

Factors affecting recruitment to breast cancer clinical trials:

**An examination of the British Association of Surgical
Oncology II trial and the International Breast Cancer
Intervention Study**

By

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Abstract

Breast cancer is the most common form of cancer among women in the United Kingdom, and there is considerable investment in research to identify the causes of breast cancer and the best means of diagnosis and treatments. The randomised controlled trial is the principal method used for evaluating diagnostic and treatment options. Trial organisers depend on recruitment of sufficient numbers of patients in order that the results are statistically significant and generalisable, but accrual to cancer clinical trials is poor.

This research analyses factors affecting the accrual of women to two breast cancer trials, the British Association of Surgical Oncology (BASO) II trial (a treatment trial) and the International Breast cancer Intervention Study (IBIS) (a prevention trial). The aims were to identify the factors affecting the recruitment of women to breast cancer clinical trials from the surgeons' and multi-disciplinary teams' perspectives and, importantly, from the perspectives of women approached to participate in clinical trials, and their reasons for participation, or non-participation in the trials.

There were three phases to the study using multiple methods. In the first phase quantitative methods were used in the form of a questionnaire, sent to consultant surgeons responsible for collecting audit data regarding breast cancer in the United Kingdom. The second and third phase incorporated qualitative methods of data collection; the second phase included in-depth interviews with multi-disciplinary teams; and the third phase involved focus group and individual interviews with women approached to join a breast cancer clinical trial. These three phases were carried out in both the trials examined.

The findings contribute to the debate and knowledge of the recruitment of women to breast cancer clinical trials in a number of ways. Firstly, by including the views of all

the key stakeholders concerned with breast cancer clinical trials. Secondly, by highlighting the factors affecting recruitment to these two breast cancer clinical trials. Thirdly, by making recommendations on methods to enhance recruitment.

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Glossary of terms

BACUP	British Association of Cancer United Patients
BASO	British Association of Surgical Oncology
BASO II	British Association of Surgical Oncology II trial
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CRC	Cancer Research Campaign
DOH	Department of Health
DCIS	Ductal Carcinoma In Situ
EBCTCG	Early Breast Cancer Trialists' Collaborative Group
GP	General Practitioner
IBIS	International Breast cancer Intervention Study
ICRF	Imperial Cancer Research Fund
LREC	Local Research Ethics Committee
MREC	Multi centre Research Ethics Committee
NHS	National Health Service
NHSBSP	National Health Service Breast Screening Programme
RCT	Randomised controlled trial

PREFACE

Introduction

This thesis represents work undertaken on behalf of the NHS National Cancer Research and Development Programme and NHS Executive Trent. It was developed to examine factors affecting recruitment to breast cancer clinical trials and these findings contribute to the debate on the recruitment of people to clinical trials.

Breast cancer is the most common form of cancer among women in the United Kingdom. There is considerable investment in research to identify the causes of cancer and treatments, and randomised controlled trials are the primary method used, but accrual to cancer clinical trials is poor. In response to this, this thesis is a detailed analysis of factors affecting the accrual of women to two breast cancer trials. Because of the importance of establishing different views regarding clinical trials these issues have been examined from the perspectives of clinicians, multi-disciplinary teams and women.

The research questions

The specific questions of the research were:

1. What are the factors affecting the recruitment of women to breast cancer clinical trials from the:
 - a) Surgeon's perspective?
 - b) Multi-disciplinary teams' perspective?

2. What are the views of women who are approached to participate in a clinical trial, and what are their reasons for participating or not participating in the clinical trial?

The studies described in this thesis start to address these questions and offer suggestions on how recruitment to clinical trials might be increased by identifying and addressing these factors.

The structure of the thesis

The thesis is divided into five chapters. Chapter 1 provides a background to the thesis with a review of the pertinent literature, placing the research in context. Chapter 2 presents the design of the research and the methods of data collection used. This provides an account of the research strategy and a critique of the methods of data collection employed and highlights how the research strategy aims to bridge the gaps in the research literature and add to the existing knowledge.

Chapters 3 and 4 present the main findings emanating from the study. Chapter 3 examines the British Association of Surgical Oncology II (BASO II) trial, a treatment trial for women with breast cancer. A number of separate phases were undertaken including a survey of clinicians; in-depth interviews with multi-disciplinary teams; retrospective and prospective audits; and individual and focus group interviews with women who entered the trial, and with women who refused to participate. Chapter 4 replicates the research design used for chapter 3 and provides results on the factors affecting recruitment to the International Breast cancer Intervention Study (IBIS), a preventative trial for women with a family history of breast cancer.

Chapter 5 pulls together the results from the two trials examined – the BASO II and IBIS trials, and discusses how these contribute new knowledge on factors that might influence recruitment to these breast cancer clinical trials. It also includes unexpected outcomes from the two studies. This chapter concludes the thesis through reflection on

the techniques used in the research process and also makes recommendations for further research.

CHAPTER 1 LITERATURE REVIEW

- 1.1 Introduction
- 1.2 Incidence and population mortality
- 1.3 Current health policy
- 1.4 Clinical trials
- 1.5 Medical research ethics as applied to clinical trials
- 1.6 Clinicians position regarding recruitment to clinical trials
- 1.7 Lay position regarding recruitment to clinical trials
- 1.8 Summary and conclusion

CHAPTER 1 LITERATURE REVIEW

1.1 Introduction

This chapter reviews the pertinent issues and the literature, which provide the background to the thesis. The chapter is divided into sections and starts with a brief overview of breast cancer and policy relating to the management of breast disease in the United Kingdom. Medical research ethics in the twentieth century, as applied to clinical trials and a review of the role of randomised clinical trials, follows. There is a critique of the literature on recruitment to clinical trials from the clinician and patient perspective, highlighting the gaps apparent in the literature.

Over the last twenty years there have been considerable advances in the treatment of patients with cancer. Yet there continues to be a widespread difficulty recruiting eligible people to cancer clinical trials (Tannock, 1995). A lack of data, either describing or testing recruitment strategies, is characteristic of both treatment and prevention trials, although it is known that recruitment is a problem in the majority of clinical trials.

Participation rates are low in many trials, even in those trials that succeed in recruiting large numbers of patients. In 1979 it was estimated that in the United Kingdom only 8% of all patients with breast cancer were recruited to clinical trials (Tate et al. 1979).

Twenty years on still less than 13% of patients are enrolled in breast cancer clinical trials in the United Kingdom (Twelves et al. 1998; Jenkins et al. 1999).

Search strategy

To access a range of sources a number of computer databases were used, including Medline, Cumulative Index to Nursing and Allied Health Literature (CINAHL) and Bath Information & Data Services (BIDS) from 1980 to 1999, using the following search

strategy: clinical and trial*, breast cancer*, recruitment* and consent*. The 'completeness' of any database can be questioned, therefore, in addition, recent volumes of key journals were also searched by hand, and references cited in key papers were also examined. This search strategy was deliberately broad in an attempt to capture as much recent literature as possible.

1.2 Incidence and population mortality of breast cancer

England and Wales has one of the highest age-standardised incidence and mortality rates for breast cancer in the world (McPherson et al. 1995; Office for National Statistics and London School of Hygiene and Tropical Medicine 1999). Breast cancer is the most commonly occurring cancer in women in the United Kingdom. There were 33,040 new cases of breast cancer in the United Kingdom in 1995 (Cancer Research Campaign (CRC) 2000), and approximately 14,500 deaths from breast cancer a year (Imperial Cancer Research Fund (ICRF) 2000). The cumulative incidence of breast cancer rises steadily from the age of 35 years with a slight increase in incidence rate with age (Liberati and Grilli 1996). However, breast cancer is rare in young women, with only 2% of women developing the disease before the age of 50 years. Lifetime incidence (by 70 years) is such that 1 in 12 women develop breast cancer (CRC 2000); the incidence rate is approximately 2 per 1000 per annum.

The earlier a cancer is diagnosed, the greater the chances of successful treatment (National Health Service Breast Screening Programme and British Association of Surgical Oncology (NHSBSP & BASO) 1996). Routine breast screening has been available via the NHS breast screening program for women aged 50-64 years since 1988 following the recommendations of the Forrest Report (Given-Wilson 1999). Breast screening has mortality benefits for women over the age of 50 years, and can

reduce death by 30% in this age group (Cuzick 1999); the benefits for younger women are not evident.

1.3 Current health policy

There have been variations in treatment for breast cancer in the United Kingdom; but increasingly women are treated by specialist breast surgeons, rather than by a general surgeon. The Calman and Hine Report suggested that patients are interested in the quality as well as the quantity of their survival (Department of Health (DOH) 1995). This report, 'A Policy Framework for Commissioning Cancer Services in England and Wales', emphasised that cancer care should be patient focused, with three levels of service provision integrating services and expertise. At the first level, primary care teams involved in the initial assessment and referral of patients as well as ongoing practical and emotional support. At the second level, designated cancer units responsible for clinical management including co-ordination of care and specific specialists. The third level would be cancer centres to provide specialist services to support the cancer units - radiotherapy, specialist diagnostic services and the management of rare cancers. There was a need to select, develop and provide accreditation of these specialist breast cancer units. This report, combined with pressure from consumers, other interested organisations and expert advisory groups on cancers, has led to the development of specialised multi-disciplinary teams, with the aim of making the best treatment available to all.

Multi-disciplinary team working has been shown to improve outcomes by selection of appropriate treatments for women based on scientific and evidenced-based research (Stiller 1994; Gillis and Hole 1996; Liberati and Grilli 1996; Twelves, Thompson et al. 1998; Sainsbury 1999). These teams have a range of specialists in terms of

qualifications, experience and time devoted to the management of breast cancer (British Association of Surgical Oncology (BASO) 1996). The British Association of Surgical Oncology (BASO) Breast Speciality Group is the national surgical speciality group in breast disease and has produced guidelines on the management of screen detected breast cancers (BASO 1998). Breast units voluntarily collect data that is audited regionally (NHSBSP and BASO 2000). Treatment for breast cancer shows that success rates are closely linked to the stage of the cancer presenting (CRC 1996); and women with small tumours (less than 2cms) have a greater chance of surviving 5 years compared with women with tumours over 5cms in diameter. Involvement of axillary nodes indicates a worse progress (Miller, Ellis et al. 1995).

The belief had been that women who undertake breast self-examination would detect tumours earlier and present for treatment before metastases occur, but the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) failed to show an advantage in cancer survival as a result of self-examination (EBCTCG 1990). Subsequently, the Department of Health (DOH) issued policy advice on breast awareness, rather than self-examination of the breast (DOH 1991a; DOH 1998a). Although there has been an attempt to provide an explanation as to what exactly breast awareness is, considerable confusion remains as to what it entails and how it differs from breast self-examination. However, increased consciousness among women regarding their breasts and breast cancer has also led to an increase in referrals to specialist breast clinics, and some have argued that these women expose themselves to unnecessary investigations (Baum 1999).

