51] The studies in this section tended to consider more generally the issue of trial participation rather than focusing on one particular problem with recruitment. However, one well-conducted UK study specifically addressed attitudes to randomisation and the impact of providing key study information.[50]

The majority of studies in this section either focused exclusively on patients with breast cancer or included a large group of breast cancer patients. Therefore it may be inappropriate to generalise the barriers found to patients with other cancers. One study specifically considered the recruitment of patients from ethnic minorities.[45]

Table 2

Study, Country	Issues investigated	Study design
Advani (2003)[45] US	Comparison of beliefs of African American and white oncology patients in terms of trial participation	Survey of 218 patients with various cancers.
Crowley (2003)[46] US	Using screening questions to identify patients interested in participating in disease-modifying and symptom-related research	Survey of 86 patients (all male) with various cancer diagnoses in a palliative care clinic.
Ellis (1998)[47] Australia	Knowledge of and general attitudes towards clinical trials	Focus group study of 20 breast cancer patients and 21 patients from the general community
Ellis (1999)[48] Australia	Knowledge of and general attitudes towards clinical trials	Survey of 60 patients (over 50% breast cancer patients)
Ellis (2001)[49] Australia	The association between anxiety, knowledge and attitudes on willingness to participate in trials at different time points in breast cancer care	Survey of 545 patients (83 with breast cancer, 205 being screened for breast cancer and 257 attending for diagnostic assessment).
Fallowfield (1998)[50] UK	Attitudes towards randomisation	Survey of 315 patients using the Attitudes to Randomised Trials Questionnaire (ARTQ).
Paskett (1996)[51] US	Reasons for participation and non-participation in treatment trials	Survey of 82 patients with breast cancer. Combines data on intended and actual trial participation.

3.2.2.2 Threats to validity of the evidence

In addition to problems of external validity described above, the studies in this section were also susceptible to some of the same problems of internal validity as the studies of real scenarios described above. These included potential for selection bias[49] and lack of detail on reliability and validity of survey instruments.[45]

3.2.2.3 Results

Treatment preference and uncertainty

The uncertainty and experimental nature of trials was also found to be a problem for patients in attitudinal studies.[47-49] Although a small study demonstrated that patients understood the importance of cancer trials[48] and another the need to conduct a trial where uncertainty existed,[47] there were concerns about loss of control[47,48] and uncertain side effects or outcome.[47]

Knowledge and information

One study in this group found no difference in knowledge between those who would consider joining a trial and those who would not.[48] However another study found that having further information on the suitability of both treatment arms, clinical equipoise and the possibility of leaving the study at any time together encouraged more people to be willing to participate.[50] This study also found that it is possible and useful to distinguish between those who refuse to participate in trials whatever information is provided and those who might participate given further information. Although this study did not assess actual trial participation, a further study based on real trial scenarios went on to find that participation was partly predicted by a patient's attitudes to trials in terms of the above concepts.[22]

Sociodemographic modifiers

In contrast to the studies describing real trials, two of the attitudinal studies found older patients less likely to participate in trials.[45,46] It should be noted that one of these studies[46] was comprised of only men receiving palliative care. A further study did not find an effect of the sociodemographic modifiers investigated (age, race).[51]

Other modifiers

The health professional as a modifier for trial participation was again noted in two attitudinal studies. This included the patient's perception of the health professional or the recommendations made by the health professional.[48,51] In one study, family members were found to influence patients against trial participation.[51]

Benefits
As with real trial scenarios, benefits of trial participation, as perceived by patients, were both self-motivated and altruistic. These included wanting to gain 'personal benefit' [48,51] and to have a greater chance of a cure.[49] There were motivations of furthering medical knowledge [49,51] and benefiting other people in the future. [49,51]

3.3 Health professional perspective

Twenty-five studies explored barriers to participation in cancer trials from the perspective of the health professional, the majority of whom were doctors. The eight studies investigating accrual to a specific trial have been grouped together[20,34,39,43,52-55] as have the seventeen that consider the attitudes of health professionals to trials.[15,17,31,56-69] Within these groups, barriers are discussed relating to system and organisational issues, trial design issues and personal barriers of the health professional.

3.3.1 Studies investigating accrual to a specific trial

3.3.1.1 Study characteristics

Eight studies examined barriers to recruitment to a specific trial from the health professional perspective (see Table 3).[20,34,39,43,52-55] Mainly survey methods were used with one study involving a chart review of records.[39] The number of survey participants ranged from 17 to 238.

Table 3 Studies investigating accrual to a specific trial – health professional perspective

Study, Country	Trial being evaluated	Study design
Baum (2002)[52] Across 21 countries	The Arimidex, Tamoxifen, Alone or in Combination (ATAC) adjuvant breast cancer trial in post-menopausal women	Survey of 238 trial investigators
Cook (2002)[20] UK	Cross-over trial of interventions for oral dryness in palliative care patients	Unclear
Ehrlich (2002)[53] US	Trial of minimally invasive surgery (MIS) in children with cancer	Survey of 86 surgeons
Goodwin (2000)[54] Canada	Breast Expressive-Supportive Therapy (BEST) Study, a trial of group psychosocial support in metastatic breast cancer	Survey of 17 group leaders
Hjorth (1996)[55] Sweden, Norway, Denmark	Melphalan-prednisone therapy with or without interferon in patients with newly diagnosed myeloma	Survey of 93 principal investigators
Maslin-Prothero (2000)[34] UK	British Association of Surgical Oncology Trial II (BASO II) investigating necessity for radiotherapy after surgery in women with breast cancer of low aggressive potential	Survey of 80 surgeons and focus groups with multidisciplinary teams from 14 centres
Ringberg (2000)[39] Sweden	Ductal carcinoma in situ (DCIS) trial comparing breast conserving therapy, with or without radiotherapy	Chart review
Westcombe (2003)[43] UK	A trial of aromatherapy massage in palliative care patients	Unclear

Apart from one trial,[20] the studies in this section were all multi-centre trials of different types of therapies. Most of the interventions were medical with one trial of a psychosocial intervention[54] and one of aromatherapy massage.[43] In one trial the participants were children[53] and the other trials were of adult cancer patients, mainly women with breast cancer.[34,39,52,54] There were two trials in a palliative care setting.[20,43] All of these studies except one[52] reported having problems with patient recruitment to the trial with some having to close recruitment centres.[54,55]

3.3.1.2 Threats to validity of the evidence

Potentially there is much that can be learned from the experiences of specific trials in relation to factors that prevent or enable successful patient recruitment. However, most of this group of studies investigating specific trials presented a fairly limited exploration of barriers. In some studies the methods used to explore barriers did not appear systematic or structured. As with many of the patient studies, the reliability and validity of survey instruments was not always reported in full.[52-55] Equally, problems were encountered with data collection such as not providing an opportunity for respondents to make additional comments.[54,55] Poor or limited reporting of methods of data collection and analysis was also observed in this group of studies.[20,39,43,53,55] Finally, although more than one group of health professionals were involved in individual trials, some studies focused on just one professional group thereby limiting the perspectives included.[53-55]

3.3.1.3 Results

System-related and organisational barriers

Several different system and organisational barriers were identified in the included studies. Obviously these will reflect the particular context and setting of the individual study and may not readily generalise to other settings.

The time involved in participating in trials emerged as a barrier. This included the extent of extra work generated by the study,[55] and the time needed discuss[69] and to 'sell' trials to patients and to obtain their consent.[34] Allied to time commitments were the costs involved in participating in trials.[55, 52]

Identifying patients for trials was also seen as a problem.[34] Trials competing for the same patient groups were also barriers [34,54] as were restricted trial eligibility criteria.[54] In one study of recruitment to a trial of breast conserving therapy with or without radiotherapy, accrual was found to be highest where mammography screening centres were well integrated with specialist breast clinics.[39]

Trial design barriers

The scientific rationale of the trial was seen as important to the success of engaging health professionals.[43,52] If the design was thought to be poor, clinician gate keeping might occur.[43] A more pragmatic design in line with standard practice, easier to explain to patients and a logical extension of earlier trials encouraged participation in the ATAC breast cancer trial.[52] Reluctance to participate in a trial arm seen as less than standard practice was identified as a barrier in a further study.[34]

Individual health professional barriers

In one study, type of hospital and specialism did not affect participation in trials.[55] However the need to engage and maintain the interest of all members of the healthcare team involved in trial participation was identified.[20]

One study found that a physician's interest in participating in a trial might reflect their perception that their clinical work is valued above their scientific work.[34] In contrast, research experience or academic qualifications of the principal investigator did not affect participation in another study.[55]

Health professional gate keeping of trials might occur due to bias towards or against a particular trial treatment arm [43,53,55] or concerns about treatment toxicity.[52]

3.3.2 Attitudes to recruitment to trials

3.3.2.1 Study characteristics

Seventeen studies examined attitudes of health professionals to participation in cancer trials.[15,17,31,56-69] Three studies examined barriers to recruitment of ethnic minority groups to cancer trials from the perspective of health professionals.[62,66,67] All of these studies were carried out in the United States. Three studies explored the views of professionals involved with trials other than doctors. Two were conducted with Clinical Research Associates (CRAs)[61,69] and one with oncology nurses.[57] Both the studies of CRAs used focus groups whereas the study of nurses used a survey approach. One study investigated the issue of recruitment of older patients to cancer clinical trials from the health professional perspective.[63] Three studies focused on the views of specific types of clinicians or a specific health professional related barrier.[56,58,65] Finally,

seven studies investigated general issues and attitudes in relation to barriers to participation in cancer clinical trials.[15,17,31,59,60,64,68] A variety of study designs were used including focus groups and surveys. Surveys had between 47 and 706 participants.

Table 4 Attitudes to recruitment to trials – health professional perspective

Study, Country	Issues investigated	Study design
Albrecht (1999)[56] US	The relationship between physician communication and patient accrual	Analysis of 48 videotaped interactions between 12 medical oncologists and 48 patients where the patient was presented with the option to participate in a trial
Burnett (2001)[57] US	Oncology nurses' attitudes and beliefs toward trials and their perceptions about factors influencing patient participation	Survey of 250 oncology nurses in a free-standing National Cancer Institute designated comprehensive cancer centre
Crosson (2001)[58] US	Primary care physicians' knowledge, attitudes and practices related to cancer trials	Survey of 706 primary care physicians
Ellis (1999)[59] Australia	269 surgeons, radiation oncologists and medical oncologists	Survey using a questionnaire on attitudes to and participation in current RCTs and perception of barriers to patient participation
Fallowfield (1997)[60] UK	154 clinical oncologists, 56 medical oncologists and 143 surgeons with a special interest in oncology	Survey using Physician's Orientation Profile questionnaire. They were asked to name the trials in which they were participating and the characteristics that made patients easy/difficult to approach
Grunfeld (2002)[61] Canada	Views of Clinical Research Associates (CRAs) on barriers and facilitators to the accrual of patients	Focus groups with 24 CRAs and 5 data managers at six of eight tertiary cancer treatment centres in Ontario
Kaanoi (2002)[62] US	Physician referral of Native Hawaiian patients to trials	Survey of 47 cancer speciality physicians practising in Hawaii
Kornblith (2002)[63] US	Oncologists' perceptions of barriers to accrual of older patients with breast cancer to trials	Survey of 156 medical, surgical and radiation oncologists and general surgery physicians and fellows from 10 institutions
Langley (2000)[64] UK	7 oncologists, 5 urologists, 4 general/breast surgeons and 4 haematologists	Interviews using a semi-structured questionnaire
Lara (2001)[31] US	12 medical oncologists and six fellows	Questionnaire assessing decisions about trial referral and non-referral of specific patients
Martin (2003)[65] US	The prevalence of patient enrolment in trials by recent surgical graduates and reasons for participation or non-participation	Survey of 201 surgical oncology or general surgery graduates from one of three institutions.
Outlaw (2000)[66] US	Recruitment of black Americans	Survey of 39 oncologists and 17 data managers at a large urban cancer centre
Pinto (2000)[67]; US	Enrolment of minority patients as part of an Eastern Cooperative Oncology Group (ECOG) initiative	Focus groups with 40 community physicians affiliated with the National Medical Association and 33 ECOG investigators from four US cities
Siminoff (2000)[68] US	107 surgeons providing care to breast cancer patients and 40 oncologists	Interviews using an interview guide exploring referral decisions in relation to specific patients
Skeel (1998)[17] US	136 Eastern Cooperative Oncology Group (ECOG) who were mainly medical oncologists	Survey using Physician's Orientation Profile II questionnaire
Tripathy (1998)[15] US	Medical oncologists and other specialists	Not stated
Wright (2002)[69] Canada	CRAs' views on factors that influence patients' decisions about trial entry	Focus groups with 13 CRAs at a regional cancer centre

3.3.2.2 Threats to validity of the evidence
Two studies could not be quality assessed due to lack of information.[15,17]

Quality assessment of the remaining studies revealed threats both to the internal and external validity of the research. Firstly, none of the included studies on barriers to ethnic minority participation in cancer trials were based in the UK. It is unlikely that the barriers identified by these three studies are directly transferable to the UK.[62,66,67] This is partly because some of the cultural issues addressed may be specific to the setting in which they were carried out and also because they were very small studies.

Three studies explored barriers to clinical trials from professionals involved other than doctors.[57,61,69] Although it is useful to have the views of other important stakeholders in the process of patient accrual to clinical trials these were all fairly small studies, two of which were carried out at a single centre. None of them were carried out in the UK and the transferability of the findings is unclear.

Similar threats to validity were found in this group of studies as have been previously discussed. These included the potential for selection bias.[63] Once again the reliability and validity of survey instruments was unclear in terms of survey design and piloting.[31,57-59,62,63,66] Again concerns were raised that the barriers to trial participation identified in several of the studies might be a reflection of the researchers' rather than the participants' views. Other problems included not providing respondents with the opportunity to make additional comments.[31] Poor or limited reporting of methods of data collection and analysis made it difficult to assess the introduction of any bias in several studies.[31,67-69]

3.3.2.3 Results
System-related and organisational barriers
This group of attitudinal studies also identified system and organisational barriers. As before, the time involved in participating in trials emerged as a barrier. In attitudinal studies this included the extent of extra work generated by the study,[60] the time needed to discuss trial participation,[61,63] the time needed for ethics submissions[64] and office staff time.[15] Also mentioned again were resource issues. These included costs involved in participating in trials,[64] paperwork[59] and provision of data management facilities.[59] An infrastructure with appropriate support from formal and informal bodies was felt to be crucial to the success of the trial.[64]

Identifying patients for trials was also identified in this group of studies. This included the fact that an insufficient number of patients may be readily approachable.[59] Trials competing for the same patient groups were also seen as barriers.[17] The need for easier to use eligibility checklists was highlighted.[64]

Trial design barriers
The scientific rationale of the trial was again seen as important to the success of engaging health professionals in this group of studies.[59,69] Another factor was the physician's perception of the relevance of the trial to the local population.[17] There was again a desire for more pragmatic designs in line with standard practice.[68]

Individual health professional barriers
Two studies found variation in barriers according to the medical specialism, age and academic setting of the health professional.[15,68]

A further study found that a physician's interest in participating in a trial might reflect where they see themselves on the clinician-scientist continuum.[60] Lack of awareness of ongoing trials and their eligibility criteria was also identified as a barrier.[15,68]

The problem of health professional gate-keeping of trials due to bias towards or against a particular trial treatment arm was identified by studies in this group.[59,64] Gate-keeping might also reflect a perception that the patient might not be 'up to' the trial. For example, one study recommended educational programmes for physicians on the toxicity of treatments and the physical and mental abilities of elderly patients.[63]

4. DISCUSSION

We conducted a systematic review of the barriers, benefits and moderators involved in the decision to participate in randomised trials of cancer therapies. It is evident from this review that there is a wide range of literature evaluating the benefits, modifiers and barriers to participation in cancer trials. Searches between 1996 and 2004 resulted in the inclusion of 56 studies in the review. The international literature describes both the patient's and the health professional's perspective. The included studies cover a range of cancer sites and types of trial. There is clearly, then, no shortage of research in this area. However there is a shortage of good quality research.

It was considered that including a variety of research designs would bring a range of perspectives to the problem of trial participation. The study designs in the review included: surveys, qualitative studies, trial reports, observational studies and chart reviews. The choice of study design was usually appropriate to the aims of the specific study but the quality of the studies was often low. A number of threats to the validity of the studies were identified. These included concerns about the reliability and validity of research instruments (often methods of survey design were limited and questionnaires were not piloted); non-justification of sample size and the potential for selection bias.

In addition to problems of quality, some of the studies were hampered by poor or limited reporting. In several studies it was not clear how the participants (patients and health professionals) had been selected and often methods of data collection and analysis could not be ascertained. Hence the reliability of the study and the validity of the measures used were difficult to assess. Often it was unclear how data on barriers to participation in a trial had been collected.

What is clear is that the predictors of trial participation identified in many of the studies could be an artefact of what has been studied. The methods by which the researchers derive the barriers to be investigated can introduce bias. For example, if the researchers generate the barriers in a non-structured way without recourse to the population being studied, then a biased or limited set of barriers may be investigated and subsequently confirmed in analyses.

Some studies focused on specific barriers to trial participation such as doctor-patient communication or randomisation whilst others considered more general attitudes to trial participation. The strengths of the studies investigating specific barriers are that they allow for detailed examination of a particular barrier. However they do not tell the reader how that particular barrier might operate in the context of other barriers to trial participation. Studies investigating more general attitudes to trials have the potential to examine the particular interplay of barriers but they may be compromised if the set of barriers to be investigated are based solely on those defined by the researchers without recourse to the population under investigation. This was found to be an issue in studies from both the health professional and patient perspective.

The predictors of trial participation could also be an artefact of how the data have been collected. Where researchers have asked respondents for just one reason for trial participation or refusal, such as in many of the patient chart reviews, the multifaceted nature of the decision will be lost. It remains unclear whether the person would have made the same decision on participation had the major barrier they had described been addressed. Some studies only documented patient reasons for declining a trial from those who volunteered a response rather than asking the whole sample. In several studies participants did not have the opportunity to provide additional comments, thus losing potentially valuable data.

A number of studies relied on hypothetical scenarios to survey patient or health professional attitudes to trial participation. Such studies may not reflect the barriers involved in real trial participation decisions. In a few studies health professionals commented on why patients do not participate in trials, but it is unclear how useful this indirect evidence is in determining barriers to patient participation. In a study where both perspectives were examined there was not always agreement.[34] In some of the studies from the health professional perspective the focus was limited to just one professional group.

Compounding problems of limited quality, poor reporting and potentially biased approaches is the problem of generalisation. A very different set of barriers may emerge as a reflection of differences in populations (cancer sites and stages, sociodemographic variables), settings (infrastructure and staff) and the trial or trials that are on offer. The included studies presented a variety of study populations with some studies considering only one form of cancer such as breast cancer or prostate cancer. These studies are potentially valuable in their focus on a particular patient group but generalisation to other cancer sites may not be appropriate. The relative importance of barriers to participation will also vary according to the setting. Where a centre has very good infrastructure for research, for example, barriers may reflect quite different issues from one where staff time for informed consent interviews is limited. A further variable is the trial or trials that are on offer. For example, where patients are likely to have preconceived ideas and preferences about treatments (such as in a trial of chemotherapy) worries about randomisation and uncertainty may prevail over practical difficulties such as transport. Ascertaining universal barriers or barriers applicable to particular subgroups based on cancer site or type of trial, for example, is difficult given the threats to validity observed in the included studies.

We cannot exclude the possibility of having missed studies given the challenges of searching this poorly indexed topic area. However we developed a comprehensive search strategy and searched a range of databases in addition to using supplementary search methods. It is unlikely that a missed study would change our overall conclusions. In terms of other limitations, we attempted to minimise bias in extracting qualitative data by using a second reviewer to check data extraction. Our quality assessment, although thorough, did not enable us to establish a hierarchy of included studies based on their potential bias. Finally we did not contact authors to clarify poor reporting of study methods.

5. CONCLUSIONS AND RECOMMENDATIONS

The themes we have identified in this review are similar to those highlighted in Prescott et al,[1] a review which also included patients with diseases other than cancer. In common with this review, we found issues such as time constraints, resource issues, the importance of the research question, patient preference for a particular treatment (or no treatment), worry about uncertainty of trials as well as concerns about information and consent. Our review also lends support to their findings of the clinician acting as a barrier to patient participation. However crucially our review, through an assessment of the quality of the included studies, also identifies the limitations of the research literature in identifying in a clear, reliable and consistent way the barriers involved in trial participation.

The methodological limitations we have identified compel us to be more cautious in identifying what is and is not a barrier and in recommending interventions to overcome barriers.

The decision to participate in a trial is a multifaceted one that has tended to be approached in a more unidimensional manner in the research. Many of the studies have no theoretical basis and do not fully address the complex relationship between attitudes and behaviours. A recent study (unfortunately not specific to cancer) used an extended form of the Health Belief Model to explain trial participation.[70] Studies within the field of cancer would be strengthened by such a theoretical underpinning.

Many studies were of poor quality and were further hampered by poor reporting. A major concern is that the predictors of trial participation identified in much of the research could be partially an artefact of what has been studied, how the data has been collected or how it has been analysed. The limitations we have identified in interpreting the research compel us to be cautious in stating what is and is not a barrier to participation in cancer trials. Instead we recommend the following:

- The interplay of barriers, modifiers and benefits relevant to participation in a particular cancer trial needs to be prospectively identified by trialists in the light of issues identified in the research literature.

- Evidence of having identified and addressed the barriers that might apply to a given trial should be a prerequisite for gaining research ethics approval.

- The involvement of patients in the design of trials and identification of barriers appears to be a beneficial way forward.[71]

Further research in this area should address the complexity of the problem and the multidimensional nature of the decision to participate in a trial. Ideally it should have a theoretical underpinning or a clear rationale for the approach taken and maximise the strengths of the study design chosen. Those using surveys need to carefully consider the sampling frame and design and piloting of the research instruments. More planned, prospective collection of data on accrual in actual trials would lend support to the research literature.

Potentially there is much to be learned from trials that successfully overcome barriers to participation. The publication of these successful strategies could aid other trialists.

The following checklists, based on themes identified in the literature, can be used as a starting point to identify barriers for a particular setting or trial.

Checklist - patient perspective

- 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?

Checklist – health professional perspective

- 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?

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APPENDIX 1: SEARCH STRATEGY FOR REVIEWS

Search strategies to locate systematic reviews are as follows:

Cochrane Database of Systematic Reviews (CDSR) & Cochrane Database of Methodology, the Cochrane Library Database Issue 4 2003.
Searched 23.1.04 http://www.nelh.nhs.uk/cochrane.asp

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Database of Abstracts of Reviews of Effects (DARE)
http://www.york.ac.uk/inst/crd/crddatabases.htm
searched 23.1.04

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Health Technology Assessment Database (HTA) http://www.york.ac.uk/inst/crd/crddatabases.htm
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National Coordinating Centre for Health Technology Assessment
http://www.hta.nhsweb.nhs.uk/
Searched 23.1.04

Searched the following words:

Participate, participation, recruit, recruitment, enrol, enrolment, enroll, enrolment, accrual, accrue, enlist.

Centre for Reviews and Dissemination Ongoing Reviews Database (CAIRS T internal system) Searched 26.1.04

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TRIP Database Plus
http://www.update-software.com/scripts/clibng/html/tripusernamelogon.htm
Searched 27.1.04

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APPENDIX 2: SEARCH STRATEGY FOR PRIMARY STUDIES

MEDLINE 1996-2004 Feb week 1
Accessed via Ovidweb http://gateway/uk.ovid.com
Search date: 13.2.04

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HMIC (Health Management Information Consortium) 1996- 2004/Jan
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10. exp clinical trials/
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15. patient participation/
16. client participation/
17. human research subjects/
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21. ((difficult$ or problem$ or obstacle$ or barrier$) adj2 (accru$ or recruit$ or enrol$ or participat$ or nonparticipat$ or enlist$)).ti,ab.
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APPENDIX 3: QUALITY ASSESSMENT TOOL FOR THE APPRAISAL OF SURVEYS

Design
Are the aims clearly stated?
Is the design appropriate to the stated objectives?
Was the sample size justified?
Are the measurements likely to be valid and reliable?
Are the statistical methods described?
Is there a suggestion of haste?

Conduct
Did untoward events occur during the survey?

Analysis
Were the basic data adequately described?
Do the numbers add up?
Was the statistical significance assessed?
Were the findings serendipitous?

Interpretation
What do the main findings mean?
How could selection bias arise?
How are null findings interpreted?
Are important effects overlooked?
Can the results be generalised?
How do the results compare with previous reports?
What implications does the study have for your practice?

APPENDIX 4: QUALITY ASSESSMENT TOOL FOR THE APPRAISAL OF QUALITATIVE RESEARCH

Was the research design appropriate to address the aims of the research?

Was the recruitment strategy appropriate to the aims of the research?

Were the data collected in a way that addressed the research issue?

Has the relationship between researcher and participants been adequately considered?

Have ethical issues been taken into consideration?

Was the data analysis sufficiently rigorous?

Is there a clear statement of findings?

How valuable is the research?

APPENDIX 5: DATA EXTRACTION

Studies are presented in alphabetical order of author surname.

Author, Year Advani 2003 [45] **Study aim** To compare the beliefs of African American and white oncology patients regarding cancer, clinical trials, and willingness to participate in a clinical trial. **Setting** Multiple hospitals **Country** USA	**Study design** Survey **Sample size, Type** 218 Patients **Sample characteristics** Age (Median) African American participants 63 years; White participants 61 years Gender Not stated Cancer stage African-American participants: low stage (including carcinoma in situ) 48.5%; intermediate (including stage II or III disease or regional lymph node involvement) 39.4%; high (including stage IV metastatic disease) 12.1%. White participants: low stage 41.1%; intermediate 36.3%; high 22.6% Previous trial experience African American participants 8.3%; White participants 9.6% Misc Ethnicity:African American n=72; White n=146 Income <$15,000: African American participants 67.8%; White participants 34.2% Education < high school:	**Data collection** Participants were recruited from the Duke Cancer Clinic (DCC) and Duke Oncology Outreach Clinics (DOORS). Eligible patients were those who had been diagnosed with cancer in the previous 5 years; were of African American or white ethnic background; over 18 years; had a solid or haematologic malignancy (excluding melanoma); with consent from primary care physicians and patients. Data were collected by telephone interview using a 20 minute standardised questionnaire including questions on knowledge of cancer, religious beliefs, satisfaction with their oncologist and clinic, financial and/or transport issues, demographics, knowledge of clinical trials and reasons why they would or would not participate in a trial. Response were scored as yes/no or on a 5-point Likert scale rating strong agreement to strong disagreement. DOORS patients were selected consecutively based on the clinic appointment schedule and DCC patients were selected from the tumour registry with those with the most recent diagnosis selected first. Factors that affected patient's decision to participate were rated 0 to 10 for importance. **Data analysis** African American patients were compared with white patients and DCC patients were compared with DOORS patients using chi square for dichotomous responses and the Wilcoxon test for responses from a Likert scale. Logistic regression was used to assess whether questionnaire items were associated with a willingness to participate in a clinical trial (yes versus no or don't know) with race, clinic and disease stage controlled and not controlled for.	**Response rate** 52% (218/420) **Results** There was no significant difference between ethnic groups and clinic groups in the percentage of patients who had heard of a clinical trial, knew what a clinical trial was, or had been asked to participate in a clinical trial (data reported). African American patients ranked physician advice significantly lower than white patients with regard to its influence on their decision to participate in a clinical trial (mean rating 7.1% versus 8.4%, p<0.05) and were significantly less likely to participate in a trial because the trial may benefit others (mean rating 7.1% versus 8.5%, p<0.05). African Americans were significantly more likely than white patients to strongly agree that 'God would determine whether or not they would die from their cancer' (95% versus 78%, p<0.05). African Americans were also more likely than white patients to report that transportation (28% versus 15%, p=0.02) and cost (31% versus 15%, p=0.005) were problems for them getting to the clinic. Willingness to participate in a clinical trial All participants: 40% said they would be willing to; 22% said they would not and 39% said they did not know. 45% of white participants willing to participate versus 31% of African Americans (p=0.05); 47% DCC patients versus 36% of DOORS patients willing to participate. Multivariate analysis When adjusted for race, clinic and stage of disease, willingness to participate in a clinical trial was significantly associated with age; knowledge of trials (4 items); the risk of experiencing side effects; and the chance that the trial may benefit others (odds ratio) and 95% confidence intervals	**Conclusions** The major barriers to clinical trial participation may be factors associated with religion, education and income, rather than race. **Recommendations for research** The authors state that future research should be directed at determining whether various interventions help improve clinical trial accrual and reduce disparities between African Americans and whites and DCC and DOORS patients. Interventions suggested were community recruitment, offering clinical trials at outlying clinics, patient advocate model, and helping with medical costs. **Recommendations for practice** The authors state that interventions that target education and income may increase the recruitment of African American oncology patients into clinical trials. They also suggest that offering trials at outreach clinics and helping with medical costs would make clinical trials more readily available to patients of lower socioeconomic class who live in outlying communities.

	African American participants 53.5%; White participants 19.3%		reported).	**Reviewers' comments** This study did not investigate reasons for participation/non-participation in an actual trial. There was a fairly low response rate to the survey and many of the issues addressed may be culturally specific.

Author, Year Albrecht 1999 [56] **Study aim** To explore the relationship between physician behaviour and patient accrual to a clinical trial by videotaping the interaction. **Setting** Single hospital **Country** USA	**Study design** Observational **Sample size, Type** 48 Both **Sample characteristics** Health professionals 12 medical oncologists (10M, 2F, average age 55 years). Patients n=48 Age Accrued and nonaccrued patients were similar in age (57.8 years (SD 12.34) vs. 59 years (SD 10.36). Gender Of the 32 who agreed to participate in a trial 28%M, 72%F. Of those who did not agree 23%M, 72%F. Trial participation status Patients were eligible for a phase II or phase III trial. 31 of 48 (65%) agreed to take part in a trial (16 phase II, 15 phase III). The 15 patients who accrued to phase III studies were distributed across eight different protocols. 12 patients did not agree to participate in phase III	**Data collection** Patients attending one of several multidisciplinary (thoracic, malignant haematology, breast, neuro-oncology, pain management, senior adult, gastrointestinal oncology) clinics at the H Lee Moffit Cancer Center and Research Institute were selected according to their eligibility for a phase II or phase III clinical trial. In most cases the patient was told that a clinical trial was a possible treatment option (before consent was sought to videotape the more formal process). Interactions between physicians and patients were videotaped during the time the eligible patient was formally presented with the option to participate in a trial. Three research nurses assisted in four interactions although each nurse was under the supervision of one of the 12 oncologists in the study. The patient was offered a copy of the videotape free of charge. Two small video cameras were set to record the physician and the patient. **Data analysis** The videotapes were reviewed several times for analysis through two videocassette recorders connected to an audiovisual mixer unit. The unit enabled simultaneous viewing of the tape of the physician / health professional and patient via a split screen format on a single video monitor enabling analysis of communication patterns. The split view was then recorded onto a standard VHS cassette. Coders then inserted the videocassettes into standard VCR units to code the interactions. Videotapes were reviewed and coded by four trained analysts using the Moffitt Accrual Analysis System (MAAS) developed by the study investigators. The coding system addressed both content and strategic influence aspects of the accrual interaction in two major sections and was based on four initial videotaped interactions. The first section is a checklist for coders to record the occurrence or non-occurrence of key messages and behaviours relating to the legal / informational process of gaining informed consent. The second section includes a series of global judgements by	**Response rate** NA **Results** Results of intercoder agreement were 0.67 (SD 0.16, range 0.30, 0) for the checklist items and 0.64 (SD 0.11, range 0.53, 0.82) for global judgement items. (The value of the intercoder agreement for the checklist items is outside the range given). Accrued patients had significantly higher average scores for hierarchical rapport based on cordiality (mean value of 5.87 vs.4.21), patient physician connection (5.06 vs. 3.21), trust (5.29 vs. 3.92) and greater physician responsiveness to patient concerns (5.77 vs. 4.64). In addition the physicians of accrued patients were judged to adhere more closely to the legal consent form (r=9.82) and to give more appropriate forms of information (r=16.90). None of the following were found to be statistically significant. Physician's use of technical and medical jargon, patient use of technical and medical jargon, physician's momentum to sign consent, sharing of floor time, physician orientation to personal opinion or to accepted scientific findings. Physicians interacting with accrued patients tended to mention study benefits, side effects, patient concerns and resources to manage the concerns more often than physicians interacting with patients who did not accrue. The average length of the interaction (in minutes) did not differ between accrued versus nonaccrued patients for the presentation of phase III trials (24.31 minutes (SD 12.97) vs. 23.75 minutes (SD 11.41).	**Conclusions** The authors concluded that their research has implications for modifying physician behaviour and thus to increase the numbers of patients accruing to cancer clinical trials. **Recommendations for research** The authors stated that it is important to explore whether nonverbal behaviours enhance or detract from the legal-informational content. Further investigation is needed regarding the impact of a third party companion accompanying the patient. **Recommendations for practice** The physician behaviours found to be associated with patient trial participation could be addressed directly by the physician, or patients could be referred to other sources. Training programmes might provide guidelines for physicians to use in presenting clinical trials to their patients. **Reviewers' comments** Although a small study it is useful in highlighting the influence of the physician in patient accrual to trials. The

	trials. Misc 45 of 48 were white, 2 black and one Hispanic.	coders on the effectiveness of the physician-patient communication process including aspects of rapport, language, trust, responsiveness of physician to patient's concerns, adequacy of information given and manner of managing the encounter. 15% of the videotaped interactions were randomly selected to analyse intercoder agreement. Validity of global judgement items on the MAAS scoring system was assessed for convergent and discriminant validity (details are provided in the paper).		study included both phase II and phase III participants but did not assess the influence of physician behaviours on the groups separately. Further research would be needed to determine if phase III recruitment requires different physician behaviours. The study had a high accrual rate possibly due to specific characteristics of the centre therefore it would be important to examine generalisability to other situations.

Author, Year Baum 2002 [52] **Study aim** To identify possible reasons for the rapid rate of recruitment into the ATAC trial with a view to building on this success and providing ideas for future good practice to other clinical trial organisations. **Setting** Multiple hospitals **Country** Various	**Study design** Survey **Sample size, Type** 238 Health professionals **Sample characteristics** The participants were clinicians who had participated in the ATAC trial. The ATAC trial recruited over 9366 patients from 381 centres in 21 countries over 45 months. The demographic and professional characteristics of the clinicians were not reported.	**Data collection** When patient recruitment had been completed, all ATAC trial investigators worldwide (n=381) were asked to anonymously complete a postal questionnaire. The questionnaire was designed by a member of the ATAC Steering Committee. It included 11 statements regarding recruitment to the ATAC trial each of which respondents rated for importance on a three-point scale (very important, somewhat important, not important). An additional question asked for any other reasons that may have encouraged investigators to recruit into the trial. Participants were also asked to select the single statement from the 11 provided that they considered the most important reason for recruiting patients into the trial. **Data analysis** The results were presented descriptively as percentages.	**Response rate** 62% (238/381) **Results** I found the scientific rationale of the trial attractive very important 84%; somewhat important 15%; not important 1%; single most important reason 30% I found the design of the trial easy to explain to patients very important 79%; somewhat important 15%; not important 3%; single most important reason 8% The pragmatic design of the trial, which was in line with standard clinical practice and which allowed me to select appropriate primary therapy and chemotherapy prior to randomisation, made the ATAC trial attractive very important 76%; somewhat important 21%; not important 3%; single most important reason 17% The infrastructure of the trial was well organised and this made randomising patients easy very important 70%; somewhat important 26%; not important 4%; single most important reason 4% Accepting that proposed treatment arms were appropriate for evaluation in this large early breast cancer trial, the fact that the treatments themselves were oral and relatively non-toxic encouraged me to enter very important 69%; somewhat important 28%; not important 3%; single most important reason 6% This trial was a logical extension of earlier trials of endocrine therapy that had helped establish tamoxifen as a standard hormonal treatment in early breast cancer very important 67%; somewhat important 29%; not important 4%; single most important reason 12%	**Conclusions** In the future, studies (either in the field of oncology or in other therapeutic areas) that consider the factors outlined in this paper in the trial design may maximise the potential recruitment rate. **Recommendations for research** None stated **Recommendations for practice** None stated **Reviewers' comments** This is a reasonably well-conducted survey which focuses on the reasons why there was successful recruitment to a specific clinical trial. A weakness of the study is that no information is provided on the method of questionnaire construction therefore the reliability and validity of the measure is unclear. It is also unclear how respondents may have differed from nonrespondents.

			The provision of trial medication free of charge from the sponsors encouraged me to join the trial very important 47%; somewhat important 33%; not important 20%; single most important reason 2% At the time, there was no other trial of adjuvant endocrine therapy open for recruitment very important 36%; somewhat important 36%; not important 28%; single most important reason 5% The international nature of the trial encouraged my participation very important 30%; somewhat important 40%; not important 30%; single most important reason 4% The level of financial support provided very important 29%; somewhat important 45% not important 26%; single most important reason 10% Endorsement by Consumers Advisory Group for clinical trials encouraged me to put patients into the trial (UK only) very important 6%; somewhat important 28%; not important 66%; single most important reason 0% Other key reasons that encouraged investigators to recruit patients into the study included: the timely initiation of the study (patients were asking for alternative treatments to tamoxifen); previously good cooperation between the researchers and AstraZeneca; patients are keen to try new, modern pills; the trial was addressing the question of whether two drugs are more effective than one; there are many publications in this field and this study was a logical progression of the 1998 Early Breast Cancer Trialists' Collaborative group; and trials of this size always provide interesting additional results to the primary and secondary endpoints.	

Author, Year Brown 2000 [18] **Study aim** To assess differences between African-American and Caucasian women in factors affecting clinical trial accessibility and participation. **Setting** Single hospital **Country** USA	**Study design** Survey **Sample size, Type** 196 Patients **Sample characteristics** Age Not stated. Gender All female. Cancer site All breast cancer. Misc 61 of 196 (31%) were African American. 5% of African American women enrolled in a breast cancer trial compared with 11% of the primarily Caucasian sample.	**Data collection** The target population consisted of all new breast cancer patients treated during a 1-year period at Harper Hospital, a large university-based hospital affiliated to a cancer institute in Detroit, Michigan. Data were gathered on patients from three sources. Firstly, interviews with women newly diagnosed with breast cancer (within 8 weeks). Secondly data were gathered from the women's oncologists to obtain an assessment of eligibility for available clinical trials. The third source of data was the clinical trials office who had documented whether or not a women had participated in a trial. The three sources of data were integrated. **Data analysis** Not reported.	**Response rate** NA **Results** African American women were less familiar with the term 'clinical' trials than caucasian or other women (n=21 vs. n= 81, p <0.001), were less likely to know someone who had participated in one (n=5 vs. n=27, p <0.05) and to indicate that their oncologist had talked to them about participating in a trial (n=12 vs. n=58, p <0.001). Data from the oncologists' assessment of eligibility showed that African American women were less likely than caucasian and other women to be offered clinical trial participation by their physicians (19% vs. 35%). Even if offered clinical trial participation African American women were less likely to enrol (10% vs. 26%). However African American women were more likely to have advanced stage disease along with poorer performance status and greater experience of pain in the last week (no data presented). They were less likely to have health insurance coverage for clinical trial participation or to have the necessary transport for medical visits (no data provided).	**Conclusions** The authors concluded that among the barriers for African American participation in breast cancer trials were lack of knowledge and awareness of available protocols. African American women tended to have a more advanced disease stage and poorer functioning. They experienced economic barriers such as health insurance and transport. They were less likely to be offered a place in a trial. **Recommendations for research** Not stated. **Recommendations for practice** The authors concluded that there was a need to provide educational materials and information on available trials. **Reviewers' comments** A very brief report so it is not possible to assess the quality of the survey instrument or other methods of data collection. The other three studies in this paper do not refer exclusively to cancer patients and data has not been extracted.

Author, Year	Study design	Data collection	Response rate	Conclusions
Burnett 2001 [57] **Study aim** To identify nurses' attitudes and beliefs toward cancer clinical trials and their perceptions about factors influencing patients' participation in these trials. **Setting** Single hospital **Country** USA	Survey **Sample size, Type** 250 Health professionals **Sample characteristics** Oncology nurses working in a free-standing National Cancer Institute (NCI)-designated comprehensive cancer centre (Roswell Park Cancer Institute, RPCI) where conduct of clinical trials is a primary mission. 90% (n=226) of participants were female; 57% (n=142) were 40 years or older; 88% (n=219) were white; 37% (n=92) had a Bachelor's degree and 10% (n=24) had a Master's degree. Practice setting: inpatient 19% (n=48); intensive care unit/bone marrow transplant unit (ICU/BNT) 19% (n=48); outpatient clinic 16% (n=41); operating room 8% (n=20); clinical research 11% (n=27); other 15% (n=37); no answer 19% (n=47). Number of patients on clinical trials treated per year: no trials 8% (n=20); 1-10 10% (n=26); 11-20 13% (n=32); 21-50 15% (n=37); 51-100 18% (n=46); >100 14% (n=35)	All 417 registered nurses (RNs) employed at RPCI at the time of the survey, identified using personnel records, were invited to complete a self-administered questionnaire. Questionnaires were coded to ensure respondent confidentiality. The 59-item questionnaire was developed by the authors based on the literature, clinical practice and discussions with oncology experts. It addressed nurses' perceptions about patients reasons for participating in clinical trials and there were two 6-item subscales on nurses' attitudes toward the benefit of trials and nurses' perceptions of patients' understanding of trials. Items were rated on a 5-point Likert scale ranging from strongly agree to strongly disagree. Sum scores generated from each of the subscales: a higher score on subscale 1 suggested a more positive attitude to clinical trials; a higher score on subscale 2 suggested that nurses were more likely to believe that patients were well informed about trials. Face and content validity were assessed based on an 'extensive' literature review and a review of the instrument by three medical oncologists and two oncology nurses. Revisions were made to the questionnaire based on the comments of the expert reviewers. **Data analysis** Scores for missing items on the subscales were imputed by calculating the mean score of the nonmissing items provided more than two items had been completed. Cronbach alphas were calculated for the two subscales (alphas=0.78 and 0.63 respectively). Descriptive statistics were used to describe the study population. 95% confidence intervals (CI) calculated based on binomial distribution. Chi-square, t-tests and analysis of variance were used to examine the bivariate associations between variables of interest. Multiple regression analysis was used to explore the predictive relationship of selected variables (including age, educational level, race/ethnicity and practice setting) and the subscale scores.	60% (250/417) **Results** 96% (95%CI: 93%, 98%) of respondents agreed that clinical research was important in improving future standards of care; 56% (95% CI: 50%, 63%) agreed that patients should be encouraged to participate in research; 35% (95% CI: 29%, 41%) stated that they would prefer treatment in a clinical trial if they had cancer. Half of the respondents believed that an experimental therapy should have at least 50% chance of benefit before being offered to patients. Compared to other nurses, research nurses felt that a new therapy should have median 25% chance of benefit before entering a clinical trial (p=0.02). Motivations for patient participation in clinical trials as identified by nurses Wish for cure 92% (n=230); wish for other benefit to health 85% (n=212); wish to help others 69% (n=173); no other option 69% (n=173); hope of better medical care 68% (n=170); inability to accept that nothing can be done 61% (n=153); inability to accept death 60% (n=150); family wishes 59% (n=148); desire to please physician 44% (n=110); pressure from physician 34% (n=85). Attitudes toward benefit of clinical trials Multivariate analysis: positive attitudes toward clinical trials and patients' participation in these trials were predicted by age and practice setting. Nurses who were 40 years and older and nurses from settings other than ICU/BNT predicted a positive attitude compared to nurses 20-39 years and from ICU/BMT settings controlling for race and education level (R2 10%, p<0.05) (bivariate analysis also reported). Nurses perceptions of patients' understanding Multivariate analysis: nurses' perceptions of patients' knowledge of clinical trials was predicted by being a research nurse or practice in other settings compared to ICU/BMT, controlling for age, race and educational level (R2 9%, p<0.05) (bivariate analysis also reported).	Nurses generally reported that clinical trials are important to improve standards of care; however, attitudes concerning patient participation in clinical trials and perceptions of patient understanding differed by work setting. Nurses have high expectations regarding the benefits of investigational therapy. **Recommendations for research** The authors state that similar research is required with other comprehensive cancer centre nurses and with nurses from other work settings. **Recommendations for practice** The authors state that targeted interventions that involve nurses to enhance appropriate patient accrual, patient understanding, and patient decision-making should result in improved patient care in centres conducting clinical trials. **Reviewers' comments** This study investigates general attitudes to aspects of trials but does not investigate barriers or factors that encourage trial participation. It also relies on nurses' perceptions of patients views. Given that it has been carried out in a single specialist cancer centre in the US, the findings may have limited applicability.

Author, Year	Study design	Data collection	Response rate	Conclusions
Camerini 1999 [19] **Study aim** To describe the accrual experience of the multicentre breast cancer study with fenretinide (4-HPR) at the Istituto Nazionale Tumori of Milan. **Setting** Single hospital **Country** Italy	Chart review **Sample size, Type** 4030 Patients **Sample characteristics** Trial participation status 4030 patients were screened by prospective or retrospective methods for entry into the 4-HPR trial. Screened patients were classified into the following categories: 'not eligible' if the eligibility criteria were no longer met (827 of 4030 (20.5%)); 'refusal' if the patient was eligible but refused to enter the trial (1388 of 3203 (43.3%)) and 'randomised' if all the selection criteria were met and the patient was included in the trial (1815 of 3203 (56.7%)).	The aim of the trial was the prevention of a contralateral breast cancer in women already operated on for T1-T2 breast cancer without axillary lymph node involvement and without evidence of local recurrence and / or distant metastases. Patient randomisation lasted from March 1987 to July 1993. Retrospective accrual was undertaken in addition to prospective and involved reviewing the medical records of the patients operated on for breast cancer at the institute starting from January 1978. All information about accrual management was stored in a database. **Data analysis** Not stated.	NA **Results** Refusal was more frequent among patients accrued retrospectively (787 of 1612, 49%) than among those accrued prospectively (601 of 1591, 38%). Reasons for refusal to enter the trial were: (n=1388) unspecified 424 (30.5%); refusal of randomisation 17.3%; psychological motivations 216 (15.6%); familial or medical advice 160 (11.5%); difficulties in reaching the institute 103 (7.4%); drug refusal 92 (6.6%); follow up refusal 88 (6.4%); trial too long 33 (2.4%); patients followed elsewhere 21 (1.5%); fear of side effects 11 (0.8%). For women recruited retrospectively the time from surgery to first contact did not appear to impact on the frequency of refusal. Frequency of refusal was stable for intervals up to three years, 40% on average. However in the 3-10 year interval representing most patients the refusal frequency increased sharply to 58%. For both accrual methods the frequency of refusal tended to increase with time from first contact to randomisation. Around 65% were randomised at a 0-6 month interval whereas only 38.9% were randomised at over 2 years (14.9% for the retrospective method). The frequency of refusal increased with patient age. Among retrospectively accrued women it was 41.1% between ages 30-40 and 60.9% between ages 61-70) . In the prospectively accrued group the refusal levels were 35.8% and 41.9% respectively.	The authors state that the reasons for the different yield of retrospective and prospective accrual are many and are mainly related to the time interval since surgery. Women were expected to be strongly motivated to enter the trial as the treatment was not available outside of it and the women had all had primary breast cancer. In the light of these issues the refusal rate was unexpectedly high. The authors further ask for caution in the planning of trials where accrual is likely to be even more challenging in the context of chemoprevention. **Recommendations for research** **Recommendations for practice** Accrual to trials needs careful monitoring to ensure early identification of problems. The outcome of the accrual processes should be reported with the study results in order to improve recruitment strategies in the future. **Reviewers' comments** In this chart review it appears that patients who refused were permitted only one reason for refusal. It is also unclear how the authors elicited reasons for refusal and how they defined the reasons. There are likely to be problems with generalising the results of this study but the time interval between first contact and randomisation is an issue worth considering.

Author, Year	Study design	Data collection	Response rate	Conclusions
Cook 2002 [20] **Study aim** Failure to recruit to a randomised trial of the effects of three potential xerostomia-relieving products on patients presenting with mouth dryness within the Holme tower, Marie Curie Centre in Cardiff, Wales led to a feasibility study into the future of palliative care research at the centre. A simplified trial (crossover design) was introduced and aimed to raise the profile of research and get staff involved in all stages of the process. **Setting** Palliative care centre **Country** UK	Feasibility study **Sample size, Type** 140 pts Both **Sample characteristics** Age Not stated Gender Of 35 trial participants 14 were male and 21 were female. Cancer sites Not stated. Palliative care Trial participation status 140 patients were approached. 35 were entered onto the study. No patient crossed over to the other treatment. It is unclear how many professionals were involved in the study.	Not stated. **Data analysis** Not stated.	NA **Results** The new approach was successful in raising the profile of research in the centre and involving staff in the process throughout. Interward referral competitions were well received. Introduction of key workers was less successful as the nurses seemed to wane in enthusiasm quite quickly. No patients were crossed over to the other product after seven days as planned due to decisions by nursing staff. Some referrals were inappropriate as they did not fit the selection criteria.	Even though there has been a growth in the extent of palliative care research in recent years resistance still exists within the professional community. **Recommendations for research** More responsibilities could be given to ward staff in future studies but this will require co-operation between the researchers and nurses. Good quality research answering much needed questions should result in better care. **Recommendations for practice** Avoid overlong project duration as staff interest in the research study may wane and referrals decrease. Involve staff in all stages of the research process and ask for their opinions and advice prior to commencement of the study. Constantly update on progress and disseminate findings at project completion. Study methods and assessment of patient and documentation should be kept simple to aid recruitment and retention. Keep patient assessment periods as short as possible. **Reviewers' comments** No quality assessment is possible due to lack of information on study methodology. It was unclear how the data gathered on how the feasibility study progressed and barriers to its success. It appears to be entirely from the researcher's perspective. The authors do not appear to have obtained information from the staff involved into the barriers they experienced.

Author, Year	Study design	Data collection	Response rate	Conclusions
Crosson 2001 [58] **Study aim** To provide more detailed information about primary care physicians knowledge, attitudes and practices related to cancer clinical trials. **Setting** Community **Country** USA	Survey **Sample size, Type** 706 Health professionals **Sample characteristics** 706 primary care physicians practising in the United States. There were approximately equal numbers from general and family practice, internal medicine and obstetrics and gynaecology. 78% were male; 59% spent 40 hours or more in direct patient care; 20.5% worked in a rural area; and 42.1% were affiliated with a university or medical school (data also broken down by professional group)	A national probability sample of 1,405 physicians was selected from the American Medical Association and American Osteopathic Association Lists. The sample was drawn from general and family practice, internal medicine and obstetrics and gynaecology at different sampling rates. Up to 30 attempts were made to contact physicians by telephone. 481 completed the interview by telephone and 225 completed a self-administered version of the questionnaire. **Data analysis** The statistical package SUDAAN was used to generate estimates and standard errors of the estimates.	61% of eligible physicians **Results** 49.2% (CI: 45.2, 53.2) of physicians said they brought up the topic of clinical trials with none of their patients, 39.1% (35.3, 42.9) brought it up with only a few patients. The two reasons most frequently cited for not doing so were a preference to leave discussions about clinical trials to the oncologist (40.9%, CI: 36.8, 45.0) and not being aware of any trials that might be available to their patients (37.0%, 95%CI: 32.9, 41.1). 94.1% (95%CI:92.1, 96.1) said they would be very or somewhat supportive of oncologists' recommendations that patients participate in trials. Physicians' opinions of possible barriers to patients enrolling in clinical trials (a large barrier; somewhat of a barrier; not a barrier at all). Patients fear being a clinical research subject or a 'guinea pig': 53.5% (SE 3.9);41.7% (SE 3.7); 4.8% (SE 1.8) Patients believe that a clinical trial investigator is more interested in the research than in the patient's well-being: 24.6% (SE 3.3); 57.8% (SE 3.9); 17.6% (SE 2.9) Patients believe that a particular treatment or intervention is ineffective: 24.4 (SE 3.3); 53.7 (SE 3.9); 21.9 (SE 3.1) Patients do not realise that they would be receiving state of the art treatment: 22.9% (SE 3.3); 53.0% (SE 3.9); 24.1% (SE 3.3) Patients think the intervention or treatment in a clinical trial will have more undesirable side effects than the standard treatment: 22.0% (SE 3.1); 60.8% (3.7); 17.2% (2.9) Patients assume that the intervention or treatment is more invasive than the standard treatment: 14.0% (SE 2.7); 55.1% (SE 3.9); 31.9% (SE 3.5) Patients tend to lose confidence in their physicians when the physicians recommend a clinical trial for their cancer therapy: 3.6% (SE 1.4); 23.3% (SE 3.3); 73.0% (SE 3.3) The importance of possible obstacles to patients enrolling in clinical trials (very important; somewhat important; not at all important) Health insurance and managed care providers do not always cover all patient costs: 64.7% (SE 3.7); 29.6% (SE 3.5); 5.7% (SE 1.8) Transportation and travel times are problematic: 47.1% (SE 3.9); 43.0% (SE 3.9); 9.9% (SE 2.4) Access to trials is limited: 41.6% (SE 3.9); 47.0% (SE 3.9); 11.3% (SE 2.5) Language, ethnic and cultural differences present special problems: 26.7% (SE 3.3); 48.6% (SE 3.9); 24.8% (SE 3.3) Information about the trial is too technical: 19.6% (SE 3.1); 58.4% (SE 3.7); 22.0% (SE 3.1) Too much time is required for participation: 19.4% (SE 3.1); 53.9% (SE 3.9); 26.6% (SE 3.3) Data are also reported sources of cancer information used by physicians and knowledge of National Cancer Institute (NCI) resources.	Primary care physicians may represent an important untapped resource for introducing the concept of clinical trials as an option to newly diagnosed cancer patients. **Recommendations for research** None stated **Recommendations for practice** Given the physicians' reliance on colleagues and journals for information, potential ways to reach them to promote awareness of NCI resources and services on clinical trials include national medical association meetings as well as association journals. **Reviewers' comments** This is a well conducted survey; however the findings may not be generalisable to the UK context. No information is provided on the method of questionnaire construction therefore the reliability and validity of the measure is unclear. Care needs to be taken in drawing implications from the patient barriers identified as these are based on the physicians' perceptions and they rarely discussed clinical trials with their patients.

Author, Year	Study design	Data collection	Response rate	Conclusions
Crowley 2003 [46] **Study aim** To evaluate the strategy of using screening questions to identify patients interested in participating in research. **Setting** Palliative care clinic **Country** USA	**Study design** Survey **Sample size, Type** 86 Patients **Sample characteristics** Age Mean age 67 years (range 41-88 years) Gender 86M (100%) Cancer sites Lung: 22 (26%); Colon: 17 (20%); Head and Neck: 11 (13%); Prostate: 9 (10%); Other: 27 (31%) Trial participation status Not stated. Previous trial experience Not stated. Misc Enough or more than enough money at the end of the month: 41 (48%); Estimated prognosis < 6 months: 39 (46%). Race: African American 56 (65%); White 27 (31%); Hispanic 1 (1%); Asian 2 (2%).	During the intake process at the first clinic visit all patients were asked two screening questions assessing their interest in participating in disease-modifying and symptom-related research. Patients were told that affirmative answers to either of the two screening questions might result in review of their medical records to ascertain eligibility and possible recruitment for research. Patients were asked to explain their answers to both questions. Explanations for interest in research were categorised into potential benefits, indirect or collateral benefits and altruism. Explanations for reluctance to taking part in research were divided into four categories: physical limitations, ' hassles', perception of no benefits and concerns about risks. These codes were generated and revised by consensus by two individuals blinded to patient characteristics. Multiple codes were used to define each response if patients gave more than one explanation. Additional questions assessed demographic characteristics, clinical and social history, needs for social services and preferences regarding life-sustaining treatment. Symptoms were assessed using the Global Distress Index (GDI) of the Memorial symptom Assessment Scale. Functional status was assessed using the Eastern Cooperative Oncology Group (ECOG) scale. The clinic physician assessed prognosis. **Data analysis** Patients who were interested in learning about research were compared using the sign test and patients' characteristics associated with interest in either type of research were evaluated using either the Wilcoxon rank sum test or the fisher exact test. The same tests were used to evaluate relationships between patient characteristics and the explanations they gave for their interest or lack of interest in research. Concordance of responses to the two screening questions was assessed using the Kappa statistic with a corrected p value of 0.007 for multiple comparisons. Logistic regression was used to identify characteristics that were independently associated with interest in symptom related and	NA **Results** Patients were less likely to be interested in symptom-related research than in disease-modifying research (32 of 86 (37%) vs. 46 of 86 (54%), p=0.009. Patients' responses to the screening questions for symptom-related and disease-modifying research were moderately associated: kappa =0.41; p < 0.001. In the logistic modelling (based on 32 responses) independent predictors of interest in symptom management research included younger age (OR=0.90 (95% CI: 0.86, 0.96), p =0.001) , white race (OR=10.50 (95% CI: 3.24, 33.8), p < 0.001) and a lower mean GDI symptom distress score (OR=0.08 (95% CI: 0.02, 0.43) p =0.004). In the logistic modelling (based on 49 responses) independent predictors of interest in disease-modifying research included younger age (OR=0.92 (95% CI: 0.88, 0.97) p=0.003) and white race (OR = 21.19 (95% CI: 5.12, 87.7) p< 0.001). Patients were less likely to cite a hope of potential benefit for symptom research (i.e. that the intervention being tested would improve health, survival or quality of life) than for disease modifying research (9 (10%) vs. 28 (33%), p < 0.001). Expectations of the benefits of either type of research were not related to GDI score, age or performance status. Patients cited expectations of collateral benefits (e.g. improved care due to better monitoring) approximately equally for both symptom-related and disease modifying research (9 (10%) vs. 7(8%), p = 0.625). Patients who cited collateral benefits for either type of research (10 (12%)) had a lower symptom burden (0.48 vs. 0.74, p =0.027) and were younger (58 vs. 68 years, p < 0.001) than those who did not. A similar percentage of	Screening questions may be useful in identifying patients who are willing to be recruited for research. The challenges of recruiting patients for symptom management and disease modifying research are surmountable. **Recommendations for research** Further study is needed to determine whether screening questions introduce selection bias in the recruitment process. Determining the influence of patient characteristics such as socioeconomic and racial factors deserves further research. **Recommendations for practice** Efforts to enhance recruitment of particular subgroups may be more effective if they highlight aspects of a study that are more likely to be important to those patients. **Reviewers' comments** Numbers are relatively small and when comparing subgroups analysis may be underpowered to detect effects. All study participants are male and almost half have a poor prognosis which will limit generalisability of results. Explanations are categorised by authors and effects are based on this.

		disease-modifying research with all variables that reached a significance level of p less than 0.25 in bivariate tests considered for inclusion in the model. Variables were subtracted from the model sequentially. The resulting model pairs were compared with the likelihood ratio test. Variables that resulted in a significant likelihood ratio test on subtraction were restored and retained in the final model. The sample size had 0.80 power to test the hypothesis that patients would be at least 20% more likely to express an interest in learning about disease-modifying research than they would be to learn about symptom-related research.	patients cited altruism as a motivation for both types of research (12 (14%) vs. 19 (22%) , p=0.119). Patients who cited altruism for either kind of research (23 (27%)) were older (72 vs. 65, p=0.010) and more likely to be white (17 of 23 (74%) vs. 10 of 63 (16%), p =0.001). Patients cited physical limitations as an explanation for their reluctance to learn about both types of research. They were more likely to cite physical limitations in symptom related research than disease-modifying research (25 (29%) vs. 16 (19%), p=0.023). Patients cited inconveniences for both types of research but more for symptom related (16 (19%) vs. 9 (11%), p=0.065). Patients cited the absence of benefits for both types of research but to a greater degree for symptom related research (12 (14%) vs. 5 (6%), p =0.009). Patients who cited this reason for either kind of research (14 (16%) had lower GDI scores than those who did not (0.75 vs. 0.54, p = 0.027) Patients cited risks of research participation such as medication side effects only in relation to disease modifying research (9 (10%) vs. 0 (0%), p = 0.004). Patients' concerns about research were not related to age, GDI score or ECOG performance status.	Different categorisation of results might change the overall picture. This study is not about trial participation but about a patient's interest in learning about studies that are being undertaken in the unit. There are no data on the patients who actually went on to participate in a trial.

Author, Year	Study design	Data collection	Response rate	Conclusions
Diener-West 2001 [21] **Study aim** To study and compare predictors of patient participation in two related multicentre trials conducted concurrently in North America by the same group of investigators. **Setting** Multiple hospitals **Country** USA	**Sample size, Type** 6906 Patients **Sample characteristics** The Collaborative Ocular Melanoma Study (COMS) consists of two multicentre randomised trials to evaluate the effectiveness of radiotherapy in comparison to standard enucleation in prolonging survival of patients with choroidal melanoma. One trial was for patients with large tumours, the other for patients with medium-sized tumours. The study was designed to encourage the enrolment of every patient seen at any of the 43 participating clinical centres during the course of the study with the exception of patients who failed to satisfy one or more of the eligibility criteria. Age The median age of the study participants was 60. Gender Medium tumour trial: 652F (49%) and 665M (5 .,1%) enrolled, 746F (48%) and 813M (52%) not enrolled. Large tumour trial: 425F (42%) and 587 (58%) enroled,140F (48%) and 155M (52%) not enrolled. Cancer sites All ocular melanoma. Of 6906 reported patients 1860 were large tumour patients and 5046	The investigators reported to the co-ordinating centre of the study in Baltimore every patient with choroidal melanoma examined in a COMS centre regardless of whether eligible and enrolled, eligible and not enrolled or ineligible. Checks were made for multiple reporting of individuals. Baseline sociodemographic and clinical data were collected for both enrolled patients and eligible patients who did not enrol in the randomised trials in the COMS study during the first three years of recruitment. Partial information was collected thereafter. An eligible patient who did not enrol was taken to be one who had refused enrolment or who may not have been given the opportunity by clinical centre staff to participate. An ophthalmologic evaluation was performed for all patients and a short personal interview was conducted to obtain the sociodemographic information. **Data analysis** Logistic regression methods were used to identify factors predictive of trial participation. Both univariate and multivariate models were used (the latter covering the combined effects of sociodemographic and clinical characteristics on the likelihood of enrolling in the study). Individual characteristics that were potentially associated with enrolment for either trial at a significance level of p <0.15 in the univariate regression models were included in the multivariate logistic regression analyses. The final multivariate models included all variables achieving statistical significance at the 0.05 level for either trial. The primary analyses were based on all patients evaluated by July 31 1998, the end of patient enrolment and included only the variables that were collected throughout the course of the study. Secondary analyses were also performed on the subset of patients evaluated before January 1990 for whom complete sociodemographic and clinical information was available to assess the stability of these findings. Other analyses were performed to adjust for differences in enrolment rates among clinical centres A dummy variable was constructed to	NA **Results** In univariate models in the medium tumour trial patient age 60 years or older were more likely to participate (p <0.15), as was having a less than college education, non-managerial occupation, current smoking and residing in the same state as a COMS clinical centre. In univariate models in the large tumour trial the following were more likely to participate in a trial: males, individuals who were not college educated, those living with other adults or children in the same household and individuals residing in the same state as a COMS clinical centre. In univariate analysis in both trials patients with larger tumour dimensions and initial visual acuity worse than 20/20 in the study eye were more likely to enrol. In multivariate regression models variables that were significantly predictive of trial enrolment in the medium tumour trial were (p <0.05): age greater than or equal to 60: Adjusted OR= 1.20(95% CI: 1.03,1.39), residence in the same state: Adjusted OR=1.38(95% CI: 1.16, 1.64) and worse initial visual acuity in the study eye: Adjusted OR=1.26(95% CI: 1.07, 1.48). Larger tumour basal diameter was not significant: Adjusted OR = 1.12 (95% CI: 0.97, 1.30). In multivariate regression models variables that were significantly predictive of trial enrolment in the large tumour trial were (p <0.05): residence in the same state: OR=2.20(95% CI: 1.62, 3.00), larger tumour basal diameter: OR=1.38 (95% CI: 1.05, 1.82). Neither age 60 years or over (Adjusted OR = 0.98 (95% CI: 0.74, 1.30) and worse initial visual acuity in the study eye (Adjusted OR=1.39 (95% CI: 0.95, 2.04) were significant predictors of trial participation.	Patient enrolment in clinical trials may be increased by heightened physician awareness of sociodemographic and clinical predictors of trial participation, strategies for addressing these differences and enhanced communication between physicians and patients. **Recommendations for research** Not stated. **Recommendations for practice** Not stated. **Reviewers' comments** The analysis does not differentiate between those eligible for trial participation but not approached to take part and those approached who refused. Patients' reasons for non-participation are not investigated. It examines predictors of enrolment in a fairly large group of patients.

	were medium tumour patients. Trial participation status 70% of the large tumour patients were eligible and of these 77% were enrolled. 57% of the medium tumour patients were eligible and of these 46% were enrolled. Previous trial experience Not stated. Misc Patients were almost exclusively non-Hispanic whites (98%). Slightly less than half were employed and about one quarter of the patients were college graduates. Based on data reported during the first three years of COMS Data collection nearly one third held managerial positions and one third held technical positions. Over 40% had never smoked and only 20% were current smokers. Almost three quarters of the patients for whom the information was requested stated a religious affiliation. Approximately 70% were married; only 15-20% were living alone. Most patients did not live in households with children. Over 70% resided in the same state as the reporting COMS clinical centre.	represent low versus high overall enrolment (based on median enrolment across centres). All statistical analyses in this report were based on all information available as of December 31 2000 and used SAS statistical software.	The magnitude of the adjusted odds ratios remained robust when an indicator variable (high versus low enrolling clinic) was included in the models to adjust for differences in enrolment rates among clinical centres. Analysis of the smaller subset of eligible patients evaluated prior to 1990 resulted in similar trends although the associations were not statistically significant (data not shown).	

Author, Year	Study design	Data collection	Response rate	Conclusions
Ehrlich 2002 [53] **Study aim** To evaluate and describe those factors that impacted on failure of two randomised controlled trials on the role of minimally invasive surgery (MIS) in children with cancer to help ensure future successful surgical clinical trials. **Setting** Multiple hospitals **Country** USA	Survey **Sample size, Type** 86 Health professionals **Sample characteristics** The sample consisted of 86 surgeons, from across 77 institutions, who were members of the two groups that had received funding for two RCTs on MIS, the Children's Cancer Group (CCG) and the Pediatric Oncology Group (POG). The two studies opened in 1996 and closed in 1998 due to lack of patient accrual (26 patients in the thoracoscopic arm and 6 in the laparoscopic). Further demographic and professional characteristics were not reported.	The sample was identified from CCG and POG rosters, checked for eligibility and addresses were confirmed from professional body directories. Surgeons completed a postal self-report questionnaire. It consisted of 19 items, with responses as a yes/no format, or on a 5-point scale from strongly agree to strongly disagree and the opportunity for written comments. The questions were based on six hypotheses the authors had formulated as to why trial accrual had been unsuccessful. **Data analysis** The authors stated that descriptive statistics, chi-square tests, analysis of variance and an extensive correlation analysis were used when appropriate. 18 of the 86 respondents did not answer any survey questions and were excluded from most of the analyses.	62% (86/140) responded and 48.5% (68/140) completed the survey **Results** Hypothesis one: the study failed due to poor organisation, processing and publication 92% (59/64) knew about the two studies. They heard about them through CCG/POG meetings (72%); CCG/POG publications (14%); from other surgeons (7%) and oncologists (7%). 65% (n=41) knew the National Cancer Institute had funded the study and 50% knew the studies had a randomised and nonrandomised arm. 73% (n=47) reported receiving the protocol from the principal investigator (PI, usually an oncologist) at their institution. Many waited for up to one year after the trial opened before receiving the protocol (n not specified). 72% (n=43) said they had supported the aims and objectives. Hypothesis 2: the study failed due to the process of the Institutional Review Board (IRB) being overwhelming and a limiting step For this study it was the responsibility of surgical principal investigators to obtain IRB approval whereas it was historically carried out by oncologists.26/61 institutions submitted a protocol, 17 did not and for 18 institutions it was unknown whether they did so. 33% (n=20) were submitted by a surgeon; 18% (n=11) by an oncologist and 48% (n=29) did not know. One submitted protocol was not approved. 50% of respondents stated that a universal IRB form or assistance from CCG/POG would have been helpful. Hypothesis 3: the coinvestigators (paediatric oncologists) did not support the study 75% (n=51) believed their institution's oncologists were aware of the study: 36% (n=25) felt their oncologists supported the study objectives; 20% (n=14) felt they did not support it and 28% (n=19) did not know. 76% (n=43) did not feel that the referral pattern of their oncology service affected study enrolment. Hypothesis 4: the study was limited by the inability of	The study failed because of lack of accrual for a variety of reasons: failure to submit to the institution's IRB, lack of surgical expertise with MIS procedures and preconceived surgeon bias toward either an endoscopic or traditional open approach. **Recommendations for research** None stated **Recommendations for practice** In future studies, greater attention and utilisation of the resources of cooperative study groups is required. **Reviewers' comments** This is a poorly reported survey which focuses on the reasons why a specific clinical trial failed due to poor accrual. No information is provided on the method of questionnaire construction therefore the reliability and validity of the measure is unclear. The analysis was poorly reported. It is also unclear how respondents may have differed from nonrespondents.

			surgeons to perform the MIS procedure. 37% (29/70) were not actively practicing thoracoscopic procedures and 35% (27/60) were not actively practicing laparoscopic procedures when the study opened (This analysis included 10 surgeons who had not completed the questionnaire because they stated they were not actively practicing MIS at the time of the study). Hypothesis 5: Patient recruitment was poorly organised The authors state that because of the small number of recruited patients it is not possible to assess whether recruitment methods affected study failure. Hypothesis 6: Preconceived biases by surgeons, oncologists and families prevented the studies from being successful Were surgeons biased toward a particular approach? Strongly agree (n=12); agree (n=21); neutral (n=13); disagree (n=8); strongly disagree (n=3) (a significant number of respondents believed their speciality was biased to a particular approach, p<0.001. Were oncologists biased toward a particular approach? Strongly agree (n=7); agree (n=26); neutral (n=17); disagree (n=13); strongly disagree (n=4) (a significant number of respondents believed oncologists were biased to a particular approach, p<0.001). Were the study's questions already answered? Strongly agree (n=4); agree (n=11); neutral (n=19); disagree (n=7); strongly disagree (n=12). 2/54 respondents said the family was biased toward an open surgery approach and 14/54 said the family were biased towards an MIS approach. The authors analysed the factors that affected surgeon and oncologist support of the study. Surgeon support was related to whether they received a copy of the study protocol (p<.001) and whether they were participating in MIS (p<.016). The oncologist's knowledge and support of the study (as perceived by surgeons) related to whether MIS was practiced at their institution (p<.03).	

Author, Year	Study design	Data collection	Response rate	Conclusions
Ellis 1998 [47] **Study aim** To explore knowledge of and attitudes towards randomised controlled trials among women in the community and breast cancer patients. **Setting** Single hospital **Country** Australia	Qualitative **Sample size, Type** 41 Patients **Sample characteristics** 21 respondents were women in the community, only 20 were women previously treated for breast cancer. Age Median decade for women in the community was 30-39 and for women previously treated for breast cancer 50-59. Gender All women Cancer sites Breast cancer Trial participation status Not stated Previous trial experience Not stated Misc Of the 20 breast cancer patients 15 were married, 3 widowed / divorced and 2 were single. 15 had a family history of cancer and 10 specifically of breast cancer.	The breast cancer patients were identified from the records of the Medical Oncology department at the Royal Prince Alfred Hospital. They had all been diagnosed with breast cancer in 1995. Contact was made by telephone and an invitation to attend a focus group was posted to interested participants. Eight focus groups were held which also included 21 mothers or grandmothers not suffering from breast cancer. Four to eight women were included in each group. An outline for the discussion was developed following a review of the literature and consultation with psychologists and medical oncologists experienced in the conduct of clinical trials. This included points on clinical decision making, understanding and knowledge of clinical trials including treatment allocation and randomisation, willingness to participate in a trial, advantages and disadvantages of trials, types of treatment in trials and the need for clinical trials to benefit others. Separate focus groups were carried out for those with cancer and the community group. Focus groups with breast cancer patients were conducted at the Medical Psychology unit at the hospital. Participants completed a brief demographic sheet prior to the focus group. A facilitator and observer were present in all groups. All focus groups were audio taped and transcribed in full and salient issues were also noted during the discussion by one of the study authors. As no new or additional information was discussed at the last two groups no additional focus groups were conducted. **Data analysis** The analysis of transcribed material was informed by grounded theory. Analysis of points identified from the transcripts were compared with individual points identified by one of the study authors in the discussion. Points were organised into themes by both the authors and responses summarised according to the original questions posed. The final list of issues was discussed by both of the study authors.	NA **Results** Most women in both groups (breast cancer and community) wanted to receive all information about their disease but they varied in their preferences for involvement in decision making. The majority of women in both groups did not have a good understanding of the need for clinical trials or the manner in which they were conducted. They were more likely to think that trials were conducted to determine safety rather than efficacy of treatments. Most women were aware of the use of a comparator in trials but were unsure how this would happen or felt that a placebo might be used. Reasons for randomisation were poorly understood. A number of women thought that trials were only appropriate for the terminally ill or conversely were not appropriate for cancer. The majority of women acknowledged the need for clinical trials but felt they would not participate. A number of breast cancer patients reported feeling very insecure around the time of their diagnosis and felt discussion about clinical trials would add to their anxiety. Both groups perceived the uncertainty of trials and randomisation as negative aspects. Additional or unknown side effects from the new treatment and feeling coerced to take part were also fears. Differences emerged between the groups in their perceptions of the advantages and disadvantages of participating in clinical trials: women in the community were more likely to mention practical issues such as disruption to family life and activities whereas breast cancer patients were more likely to mention emotional issues such as the stress of participating in a trial and potential loss of control. Most women could see the advantages of participating in trials such as furthering medical knowledge or benefiting other people in the future, cheaper care or more intensive follow up and a greater sense of hope. However among breast cancer patients a number felt that a clinical trial did not benefit individual patients and that their decisions would be motivated by what was best for themselves rather than others. There was almost uniform agreement that women should be offered a clinical trial if one existed and some women emphasised the altruistic aspect of taking part in a trial. A number of women commented at the end of the focus groups that they would be more willing to consider a clinical trial now they understood more clearly what was involved. They emphasised the need to give information on trial conduct.	The results suggest that greater community awareness of clinical trials may be needed to improve participation in clinical trials. **Recommendations for research** These focus group findings require validation in a larger sample. More research is needed on whether being better informed leads women to participate in clinical trials. **Recommendations for practice** Strategies to improve recruitment should examine ways to reduce the perceived disadvantages of trial participation. **Reviewers' comments** Small study, not necessarily generalisable. Difficult to separate out views of community women from breast cancer patients.