Over a decade ago 11-12% of breast referrals proved to be carcinoma, recent surveys have demonstrated a detected carcinoma rate for symptomatic referrals of 6.3% and 5.9% (Austoker 1999). This 50% fall in incidence rate could be explained by an increased awareness of breast disease due to education, breast screening and media

coverage (Dey et al. 1997; Baum 1999).

From 1st April 1999, with the introduction of National Guidelines, all urgent referrals for breast cancer investigation must now be seen within two weeks for early recognition and diagnosis of breast cancer (NHS Executive 1998). This means that non-urgent referrals have to wait longer before the breast team sees them. Early data from the BASO Breast Speciality Group (unpublished data) suggests that 50% of cancers lie in the non-urgent referrals; therefore rather than advancing the detection rate of all breast cancers, this new policy means that women with breast cancer take longer to be seen. A factor contributing to this increased pressure on multi-disciplinary teams is because of 'inappropriate' referral of women with breast lumps by General Practitioners (GPs). To address this problem breast referral guidelines for GPs were produced in December 1995 to make referral easier, effective and more efficient (Austoker et al. 1995), with a second edition in 1999 incorporating the new National Guidelines (Austoker and Mansel 1999).

There are number of different treatment options for women with breast cancer, and clinicians have access to a comprehensive portfolio of research-based evidence on which to base their therapeutic decisions (Early Breast Cancer Trialists' Collaborative Group (EBCTCG) 1992; EBCTCG 1996; EBCTCG 1998; EBCTCG 2000). Decisions regarding treatment vary with how clinicians weigh the potential benefits of known treatments against potential harms, and length of life versus quality of life.

1.4 Clinical trials

The evaluation of possible improvements in the treatment of disease has historically been an inefficient and haphazard process; in the past healthcare has been based on

historical legacy, personal treatment preference and ritual. Concurrent controls were used in the 1930s and 1940s as a means of evaluating treatments, with alternate patients allocated a treatment (Doll 1998), but there was a risk of bias in selection, as the clinician knew which treatment a patient was going to receive. In 1948 Bradford Hill first described a randomised controlled trial using streptomycin for the treatment of pulmonary tuberculosis (Yoshioka 1998; Fisher 1999), and Paterson in 1947 suggested the first randomised controlled trial for breast cancer to test the efficacy of radiation therapy to the breast (Paterson 1962). Through hypothesis testing and a discovery process, the worth of different therapies were evaluated. One of the many achievements of the 20th century has been the development of the randomised controlled trial; these clinical trials are the method by which different treatment options are evaluated.

Yet some health professionals continue to use clinical interventions known to be ineffective and fail to implement other proven treatments known to have good outcomes (Tattersall and Simes 1992; Walshe 1998). There is increasing pressure for a more systematic approach to healthcare delivery based on clinical and cost effectiveness, with the ultimate aim of enhancing patient care (Cochrane, 1972). Though, as Thomas (1994 cited in Fisher 1999 p1965) stated: “... *hunches and intuitive impressions are essential for getting work started*”, then these hunches need to be assessed. Evidence-based medicine emphasises the examination of evidence from clinical research, where the evidence is critically appraised for its validity and usefulness, and where the results of the appraisal are applied to clinical practice and evaluated.

Properly conducted clinical trials provide a reliable basis for evaluating the efficacy and safety of new treatments. Clinical trials are a means by which clinical questions are

answered, and they have made major contributions to the development of new and improved treatments for patients with cancer (Catalottini et al. 1999). The randomised controlled trial is recognised by clinicians as having the rigour to inform clinical decision-making and is viewed as the 'gold standard' for evidence-based healthcare (Paterson 1962; Black 1996). Clinical research uses random allocation to eliminate bias and examines individuals by comparing those receiving a treatment with untreated individuals, as a means of ascertaining the benefits and effects of a treatment versus the adverse effects of treatment. Randomisation involves the allocation of individuals to control and experimental groups at random, so that the selection process introduces no bias. Random allocation to treatment groups theoretically distributes evenly both the known and unknown variables that can influence treatment outcomes; the aim is to ensure that the results are a reasonably accurate reflection of how other similar groups of patients might respond under the same regimen in future (Doll 1998). Yet there can be ethical concerns about the justification of randomising patients to treatments that might compromise survival.

The ability of a clinical trial to deliver valid, safe results depends upon the recruitment of sufficient numbers of patients, so that results are statistically significant and therefore generalisable (Peto and Baigent 1998). Clinical trials require groups of eligible patients who fit the criteria, to volunteer to participate in the trial. A large number of patients are eligible to participate in clinical trials for cancer therapy, however recruiting sufficient eligible patients into randomised clinical trials, so that treatment studies and outcomes can be reliably compared is difficult - accrual in clinical trials of cancer treatment is low (Ward et al. 1992). In spite of the generally high attention to breast cancer by the media in recent years, recruitment of patients to all breast cancer clinical trials remains poor in the United Kingdom (Tate et al. 1979; Twelves et al. 1998); despite some

studies indicating that public attitudes to trial participation remains favourable (Cassileth et al. 1982; Slevin et al. 1995). The research to date, although relatively scarce, suggest a number of factors that contribute to this low accrual rate.

Researchers frequently have difficulty in gaining patients' agreement to take part in clinical trials - there are dichotomies between health professionals who want to provide evidence-based care, but have concerns about aspects of the research process (Baum 1990; Tobias and Souhami 1993); and the public who want effective healthcare but are ambivalent, or even resistant, to participating in clinical trials (Llewellyn-Thomas et al. 1991). Analyses of recruitment to breast cancer trials indicate two broad reasons for failure to recruit to clinical trials: firstly, exclusion on clinical grounds by clinicians and secondly, decline of random allocation by patients (Maslin-Prothero et al. 1999).

Literature on accrual to cancer trials suggests that both clinician and trial protocol characteristics are important correlates of recruitment success (Thornton 1997). The clinician related characteristics include clinician's attitude to clinical trials, and their motivations for entering patients (Taylor et al. 1994). The characteristics of the trial that influence accrual from the clinicians perspective include trial designs with a no treatment arm, arms of unequal attractiveness, the process of informed consent, and the method of presenting the trial (Gotay 1991; Tannock 1995). Difficulties with equipoise may lead to a lack of commitment in presenting the trial to eligible patients.

Design of the trial

Thorough planning of the recruitment phase is essential to the success of any clinical trial. This phase includes staff participation and training, developing detailed profiles of the study subjects, and testing specific recruitment strategies (Swanson and Ward 1995; Farrell 1998). For prevention trials specifically, but also for treatment trials, the

component most often overlooked is the development of detailed profiles of the communities, populations, clinics, and hospitals from which participants will be recruited. These profiles often require a survey of the population, a summary of population or clinic demographics, and a determination of literacy and language levels amongst the proposed populations. Pilot studies of proposed recruitment strategies are recommended in determining the most effective methods, but are infrequently done (Swanson and Ward 1995).

Detailed procedures for managing clinical trial recruitment and active participation by the investigators are essential if high recruitment rates are to be attained. Monitoring of the recruitment progress, preferably through computerised tracking systems, is essential to meet study objectives and to identify and correct problems (Swanson and Ward 1995). Multi-centre studies present additional challenges to recruiting subjects, since each site will have different recruitment rates due to other variables (Warlow 1990). Studies that have had the highest participation rates are those that have included recruitment co-ordinators and experienced investigators (Farrell 1998).

A few studies have identified both effective and ineffective strategies for clinical recruitment. Swanson and Ward (1995) identified factors to enhance recruitment: involve primary care providers; media promotion; public education; clinician and nurse education; nurse as recruitment co-ordinator; and direct telephone, mail or in-person recruitment.

For the purpose of external validity, the study population must be representative of the population, and for internal validity, prognostic factors must be equally distributed among patients in the study population. Unbiased patient recruitment, logical and

precise inclusion, random allocation - preferably stratified, and minimal patient attrition are important to enhance the validity of the study (Rinck et al. 1997).

Unbiased patient recruitment begins with the identification of all eligible cases, yet as Bush asserts (Bush 1994) no one wants uniform inclusion of *all* patients *all* the time. It is more a matter of obtaining valuable information and performing a proper analysis. What is necessary are methods to predict where there might be clinically important differences among various sub-groups, and the strategies in place for recruiting the representative patients, retaining them, and properly analysing the data obtained from them.

A threat to unbiased patient recruitment is patient or clinician refusal. Patients and their clinician may have serious misgivings with randomisation, or have specific wishes about further care. Therefore, registration and evaluation of these non-participating patients are necessary to judge the generalisability of the investigation (Rinck et al. 1997). The criteria should reflect important prognostic factors, include clinical and health parameters, and take the objective of the intervention into consideration. Overall patient attrition must be accounted for (Rinck et al. 1997).

It is a challenge for future research to link patient outcomes with the quality of care, independently of the autonomous course of the disease and personal characteristics. For this it is necessary to apply study designs with baseline measurements and multiple follow-up measurements. Controlled studies with random allocation to the study groups are preferred, because random allocation can ensure unbiased allocation and help to control the many known and unknown person-related, disease-related, and care-related factors that influence patient outcomes (Rinck et al. 1997; Doll 1998).

1.5 Medical research ethics as applied to clinical trials

Medical research that involves human subjects has an obligation to ensure that the research adheres to ethical principles, whether using laboratory research or clinical trials. Clinical trials involve experimentation on the healthy and those with health problems and must therefore be constrained by ethical considerations.

Ethical considerations

A clinical trial requires careful assessment of whether it is ethically acceptable for patients to participate. It is of paramount importance that unnecessary suffering, inconvenience to the patient as a result of participating in a trial, and any experience of loss of freedom is discussed with the proposed participant. The balance between medical progress and ensuring individual patient care is the basis of the ethical dilemma. The key ethical dilemma is whether each patient should be (and is) informed, and his or her consent sought, prior to inclusion in a clinical trial. Where individuals are being asked to participate in research they have certain rights, and the researcher has responsibilities to ensure that the participants experience no abuse or harm.

Medical research has a particular tradition of ethical concern emanating from unacceptable experimentation undertaken by medical practitioners in the Second World War. These experiments were exposed at the Nuremberg Trials and resulted in the Nuremberg Code setting out ethical principles for medical research. These principles of general ethical requirements of clinical research worldwide are outlined in the Declaration of Helsinki (World Medical Association 1983). Internationally this document has generally been accepted as the basis for ethical research, though the interpretation of this document varies between countries, and individuals.

Individual verses collective ethics

Schwartz et al (1980) argue that in any clinical trial there is a tension between the ethics of individual benefit and the ethics of collective benefit. Individual ethics refers to treatment that is believed to be beneficial to the patient's condition, a primary aim of most clinicians being that together, the clinician and patient should identify the most relevant and beneficial treatment. Patients usually depend on their clinicians to recommend the most appropriate treatment based on the clinicians knowledge, experience and opinion. Individual ethics is concerned with present treatment. In contrast, collective ethics look to the future achievement of medical progress; the prime motivation here is to identify the most effective treatment for future patients. Each clinical trial requires a balance between individual ethics and collective ethics.

Moral principles for healthcare research ethics

Beauchamp and Childress (1994) distinguish four moral principles, which can be used as a basis for healthcare research ethics: beneficence, nonmaleficence, respect for autonomy, and justice. Beneficence refers to the obligation of research to provide benefits, and to balance these benefits against the risks of participation.

Nonmaleficence relates to the researcher's obligation to avoid harm to either individuals or society. Respect for autonomy is the obligation to respect the decision-making ability of autonomous individuals. Finally, justice is the moral obligation to act on the basis of fair adjudication between competing claims for benefits and risks. These four principles can conflict with each other, and it is for the researcher to determine and resolve any contradicting points in order to maximise the overall benefit to the patient.

Ethical control of research in the NHS

Since the 1960s in the United Kingdom there has been a development of a system of Local Research Ethics Committees (LREC) at local NHS Trust levels, and regionally, Multi-centre Research Ethics Committees (MREC). These ethical committees have a remit to protect the autonomy and rights of potential participants in clinical research, as well as acting as regulators. A clinical trial must have its protocol approved by such a committee before it commences, although it remains the responsibility of the trial organisers to ensure that is ethical and that patients do not suffer as a result of clinical research. Through regulation, by LRECs and MRECs the incidence of abuse, exploitation and trauma should be prevented.

Guidelines from the Royal College of Physicians (1990) emphasise that research benefits to society should not be hindered without good cause, and that the objectives of LRECs are to:

“...maintain ethical standards of practice in research, to protect subjects of research from harm, to preserve the subjects’ rights, and to provide reassurance to the public that this is being done.” (Royal College of Physicians 1990 p 3)

In 1991, the Department of Health formally required the inclusion of lay members on these committees (DOH 1991b). These groups work variously and there is no common practice across districts or between NHS Trusts.

MRECs and LRECs provide methodological and ethical surveillance on behalf of patients in the United Kingdom. They check that the researchers are qualified to carry out the trial, the protocol is suitable for the needs of the trial, the probable benefits of a

new treatment outweigh the side effects, there is enough information for participants, and the local health facilities are able to support the trial.

Informed consent

The Declaration of Helsinki cited by (World Medical Association 1983) states that in clinical research the doctor should obtain the individuals freely given informed consent, preferably in writing. Informed consent does not only involve disclosure of all relevant information but also ensures that the individual understands the information provided.

Informed consent relates to the interaction that occurs when an individual consents to treatment or participation in research. The following components should be evident: that the individual is mentally competent to give consent; that consent is freely given without coercion; and that the individual is given adequate information on which to base their decision (Royal College of Physicians 1990). Obtaining informed consent involves the clinician describing the situation to a patient in order that the patient does not lose confidence in the clinician, fully understands the proposed study, is willing to take part in the study, understands the effects of the proposed treatment, and understands that the treatment will be allocated at random. The clinician has a duty of care to their patients, which includes informing them of the most appropriate course of treatment for each patient and the information necessary to make that decision (Kirby 1983). It is not a legal duty in the United Kingdom to obtain informed consent, but is an expected requirement (Kirby 1983; Baum 1986).

Obtaining informed consent is not simple; there is considerable debate regarding the kind of information to be given to patients, by whom and in what form. Some clinicians reason that patients do not want full informed consent prior to inclusion in a clinical trial

(Taylor and Kelner 1987), and that the process of gaining consent can act as a barrier to recruiting patients to clinical trials. This is associated with the clinicians' concern that -recruiting patients to a clinical trial exposes the uncertainty of the clinical community, to the patient, as to which is the most appropriate treatment for them, and this uncertainty is then passed on to patients (Tobias and Souhami 1993). Maguire (Maguire 1999) argues that most cancer patients want to know their diagnosis, prognosis, possible treatment options and relevant side effects, and that only a minority prefer not to know. Problems arise when there is a discrepancy between what the patient wants to hear and the way the clinician delivers information.

There is a degree of unfamiliarity regarding the meaning of randomisation; some patients are concerned about the process, and would prefer the clinician to make the decision regarding their treatment, not a computer (Gotay 1991; Llewellyn-Thomas et al. 1991). Patient consent to treatment is now almost always sought prior to randomisation. This involves the clinician revealing a degree of uncertainty regarding the best treatment, and obtaining agreement from the patient to participate in the trial without either party knowing which treatment they will receive. The use of the double blind procedure, in which the patients and the doctors administering the treatment are unaware of the group to which the participant has been allocated, is often used in randomised controlled trials. Yet where a patient's preferred treatment is so strong that they refuse randomisation, sample representativeness can be compromised (Hicks 1998).

Other concerns may be related to the extent of difference between treatment options. Where therapies are similar in nature then obtaining informed consent is less complex. However, where treatments are completely different, then obtaining fully informed

consent may be more difficult. The ethical problems associated with placebo treatments are well documented (Pocock 1983) and influence the decision of patients who are prospective participants. The use of a placebo is preferable to the continued use of an unproven clinical treatment. It is essential that prospective patients be informed in advance about experimental procedures and any associated risks.

There is evidence to suggest that even for those patients who have given consent to participate in a clinical trial, their consent may not have been informed or educated (Montgomery et al. 1997). For clinicians experiencing difficulties in discussing informed consent, this will reduce the numbers of eligible patients enrolled on trials (Taylor et al. 1984; Taylor and Kelner 1987; Taylor et al. 1994).

Equipoise

If the clinician seeking consent can truly tell the patient that they do not know which treatment is better, then the clinician is in equipoise. However, Baum (Baum 1994) and others have argued that the management of breast cancer is a subject of debate and choice among clinicians, and that patients are unaware of this uncertainty. Equipoise is unlikely where the clinician hypothesises that one treatment is superior to another; if the clinician shares this suspicion with the patient, that one treatment maybe superior, then consent to randomisation may be less likely (Gotay 1991; Stephenson and Walker 1996).

Peto and Baigent (Peto and Baigent 1998 p 1170) refer to the uncertainty principle, suggesting that:

“A patient can be entered [to a trial] if, and only if, the responsible clinician is

substantially uncertain which of the trial treatments would be most appropriate for a particular patient. A patient should not be entered if the responsible clinician or the patient are for any medical or non-medical reasons reasonably certain that one of the treatments that might be allocated would be inappropriate for this particular individual."

Baum (Baum 1993) argues that it is not possible for clinicians to obtain fully informed consent to a randomised controlled clinical trial from patients soon after notifying them of a life-threatening illness. He suggests that both the clinician and the patient need to be in equipoise before the patient agrees to be randomised:

"[There is] the cruelty and risk of moral compromise, in trying to force patients to consent to randomisation shortly after the diagnosis of a life-threatening illness...How can we truly expect to receive informed consent for treatment of breast cancer within a controlled trial when the subject is so complex that very few medically qualified individuals can grasp the issues?" (Baum 1993 p 813)

Clinicians are now more likely to admit uncertainty and see this as an ethically honest and open issue rather than a defeatist approach. The clinician's views about patients' requests to be informed and consulted are influenced by their own convictions about good practice, as well as by the patients' preferences.

Informed patients

The degree to which individuals want to be involved in decision-making varies.

Cassileth et al (Cassileth et al. 1982) suggested that it was younger and well-educated people who most wish to be involved in the decision-making process. Others have

suggested that a patient's role in decision-making was based on their level of illness – the more serious the illness, the less involved they wanted to be (Thompson et al. 1993). Conversely, Fallowfield et al (Fallowfield et al. 1990) identified that women with early stage breast cancer who perceived that they were given a choice between mastectomy and breast conserving surgery, experienced less anxiety and depression than women who had no choice. Maslin (Maslin 1994) in her study of women attending a breast unit identified women's need for the following regarding clinical trials: verbal and written information, an indication of the time commitment, an outline of the information the trial will produce, probable and possible side effects of treatments, physical and emotional discomforts, the right to withdraw from the trial, and the need for on-going support and information.

Yet there is a body of evidence to suggest that patients do not perceive that they have a role to play in the decision-making process, or choose to adopt a passive role, reinforcing the power and status doctors have because of their assumed knowledge, expertise and social standing (Cassileth et al. 1980; Strull et al. 1984; Tobias 1988; Sutherland et al. 1989; Degner and Sloane 1992; Baum 1994). The skill lies with the healthcare professional's ability to identify the information requirements of each individual, and communicate the options available to them, in order that each individual is able to participate at a level that suits their requirements.

Baum (Baum 1993) considers that an organisation of well women could be drawn together to improve the treatment of cancers experienced by women such as breast and cervical cancer. They would be educated about cancers and about the need for randomised controlled trials to "*...exploit the latest developments in translating laboratory findings into novel and effective therapies.*" He argues that they could be

educated about the personal benefits of being involved in randomised controlled clinical trials. For example, improvements in clinical outcomes have come about because clinicians base their practice on series of trials rather than pursue treatments selected on the basis of individual clinical judgement, irrespective of any broad evidence. Women could be kept up to date with current listings of actively recruiting clinical trials, with the various treatments on offer, and with their scientific rationale. This would then provide a group of women who, should they develop cancer, not only expect to be offered entry into a randomised controlled trial, but perhaps even demand it, knowing that their chances will be better if they receive treatment from an expert clinician who is committed to controlled trials methods. Furthermore, at the time of diagnosis, they will no longer have to absorb masses of information about the nature of their disease, the need for randomisation, and the rationale for the various treatments on offer. There needs to be an acknowledgement that any information must be presented in a simple and straightforward manner. Stephenson advocates individuals invited to enter a randomised control trial be made aware that experimental treatments have given better outcomes (Stephenson and Walker 1996).

Decision-making

The attitudes and expectations of both clinicians and their patients have changed since the 1960s. Clinicians tend to be less paternalistic about what should or should not be disclosed to patients in their care, and patients tend to be more, although not necessarily better, informed about disease and treatment options through the media. There is a greater expectation for health professionals to involve the patient in the decision-making process (Bond and Thomas 1992).

There has been a growth in policy documents that emphasise the patient's perspective

regarding healthcare provision, for example the Patients Charter (DOH 1991c). There is an assumption that all patients should be provided with all information and given the time to consider the facts in order that they can arrive at an informed decision. This assumes that all patients have the same ability to understand information prior to making an informed decision regarding their treatment, and that clinicians are willing and able to communicate with patients and their families.