Author, Year	Study design	Data collection	Response rate	Conclusions
Ellis 1999 [48] **Study aim** To assess the understanding of and attitudes towards randomised clinical trials amongst patients attending oncology outpatient clinics. **Setting** Single teaching hospital **Country** Australia	**Study design** Survey **Sample size, Type** 60 Patients **Sample characteristics** Age 55.2 (SD 14) years Gender 14M (23%), 46F (77%) Cancer sites Breast: 32 (53%); Gastrointestinal: 8 (14%); Lymphoproliferative: 6 (10%); Gynaecological: 4 (7%); Testicular: 3 (5%); Lung: 2 (3%); Other: 5 (8%). Trial participation status 24 respondents stated that they had been invited to participate in a clinical trial. Of these 17 indicated that they believed they were participating in a clinical trial of whom 6 were. Previous trial experience In total 8 (14%) were enrolled in a clinical trial. Misc Marital status 4 (7%) single; 40 (66%) married / de facto; 16 (27%) widowed / divorced / separated. Respondents were a median of 1.7 years (interquartile range 0.7-4.4 years) following the diagnosis of their cancer.	Survey was informed by literature review and focus group interviews as described in Ellis 1998[47]. During 1996 a cross-sectional survey was undertaken of patients attending medical oncology outpatient clinics at the Royal Prince Alfred Hospital, Sydney. All were eligible except non-English speaking patients and patients attending for their first consultation. Patients were approached prior to a scheduled outpatient appointment. Demographic data were collected as were respondents' information needs (3 point scale) and preference for involvement in clinical decision making (5 point scale). Knowledge and attitudes towards RCTs were measured using a 5 point Likert scale. Respondents were asked to indicate their willingness to participate in a hypothetical RCT and using a 5 point likert scale to rate 20 items of lt potential influence. **Data analysis** Data analysis was undertaken in SPSS. The major outcome as respondents' willingness to participate in a RCT. Answers to knowledge questions were summed and the total score (range 0-7) used as an indicator of knowledge about the trial process. Analysis of variance was used to explore the relationship between knowledge scores and trial participation. A principal components analysis (with varimax rotation) was undertaken on the items assessing attitudes to clinical trials and scores calculated for the resulting factors. A multivariate logistic regression analysis was undertaken to examine the relative influence of the factors identified in the principal components analysis on patients' decision to join a clinical trial. A sample of 60 patients had a power of 0.80 at a significance level of 0.05 to detect a difference of 1.5 (approximately 1 SD) or greater in mean knowledge scores amongst patients willing to participate in a clinical trial compared with patients who were not.	100% **Results** 88% of respondents thought that patients should be asked to participate in trials testing new treatments. 33% would consider participating in a randomised trial themselves. If a trial was endorsed by an independent cancer information service respondents would be more likely (72%) to participate. Knowledge about randomised trials was not high. Respondents scored a median of 3 out of 7 (interquartile range 2-4) correct answers to a series of questions about randomised trials. 11 (19%) knew the correct responses to five or more of the seven questions. 51% agreed that randomised trials were the best way of finding out whether one treatment was better than another yet 31% were unaware that treatment is allocated by chance in such trials. 24% thought that the doctor would know that one of the treatments offered in the trial was better than the other and 74% thought that the doctor would ensure that they received the best of the treatments on offer. 18% thought that clinical trials are offered only when the doctor considers the situation hopeless and 19% that clinical trials test treatment which nobody knows anything about. There was no difference in mean knowledge scores between respondents who would consider joining a trial (3.2, SD 1.4) and those who would not (3.2, SD 1.7) or between respondents receiving treatment as part of a trial and those not. There was no evidence of an association between decision making preferences and willingness to join a clinical trial. One item was omitted because it lowered the overall internal reliability. In factor analysis a six factor solution explaining 66.5% of the variance in respondents' willingness to join a trial suggested the following factors: perception of the doctor; personal benefit; perception of inconvenience / loss of control on clinical trial; sense of obligation to the doctor; attitudes towards experimentation and uncertainty and one difficult to categorise. In logistic regression willingness to participate in a randomised trial was	Patient understanding of the need for and conduct of clinical trials is not good. Evaluation of new strategies to educate the public and patients about trials is needed. **Recommendations for research** The findings of the study require validation in a larger sample of people considering entry into a real clinical trial. **Recommendations for practice** Involvement of consumers in the design and conduct of clinical trials and in evaluation of strategies to improve doctors' communication of clinical trial information is needed. **Reviewers' comments** Respondents' willingness to participate in a randomised trial reflects a hypothetical decision. The number of actual trial participants was very small. The study may have a gender bias as the issues covered in the questionnaires were based on a focus group study of women only.

			most strongly influenced by the patients' perception of the doctor (OR=1.8, p=0.05) attitudes to experimentation and uncertainty in treatment allocation (OR= 0.58, p=0.05). There was a trend for decisions to be influenced by patients' perception of inconvenience / loss of control on a clinical trial (OR 0.77, p = 0.09). The remaining factors did not appear to influence patients' willingness to participate in a clinical trial. Data on preferences for information and involvement in clinical decision making was also provided but was not extracted here.	

Author, Year	Study design	Data collection	Response rate	Conclusions
Ellis 1999 [59] **Study aim** To identify barriers to participation in current randomised trials for early breast cancer. **Setting** Other **Country** Australia	Survey **Sample size, Type** 269 Health professionals **Sample characteristics** 246 surgeons(S), radiation oncologists (RO) and medical oncologists (MO) involved in the treatment of breast cancer across Australia. Mean age: MO 42.1 years (40.7-43.5), RO 44.3 years (42.2-46.4), S 50.2 (48.2-52.2). Male: MO 82%, RO 77%, S 99%. Post graduate qualifications: MO 33%, RO 16% S 16%. Access to data management MO 79%, RO 82%, S 59%. Participant in the Australian and New Zealand Breast Cancer Trials Group (ANZBCTG) MO 71%, RO 37%, S 77%	All medical and radiation oncologists across Australia and surgeons who were listed as participants in ANZBCTG residing within Australia were sent a postal questionnaire to be completed anonymously. A reminder letter was sent two weeks later and a second copy of the questionnaire was sent to respondents after one month. The questionnaire asked about attitudes towards and participation in current (RCTs), in addition to their perceptions of the barriers to participation. Participants were also asked to estimate how many of their breast cancer patients were enrolled in breast cancer trials in the past 12 months. **Data analysis** 23 participants were excluded as more than 25% of the questionnaire was unanswered therefore 246 questionnaires were included in the analysis. Descriptive statistics were used to report demographic data and questions about barriers to participation; chi square analysis was used for demographic data; and analysis of variance (ANOVA) was used to examine the relationship between age and categorical variables. Estimates of number of referrals to trials were grouped into non-accruers (0 patients); low accruers 1-9 patients); and high accruers (10 patients).	71% (269/381) **Results** Radiation oncologists were significantly less likely to be high accruers to clinical trials in breast cancer (p=0.01): high accrual MO 22%, RO 17%, S 31%. Higher rates of accrual were also associated with being a participant in ANZBCTG (p=0.00001), having access to data management (p=0.002), being male (p=0.01) and seeing a greater number of new cases of breast cancer per month (p=0.0007). (n=201 participants were included in this analysis) Factors limiting participation in trials (180 participants were included in this analysis) Resources problems 44.4% (n=80): too difficult overall (n=44), no/limited access to data management (n=52), other (n=20). Issues specific to current breast cancer trials 44.4% (n=80): relevance of the study question (n=54), inappropriate standard therapy arm (n=46), bias against radiotherapy (n=12), other (n=10). Too few breast cancer patients 16.7% (n=30); patient factors 15.6% (n=28); decision made by someone else 11.1% (n=20); problem with trial organisation 6.1% (n=11); lose patients or professional standing 5.6% (n=10); prefer to make own decisions about treatment 2.8% (n=5). There was no significant difference between the professional groups on these responses. Suggestions to improve participation in clinical trials (146 participants were included in this analysis) Resource issues (n=95) Ease of administration (n=61): provide data management, minimise paperwork Help in patient identification (n=36): summary trial information, early use of clinical trial personnel Increase funding (n=34): compensate doctors, more funding, increase number of oncologists Improve aspects of study design (n=44): more clinically relevant trial questions, include all groups in study design, avoid drug company sponsered trials. Improve aspects of trial conduct (n=35): improve communication between specialists, better feedback on trial progress, better recognition of individual clinicians. Promote RCTs among doctors (n=24): educate doctors/students, incorporate into accreditation/continuing medical education, make departmental funding dependent upon clinical research. Promote RCTs among patients (n=27): educate the community, short patient information/handout, involve patients in the design/conduct of trials. There were differences between the professional groups in their suggestions to improve clinical trials (see paper).	The results of this study suggest that efforts to improve doctors' participation in clinical trials need to address a number of issues. More empirical research is needed to evaluate new strategies to raise participation in clinical trials. **Recommendations for research** The authors state that attempts should be made to incorporate the views of surgeons, radiation and medical oncologists involved in the management of breast cancer in setting future research priorities. **Recommendations for practice** The authors state that mechanisms to seek and allow input from a broader range of breast cancer specialists in the design phase of clinical trials merits consideration. They also suggest that consideration is given to the promotion of RCT and an evidence-based approach to decision-making in specialist training programmes, or the integration of clinical research into continuing medical education/hospital accreditation programmes. **Reviewers' comments** There was a good sampling frame for the medical and radiation oncologists. No information is provided on the method of questionnaire construction therefore the reliability and validity of the measure is unclear. The data were adequately though there were some limitations.

Author, Year	Study design	Data collection	Response rate	Conclusions
Ellis 2001 [49] **Study aim** To explore the association at different time points in the trajectory of breast cancer care, between anxiety, knowledge and attitudes on women's willingness to participate in randomised clinical trials. **Setting** Breast clinic **Country** Australia	**Study design** Survey **Sample size, Type** 545 Patients **Sample characteristics** Age Mean age 48.9 years (SD 11.3 years), Range 17 to 87 years Mean age breast cancer patients 51.3 years; women at diagnostic clinic 45.4; screening 52.1 Women attending for diagnostic assessment were significantly younger than breast cancer patients and mammography patients (p<0.0001). Gender All women Cancer sites 83 Breast cancer (newly diagnosed), 205 being screened for breast cancer and 257 attending for diagnostic assessment. Trial participation status Unclear Previous trial experience Not stated Misc Women with breast cancer were less likely to work outside the home than the other two groups. Otherwise the groups were similar on the demographic variables assessed.	All women attending the Medical Benefits Fund (MBF) Sydney Square Breast Clinic (SSBC) for a screening mammogram or diagnostic assessment over a 4 week period during late 1997 were eligible to participate in the survey. Women undergoing treatment for early stage breast cancer at the Sydney Breast Cancer Institute (SBCI) during 1998 were also eligible. They were approached within 7 days of undergoing a definitive surgical operation for early stage invasive breast cancer before seeing a medical oncologist. Women with locally advanced breast cancer treated with initial chemotherapy or radiotherapy were not eligible. Women were excluded if they had metastatic disease at presentation, were unable to read English or unable to complete a questionnaire. Women were approached by one of the study authors who explained the purpose of the research and gave them an information sheet. The questionnaire was developed using information obtained from focus group interviews (Ellis 1998[47]) in conjunction with a review of the literature. The questionnaire had been previously used in a sample of patients attending medical oncology outpatient clinics (Ellis 1999[48]). The questionnaire covered the following areas: demographic data; The Hospital Anxiety and Depression Scale (HADS) which scores respondents into 3 groups: noncase, possible case and definite case; Women's preferences for the amount of information they wish to receive from their doctor (3 item scale) and their level of involvement in clinical decision making (5 item scale); knowledge about the need for clinical trials and about the manner in which randomised clinical trials are conducted which was measured using a 7 item scale developed for this study; attitudes towards randomised clinical trials which was measured using a 36 item scale developed from focus group data and a review of the literature that measured the impact of individual items on women's willingness to participate in randomised clinical trials on a 7 point Likert scale; general willingness to participate in a randomised clinical trial and reasons to consider joining / not joining a clinical trial.	545 of 728 (75%) overall. 87% for breast cancer patients, 76% for those attending the screening clinic and 71% for women attending the diagnostic clinic. **Results** There was no evidence of any differences in preferred decision making roles among the three groups of women (data not extracted) Women attending the clinic for diagnostic assessment and women with breast cancer were more likely to be classified on HADS as having a possible / definite case of anxiety than women attending for screening (47%, 47%, 30%, p=0.0004). This difference remained when adjusted for age. There was no evidence of any difference in the proportion of women classified as possible / definite cases of depression (women with breast cancer 13%, women undergoing diagnostic assessment 7%, women undergoing screening 5% (p=0.08). There was no significant difference in the mean knowledge scores among women in the three groups. This was unchanged for age (data not extracted). Women with breast cancer were significantly more likely to decline to participate in a trial (31%) than women attending for screening mammography (15%) or diagnostic assessment (15%) (p=0.0002). 44% of breast cancer patients answered 'don't know' and 25% would accept. Older women were more likely to decline to participate in a randomised trial (women 40 years old or less, 10%; 41-50 years, 13%; 51 to 60 years, 16%; 61 years or older 25%; p = 0.02). More than 80% would be more willing to join a clinical trial if it was endorsed by a nationally recognised organisation such as the National Breast Cancer Centre. Women who might consider participating in a trial ('yes' and 'don't know' groups combined) had a higher knowledge score about clinical trials than those who would refuse to participate (mean difference 0.7: 95% CI: 0.2, 1.2; p =	Women who have a better understanding of issues about clinical trials have more favourable attitudes towards randomised trials and are more willing to consider participating in one. **Recommendations for research** There is a need for research examining how doctors communicate information about clinical trials to potential participants. **Recommendations for practice** When a randomised clinical trial is available at an institution it should be presented as one of the standard treatment options to all patients. Physicians should take time to elicit and address patients' concerns and understanding about a clinical trial. **Reviewers' comments**

		Data analysis Sample size calculations were based on the question of whether women's willingness to participate in RCTs varied at three different time points in the trajectory of care. A sample of 500 women had a power of 0.80 at a significance level of 0.05 to detect a difference as small as 15% among the three groups of women in their willingness to join a randomised clinical trial. Data analysis was undertaken in SPSS and data were summarised descriptively. Answers to knowledge questions were summed to give a total score. A principal components factor analysis with varimax rotation was conducted on the 36 attitudinal items and standardised scores were calculated for the resulting factors. A stepwise backward multivariate logistic regression analysis was conducted in relation to the issues surrounding decision making for participation in randomised clinical trials.	0.003). There was no evidence of an association between either anxiety or depression and women's willingness to join a clinical trial. The major reasons to consider participating in a randomised clinical trial were possibility for a greater chance of cure, furthering medical research and benefiting others and self. These findings were the same for all 3 groups (no data given). The top reasons to decline were: possibility of side effects being worse on the trial, the treatment might be worse and the doctor might not know as much about the treatment. Breast cancer patients stated that the trial would feel like a gamble and that they would prefer to choose the standard treatment. Univariate analysis suggested that the following were associated with willingness to participate in a RCT: women with no cancer diagnosis (p =0.003), single women (p=0.05), women with higher education (p=0.03), women who prefer an active decision making style (p=0.003) and all four factors that emerged from factor analysis were associated with greater willingness to enter a RCT. There was a trend suggesting greater willingness among women in professional occupations (p=0.10). Multivariate analysis found the following: older women were less likely to join a RCT (OR=0.96; 95% CI: 0.93, 0.99); women who wanted to adopt an active role in decision making were more willing to participate than those who wanted a collaborative or a passive role in decision making (OR=3.2; 95% CI: 1.3, 7.6); women who reported a greater impact from the positive aspects of clinical trials (OR=2.2; 95% CI: 1.3, 3.8) and less impact from the negative aspects of clinical trials (OR = 2.2; 95% CI: 1.3, 3.2) were significantly more willing to join a trial. There was a trend suggesting that women who were more altruistic were more willing to join a trial (OR=1.6; 95% CI: 0.91, 2.9). The suggestion that a new diagnosis of breast cancer was associated with a reduced willingness to join a RCT was no longer significant in multivariate analyses.	

Author, Year	Study design	Data collection	Response rate	Conclusions
Fallowfield 1998[50] **Study aim** To assess patient attitudes to randomisation and to assess whether their attitudes could be modified after further explanation. To test an instrument which might be useful for doctors in explaining the randomisation procedure to an individual patient. **Setting** Two major cancer centres **Country** UK	**Study design** Survey **Sample size, Type** 315 Patients **Sample characteristics** 315 completed the questionnaire. Age and gender (n=307) < 25 15M (8.6%) 4F (3.0%) 25-44 63M (36.0%) 26F (19.7%) 45-64 36M (20.6%) 72F (54.5%) > 65 61M (34.9%) 30F (22.7%) Cancer sites (n=315) Breast 70 (22.2%) Testicular 66 (21.0%) Prostate 61 (19.4%) Bone 29 (9.2%) Other 89 (28.3%) Trial participation status Not stated. It was not necessary for patients to be eligible for trial entry when approached to take part in the study. Previous trial experience 100 (31.7%) of patients had previous experience of having been in a trial. No information on the trial experience of 21 patients (6.7%) was available. 194 (61.6%) were described as 'trial naïve'. Misc Some were attending for their first appointment at an oncology clinic, others for routine follow-up visits and prechemotherapy consultations.	The sample was patients with cancer attending for out-patient appointments and / or chemotherapy treatment in two major cancer centres. Respondents completed a self-report questionnaire - The Attitudes to Randomised Trials Questionnaire (ARTQ). The ARTQ was designed by three of the study authors and was based on a review of the literature and comments from colleagues and patients about their attitudes to trials and randomisation. The instrument had been previously piloted. Fifty people with and without cancer were asked to comment on the wording or terminology of the questionnaire and the instrument was slightly modified before being piloted on a further sample of approximately 50 patients on oncology outpatient clinics at University College Hospitals, London to check its comprehensibility, ease of administration and acceptability to patients. The questionnaire examined positive or negative attitudes to medical research in general, a personal willingness to be involved in research and research involving randomisation. It comprised three questions assessing willingness to take part in trials. If the respondent answered 'no' or 'don't know' to the question 'would you be prepared to take part in a study where treatment was chosen at random?' they went on to answer four further questions regarding factors that might influence their decision. Questions took a 'yes' 'no' or 'don't know' format but there was space after the final question to enter information which the patient might need before making a decision on whether to take part in a study. Patients responded to the questionnaire unassisted. **Data analysis** Descriptive data were reported for the patients who were known to have had trial experience, those who were known to be trial naïve and for the whole group.	315 of 323 (97.5%) **Results** The majority of respondents (287 of 315, 91.1%) believe that patients should be asked to take part in medical research, 8 (2.5%) said no and 20 (6.3%) did not know. 242 of 315 (76.8%) would be prepared to take part in a study comparing two treatments, 26 (8.3%) said no and 47 (14.9%) did not know. If treatment was randomised 141 of 315 (44.8%) would agree to participate, 92 (29.2%) would not and 82 (26%) did not know. For questions 1-3 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 would not agree to participate in a randomised trial (72 of 194, p=0.00008). The remaining questions were completed by those who answered 'no' of 'don't know' to question 3. When given further information about the suitability of both treatments and clinical equipoise 115 of this group (66%) then felt encouraged to take part. Knowing that they could leave the study and receive another appropriate treatment would encourage 125 (73.1%) to participate and awareness that the doctor would give information on both treatments before the trial would encourage 132 (76.3%) to take part. When considering the above points together, 119 (68.4%) of the 174 (55.2%) who initially refused randomisation or who were unsure would change their minds and take part in a trial. Overall, then, 260 of 315 (82.5%) would take part in a RCT, 21 of 315 (6.6%) were uncertain and 33 of 315 (10.5%) would not participate whatever information was provided. There were no differences in responses to questions 4-7 between those patients with previous trial experience and those without.	The ARTQ discriminated between three categories of patient with the following prevailing attitudes: a) those who appear comfortable with the concept of randomisation, b) those with some concerns who after a more detailed 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. **Recommendations for research** The authors conclude that the ARTQ and Patient Preference for Information questionnaire should now be compared with the standard methods of discussion to determine their usefulness in discussing trials with patients. **Recommendations for practice** Not stated. **Reviewers' comments** Trial participation is hypothetical and so may not reflect actual participation. There are some features of the sample that may affect the generalisability of the issues raised. The distribution of cancers reflects the specialised nature of some of the clinics. A large number of patients were less than 45 years of age. The sample comprised patients who had relapsed and those who had not. This is a useful study in distinguishing between those patients who might be open to trials but need information and those who would be hostile whatever explanation was given.

Author, Year	Study design	Data collection	Response rate	Conclusions
Fallowfield 1997 [60] **Study aim** To examine the attitudes of U.K. cancer specialists towards trial participation. **Setting** Multiple hospitals **Country** UK	**Study design** Survey **Sample size, Type** 357 Health professionals **Sample characteristics** 154 clinical oncologists, 56 medical oncologists and 143 surgeons with a special interest in oncology, working in the UK (4 did not specify their speciality). 84% of respondents were male and the majority were over 45 years. 99% (n=353) stated they were currently involved in clinical trials. Mean (SD) number of trials in which they reported being involved: Medical oncologists: 5.5 trials (6.3); clinical oncologists 4.3 trials (5.2); surgeons 2.6 trials (1.4). Respondents estimated that they would enter a median of 20 patients (range 0-600) in the next 6 months. 76% (n=269) said they were entering fewer than 50% of all eligible patients.	301 medical and clinical (radiation) oncologists were identified from a directory of specialities and addresses published by the National Cancer Alliance, UK and 252 surgeons were identified via a regular mailing to approximately 350 members of the British Association of Surgical Oncology. A postal questionnaire was sent out with a pre-paid envelope and an accompanying letter assuring respondents of confidentiality. Basic demographic details were requested but questionnaires were confidential. The questionnaire was a slightly modified version of the Physician's Orientation Profile (POP) which had been used previously in a similar US study. Clinicians were also asked to name the trials in which they were participating, the characteristics that made patients easy or difficult to approach and were invited to make any other comments they had about clinical trials. **Data analysis** Descriptive statistics (%) were used to report overall group responses to individual items on the POP questionnaire. These were compared to data from an earlier US study and categorised as less than a 10% difference; an 11-20% difference; and a difference greater than 20%. A stepwise discriminant function analysis was performed to determine whether or not the different professional groups could be separated on the basis of their responses to the questionnaire. 18 of the 45 items from the questionnaire were used to compute scores for each oncologist on five POP subscales which measured attitudes of clinicians to their clinical and scientific work. Factors influencing the ease or difficulty of communicating with patients were grouped into thematic categories.	Overall 65% (68% clinical oncologists; 77% medical oncologists; 57% surgeons) **Results** Two discriminant functions were calculated (a combined chi square (16) of 192, $p<0.00001$). The first function maximally discriminated medical oncologists from clinical and surgical oncologists. Using a cut-off of >0.3 there were six items which loaded: medical oncologists spent more time on research related activities; devoted a high level of time on publications and other research commitments compared with clinical work; authored or co-authored more publications; were more likely to be the principal investigator on one or more research grants; participated more actively in professional organisation based on their research activities; and were more likely to place importance on being known by national and international colleagues. (Further information on these items is available in the paper.) The second function discriminated surgical oncologists from medical and clinical oncologists: surgeons were more likely to report that doctors in the hospital setting are given more reward for clinical skills with patients; more likely to encourage a patient from a trial to stay on the trial when a patient on a protocol relapses or progresses and the protocol dictates additional treatment that the patient does not want; less likely to report benefits to their institution as a major reason for trial participation; and when there is controversy in the literature as to which treatment is best were less likely to report that the would enter the patient in a trial, if one exists. (Further information is available in the paper.) Overall group responses to individual items on the POP questionnaire are reported in the paper. Based on the 5 POP subscales assessing the clinician-scientist continuum, in general all respondents were more oriented toward the clinician end of the continuum though medical oncologists were statistically significantly more	The survey identified constraints imposed by the healthcare system which impede trial participation including lack of time, communication difficulties and conflicts between the role of clinician and scientist. Such factors need consideration when trials are designed. Comparison of British data with those from the US clinicians were broadly similar. The few differences found suggested that the more protocol driven culture of the US might encourage recruitment and a greater commitment to keep patients on trials. **Recommendations for research** The authors state that research is required to design and evaluate interventions and innovative approaches aimed at helping doctors and patients when trials are discussed. **Recommendations for practice** The authors stated that the influence that the type of institution in which a doctor works and their speciality needs consideration by those involved with trial design, especially when predicting the likely accrual rates. Account also needs to be taken by those involved in trial design and protocol

			oriented towards the researcher/scientist end of the continuum than the other two professional groups on four of the subscale (data reported). 327 different factors (from 249 clinicians) were suggested that influence the ease of communicating with patients about clinical trials. These were grouped into 11 thematic categories. In increasing level of frequency these categories were: cultural; relatives; gender; self-identification; social class; specific trial situation; age; disease/prognosis; other; personality/emotional; and perceived intelligence. 366 patient characteristics (from 264 clinicians) were suggested that impeded the ease of communicating with patients about trials. In increasing level of frequency the responses were grouped in the following categories: gender; self-identification; relatives; cultural barriers; social class; other; specific trial situation; personality/emotional; age; disease/prognosis; perceived intelligence. 36% (n=129) wrote 159 additional comments. Almost 60% commented on the lack of time or resources preventing them from trial involvement. The authors state that other comments revealed differing attitudes to trials; concerns about the difficulties of obtaining informed consent and potential professional repercussions of trial involvement.	development of the need to take account of overoptimistic assessments made by clinicians about likely accrual of patients. They also stated that there was a need for better communication skills training. **Reviewers' comments** This was a well-conducted survey carried out in a UK setting with a national sample of oncologists, though it is unclear how respondents may have differed from nonrespondents. The reliability and validity of the questionnaire is unclear.

Author, Year	Study design	Data collection	Response rate	Conclusions
Fleissig 2001 [22] **Study aim** To report on an intervention to improve communication during doctor-patient consultations about randomised clinical trials of cancer therapy. It was hypothesised that providing doctors with patient questionnaires detailing their information requirements and their attitudes to trials would increase patient and doctor satisfaction, improve recruitment and reduce consultation time. A secondary aim of the study was to examine the validity of the Patients' Attitudes to Trials Questionnaire as a predictor of patient behaviour. (See also Jenkins 2000[28], Fallowfield 1998[50] and Jenkins 1999[28]) **Setting** Multiple hospitals **Country** UK	Survey **Sample size, Type** 265 Both **Sample characteristics** 43 doctors were invited to join the study and 15 eventually participated (8 clinical / radiation oncologists, 6 medical oncologists and one surgeon). 10M, 5F. There did not appear to be any differences between doctors who participated and those who did not based on sex, seniority or specialty. 265 patients completed a questionnaire after the consultation. Age Age ranged from 19 to 83 years with the majority (54.0%) between 45-64 years of age. Gender 74 M(27.9%) 191F (72.1%) Marital status 207 (78.4%) married or cohabiting, 57 (21.6%) other. Cancer site Breast 146(55.1%) Ovary 36 (13.6%) Testicular 29 (10.9%) Prostate 20 (7.6%) Colorectal 14 (5.3%)	Doctors at District General and University Teaching Hospitals involved in an earlier phase of the study were invited to participate. Clinic staff identified patients with cancer aged 16 years or older eligible for a RCT. Patients were recruited between April 1997 and February 2000. These patients were invited to participate in a communication study and given an information sheet to read. All patients who accepted completed questionnaires about patient information preferences and attitudes to trials prior to discussion about trial entry (Patient Preferences for Information Questionnaire and Patient Attitudes to Trials Questionnaire and the Spielberger State Trait Anxiety Inventory). Only half of these (those completed by the intervention group) were shown to the doctor. Doctors were randomised into two groups which varied the order of intervention and control group consultations. Doctors in the intervention group were expected to provide information on trials according to individual preferences whilst the doctors in the control group could use their discretion. The study included 40 trials involving different types of treatment (chemotherapy, radiotherapy, endocrine treatment and immunotherapy) or different screening regimens. Thirteen trials involving 106 of 265 (40.0%) of patients included an inactive (placebo or 'no treatment') arm. Four patients were asked to join more than one trial. Consultations were audio taped. Following the consultation with the clinician 108 of 264 patients (40.8%) were given additional information about the trial by another health professional. After the consultations two questionnaires were given to be returned by post: a 17 item questionnaire to assess satisfaction with the doctor-patient interaction adapted from the Medical Outcomes Study PSQIII and a 16 item questionnaire describing reasons for accepting or declining treatment within a clinical trial. After each consultation doctors assessed the interview and rated patient distress using visual analogue scales. **Data analysis** Intervention: Audiotapes of the consultation were timed and assessed against a grid matrix covering the main items to check whether doctors altered their consent procedure. Thirty randomly selected tapes were	265 of 325 (81.6%) returned a questionnaire after the consultation. **Results** 205 of 265 (77.4%) agreed to trial entry and this was predicted by the Patient's Attitudes to Trials questionnaire with 80.4% accuracy (excluding the 'unsure' patients). 53 (20%) declined and 7 (2.6%) did not know. Patient Preferences for Information Questionnaire. Over 95% of participants in both intervention and trial groups wished to have information given to them on aspects of the trial: likelihood of a cure, whether the treatment would control but not cure the disease, whether the treatment would reduce symptoms but would not control the disease, all possible available treatments, all possible side-effects of the treatment, exactly how the treatment works for the illness and the research evidence that the treatment being offered works. Patients attitudes to trials - data extracted in Fallowfield 1998[50]. 83.1% of the patients who said they would participate in a randomised trial on the attitude questionnaire joined the specific trial offered to them, 30 declined and 6 did not know. 7 of 16 who said they would decline on the attitude questionnaire did decline but 9 changed their minds and accepted the trial. 18 of 35 who were unsure on the attitude questionnaire participated in a trial, 16 declined and one patient was still undecided. A decision to participate was not significantly associated with whether or not the doctor had been given the patient's questionnaires. 96 (73.8%) of the control group accepted participation and 109 (80.7%) of the intervention group accepted, p =0.463). Trial participation was not associated with age or gender but it was associated with the type of	Providing doctors with a copy of their patients' requirements for information and attitudes towards participating in research trials before asking them to participate in a trial made little difference to the outcomes measured in this study. **Recommendations for research** Further research to explore the potential use of written interventions to facilitate communication and accrual to randomised clinical trials is recommended. The part other professionals play in explaining and recruiting patients to trials should also be examined. **Recommendations for practice** Not stated. **Reviewers' comments** The rate of accrual to trials was high and may reflect the doctors who participated, the nature of the trials or the patients involved.

	Lung 8 (3.0%) Other 12 (4.5%) Trial participation status Participation being requested. Previous trial experience Yes 28 (10.6%) of whom 26 were female. No 237 (89.4%) Misc Mean anxiety of both groups was 35.9 (SD=9.66). Assessment of patient distress did not differ between patients in the control group and the intervention group. Patients in the control and intervention groups were well matched for age, gender, marital status, trait anxiety, site of cancer and previous participation in clinical trials.	reassessed by an independent assessor who did not know whether patients' questionnaires had been shown to the doctor. Data from all control group consultations were combined in the analyses and contrasted with the intervention data. Questionnaire data were analysed using SPSS and significance was deemed to be 5% or less. Missing or inadequate data were excluded. The intervention aspect of the trial is not relevant to this review.	treatments involved in the trial. Patients were less likely to participate in chemotherapy trials which involved a 'no treatment' arm than other trials (25 of 45 (55.6%) versus 178 of 208 (85.6%), $p < 0.001$). Reasons for accepting or declining trials are discussed in Jenkins 2000[28]. Factors that influenced the decisions were not associated with whether the patients were in the control or the intervention group.	

Author, Year	Study design	Data collection	Response rate	Conclusions
Goodwin 2000 [54] **Study aim** To examine recruitment for the Breast Expressive-Supportive Therapy (BEST) Study, a randomised trial of group psychosocial support in metastatic breast cancer. **Setting** Multiple hospitals **Country** Canada	Trial report+Survey **Sample size, Type** 17 Health professionals **Sample characteristics** Demographic details of group leaders were not reported.	The BEST Study compared a specific manual-based form of group psychosocial support (expressive supportive therapy) combined with educational materials and usual medical and psychosocial care against usual medical and psychosocial care alone. The intervention arm met weekly for a 90 minute therapist-led support group. The outcome of interest was survival. It was a multicentre trial co-ordinated at Mount Sinai Hospital, University of Toronto. Centres received a stipend for each women enrolled. Recruitment began in June 1993 and ended in December 1997. Participating centres prospectively maintained logbooks which formed the basis for the analysis of recruitment, eligibility and refusal rates and for the assessment of the feasibility of different randomisation ratios. In November 1996 group leaders completed a questionnaire recording their satisfaction with recruitment, perceived barriers to recruitment which were graded as 'major obstacle', 'minor obstacle' or 'not a problem' and sources of recruitment. Enrolment rates and required population base were also assessed. **Data analysis** Statistics Canada data (1991 census) were used to calculate the population residing within one hour of each study centre and the proportion having English as a mother tongue. Breast cancer mortality rates were obtained from the Canadian Cancer Society. These data were used to calculate the target population of women with metastatic breast cancer residing within one hour of the study centre assuming a steady state of mortality rates. This estimate of the target population was compared to the number of women approached and randomised into the study to calculate enrolment of potentially eligible women in the study with adjustments made for prevalent cases of metastatic breast cancer at the start of the study.	100% (all 17 active group leaders responded). **Results** Trial participation status 652 women were assessed (just under 25% of potentially eligible women). 96 of the 652 (14.7%) were ineligible on initial contact. Of the remaining 556 women 299 (53.6% of eligible women, 45.9% of all women) declined participation in the trial. 182 (32.7% of eligible women, 28.1% of all women) of these declined after being provided with a brief description of the trial. 116 (20.9% of eligible women, 17.8% of all women) expressed interest but did not return questionnaires even after telephone reminders. 9 women (1.4%) were found to be ineligible for psychological reasons during an interview with group leaders and 11 (1.7%) withdrew after this interview. 237 were randomised (43.3% of all medically eligible women assessed and 36.3% of all women assessed for the trial). Using population-based estimates 24.3% of women with metastatic breast cancer were assessed for the study and 8.7% randomised. A population of approximately 600,000 living one hour from the study centre was necessary to establish and maintain a study group. This translates as at least 75 English-speaking women with newly diagnosed metastatic breast cancer per year. Centres with a population base of 300,000 or less were unable to establish study groups. Two participating centres both having a population of just over 600,000 had problems establishing and maintaining study groups. Both centres closed after 3 years because of inadequate recruitment. Group Leaders' perception of recruitment: When asked about satisfaction with recruitment at their centre none of the group	Five lessons were learned from recruitment to the BEST trial: multicentre randomised trials of psychosocial interventions are feasible even in very ill patients; the use of a group interventions increased the required sample size by 50%; similarity of randomisation rates suggests that the study results are generalisable; multidisciplinary collaboration and involvement of experienced researchers facilitated enrolment; and that most challenges encountered in recruitment were similar to those seen in all clinical trials. **Recommendations for research** Further research is needed to investigate the influence of patient characteristics on participation in psychosocial trials. The role of psychosocial attributes such as coping style, mood and social support on participation should also be investigated. **Recommendations for practice** Not specifically stated but implicit in the lessons learned from the study. **Reviewers' comments** This was a study of barriers to participation in an actual trial and the nature of the intervention make it difficult to assess the generalisability of the research. The barriers are examined almost exclusively from the point of view of the group leaders not the patients.

			leaders was 'very satisfied', 9 (52%) were somewhat satisfied, seven (41.2%) were somewhat unsatisfied and one (5.9%) was very unsatisfied with recruitment. Eight group leaders perceived themselves as the most frequent source of recruitment at their centre, three reported data managers / clinical trial nurses and two medical staff to be the most frequent. Medical staff were thought to be common (but not most frequent) sources of medical recruitment by eight additional group leaders. Competing clinical trials, notably bone marrow transplantation studies were perceived to be the most common major obstacle to recruitment (6 of 17 (35.3%) major obstacle, 8 of 17(47.1%) minor obstacle and 3 of 17 (17.6%) found it not to be a problem. Medical staff cooperation: a 'major obstacle' by 4 of 18 (23.5%), a 'minor obstacle' by 6 of 17 (35.3%) and by 7 (41.2%) as 'not a problem'. Geographical factors: major obstacle 3 (17.6%), a minor obstacle for 11 (64.7%) and not a problem for 2 (11.8%). Eligibility criteria: a major obstacle for 3 (17.6%), a minor obstacle for 9 (52.9%) and not a problem for 4 (23.5%). Competing nonstudy support groups was a major obstacle for 3 (17.6%), a minor obstacle for 8 (47.1%) and not a problem for 6 (35.3%). Inadequate support from recruitment personnel was a major problem for 3 (17.6%), a minor problem for 6 (35.3%) and not a problem for 6 (35.3%). Language was perceived as a major obstacle by 2 (11.8%), a minor obstacle by 5 (29.4%) and not a problem by 8 (47.1%). Lack of patient interest was a major obstacle for 1 group leader (5.9%), a minor obstacle for 10 leaders (58.8%) and not a problem for 4 leaders (23.5%). Of the 183 patients who refused participation on initial contact reasons were support by family and friends considered adequate (85), lack of time (44), unwillingness to be part of a group (35) and transportation (18).	