Maslin et al (1993) suggested that most women diagnosed with early breast cancer were rational, mature adults who were able to choose whether or not to be involved in the decision-making process regarding their disease. However Maslin (1994) later noted that healthy volunteers understood the implications of trial participation better than did those with cancer. Degner et al (1997) explored the information needs and decisional preferences of 1012 women with breast cancer in oncology clinics. 22% preferred to take the lead, 34% wanted the clinician to make the decision and 44% wanted to share the decision; the researchers found that less than half these women achieved their preferred level of control. Miller and Managan (1983 cited in Maguire 1999) referred to two groups of patients: information seekers (monitors) who try to find out as much information as possible, and the avoiders of information (blunters) who put up barriers to information provided. These are different coping mechanisms and it becomes the responsibility of the multi-disciplinary team to identify which one each patient is presenting.

The studies reviewed suggest that patients' willingness to be involved in decision-making varies considerably. It is the duty of the clinician to find out how much patients want to be involved, regardless of their disease status (Degner et al. 1997; Maguire 1999). This appears to be associated with the clinician's ability to communicate

effectively with their patients and vice versa (Fallowfield et al 1998; Maguire 1999).

Barriers to effective communication exist on both sides. Patients may be reluctant to disclose what they are feeling about their diagnosis, treatment options, and how these might affect their life - they believe that health professionals are not interested in their concerns. On the other hand, clinicians are concerned about patients asking difficult questions, displaying strong emotions, plus the difficulty of explaining complex information.

Work has been done using audiotapes of consultations allowing patients and their families to hear what was said in the consultation; whilst patients and families appreciate these summaries, there is conflicting information regarding their benefit. Hogbin and Fallowfield (1989) and Knowles (1992) were in favour, whilst others found the tapes did not improve recall or reduce anxiety and depression (Fallowfield, et al. 1998).

1.6 Clinicians position regarding recruitment to clinical trials

Overall, very small proportions of patients undergoing treatment for cancers take part in randomised controlled trials. One of the possible reasons for poor accrual is addressed by Slevin et al (1995) who found that, when patients were informed of a hypothetical randomised controlled trial for their disease, 42% agreed to participate, 48% were undecided, and only 10% refused. These data suggest that very low recruitment rates do not occur because of patient refusal, but that physicians fail to recruit, and the health system fails to make it easy for them to do so (Taylor et al. 1984). Cassileth et al (1982) suggest that clinicians assess patients before inviting them to participate in clinical trials, in order to reduce the numbers of people refusing to take part in these trials. Another important factor is in who controls the trial recruitment. Direct control by

the researchers is preferable since they may experience difficulties if they depend on others for recruiting. People who have the power to recruit potential participants can be very helpful, but others can be less so, and even obstructive. Reasons for antagonism include lack of interest, concerns about evaluating their own practice, concerns about the trial design, or the time required to enter an individual to a clinical trial.

Improved survival should not be the only end-point of interest in randomised controlled trials; improved quality of life and/or decreased toxicity is also important. One method of assessing if a clinical trial is important is to ask expert clinicians if they would agree to enter into a randomised controlled trial if they had a disease that would render them eligible. One such study looked at options of radical prostatectomy and radical radiotherapy for T2 prostate cancer (Freedman, 1987) with about 50% of physician surrogates opting for each, suggesting that a randomised controlled trial which compared these strategies was of critical importance. Unfortunately, respondents had such strong personal bias that only 30% would have agreed to enter themselves on such a trial. When the results of the survey were presented to the respondents, 58% stated that they would be willing to offer the trial to an eligible patient. But how successful would recruitment be in the face of this personal bias (Moore et al. 1990).

One of the most common reasons that a cancer patient is not enrolled in a trial is that the patient's clinician made the decision not to enter the patient in the trial (Swanson and Ward 1995). Generally these issues are related to the clinician's concern for the patient, concerns about the conduct of studies and concerns about the clinicians' roles. The three major barriers seem to be the time and effort required for both the clinician and the patient to participate in trials, concern that the trial may interfere with the doctor/patient relationship, and conflict between the clinician's dual roles as caregiver

and as scientist. With regard to the last issue, many clinicians experience both cognitive and emotional tension between the role they define as that of the clinician, which places the interests of the individual patient first, and the role they define as that of scientist, which places the benefit to humanity in general first (Taylor et al. 1984; Freedman 1987).

Eligibility criteria of clinical trials need to reflect the patient population. Multi-disciplinary teams of researchers should be involved in the planning, recruitment, and study design phase to ensure that complete information about the study population is obtained. In addition to clinicians and nurses, these study teams should include psychologists, anthropologists, epidemiologists, and biostatisticians, with a focus on removing the barriers to participation among the target populations. Others have endorsed the inclusion of patients to the committees planning clinical trials (Farrell 1998; Hanley 1999).

1.7 Lay position regarding recruitment to clinical trials

Women's attitudes and beliefs towards breast cancer have been extensively studied (Fallowfield and Clark 1991; Moch 1995) and described (Thornton 1997; Picardie 1998). The fact that women want to be properly informed does not imply that they want to be responsible for the final treatment decisions (Hack et al. 1994). Yet little is known about women with breast cancer (or those that have high risk of breast cancer) and their views of clinical trials, how women make the decision to participate (or not) in clinical trials, and women's decision making about research and treatment options (Fallowfield et al. 1998). There is a requirement to identify their views regarding why there is low recruitment to clinical trials, including their concerns about clinical trials, their reluctance to be randomised, and their difficulties in accepting and understanding

clinical uncertainty.

There is literature relating to the clinician's perspective of why patients participate in clinical trials. They perceive patients' preferences for participation vary widely with some patients choosing to play an active role and others a passive role (Waterworth and Luker 1990; Degner et al. 1997; Maguire 1999). Fallowfield et al (Fallowfield et al. 1998) also examined the attitudes of patients to randomised controlled trials. 91% stated they should be asked about their willingness to enter a randomised controlled trial; 77% said they would participate in a randomised controlled trial if it compared two treatments; 45% stated they would participate in a randomised controlled trial, although the remaining would consider participation in a randomised controlled trial if it were explained properly.

Patients' concerns are in three general categories. These are the time and inconvenience associated with participating, negative personal and family attitudes regarding clinical trials (such as interventions or side effects that are seen as unpleasant), and inadequate evidence of benefits from trial participation, including the belief that the clinical investigator is more concerned about the trial than about the patient. Studies suggest that women's experiences are enhanced when there is evidence of staff-patient communication, patient involvement in decision-making, the provision of clear and relevant information and sufficient opportunity for questions and expressions of concern (Degner and Sloane 1992; Hack et al. 1994; Maslin 1994; Degner et al. 1997; Fallowfield et al. 1998).

Some studies have found that public attitudes and expectations to trial participation are favourable (Cassileth et al. 1982; Slevin et al. 1995). Stiller (Stiller 1992; Stiller 1994)

comments that for trial participants, outcomes tend to be better, irrespective of the arm of the trial to which they are assigned, than those receiving ad hoc treatment outside such a trial. Reasons for participating in clinical trials include the expectation of receiving better care through better access to specialists and facilities, more frequent visiting and closer monitoring, little or no waiting at clinic visits, closer relationships with staff, increased receipt of information, the opportunity to discuss other health and social problems, altruism and benefiting future generations (Hart 1993; Dongen and Velde 1996; Bottomley 1997; Wilson and Rose 1998).

The rhetoric of user involvement has featured in health policy documents for over a decade (DOH 1989; DOH 1991c; DOH 1997; DOH 1998b; DOH 1998c). In the United Kingdom there has been a spate of policy directives emphasizing the role of the consumer in determining, shaping and evaluating health services. In addition, there is a requirement to evaluate the effectiveness of services from the user perspective, including an annual national survey of user experience. In future,

“...the health service will measure itself against the aspirations and experiences of its users.” (DOH 1997 p 66).

User involvement incorporates a range of relationships between those providing healthcare services and those who receive them, from simple information giving through to user participation in decision-making. Patient participation in various aspects of healthcare is rapidly expanding; their involvement in decision-making takes a variety of forms from activity in patients' association through to healthcare commissioning. Healthcare professionals are increasingly being required to demonstrate that their care is patient sensitive and needs led. Smith refers to this: *“...as the balance of power in*

the doctor-patient relationship shifts towards the patient." (Smith 1997). The call from the government (DOH 1998c) is for participative research involving patients, carers, and the public, in healthcare decision-making.

1.8 Summary and conclusion

In summary this review of the literature has shown that recruitment to randomised clinical trials continues to be a problem. The ability of a clinical trial to deliver a valid result depends upon the recruitment of eligible people who fit the trial criteria and volunteer to participate in the trial. Although many are eligible to participate in clinical trials of cancer therapy, accrual in clinical trials of cancer treatment is very low (Ward, Fielding et al. 1992; Fallowfield, Radcliffe et al. 1997).

There appear to be three factors that can inhibit the clinical trial process. These are firstly, that the trial design may influence accrual because of designs with a no treatment arm, arms of unequal attractiveness, the process of informed consent, and the clinician's method of presenting the trial. Secondly, clinician related variables such as their attitude to trials, their motivations for recruiting patients, screening patients prior to recruiting, and difficulties with equipoise may lead to a lack of commitment in presenting the trial to eligible patients. Finally, patient-related factors including patients' decline of random allocation to treatment and exclusion on clinical grounds.

Chapter 2 identifies the research questions that arise from this review and how the research planned to bridge the gap and add to the existing knowledge.

CHAPTER 2 RESEARCH DESIGN

- 2.1 Introduction
- 2.2 Towards and refining research questions
- 2.3 The research context
- 2.4 Methodological considerations
- 2.5 Research design
- 2.6 Ethical considerations and procedure
- 2.7 Summary and conclusion

CHAPTER 2 RESEARCH DESIGN

2.1 Introduction

The use of clinical trials are vital in evaluating new treatments for individuals with cancer but the review of literature has revealed that there are problems associated with recruiting patients to clinical trials, which this research addresses. This chapter reviews the research design and is in two parts; the first part places the research in context by stating the research aim and the research questions and describes the two breast cancer clinical trials studied. The second part identifies the methodology, research design, methods of data collection, ethical considerations and the negotiation of access for the research.

2.2 Towards and refining the research questions

The research questions aim to add to existing knowledge regarding why people participate in clinical trials and what might improve recruitment. By identifying these factors guidelines for best practice may be developed for use by multi-disciplinary teams. For this research an examination was made of two randomised controlled clinical trials - a treatment trial, the British Association of Surgical Oncology (BASO) II trial and a prevention trial, the International Breast cancer Intervention Study (IBIS). These are both established and were chosen for closer examination because they have experienced difficulty in recruiting sufficient numbers of patients.