Author, Year	**Study design**	**Data collection**	**Response rate**	**Conclusions**
Grant 2000 [23] **Study aim** The purpose of the study was to examine the relations among patients' perceptions of their physicians' communicative behaviour during the informed consent interview, the patient's feeling of being confirmed by the physician and satisfied with care delivered by the physician, and the patient's decision to participate in a clinical trial or not. **Setting** Major regional cancer hospital **Country** USA	Survey **Sample size, Type** 130 Patients **Sample characteristics** Age The mean age of the included patients was 59.46 years. Gender Trial participants: 42M, 50F Trial decliners: 27M, 11F In this group men were more likely to decline to take part in a trial than women (chi squared=7.44, p<0.01). Cancer sites The sample included patients diagnosed with various types of cancers at different stages (e.g. breast, lung, prostate, brain, cervical, melanoma, lymphoma) who were eligible for at least one ongoing or upcoming clinical trial. Trial participation status 92 trial participants, 38 trial decliners. Previous trial experience Misc	Data were gathered through interviewing which consisted of 4 'established' measurement instruments adapted for the telephone interview format. Physician communication style was assessed using a modified version of the Communicator Style Measure (CSM) on a 6 point Likert scale. The Perceived Confirmation Scale was used to measure the extent to which a patient feels confirmed by his or her doctor and the Patient Satisfaction Questionnaire was used to assess patients' satisfaction with care provided by the doctor. Decision-making and information-seeking preferences of patients were assessed with the Autonomy Preference Index (API). **Data analysis** Discriminant analysis was used to determine the best set of dependent variables of distinguishing between patients who said 'yes' and those who said 'no' to participation.	Not stated. **Results** Based on discriminant function patients who said 'no' to clinical trials perceived their physician to be more attentive (e.g. the doctor was a good listener); less friendly (e.g. not acknowledging the patient's contributions to the interview and not being an extremely friendly communicator); as having a less favourable image (e.g. compared to other physicians the patient has had, this doctor was not an extremely good communicator, and it was not easy to maintain a conversation with this doctor). These patients characterised themselves as less satisfied with their medical care, and as more autonomous decision makers. Patients who said 'yes' perceived physicians as being more friendly, having a better communicative image and less attentive, they perceived themselves as being more satisfied with medical care and as less autonomous decision makers. The study found no significant difference for the perception of being confirmed by doctors between accepters and decliners. However almost all respondents in both groups were highly confirmed by doctors.	The authors concluded that physicians' affiliative communicative behaviours and patient satisfaction were clearly important to patients who agreed to participate. Motivations for patients who declined were less clear. Specific communication skills may enhance patient satisfaction and may help increase enrolment in clinical trials. **Recommendations for research** Analysis of the discourse between physicians and patients on accrual to trials to determine how decisions are made. **Recommendations for practice** Not stated. **Reviewers' comments**

Author, Year	Study design	Data collection	Response rate	Conclusions
Grunfeld 2002 [61] **Study aim** To identify barriers and facilitators to the accrual of patients to cancer trials by learning the views of Clinical Research Associates (CRAs) on this subject **Setting** Multiple hospitals **Country** Canada	Qualitative **Sample size, Type** 29 Health professionals **Sample characteristics** Five data managers and 24 CRAs working at 6 of 8 tertiary cancer trearment centres in Ontario province, Canada.	Centres were selected for participation in focus groups to represent a range of perspectives (e.g. urban vs rural, small vs large, north vs south). A semi-structured interview was developed, based on topics identified in the literature, to address system, physician and patient factors that may have an effect on stduy accrual. All groups were led by the same facilitator. Co-facilitators provided assistance. The focus groups were audiotaped and transcribed by individuals employed outside the cancer centre. **Data analysis** After each focus group, notes taken during the session were reviewed. Emergent topics were discussed with subsequent focus groups. Focus groups were held until the research team noted a repetition of themes. The transcripts of each focus group were coded independently by 2 researchers with descriptive titles. Codes were then categorised intoa set of preliminary main themes and sub-themes. Based on discussion the two reviewers created one comprehensive list of main and sub-themes. Quotes that best represented themes were identified.	N/A **Results** Physician barriers/facilitators The factors identified were all related to physician attitudes toward the suitability of a patient for specific trial, despite the patient meeting eligibility criteria. CRAs said that although physicians may agree to take part in a trial at times they did not believe in a specific trial and implicit physician attitudes can influence patient decision-making. Patient barriers Logistic and attitudinal barriers were identified. Logistic barriers: extra burden of tests, potentially greater toxicity, travel, care giving responsibilities. Attitudinal barriers: their views towards trials, their physicians expertise, concerns about being a 'guinea pig', their physician's view that they should not participate; their level of acceptance of their disease. Patient facilitators: belief that a trial will be beneficial, participation if standard treatment had failed, hope for a potential cure, better care, benefit furture generation, please physician. Patient modifiers (these may act to encourage or discourage patient involvement) Views of family members; first language other than English or French (an issue at one centre but not others) and media coverage. Patient knowledge of trials CRA's commented that patients were much more knowledgeable about clinical trials than in the past and wanted to participate. The CRA's who participated in this study did not think that patients limited accrual but that system factors were responsible. System factors Increasing trial and pharmaceutical requirements and tight timelines but diminishing resources including time to discuss participation.	The impact of greater demands in a climate of decreasing health care resources is perceived by CRA's as having a negative affect on accrual. **Recommendations for research** None stated **Recommendations for practice** The authors state that CRAs need to be involved in trial design from the earliest stages of development so they can provide input on both form design and trial procedures, helping to ensure that requirements are relevant and reasonable. **Reviewers' comments** The method of data collection and data analysis were reasonably clearly outlined. Participants from 6 tertiary cancer centres participated. The authors state that the focus groups were stopped because saturation was reached. The issue of reflexivity was not addressed. The findings are likely to be more relevant to similar tertiary cancer centres where multiple CRAs are working.

Author, Year	Study design	Data collection	Response rate	Conclusions
Hietanen 2000 [24] **Study aim** To determine the communicative needs of patients in the context of being invited to participate in a clinical trial in order to lead to an improvement in the quality of informed consent in trials. **Setting** Multiple hospitals **Country** Finland	Survey **Sample size, Type** 299 Patients **Sample characteristics** Age Mean age was 65 (range 48-87) Gender All female. Cancer site All breast cancer Trial participation status All had participated in an endocrine trial (see below). Misc For 138 (55%) the highest educational level was secondary school. 132 (51%) were married or living with a partner or spouse, 129 (49%) were living without a partner or spouse.	A pilot questionnaire with 24 structured and 5 open questions was developed to find out about the adequacy of the oral and written information given prior to recruitment into the trial, aspects of decision making, satisfaction with and usefulness of information, understanding of how treatment was chosen, reasons for participation, whether the same decisions would be taken after the experience and the interests of the patient when offered participation in a clinical trial (open questions). The draft questionnaire was piloted on 10 patients with breast cancer who were on follow up without recurrence and their feedback was incorporated into a final version. The final questionnaire included 20 questions, four of which were open. The question 'why did you decide to participate in the trial' had 5 response options. The final version of the questionnaire was sent in May 1998 to patients with breast cancer who had been randomised into an adjuvant trial evaluating different types of endocrine therapy across five Finnish hospitals. It was estimated that more than 95% of the eligible patients accepted randomisation. The mean time from recruitment to completion of the questionnaire was 11 months (range: 5-17 months). Those who did not return the questionnaire were requested to give a reason in writing and to return it anonymously. 14 of them answered. The most common reasons for non-completion were older age and other medical diseases, tiredness with multiple questionnaires or just unwillingness to answer. Four patients found the questionnaire too difficult. **Data analysis** Associations of age and education with how information was regarded and understood, and with decision-making, were assessed using two-way contingency tables and Chi square analysis. Significance tests were not corrected for multiple comparisons. A level of significance of $P < 0.05$ was used.	261 of 299 (87%) **Results** 231 of 255 patients (91%) regarded the information provided as easy or quite easy to understand. Most patients (203 of 252 (81%) said that the doctor told them about the side effects of the treatment in a way that was easy or quite easy to understand. 35 of 252 (14%) did not remember any discussion of side effects and 2 of 252 (1%) found this information very or quite difficult to understand. All patients were aware that they were on a clinical trial. The method of treatment allocation was unclear to most patients: 128 of 251 thought that the doctor had chosen the treatment while only 57 of 251 knew that they had been randomised and were also able to explain what randomisation meant. 18 of 251 (7%) thought that they had chosen the treatment. 26 of 251 (10%) thought that the treatment had been chosen in another way. 184 of 254 (72%) regarded the information provided as adequate for decision making while 37 of 254 (15%) had found it less than adequate and 10 of 254 (4%) very insufficient. Only 1 patient (0.4%) felt the information provided was too much. 125 of 226 (55%) found written information helpful in decision making while 15 of 226 (7%) did not find it helpful and (86 of 226) 38% were not able to say. 174 of 255 (68%) of the patients thought that they had enough time for decision making while 43 of 255 (17%) would have liked more time to consider. The rest (38 of 255, 15%) did not know. Major reasons for participation were to benefit future patients (162 of 261, 62%) and to gain personal satisfaction (101 of 261, 39%). 157 of 261 (60%) desired a more effective follow up. 110 of 261 (42%) expected to see the same	The needs of the patients when offered participation in a trial are clear information, enough time to consider the options and psychological support. **Recommendations for research** More research is needed to determine the optimal way of informing older and less educated patients about trials. **Recommendations for practice** The quality of informed consent would be improved if clinicians who recruit them used more time and adjusted their language according to the patient. Communication should be modified especially for older and less educated patients. **Reviewers' comments** This study only considers participants rather than non-participants in a trial. It is obviously specific to a particular trial and as such may not easily generalise. However patients are asked in detail about their decision making process and factors involved in the decision to participate in the trial. There may be problems of recall bias due to the time delay between randomisation and filling in the questionnaire.

			doctor more often and 100 of 261 (38%) it was important that follow up would take place in the same hospital as the treatment. 218 of 251 (87%) were happy with their decision to participate and would enrol again, 4 of 251 (2%) reported that they would decline and 29 of 251 (12%) were not sure of what their decision would be. Answers to the open questions on factors considered important when offered participation in a trial were grouped into categories of information, communication and attributes referring to doctors and nurses. The major requests for information involved the trial itself and its structure 45 (25%), side effects of the treatment 42 (23%), cost and benefit 27 (15%) and the importance of the trial for future patients 19 (11%). In terms of communication patients mainly wanted clarity of explanation (no jargon) 40 (22%) and an unhurried discussion with opportunity to ask questions and check understanding 28 (16%). Attributes of staff valued most highly were honesty and openness 18 (10%).	

Author, Year	Study design	Data collection	Response rate	Conclusions
Hjorth 1996 [55] **Study aim** To investigate the reasons for differences in accrual rates in a multi-centre trial and identify the most important factors influencing the investigators readiness to enter patients into clinical trials. **Setting** Multiple hospitals **Country** Sweden, Norway and Denmark	Survey **Sample size, Type** 93 Health professionals **Sample characteristics** 93 principal investigators on a two and a half year trial, carried out in Sweden, Norway and Denmark, comparing melphalan-prednisone therapy and melphalan-prednisone with interferon in patients with newly diagnosed myeloma. Median age: 46 years; Sex: n= 80 males; university hospital n=13, county hospital n=80. Speciality: internal medicine only n=54, internal medicine and subspeciality in haematology n=36; oncology n=3. Research experience: academic degree beyond MD n=16, not PhD but spending at least 25% of working hours on research activities n=3. 53% of all reported cases were included in the trial; 37% of reported cases were ineligible for the trial, 8% were unwilling to participate, and 2% were excluded for physician related reasons.	Principal investigators at the 99 institutions in Sweden, Norway and Denmark participating in the myeloma trial were ask to complete a self-administered postal questionnaire. A reminder was sent to non-respondents one and six months later. Eight hospitals in Finland and Iceland who had enrolled patients for only 10 months were excluded due to language barriers and their short period of participation. The questionnaire was developed by the authors. Thirty-two of the 66 questions addressed general attitudes of the investigators that could have had an important influence on patient accrual (only the findings for these are reported). There were 21 forced choice questions with 2-5 response options on opinions and attitudes to clinical trials. Respondents were asked to rank 5 items for their level of importance in their decision to participate in the trial and rank 8 factors for their importance in influencing their readiness to enter patients into the trial. They were also asked to rate the importance of nine factors possibly influencing trialists' readiness to enter patients into trials. **Data analysis** The response options were dichotomized: they were grouped into positive attitudes and negative attitudes or more positive and less positive responses. The patient inclusion rate for each participating centre was calculated using an estimate of the expected number of newly diagnosed cases for each centre (further details provided in paper). Student's t-test was used to compare the inclusion rate between centres. Mean inclusion rate and 80% confidence intervals were reported.	94% **Results** Inclusion rate: mean 40% (80% CI: 38%, 43%); Danish hospitals mean=24%; Swedish hospitals mean=43%; Norwegian hospitals mean=41%. There were no statistically significant differences in inclusion rate for hospital category, specialisation, research experience or academic qualifications of the principal investigator (details of analysis not reported). Decision to participate in the trial The five variables were ranked from highest to lowest as follows: scientific benefits; medical care benefits; educational benefits; collaboration benefits; and monetary benefits. Investigators' perceptions of factors of importance for patient accrual in multicentre studies (very great or great importance vs. little or no importance) Scientific aim of study: n=90 vs. n=3 Simplicity of protocol and forms: n=87 vs. n=6 Rightness of ethical aspects: n=77 vs. n=16 Communication with study organisation: n=77 vs. n=16 Participation in regional investigators meetings: n=77 vs. n=16 No increase in workload due to study: n=59 vs. n=34 Sense of participation in elaboration and implementation: n=57 vs. n=35 Improvement in academic qualifications through participation: n=26 vs. n=67 Monetary reimbursement for entered patients: n=14 vs. n=79 Investigators own incentives for entering patients in the trial The eight variables were ranked from highest to lowest as follows: scientific aim of study; rightness of the study ethics; sense of participation; participation in investigators meetings; no increase in workload; communication with the study organisation; improvement in academic qualification; and monetary reimbursement for entered patients. In 8 of 21 questions assessed, there was a statistically significant association between the response and patient accrual. These were the inclusion of a quality of life analysis; treatment preference for patient; ease of complying with the protocol; the extent of extra work generated by the study; ; participation in regional meetings; medical benefit to patients; hesitated to participate due to an anticipated increase in health care expenses; views on the level of reimbursement to investigators (further details in paper).	This survey revealed associations between patient accrual rate and participators attitudes for 8 of 21 questions concerning several aspects of the clinical trial process, including the importance of the scientific aims of a study, ethical considerations, the communication between participators and study organisation, and the awareness of the importance of costs and reimbursement. **Recommendations for research** None stated **Recommendations for practice** The planning and implementation of cancer clinical trials should account for all of these factors (see above), with emphasis on the scientific purpose. **Reviewers' comments** This study obtains the views of investigators in relation to a specific trial. Some aspects that principal investigators were asked about were specific to that trial therefore it is possible that some of the findings are limited to similar trials. No information is provided on the method of questionnaire construction therefore the reliability and validity of the measure is unclear. Only the perspective of the principal investigator is obtained in relation to this trial.

Author, Year	Study design	Data collection	Response rate	Conclusions
Holcombe 1998 [25] **Study aim** To summarise the experience at Louisiana State University Medical Center (LSUMC-S) in enrolling black Americans in oncology treatment and prevention trials coordinated by the South-west Oncology Group (SWOG). **Setting** Single hospital **Country** USA	Chart review **Sample size, Type** ? Patients **Sample characteristics** Not stated.	The researchers compared the accrual of black Americans for all SWOG institutions and the accrual of all minority patients at SWOG institutions with accrual of black Americans at LSUMC-S. Yearly and composite data for 1992-1996 is presented in the report. Accrual information for two chemoprevention trials is also presented but is not relevant here. The barriers discussed do not appear to be the results of a study but are based on the experience at the center. **Data analysis** Not stated.	**Results** Enrolment of black Americans at LSUMC-S from 1992 to 1996 is significantly higher than that achieved by SWOG institutions (38% vs. 12%, p <0.0001). It is unclear how these barriers have been derived and no precise data are given. Patients don't 'fit' the protocol - they often present too late with advanced disease and comorbid conditions. Time required to explain trial protocol, side effects, informed consent and paperwork. This has been helped by securing additional support staff but there are still pressures to see more patients. Access to health care, Cost (lack of insurance coverage, outpatient medication costs, excessive protocol-related costs, transport. Illiteracy remains a problem despite providing alternatives to written information and one to one doctor time. Informed consent - use of simplified forms helps but they are still too detailed and complex. Cultural / family concerns about research (helped by education and peer groups but still a problem of doctor time). Suspicion / distrust - helped by community outreach but this has cost implications.	Although major strides must still be made in the area of cancer prevention, LSUMC-S's experience demonstrates that black Americans can be encouraged to participate in cancer clinical trials. **Recommendations for research** Not stated. **Recommendations for practice** Not stated. **Reviewers' comments** Accrual percentages include prevention in addition to treatment trials. It is unclear how the data on barriers have been collected and therefore how reliable they are. It is difficult to generalise this data. It is not possible to quality assess the study.

Author, Year	Study design	Data collection	Response rate	Conclusions
Huizinga 1999 [26] **Study aim** To investigate the decision-making process that cancer patients go through when they have been asked to participate in a phase III clinical trial. **Setting** Single hospital **Country** Holland	Qualitative **Sample size, Type** 14 Patients **Sample characteristics** Age Mean 43.9 years (range 27-51 years) Gender 2M, 12F Cancer sites 10 patients had locally advanced breast cancer, 1 had metastatic breast cancer, 2 had testicular cancer and 1 had melanoma Trial participation status 13 of 14 had been recruited into trials. One did not give consent to participate. Misc All patients were diagnosed and had received primary surgical treatment before being referred to the Department of Medical Oncology for additional treatment. Patients were eligible for this study when they had fulfilled inclusion criteria to participate in one of four phase III cancer clinical trial and after they had made their decision to participate. Trials included chemotherapy drugs,	After making the decision to participate in the relevant trial each patient was interviewed by a research nurse. The interviews were semi-structured and guided by a questionnaire. They required approximately 60 minutes. The questionnaire was especially developed for the study and assessed the patient's approach to decision making and information disclosure regarding his or her medical treatment. It focused on primary information about the clinical trial provided by the referring specialist, information provided by the medical oncologist and / or oncology nurse, reflection time and randomisation procedure phase and treatment and posttreatment phase. The patient's responses to the questionnaire and additional remarks were written down during the interview. Patients were asked to provide information about their sociodemographic situation. Clinical characteristics such as the diagnosis, date of diagnosis and medical treatment were derived from the patient's medical file. **Data analysis** Descriptive statistics were used to describe and synthesise the sociodemographic data and the clinical characteristics of the patients. A qualitative content analysis was performed to evaluate the interview responses. The results of the interviews were also discussed by two medical oncologists, a psychologist and the research nurse.	NA **Results** All patients claimed they were aware of the risks and benefits associated with the experimental and standard treatments but in reality only one patient commented spontaneously on potential fatal complications. Randomisation was not understood by two patients and was displeasing to 13 patients, making them feel 'like guinea pigs'. The large amount of information was new and overwhelming for most patients. Thirteen received the written patient trial information sheet, one patient could not remember having received it. All patients who received the information sheet stated that they understood it. 13 patients also took supplementary brochures. All patients discussed participation with their accompanying partner during the first visit to the outpatient clinic. Five patients consulted their GP. Thirteen of 14 patients made their decision concerning participation immediately after or during the first visit to the outpatient clinic. Eleven stated that they did not need a week to reflect on their decision. One patient used the time but it did not influence her decision. For one patient the extra time was very important in reaching a well-considered decision. All patients reported that they played an active role in the decision-making process. Thirteen patients did not feel they were influenced by the oncologist, the oncology nurse, the GP, their partner or other relevant people. One person had the impression that the medical oncologist pressured him to participate but ultimately made the decision himself. Six patients claimed they made their decision independently whereas the other patients decided in harmony with their partners. All 13 patients mentioned the following factors as reasons for participating in the clinical trial: the desire to get well, the hope for a cure or	The results of the study suggest that patients asked to participate in a cancer trial make their choice instantaneously. This raises questions about the quality of their decision and the fact that predecisional support may be needed to ensure that the best procedure for making a decision is followed. **Recommendations for research** There is a need to study patients who refuse to enter trials. Objective criteria for evaluation of a (sound) decision making procedure and instruments to improve the decision-making process need to be developed. Such instruments might include information aids to assist patients in accessing information about their illness and treatment; decision aids that encourage patients to participate with their physician in medical decision making and that help patients make decisions corresponding with their personal values. In a future study it might be useful to integrate qualitative data and quantitative data (e.g. objective measurement of the decision making process) to enhance the reliability and validity of the research findings. Studies need to explore how patients reach their decision on a content

	stem-cell transplantation and adjuvant inteferon. 13 patients were married and one was living with a partner. 8 had a least a high school education. 7 had part-time jobs, 4 had full-time jobs and 3 were housewives.		prolongation of life and the opportunity to help other future patients. For four patients family reasons played a decisive role in the choice to participate because these patients regarded the trial treatments as superior to standard treatment. All the patients who went through the randomisation procedure mentioned that waiting for the outcome of the random selection was very stressful. Thirteen patients were satisfied with their decision retrospectively.	and on a procedural level. The role of the oncology nurse in improving the quality of decision making should be investigated as should the effects of predecisional support on participation in cancer clinical trials. **Recommendations for practice** The oncology nurse would probably be best placed to offer predecisional support which might take the form of: participating in the informed consent procedure, helping the patient to gather more information, encouraging the patient to define his or her own reasons for participating in a clinical trial and searching for alternatives and supporting the patient in making decisions in accordance with his or her personal values. **Reviewers' comments** Small sample, mainly female, only one person had refused a trial. There may be the potential for recall bias as the study was retrospective and patients had to recall their thoughts and feelings now that they were actually participating in a trial.

Author, Year	Study design	Data collection	Response rate	Conclusions
Jenkins 1999 [27] **Study aim** This study forms part of a larger study on doctor-patient communication and as such reports on consultations between doctor and patient when discussing trials. See also Jenkins 2000[28], Fleissig 2001[22] and Fallowfield 1998[50]. **Setting** Multiple hospitals **Country** UK	Observational **Sample size, Type** 100 Patients **Sample characteristics** Based on 82 patients with tapes available for analysis. Age and gender 25-44 years 1M, 6F 45-64 years 13M, 33F Over 65 years 14M, 15F. Cancer sites Breast 41 (50%) Prostate 15 (18.3%) Ovarian 10 (12.2%) Other 16 (19.4%) Trial participation status Request to participate. Previous trial experience 95% had no previous trial experience.	The sample was 100 newly diagnosed and relapsed patients with cancer who were eligible to participate in randomised clinical trials and were referred to senior clinical oncologists at two district hospitals and a university teaching hospital. These patients were invited to participate in a communication study and given an information sheet to read. All patients who accepted completed questionnaires about information preferences and attitudes to trials prior to discussion about trial entry (Patient Information Needs Questionnaire and Patient Attitudes to Randomised Clinical Trials Questionnaire (together forming the Patient Profile) and the Spielberger State Trait Anxiety Inventory). Each clinician saw 20 patients who were eligible for trials over a period of between 6 and 12 months. The clinician performed their usual Standard Consent (SC) procedure for half of the patients and had access to the Patient Profile to provide Individual Consent (IC) for the others. Doctors were randomised into two groups which varied the order of intervention and control group consultations. Consultations were audiotaped. After the consultations two questionnaires were given to be returned by post: a questionnaire to assess patient satisfaction with the doctor-patient interaction and a questionnaire examining reasons for accepting or declining treatment within a clinical trial. After each consultation doctors assessed their own satisfaction with the interview and rated patient distress using visual analogue scales. **Data analysis** There were 10 tape failures and eight questionnaires were not returned so 82 tapes were available for analysis. Audiotapes were content analysed by one researcher against a grid matrix developed by the authors. This consisted of the main items that a clinician and patient would cover when discussing randomised trials of cancer therapy. A random sample of 15 tapes (18%) was double coded by a second researcher to assess intercoder reliability. The average correlation between the two coders was 0.78. Results are presented descriptively and are based on the audiotaped consultations.	NA **Results** 24 patients (29.3%) were actively encouraged to take part in the trial. In 50% of the consultations patients were asked to make a decision immediately even though in 53 of 82 cases (64.6%) they were not told they could leave the trial at any time. 35 patients (43%) did not have a friend or partner present to ask for support and advice. 70 patients (85.4%) raised general questions about the trial. These included a fear of being experimented upon and concerns that the treatments within the trial would be at least as good as each other. 38 (46.3%) specifically asked about side-effects of treatment. 27 patients (32.9%) expressed uncertainty in treatment choices and 7 (8.5%) showed concern about randomisation. 12 (14.6%) of patients mentioned during the consultation that the research may benefit other patients in the future yet altruism was found to be one of the top three reasons in the post consultation questionnaire for agreeing to take part in a trial 22 (26.4%). 18 (22%) had fixed views on treatment choices. 69 (84.1%) did not express a wish for the doctor to choose the treatment. 8 (9.8%) were concerned about the fact that the doctor did not choose the treatment even after explanation had been given. The highest refusal rate was found in the chemotherapy versus standard therapy (21 of 40 (52.5%)) compared with 5 of 23 (21.7%) and 1 of 15 (6.7%) in the hormonal studies.	Clinicians adopt individual methods when presenting trial information to patients. Although the majority discussed the treatments on offer and their side effects in great detail the reasons for randomising treatment were kept to a minimum. **Recommendations for research** Not stated. **Recommendations for practice** Not stated. **Reviewers' comments** This is a descriptive study of preliminary data.

Author, Year	Study design	Data collection	Response rate	Conclusions
Jenkins 2000 [28] **Study aim** To examine the reasons given by patients for accepting or declining entry to different types of randomised trials of cancer therapy following discussions conducted by clinicians in both District General and University Hospitals. **Setting** Multiple hospitals **Country** UK	Survey **Sample size, Type** 204 Patients **Sample characteristics** 240 patients with cancer who were eligible to participate in RCTs were approached to participate in the main study on communication (see Jenkins 1999[27]). Of the 221 who agreed to participate, 204 (92.3%) returned questionnaires. This study reports on the findings from one of these questionnaires. Age and sex distribution (total n=204) Under 25 years: male n=3 female=0; 25-44 years: male n=9 female n=19; 45-64 years: male n=22 female n=84; over 65 years: male=28 female=39. Cancer sites (n=204) Breast cancer (n=112; 55%) and prostate cancer (n=23; 11%) were the two most common cancer sites with the remaining participants having testicular, lung, colorectal, ovarian, melanoma, lymphoma, bladder, pancreas and brain cancer. Trial participation status Of the participants who returned questionnaires, 147 (72.1%) had agreed	Patients completed a postal self-report questionnaire on reasons why they agreed or declined to participate in a clinical trial. The questionnaire was completed at home after a consultation with their clinician when the appropriate trial for that individual was discussed (there were 35 different trials). Some patients also received additional information from a research nurse. The authors state that the questionnaire was a similar design to an earlier questionnaire which had been piloted on 50 patients with cancer who had agreed to participate in cancer trials. Respondents rated 16 items on a 5-point scale of 1 (strongly agree) to 5 (strongly disagree). They were also asked to indicate which of the 16 items was the most important reason for their decision to accept or decline to take part in the clinical trial. **Data analysis** Data were analysed using SPSS. The categories 'strongly agree' and 'agree to some extent' were combined. Data were only reported for this combined response. Differences between those who had agreed and those who had declined to participate in a RCT on each of the 16 questions were analysed using the Mann-Whitney test. (The 6 patients who did not know whether they were in a trial or not were excluded from the analysis). The following additional analyses were carried out (though these did not appear to be pre-specified):(1) the 35 different trials available were categorised as chemotherapy, radiotherapy, hormone therapy and miscellaneous and participation rates were compared for each of the four categories; (2) trials were classified as having two or more active treatment arms, no treatment arm or placebo arm and participation rates were compared for each of the three categories.	204 of 240 (85% of those approached to take part) **Results** Number of patients who 'strongly agreed' or 'agreed to some extent (accept trial total n=147; decline trial total n=51) 'I thought the trial offered the best treatment available: Accept trial n=121 vs. decline trial n=6 (p=0.0001). I believed the benefits of treatment in the trial would outweigh the side-effects: accept trial n=116 vs. decline trial n=6 (p=0.0001) I was satisfied that either treatment in the trial would be suitable: accept trial n=119 vs. decline trial n=7 (p=0.0001) 'I was worried my illness would get worse unless I joined the trial: Accept trial n=25 vs. decline trial n=5 (p=0.24) The idea of randomisation worried me: accept trial n=56 vs. decline trial n=32 (p=0.049) I wanted the doctor to choose my treatment rather than be randomised by a computer: Accept trial n = 75 vs. decline trial n=39 (p=0.0039) The doctor told me what I needed to know about the trial: Accept trial n=141 vs. decline trial n= 45 (0.0553) I trusted the doctor treating me: Accept trial n = 143 vs. decline trial n=48 (p =0.2935) I was given too much information to read about the trial: Accept trial n = 11 vs. decline trial n= 11 (p=0.0982) I was given enough information to read about the trial: Accept trial n = 120 vs. decline trial n = 29 (p=0.0003) I knew I could leave the trial at any time and still be treated: Accept trial n=143 vs. Decline trial n=46 (p=0.0345) I did not feel able to say no: Accept trial n = 15 vs.	The authors state that the results from the study show that patients are generally very willing to participate in studies but that type of trial and probably communication style of the health professional explaining the study exerts a considerable influence on patients' preparedness to accept or decline. **Recommendations for research** None stated **Recommendations for practice** None stated **Reviewers' comments** Some barriers to trial participation may not have emerged as the barriers were pre-defined and there were no open-ended questions. This study showed a higher than usual participation rate. The survey was piloted on trial participants rather than decliners.

	to participate in a clinical trial; 51 (25%) had declined; and 6 (2.9%) said that they did not know whether they agreed to take part in a trial. Previous trial experience 11 of 204 (5.4%) had previous experience of trials. Misc 17 of 204 (8.3%) had previous experience of chemotherapy. 9 of 204 (4.4%) were expecting to discuss trials with the clinician during the consultation.		Decline trial n= 8 (p=0.1039) I wanted to help with the doctor's research: Accept trial n=136 vs. Decline trial n=23 (p=0.0001) I feel that others with my illness will benefit from the results of the trial: Accept trial n= 143 vs. Decline trial n=30 (p=0.0001) The doctor wanted me to join the trial: Accept trial n= 77 vs. Decline trial n=16 (p=0.0144) Others e.g. family or friends wanted me to join the trial: Accept trial n=64 vs. Decline trial n=2 (p=0.0002). Top reasons for accepting trial entry (n=138) I feel that others with my illness will benefit from the results of the trial n=34 (23.1%) I trusted the doctor treating me n=31 (21.1%) I thought the trial offered the best treatment available n=24 (16.3%) Top reasons for declining trial entry (n=47) I trusted the doctor treating me n=11 (21.6%) The idea of randomisation worried me n=10 (19.6%) I wanted the doctor to choose my treatment rather than be randomised by the computer n=9 (17.6%) chemotherapy (n=90): accept n=60 vs. decline n=30 radiotherapy (n=25): accept n=15 vs. decline n=10 hormone therapy (n=76): n=65 vs. n=11 miscellaneous (n=7) accept n=7 vs. decline n=0 active treatment arm (n=98): accept n=79 vs. decline n=19 no treatment arm (n=76): accept n=46 vs. decline n=30 placebo arm (n=24): accept n=22 vs. decline n=2 There was a significantly higher acceptance rate in trials with an active treatment in every arm compared with trials with no treatment arm (80.6% vs. 60.5% chi square test; p=0.003) The authors report that there were no differences between participants who accepted or declined participation in a trial according to marital status, age or level of anxiety.	

Author, Year	Study design	Data collection	Response rate	Conclusions
Kaanoi 2002 [62] **Study aim** To identify barriers to physician referral of Native Hawaiian patients to cancer clinical trials and to recommend interventions to increase accrual and retention **Setting** Multiple hospitals **Country** USA	Survey **Sample size, Type** 47 Health professionals **Sample characteristics** Participants were cancer speciality physicians practising in the state of Hawaii. Primary speciality: medical oncology 49% (n=23); surgery 36% n=17); radiation oncology 15% (n=7) Ethnicity: caucasian 51% (n=24), Chinese 11% (n=5), Filipino 2% (n=4), Japanese 17% (n=8), Native Hawaiian n=1, mixed or other 9% (n=4). Location of practice: O'ahu urban 70% (n=33); O'ahu rural 6% (n=3); neighbour island 21% (n=10) Proportion of patients Native Hawaiian: <5% n=8; 5-10% n=16; 11-20% n=15; >20% n=6	A self-report questionnaire was mailed to all 88 cancer speciality physicians practising in the state of Hawaii. Non-respondents were mailed another questionnaire two weeks later and two weeks after that three or more reminder phone calls were made to remaining nonrespondents. The questionnaire was constructed by the authors based on a review of the literature on patient accrual to clinical trials. In addition to demographic items, there were 5 items addressing interest in clinical trials, comfort with discussing trials, number of cancer patients seen each month, the number with whom a clinical trial was discussed and the number who entered a trial. There were also 17 items that might deter physicians from discussing trials with patients to which participants were required to indicate agreement or disagreement. There were open-ended questions which provided opportunities for respondents to add further remarks and suggest why few Native Hawaiians participate in trials. **Data analysis** Means and frequencies were calculated.	53% **Results** Level of interest in cancer treatment trials: very interested 64% (n=30); somewhat interested 28% (n=13); not at all interested 6% (n=3) Level of comfort in discussing trials with patients: very interested 64% (n=30); somewhat interested 28% (n=13); not at all interested 6% (n=3) 85% (n=40) had discussed clinical trials with patients in the past year; for 11 physicians none of the patients they had discussions with entered trials and the remaining 29 reported an average of 7 patients entering trials in the past year. Do you feel you are well informed about available cancer treatment clinical trials? Very well informed 53% (n=25); somewhat informed 34% (n=16); not at all well informed 4% (n=2). Wants information on clinical trials: 60% (n=28) From which sources? Cancer Research Center 60% 9n=28); tumor boards 36% (n=17); conferences 32% (n=15); journals 30% (n=14); internet 28% (n=13); one hour meetings19% (n=9); CD-ROM 17% (n=8); Cancer Information Service 17% (n=8); grand rounds 11% (n=5); other 15% (n=7) Barriers to discussing trials with patients Physician factors: not enough support staff 47% (n=22); preference for one of the treatment arms in the study 38% (n=18); providing informed consent too difficult and time consuming 26% (n=12); not adequately compensated 26% (n=12); trials not important in my practice 19% (n=9); not comfortable subjecting patients to trials 4% (n=2); conflict between role as clinician and researcher 6% (n=3); undermines patient's confidence in me 6% (n=3); interferes with doctor/patient relationship 2% (n=1); patient may transfer to another doctor 2% (n=1). Patient factors: patients refuse to participate 49% (n=23); patients have comorbidities 38% (n=18); patients lack transportation 26% (n=12); patients lack insurance 17% (n=8). Trial factors: trials are too time consuming 32% (n=15); trials are not innovative 30% (n=14); trials do not address questions relevant to my patients 26% (n=12) Factors deterring Native Hawaiian participation (this was an open-ended question) Cultural factors such as a bias against Western medicine (n=5); fear of diagnosis and therapy (n=3); a preference for traditional Hawaiian remedies or alternative approaches (n=4); difficulty in obtaining informed consent (n=2); Hawaiian perspective on quality of life (n=2). Access issues: socioeconomic barriers (n=4); lack of Native Hawaiian physicians (n=1); lack of information about cancer and screening recommendations (n=3); poor understanding of the process and benefits of clinical trials (n=5). Physician issues: clinical trials are not offered by doctors (n=5); physicians are not interested in trials (n=1); clinical research is not supported by the medical community (n=1).	Although most cancer patients in Hawaii do not participate in clinical trials, this study showed that Hawaii oncologists have positive attitudes about the value of clinical trials for their patients. **Recommendations for research** None stated **Recommendations for practice** The authors state that: Native Hawaiian health professionals could be enlisted to help recruit Native Hawaiian participants to clinical trials; educational programmes for clinical trials should provide culturally appropriate materials and public service announcements should be made to appropriate media and organisations; peer counselling programmes could link trial eligible individuals with current and former participants in trials. **Reviewers' comments** This study had a relatively low response rate and it is unclear how respondents may have differed from nonrespondents which may affect the generalisability of the findings. The reliability and validity of the measure is unclear. Some of the findings are likely to be culturally specific.

Author, Year	Study design	Data collection	Response rate	Conclusions
Kemeny 2003 [29] **Study aim** To assess whether older patients are significantly less likely than younger patients to be offered a trial and to refuse participation when offered a trial. **Setting** Multiple hospitals **Country** US and Jamaica	Survey+Case Control **Sample size, Type** 154 Both **Sample characteristics** Age Mean age of younger group was 48 years and of older group 74 years. Gender All female. Cancer sites All breast cancer. Stage I: 52% of younger group, 57% of older group; Stage II 45% of younger group, 40% of older group; Stage IV: 3% in both groups. Previous trial experience Not stated. Misc Ethnicity: 81% white in younger group and 74% in older group; 19% of younger group were black / Hispanic and 26% of older group. Employment status 71% of younger group were working full or part-time as opposed to 7% of the older group; 8% of the younger group were retired vs. 81% of the older group; 21% of the younger group were described as 'other' (homemaker, disabled, unemployed) as opposed	Breast cancer patients at 10 cancer and leukaemia Group B (CALGB) institutions who were eligible for enrolment in an open treatment trial were identified retrospectively. The institutions were specifically selected for having the highest accrual to breast cancer trials in the CALGB group of 30. Each of the 10 institutions was asked to contribute 10 pairs of patients (one woman younger than 65 years and one woman 65 years or older) matched as to their disease stage (I, II or IV) and to their physician who could either be a surgical, medical or radiation oncologist. Patients were no more than 2 years since diagnosis. Physicians received a written questionnaire about their reasons for offering or not offering a trial. This included a list of 14 reasons including treatment toxicity, comorbid conditions, inadequate treatment arm, patient lack of assistance at home, lack of transport and patient difficulty understanding the trial. Physicians were also asked why they thought a patient had refused participation. Patients were interviewed usually over the telephone as to reasons for participating or refusing to participate in a trial. A list of 17 reasons for participating or refusing were offered to patients reflecting treatment side effects, outcome and cost, research-specific issues, the consent form, the doctor's and family's wishes and altruism. Patients were asked to rate each reason as to importance for their decision on a 4 point Likert scale ranging from 'not important' to 'very important'. Patients were then asked to rate which were the three most important reasons that influenced their decision. Comorbid conditions which might explain differential enrolment were assessed using a 14 point list with a 3 point scale rating from 'not at all' to 'a great deal' to assess the degree with which it interfered with daily functioning. A modified version of the Revised Rand Functional Limitations Scale was used to assess physical functioning. Background information on sociodemographic details also collected.	NA **Results** There was a trend towards older patients being offered a trial less frequently than younger patients (19 pairs where younger person was offered a trial but not the older, 9 where the older person only was offered). The remaining 39 pairs were concordant. Age did not predict being offered a trial in stage I patients. However 68% (25 of 34) of younger stage II patients were offered a trial compared with 34% of the older patients (25 of 71) (p=0.0004). In univariate analyses age (p=0.006), disease stage (p=0.01) and number of comorbidities (p=0.03) were significant predictors of being offered a trial. In multivariate analyses disease stage and age remained highly significant in predicting trial offering (p=0.0008) which remained when controlling for physical functioning (p=0.04) and comorbidity (p=0.02). The most frequently cited reasons for younger patients not being offered trials were unaware that a trial was open (30%); thought the patient was not eligible (15%), thought the best treatment was not included in the trials (15%) and thought one arm in a randomised trial would be less effective (15%). Among the 33 older patients not offered a trial reasons physicians gave were as follows: treatment too toxic for the patient (33%); the best treatment was not included in the available clinical trials (27%); unaware that a trial was available (21%); thought the patient was not eligible (18%) and concerns about comorbidity even if this did not affect trial eligibility (18%). Of those offered a trial (60 patients) there was no significant difference in participation rates between younger (56%) and older (50%) patients (p=0.67). Primary reasons for participating among younger patients (n=20) were they expected their health to	When controlling for comorbid conditions age and stage were the only predictors of whether a patient was offered a trial. There are likely to be multiple reasons for this observation. However the greatest impediment to enrolling older women was the physicians' perceptions about age and tolerance of toxicity. **Recommendations for research** Not stated. **Recommendations for practice** **Reviewers' comments** This is a retrospective study with the possibility of recall bias given the length of time since being offered a trial. This pilot study used closed rather than open questions limiting patient generated responses. Findings are based on small numbers of patients in centres relatively successful at recruiting patients to trials and thus the results may be difficult to generalise.

	to 13% of the older group. 49% of older and 5% of younger were widows. In terms of functional limitations 35% of the older and 55% of younger were able to do the vigorous activities they used to do. Older patients had significantly more comorbid conditions than younger patients (mean 3.2 vs. 1.9, p<0.0001). The most commonly reported comorbid conditions in older patients were arthritis, rheumatism or other connective tissue disorders(71%), high blood pressure (58%), circulation trouble in arms or legs (30%) and heart disease (29%). There was no significant difference between older and younger patients in the degree to which comorbid conditions interfered with their daily functioning (1.5 vs. 1.4, p=0.43).	The number of trials offered to the two groups was compared. **Data analysis** The power calculation was based on 100 pairs of women but only 77 pairs were recruited. McNemar test was used to test the association of age with being offered a trial. In all further analyses repeated measures logistic regression (i.e. with generalised estimating equations) was used to test the univariate and multivariate association of being offered a trial with age and other potential predictors including race, education, marital status, comorbidities and functional limitations. 4 patients who had stage IV disease were grouped with the stage II patients. The chi squared test was used to test the association of age group with whether or not patients who were offered a trial accepted trial participation. A two sided type I error of 0.05 was used for all statistical tests.	improve (85%); they wanted to help find a cure for cancer (75%) and they wanted the latest treatment (55%). Among the 12 older patients reasons were: it was the best treatment available (67%); they expected their health to improve (67%) and they wanted to help find a cure for cancer (50%). The primary reason for not participating among 16 younger patients was that they wanted to choose their own treatment (69%). 25% of younger patients also said they wanted a treatment that was not offered, they did not want to be in an experiment and that they felt that the treatment would be life threatening. Views of the older group were similar (n=12): choose own treatment (75%); a treatment that was not offered (33%) and did not want to be in an experiment (25%). The two main reasons physicians gave for patients refusing to participate were the same for both age groups: patients did not want to be in a study with an experimental treatment and the patient did not wish to be randomised.	