Most studies regarding recruitment to clinical trials are either commentaries or descriptive analyses focusing on the roles of clinicians, clinics, and hospital in-patient accrual rates. When patient attributes are discussed, information provided rarely moves beyond demographics and exclusion criteria. There has been an increasing

interest and recognition of the role users of health services have to play in the development of the NHS (Hanley et al. 2000). With an emphasis on the importance of patients' involvement in decision-making; their views can be used to develop policies and practices that meet their needs as well as the requirements of the service.

Aim

The aim of this research was to identify the factors influencing the recruitment of patients into clinical trials, by examining the recruitment to two clinical trials for breast cancer, from the perspective of both the healthcare professionals and the patient, and to make recommendations on how recruitment might be improved.

Research questions

1. What are the factors affecting the recruitment of women to breast cancer clinical trials from the:
 - a) Surgeon's perspective?
 - b) Multi-disciplinary teams' perspective?

2. What are the views of women who are approached to participate in a clinical trial, and what are their reasons for participating or not participating in the clinical trial?

2.3 The research context

The two breast cancer clinical trials examined had both experienced, at sometime, difficulty recruiting women.

The first was simple and ethically uncomplicated, the British Association of Surgical Oncology Trial II (BASO II) which investigated the treatment of small, well-differentiated,

node negative tumours of the breast. The second, the International Breast cancer Intervention Study (IBIS), coordinated by the Imperial Cancer Research Fund (ICRF) and the Cancer Research Campaign (CRC), is a trial of well women, who have a higher than normal risk of breast cancer identified by their familial history and has the ethical problems of administering medication to well women.

Background to the British Association of Surgical Oncology II (BASO II) trial

Trials of breast screening demonstrate that well-differentiated tumours are found in a high frequency in the screened population (BASO Breast Group, 1995): 30 per cent are found to be well-differentiated, node negative and measure less than or equal to 2 cm in diameter. Although the prognosis, in terms of survival of such tumours is excellent (Dixon, 1985; Ellis, 1992), there remains the danger of local relapse in the treated breast when treatment includes breast conservation. Prior to the BASO II trial, standard treatment was to administer radiotherapy to the affected breast following complete excision of the primary breast cancer. Many surgeons also gave Tamoxifen for 5 years after surgery, which has been effective in deferring recurrence of breast cancer (Early Breast Cancer Trialists' Collaborative Group (EBCTCG) 1998).

These treatments have a number of effects. For example, in the case of radiotherapy an increased workload for clinical oncologists and radiotherapy departments; patients' incur time and travel costs during radiotherapy treatment including obtaining time off work or other responsibilities for treatment; and the side effects of radiotherapy.

Treating women with breast cancer with radiotherapy reduces local recurrence in some women, whilst the majority do not require this treatment (EBCTCG 2000).

Considerable savings might be made to the NHS if those women who do not require radiotherapy could be identified.

The BASO II trial tests whether radiotherapy is necessary for breast cancer of low aggressive potential following breast conserving surgery. These cancers carry the best possible combination of prognostic factors: a histological grade 1 tumour, tumour size not greater than 2 cm, with no axillary lymph node involvement. BASO II trial has a 2x2 design so that those centres recruiting women to the trial do not have to enter into all 4 treatment arms - there is an elective element in that clinicians can choose which arm of the study to randomise women. This provides clinicians with a degree of choice:

- wide local excision and Tamoxifen (centres could elect to give radiotherapy, or not give radiotherapy);
- wide local excision and radiotherapy (centres could elect to give Tamoxifen, or not give Tamoxifen);
- wide local excision and radiotherapy and Tamoxifen.

The primary outcome measure for the BASO II trial is local recurrence in the treated breast. Secondary endpoints include regional recurrence, distant recurrence, death from breast cancer and the incidence of contralateral breast cancer.

This trial was selected for this study because:

- i. breast surgeons are an accessible group, identifiable through the BASO breast group;
- ii. there is a ready supply of women with these tumours; and
- iii. the trial initially experienced slow recruitment and between February 1992 and December 1996 only 460 women had been recruited (out of a target of at least 800).

Background to the International Breast cancer Intervention Study (IBIS)

IBIS is a preventative trial, to evaluate the reduction in incidence from breast cancer, associated with taking Tamoxifen daily for five years. The IBIS trial forms part of an international study but the focus will be on United Kingdom recruitment only.

Tamoxifen is a widely and successfully used drug in the treatment of breast cancer, but its efficacy in the prevention of cancer is unknown. Some breast cancers are dependent on oestrogen and Tamoxifen blocks the effect of oestrogen within breast tissue (Baum et al. 1994), and may by this hold back the growth of breast cancer. It may also affect the development of tumours in the contralateral breast and this is the rationale for the study. All women joining the study are asked to take medication or placebo for five years, half receive Tamoxifen 20mg daily and half receive an inactive placebo.

IBIS aims to recruit 7000 women worldwide who are at higher risk than normal of developing breast cancer.

a. Women aged 45-70 years, with one or more of the following:

- a mother, sister or daughter who has had breast cancer at the age of 50 years or younger;
- two close, blood relatives who have had breast cancer at any age;
- a biopsy of the breast showing pre-cancerous changes (atypical hyperplasia or lobular carcinoma in situ).

b. Or, women aged 35-44 years, with one or more of the following:

- a number of women in the family (blood relatives) who have had breast cancer;
- a mother or sister (blood relative) who has had breast cancer at the age of 40 or less;

- a biopsy of the breast, showing pre-cancerous, changes (atypical hyperplasia or lobular carcinoma in situ).

The primary aim of the IBIS trial is the incidence of breast cancer in women taking Tamoxifen daily for five years, versus placebo.

This trial was selected for study because:

- I. breast surgeons are an accessible group, identifiable through the BASO breast group;
- II. the study had experienced slow recruitment (between 1993 and 1996, in that only 1727 women had been recruited to IBIS in the UK);
- III. the contrast in the ethical issues compared to the BASO II trial.

2.4 Methodological considerations

In the past there had been an emphasis on the quantitative approach to health services research that produced statistical data; it was the preferred approach by policy makers and the funders of research (Pope and Mays 1993; Ong 1993; Avis and Robinson 1996). With the influx of other researchers into the health field, such as medical sociologists, there has been a growth in the use of qualitative research and data being used to validate and confirm the findings generated by the quantitative methods (Murphy et al. 1998; Popay and Williams 1998). Funders have begun to actively encourage researchers to use a range of methods and theoretical perspectives when submitting proposals for review.

Quantitative and qualitative research methodologies have been seen as being opposed to one another; yet there are differences of opinion and methods within each of these approaches (Silverman 2000). Increasingly, there has been a move toward the

recognition that different methods of data collection can be complementary to the research process rather than exclusive (Popay et al. 1992; Pope, 1995a; Mays, 1995b; Murphy et al. 1998).

Strengths and weaknesses of quantitative and qualitative methods

The strengths of an experimental design are that they provide sufficient information about the relationship between variables under investigation to enable prediction of and control over future outcomes (Clifford, 1997). The positivistic approach represents the historical dominant tradition and can provide evidence on causal relationships, the testing of hypotheses, the capacity to compare interventions and to generate confidence levels for the effect of estimated values, uncovering influences and patterns of interactions (Wilson-Barnett, 1991). Randomised controlled trials are an example of a quantitative research approach adopted by the medical community to test drugs and surgical procedures, an experimental design used to demonstrate the most appropriate treatment (Doll 1998). The quantitative approach is seen as value free and objective, where the emphasis is on a deductive approach, where empirical data is collected and used to test a hypothesis.

This perceived strength can also be seen as a weakness, in that the experience of the individual, the organisation where they work, and the interaction that occurs between different groups maybe missed or dismissed as unimportant (Popay and Williams 1998).

The strengths of qualitative techniques are that they are able to elicit individual perspectives (Bowling 1997; Denscombe 1998). The relationship between the researcher and the subject can be seen as a strength, allowing the researcher to obtain

first hand experience of the subject, consequently adding meaning to the data (Oakley 1981; Robson 1993; Murphy et al. 1998). Qualitative researchers utilise techniques that allow the subjects of the study to provide accounts of their actions, without imposing any pre-defined criteria (Popay and Williams 1998). Bryman (1988) argues in its favour, that the more time the researcher and the subject spend together; the more the data are likely to be honest and valid.

The weakness is that a qualitative approach can be seen as unscientific, personal, biased and journalistic. Qualitative research methods recognise that subjectivity cannot be eliminated, but that they allow the research participants to raise issues and topics that the researcher may have not included, had a more controlled research design been chosen (Murphy et al. 1998; Popay and Williams 1998). Qualitative researchers aim to immerse themselves in the social worlds of those they are researching and their experiences, without imposing the barriers of formal theory or preconceived typologies between themselves and the participants.

A qualitative approach can contribute to enhanced communication among those involved in the research, but the objectivity of the researcher must not be lost, otherwise the research may lack rigour and reproducibility (Bryman, 1995; Murphy et al. 1998). The researcher, by being systematic in the research design, collection, interpretation and communication can overcome these by keeping concise, detailed records of interviews and observation, and reliability can be assured. Finally, validation can be achieved by providing feedback of the research findings to the participants in the research, to ensure the inference reflects their experience (Pope, 1995a; Mays & Pope, 1995), reducing the chance of researchers imposing their views on the people being researched.

Mixed methods approach

The aim of this research was to appraise recruitment to breast cancer clinical trials from the different perspectives of consultant surgeons, multi-disciplinary teams and patients, with different aims and priorities, at different levels. Increasingly researchers working in the complex field of healthcare are acknowledging the advantages of adopting a mixed method approach to their research. To adhere to one research approach would have been inappropriate in work that aims to undertake a number of phases, each assessing the process, impact and outcome for a specific group. In order to address different research needs, by using a number of different methods for data collection, the researcher may be able to meet the requirements of these different situations. A mixed methods approach, can provide a greater variety of individual experience, generating new insights, a more comprehensive understanding of the factors affecting recruitment to breast cancer clinical trials, not easily reached by one method alone.

The approach taken has been that of the multi-method approach applying the principles of triangulation. According to Denzin (Denzin, 1978) any study reliant on only one data source is method bound. Triangulation is defined as:

“...the combination of methodologies in the study of the same phenomenon.”