Author, Year	Study design	Data collection	Response rate	Conclusions
Klabunde 1999 [30] **Study aim** To provide an overview of factors influencing enrolment of cancer patients in National Cancer Institute sponsored clinical trials with particular reference to the possible influence of insurance coverage. **Setting** Multiple hospitals **Country** USA	**Study design** Chart review **Sample size, Type** 573 Patients **Sample characteristics** Facility type CCOP 487 (of whom 24.8% enrolled) Academic medical center 86 (of whom 52.3% enrolled) Age Not stated. Gender Of 573 eligible for enrolment on a specific trial 231M (of whom 29.4% enrolled), 342F (of whom 28.7% enrolled). Cancer sites (based on 573 eligible patients) Breast 228 (25.4% enrolled) Colorectal 119 (18.5% enrolled) Prostate 89 (23.6% enrolled) Other 89 (56.2% enrolled) Lung 48 31.2% enrolled) Trial participation status 936 of 2339 (40%) patients had at least one available protocol suitable for them. Of these 573 were clinically eligible for enrolment (61%). Of these 166 (30%) were successfully enrolled. 42% of 82 patients eligible for Phase I or II enrolled whilst 26.8% of 491 patients eligible for phase III or other enrolled. Misc Of 409 white patients 29.9% enrolled, of 164 black patients 29.3% enrolled. Of 519 with a new diagnosis 28.3% enrolled and of 54 with recent progression 32.0% enrolled. Of 94 patients at cancer stage 1 18.1 enrolled, at Stage 2 it was 20.4% of 255, at Stage 3 it was 30.1% of 93, at Stage 4 it was 52.6% of 78 and where it was unknown 52.8% of 53 enrolled.	Between June 1997 and January 1998 data were collected on all adult (20 years or older) cancer patients evaluated for enrolment in National Cancer Institute sponsored clinical trials at 15 medical facilities in the south-eastern United States. Data was entered onto a standardised log sheet adapted from an earlier study of clinical trial enrolment barriers by clinical co-ordinators. The following were abstracted: patient and facility identifiers, primary diagnosis and disease stage, any progression of cancer to a new stage, sex, race / ethnicity, insurance coverage and details of any NCI sponsored trial protocols available for the patient's cancer type. Coverage of protocol care by the patient's insurance, clinical eligibility and ultimate enrolment were also recorded. During the data collection period at least 140 NCI-approved protocols were open for enrolment at the centres. For clinically eligible patients who were not enrolled the primary reason for nonenrolment was noted. Clinical co-ordinators received on-site training sessions on collecting data. **Data analysis** Factors predictive of enrolment of clinically eligible patients were assessed using chi-square tests and logistic regression modelling.	NA **Results** Neither patient race (OR = 0.82 for black patients (95% CI: 0.52, 1.29) nor sex (OR= 1.13 for female gender (95% CI: 0.62, 2.05) nor trial phase ((1.42 for phase III or other (95% CI: 0.75, 2.66) predicted enrolment. Newly diagnosed patients were not more likely to be enrolled than were previously diagnosed patients whose cancer had advanced to a new stage ()R for new diagnosis 0.56 (95% CI: 0.29, 1.07). Patients with fee-for service coverage were more likely to be enrolled compared with patients with other types of coverage including managed care. Patients with later stage disease (for Stage 3 OR=2.13 (95%CI: 1.01, 4.52), for Stage 4 OR= 4.07 (95% CI: 1.90, 8.74) or whose primary site was a cancer other than breast, prostate or colorectal were more likely to participate in a trial (ORs from 0.30 to 0.46). The following were noted as the major reason for refusal: concerns about experimentation (15%), cost (5%) or toxicity (5%) or unspecified concerns (13%). Additional eligibility problems, comorbidities and anticipated problems with follow-up were cited for 22% and physician preference for a specific therapy for 17%. Insurer refusal to cover protocol care was listed for 7% and 5% were not enrolled because they were referred to another facility or placed on non-NCI protocols. Other or unknown was indicated as the primary reason for nonenrolment for 10%. Bivariate analysis demonstrated that patients who refused enrolment were more likely to be newly diagnosed ($p < 0.05$) and self pay or to have other type of coverage ($p < 0.005$). Compared with clinically eligible patients who were enrolled patients who refused enrolment did not differ by sex, race cancer site or stage or type of facility at which evaluated.	Although multiple factors were found to influence enrolment in clinical trials for cancer, results suggested that insurance coverage played a role. Patient refusal, a substantial reason for nonenrollment, points to the need for continued efforts to educate physicians and the public in the value of clinical trials. **Recommendations for research** Additional investigations are needed to confirm the study results and to enhance understanding of barriers to clinical trials enrolment. **Recommendations for practice** Not stated. **Reviewers' comments** This study includes phase 1 and 2 studies but trial phase was not found to be a modifier of enrolment.

Author, Year	Study design	Data collection	Response rate	Conclusions
Kornblith 2002 [63] **Study aim** To assess physicians' perception of the difficulties in entering older patients with cancer on clinical trials **Setting** Multiple hospitals **Country** USA	Survey **Sample size, Type** 156 Health professionals **Sample characteristics** Participants were from 10 institutions that had the largest accrual of patients with breast carcinoma to treatment trials across all ages in Cancer and Leukemia Group B (CALGB). They were involved in the treatment of patients with breast carcinoma. Medical Speciality: medical oncology 48% (n=75); surgical oncology 21% (n=32); radiation oncology 16% (n=25); general surgery 12% (n=18); Fellow 3% (n=5) Practice setting: academic medical centre 71% (n=106); private practice 25% (n=37); community-based hospital 5% (n=7). Male 69% (n=105); white 87% (n=132); median age 43 years (range, 29-74 years)	Physicians were asked to complete a questionnaire about their perception of the difficulties in placing older patients with carcinoma in trials. Copies of the questionnaire were sent by Clinical Research Associates, by interoffice or regular mail, to physicians involved in the treatment of patients with breast carcinoma. Completed questionnaires were retuned to them. The questionnaire was constructed by two of the authors. Multidimensional items were included on barriers to accrual and physicians were given the opportunity to suggest reasons for difficulty in recruiting older patients. They were asked to rank the three most important reasons why it was difficult to accrue older patients to cancer trials. They were asked to identify which of seven possible interventions they thought might be effective to improve accrual and rank the three interventions that might be most effective. They also had the opportunity to suggest additional intervention. **Data analysis** Percentages and frequencies were reported.	This was measured in only 3 of the 10 institutions. Where it was measured, it ranged from 33%-100%. **Results** There were eight reasons endorsed by 25% or more of physicians as to why it was difficult to accrue older patients with breast carcinoma to clinical trials: transportation needs (68%, n=106); comorbid conditions that are not excluded but may affect response (53%, n=78); patient difficulty in understanding the trial (50%, n=80); toxicity of treatment regimens (51%, n=78); assistance at home for treatment administration not available (40%, n=63); often do not meet eligibility criteria (36%, n=56); some costs not covered by medical insurance (34%, n=53); physician concerns that a treatment arm is less effective or unacceptable (25%, n=39). The most important barriers to accrual were: comorbid conditions (16%, n=25); patient difficulty in understanding the trial (16% n=24); toxicity of treatment regimens (14%, n=22); and elderly often do not meet eligibility criteria (15%, n=23). Seven suggestions for improving accrual were endorsed by 19% or more of physicians: make personnel available in the clinic to explain trials (69%, n=108); provide better educational materials for patients (63%, n=99); provide transportation (63%, n=98); provide better educational materials for family members (59%, n=92); protocols with few inclusion criteria related to comorbid conditions (49%, n=77); provide MDs with lectures, courses and articles on toxicity of cancer treatments in elderly (45%, n=70); provide MDs with courses, lectures and articles concerning physical and mental capabilities of elderly (19%, n=29).	Physicians viewed barriers to accruing older patients with breast carcinoma to clinical trials as multidimensional, with the most important involving protocol requirements, treatment specific issues, and older patients' medical and cognitive characteristics. **Recommendations for research** The authors state that the questionnaire focused on areas that had previously been identified as barriers to older patients. There may be general barriers to all age groups which are relevant to older people so the questionnaire should be revised to include the full range of reasons why it is difficult to enter older patients with cancer into trials. They also state that additional research is required to validate their findings. **Recommendations for practice** Accrual of older women may be improved by providing oncologists with medical information to help them determine whether a clinical trial should be offered to their older patients with cancer. **Reviewers' comments** This was a poorly conducted study which has limited generalisability given the sample of oncologists used and the lack of a protocol for how individuals within the institution were chosen. The reliability and validity of the questionnaire is unclear.

Author, Year	Study design	Data collection	Response rate	Conclusions
Langley 2000 [64] **Study aim** To explore attitudes to and problems experienced with recruitment into randomised trials in cancer care **Setting** Multiple hospitals **Country** UK	**Study design** Qualitative **Sample size, Type** 20 Health professionals **Sample characteristics** Speciality: oncology (n=7); urology (n=5); general surgery/breast (n=4) haematology (n=4) Main location: teaching hospital/cancer centre (n=7); associated teaching hospital (n=3); district general hospital (n=10) Involvement in randomised trials (number in last 2 years): 0 trials (n=2); 1-3 trials (n=9); 4-6 trials (n=4); 7-10 trials (n=4); more than 10 trials (n=1)	Clinicians caring for bladder, breast, lymph glands, lung, ovarian and head and neck cancer in the South West of England (n=403) who responded to a survey on trial participation were invited to participate in the qualitative part of the study. A purposive sample of 20 was drawn from the 55 who agreed to participate with the aim of covering a range of cancer specialities, geographical areas, types of hospital and degree of previous involvement in randomised trials. Clinicians were interviewed, using a semi-structured interview for 30-60 minutes at the hospital in which they were working during the second half of 1997. The interviews focused on the concerns they had highlighted in the survey questionnaire. Interviews were audio taped and verbatim transcriptions were made by the interviewer. **Data analysis** Data were analysed by comparing transcripts and describing identified and emergent themes. All members of the team examined five transcripts initially and identified 22 categories of responses which came under four themes: organisational issues, clinician perspectives, patient issues and trial characteristics. The transcripts were coded according to these categories by members of the team and differences were resolved by discussion. The NUDIST qualitative analysis program was used to collate all extracts for each category. These were inspected and summarised and some categories were amalgamated. Following analysis the major findings were collated under the following four headings: decision to participate; requirements of the general clinical situation; difficulties experienced/practical needs; and collaboration.	NA **Results** Decision to participate Nearly all those interviewed were in favour of research. In general, higher recruiters were more positive about research and lower recruiters expressed more concerns. Many viewed involvement in trials as an additional burden whereas others felt a responsibility to involve patients in trials as part of their day-to-day clinical practice. Awareness of ongoing trials, remembering the trials and the eligibility criteria in the clinical situation, belief in the effectiveness and safety of different treatment arms, a trial addressing important practical issues and the likelihood of recruiting sufficient numbers were identified as important issues. Practical support provided by the body organising body also affected the interest shown in a trial. Provision of regular feedback was viewed as necessary to encourage continuing participation. Requirements of the clinical situation All clinicians commented that gaining patient consent for trials took much more time than standard treatment. Although the additional support from trial nurses was regarded as essential many felt it was the doctor's role to initiate discussion with the patient. Difficulties experienced and practical needs Many comments were made on the difficulty and time required for preparing submissions to ethics committees. Many thought there should be a national streamlined process. If there was no administrative support available the ongoing data requirements after patients have entered a trial were a barrier to clinician participation. The expense of treatments, lack of facilities and lack of support in the hospital setting were also identified as barriers. Aspects of randomisation viewed as problematic were: that the clinician felt it was not the right way to make treatment choices, that the concept was poorly understood	Barriers to recruitment depend on the clinicians' individual situations and on a complex combination of factors. Action is needed to promote awareness of randomised trials under way, to ensure that trials address issues of importance, are acceptable to patients and clinicians, and that practical support is provided for participating centres. **Recommendations for research** None stated **Recommendations for practice** None stated **Reviewers' comments** The method of data collection and data analysis were reasonably clearly outlined. The recruitment strategy identified a planned and diverse group of clinicians. The sample size was not justified and it is unclear whether saturation was reached. The issue of reflexivity was not addressed. The possibility of how a researcher interviewing participants about participation in research and the fact that members of the team were researchers from a medical background may have influenced all aspects of the research process should have been examined.

			by patients and often unacceptable to them. Clinicians were concerned that they did not have the necessary support staff or time to discuss trials with patients. Collaboration More active recruiters to trials were in close contact with trial organisers and national and regional groups. There was very limited collaboration between clinicians in different hospitals and some felt professional rivalry prevented collaboration. Some clinicians not in contact with the trials network were unaware of interested clinicians. Views on improving recruitment into cancer trials Trial organisers: involve clinicians at an early stage to optimise relevance and feasibility of trials; communicate trial summaries more widely and provide regular feedback; opportunity to attend meetings to hear results and study progress; funding and/or practical support with administration and data handling; provide 'at a glance' eligibility checklists for use in clinics. Providers and purchasers of healthcare: promote policies that actively support involvement in trials; provide the necessary infrastructure; provide a structure that can handle research monies easily. Formal and informal professional bodies: increase central organisation to minimise research demands on clinical time; use meetings and research networks to increase clinician involvement; monitor efficiency of ethics procedures; consider how patients could become more knowledgeable about clinical trials. Research active clinicians: communicate about trials you would like to see completed; collaborate across district and trust boundaries; share administrative burdens and research staff; increase the scope of local networks.	

Author, Year	Study design	Data collection	Response rate	Conclusions
Lara 2001 [31] **Study aim** To determine the overall accrual rate of new patients into available clinical trials, to evaluate the factors that might affect protocol eligibility, to study the characteristics of patients who did not enrol despite being eligible and to evaluate the impact of the findings on the design and development of future studies to increase awareness for greater trial participation. **Setting** Cancer Centre **Country** USA	Survey **Sample size, Type** 276 Both **Sample characteristics** 276 patients assessed by oncologists and eligible for analysis. Age Median age 62 years (range 17-88) Gender 157M (43%), 119F (57%) Cancer sites Not stated. Trial participation status 171 (62%) were considered by physicians for participation, 105 (38%) were not considered. Of those considered for participation 91 (53%) had an appropriate protocol available for site and stage of disease, 80(47%) did not. 76 of 90 patients with available protocols (84%) met eligibility criteria for a particular study, one patient's eligibility could not be determined and 14 (15%) were found to be ineligible. 39 of 76 (51%) agreed to participate. 37 of 76 (49%) declined to participate. Overall accrual rate was therefore 39 of 276 (14%). Previous trial experience Not stated. Misc Race Caucasian: 211(76%), Hispanic: 23(8%), Unspecified: 18(7%), Other: 24(9%).	Prospective tracking of factors affecting patient accrual in trials available at the University of California Davis (UCD) Cancer Center during three time periods: Jan 15 to June 15 1997; Sept 1 to Dec 1 1998 and Jan 1 to April 30 2000. Twelve medical oncologists and six fellows saw patients during these time periods. Physicians were alerted to the availability of protocols by dissemination of a paper copy of a quarterly protocol list. Other relevant protocol information is available electronically. Medical oncologists were asked to complete questionnaires about patient characteristics and clinical trial eligibility appended to progress notes of most new patients seen at the centre. Standardised questionnaires asked first whether the physician had considered enrolling a particular patient in a trial and if not to give the reason. The second question was about the availability of an appropriate protocol. The third asked whether the patient met eligibility requirements as defined in a particular trial. Finally the physician was asked to record the patient's decision whether to participate and if they refused their reason for doing so. **Data analysis** Data was recorded in MS Excel. Descriptive statistics were generated. Univariate analyses were performed to evaluate associations of patient characteristics with protocol accrual. Associations were assessed using the chi squared test. Odds ratios and confidence intervals were generated. All statistical analyses were performed using SAS and statistical significance was set at $p < 0.05$.	Not given (350 forms were completed with 276 patients eligible for analysis) **Results** None of the patient characteristics were found to be statistically significant (in univariate analysis) in influencing physician decision-making about considering enrolling a patient: age group, gender, race, referral source and insurance status. The primary reasons physicians did not consider patients for trials were: no available protocol in 22 patients(21%), poor performance status in 20(19%), patient not expected to return in 12 (11%), previous therapy in 11(10%), no evidence of disease in 9(9%), no pathologic diagnosis in 8(8%), synchronous primary tumours in 5(5%), unknown primary cancer in 5(5%) and other reasons in 13(12%). None of the patient characteristics (age, gender, race, referral source) were found to be statistically significant (in univariate analysis) in predicting patient participation apart from patients being less likely to participate if they had private insurance (OR=0.34 (95% CI: 0.13, 0.9, p=0.03). The most common reasons (37) for patients to refuse participation in a trial were as follows: desire for other treatment: 13 (34%), distance from clinic: 5(13%), no reason given: 4(11%), insurance denial: 3 (8%) and fear of randomisation: 2(5%).	Barriers to cancer clinical trials from the point of view of the physician, protocol or eligibility, patient and funding can be prospectively identified and addressed in the development and conduct of future studies. **Recommendations for research** Investigation of patient perceptions regarding the clinical trials process and the role of third party payers is needed. **Recommendations for practice** Not stated. **Reviewers' comments** It is unclear if patients were allowed to record more than one reason for refusal to participate in trials which may have resulted in relevant data being lost. Those who accepted to take part in a trial were not asked why they had participated.

Author, Year	Study design	Data collection	Response rate	Conclusions
Madsen 2002 [32] **Study aim** To compare attitudes to clinical research amongst cancer trial participants and nonparticipants and to compare results with those from previous studies amongst participants in non-cancer trials. **Setting** Multiple hospitals **Country** Denmark	Survey **Sample size, Type** 88 Patients **Sample characteristics** Age Cancer trial participants were statistically significantly older than decliners (Median age 59 vs. 46). Gender 24M, 64F Cancer sites Participants Nonparticipants Premenopausal breast cancer 11(0M) 41(0M) Duke C type colon cancer 3 (6M) 3 (2M) Disseminated colorectal cancer 17 (14M) 3 (2M) Trial participation status All were eligible to participate in cancer clinical trials including chemotherapy. 41 participants (20M, 21F) and 47 nonparticipants (4M, 43F) in cancer trials. Previous trial experience 9 trial participants and 5 nonparticipants had previously participated in a trial.	Data were gathered over a 2 year period (1997-1999) at the oncological departments of two university hospitals. Cancer patients accepting or declining randomisation to trials including chemotherapy were included. In the breast cancer group only premenopausal women were included. The survey used a self-administered questionnaires. Trial participants and non-participants completed a questionnaire on attitudes to participation in trials at the first visit after their decision to accept or decline participation. Participants only completed 2 further questionnaires. Only the first questionnaire probing attitudes to participation is relevant here as the remaining questionnaires were concerned with satisfaction with participation in a trial. Most questions were multiple choice with additional space free text. **Data analysis** Nonparametric statistical tests (Kruskal-wallis, Mann-Whitney) with a significance level of 0.05 were performed using GraphPad software. The possible influence of age and sex on results was investigated with a multinomial logistic regression analysis using SPSS.	93% (82 of 88) **Results** No significant differences were seen between participants and nonparticipants in answer to the question 'Which motives do you think doctors have to plan and conduct medical research'. No significant influence on results of age or sex were seen for this question. No significant difference was noted between groups on whether declining participation constituted a moral problem (cancer trial participants 24% vs. decliners 12%). Again no effects of age or sex were found. No significant differences between groups were noted on the need to examine new drugs and investigations. Attitudes towards clinical research were generally positive in all groups with participants being significantly more positive than decliners. Age or sex did not influence the results. In response to the question 'How is your general attitude towards your own potential participation in a clinical trial?' cancer trial participants were more positive than decliners with no influence of age or sex (68% vs. 15%). There was a similar level of positiveness towards participation of family and friends with participants being more positive than nonparticipants. . 'Several' trial participants stated that their reasons for a positive attitude to trials were: hopes for a personal benefit and a wish to help future patients. 'Several' decliners stated an anxiety about 'the unknown' and a wish to maintain a personal influence on decisions (data not reported). Decliners were significantly more negative towards randomisation than participants (34% vs. 7%). Age significantly influenced results with younger respondents being the most positive. The odds for a positive versus a hesitating / negative opinion were 2.65 (95% CI: 0.95, 7.42) for respondents younger than 36 years. Free text tended to reveal comments on the fairness of randomisation from cancer participants though most would have liked to choose their treatment themselves) and from decliners resentment towards drawing lots when a life threatening disease was involved and a wish to choose their own treatment or let the doctor choose it for them. Cancer trial participants were asked to rate on a 4 point scale the importance of a number of reasons for their choice to participate in an actual trial. The wish to get the new drug / investigation was felt important or very important by 78% (n=32); the wish to be more closely monitored by 69% (n=28); the wish to develop a good 'relation' with the treating department by 35% (n=14), the wish to help future patients by 71% (n=29) and positive experiences from former participation in trials by 22% (but only 9 people responded to this question). A majority of decliners stated a fear of adverse events and / or fear of the unknown. Several felt uneasy with randomisation, mentioned a lack of personal resources, a lack of information, saving the 'new' treatment for a possible recurrence of the disease and some explained their choice as purely emotional. Numerical data were not provided for these items.	Attitudes towards clinical research are generally positive even in cancer nonparticipants. Both personal and altruistic motives for participation were highly rated. A fear of the unknown and resentments towards randomisation were primary reasons to decline participation. **Recommendations for research** Not stated. **Recommendations for practice** Not stated. **Reviewers' comments** Concern about sample size for multiple testing so may merit a more cautious interpretation of results. Data appears to be reported for some questions but not for others. It is unclear how free text was analysed. It is interesting that even trial decliners are positive about clinical trials.

Author, Year	Study design	Data collection	Response rate	Conclusions
Mannel 2003 [33] **Study aim** To analyse the role of individual physicians in recruiting patients to clinical trials. **Setting** Single hospital **Country** USA	Chart review **Sample size, Type** 248 Patients **Sample characteristics** Age Not stated. Cancer sites Untreated Endometrial, Cervical or Ovarian cancer Trial participation status 248 of 303 were eligible for a multi-institutional phase III trial. 190 of 248 (77%) of all eligible patients were offered a trial. 120 (48% of total sample, 63% of those offered a protocol) were enrolled in a trial.	A retrospective review was undertaken of all patients with untreated endometrial, cervical or ovarian cancer potentially eligible for a multi-institutional phase III trial cared for by the Section of Gynecologic Oncology at the University of Oklahoma from July 1 1998 to September 30 1999. The section has four faculty physicians who have equal access to a centralised research infrastructure of data managers, research nurses and protocol trained chemotherapy nurses. All new patients are reviewed for trial eligibility during a weekly mutlidisciplinary tumour board. The chart review in this study determined eligibility for participation, age, insurance status and reason for not enroling on a study. **Data analysis** The information from the chart review was correlated to individual faculty physicians and comparisons were made using chi-square analysis. All statistical analysis was performed using the Statistical Analysis System (SAS) version 6.12	NA **Results** There was no difference in patient age, type of cancer or insurance status between the four faculty practices but there was a difference in percentages of patients enrolling in trials according to attendant physician (range 27% to 80%). Physicians who were primary investigators for the research trials were significantly more likely to enter patients on trials (71% vs. 31% for enrolled patients, $p < 0.0000001$). There was a difference in the rate of faculty offering protocol therapy ranging from 61-97%. When analysing the subset of patients who were offered protocol therapy there remained a difference between individual physicians in successful enrollment (44% to 83%). Principal investigators were significantly more successful in enrolling patients once protocol was offered (76% vs 49%, 0.00001). Referring physicians assuming patients care off protocol remained a small reason for nonenrolment (4%).	Individual physician factors play a greater role in enrollment of patients onto clinical trials than do patient and institutional factors. **Recommendations for research** **Recommendations for practice** The authors concluded that efforts to increase enrollment of patients onto cancer clinical trials should be focused primarily at the individual physician level through education and recognition of the importance of patient participation in trials. **Reviewers' comments** The study minimises the patient variables and is based on one centre with good research support so it focuses on the individual physician barriers. However its limitation is that it is based on results from just four physicians.

Author, Year	Study design	Data collection	Response rate	Conclusions
Martin 2003 [65] **Study aim** To evaluate the prevalence of prospective randomised controlled trials (PRCT) written and participated in by recent graduates of surgical fellowships and general surgery graduates and the reasons for participation or non-participation. **Setting** Multiple hospitals **Country** USA	Survey **Sample size, Type** 201 Health professionals **Sample characteristics** All the participants were surgical oncology or general surgery graduates from one of three institutions: 50% (n=100) had completed a surgical oncology fellowship; 17% (n=35) had completed general surgery training only; and 33% (n=66) had completed another type of fellowship. Current position: academic full-time 46% (n=92); academic part-time 9% (n=18); solo private practice 14% (n=28); group private practice 28% (n=56); health management organisation 1% (n=1); administration 1% (n=2); other 1% (n=4). Academic rank: 23% (n=47) were not associated with academic centres; the remaining participants were professor/clinical professor or assistant professor/clinical professor.	All surgical oncology graduates of Memorial Sloan-Kettering Cancer Centre (n=100) and general surgery graduates of the University of Louisville (n=100) and New York University (n=100) from 1985-1999 were asked to complete a postal self-administered questionnaire. Nonrespondents were mailed a further questionnaire two months later and then one month later. The questionnaire was developed for the study and piloted on a small number of current surgical oncology fellows. It comprised 15 questions on two pages and covered the following areas: current academic position; utilisation of data from PRCTs; their opinion of PRCTs; if a PRCT had changed their practice; ; if they participated in a PRCT; and where they felt they had received the information that helped them for decisions for their current practice. Participation in a PRCT was defined as enrolling a patient in a trial.(Only data related to participation in RCTs and barriers was extracted for this review.) **Data analysis** Descriptive data were presented.	67% (201/300) **Results** Participation in PRCTs: 89% of surgical oncology graduates, 42% of general surgical graduates and 54% of other fellowship graduates had participated in a PRCT. The most frequent reason for lack of participation in a PRCT was not being asked to participate (80%), with the second most common reason lack of time (18%). The barriers were not reported for surgical oncology graduates for this item. 50% of surgical oncology graduates had not written a PRCT; the two most common reasons given were no time available (63%) and no support from their institutions (38%)	Participation in PRCT is significantly higher in surgical oncology graduates when compared with general surgery graduates and other fellowship trained graduates, with lack of involvement being the primary reason. **Recommendations for research** None stated **Recommendations for practice** The authors state that continued emphasis during training and actively involving academic as well as community surgeons, will increase the number of patients involved in PRCTs. **Reviewers' comments** This study addresses barriers in only a limited way and barriers to accruing patients are reported only for the general surgery and other fellowship graduates.

Author, Year	Study design	Data collection	Response rate	Conclusions
Maslin-Prothero 2000 [34] **Study aim** To identify the factors affecting the accrual of women to breast cancer clinical trials from the perspective of surgeons, multidisciplinary teams and of women approached to participate in trials who either participated or did not. **Setting** Multiple hospitals **Country** UK	**Study design** Mixed methods **Sample size, Type** see bel Both **Sample characteristics** Demographic characteristics of the surgeons and multidisciplinary team were not reported. Patients with breast cancer Age: 40-49 years n=1, 50-59 years n=18, 60-69 years n=11, >70 years n=3 Marital status: married, n=27; single n=2, cohabiting n=1, divorced n=3	The BASO II trial investigated whether radiotherapy is necessary for breast cancer of low aggressive potential following breast conserving surgery. It had a 2x2 design so that those centres recruiting women to the trial do not have to enter into all four arms. Surgeons All BASO nominated breast group surgeons were asked to complete a specically constructed postal questionnaire regarding their views on clinical trials and their experiences of joining the British Association of Surgical Oncology Trial II (BASO II) l or their reasons for not doing so. Multidisciplinary teams Members of multidisciplinary teams at 14 centres recruiting to the BASO II trial were interviewed individually or as a group using a piloted semi-structured questionnaire with open-ended questions. Interviews were tape-recorded and transcribed by an independent professional. The 14 centres were chosen to give a spread of low, medium and good recruitment success (self-assessed) Patients Four focus groups and three individual interviews were carried out with 21 women who had participated in the BASO II trial and individual interviews with seven women who had declined participation. Piloted discussion guidelines were used. Where agreement was obtained the sessions were recorded. An additional patient responded by letter. **Data analysis** Clinician questionnaire: data were analysed using descriptive statistics Interviews with multidisciplinary teams and patient focus groups: notes were made on the general themes emerging from each of the transcripts, these were coded and analysed with the main themes agreed with independent researchers.	80/118 surgeons (68%) **Results** Surgeons (49% of questionnaires were from surgeons entering patients into BASO II trial) General issues: 84% (n=63) thought they were given more acknowledgement for their clinical work than for any contribution to scientific knowledge. 56% (n=44) were reluctant to participate in a trial that had a treatment arm that involves a treatment that is seen as being less than standard practice. 46% (n=37) felt that having to explain the details of a clinical trial discouraged them from approaching eligible patients. Factors causing difficulty in joining the BASO II trial: The majority of participants had no difficulty with any of the following potential barriers: making ethics application, and obtaining approval, number of eligible women seen, conflicting trials, adapting local practice to protocol. Scientific design of the BASO II trial, relevance of trial to practice, obtaining appropriate pathology reports and obtaining information on BASO II trial. Two of these issues prevented more than 10% of clinicians in joining the BASO II trial: conflicting trials and adapting local practice to protocol with small numbers being prevented from joining due to the other factors. Based on analysis of the open-ended questions, clinical workload and obtaining the agreement of colleagues to work to the trial protocol were also important factors (data not reported). Factors causing difficulty in the recruitment of women into BASO II trial in registered centres (n=39)(these data are presented by centre not by clinician) The main difficulties experienced were in relation to patients expressing a treatment preference (prevented entering women 26% (n=9), caused some difficulty 66% (n=23)) and eligible patients refusing to join the trial (prevented entering women 34% (n=12), caused some difficulty 60% (n=21). Clinician related factors causing some difficulty were time explaining the trial to patients (46%, n=16), poor design of informed consent information (21%, n=7), relinquishing doctor decision-making to randomisation (15%, n=5), effect on doctor-patient relationship 14%, n=5) Multidisciplinary teams Lack of appropriate systems to identify eligible woman was	There were similarities and differences between the views of clinicians, multidisciplinary teams and patients. There was agreement that women do have treatment preferences, the time when they are first approached to join the trial was not a good one, and that they pick up on any uncertainty displayed by the multidisciplinary team. Differences mainly relate to practicalities such as insufficient staff and time available for recruiting women and the commitments associated with trial participation for the women. **Recommendations for research** To undertake a comparative study to examine whether incentive payments make a difference to the recruitment of patients to trials. To examine recruitment to other clinical trials, in other areas of healthcare, to identify if the factors affecting recruitment are the same for all trials. (These are based on the findings in relation to the BASO II trial as well as the findings in relation to another trial that were not extracted as the trial was of healthy women) **Recommendations for practice**

			not identified as a barrier to recruitment. The main reason for failure to recruit was identified as the refusal of eligible women to participate. The author states there was little evidence to suggest that differences in the characteristics of eligible women between centres could account for variation in recruitment rates, with the exception of centres with a large rural population, who found that women in outlying areas were less willing to accept radiotherapy. This could be explained by the commitment of travelling daily for 6 weeks of treatment. Key themes identified 1. 'Selling the trial had three sub-themes: encouraging trials, difficulties with design of a trial and backtracking of the multi-disciplinary team'. Centres with the best recruitment approached 'selling the trial' by providing a positive message, with random allocation presented as a rational policy when the benefits of the treatment arm are unproven. The idea of selling the trial was viewed as pejorative by some clinicians and there were concerns about meeting the requirements for informed consent. Lack of consistency in the explanations given to women was perceived as a problem. This happened when women were given a likely treatment plan before surgery but then after surgery if they were eligible for the trial, clinicians had to 'backtrack' on the initial treatment plan. 2. Methods of obtaining consent had four themes: entering patients into BASO II, eligibility issues, factors affecting asking women and organisational issues. Entering patients was more difficult in some centres because of factors such as local surgical practice or clinical workload. Where centres are positive when explaining the trial, they find recruitment straightforward. Local policies about routine auxillary node sampling meant that for some centres extra work was required to identify eligible women. It was felt that women were approached for participation at a very stressful time. Also there was a general feeling that the longer women had to think about whether they should participate, the less likely they were to do so. There was a view that factors such as clinics specifically for trial recruitment and sufficient staff including data managers and research staff could enhance recruitment. Regional trials meetings were seen as helpful for sharing advice on recruitment. 3. Patient preference had four subthemes: concerns about treatment, dislike clinical trials, choice about treatment and lack of continuity. It was felt that lack of staff continuity contributed to patient concerns about treatment. Some women wanted orr expected a different treatment. Because	Trial design Trials should address a relevant issue and have a high probability of changing/confirming practice. Design should be kept as simple as possible A clear recruitment plan including professionals and patients. Flexibility in recruitment strategies. Health professionals Participation for professionals should be an expected part of practice with non-participation requiring justification. Adequate funding of trials to meet staff and participant requirements. Financial incentives for recruiters Education on trials and communication. Funders of routine healthcare must be informed that evidence-based practice is usually more cost-effective than traditional practices or use of unproved treatments. Patients Financial incentives to cover costs. Treatment nearer to place of work or home. Use of media and setting up of information centres to educate and inform people about clinical trials. Making the clinic environment more comfortable for women. Talks from previous trial participants. (These are based on the findings in relation to the

			of the time commitment and long travel distance associated with radiotherapy was seen as a barrier to participation for some women. Some women simply did not like the idea of a clinical trial and random allocation. There was also a concern about receiving less than the standard treatment. Patients who had participated in the BASO II trial (21 women) The focus groups were summarised as follows: The benefits of participating in the trial should be explained to women; there should be a better awareness among health professionalss of how anxious women are at the results clinic and how this impacts on their ability to deal with additional information; More information, that can be taken away for later consideration about the trial and different treatment options should be available.The cost to women in terms of treatment side-effects, travelling and the time commitment were also noted. Patients who had declined participation in the BASO II trial (8 women) Key themes 1. Women's attitudes had three sub-themes: the optimists, responsibility to society and the pessimists. Attitudes seemed to be diverse, varying between optimistic about future health with a recognition of the importance of clinical trials for improving treatments for breast cancer to being pessimistic about their future health. Among the women who were pessimistic there was a concern about receiving less than standard care if they entered the trial. 2. Costs to women had two subthemes: treatment options and travel and time commitments. A couple of women were concerned about overtreatment and there were concerns about side-effects of radiotherapy especially if it was unclear that there would be any benefit. Some of the women were already involved in other clinical trials. Travel and time commitments was the main barrier for some women. 3. Thoughts about the BASO II trial had two subthemes: positive and negative. Conflicting information from clinicians was an issue. Also some found it difficult to deal with information about a trial just after hearing what their prognosis was. All of the women said that they had not received any written information about the trial. Although declining participation, these women recognised that cancer trials were important and the majority believed that the multi-disciplinary team had involved them in the decision-making process.	BASO II trial as well as the findings in relation to another trial that were not extracted as the trial was of healthy women)

Author, Year Maslin-Prothero 2003 [72] **Study aim** This study duplicates Maslin-Prothero 2000[34] which has been extracted in full. **Setting** Multiple hospitals **Country** UK	**Study design** Qualitative **Sample size, Type** Patients **Sample characteristics**	**Data collection** **Data analysis**	**Response rate** **Results**	**Conclusions** **Recommendations for research** **Recommendations for practice** **Reviewers' comments**

Author, Year	Study design	Data collection	Response rate	Conclusions
McCaskill-Stevens 1999 [73] **Study aim** This is the same study as Pinto 2000[67] which has been extracted in full. **Setting** **Country** USA	Survey **Sample size, Type** **Sample characteristics**	**Data analysis**	**Results**	**Recommendations for research** **Recommendations for practice** **Reviewers' comments**

Author, Year	Study design	Data collection	Response rate	Conclusions
Mills 2003 [35] **Study aim** To explore patients' perceptions of randomisation and to understand their reasons for consenting or refusing randomisation within a controversial trial of treatments for localised prostate cancer (ProtecT study). **Setting** Multiple hospitals **Country** UK	Qualitative **Sample size, Type** 21 Patients **Sample characteristics** Age Men aged 50-69 years old. Gender All male. Cancer sites Localised prostate cancer Trial participation status 10 participants, 11 nonparticipants.	In-depth interviews were conducted with participants in the ProtecT study, an unblinded randomised trial of treatments for localised prostate cancer. Interviewees were selected from three clinical centres to ensure the inclusion of similar proportions of those agreeing or refusing random treatment allocation in each of the treatment groups. Patients were invited to interview by letter followed by a telephone call a few days later. The interviews, which were undertaken by one of two members of the study team, took place in the men's home approximately 10 days after they had made their decision to consent to or decline randomisation. All interviews were conducted by one of two interviewers with a checklist of topics developed by the study team to ensure that similar questions were asked of all interviewees with flexibility to allow discussion of issues of importance to the men. Men were asked about their understanding of the ProtecT study, the treatments involved, their recall and understanding of the study design, the acceptability of the treatment decision reached and the factors involved in their decision to accept or reject randomisation and / or treatment allocation. Interviews lasted between 45 and 105 minutes (average 60 minutes). All interviews were audio tape-recorded. **Data analysis** Interviews were transcribed verbatim and anonymised. Transcribed text was methodically coded and themes were identified using the method of constant comparison. Analysis was carried out initially by the interviewers with checking of coding and interpretation by two other members of the study team. The team met regularly to compare coding and to discuss findings and theoretical development. A grid developed previously was used to determine levels of recall and understanding of chance, comparison and clinical equipoise. Relevant text segments from each transcript were extracted onto the grid independently by three members of the study team. Clear evidence of recall and understanding was marked with a tick, no recall or understanding with a cross and a question mark where there was discussion but understanding was unclear. Two members of the team jointly reviewed the grid with the original transcripts to resolve discrepancies and to complete the final version.	NA **Results** Recall and understanding of the major principles of randomisation were good and were similar for 'chance' and 'comparison' between those who consented to and refused randomisation. Almost all particpants recalled and understood the consent of clinical equipoise. However belief in clinical equipoise was key to participants' consent to randomisation. Ten of the 11 who refused randomisation did not find equipoise acceptable. Five of the six who clearly accepted equipoise consented to randomisation. Five men consented to randomisation even though they did not accept equipoise (two were by chance allocated their preferred treatment and accepted it; two were not allocated their preferred treatments and subsequently rejected random allocation and chose a treatment; one struggled to understand any of the concepts and wanted a clinician to decide his treatment.	Only if the men could accept that the clinician was genuinely uncertain and the treatments similarly effective could randomisation be seen as an acceptable method of deciding treatment. Belief in clinical equipoise was key to participants' consent to randomisation. Ensuring patients understand and accept equipoise may thus increase their readiness to consent to participate in trials. **Recommendations for research** The authors state that a priority for future research is to focus on the provision and presentation of suitable and effective trial information concentrating particularly on the presentation of information by clinicians including the concept of clinical equipoise. Some participants consent to randomisation even when they have a strong personal preference then subsequently decline their allocation. The authors state that this issue requires further investigation. **Recommendations for practice** Not stated. **Reviewers' comments** This appears to be a well conducted qualitative study although it focuses on one specific potential barrier to participation in trials. All the participants were male and 50-69 years therefore it is unclear how relevant the findings may be to other groups.