(Denzin, 1978 p291)

Triangulation maximises the strengths and weaknesses of each research approach. In some senses different research methods such as questionnaires, interviews, observations and documents could be seen as competing with each other (Denscombe 1998); yet they can be combined to complement one another. The more dissimilar the

methods used, the more likely they are to make up for the weakness of one another. Thus triangulation can result in the creation of deeper and richer research findings, enhancing the completeness and comprehensiveness of the data. This research utilises between methods triangulation; where a quantitative approach (the use of questionnaires and statistical analysis), is combined with a qualitative approach (in-depth interviews and focus groups utilising content analysis), thus strengthening the credibility of the data and its external validity. Where convergence occurs the researcher can be more certain that this is a more accurate reflection of the truth. Where conflict arises, the researcher cannot be sure whether the differences are because of the methods chosen or other factors (Murphy et al. 1998). This approach can present difficulties, such as combining and comparing data collected from different sources. Though, through the use of multiple methods, multiple sources of data and different perspectives, rigour, depth and breadth can be ensured (Denzin 1978; Denzin and Lincoln 1998; Popay and Williams 1998; Denscombe 1998).

2.5 Research design

To investigate the experience of recruitment to the two clinical trials each study was divided into three phases. In phase one the views of consultant surgeons were sought using questionnaires. The findings from the questionnaires led to the development of an interview schedule for the second phase of the study; this focused on the development of questions to reflect the issues raised in the questionnaires and the literature to enable the collection of data from the multi-disciplinary teams, and an audit to examine the recruitment before and after feedback from the research. The final phase involved interviewing women who had been approached to participate in the clinical trial to elicit their opinions. The three phases were replicated in both of the breast cancer clinical trials under investigation.

Description of research method chosen

Questionnaires

The first phase involved the collection of data by means of a self-completed questionnaire by clinicians. This provided the base line for information regarding accrual to clinical trials. Subsequently, this information was used in the planning of in-depth, semi-structured interviews with the multi-disciplinary teams and women's focus groups. Using self-completed questionnaires allows large numbers of respondents to be approached; the method is cost effective and not as time consuming as other methods (Edwards et al. 2000). Questionnaires can offer anonymity to the research participants and avoid interviewer bias in the responses - reliability and validity are more likely to be achieved with questionnaires as opposed to interviews. The problems associated with questionnaires are that respondents may be constrained by the use of closed questions and do not have the opportunity to ask the researcher questions, which are often associated with poor response rates; there is little or no opportunity for the researcher to clarify returnees' responses.

Questionnaire formulation

The process of questionnaire design requires careful consideration of the purpose of questions and the data they seek to gain (Denscombe 1998; Robson 1993). The decision was made to devise a questionnaire. From the literature review a few existing questionnaires were identified as being of potential benefit, because they had previously been used with clinicians, and so some questions were used in the questionnaire (Taylor et al. 1994). Closed and open questions were employed; closed questions were to minimise the time required to complete the questionnaire, and open-ended questions were also incorporated to allow the respondents to express opinions.

Special consideration was given to the format of filter questions, which routed respondents through the different sets of questions. This approach enabled the collection of numerical and measurable data, amenable to statistical analysis.

The questionnaire was in four sections (see Appendices A and B). The first section collected data on consultant surgeon's general views on clinical trials and on the number of clinical trials entering patients at their centre. The second section examined their reasons for joining, or not joining, the trial. Only those centres registered to enter patients to the trial were asked additional questions, in the third section, regarding their method for identifying and approaching eligible women; the difficulties encountered in entering eligible women into the trial. The fourth section included an estimation of their recruitment rate over the previous twelve-month period, and their expected recruitment for the next twelve months. A statistical package SPSS Version 9.0 for Windows was used for analysis of the questionnaires.

Sample to be sent the questionnaires

All BASO nominated breast group surgeons (n=118) were identified through the 'Quality Assurances Guidelines for Surgeons in Breast Screening' (NHSBSP & BASO 1996).

These nominees are responsible for the treatment of women detected with cancer through the NHS breast screening programme and for the collection of data on breast screening at each centre in the United Kingdom. They could be expected to have an interest in the scientific evaluation of breast cancer treatments, and to see numbers of women with cancers eligible to be entered into the BASO II and IBIS trials. They are also local specialist breast surgeons, to whom women with a family history of breast cancer are referred for advice.

Phase 1: Questionnaire implementation

Questionnaire for the BASO II trial

Phase 1 was to elicit clinician's opinions regarding clinical trials. A questionnaire was sent in February 1997 asking the surgeons for their views on clinical trials, the number of clinical trials of adjuvant treatment currently offered at their centre, their experiences of joining the BASO II trial or their reasons for not joining (Appendix A). Surgeons who were randomising patients into the BASO II trial at the time were asked further questions about their method for identifying and approaching eligible women, the difficulties they experienced in entering eligible women into the trial, and for an estimation of their recruitment rate during the previous 12 months.

Questionnaire for the IBIS trial

A second questionnaire was sent in August 1998 to the same surgeons, and to a further four centres recruiting women to IBIS, who were not local screening surgeons. This questionnaire replicated the questions used in the BASO II questionnaire on clinicians' views about clinical trials, the number of clinical trials currently offered at their centre, their experiences of joining IBIS or their reasons for not joining (Appendix B). The clinicians randomising women to IBIS were asked further questions about their method for identifying and approaching eligible women, the difficulties they experienced in entering eligible women, and their estimated recruitment rate in the previous 12 months.

The data from the questionnaires were analysed using SPSS version 9.0. Each column was labelled using the questions from the questionnaire and the data entered directly from the questionnaires. Initially, the code (.) automatically assigned by SPSS was used for missing data; this was not satisfactory therefore missing values were coded: 999 (question not completed), 555 (all options ticked) and 333 (centre not registered for

the trial). The data was checked for errors visually and by undertaking random checks of the questionnaire; a number of inaccuracies were identified.

The data was analysed using descriptive statistics, which highlighted patterns and trends. All the percentages were rounded up or down to the nearest whole number.

Phase 2: Interviews with multi-disciplinary teams

Semi-structured interviews were chosen to explore factors affecting recruitment to clinical trials with a number of multi-disciplinary teams, who had completed the questionnaire in phase 1. The interview can be viewed on a continuum, at one end is the structured interview where the wording and order of the questions are the same for each respondent; at the other end is the unstructured, in-depth interview which allows the respondents to talk about the subject using their own frame of reference (May, 1993; Fontana, 1994). Semi-structured interviews were chosen because they allow the researcher to pursue the aim of the research, while facilitating the interviewees to provide their experience and perspectives of recruiting women to the trials - an effective means for collecting information regarding opinions and perceptions (Fontana and Frey 1994). The possibility of misinterpretation by the interviewee can be minimised as the interviewer can check responses. Finally, observations made by the researcher during the interview may be a further source of information.

The interview schedule was developed using issues raised in the questionnaire. This allowed the researcher to pursue these lines of enquiry in greater detail and depth, thus complementing the questionnaire data. The schedule was piloted locally, and where necessary, adjustments made (Appendix C & D).

Interviewing requires interpersonal skills by which the subject is put at ease, questions are asked in a manner, denoting interest, and the researcher is supportive without introducing bias. The researcher's experiences as a nurse, lecturer and researcher have helped developed these skills. Participants were encouraged to speak freely on the factors affecting recruitment. Anonymity and confidentiality were assured in writing and verbally; the interviews took place in a location that avoided interruption. The duration of the interviews ranged from 45 minutes to 120 minutes. Tape recording of each of the interviews ensured accurate verbatim data and allowed the researcher to concentrate and attend to the participants fully, observing the non-verbal aspects of the interview. The presence of a tape recorder can inhibit respondents, but this was not evident and none of the multi-disciplinary team interviewees refused to have interviews recorded.

The researchers needed to be aware of their own influence on the interview in terms of their interaction with participants. It is not possible to have a completely bias free research process and the researcher needs to recognise and acknowledge possible sources of bias, and that they only portray the 'truth' as they interpret the information provided by the interviewee at that time. Individuals will provide different descriptions of the same experience, and their perspective may change over time. Selective reporting may occur, particularly in the group setting where interviewees might be reluctant to reveal their personal opinions. The strengths of the interview technique and information gathered outweigh any inherent method weakness.

An independent professional transcribed the interview data. The accuracy of the transcripts were checked and corrected against the recording. There are computer packages available for the analysis of qualitative data for example Non-numerical

Unstructured Data Indexing, Searching and Theorising (NU.DIST), Atlas and Ethnography. These were considered, as data can be quantified, however these were disregarded for a more traditional approach because the majority of interviews were group interviews; the quantifiable element of the package could be applied, but it would have no meaning, as it would not represent the group perspective, only an individual comment. Analysis of the information was by a combination of methods. Norman et al (Norman et al. 1992) suggests the use of inductive classification of the information and the construction of a hierarchy of categories that enables the information to be described at increasing levels of specificity, and thematic content analysis (Burnard, 1991; Robson 1993; Ritchie and Spencer 1994). The analysis of qualitative data is a highly personal activity involving interpretative and creative processes while trying to ensure that the results represent the participants' world as they see it. Notes were made on the general themes emerging from each of the transcripts; these were coded. When generating categories and themes, the researcher was mindful of bias and so these were externally verified.

Multi-disciplinary team selection

The 21 multi-disciplinary teams selected for interview were chosen from those centres, which responded to the questionnaires. The interviews were to investigate the group's experiences of recruiting women to clinical trials and allowed exploration of points raised in the questionnaires in greater depth.

Visits and interviews took place at 14 centres recruiting to the BASO II trial and 7 centres recruiting to IBIS, across the UK. Each centre was classified according to their own estimation of recruitment rate to the clinical trial, identified in the questionnaire as good, medium and low recruiters. Members of the multi-disciplinary team were

interviewed using a semi-structured, in-depth interview schedule in either a group or individual setting. The questions were open-ended and the same format was used with each interview. The interviews developed a structure of their own depending on the interactions within the group; there was a degree of flexibility, to explore the subject and draw out meanings (Ely, 1997).

These interviews were tape-recorded and lasted between 45 and 120 minutes, and were professionally transcribed. These were independently analysed and the main themes agreed, with independent researchers.

Retrospective and prospective audit

The retrospective and prospective audit was to identify the number of women eligible for recruitment to both clinical trials. Retrospective studies are a descriptive survey of a population at a particular point in time, usually looking back to before they entered the study (Bowling 1997). Criticisms have been made regarding the difficulty of establishing an association in retrospective studies (Robson 1993; Bowling 1997).

Prospective studies are analytical surveys that take place over the forward passage of time (Bowling 1997). The aim in this research was to identify the numbers of eligible women for both the clinical trials, and ascertain, where possible, women's reasons for participating or not in each of the two trials.

The retrospective and prospective audit undertaken was different for each of the two trials examined. The primary aim was to use the retrospective audit to establish the numbers of eligible women for the two breast cancer clinical trials. The findings would provide a basis for the third phase of the research. A secondary aim was to test whether there were difficulties obtaining appropriate pathology reports for the BASO II

trial; the number of true, eligible cases for the trial could be identified by examining the individual patient record, the breast care/research nurse records, and the pathology database. The same method could not be used for IBIS because women eligible are found or referred by the IBIS co-ordinating centre in London.