Author, Year	Study design	Data collection	Response rate	Conclusions
Moritz 2002 [36] **Study aim** To examine the accrual process for prostate cancer clinical trials to elicit reasons why patients are not being accrued at higher rates at two Canadian cancer centres. **Setting** Two cancer centres **Country** Canada	Chart review+Survey **Sample size, Type** 359 Patients **Sample characteristics** Age Not stated. Gender All male. Cancer sites All prostate cancer. Trial participation status Of 359 patients attending the two centres during the study 173 (48.2%) were eligible for at least one trial. Reasons for ineligibility were (n=186): no trial available for disease characteristics: 114 (61%); health care system delay: 23 (12%); symptomatic problems: 21 (11%); life expectancy / Performance status: 13 (7%); second primary cancer: 11 (6%); equivocal radiology: 3(2%); other illness: 1 (0.5%). 117 (67.6%) of the 173 eligible patients were approached to participate in a trial. Reasons for not approaching patients were as follows (n=56): doctor's decision (i.e. chose alternate treatment): 35(63%); study reasons (waiting time too long): 13 (23%); patient reasons (i.e. patient wanted specific treatment): 4 (7%); disease reasons; 3 (5%); no reason given: 1 (2%). 54 (46.2%) of the 117 approached were recruited (an overall recruitment rate of 15.0%). 29 of these were interviewed about their treatment decision (18 trial participants, 11 nonparticipants). Previous trial experience Not stated.	A chart review was conducted on all prostate cancer patients who were referred for a treatment consultation at the centres during two one month periods. Patients were prospectively tracked for trial eligibility, whether they were approached for trial participation (if not why not) and if approached whether they accepted or declined. There were seven available clinical trials: five were open at both centres and the remaining two were exclusive to each centre. Telephone interviews were conducted in one of the centres with those patients who were approached to determine their reasons for trial participation decisions. Interviews were audio-taped and interrater reliability checked. Interviews included questions about patients' attitudes towards clinical trials and the factors that played a role in the decision-making process for joining a trial. The interview began with questions to remind patients of being approached about trial participation. Patients were asked about their level of comfort with the idea of participating in research, the idea of randomisation, comfort with treatments offered, who they wanted to choose their treatment, the degree to which they knew what treatment they wanted prior to coming to the cancer centre as well as who and what influenced their decision. Finally patients were administered a questionnaire to determine the reasons that might have influenced their decision to accept or decline participation. Patients were asked to respond to statements on a five point scale from strongly disagree to strongly agree. Only 29 interviews could be conducted as 28 patients were too ill to be interviewed, were deceased, incorrect contact information was available or the interviewer was not able to reach a patient after several attempts. Of the 36 who were contacted 7 did not remember enough details about being approached about a clinical trial to answer the interview questions and therefore these interviews were excluded from the analysis. **Data analysis** For analysis purposes responses to the questionnaire were grouped as 'agree', 'disagree' or 'unsure'. The responses to each statement were analysed using the Chi-square test to determine if there was a difference between those patients who accepted trial participation versus those who declined with a significance level set at $p < 0.05$.	29 of 64 patients approached (45%). Interviews were obtained from 25% of patients approached for trial participation. **Results** The majority of patients who decided to participate in a trial were most frequently influenced by the nurse (63%), the doctor (58%) and the patient's emotional state (53%). The reasons for patients to decline clinical trials were more diverse but they were most frequently influenced by their cancer centre doctor (35%). Overall the majority of patients were comfortable with the idea of participating in research (72%) but patients who declined to participate were significantly more likely to be uncomfortable ($p < 0.001$). 8 of 21 questions resulted in a significant difference in the proportion of agreeable responses between those who accepted trial participation and those who did not. They were as follows (accepters vs. decliners): I thought the trial offered the best treatment available (89% vs. 27%, $p<0.001$); I believed the benefits of treatment in the trial would outweigh any side effects (94% vs. 9%, $p< 0.001$); I was satisfied that either treatment in the trial would be suitable for me (78% vs. 18%, $p<0.01$); I thought the standard treatment would be better (6% vs. 45%, $p<0.01$); I was concerned I might be subjected to unnecessary tests (0 vs. 27%, $p <0.05$); I know that I could leave the trial at any time and still be treated (78% vs. 36%, $p <0.05$); I wanted to help with the doctor's research (78% vs. 24%, $p <0.05$) and I feel that others with my illness will benefit from the results of this trial (94% vs. 55%, $p <0.05$). Data were also reported on reasons for patient ineligibility for trials (data not extracted).	Accrual may be increased by broadening eligibility criteria and by emphasising the benefits of trial participation to potential participants. **Recommendations for research** Not stated. **Recommendations for practice** Broadening eligibility criteria may be the single most effective strategy for improving accrual to clinical trials. Trials should be designed so that patients benefit from participation and these potential benefits should be communicated to those considering participation. **Reviewers' comments** Multiple statistical tests in a small sample. Concern that those not approached for their views may be different from those approached.

Author, Year	Study design	Data collection	Response rate	Conclusions
Motzer 1997 [37] **Study aim** To summarise recruitment and retention experiences, to review accrual and retention issues identified in the Family Home Visitation Program: Nurse as Coach programme funded by the National Cancer Institute and to suggest specific strategies to maximise sample size for future clinical trials involving families. **Setting** Community **Country** USA	Trial Report **Sample size, Type** 96 Patients **Sample characteristics** Age Not stated. Gender All women together with their male partners and children Cancer site Early stage breast cancer (diagnosed within 8 months at Stage 0, I or II) Trial participation status 313 eligible referrals from 91 sites: 217 were accrued (69.3%). 96 families (30.7%) refused. Target sample size of 200 therefore was attained. 181 (83.4%) were retained, 11 (5.1%) were dropped because of changes in eligibility status or because of scheduling error and another 25 (11.5%) elected to withdraw. Previous trial experience Not stated.	The trial was a 3 year (1992-1995) multisite randomised clinical trial of a home-based nursing intervention for child-rearing families where the mother had nonmetastatic breast cancer. The goal of the 10 month intervention was to facilitate the family's management of the impact of the mother's illness on the family. Data collection on trial refusers Families were considered to be refusals if they initially declined to participate or if they subsequently declined prior to signing informed consent and completing the first in-home visit. Multiple reasons for non-participation were often given and it appears that all were recorded. Categories of responses were predetermined by the researchers or were derived by the researchers from families' verbatim responses. Apart from information on reasons for non-participation the authors did not appear to carry out a formal evaluation of recruitment issues. Descriptive information is provided on barriers faced. **Data analysis** Not stated.	NA **Results** Refusals were nearly equal between families who were randomised as coached (47) and as evaluation (49). More coached (24) than evaluation (12) families did not complete the study. Final group sizes were 84 coached and 97 evaluation families. Predetermined category - PC, Verbatim responses - VR. Of 96 families refusing to participate in the programme responses were given as follows: Mother interested, partner refused 28 (PC), Not enough time to participate 26 (PC), Mother did not want to participate or be bothered 17 (PC), Decided against participating after initial verbal agreement 9, Mother felt study would create additional problems or worries 8 (PC), Mother wanted to move past the breast cancer 8 (VR), No issues or not right for them 6 (VR), Mother felt she was doing fine 5 (VR), Assigned to the evaluation group but preferred coaching group 5 (PC), Mother sick to participate 4 (PC), Felt they were 'too private' to participate 3 (VR), Unable to participate because of illness in other family members 3 (VR), unable to participate because of new baby in the family 3 (VR), overwhelmed by chemotherapy or radiation therapy 2 (VR), too concerned about the children 2 (VR), Other 13. Rate of refusal was higher in Seattle (84 of 240 (35%)) than Portland (12 of 73 (16.4%)). The site co-ordinator in Portland had a closer working relationship with fewer intermediaries than the project manager in Seattle. There was a strong, lengthy history of face to face relationships between the site co-ordinator and Portland recruitment sites. The greatest impediment to accrual in working with intermediaries was a downsizing of health care services and personnel. Despite a nominal fee for accrual of patients intermediaries often relegated research time to a lower priority. There was also competition for participants from other Cancer Institute Community Clinical Oncology Program (CCOP) trials. Making contact with families and accommodating to their needs were important (this often needed multiple telephone calls). Scheduling visits when all the family were available and the mother feeling well enough were also problematic. There was a need to chase up incomplete or misplaced questionnaires.	Recruitment costs should be anticipated a priori. A formal plan of recruitment helps ensure attainment of the target sample size. **Recommendations for research** Not stated. **Recommendations for practice** Specific recommendations made by the authors relating to accrual and retention for future clinical trials involving families in longitudinal designs were listed in the paper. **Reviewers' comments** There may be problems in generalisation as this trial is concerned with the recruitment of families, the intervention was not for treatment of cancer but in relation to enhancing long-term adjustment of the breast cancer's effect on family functioning. Allocation to treatment or control was known beforehand and payment was made to the control group.

Author, Year	Study design	Data collection	Response rate	Conclusions
Outlaw 2000 [66] **Study aim** To identify factors physicians and data managers believe prevent the participation of black Americans in clinical trials. **Setting** Single hospital **Country** USA	Survey **Sample size, Type** 56 Health professionals **Sample characteristics** 39 oncologists 17 data managers Age 40 years or younger: Oncologists 17 (45%), Data Managers 9 (53%); 41-50 years: Oncologists 13 (34%), Data Managers 5 (29%); 51-60 years: Oncologists 6 (16%), Data Managers 2 (12%); 61+ years: Oncologists 2 (5%), Data Managers 1 (6%). Race White: Oncologists 34 (94%), Data Managers 16 (100%) Black American: Oncologists 1 (3%), Data Managers 0 Asian: Oncologists 1 (3%), Data Managers 0 Length of time in practice 5 years or less: Oncologists 13 (35%), Data Managers 8 (47%); 6-10 years: Oncologists 8 (22%), Data Managers 4 (24%); 11-20 years: Oncologists 11 (30%), Data Managers 4 (24%); 20+ years Oncologists 5 (14%), Data Managers 1 (6%). Length of time involved in clinical trials 5 years or less: Oncologists 12 (32%), Data Managers 15 (88%); 6-10 years: Oncologists 11 (30%), Data Managers 1 (6%); 11-20 years: Oncologists 9 (24%), Data Managers 1 (6%); 20+ years: Oncologists 5 (14%), Data Managers 0. Age, time in clinical practice and duration of involvement in clinical trials were all found to be correlated ($p < 0.001$).	Personnel likely to enrol patients in clinical trials at a comprehensive cancer centre were asked at departmental meetings to complete a questionnaire regarding recruitment of minority participants into their clinical trials. Content of the questionnaires was based on a review of the literature on barriers to ethnic minority participation in trials from a physician and patient perspective. Questionnaires included demographic questions and questions to elicit reasons for recruitment and barriers and perceptions about ethnic minority group participation in trials. **Data analysis** Chi squared tests were performed to determine the degree of similarity in demographics among the three oncologic specialisms and data managers. No demographic differences were found between the three groups of oncologists. Data for all the oncologists are reported together.	89% **Results** Personal reasons for recruiting participants: All the oncologists and 94% of the data managers said they were interested in studying new treatments for patients with cancer. 62% of oncologists and 47% of data managers believed that clinical trials offer the best option for patients. 49% of oncologists and 47% of data managers recruited patients into clinical trials because of requests by patients or family members. 39% of oncologists and 24% of data managers recruited patients because of clinical research infrastructure availability. At least 30% of the oncologists thought that Hispanic men and women as well as black American men and women were difficult to recruit to trials. 21% of them thought that Asian women were difficult to recruit and 10% or less thought that Asian and white men and women were difficult to recruit. Oncologists were asked on the basis of their own experience to identify reasons why they think minority patients choose not to participate in trials. They answered in the positive to the following: complexity of clinical trials 25 (64%); value of research not recognised 22 (56%); Fear of the health care system 20 (51%); Lack of education or illiteracy 17 (44%); additional burden to the patient 16 (41%); the Tuskegee syphilis experience 15 (38%); Patient lack of comfort with high technology care 13 (33%); Negative experience with the health care system 12 (31%); Language 11 (28%); Health care system perceived as unfriendly to minorities 9 (23%); Lack of family support 7 (18%); Late stage of disease 6 (15%); Perceived discrimination 5(13%); Lack of access to health care system 5 (13%); Religion 4 (10%) and Cost 3 (8%). Oncologists and data managers identified and ranked from 1 to 5 the top five barriers that physicians face in recruiting minority patients into clinical trials. (The number 1 indicated the greatest barrier): small percentage of patients who are minorities: Physicians 10 (28%), Data Managers 7 (41%); Lack of staff to support participation: Physicians 8 (23%), Data Managers 3 (18%); Additional time required: Physicians 6 (18%), Data Managers 3 (18%); Concerns about patient: Physicians 5 (15%), Data Managers 2 (12%); Lack of funds to cover patient costs: Physicians 5 (15%), Data Managers 1 (6%); Language barriers: Physicians 2 (5%), Data Managers 1 (6%); Patient's ability to comply with trial: Physicians 1 (3%), Data Managers 0; Ethical concerns about being more aggressive regarding recruiting minorities: Physicians 1 (3%), Data Managers 0.	Findings from this study are in accordance with those from the research literature. **Recommendations for research** Survey cancer centres to determine trends in minority use of these centres. **Recommendations for practice** The planning phase of a clinical trial should include active participation by all the healthcare team so that detailed procedures for recruitment into the trial can be developed and adhered to by all members of the team. Physicians need to develop through core components of a curriculum the skills needed to communicate effectively across racial, ethnic, socioeconomic and cultural divides. **Reviewers' comments** Patient barriers are as cited by physicians. This study focuses on cultural issues therefore it may have limited generalisability. In addition the participants are from one centre and applicability to other settings is unclear.

Author, Year	Study design	Data collection	Response rate	Conclusions
Paskett 1996 [51] **Study aim** To investigate reasons for participation or non-participation in clinical treatment trials among women with breast cancer. **Setting** Multiple hospitals **Country** USA	Survey **Sample size, Type** 82 Patients **Sample characteristics** Age 45 (55%) under 65 and 37 (45%) 65 years or older. Gender All women Cancer sites Breast cancer (diagnosed within the last 6 months). 59 (72%) were at the early stage (I-IIIa) and 23 (28%) at the late stage (IV). Trial participation status 2 patients' eligibility for trials could not be determined (2%) neither of whom were asked to participate (1 would have agreed if asked), 34 (43%) of patients were eligible for trials and of these 20 (59%) were asked by physician to participate in trials. Of those asked, 14 (70%) agreed to participate. Those ineligible or not asked were asked if they would have participated and 7 (50%) of those not invited and 32 (70%) of those ineligible stated that they would have participated. Previous trial experience Not stated.	Pilot retrospective, descriptive study involving 30 minute face to face interviews. Women were selected from tumour registry data at a University-based medical centre in an urban county and a rural community hospital in in North Carolina. Some subgroups of women for example women with late-stage cancer, older women and African American women were oversampled to provide better estimates of reasons for participation or non-participation. After approval by the woman's oncologist patients were contacted by letter and then were contacted by telephone to arrange an interview at home or in their doctor's office. Both open and closed questions were used in the survey instrument. Data were collected on demographics, medical history, breast cancer screening practices, diagnosis and treatment factors and clinical trial beliefs, knowledge and participation items. Data on the availability and eligibility status for participation in a current clinical treatment trial were obtained from medical chart review and a comparison of current breast cancer studies available at each clinic. Medical charts were reviewed to determine if patients were invited to join a clinical trial and if patients were participating in a clinical trial. **Data analysis** Responses to open-ended questions were coded verbatim and grouped into similar categories. Groups for reasons to participate were: personal benefit, altruism, doctor recommendation, to foster medical research and previous experience with cancer research or medical research or both. For non-participation groups were negative beliefs about clinical trial research (e.g safety concerns and uncertainty including randomisation); lack of knowledge about clinical trial research, personal issues (e.g lack of family support or stressful time) and protocol factors (e.g. longer duration of treatment). Participation was coded positive if the patient either participated in a trial or would have participated if asked. A range of variables was examined for their association with clinical trial participation. Many of the variables were combinations of several questionnaire items. Research	100% **Results** Logistic regression analysis identified two areas that predicted participation: knowledge about research studies : OR = 3.98 (p=0.05) and attitudes about research studies: OR = 3.59 (p=0.03). Working status (not working OR= 3.23), cancer detected by a physician (OR=2.60) and knowledge of signs and symptoms of cancer (OR=4.60) were modestly associated with participation (not significant). Age, race, stage of disease and site were not significantly associated with participation in a trial. Women who were not offered participation (and thus did not receive information about clinical trials) reported negative beliefs and lack of knowledge as reasons for not paticipating. Women who had been offered participation but declined reported protocol factors and dislike of randomisation as reasons.(No data) Reasons for trial participation (n=54, 14 actual, 40 intended) were not mutually exclusive and were as follows: Personal benefit: 18(33%), Altruism: 13(25%), Recommendation of doctor: 10 (19%), To foster progress of medical research: 7(14%), Obtained information about research: 5(10%), previous experience with cancer: 2(4%) and family benefit: 1(2%). Reasons for trial refusal (n=28, 6 actual, 22 intended) were not mutually exclusive and were as follows: Past negative beliefs about research: 9(35%), poor knowledge and attitudes: 5(19%), protocol factors: 3(12%), stressful time: 1(4%) and unsupportive family: 1(4%). Among eligible women those who were not offered trial participation were older than those offered participation (63 vs. 54 years, p=0.025).	The authors conclude by giving recommendations for research and practice as detailed below. **Recommendations for research** Research to improve participation in clinical trial research needs to focus on both the oncologist who develops trials and offers trial participation and on women with breast cancer (to promote good knowledge and positive attitudes). **Recommendations for practice** Three areas of intervention were identified that would foster clinical trial participation for breast cancer: protocols need to be designed with broader eligibility criteria or more protocols written; physicians should be encouraged to invite all eligible patients to participate and knowledge and attitudes of patients regarding clinical trials needs to be improved. **Reviewers' comments** The data on intended and actual participation (and non-participation) are combined making it difficult to draw clear conclusions.

	Misc 48 (58%) white and 34(42%) African American 40 (49%) were from the community hospital and 42 (51%) from the University hospital. 10 (12%) were homemakers, 18(22%) working part or full time and 54 (66%) not working. Women at both sites were comparable in terms of age, race, stage of disease, marital status, education and working status. Study population said by authors to be different from the general population of breast cancer patients.	attitude was considered positive if survey participants responded positively to five or more of the seven questions about research. Knowledge of research studies was considered positive if survey participants responded positively to all four questions about research. Chi-squared tests were used to assess the univariate association of these variables with clinical trial participation. Logisitic regression was used to determine which variables were jointly predictive of participation. A forward stepping algorithm was used in which variables were entered into the model until none were significant at the 0.15 level of significance.		

Author, Year	Study design	Data collection	Response rate	Conclusions
Pinto 2000 [67] **Study aim** To identify barriers to the accrual of minority patients to trials and to develop solutions to those barriers. McCaskill-Stevens 1999[73] is a related publication but adds no further data to this study. **Setting** Community **Country** USA	Qualitative **Sample size, Type** 73 Health professionals **Sample characteristics** 40 were community physicians from a variety of clinical disciplines. Thirty-three were physicians formally associated with the ECOG cancer clinical trials programme in their region. All of the ECOG physicians had experience of enrolling, referring or treating patients on ECOG trials but 20% had not enrolled any patient within the past year. Many community physicians had experience of trials in an area other than cancer but 57% had not referred a patient to a cancer clinical trial in the past year. 27% of cancer program physicians had not entered or referred a patient to a cancer clinical trial in the past year.	A series of focus groups was held between 1993 and 1996 in four US cities (Cleveland, Indianapolis, Philadelphia and Santa Clara County). The communities were chosen because each had a large minority population in the service area and the particular ECOG institution / programme had not succeeded in enrolling minority patients. Each area also had an active National Medical Association (NMA) organisation that provided the structure for outreach to the minority community. The project involved a four step process. In step one minority community physicians and cancer programme physicians met separately in focus groups to report on barriers and offer solutions. In step two minority community and cancer programme physicians discussed specific barriers and solutions to specific problems. Project staff served as facilitators for these discussions. In step three specific trials were analysed by the group of participants who had committed themselves to developing solutions in the context of specific trials. In step four the procedures and programmes identified by the physicians were implemented. The first focus group agenda covered a general discussion of cancer clinical trials, scientific knowledge about ethnic differences in cancer incidence and mortality and factors that intersect with cancer clinical trial participation. At the first meeting the participants were asked to name the most important barriers to participation and suggest ways that these barriers could be overcome. At the end of the session participants completed an open response questionnaire to answer three questions: What are the three most important barriers that make physicians less likely to recommend clinical trials to their minority cancer patients? What are the three most important reasons why minority cancer patients are under-represented in clinical trials? What are the three most important things that ECOG could do to increase enrolment of minority cancer patients into clinical trials? At a second meeting (attended by 66% of the original group) participants were asked to suggest specific solutions to barriers they had named ion the first focus group. The questionnaire asked the following: What would you recommended to ECOG in the way of specific	95% of the physicians answered all the questions on the questionnaire. **Results** In response to the question on factors that make physicians less likely to recommend clinical trials to minority cancer patients the following emerged: lack of information about the trial (Community physicians (CP) 75%, Cancer program physicians (ECOG) 36%, all 58%); Fear of losing patients / distrust / racism (CP 60%, ECOG 21%, All 42%); Takes too much time / insufficient resources CP 28%, ECOG 36%, all 32%; Cultural barriers CP 23%, ECOG 12%, All 18%; Lack of support from primary care physician (CP 23%, ECOG 9%, All 16%; No access to institution conducting clinical trial (CP 15%, ECOG 15%, All 15%); Cost to patient / patient poverty(CP 13%, ECOG 18%, All 15%);Lack of support (CP7.5%, ECOG 21%, All 14%); Physician thinks patients are not interested (CP 7.5%, ECOG 18%, All 12%); Informed consent too complex (CP not stated, ECOG 21%, all 9.6%); Patient comorbidity (CP 7.5%, ECOG 12%, All 9.6%); Protocols too complex (CP 5%, ECOG 12%, all not stated); Lack of minority patients (CP 2.5%, ECOG 12%, All 6.8%); Physician not interested in research (CP 5%, ECOG 9.1%, All 6.8%); Study design - randomisation (CP 2.5%, ECOG 3%, All 2.7%). The physician cited reasons that minority cancer patients are underrepresented in clinical trials were: patient suspicious or afraid (CP 73%, ECOG 67%, All 70%); Lack of information about the trial (CP 48%, ECOG 33%, All 41%); Physicians do not offer trials (CP 40%, ECOG 33%, All 37%); Racial bias (CP 45%, ECOG 18%, All 33%); Cost to patient / patient poverty (CP 23%, ECOG 36%, All 29%); Social factors (CP 13%, ECOG 30%, All 21%); Protocols too complicated (CP 5%, ECOG 15%, All 9.6%); Patient presented too late (CP 2.5%, ECOG 6.1%, All 4.1%); minority patients seen as not compliant (CP 5%, ECOG 3%, All 4.1%); Takes too much time / insufficient resources (CP not stated, ECOG 9.1%, All 4.1%); Loss of control of patient (CP 2.5%, ECOG 3%, All 2.7%); Lack of preventive medicine (CP 2.5%, ECOG not stated, All 1.4%).	Outreach efforts to educate patients, their families and community physicians about trials should be directed at overcoming patient suspicions and providing practical information to physicians about specific trials and how to enrol patients. **Recommendations for research** Not stated. **Recommendations for practice** As per conclusions. **Reviewers' comments** Patient barriers are as cited by physicians. It is difficult to know how generalisable this research is in terms of the cultural context.

		actions to increase minority accrual? What specific procedures or methods can you suggest for disseminating information on specific clinical trials to physicians in the community? What specific solutions can you suggest to deal with the problem of losing control over the care of a patient? **Data analysis** The responses to the questions were reviewed and initially coded into 28 barriers. They were subsequently combined into nine general categories after review by the investigators.	Potential ECOG strategies to increase minority enrolment in cancer clinical trials were: improve communication and outreach (CP 78%, ECOG 57%); develop educational materials (CP 40%, ECOG 27%); allow primary physicians to participate directly (CP 35%, ECOG 3%); improve consent forms (CP 2%, ECOG 39%); increase resources for physicians (CP 7%, ECOG 33%).	

Author, Year	Study design	Data collection	Response rate	Conclusions
Richardson 1998 [38] **Study aim** To describe the recruitment experience of a complementary / alternative medicine (CAM) trial, provide details of reasons for non-participation and compare participants and non-participants on demographic, clinical and treatment-related variables. **Setting** Single hospital **Country** USA	Chart review **Sample size, Type** 158 Patients **Sample characteristics** Gender All female Age 35 of 158 eligible patients were aged < 40 (22%), 42 of 158 (23%) were aged 40-45, 40 of 158 (25%) were aged 46-54 and 41 of 158 (26%) were over 54 years old. Mean age was 48.0 (SD 11.9). Participants were more likely to be 40-54 years of age versus younger or older (OR=2.4 (95% CI: 1.1, 5.1). Cancer site All breast cancer. Participants were a mean 11.7 months (SD 7.8) posttreatment. Trial participation status 173 of 4777 met inclusion criteria, 158 of these were eligible and 47 participants consented (30%). Non-participants and participants were comparable on clinical, treatment, geographic distance from the centre and religious affiliation. Previous trial experience Not stated. Misc 94 of 158 eligible patients were married (60%), 38 were divorced or separated (24%), 14 were single (9%) and 12 were widowed (8%).	Patients were informed of the requirements of the trial which was presented as a study of how emotions might influence health and recovery after breast cancer. Following a letter research staff telephoned potential participants and explained the nature of the interventions. Randomisation was to a 6 week support or imagery group Reasons for non-participation were recorded during each recruitment call. 45 of the 111 non-participants were contacted two or more times during the study period and the reason cited at the last call was coded as the primary reason for non-participation. Demographic variables were observed from hospital records. **Data analysis** Participants and non-participants were compared on demographic, clinical and treatment variables. Chi-square tests assessed binary and categorical variables and the analysis of variance evaluated continuous variables. Variables identified in the contingency tables as significant at the $p < 0.10$ level were selected as possible predictor variables and tested in univariate logistic models. The univariate model describes the relative odds of participating versus not participating. Stratified analyses were used to assess the effect of bivariate relationships on participation. The multivariate logistic regression model was used to confirm the stratified analysis. A step down variable selection procedure was used in the logistic model. The Hosmer-Lemeshow chi-square goodness of fit tested optimal correspondence between obtained and expected outcomes for the final model.	NA **Results** Primary reasons for non-participation included work / childcare (37 of 111 (33.3%)), transportation / travel (34 of 111 (30.6%)), lack of interest (27 of 111 (24.3%)), time conflict (7 of 111 (6.3%), illness (3 of 111 (2.7%)), no show after consenting (3 of 111 (2.7%) Of the 27 that cited 'no interest' 11 stated clearly that they were not interested in participating in the study, 5 reported that they disliked or feared support groups, 3 cited concerns about the hospital and 7 reported as being too busy. Nonparticipants and participants were comparable on clinical (i.e. disease stage), treatment (i.e. surgery type, adjuvant therapy and time posttreatment), geographic distance from the medical centre (i.e. country of residence) and religious affiliation. Participants were more likely than non-participants to be divorced / separated (OR=2.2(95% CI 0.98, 4.8). Women who were unable to pay any medical expenses were more likely to refuse participation than women with partial or full medical coverage. (OR = 2.8 (95% CI: 1.2, 6.96) . 21 of 158 eligible patients were African American (13%), 25 were Hispanic (16%), Hispanics tended to be more likely to join than other ethnic groups to join the trial (OR=1.8 (95% CI: 0.72, 4.6) whereas African-Americans were more likely to refuse than other ethnic groups (OR=4.6 (95% CI: 1.04, 20.8)). Stratified analyses suggested an interaction between pay and marital status. Married women who were indigent were less likely to participate (OR=0.07 (95% CI: 0.01, 0.56)). The logistic regression model confirmed the main effects of age, marital status and pay status. The combined effect of being divorced / separated and indigent and their interaction was demonstrated. (OR=1.67, 95% CI: 0.5, 5.4).	Researchers must assess the impact of exclusion criteria on accrual and recognise the needs of their target population. Although age, marital status and pay status were the strongest predictors of participation these factors cannot be altered by intervention. Other factors as detailed below may be amenable to change. The low accrual seen in this trial, however, may reflect the complexity of conducting a trial with two intervention arms and requiring participants to be available for assignment to either arm prior to randomisation. **Recommendations for research** Issues specific to the recruitment of minority populations should be considered. **Recommendations for practice** Researchers might boost accrual by providing interventions available during the day and evening to accommodate working women, child care services, transportation or reimbursement for travel costs. **Reviewers' comments** The study did not assess reasons for non-participation had barriers related to practicalities been removed. Participants appeared to have only been allowed to document one reason for refusal.

Author, Year	Study design	Data collection	Response rate	Conclusions
Ringberg 2000 [39] **Study aim** To assess patient accrual to the DCIS trial, to identify limiting factors and to evaluate possible ways to influence these factors in order to increase patient accrual. **Setting** Multiple hospitals **Country** Sweden	Chart review **Sample size, Type** 331 Both **Sample characteristics** Age Not stated Cancer sites All ductal carcinoma. Trial participation status 18 of 331 were incorrectly diagnosed. 96 of 331 were randomised into the study.	Between 1987 and December 1991 331 patients had been registered with the DCIS trial in the regional tumour registry. All 331 were subjected to chart review studying clinical data, mammography reports, cytology and pathology reports to identify inclusion and exclusion criteria according to the trial. The trial was comparing breast conserving therapy with or without radiotherapy. For DCIS patients not entered into the trial the recommended treatment was mastectomy or subcutaneous mastectomy without axillary clearance. Reasons for non-randomisation of patients were sought. **Data analysis** Not stated.	NA **Results** Of the 235 not randomised 172 had exclusion criteria, the most common reason being lesion size. However in 63 of the non-randomised patients no exclusion criteria was present (19%). In 38 cases this implied hesitation on the part of the treating surgeon in implementing proper treatment based on the pathologist's report although the patients were eligible for the study. In 8 cases the treating surgeon was unaware of the trial. 39 patients were not interested in participating in a randomised trial (12%). Eleven of these preferred mastectomy and 6 radiotherapy after breast conservation therapy. 14 did not want radiotherapy (13 had BCT, 1 mastectomy as definitive treatment). In 8 cases treated with BCT the patient could not specify a reason for not wanting to participate. Highest accrual was seen where mammography screening centres were well integrated with specialist breast clinics. Rates of the five major contributing hospitals showed a variation between 9 and 45%.	Increased information to participating hospitals and a raised awareness of limiting factors from the physician's and patients' points of view should increase accrual to trials of this nature. **Recommendations for research** Not stated. **Recommendations for practice** Continuous information should be provided to hospitals and physicians involved in treating DCIS to assure proper accrual. **Reviewers' comments** This study considers accrual to an actual trial using a retrospective chart review. It is unclear how the authors elicited information from patients on why they did not take part in the trial. It is also unclear how surgeon 'hesitation' on trial referral was defined.

Author, Year	Study design	Data collection	Response rate	Conclusions
Siminoff 2000 [68] **Study aim** To examine physician referral practices to clinical trials. The study investigated (1) why physicians are generally reluctant to participate in clinical trials and (2) why participating physicians refer only a small percentage of their patients to trials. **Setting** Multiple hospitals **Country** USA	Survey **Sample size, Type** 147 Health professionals **Sample characteristics** The sample consisted of 107 surgeons who provided surgical care to breast cancer patients and 40 oncologists. Age Average age: surgeons 47.8yrs, oncologists 45.2yrs Gender surgeons 94.4% male (n=101),oncologists 85% (n=34); Cancer sites Up to 4 of the surgeons' most recent breast cancer patients were chosen for discussion with the surgeon (or medical oncologist if the case was referred on) and demographic details of these patients are provided in the paper. Trial participation status Of 245 eligible patients 93 had been offered a trial (38.1%) with 49 (52.7%) agreeing to participate. Misc white: surgeons 84.1% (n=90) and oncologists 100% (n=40)	The study was carried out over two years (1993-95) in a large metropolitan region in Pennsylvania. Through data provided by county medical associations, a list was drawn up of all physicians (n=272) who possibly provided primary surgical care to breast cancer patients. A telephone screening identified 198 surgeons who provided care to breast cancer patients. Of the surgeons who agreed to participate and had eligible patients, up to four of their most recent breast cancer patients were identified from a chart review. Only patients who were eligible for participation in at least 1 Phase III breast cancer treatment trial at the time surgical care was provided were included. Cases that were referred to a medical oncologist by the surgeon for consideration of adjuvant therapy were discussed directly with the oncologist by the researcher. Each patient case was reviewed with the physician. Trained nurse-interviewers used an interview guide, with structured probes of responses) to obtain patient-specific and general attitudes about adjuvant therapy and phase III clinical trials. Physicians were asked about their attitudes towards trial participation from their point of view and the patients'. Further details are provided in the paper of the issues covered in the interviews. **Data analysis** Descriptive statistics were used to examine physicians' attitudes towards trial participation. Five logistic regression analysis were carried out on the effects of the following sets of variables on physician referral to trial (separate analyses were carried out for surgeons and oncologists): physicians' demographic and professional characteristics; patients' demographic and disease characteristics; patient-physician interactions concerning adjuvant therapy; trial related factors; and physicians' attitudes and expectations. Variables in each of the five logistic regression models with a p value less than or equal to 0.1 were then used as independent variables in final regression models examining significant predictors of surgeons and oncologists trial referrals.	An acceptance rate of 75.8% of surgeons was reported though only 54% provided data. The response rate for oncologists was 72.3%. **Results** The results of the five preliminary logistic regression for surgeons and oncologists are reported in the paper. The final model of factors explaining surgeons' decision-making concerning referral to clinical trials (n=244; x2=33.06; p</=0.01; R2=0.5377). The following factors were determinants of decision to refer to trial in the final model: frequency of physicians referral to trials (OR 2.4725; 95% CI 1.5326, 3.9888); knowing which trial the patient was eligible for (OR 6.7123; 95% CI 2.1257, 21.1955); fewer affiliations with cooperative groups (OR 0.3301; 95% CI 0.1549, 0.7036); receiving cooperative group's support (OR 8.3153; 95% CI 2.0986, 32.9485); those who did not want to stray from protocols (OR 25.6282; 95% CI 1.4687, 447.2090); more surgeon involvement with adjuvant therapy decision (OR 2.0255; 95% CI 1.3083, 3.1358); tamoxifen treatment not started by the surgeon (OR 0.1396; 95% CI 0.0194, 1.0036); patient involvement with the trial decision (OR 2.6815; 95% CI 1.6029, 4.4857); and patient delay in seeking adjuvant therapy (OR 8.0162; 95% CI: 1.4674, 43.7922). The final model of factors explaining oncologists decision-making concerning referral to clinical trials (n=170; x2=169.07; p</=0.01; R2=0.7340). The following factors were determinants of decision to refer to trial in the final model: university practice (OR 56.2394 95% CI 2.0741, 1,524.9260); surgeon involvement with decisions about adjuvant treatment (OR 2.5280 95% CI 1.3173, 4.8513); knowledge of which trial the patient was eligible for (OR 5.3331; 95% CI 1.3559, 20.9774); patient involvement with trial decision (OR 24.2149; 95% CI: 5.4765, 107.0680); oncologist involvement with the trial decision (OR 6.8784; 95% CI: 2.3605, 20.0437); paperwork not too time consuming (OR 0.1785; 95% CI: 0.0426, 0.7480).	The authors concluded that physicians still need to overcome attitudinal and practical barriers to trial participation; more support for physicians is needed; surgeons play a pivotal role in the recruitment of patients to adjuvant therapy trials; and garnering patient enthusiasm for trial participation and involving them in the choice of adjuvant therapy may be key components to increasing trial enrolment. **Recommendations for research** None stated **Recommendations for practice** None stated **Reviewers' comments** Although this study was appropriately designed to provide in-depth information about the referral decisions of physicians, only limited conclusions can be drawn due to the weaknesses in the data analysis and reporting.

	solo professional practice: surgeons 40.2% (n=43) and oncologists 12.5% (n=5) university practice: surgeons 9.3% (n=10) and oncologists 12.5% (n=5) private group practice: surgeons 49.5% (n=53) and oncologists 75% (n=30) physician refers patients to a trial regularly (4-point scale): average surgeons 2.38, oncologists 3.11 number of hospital affiliations: average surgeons 2.27, oncologists 3.60 cooperative group affiliation (4-point scale): average surgeons 0.46, oncologists 2.10			

Author, Year	Study design	Data collection	Response rate	Conclusions
Sinnott 2002 [14] **Study aim** The paper describes problems recruiting to a randomised study of amitriptyline and sodium valproate for patients with cancer-related neuropathic pain. **Setting** Multiple hospitals **Country** UK	Chart Review **Sample size, Type** 152 Patients **Sample characteristics** Age Not stated. Gender Not stated Cancer sites Not specified but only related to palliative care for cancer-related neuropathic pain Trial participation status 10 patients were recruited over 18 months. 142 failed to be recruited hence the trial was terminated. Previous trial experience Not stated.	The six centres involved in the drug trial kept records of patients referred as possible recruits to the trial. One centre kept a complete screening record of all patients referred to the palliative care team with neuropathic pain. **Data analysis** Not stated.	NA **Results** The predominant reasons for failure of recruitment related to the inclusion / exclusion criteria for the study (n=142 across the centres): patient already started on drug treatment for neuropathic pain (64); patient due to receive radiotherapy or chemotherapy for the pain (16); other inclusion / exclusion criteria not met (18); too ill or distressed to approach (8); not able to cope with paperwork (5); refused participation in trial (no reason recorded) (8); other (17); not recorded (6).	There are problems in establishing a research culture in palliative care which need to be addressed. **Recommendations for research** It is important to recognise the difficulties of conducting research in palliative care in order to design successful clinical trials. However there is a need to identify acceptable alternatives to RCTs when such trials are unachievable. These might include phase II studies, n of 1 studies and qualitative research evidence. **Recommendations for practice** Not stated. **Reviewers' comments** This letter reports on problems with a specific trial and is perhaps most useful in outlining the potential barriers of eligibility criteria. Data appeared to be gathered prospectively. It is not possible to quality assess this paper in detail.