The audits used multiple sources including nursing and medical records, pathology data, and the BASO and IBIS databases, to identify and compare the number of eligible women for both trials. The number of women actually recruited to the trials and, where recorded, the reasons for women not participating in the trials. Analysis was undertaken using SPSS.

Retrospective audit: the BASO II trial

With the BASO II trial a retrospective study of six months practice (1 July to 31 December 1997) in each of the fourteen centres was undertaken. All suitable cases diagnosed over the period were identified from the pathology database, breast screening data and patients clinical notes. Having identified the eligible women, where possible their records were accessed and the reasons for women not being recruited to the BASO II trial were identified. A validity check was undertaken by comparing the numbers of women recruited to the BASO II trial by the 14 centres, with the actual numbers of women randomised and entered according to the BASO database. Thirteen of the 14 centres provided data for analysis, with one centre still waiting for LREC approval to retrieve data from their pathology database.

Following the retrospective analysis and the findings from the multi-disciplinary team interviews, written general and specific feedback were given to the fourteen centres on how they might improve recruitment to the BASO II trial.

The prospective audit included the use of a form devised to identify all eligible women for the trial, and if the women refused to enrol on the trial their reasons documented. Comparisons were made between the retrospective and prospective audits to see if recruitment to the trial was increased.

Retrospective audit: the IBIS trial

The method adopted for phase 2 for IBIS differed. There was no facility for identifying all potential women for IBIS in each of the centres, instead a six-month retrospective analysis of recruitment in the seven centres was undertaken using the IBIS national database. Following interviews with the multi-disciplinary teams, in the seven centres about their recruitment, a national recruitment facilitator was appointed by the IBIS trial organisers; the aim was to improve recruitment to the trial. Six months after that appointment a prospective audit was undertaken, and a comparison made to establish if recruitment to the trial had increased following the development of this new post.

Phase 3: Focus groups with women

The final phase included focus groups with women from different centres in the United Kingdom who had been approached to participate in either the BASO II or IBIS trials. Previous research regarding the recruitment of patients to clinical trials has tended to focus on the clinician perspective rather than seeking the views of the subjects. There is an increasing emphasis on public accountability, quality, efficiency and cost effectiveness of health services (Coulter 1991) - feedback from users is one method of measuring effectiveness. Opinions and experiences of women invited to participate in these two breast cancer clinical trials were sought, including women randomised and women who refused to enter the trials. The purpose was to gain an understanding of

women's experience of being approached to participate in a clinical trial, participating in a clinical trial, discuss their views of the service; and elicit their suggestions of how the service might have been improved.

Focus groups are described as:

"...a carefully planned discussion designed to obtain perceptions on a defined area of interest in a permissive and non-threatening environment". (Krueger, 1988 p6).

A facilitator leads the group, ensuring that the group remains focused on the issue being discussed. They differ from other group interviews by the use of the group interaction as research data (Morgan, 1988; Kitzinger, 1994; Kitzinger, 1995). Focus groups have remained a popular method in both the social sciences and for market research (Dilorio, 1994; Macleod Clark, 1996). In healthcare, focus groups have been used to elicit clients' and carers' experience of their illness and the health service (Kitzinger 1994; Kitzinger 1995; Owen 1999).

Focus groups were the chosen approach because of their strengths, and can provide a safe environment for people to share thoughts and feelings without criticism.

Compared to an interview, the focus group is a method where the participants can interact with each other, rather than with the facilitator, emphasising the women's perspective rather than the researcher's (Morgan, 1988; Krueger, 1988). Focus groups can extend the tradition of women sharing personal information with other women, and participants often enjoy their discussions (Kitzinger, 1994). The facilitator is to ensure that women can represent a range of views, and to encourage them to feel able to

introduce issues that concerns them as users of healthcare services. An advantage of the focus group is that it does not discriminate against individuals who cannot read or write.

There are number of weaknesses related to these groups. Obtaining consensus in the group may not be possible, and if an individual in a focus group does not have a personal opinion, the group may influence and make her feel pressurised to adopt the group opinion (Janis 1982). Focus groups may exclude people who are reluctant to talk in front of others, or do not speak the common language. Finally, they rely heavily on the skills and attributes of the facilitator.

Running focus groups

The group should be between four and twelve people (Morgan, 1988; Kitzinger, 1995), less than four people in a group might not generate sufficient discussion and more than twelve people would not permit adequate participation by all group members. Over-recruiting by 20-50 percent should provide an adequate margin of safety for non-attendance (Macleod Clark, 1996).

Some of the literature recommends random sampling for focus groups (Morgan 1995), however this is not feasible where the numbers being invited to participate are small and that focus groups are not representative random samples. For this study women with breast cancer and women with a familial history of breast cancer were invited to participate in separate focus groups; therefore non-random sampling for representativeness was adopted when selecting women.

A number of authors recommend that the group be homogeneous, as this can help make the participants feel more at ease with each other and more willing to express

personal views without feeling inhibited (Dilorio, 1994; Macleod Clark, 1996; Kitzinger, 1995; Morgan, 1988). Homogeneity can lead to dissuading participants from expressing views that differ from the majority, where group harmony takes priority over individually held views (Janis, 1982). The number of focus groups held should be determined by the amount of new information obtained at each group; at least four groups should be held, beyond this there can be repetition (Basch, 1987; Nyamathi-Shuler, 1990; Kitzinger, 1995).

The facilitator of the focus group is usually the key researcher, who guides the discussion and ensures that the data generated meets the research objectives. The researcher should be knowledgeable but not 'all knowing' for this might lead to deference towards the facilitator's opinion and inhibit the flow of the group. The facilitator needs to make clear from the outset that confidentiality is ensured. The facilitator's role involves gaining quality data through making the focus group participants feeling comfortable, enabling them to express their views as well as listening to the views of other group members. A co-facilitator can assist the facilitator by carrying out other functions including handing out refreshments, monitoring recording equipment and taking notes. They can record the different forms of communication that occur within the group including interactions (both verbal and non-verbal), jokes, anecdotes and any argument.

The location for the focus group needs to be accessible to all participants and be a non-threatening environment. Distractions are to be avoided and the room should seat everyone comfortably. A circular seating arrangement will allow the participants to see all members of the group as well as fostering a feeling of equality.

Discussion should be tape-recorded, with informed consent for discussion and recording obtained. The complexity of the material, together with the number of different participant voices, accents, background noise, and people talking at the same time, all add to the difficulty of transcription. In a focus group, it is the group not the individual that is the unit of analysis. This further complicates transcribing of the audiotapes because the transcriber must ensure that nothing is taken out of context. Kitzinger (1995 p301-302) highlights the:

“...need to indicate the impact of the group dynamic and analyse the sessions in ways that take full advantage of the interaction between research participants.”

The disadvantages of the focus group are largely practical. The groups are time consuming to arrange, run and transcribe. Careful and rigorous planning is essential for focus groups to run smoothly. Difficulties associated with the interpersonal dynamics, such as ‘groupthink’, clashes of personalities, dominant people and the more reserved participant is the responsibility of the facilitator.

Focus group sample selection for BASO II trial

Four centres recruiting women to the BASO II trial were approached to participate in this phase of the research and included centres that were good, moderate and poor recruiters. MREC approval was obtained and LREC approval was sought from each of the centres, approval was achieved in three of the centres. In one centre, the consultant surgeon failed to pass on the protocol form to the LREC. The committee had received the completed forms from the researcher, and approved the research. However, in spite of frequent reminders the consultant surgeon had not forwarded the necessary information to the LREC, and at the time of writing the researcher has still

not obtained approval.

Four focus groups and three individual interviews were held with women randomised to the BASO II trial – a total of twenty-one women. A further eleven individual interviews were undertaken with women who had been invited to participate in the BASO II trial but had refused. There was a further letter from a woman, giving her reasons for not joining the trial.

Focus group sample selection for IBIS

The original aim had been to undertake four focus groups with women in IBIS; instead the number who responded to the letter of invitation exceeded expectations. The researcher could have excluded the extra women (Macleod Clark, 1996) but a decision was made to include all those women who volunteered. The reasons for this were:

- The women's enthusiasm and their wish to take part in the focus group discussion.
- The group would provide women with an opportunity to meet other women in the trial.
- The data from the focus group would provide an in-depth analysis of these women's experiences.

Discussion guidelines were developed for the two different trials. The same guidelines were used for individual interviews with women. The guidelines were piloted with a group of women prior to conducting the groups and changes made (A copy of the focus group discussion guidelines can be seen in Appendix E). These consisted of a list of open-ended questions designed to explore and elicit information on how women were approached to participate in the clinical trial, why they decided (or not) to participate, and how they felt about being involved. The guidelines allowed additional questions to

be asked, and for women to introduce their own questions.

2.6 Ethical considerations and procedure

It is important to ensure that participants are fully aware of the implications of the research of which they are a part. The execution of the research must be dependent on the participant's informed consent.

Negotiating and gaining access

The research covered a number of different sites across the United Kingdom, and required the negotiation of access to the multi-disciplinary teams and the women in their care. This was not straightforward. The Professor of Surgery at Nottingham City Hospital was one of the lead researchers in the initial research project, and was very supportive of the need to identify why so few women were recruited to breast cancer clinical trials. Permission to invite the multi-disciplinary teams to take part in the research project was sought via the BASO nominated surgeons in each centre.

Ethical approval for the focus group interviews with the women was applied for and obtained from MREC. Permission was sought from the consultant surgeons responsible for recruiting women to these two clinical trials, before securing LREC approval at each centre accessed. This was a time consuming but important activity not only because it ensured that those being researched would not be disadvantaged, but it also enabled the researcher to establish a link with each research location, and develop a relationship with personnel at each site.

Observation

Some time was spent in one centre observing the multi-disciplinary team at work - such

as at pathology meetings, results clinic and follow up clinics in the hospitals outpatient department. Through this the researcher was able to develop an understanding of the context in which these two breast cancer clinical trials were taking place. By observing these different environments and interactions a greater understanding of the relationships between the multi-disciplinary teams and women attending hospital was made.

The researcher was aware of the effect she might have on the setting, and that her presence might modify the research context and behaviour of the group being observed (Burgess 1984). She was introduced to key members of staff and others. Permission was sought from the multi-disciplinary teams and patients before being present in any consultation. The researcher was aware of the ethical principles of the rights of the participants to informed consent, confidentiality, privacy and protection from harm, but applying these was complex. Informed consent was sought from the multi-disciplinary teams, and they sought the women's permission for the researcher to observe any consultation; the premise was that the women might feel more able to refuse the request if it came from the multi-disciplinary team.

This observation experience was used by the researcher to explore and clarify points when it came to undertaking the in-depth interviews with the multi-disciplinary teams, and the focus groups and individual interviews with women.