Author, Year	Study design	Data collection	Response rate	Conclusions
Skeel 1998 [17] **Study aim** The authors state that a substantial drop in accrual in 1996 prompted a survey of Eastern Cooperative Oncology Group (ECOG) physicians to compare accrual barriers with those found in the 1987 survey and to provide data from which evidence-based interventions to approve accrual could be developed. **Setting** Multiple hospitals **Country** USA	Survey **Sample size, Type** 136 Health professionals **Sample characteristics** Participants were predominantly male (89% and medical oncologists (77%). Primary income source: fee-for-service (44%), managed care (30%), and salary (26%).	The Physician Orientation Profile II was administered to a random selection of 136 physicians using a telephone with a faxed document. Anonymity and confidentiality were guaranteed. **Data analysis** Not stated	Not stated **Results** The three main barriers to patient enrollment in ECOG trials: lack of relevance to own patient population; patient discomfort with randomisation; and competing trials. Fulfilling clinical requirements placed a conflicting demand on participants. Senior investigators reported putting more patients in studies. Non senior investigators reported facing difficulties receiving reimbursement. (Abstract only; data not reported)	The authors concluded with Recommendations for practice (see below). **Recommendations for research** None stated **Recommendations for practice** The authors state that strategies to improve accrual at community hospitals will need to address the diverse problems of senior and non-senior investigators. The latter group offer the greatest potential for increases in accrual but will require demonstrating the importance of trials to their clinical work and professional advancement. **Reviewers' comments** This is an abstract therefore only limited information is available. It is not possible to comment on the quality of the study or its generalisability.

Author, Year	Study design	Data collection	Response rate	Conclusions
Spiro 2000 [40] **Study aim** To assess the reasons why patients with non-small cell lung cancer did not enter a randomised trial of cisplatin-based chemotherapy as an adjunct to treatment by surgery, radiotherapy or best supportive care. **Setting** Multiple hospitals **Country** UK	Chart review **Sample size, Type** 688 Patients **Sample characteristics** Age The median age of the 688 patients identified was 67 (range 32-94). Trial entrants were younger than non-entrants (61.3 vs. 65.7 years, mean difference 4.4 years (95% CI: 1.9, 6.9)). Gender 488 (71%) of the original 688 patients were male. Cancer sites Recently diagnosed non-small cell lung cancer patients. Trial participation status 274 were ineligible for the trial (39.8%) for clinical reasons (frailty and poor performance status: 72; comprehension / language barrier: 21; co-morbidity: 19; inadequate renal function: 16; change in prognosis / condition during primary treatment: 15; change in diagnosis / unclear pathology: 11; complications with primary treatment: 6; suspected poor compliance: 3; depression: 2). Another 161 (23.4%) were ineligible for logistical reasons. For 84 patients (12.2%) the clinician felt that they should be offered chemotherapy. These patients were younger with a mean age of 58.1 years compared with 66.9 years for the other non-entrants (difference between means 8.8 years (95% CI: 6.6, 10.9). Of 253 potentially eligible patients only 63 (24.9% of those eligible, 9.2% of total) agreed to enter the RCT, four entered another study and 186 (73.5%) refused to enter. Previous trial experience Not stated.	The study was carried out in two large London institutions (University College London Hospitals NHS Trust and St Bartholomew's and the London NHS Trust) with a special interest in recruiting patients to lung cancer trials. Patients were prospectively identified between November 1995 and July 1998 and followed to see whether they entered the RCT described above and if not to identify their main reasons for refusal. For all patients identified (through ward visits, medical records and list and outpatient clinics) a record was made of sex, date of birth, primary treatment, whether or not they entered an RCT and if not the main reason for non-entry. Where multiple reasons for non-entry were recorded for an individual, one main reason was used. Patients were not asked why they were refusing and data is from those who volunteered a reason. **Data analysis** During the survey reasons for non-entry were grouped together into common categories and are reported here.	NA **Results** Of those who did not enter, 77 (41.4%) declined without stating a reason, 61 (32.8%) did not want chemotherapy, in 23 cases the patient's family dissuaded the patient, 9 did not want involvement in research, eight (4.3%) expressed a wish to have chemotherapy and 8 (4.3%)gave other reasons. Refusal rates were highest in the surgical group (83.5% of those asked) and similar in radiotherapy (67.5%) and best supportive care groups (68.6%). There was a higher proportion of men in the trial entrants group than the non-entrants (87.3% vs. 69.2%, p =0.003). 161 of 688 patients were ineligible for logistical reasons (further treatment was planned at hospitals not involved in the trial or there was a delay in referral or identification. 274 of 688 were ineligible for clinical reasons (e.g. clinical decisions not to give chemotherapy due to frailty and comorbidity)	Despite considerable time and effort the proportion of patients recruited was small. Many seen were ineligible but 73.5% of those eligible refused to participate. **Recommendations for research** Not stated. **Recommendations for practice** Not stated. **Reviewers' comments** This is a prospective study but there are a number of limitations. Patients were not asked to give a reason for declining to participate in a trial, so only those who volunteered a response had their views documented. Only the main reasons were recorded, therefore some data will have been lost.

Author, Year	Study design	Data collection	Response rate	Conclusions
Stevens 2004 [41] **Study aim** To explore the reasons why breast cancer patients decline entry into randomised clinical trials of adjuvant cancer therapy **Setting** Multiple hospitals **Country** UK	Qualitative **Sample size, Type** 22 Patients **Sample characteristics** Age Median age 58 years (range 42 to 70) Gender All female (n=22) Cancer sites All newly dignosed breast cancer (n=22) with mixed disease stage and prognosis Trial participation status Of the 136 patients who agreed to participate, 20 were taking part in a clinical trial, 94 had not been offered the opportunity to take part in a trial and 22 had declined participation in a trial that had been offered to them. Previous trial experience Not stated Misc Employed n=11; housewives n=4; retired n=7 No formal qualifications n=8; O levels n=6; A levels n=1; NVQ n=1 OND/HND n=3; degree n=3 All classified themselves as white	Consecutive, newly diagnosed women patients from 5 breast clinics who had been referred to an oncologist at Sheffield Cancer Centre between July 2000 and January 2001 were identified and sent a letter inviting participation in the study. Patients who expressed an interest were interviewed in their own home or at the hospital. At the time of the study eight different trials of adjuvant therapy were actively recruiting patients. Interviews focused on attitudes towards clinical trials, beliefs about risks and benefits of taking part and the patient's own decision about participation. Interviews were repeated at 6 and 12 months and were broadly similar though they also addressed any changes in attitudes. Interviews were audiotaped and transcribed. This paper reports data from the interviews with the 22 women who declined participation in a trial. **Data analysis** Analysis followed the Framework approach and coding was carried out by different members of the research team. Coding validity was monitored using deviant case analysis. (One of the 22 patients withdrew from the study at 3 months, one at 9 months and one died at 3 months.)	154/294 patients returned the study reply form; 136 participated (46.3%) in the overall study **Results** Fear as a reason not to participate A common theme was deep-seated fear about cancer. For some patients this was compounded by negative prior perceptions and sometimes a limited understanding of the research process. Although many patients had high levels of information need about research, fear inhibited the information seeking behaviour of some. Many felt that participation in a trial would contribute to the exacerbation of existing fears because of uncertainty of outcome. Some respondents thought they had been approached because their prognosis was poor. Opting for the treatment that was 'tried and tested' was an antidote to fears about the research process. Poor presentation of the research as a deterrent to participation The timing of the approach to participate in a trial was an important issue. Patients felt that they were approached very soon after diagnosis when they were unprepared to deal with new information about research. Some felt shocked about the way they were approached expecially when it was someone they had not previously met. Some patients misinterpreted the reasons why they had been asked to participate. Commonly. Patients felt attention was focused on the treatment protocol rather than on providing information on the alternatives. Many patients did not understand the information they had been provided with on a particular trial even though it was not a particularly complex trial. Information overload as a deterrent Patients, who were already feeling emotional and stressed, felt that the introduction of new information about research was more than they could deal with. Problems in interpreting trial information as well as as unfamiliarity with the research process itself caused patients to decline	While a minority of patients had a wholly negative belief about medical research, for the majority of patients, their decision to decline trial entry was tempered by a variety of situational and process factors that they were experiencing at that time. **Recommendations for research** Further research is required to examine why there may be a response shift over time in patient's position about participating in a trial in addition to the influence of the interviewers themselves in providing patients with additional information. Further research is also required to capture the views of non-white breast cancer patients. **Recommendations for practice** A public education campaign is required to increase awareness of medical research. Although patients have high information needs it is important to avoid information overload. Patients should have access to multiple sources of information Health professionals should adopt an integrated approach in developing their information strategies especially in the explanation

			trial participation. Others mentioned the time pressure to make their decision. An aspect of information overload was the overlap in discussions with health professionals about diagnosis, treatment plan and research options. Guilt, uncertainty and decision review In some cases the decision to decline trial participation left patients feeling 'quite upset', , feeling that they 'weren't being useful', 'selfish', 'guilty' or 'uncertain'. Some patients had also changed their mind about participation for various reasons including receiving further information addressing their areas of concern, an increase in confidence and having their fears allayed. Recommendations for increasing accrual (obtained at the 12 month interview) More information with the information being reinforced by offering it at different times. Develop innovative ways of imparting information such as the use of independent counsellors, a greater role for GPs, group discussions, poster displays in hospitals and using existing trial participants to disseminate information. 'Strong demand' for more public education about medical research. Adoption of more innovative study designs that could offer patients more choice and initiatives such as prerandomisation that could help reduce uncertainty. Many respondents felt that their limited knowledge and understanding of clinical research had been an important factor in their decision not to participate.	of protocols to participants. Information about research should be available at different time points. Patients should have access to an independent source of information and advice about medical research. More 'patient friendly' trials through greater patient involvement in the design of studies. Reduction of uncertainty through the adoption of innovative research methodologies that offer patients more choice. **Reviewers' comments** This study examines in some depth reasons for trial refusal in a group of patients who have recently declined trial participation. However, as the authors state, this is a small select sample of women. Validation of these issues would need to be undertaken in a larger population.

Author, Year	Study design	Data collection	Response rate	Conclusions
Tripathy 1998 [15] **Study aim** to report physician and patient barriers to breast cancer trials. **Setting** Unclear **Country** USA	Survey **Sample size, Type** ? Both **Sample characteristics** Patients had newly diagnosed or progressive breast cancer. Physicians surveyed provided care for breast cancer in the San Francisco Bay area. (No further information available)	Patients and physicians responded to separate surveys on trial awareness, cost, convenience, risks, potential benefits and trials in alternative medicine. No detailed information available. **Data analysis** Not stated - abstract only.	Not stated. **Results** Patient barriers were found to be: extra time requirements, side effects of new drugs and reluctance to be randomised. Younger patients had more concerns about costs. Worries about insurance coverage were found in lower income and education groups and confidentiality was a concern for married patients. Non-white patients and those citing a religious preference trusted their doctors to make decisions about trials. English speaking patients were more concerned about side effects and efficacy of experimental treatment. Physician barriers were found to be: lack of trial information, patient inconvenience, preference for one treatment arm, office staff time but not compromise on patients' care. Younger physicians were more concerned about toxicities of new agents. Medical oncologists compared to other specialists were more concerned about a greater restriction of eligibility requirements and were less worried about side effects of new agents. Private practice and non-academic physicians were more concerned about stresses to patients and interference with treatment and referral patterns. Attitudes to trials on alternative medicine were generally positive especially in younger respondents. Married and higher income patients were more concerned about negative perceptions from family and physicians for participation in alternative medicine trials. Younger physicians had less concern about interference with standard care and loss of patient / physician credibility with participation in alternative trials.	Mechanisms to target and address the physican and patient barriers found are needed. **Recommendations for research** Not stated. **Recommendations for practice** Not stated. **Reviewers' comments** No assessment of quality was possible due to lack of information.

Author, Year	Study design	Data collection	Response rate	Conclusions
Twelves 1998 [42] **Study aim** To identify the factors influencing entry of women with invasive breast cancer into clinical trials in Scotland. **Setting** Multiple hospitals **Country** UK	**Sample size, Type** 4688 Patients **Sample characteristics** 1987 - 2148 patients, 1993 - 2540 patients Age Not stated. Gender All women. Cancer Site All breast cancer. Trial participation status 501 entered trials (12.3% of those diagnosed in 1987 and 9.3% of those diagnosed in 1993). Patients entered 34 clinical trials, 18 for early or locally advanced disease, 14 for metastatic disease with two open to patients of either category. Trials included 2 phase I and 5 phase II studies as well as 27 randomised Phase III studies. Seven were industry-sponsored whilst the rest were supported by local funds of by trial groups. 15 trials were local, eight were national UK studies and 11 were international. Patients were entered into trials from 21 hospitals.	All women newly diagnosed with invasive breast cancer during 1987 and 1993 in Scotland were identified from Scottish cancer registry data records. Their case notes were reviewed by Scottish Cancer Therapy Network (SCTN) staff and entry into clinical trials was recorded along with clinical and demographic data. Trials were categorised as being for either early / locally advanced disease or metastatic breast cancer. Information on disease characteristics at presentation including clinical stage, tumour size, oestrogen recepter status and nodal status was collected. Demographic data included age, social deprivation and the area of Scotland within which the patient was first managed. Surgeons were classified according to workload and referral to an oncologist within 3 months of diagnosis was recorded. Case notes were located for 89% and 97% of registered patients diagnosed in 1987 and 1993 respectively. **Data analysis** Chi-squared tests were used to compare the clinical features of patients entering and not entering clinical trials. Univariate analysis was used to examine the effect of each demographic factor on trial entry. Multivariate regression was also used and variables were entered as unordered, categorical factors. The effect of trial entry on survival, adjusted for other factors, was investigated using a Cox's proportional hazards regression model.	NA **Results** In multivariate logistic regression analysis patients seen by surgeons with a high case load were more likely to enter a trial, adjusted OR= 7.39 (95% CI: 4.75, 11.49) ($p < 0.0001$) and those referred to an oncologist were more likely to enter a trial (adjusted OR=3.06(95% CI: 2.30, 4.07) $p < 0.0001$). The area of Scotland (Health Board) where the women was first treated influenced participation. Compared to Greater Glasgow Health Board odds ratios varied between 0.13 (95% CI: 0.05, 0.37) to 1.4 (95% CI: 1.01, 1.83). The top four positions for numbers entered into trials were taken by health boards with teaching hospitals. Social deprivation had no effect on trial participation ($p = 0.93$). Women over 65 years of age were less likely to enter studies, the adjusted odds ratio being 0.76 (95% CI: 0.57, 1.00) ($p=0.05$). For women over 80 years of age the odds ratio was 0.43 (95% CI: 0.22, 0.84) ($p=0.01$) Survival in the 1987 cohort was better in the women treated in trials for early or locally advanced disease but this did not reach statistical significance (HR=0.79, 95% CI: 0.59, 1.04). Patients first seen at one of the five regional cancer centres were more likely to be entered into trials than those treated elsewhere (18.1% versus 3.3%).	Patients seen by a specialist surgeon or oncologist are significantly more likely to enter a clinical trial. **Recommendations for research** **Recommendations for practice** The authors concluded that extending the management of patients by specialist multidisciplinary teams should increase recruitment into clinical trials. They stated that it is essential that oncologists based at cancer units are integrated into teams with specialist surgeons and have access to the resource necessary for clinical trials. The effect of a health board on trial entry highlights the need to address geographical variation in patterns of treatment and research. **Reviewers' comments** A useful exploration of 'system' barriers to trial participation.

Author, Year	Study design	Data collection	Response rate	Conclusions
Westcombe 2003 [43] **Study aim** To report on the recruitment problems of a large, multicentre randomised controlled trial of aromatherapy massage and the changes that were made to the trial's design following poor recruitment. **Setting** Multiple hospitals **Country** UK	Trial report **Sample size, Type** Unclear Both **Sample characteristics** Palliative care patients with advanced disease initially but extended to include cancer patients irrespective of disease stage. No information was available on the characteristics of the professionals.	The trial being evaluated was a multicentre RCT of aromatherapy massage initially for palliative care patients with advanced cancer. **Data analysis** Not stated.	NA **Results** 18000 potentially available patients with cancer entered the four recruitment centres each year. Recruitment rates to the trial were relatively low particularly in the first two years of the trial. Of those who did not take part 37% declined, around 8% were too ill and 11% were receiving or were about to receive either psychological therapy or medication or complementary therapy. In order to improve recruitment to the study a number of modifications to the trial design were undertaken: firstly opening the trial to all those with cancer irrespective of stage. The rate did improve but not sufficiently to improve the viability of the trial so the next step was to remove the relaxation therapy control group and reduce power to 80%. This reduced the number required from 508 to 258. The addition of an extra recruiting centre allowed for considerable increase in recruitment. Poor recruitment to the original design was thought to be due to the need to recruit across the entire structure of the cancer services potentially through hundreds of health professionals. Few of the clinicians had a stake in the trial and it was difficult to maintain the profile of the trial. Clinicians were asked to refer outside their main area of expertise. Barriers thought to be due to clinicians gate keeping arose. These were felt to be due to scepticism about complementary therapies, belief that the benefit of complementary medicine is self evident, the belief that there is a need to reduce the burden on already very ill patients and feeling uncomfortable with randomisation to a control arm. Once patients were referred to the trial exclusions and declines were higher than expected. On average it was necessary to consider 10 patients for each one randomised. One major reason for declining the trial was travel to and from the centre for a therapy that could have been delivered more locally. Other reasons for declining were wanting a specific therapy, wanting a therapy immediately and not being interested in the research generally. Throughout the trial maximising recruitment was dependent on maintaining the profile of the trial among potential referrers. Individual researchers at each site helped to keep the trial 'visible'.	Although it is not generally good practice to change a study design once recruitment has started, the changes were consistent with the original study aims and principles and allowed for successful completion of the study. **Recommendations for research** Not stated. **Recommendations for practice** Take a pragmatic approach where methodological rigour may be compromised to ensure the viability of a trial (for example being as flexible as possible in setting inclusion / exclusion criteria, keeping follow up periods short to minimise attrition, keep study design as simple as possible whilst ensuring clinical relevance, be open and flexible regarding data collection methods so that patients who have difficulty travelling can be accommodated). Invest time and money carrying out an exploratory phase prior to rolling out the full RCT (to establish acceptability / viability of methodology, outcome measures and planned recruitment / attrition levels, standardisation of treatment protocols etc and familiarise health professionals / patients with trial personnel. . Preliminary qualitative or observational work could highlight potential obstacles to success. **Reviewers' comments** It was not possible to quality assess this study due to lack of information. The authors did not state how they gathered data on the challenges encountered during the study. It was unclear how information was gathered from the professionals involved. It was also unclear how the authors elicited patients' reasons for declining trial entry.

Author, Year	Study design	Data collection	Response rate	Conclusions
Wiley 1999 [44] **Study aim** To investigate parents' knowledge and perceptions about randomisation in clinical trials for children with cancer and to determine whether parents' decisions were influenced by demographic factors, randomisation circumstances, the clinical characteristics of the child with cancer or a combination of factors. **Setting** Multiple hospitals **Country** USA	Case control **Sample size, Type** 192 Parents **Sample characteristics** Age (of parent) 15-19: 3 (1.6%), 20-24: 16 (8.3%), 25-29: 34(17.7%), 30-34: 61 (31.8%), 35-39: 44 (22.9%), 40-44: 22 (11.5%), 45-49: 9 (4.7%), 50-54; 2 (1.0%), Unknown: 1 (0.5%). Child's Gender 76 female (39.6%) and 116 male (60.4%) Cancer site Parents of children with various forms of childhood cancer mainly Acute lymphocytic leukaemia 93 (48.4%), Acute myelogenous leukaemia 26 (13.5%), Wilm's tumour 17 (8.9%), Neuroblastoma 17 (8.9%), Brain tumour 12 (6.2%), Other 27% (14.1%). Trial participation status 140 in the early randomisation group (of whom 47 refused randomisation and 93 accepted) and 52 in the late randomisation group (of whom 10 refused randomisation and 42 accepted). Early decision groups are the main focus of this report.	The researchers described the study as having a comparative case control design. Cases were parents of any patients who refused an early (front end) randomisation. Parents who made any late randomisation decision, either to accept or to refuse were also eligible for study participation. Controls were parents of the two previous patients from the same institution as the target case who was registered on a study with an early randomisation. Two controls were selected for each case. Eligible parents were invited to participate in the study by nurses in their CCG institution. Verbal or written consent was obtained. Patients were administered The Clinical Investigation Randomization Scale which had been developed during the course of a previously reported feasibility and descriptive study. The questionnaire and a postage paid envelope were provided to the parents and were to be returned to the nurse. If the questionnaire was not returned within 4 weeks the nurse made one follow up all to the parents. The CRS was administered to all participants within 3 months of randomisation eligibility on the child's clinical trial. The CIRS includes 32 questionnaire items pertaining to randomisation with responses on a 5 point Likert scale from 'strongly agree' to 'strongly disagree'. It also includes a mixture of free choice and open ended questions to obtain demographic data and information about the circumstances of randomisation. Additional descriptive data were obtained from CCG study registration forms that are completed for all newly diagnosed cancer patients at CCG institutions whether they are entered into the study or not. **Data analysis** Due to paucity of responses at the extremes of the scales on some items the two categories of similar agreement (agree and strongly agree or disagree and strongly disagree) were recategorised into single groups of 'agree' and 'disagree'. Factor analysis using varimax rotation was performed and the two factors that explained most of the variation in the data were identified. Chi square analyses of demographic data and questionnaire item responses	NA **Results** In the early randomisation group there were no significant differences between refusers and accepters in age, education, relationship to child or income. No demographic variables showed significance in chi square analyses with questionnaire items. Numbers in the late randomisation group were too small to assess significance. There were no significant differences between accepters and refusers on items pertaining to randomisation circumstances. Three questionnaire items predicted participation decisions in logistic regression analysis: 'randomisation provides the best opportunity for my child to be cured of his / her cancer with refusing parents much more likely to disagree with the statement ($p < 0.0001$). Refusers were much more likely to agree with the statement I did not have enough time to make the decision about randomisation = 0.001). Refusers were also more likely to agree with the statement randomisation will help primarily in the treatment of future children more than my child ($p = 0.04$). A predictor model was developed that accurately predicted acceptance or refusal of randomisation 85% of the time. In the early decision group the final regression model included the items 'randomisation provides the best opportunity for my child to be cured of his / her cancer to which accepters tend to agree, 'the thought of randomisation was frightening for me' to which accepters tend to disagree and 'randomisation will help primarily in the treatment of my child (more than future children with cancer) to which accepters tended to agree. At a level of 76% sensitivity the model had 93% specificity with these items combined. Responses to the open-ended item 'is there anything else you would like to tell us about why you did or did not agree to randomisation for your child' showed that accepting parents reinforced	What most distinguished parents who refused randomisation from those who accepted was not their knowledge about randomised clinical trials but their beliefs, values and perceptions. **Recommendations for research** Further research is needed to develop the predictor model and to determine whether these differences occur in a population of parents that is more ethnically, culturally, socioeconomically and linguistically diverse. Future research might assess the potential clinical usefulness of predicting willingness to participate in trials and whether predictions would be sufficiently accurate to save time and effort in recruitment to trials. Are there interventions that could ease parents' distress and fears about randomisation? Research would need to consider which factors influencing parents' decision making are innate and which are amenable to interventions. **Recommendations for practice** Not stated. **Reviewers' comments** The study focused primarily on randomisation. It would have been interesting to have had more data from the late

	Misc 76.1% white, 21 (10.9%) Latin, 14 (7.3%) African-American, 2 (1.0%) Asian and 9 (4.7%) other.	were performed for the parents who refused early randomisation compared with those who accepted. Similar comparisons were made for late randomisation. Univariate analyses compared the distribution of responses to individual questionnaire items for cases and controls. Comparisons were also made of additional patient data, family demographic data and other issues regarding the circumstances of the randomisation process. Multivariate analyses used conditional logistic regression methods for matched case control sets. These analyses initially included all the questionnaire items and other variables as candidate items for classifying participants into the two decision categories: refuse and accept randomisation. Forward stepwise logistic regression was used to identify important variables for multivariate prediction of randomisation decisions. A statistical significance criterion of $p > 0.10$ was used as a stopping rule for predictor selection and developing the final regression model. After finding the set of important predictors that comprise the model an analysis of the 'posterior classification probabilities' was performed. This classification was compared to the actual decision that each participant made to test the accuracy of prediction for the logistic regression model. Further details were provided in the paper.	their belief that the RCT afforded hope for cure for their child, their trust in the physician who presented the RCT and their reluctance to make a decision about treatment that might be 'wrong'. They commented about the value of knowing they could withdraw at any time. Those who refused tended to express fear about randomisation and a sense of pressure about accepting. They commented on the desire to have decisional control. They trusted their physicians' choice rather than a computer.	randomisations as the early randomisations reflect attitudes to trials whilst parents are still coming to terms with their child's diagnosis.

Author, Year	**Study design**	**Data collection**	**Response rate**	**Conclusions**
Wilt 2003 [16] **Study aim** To report on recruitment to the Prostate cancer Intervention versus Observation Trial (PIVOT). **Setting** Multiple hospitals **Country** USA	Chart review **Sample size, Type** 4279 Patients **Sample characteristics** The report is concerned with recruitment to the PIVOT Trial, a large randomised trial comparing treatment with surgery versus watchful waiting for the treatment of clinically localised prostate cancer. Age Under 75 years old. Gender Male Cancer sites All newly diagnosed (within 12 months) clinically localised prostate cancer without serious comorbidities. Trial participation status Of 4279 eligible for enrolment a total of 731 consented to participate in PIVOT.	Recruitment to the PIVOT trial began in November 1994 and was finished in January 2002. Men with newly diagnosed prostate cancer were identified from 44 Medical Centres and 8 National Cancer Institute sites. A variety of recruitment methods was used: one to one interviews, educational and recruitment video, colour brochure and web site. Patients who declined enrolment were compared with those who were enrolled. **Data analysis** Not stated.	NA **Results** Most men declined to enrol because they were not willing to participate in research (13%), not willing to leave decision for treatment to chance (68%) or faced family opposition to their participation (14%). Patients who declined enrolment were similar to those who accepted it on baseline demographic and tumour characteristics.	Enhancing enrolment in randomised trials of prostate cancer treatment requires addressing concerns of patients about leaving treatment decisions to chance. The greatest barrier was that many men did not want to be randomised into one of two very different treatment modes and often had predecided their treatment preferences. **Recommendations for research** Not stated. **Recommendations for practice** Not stated. **Reviewers' comments** No quality assessment was possible due to lack of information.

Author, Year	Study design	Data collection	Response rate	Conclusions
Wright 2002 [69] **Study aim** To explore the factors that influence the decision of patients with cancer regarding clinical trial entry, specifically from the perspective of the Clinical Research Associate (CRA) **Setting** Single hospital **Country** Canada	Qualitative **Sample size, Type** 13 Health professionals **Sample characteristics** Participants were CRA's, with experience of phase III trials, from the Department of Clinical Trials at the Hamilton Regional Cancer Center (HRCC). HRCC is a large, academic tertiary care cancer clinic with on average 38 phase III trials running in the period 1999-2001. The length of participant's experience with phase III trials ranged from 1-12 years. Ten were nurses and three were clinical data managers.	A convenience sample was obtained by inviting, by letter, CRA's from HRCC to participate in a focus group. Two focus groups (one with 7 and the other with 6 participants) were conducted. They were facilitated by an 'experienced focus group leader' external to the Department of Clinical Trials using an outline of areas to be addressed. There was an exploratory and confirmatory phase to each session. A HRCC physician observed and provided summary of the discussion in the exploratory phase. Based on this phase a list of factors potentially affecting patient accrual was drawn up for the confirmatory phase and these were then rated by the group, based on a consensus, as being very important, somewhat important, or of little importance (confirmatory phase). The focus groups were also audiotaped. **Data analysis** The audiotapes were reviewed and summarised. Summary notes were coded independently by the two researchers. Codes that described aspects of more comprehensive categories were combined trough a process of consensus, employing intercoder triangulation.	NA **Results** Based on the exploratory phase of the focus group and factors identified in the literature a 32 item list of factors influencing clinical trial accrual was constructed. It was grouped into physician factors, patient factors and CRA factors. Within each group the items were further grouped into general, trial specific and CRA factors. The following factors rated as very important by both focus groups. Physician factors Trial specific: role as principle investigator; impression of trial's scientific method; impression of trials toxicity. Patient factors General: cultural background. Trial specific: patients sense of personal benefit; opinion of family, friends and other supports. Encounter specific: patient's sense of strength of physician recommendation; patients's impression of recruiters personality; success of information transfer. CRA factors Trial specific: CRA's confidence with study background; CRA's impression of scientific merit. Physician factors: an enthusiastic physician with an ability to communicate well with patients, and often with a vested interest, lead to more successful recruitment. Physicians could also be barriers if they were not enthusiastic about a trial. Patient factors: patients have more trust in information about a study if it comes from an outside source such as a newspaper; patients had more negative perceptions of placebo controlled trials; disease severity and treatment options available also influenced patient decisions; ethnic background was influential; and the patient's perception of the physicians enthusiasm for the study. CRA factors: They believed that their own actions had the potential to have a positive or negative impact on recruitment. With patients they considered a good candidate they would try a bit harder to encourage their participation. CRA's regarded information transfer as an important role for them. They felt recruitment was more successful when they completely presented the pros and cons of a study. Some felt that presentations that used complementary multimedia enhanced recruitment success. Adequate time to discuss issues fully and in a personalised way was felt to be important. The necessity of an empathetic approach was emphasised.	CRAs appear to have a unique role in the process of recruiting patients to active clinical trials. They believe that they have an important influence on recruitment success. **Recommendations for research** The authors state that further research is required to validate the extent to which CRAs have an influence on recruitment success. **Recommendations for practice** None stated. **Reviewers' comments** The poorly reported study is based on a small convenience sample of CRAs, from one setting in the US, which limits generalisability. The authors state that further research is required to validate the impressions obtained from the study.

APPENDIX 6 QUALITY ASSESSMENT

Studies are presented by study type (Survey, Qualitative, Chart Review) in alphabetical order (by author surname).

Surveys

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Advani 2003[45]	The aims of the study are clearly stated and the design appears to be appropriate for the stated objectives. However, the study was hypothetical in that participants were only asked about general willingness to participate in trials. The sample size was not justified. Validity and reliability of the instrument is not specifically commented upon and did not appear to be piloted. The study does not distinguish between Phase I/II and Phase III trials.	The basic data were adequately described though the extent (if any) of missing data was unclear as only percentages were reported. This may be a particular problem in the multivariate analysis. The analysis appeared appropriate. Both adjusted and non-adjusted results were reported.	No untoward events appear to have occurred during the study.	This study was based on a fairly small sample of individuals from two clinics in the U.S. Only half the sample participated and it is unclear how participants may have differed from nonparticipants. These factors may limit the generalisability of the findings.

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Baum 2002[52]	The aims of the study were clearly stated and the design was appropriate to the stated objectives. The sample included all investigators involved in the trial. No information was provided on how the questionnaire was contructed, why and how specific questions were chosen and whether it was piloted. Respondents were given an opportunity to provide other reasons that may have encouraged them to recruit into the trial. The study only obtains the views of clinicians therefore it provides a unidimensional perspective on this trial. However the author reports that a survey of patients from the trial is planned.	The basic data were adequately described and it was appropriate to use descriptive statistics. Although the response rate was reasonable no information was provided on respondents and nonrespondents therefore it is not possible to assess how nonreponse may have affected the findings.	No untoward events appeared to have occurred during the survey.	This study obtains the views of investigators in relation to a specific trial. Some aspects clinicians were asked about were specific to that trial therefore it is possible that some of the findings are limited to similar trials.

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Burnett 2001[57]	The aims were clearly reported and a survey design was appropriate. All of the nurses in one cancer treatment centre were approached. The authors did not justify why nurses from only one centre were included. Some limited information is provided on how the questionnaire was constructed though the reliability and validity of the instrument was unclear. The questionnaire did not directly address barriers to nurse participation in clinical trials. Also the reasons identified for patient motivation for participating in trials was based on nurse perceptions' of the views of patients and not directly on the views of patients.	The basic data were reasonably adequately described. However it was unclear how many of the subscale scores used imputed data. Given that there was no response to up to 22% of individual demographic questions, this may have been substantial. Although responses to some of the questionnaire items were on a 5-point scale responses are reported as agree or disagree with no information on how the categories were collapsed.	No untoward events appear to have occurred during the study.	As the authors point out, the responses of the participants may not be generalisable to nurses not working in a comprehensive cancer centre or those working at other cancer centres. It may also have limited applicability to a U.K. setting. The study focuses on general views rather than barriers to participation. The stated implications for nursing practice do not directly relate to the findings.

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Crosson 2001[58]	The aims were clearly stated and the design was appropriate to the stated objectives. A national probability sample of physicians was used though the sample size was not justified. No information was provided on how the questionnaire was contructed, why and how specific questions were chosen and whether it was piloted. The opportunity available to respondents to make spontaneous comments was unclear.	The basic data were adequately described and the statistical analysis appears to be appropriate. There seemed to be no missing data, though for one table only percentages are reported.	No untoward events appear to have occurred during the survey.	The study used a national sampling frame however the findings may not be generalisable to the UK context. Care needs to be taken in drawing implications from the patient barriers identified as these are based on the physicians' perceptions and they rarely discussed clinical trials with their patients.

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Crowley 2003[46]	The study was not designed as a survey but as a chart review but included an element of surveying patients. Aims are clearly stated. A sample size calculation was provided. Measurements appear to be valid and statistical methods are described.	Basic data are adequately described and statistical significance assessed. Numbers are relatively small and when comparing subgroups analysis may be underpowered to detect effects. Methods of coding and analysis of the data are stated and appear to be appropriate.	No untoward events appear to have occurred in the study.	The main findings appear to be valid but should be interpreted within the context that all study participants are male and half have a poor prognosis which limits generalisability of results. There is no data on the patients who actually went on to participate in a a trial.

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Ehrlich 2002[53]	The aims are clearly stated and a survey design was appropriate to the stated objectives. However, the authors did not state on what basis the six 'hypotheses' and the questionnaire were formulated. It is therefore unclear whether all the relevant barriers to accrual were addressed. The study attempted to include all surgeons potentially involved in the failed trials in the sample. Information on the reliability and validity of the questionnaire was not reported. It does not appear to have been piloted. Although there was opportunity for additional comments in the questionnaire, it is unclear how this information was incorporated into the study. The study only obtains the views of surgeons therefore it provides a unidimensional perspective on this trial. The views of principal investigators (if they were oncologists) were not obtained directly.	Some aspects of the statistical analysis were very poorly reported and it was not possible to assess how appropriate they were. The denominator used to calculate percentages changed across questions as nonresponses appeared to be excluded. Although 26 protocols were submitted to the IRB it is reported that 31 protocols were submitted by an oncologist or surgeon. The discrepancy is not explained. Statistical significance levels were reported for some of the questions on a 5-point scale but it was unclear what tests were used and what the comparison was being made. It was unclear how the analysis assessing the factors affecting surgeon and oncologist support of the trial was carried out.	No untoward events appear to have occurred during the study.	The study focuses primarily on organisational issues, some of which are specific to how research is organised in the United States so this may limit the generalisability of the findings. Although there was a reasonable response rate, due to the lack of data it is unclear how respondents may have differed from nonrespondents.

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Ellis 1999[48]	Aims were stated. The survey design was appropriate to the objectives of the study. The sample size was justified. Two of the measures had been used in previous studies althouygh theire reliability and validity was unclear. Statistical methods are described. The survey is based on focus group interviews and literature review. It is uncertain how the patients were chosen for participation therefore the representativeness of the sample is unclear.	Basic data are adequately described and numbers tally. Statistical significance was assessed.	The authors report that three patients (5%) did not complete the final section of the questionnaire and one item of the questionnaire was omitted because it lowered the overall internal reliability.	The main findings may need to be interpreted with caution as respondents are being questioned on willingness to participate in hypothetical trials. The numbers of actual trial participants was low and the finding of no difference in knowledge between participants and nonparticipants may need to be replicated with a larger group. The survey was based on a focus group of women which may have placed less emphasis on issues relevant to men. It should be noted that over 50% of those surveyed were breast cancer patients. This will affect the generalisability of the results.

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Ellis 2001[49]	The aims of the study were clearly stated and the design was appropriate for the objectives. The sample size was justified for between group differences. Statistical methods are described. It was unclear how the women were selected to participate in the study therefore the potential for bias is unclear.	Basic data was adequately described and numbers tally. Statistical significance was assessed through a variety of methods. The extent of missing data is uncertain as the denominator for many of the responses is unclear.	No untoward events appear to have occurred in the survey.	There is a possibility of selection bias due to the 25% who refused to take part in the survey and also from those who were not approached. Both null findings and important effects are considered. It may be difficult to generalise the results beyond breast cancer patients. Trial participation is hypothetical and the authors acknowledge that this situation may not reflect being asked to participate in an actual trial.

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Ellis 1999[59]	The aims of the study were clearly stated and the design was appropriate to the stated objectives. All medical and radiation oncologists in Australia involved in the treatment of breast cancer were approached, though only surgeons involved in a clinical trial group were inclided. No information was provided on how the questionnaire was contructed, why and how specific questions were chosen and whether it was piloted. The opportunity available to respondents to make spontaneous comments was unclear (though the questionnaire is available from the authors).	The basic data were adequately described. Although there was a good response rate, presumably due to missing data, only 67% and 54% of the total respondents were included in the analysis of barriers and suggestions for improvements respectively. Missing data seemed to be excluded from the analyses with the denominator being the number of respondents from whom data was available. It is unclear whether there was any bias in the missing data. Where there were more than 3 groups in the analysis, it was unclear how they established where the statistically significant difference lay. It seems odd that although the sampling frame for surgeons was the ANZBCTG participation list, only 77% said they were an ANZBCTG participant. It would have been useful to have this discrepancy explained.	No untoward events appear to have occurred in the survey.	Some of the findings may not be generalisable to the UK context. The authors point out that because the surgeons were involved in ANZBCTG, they are likely to have different views to surgeons in general, therefore the findings may not be generalisable to all surgeons.

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Fallowfield 1997[60]	The aims of the study were clear and the design was appropriate. A national group of clinicians involved in different areas of oncology was approached though it is unclear whether the sampling frames used provided a representative sample of clinicians involved in this field. Although the questionnaire was used previously in a study no information is provided on reliability or validity. There was an opportunity for respondents to make spontaneous comments. The statistical methods used were described.	The basic data were adequately described though the extent (if any) of missing data on the POP questionnaire was unclear as only percentages were reported. The analysis appeared appropriate.	No untoward events appear to have occurred during the study.	The findings of this study are likely to be generalisable though it would have been helpful to have more demographic information on the sample such as geographical location and type of work setting. It was unclear how respondents may have differed from nonrespondents. The medical oncologists appeared to have a high level of research involvement though the authors point out that this may be typical of this speciality as it is a relatively small speciality and the appointments tend to be in teaching hospitals and cancer institutes where research activity is an explicit expectation.

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Fallowfield 1998[50]	The aims of the study are clearly stated and the design appears to be appropriate for the stated objectives. The sample size was not justified. Validity and reliability of the instrument is not specifically commented upon but the survey was designed with recourse to professionals, patients and the research literature and was piloted. Statistical methods are not described in detail.	Basic data are adequately described and numbers tally. Statistical significance is assessed for between group differrences.	No untoward events appear to have occurred during the study.	Findings suggest that it is possible and useful to distinguish between those who refuse to participate in trials whatever information is provided and those who might participate given further specific information. Null findings are presented and where these might have arisen through lack of statistical power this is noted. However willingness to participate in trials is hypothetical and so may not reflect actual participation decisions. There are some features of the sample such as type of cancer, previous participation in trials that may affect the generalisability of the issues raised.

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Fleissig 2001[22]	Aims are clearly stated. The design appears to be appropriate to the stated objectives. However the intervention might have been better designed as a cluster randomised trial so that doctors did not have to deliver the intervention as well as working with the control group. The physicians were self-selected. Sample size was not justified. Measurements are based on instruments previously described (Fallowfield 1998[50]). Statistical methods are only briefly described.	Basic data are adequately described and numbers tally (although there appear to be one or two differences between data reported here and in Fallowfield 1998[50]). Statistical significance was assessed.	No untoward events appear to have occurred during the study.	This study builds on the previous study (Fallowfield 1998[50]) which stated that people's attitudes towards RCTs could be modified with further information and that this might encourage them to take part in a trial. It is not clear just how different intervention and control group consultations were and how tailored to the patients' needs. The high accrual rate in both intervention and control groups suggests that the doctors in this study were very motivated to and effective at recruiting patients but this may not reflect usual practice. The nature of the trials or patients involved may have also influenced participation rates.

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Grant 2000[23]	Aims are clearly stated. The design appears appropriate to the objectives. Sample size is not justified. The survey was based on published research instruments adapted for the telephone interview format. Statistical methods are described. No detail on piloting of the questionnaires is provided and there appeared to be no opportunity for respondents to make their views known through free text.	Basic data are briefly described and numbers tally. Statistical significance was assessed. There may be a possibility of respondents wishing to give socially acceptable responses when questioned about, for example, the friendliness of the doctor. Aspects of the various instruments found to be unreliable were dropped from the analysis.	No comment	The main findings should be interpreted within the context of the fact that respondents all had 'very serious' cancers not necessarily recently diagnosed. Furthermore there was a gender imbalance in that significantly more men were in the trial decliners group, thus potentially biasing the results. It is unclear if the discriminant factors would apply when taking account of cancer type and trial type.

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Hietanen 2000[24]	The aims of the study were clearly stated and the design was appropriate although only trial participants were included which limits the results. Sample size was not justified. The questionnaire was designed by the researchers and was piloted on a small sample of breast cancer patients. Reasons for participation were presented in closed format but it appears that respondents could select more than one reason if appropriate.	Basic data are adequately described and statistical methods are described in outline. However statistical significance is often not reported and there may be problems in assessing the significance of multiple comparisons without appropriate adjustment.	No untoward events appear to have occurred during the study.	The findings are perhaps most applicable to informed consent and may not easily translate into overcoming barriers to participation in trials. The findings are specific to a trial of a relatively well tolerated drug and so may not generalise to other treatment trials and other cancer sites. The research highlights important points about the process of deciding to participate in a trial, but it does rely on patients' recall. Experience of participating in the trial may have influenced the judgement of the respondents. The research also raises the concern that whilst respondents felt relatively satisfied with the information they had received, this did not necessarily translate into an understanding of even the basics of the clinical trial process. The need to tailor information for age and education is highlighted.

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Hjorth 1996[55]	The aims of the study were clear and a survey design was appropriate. The sample excluded eight hospitals in Finland and Iceland who had enrolled patients for only 10 mths due partly to their short period of participation. It would have been useful to explore why they had stopped participation in the trial. No information was provided on how the questionnaire was contructed, why and how specific questions were chosen and whether it was piloted. There appeared to be no opportunity for spontaneous comments about factors affecting patient accrual. Only limited information was provided on the statistical methods. The participants appear to have been asked about factors affecting trialists' readiness to enter patients into trials. It is unclear whether these were other investigators involved in the trial or this is a more general question.	Some of the data were not adequately described. Only 8 of the 21 questions on attitudes toward the trial were reported. It was stated that these correlated positively with inclusion rate. However no information was provided on the method of correlation used or what the authors defined as a positive correlation (or has the students t-test been described as a correlation?). Although Danish hospitals had a lower inclusion rate than the other two countries this was not explored any further.	No untoward events appear to have occurred during the study.	This study obtains the views of investigators in relation to a specific trial. Some aspects of the study were poorly reported. Some aspects that principal investigators were asked about were specific to that trial therefore it is possible that some of the findings are limited to similar trials.

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Jenkins 2000[28]	The aims were clearly stated and the design was appropriate to the stated objectives. The sample size was not justified. Although there was a high response rate, it is unclear how the sample of patients invited to participate in the main study was obtained. Information on the reliability and validity of the questionnaire was not provided. It was unclear how similar the questionnaire was to the piloted questionnaire on which it was based and whether the questions were totally 'researcher driven'. There was no opportunity for participants to provide additional comments or suggest barriers/benefits outside the 16 questions they were presented with. Also, the earlier questionnaire had been piloted on patients who had agreed to participate in trials. Statistical methods are described in outline.	Participants were adequately described. The authors do not justify their reason for combining the categories 'strongly agree' and 'agree to some extent'. Despite using a 5-point response scale they report data on one collapsed category. It is unclear whether the analysis on type of treatment and type of trial was prespecified.	No comment	It is unclear whether selection bias may have arisen from how the sample from the main study may have been selected. The authors note that the high acceptance rate to placebo trials may have been confounded by the fact that most of the patients were offered the same trial for prostate cancer by one clinician. There may also have been a confounding effect between type of treatment and type of trial. 55% of patients were breast cancer patients which may affect the applicability of the study.

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Kaanoi 2002[62]	The aims of the study were clearly stated and the design was appropriate to the stated objectives. All cancer speciality physicians practising in Hawaii were approached to participate. Other than stating that a review of the literature guided the design of the questionnaire, no information was provided on how the questionnaire was contructed, why and how specific questions were chosen and whether it was piloted. There were some open-ended questions allowing an opportunity for participants to expand on their views.	The basic data were adequately described and it was appropriate to use descriptive statistics.	No untoward events appear to have occurred during the study.	The study had a relatively low response rate with just over half the participants returning the questionnaire despite the efforts of the authors. It is unclear how participants may have differed from nonparticipants. This study provides some general information on barriers but otherwise the finding are culturally specific.

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Kemeny 2003[29]	Aims are clearly stated. Survey design appears appropriate as does matched pairs design. The study failed to recruit the full number for the power calculation given. Measures may be susceptible to recall bias given the length of time since being offered a trial. Statistical methods are described. There appears to be no suggestion of haste but this was described as a pilot study. It is unclear how the suggested reasons for offering and participating in trials were actually derived.	Basic data were adequately described and numbers tally. Statistical significance was assessed. Findings on patient participation and refusal are based on small numbers of patients.	Not all data was obtainable but this was documented in the report. Although matched pairs of younger and older patients had an oncologist in common it may not have been the same oncologist who presented trial protocols to the matched pair of patients.	Selection bias could have arisen in the selection of matched pairs though this procedure was carefully documented. Null findings and main effects are presented. Results may not be generalisable as institutions involved in this study were relatively successful at recruiting patients, findings relate only to breast cancer patients and few advanced stage patients were recruited. This study provides some information on the complex reasons for lower accrual of older patients.

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Klabunde 1999[30]	Aims are clearly stated and the design was appropriate for the objectives. However this was not specifically designed as a survey of patients' reasons for refusal to participate in trials and only their major reason for refusing was documented. It was also unclear how this information was elicited.The sample size was not justified but all adult cancer patients considered for enrolment in NCI trials within the given time period were considered. Statistical methods are described in outline.	Basic data are adequately described and numbers tally. A flow diagram describes the status of all patients evaluated. Statistical significance was assessed through logistic regression models. Patient reasons for refusal to participate are documented as simple percentages and considered in regression models. Documenting one major reason for refusal does not describe the complex interaction of variables that might influence a patient's decision and this will have implications for the findings of the study.	No untoward events appear to have occurred during the study.	The findings demonstrate that for many patients there will be no protocol available or they will not be eligible. It should be noted that roughly 40% of the patients were breast cancer patients which might limit the generalisability of the results. The emphasis on insurance is not relevant to the UK context. This study does not separate out results for phase I and 2 and phase 3 trials which might also limit interpretation of the results.

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Kornblith 2002[63]	The aims of the study were clearly stated and a survey was appropriate to the stated objectives. The sampling frame was 10 institutions chosen for their high accrual rate. There did not appear to be a protocol for which physicians were approached within the institutions which may have introduced bias. There was no justified sample size and no attempt was made to consistently measure response rate. Other than stating that a review of the literature guided the design of the questionnaire, no information was provided on how the questionnaire was contructed, why and how specific questions were chosen and whether it was piloted. A fairly narrow range of barriers were addressed in the questionnaire.	It was appropriate to report descriptive statistics and the basic data were adequately described.	No untoward events appear to have occurred during the study.	As the authors note, the participants were not a representative sample of oncologists therefore the findings may not be generalisable. The poor response rate (in so far as it was measured) may also have biased the findings.

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Lara 2001[31]	Aims of the study are clearly stated. Survey design is appropriate. Sample size is not justified. It is unclear whether the questionnaire was piloted and it is of concern that respondents (both clinician and patient) may not have been able to give more than one response to a question. Statistical methods are described. The questionnaires were appended to the case notes of 'most' new patients. The total number of new patients seen in the centre over the three year period is not reported, therefore it is unclear what proportion of patients were included in this study and whether the patients included were typical of new patients seen at the centre.	Basic data are adequately described and numbers tally. Statistical significance was assessed and non-significant results reported.	There was no cancer diagnosis for 70 patients and incomplete data for 4 patients reported by the authors.	Patients' reasons for non-participation may not be comprehensive and reasons for participation are not examined. Results may not be generalisable to the UK context and no breakdown of cancer sites and stages is given. The types of trials patients were eligible for are not specified although Phase I trials appear to have been included.

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Madsen 2002[32]	Aims are stated and a questionnaire design is appropriate in this instance. However sample size is not justified and no information on validity and reliability of the instruments is available. Statistical methods are briefly described. No information is available on the design and piloting of the questionnaire. It is unclear why these particular patients were approached and how similar they are to other trial participants and nonparticipants in these two centres.	Basic data are described but there is a lack of clarity on the analysis of free text responses and some numerical data are not given in the report. Statistical significance is assessed and null findings are reported.	No untoward events appear to have occurred which reflect on the data provided.	The majority of the trial nonparticipants were premenopausal breast cancer patients which could affect the applicability of the findings to other types of cancer patients. Null findings of the influence of age and sex may need to be interpreted with caution due to the small sample size.

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Martin 2003[65]	The aims were clearly reported and a survey design was appropriate. It is unclear why the particular institutions were selected. Although the authors state that they piloted the questionnaire, no details are provided. Barriers to trial participation were addressed only in a limited manner. Participation in trials was defined at a very low level (enrollment of a patient). The study would have been more informative if extent of participation had been investigated. Additionally approxiamtely half the respondednts did not work in oncology.	It was appropriate to report descriptive statistics though only percentages are reported for the findings on barriers therfore the extent of nonresponse is unclear. There were some minor inaccuracies in the calculation of percentages. Barriers to participation in clinical trials were not reported for surgical oncology graduates presumably because they reported a high level of participation. Although the response rate was not reported separately for the different groups, it is reported that 100 of the participants were surgical oncology graduates. Therefore it would appear that there was a 100% response rate for this group and much lower for the other groups. The implications of this are not discussed.	No untoward events appear to have occurred during the study. However, they did include graduates over a 14 year period and there may have been changes in the training provided over that time. This is not discussed.	This study adressed barriers in only a limited way and barriers are reported only for the general surgery and other fellowship graduates.

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Maslin-Prothero 2000[34]	The aims of this part of the study were clear and the design was appropriate. A national group of clinicians involved in breast surgery was approached though it is unclear whether the sampling frames used provided a representative sample of clinicians involved in this field. Only a subsample of the total group of respondents were directly involved in the BASO II trial. The questionnaire did not appear to be piloted. There was an opportunity for respondents to make spontaneous comments. The statistical methods used were described.	The basic data were adequately described and numbers appear to tally. However the data from the open-ended questions was not reported in any detail.	No untoward events appear to have occurred during the study.	This study obtains the views of investigators in relation to a specific trial. The findings may not be generalisable to all trials. It would have been helpful to have more demographic information on the sample such as geographical location and type of work setting. It was unclear how respondents may have differed from nonrespondents.

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Moritz 2002[36]	Aims are clearly stated and the design is appropriate to the objectives. Sample size is not justified. Use is made of a previously published questionnaire. It is unclear how the research questions were designed and if the research instruments were piloted. It is unclear why only 64 patients were approached to take part in the study and how these were selected from the 117 patients who had been offered participation in a trial.	Basic data are inadequately described, for example basic demographic information. Numbers tally and statistical significance is assessed. Findings are based on multiple testing of a small group of patients.	Only 29 of those approached to take part in a trial were interviewed. Reasons were given for the exclusion of some of this number.	Some selection bias may have occurred as it is unclear how typical the 29 interviewees (18 trial participants, 11 refusers) are of the sample as a whole. Sample size may be inadequate to distinguish between all barriers. It may be difficult to generalise the results of this small sample and results may only apply to prostate cancer, be more applicable to males with cancer and not reflect centres with a poorer research infrastructure

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Motzer 1997[37]	Aims are clearly stated. The study was not designed specifically as a survey. Sample size was not justified and only those refusing to take part in the trial were assessed. Measurements included researcher-derived reasons for refusal and participants' verbatim responses.	Methods of data analysis were not stated.	Not applicable.	As this study is concerned with recruitment to a specific trial the results may not be easily generalisable. Allocation to treatment or control was known before the decision to participate or not.

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Outlaw 2000[66]	The aims of the study are stated. The design appeared to be appropriate to the objectives. Sample size was not justified and the sample was small. It is unclear what steps were taken to ensure validity and reliability of measures. Statistical methods are only partially described. Questions were derived from a review of the literature but it is unclear if they were piloted. The participants were from a single centre.	Basic data were described although demographic details such as gender were omitted from tables. Statistical significance of results was not always assessed / reported.	No untoward events appear to have occurred during the study.	The findings are of interest but where physicians interpret patient barriers this is less reliable. The study was based on a small sample of mainly white health professionalss from a single setting. It is unclear how generalisable this research is.

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Paskett 1996[51]	The aims are clearly stated. The survey method is an appropriate design but sample size is not justified and numbers of actual (as opposed to intended) participants and non-participants is low. It is unclear why these particular patients were selected for participation. Methods of coding data are broadly described but it is unclear how these have been validated. Statistical methods are described in some detail. This study is described as a pilot but no detailed information on the questionnaire administered was available.	Basic data were adequately described and numbers tally. Findings could have been serendipitous given the small sample and multiple testing and the fact that for some respondents the situation was hypothetical (I.e. would they participate in a trial if offered).	Two patients' eligibility for trials could not be determined but these are accounted for.	It is difficult to interpret the findings due to the inclusion of hypothetical trial participants and refusers. More data could have been provided on actual rather than intended particpation although numbers were very small. There are problems in generalising the results. The predictors of participation found here - knowledge and attitudes towards research - are very general and more information on the authors' definition of these constructs is needed.

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Pinto 2000[67]	Aims were clearly stated. Although the authors stated that they used focus groups they reported only the data from an open-ended questionnaire used at the end of the focus groups. Sample size was not justified. Statistical methods were not described. Questionnaires included open-ended, broad questions with responses categorised post-hoc.	Basic data were adequately described and numbers appeared to tally. Very little information was provided on how data were coded, therefore it is difficult to assess the rigour of the process used to categorise data. The authors appeared to report only significant findings.	No untoward events appeared to have occurred during the study.	The main findings of the factors that make physicians less likely to recommend clinical trials to minority cancer patients are noteworthy and the paper goes on to discuss strategies to overcome barriers. The reasons that minority cancer patients are underrepresented in trials were suggested by the physicians rather than patients so it is unclear how valid these are. It is also unclear how representative participants were and how individuals were selected. Additionally it is unclear how appropriate it would be to generalise this research to minority groups other than African Americans.

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Siminoff 2000[68]	The aims of the study were clearly stated and the broad design was appropriate to the stated objectives. The sampling frame for surgeons and oncologists was not justified. It was unclear why fewer than four of the surgeons' patients may have been selected for discussion in some instances. The authors provide clear justification for the use of patient case histories to elicit information on physician attitude and patient-physician interaction. Information is provided on the first half of the interview process which was concerned with the case histories. However the format of the second part of the interview on general attitudes, knowledge and practices concerning clinical trials was unclear. There may be problems of recall bias in asking physicians to refer back to particular patient details. Interviewers received training prior to data collection. No information is provided on piloting of the interview schedule. Some limited information was provided on the statistical analysis.	The form of much of the data produced from the interviews is unclear. It is unclear whether the data produced was qualitative or quantitative and how it was coded. The dependent variable appeared to be physician decision to refer to trial. However it was unclear what data was used. If the decision to refer/not refer each of the 244 patients was used, it is unclear why there was a n of 244 in the surgeon regression model as well as a n of 170 in the oncologist regression model. The total number of decisions to refer/not refer exceeds the number of patients. No rationale or description of the process to group particular variables together in the five domains for the preliminary regression analysis was provided. A different grouping may have produced different findings. Although the authors state that predictors with a p value of 0.1 or less in the preliminary regression analysis would be entered into the final models, they are not all reported as part of the final model. It is unclear whether these were not entered into the model (and why) or were not reported. There was a large number of variables entered into the models given the sample size, particularly of the oncologist group	No comment	The authors attempted to identify all surgeons who provided care to breast cancer patients in a particular region. The response rate, however, was fairly low for this group and it was unclear how similar participants were to nonparticipants. Only those oncologists who had received a case referral from one of the surgeons were eligible for inclusion and it was unclear how similar they were to other oncologists working in the region. It is unclear how typical the selected patients were of breast cancer patients seen by the physicians. Physicians' responses were specifically in relation to breast cancer patients, therefore the findings are most applicable to this group. Results may not be entirely applicable to the UK setting.

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Skeel 1998[17]	This study was reported in an abstract therefore there was not enough information to appraise the study quality.			

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Spiro 2000[40]	Aims are clearly stated. All the patients considered for entry into the trial were included. Decisions on reasons for trial participation were recorded as volunteered by respondents therefore data is not available from all patients.	Basic data are adequately described and statistical significance was assessed. Findings may be limited by the fact that 41.4% did not give a reason for non-participation. Reasons for non-participation given were grouped together with no explanation of how this was carried out.	Not relevant.	The findings reiterate the problem of non-eligibility for trials (actual and as judged by clinicians). The findings point to the influence of trial design where one trial arm presents as a less attractive option to patients. Selection bias is a concern in that trial non-entrants were older and the group contained more females. Only this group's views were taken into account. The results are difficult to generalise as they represent the results of one trial in the area of lung cancer and they reflect a particular treatment option (chemotherapy).

Author, Year	Survey design	Survey analysis	Survey conduct	Survey interpretation
Wiley 1999[44]	The aims of the study were clearly stated. The design appeared to be appropriate to the objectives. Sample size was not justified. The Clinical Investigation Randomization Scale was based on information gathered in a feasibility study and two methods were used during the study to determine its reliability. It was unclear how the target sample was selected (it did not appear to be random).	Basic data were adequately described and numbers tally. Statistical methods were described in some detail and statistical significance was assessed through a variety of tests resulting in the generation of a predictor model for trial participation.	No untoward events appeared to have occurred during the study.	A concern with the study is its emphasis on randomisation as a synonym for trial participation. The decision to take part in a trial is more than an acceptance of randomisation but all questions are framed in terms of randomisation. It is inappropriate to generalise the findings beyond parents of children with cancer.

Qualitative Studies

Author, Year	Research design	Data collection	Data analysis	Interpretation
Ellis 1998[47]	The research design was appropriate to generate a potential framework for a more systematic evaluation of knowledge and attitudes to clinical trials. The authors discussed briefly the advantages of focus groups over one to one interviews. The appropriateness of considering women in the community and breast cancer patients together could be questioned. The researcher reported clearly on the selection of participants. However it is unclear if any of the women had actually participated in trials or indeed been offered the chance to do so.	The format for the focus group discssion was developed following a review of the literature and consultation with experts in the field. Methods of data collection are explicit. Attempts appear to have been made to reduce researcher bias by consulting with experts prior to formulation of discussion outline. Two authors were involved in organisation of responses into themes. There was no discussion of the issue of reflexivity. Approval was sought from an ethics committee and each discussion group began with an introduction to the purpose of the study and its conduct.	Data analysis procedures are described in outline only.	Findings are discussed in relation to the original research questions. As the authors state, this is a small and select sample of women and validation of these issues would need to be undertaken in a larger population.

Author, Year	**Research design**	**Data collection**	**Data analysis**	**Interpretation**
Grunfeld 2002[61]	The research design was appropriate to the stated aims The cancer sentres were selected on specific characteristics though examples of the characteristics they selected on were given so it is not clear whether there were further characteristics. It is unclear how participants were recruited from the centres and why some may not have taken part.	It was clear how the data were collected and the form of data is clear. Satuaration of the data was discussed. There was no discussion of reflexivity. Approval was sought from an ethics committee, and participants gave their consent for participation in the focus groups and for the use of quotes in publications emerging from the study. The procedures used to ensure confidentiality are explained.	The process used for data analysis was described including how data were coded. Transcripts were coded by more than one researcher. A reasonable amount of data is presented to support the findings. The researchers did not critically examine possible sources of bias during analysis and selection of data for presentation.	The findings are clearly stated and discussed in relation to the original research question. The researchers did not critically examine possible sources of bias during analysis and selection of data for presentation. The authors state that due to the qualitative methods used, the specific findings presented may not be generalisable. The findings are likely to be more relevant to similar tertiary cancer centres where multiple CRAs are working.

Author, Year	Research design	Data collection	Data analysis	Interpretation
Huizinga 1999[26]	This was a pilot study and as such the design was appropriate to the research question. It is unclear how the 14 participants were selected. The study only included one person who had refused to take part in a trial so barriers to trial participation are investigated from the point of view of trial participants. It is unclear if some patients refused to take part in the pilot study and if so whether this group did represent the views of the patient population.	It was clear that data were collected in the form of a semi-structured interview and the questionnaire on which this is based is provided in the report. Methods of data collection are explicit. Patient responses were not recorded but were written down during the interview which may have led to a loss of information for the open-ended questions. The questions in the structured interview had been formulated specifically by the researchers for this study but appeared to have been phrased neutrally to invite open ended responses and comments. However there is no discussion of reflexivity. The authors reported that the study was approved by a medical ethics committee.	The researchers state that a qualitative content analysis was performed and results were discussed with other experts. However there is no in-depth description of the data coding and analysis process.	The researchers discuss some of the limitations of their study. This is a pilot study with a small sample and only one person had declined participation in a trial. The researchers acknowledge the need to confirm their findings with further research and suggest areas of potential.

Author, Year	Research design	Data collection	Data analysis	Interpretation
Langley 2000[64]	The research design was appropriate to the stated aims. Although the authors selected the participants on specified and appropriate characteristics, it was unclear how this particular group of 20 were chosen from the sample of 55. The authors do not provide justification for the size of sample.	It was clear how the data were collected and the form of the data though very little information was provided on the content of the interview schedule and how the interviews were conducted. It is unclear whether the interview was based on the concerns the 20 participants raised in the survey or the concerns of all the survey participants. Interviews were audiotaped.	The process used for data analysis was clearly described including how data were coded and definitions of the categories used. Transcripts were coded by more than one researcher.	The findings are clearly stated and discussed in relation to the original research question. The findings are discussed in relation to changes in the organisation of clinical trials and how some of the barriers identified by clinicians may have changed.

Author, Year	Research design	Data collection	Data analysis	Interpretation
Maslin-Prothero 2000[34]	Two stages of the study used qualitative methods. The research design was appropriate to the stated aims The recruitment strategy for multidisciplinary teams seemed appropriate. An attempt was made to recruit teams from centres with varying levels of recruitment, though this was based on self-assessed recruitment levels. The recruitment strategy for patients was not clearly reported. Forty-eight women who had declined trial participation did not agree to take part in this study with only seven trial decliners being successfully recruited (this is stated as eleven in one part of the report. It is unclear how many trial participants were approached.	Data collection methods were explicit and the interview/focus group guidelines were available.No information was provided on the multidisciplinary groups apart from the centre's recruitment success and it was unclear how many professionals from each centre were actually involved in the study. Except where patients refused, all focus groups/interviews were tape-recorded and transcribed independently. The issue of bias was discussed in general terms. An independent professional transcribed the tape-recordings. The author states that the categories and themes generated in the coding process were externally verified however no details of this process are provided. it is not clear if there was a critical examination of the researcher's role, potential bias and influence during formulation of research questions. The study was approved by an ethics committee.	It is stated that a thematic analysis was performed and coding was independently verified. However there is no in-depth description of the data coding and analysis process.	The findings are clearly stated and discussed in relation to the original research question. The researcher did not critically examine possible sources of bias during analysis and selection of data for presentation. A strength of this study is that it examines reasons for trial non-participation in a group of patients who have declined trial participation. However, this is a small and select sample of women. Validation of these issues would need to be undertaken in a larger population. An additional strength of the study is that examines participation in a specific trial from a range of perspectives.

Author, Year	Research design	Data collection	Data analysis	Interpretation
Mills 2003[35]	The research design was appropriate to the aims of the study. Apart from the need to include similar proportions of trial accepters and refusers from the three different centres, it is not clear how the 21 men were selected and if there were any differences between those selected and those not.	The data appear to have been collected in a way that addressed the research issue. Data were collected through structured interview, taped and transcribed verbatim. Four experienced qualitative researchers were involved in checking of coding and interpretation. However it is not clear if the researchers critically examined their own role, potential bias and influence during formulation of research questions. Ethical issues appear to have been considered adequately.	Analysis of data was checked by other members of the team thus helping to minimise bias. Members of the team reviewed the data extraction grid with the original transcripts to resolve discrepancies.	There is a clear statement of findings and these are discussed in relation to the original research questions. The researchers discuss the findings in relation to other studies and identify areas for research (addressing the specific barrier of acceptability of clinical equipoise). This was a well conducted study but it is unclear how relevant the findings would be to other groups.

Author, Year	Research design	Data collection	Data analysis	Interpretation
Stevens 2004[41]	The research design was appropriate to the stated aims. The process of recruitment to the study was clearly explained. Of the sample recruited for the overall study all patients who had declined participation in a trial were invited to participate. The authors point out the potential risk of small samples in an interview-based survey including more articulate patients. There is also the potential for a social desirability effect.	It is clear how the data were collected and the form of the data though very little information was provided on the content of the interview schedule/topic guide and how the interviews were conducted. It is not clear if the researchers critically examined their own role, potential bias and influence during formulation of research questions and data collection. Approval was obtained from an ethics committee.	The researchers state that a qualitative content analysis was performed with different members of the team involved in coding. However there is no in-depth description of the data analysis process.	The findings are clearly stated and discussed in relation to the original research question. A strength of this study is that it examines in some depth reasons for trial non-participation in a group of patients who have recently declined trial participation. However, as the authors state, this is a small and select sample of women. Validation of these issues would need to be undertaken in a larger population.

Author, Year	Research design	Data collection	Data analysis	Interpretation
Wright 2002[69]	The research design was appropriate to the stated aims. A convenience sample was taken from one setting. Given the aims of the study it would have been more appropriate to involve CRA's from a range of settings.	It is clear how data were collected (focus group) and the method chosen was justified. It is reasonably clear how the exploratory phase of the focus groups was conducted. However, the process of drawing up a list of factors for rating in the confirmatory phase was unclear. No justification is provided for why over half the factors participants were asked to rate in the confirmatory phase were not actually generated in the exploratory phase. The focus groups were audio recorded but were not transcribed. The authors stated that no new content areas were revealed with the second focus group. There was no discussion of reflexivity. The focus group facilitator was external to the Department of Clinical Trials. However, the observer, who also provided a summary of the discussion of the exploratory for the confirmatory phase, was a physician in the Department. There was no discussion of how this may have impacted on how freely participants may have expressed their views.	Only scanty information is provided on the analysis process. Summary notes of the interviews were coded independently by two researchers. The method used for coding is not explained. No data are presented to support the findings in the exploratory phase. The researchers did not critically examine possible sources of bias during analysis and selection of data for presentation.	Due to the lack of data presented the findings from this study are somewhat unclear. There is inadequate discussion of the credibility of the findings. The study is based on a small convenience sample of CRAs, from one setting in the US, which limits generalisability. The authors state that further research is required to validate the impressions obtained from the study.

Chart Reviews

Author, Year	Design	Data collection	Data analysis	Interpretation
Brown 2000[18]	It is not possible to assess the design of the survey instrument due to lack of information.	Data were collected from three sources as outlined in the report. Detailed methods were not available.	No details on analysis were available.	This study is likely to be specific to the US context and it will be inappropriate to generalise to other ethnic groups.

Author, Year	Design	Data collection	Data analysis	Interpretation
Camerini 1999[19]	A problem with this chart review is that it appears that patients who refused to take part in the trial were permitted only one reason for refusal.	It is also unclear how the authors elicited reasons for refusal and how they defined the reasons.	Not stated	This study is hampered by design and data collection problems as stated. Its generalisability is unclear.

Author, Year	Design	Data collection	Data analysis	Interpretation
Cook 2002[20]	This study was not designed to investigate barriers to trials.	It was unclear how data were gathered on barriers to the success of the feasibility study. The authors dod not appear to have obtained information from staff on the barriers experienced.	Not stated.	It is unclear how to interpret this study due to poor reporting and problems of data collection.

Author, Year	Design	Data collection	Data analysis	Interpretation
Diener-West 2001[21]	The study was designed to examine recruitment to two specific trials.	Methods of data collection are outlined.	The analysis did not differentiate between those eligible for trial participation but not approached and those approached who refused	This study examined predictors of enrolment in a fairly large group of patients but does not investigate patients' reasons for non-participation.

Author, Year	Design	Data collection	Data analysis	Interpretation
Goodwin 2000[54]	It is unclear why respondents were asked about a specific set of potential barriers and not others.	Health professionals other than group leaders were involved in recruitment but their views were not sought.	Methods of analysis are stated.	This study presents a fairly limited exploration of barriers to participation in the trial. The authors' conclusions are based on a fairly limited survey of group leaders and some routine data on recruitment. There did not appear to be any structured way for respondents to identify barriers to participation other than those that the authors chose to investigate.

Author, Year	Design	Data collection	Data analysis	Interpretation
Holcombe 1998[25]	This study did not appear to be designed specifically to investigate barriers to accrual. Those reported appear to be based on experience at the centre.	It is unclear how the data on barriers has been collected.	Not stated	There is a lack of information on methods of data collection and there are difficulties in generalising beyond the particular ethnic group and setting.

Author, Year	Design	Data collection	Data analysis	Interpretation
Jenkins 1999[27]	This study is not specifically designed to focus on barriers but forms part of an overarching study that does investigate such barriers. The design appeared to be appropriate for the investgation of doctor-patient communication about trials.	Methods of data collection are presented.	Methods of data analysis are stated	This appeared to be a well-conducted observational study raising issues of doctors adopting individual methods when describing trials to patients.

Author, Year	Design	Data collection	Data analysis	Interpretation
Mannel 2003[33]	Details of the design of the chart review were limited.	Chart review methods were described in outline.	Analysis was done at the level of the physician but differences between physicians other than being a principal investigator or not were not investigated.	This study is based on one centre with good research support so the focus is on the barriers generated by individual physicians. However a limitation of the study is that it is based on just four physicians.

Author, Year	Design	Data collection	Data analysis	Interpretation
McCaskill-Stevens 1999[73]	This study was reported in an abstract therefore there was not enough information to appraise the study quality.			

Author, Year	Design	Data collection	Data analysis	Interpretation
Richardson 1998[38]	This study is designed to decribe the recruitment experience rather than as a study of patient barriers.	It is not clear how the reasons collected were derived (researcher-defined or patient comments).	Within the limitations of design and data collection analysis appears to be appropriate.	Interpretation of this study is made more difficult by the fact that patients appeared to have only been allowed to document one reason for trial refusal. Demographic issues highlighted here may be specific to the US context or even to trials involving complementary medicine..

Author, Year	Design	Data collection	Data analysis	Interpretation
Ringberg 2000[39]	This study was designed to assess patient accrual to a specific trial.	It is unclear how the study authors elicited information from patients on why they did not take part in the trial and it appears that patients only documented one reason.	Not stated	Problems with data collection and poor reporting of analysis make the issues highlighted in this chart review difficult to interpret.

Author, Year	Design	Data collection	Data analysis	Interpretation
Sinnott 2002[14]	This study was reported in a letter therefore there was not enough information to appraise the study quality.			

Author, Year	Design	Data collection	Data analysis	Interpretation
Tripathy 1998[15]	This study was reported in an abstract therefore there was not enough information to appraise the study quality.			

Author, Year	Design	Data collection	Data analysis	Interpretation
Twelves 1998[42]	The design appears to be appropriate to the stated aims.	Methods of data collection appear to be appropriate.	Methods of analysis appear to be appropriate.	This appears to be a well-conducted chart review focusing on demographic and physician-related barriers.

Author, Year	Design	Data collection	Data analysis	Interpretation
Westcombe 2003[43]	This was a report of recruitment problems rather than a specific study of barriers to trial participation.	It was unclear how the authors elicited patients' reasons for declining trial entry. It was unclear if and how information was gathered from the professionals involved in the trial or whether the barriers identified are based solely on the authors' perceptions.	Not stated	It is difficult to assess the robustness of the information on barriers to trial participation in this study due to the lack of information on how the information on barriers was actually gathered and collated

Author, Year	Design	Data collection	Data analysis	Interpretation
Wilt 2003[16]	This study was reported in an abstract therefore there was not enough information to appraise the study quality.			