Gaining access to multi-disciplinary teams and women

Having obtained co-operation from the consultant surgeons in each of the centres, arrangements were made to interview the multi-disciplinary teams. For 13 of these interviews, a consultant breast surgeon also took part, to assist access, and expertise in

clinical aspects of breast surgery and treatment.

The focus groups were run over an 18-month period. Access to the women was gained initially through the breast care or research nurses at each centre responsible for supporting the women on the two clinical trials. All the women were provided with information regarding the study, an invitation to attend a focus group, details of when and where the groups would take place, a consent form and an opportunity to contact the researcher for further information. This personal contact was to answer queries, and allay fears or concerns the women might have had.

Organising the focus groups was complicated. There was no venue where women met on a regular basis. The first two focus groups were organised to coincide with a meeting associated with Breast Cancer Awareness month (October 1998). In the majority of focus groups a co-facilitator was present. Very few of the women knew each other, but they had the shared experience of the clinical trials under examination.

One person refused to participate in a focus group, though asked to take part in an unrecorded, one-to-one interview because she felt she would be inhibited in a group; in this situation notes were made of the interview. Individual interviews took place, instead of focus groups, if this was more convenient. The decision was made that a planned focus group would proceed even when the numbers of women attending were low.

Following each of the focus groups reflections of the researcher were recorded in a fieldwork diary. The same method of analysing the data was used as with the semi-structured interviews.

The relationship between the researcher and the researched

Much healthcare research is seen to focus on relatively powerless groups, for example women and people with mental health problems, where researchers could exploit their subjects' powerlessness. This imbalance of power between the researched and the researcher centres on perceptions of status, knowledge and training (Oakley 1981; Braye and Preston-Shoot 2000). Even where the researcher and researched are seen as social equals, power is still exerted because it is the researcher who decides the nature and purpose of the research as Oakley (Oakley 1981) p 40 surmised:

“... interviewers define the role of interviewees as subordinates; extracting information is more to be valued than yielding it; the convention of interviewer-interviewee hierarchy is a rationalisation of inequality; what is good for interviewers is not necessarily good for interviewees.”

Add the dimensions of gender, ethnicity and class between the individuals involved, and an imbalance can occur because those who may perceive themselves less powerful are reluctant to speak and the interaction is affected (Burgess, 1984). The ability of the researcher to be neutral and objective is problematic. In this research there was an attempt to reduce any imbalance by involving the participants in the research process, in order to gain their insight and perceptions of treatment and its value. Criticism may be levelled at the researcher who becomes too closely involved in the research process and the people studied. This is explored in the discussion and concluding chapters.

2.7 Summary and conclusion

This chapter has identified the research design chosen for this research. It takes the

research questions emanating from the literature review to the problems encountered in securing access to the researched and negotiating relationships in the field, and the methodological approach taken to collect and analyse the data. As health care professionals working in an increasingly complex arena, with complex issues, any research needs to be able to clarify issues and provide solutions. A multi-methods approach was seen as the most appropriate means of eliciting the various views of the different people involved in these two breast cancer clinical trials. By using a mixed methods approach the aim was to generate data that uncovered the actions of individuals, the differences between them and began to explain how and why these variations occur. As Avis and Robinson (1996, p 9) state:

“...non-quantitative research methods can reach the parts that quantitative methods cannot reach.”

CHAPTER 3 THE BRITISH ASSOCIATION OF SURGICAL ONCOLOGY II (BASO II) TRIAL

- 3.1 Introduction
- 3.2 Questionnaire regarding the BASO II trial
- 3.3 Interviews with selected multi-disciplinary teams
- 3.4 Retrospective and prospective audits
- 3.5 Focus group and individual interviews with women
- 3.6 Discussion of key findings
- 3.7 Summary and conclusion

3.1 Introduction

The aim of this chapter is to present the results from this research which has examined the factors affecting the accrual of patients into the British Association of Surgical Oncology II (BASO II) clinical trial. The chapter starts by placing the research in context then presents each phase of the research: phase one presents the methods and results from a survey of clinician opinion; phase two consists of the in-depth interviews with selected centres, and a retrospective and a prospective audit of recruitment. Phase three represent the results from women approached to participate in the trial, including those who entered and those who refused. Finally there is a discussion of all these findings.

Context of the BASO II trial

The BASO II trial tests whether radiotherapy is necessary for breast cancers of low aggressive potential following breast conserving surgery. The BASO II trial has four treatment options: wide local excision alone (with clear margins on histology); wide local excision and radiotherapy; wide local excision and Tamoxifen 20 mg daily for five years; or wide local excision with both Tamoxifen and radiotherapy. The trial has a 2x2 design; and centres do not have to enter into all four arms.

The primary outcome measure is local recurrence in the treated breast. Secondary endpoints include regional recurrence, distant recurrence, death from breast cancer and the incidence of contralateral breast cancer.

3.2 Phase 1: Questionnaires regarding the BASO II trial to BASO nominated breast surgeons

Method

For the first phase of the research all the BASO nominated breast surgeons, identified in the Quality Assurance Guidelines for Surgeons in Breast Screening (NHS Breast Screening Programme and BASO 1996) were approached. There are 118 surgeons nominated by the BASO Breast Group; each is responsible for the collection of relevant data on breast screening at their screening unit. These surgeons are expected to have an interest in the scientific evaluation of breast cancer treatments and they treat large numbers of women who are eligible for the BASO II trial.

The first phase involved the collection of data by means of a self-completed questionnaire. This provided the base line for information regarding accrual to clinical trials. A questionnaire was sent in February 1997 asking the surgeons for their views on clinical trials, the number of clinical trials of adjuvant treatment currently offered at their centre, their experiences of joining the BASO II trial or their reasons for not joining (Appendix A). Surgeons who were randomising patients into the BASO II trial at the time were asked further questions about their method for identifying and approaching eligible women, the difficulties they experienced in entering eligible women into the trial, and for an estimation of their recruitment rate during the previous 12 months.

Results from the questionnaires regarding the BASO II trial

Of the 118 surgeons, eighty completed questionnaires were returned giving a 68 % response rate. Thirty-nine out of the completed questionnaires (49%) were from surgeons who were entering patients into the BASO II trial. A statistical analysis of the questionnaire was conducted using SPSS Version 9.0 to identify reasons stated for not

joining the trial, the difficulties in recruiting and the surgeon's estimation of their own recruitment rate. The analyses of these questionnaires are to be found in Appendix G.

Forty six (58%) of clinicians answered that they had experienced significant pressure to participate in clinical trials; but 63 (84%) thought that they were given more acknowledgements for their clinical work than for any contribution to scientific knowledge. Clinicians referred to fact that their peers valued them for their scientific work, whereas their employing NHS Trust valued them only for their clinical work. Forty four clinicians (56%) 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. Thirty-seven (46%) felt that having to explain the details of a clinical trial discouraged them from approaching eligible patients. Sixty-three (81%) were involved in treatment trials of adjuvant therapy; the median number of other trials was 2, with a range from 1 to 12.

Factors affecting recruitment to the BASO II trial (Table 3.1)

The answers to the questions on possible difficulties in joining the BASO II trial are summarised in Table 3.1. The responses have been separated into those centres recruiting and those not recruiting patients to the BASO II trial in order to highlight any differences.

Table 3.1 Factors causing difficulty in joining the BASO II trial, (respondents, n = 80)

Factor	Frequency of response					
	No difficulty for clinicians		Some difficulty for clinicians		Prevented clinicians	
	Recruiting to trial	Not recruiting to trial	Recruiting to trial	Not recruiting to trial	Recruiting to trial	Not recruiting to trial
Making ethics application	26 (36%)	19 (27%)	13 (18%)	11 (15%)	0 (0%)	3 (4%)
Obtaining ethics approval	27 (38%)	19 (27%)	12 (17%)	9 (13%)	0 (0%)	4 (5%)
Number of eligible women seen	27 (36%)	25 (34%)	12 (16%)	8 (11%)	0 (0%)	2 (3%)
Conflicting trials	30 (42%)	15 (21%)	8 (11%)	11 (15%)	0 (0%)	8 (11%)
Adapting local practice to protocol	28 (38%)	16 (22%)	8 (11%)	11 (15%)	3 (4%)	7 (10%)
Scientific design of the BASO II trial	34 (47%)	23 (32%)	3 (4%)	9 (13%)	2 (3%)	1 (1%)
Relevance of trial to practice	32 (44%)	24 (33%)	6 (8%)	6 (8%)	1 (1%)	3 (4%)
Obtaining appropriate pathology reports	35 (48%)	28 (39%)	4 (6%)	5 (7%)	0 (0%)	1 (1%)
Obtaining information on BASO	37 (50%)	29 (39%)	2 (3%)	3 (4%)	0 (0%)	3 (4%)

The majority of respondents had no difficulty with any of these factors. Two factors accounted for half of the respondents not being registered for the BASO II trial; those centres that had difficulty in adapting to the trial protocol were evenly divided between participation in other trials and difficulties in adapting local practice that is the use of Tamoxifen and/or radiotherapy for all women. Another reason was the difficulty in obtaining local ethical approval; this factor is surprising because the trial organisers had a partially completed ethics approval form, which could be adapted by centres.

Analysis of responses to open questions suggested that clinical workload and obtaining the agreement of colleagues to work to the trial protocol were other important factors.

Twenty four surgeons said they experienced other difficulties joining the BASO II trial including: lack of time to participate in more trials (n=9); lack of research infrastructure (n=6); patients not keen to join trials (n=6); 2x2 randomisation can be difficult for patients to understand (n=4); give radiotherapy to all women (n=3); axillary node biopsy not routinely undertaken (n=2); clinical oncologists not complying with protocol; no patient information leaflets; no agreement among multi-disciplinary members.

Difficulties entering patients into the trial

Each centre randomising patients into the BASO II trial answered questions on the process of entering patients into the study (Appendix A). Half the centres identified eligible patients at a multi-disciplinary meeting. In the majority of cases the surgeon was responsible for approaching eligible patients. The proportion of eligible patients estimated to be recruited varied between 0% (for centres who had yet to enter a patient) and 100%. The mean estimated recruitment rate was 31%.

The main difficulties encountered in entering patients were patients expressing a preference for treatment or refusing to be randomised. Table 3.2 summarises the factors causing difficulty in recruitment of women into the BASO II trial.

Table 3.2 Factors causing difficulty in the recruitment of women into BASO II trial (in registered centres) (n=39)

Factor	Frequency of response		
	No difficulty in entering women to BASO II trial	Some difficulty in entering women to BASO II trial	Prevented entering women to BASO II trial
Clinician factors			
Time explaining the trial to patients	19 (54%)	16 (46%)	0 (0%)
Poor design of informed consent information	27 (79%)	7 (21%)	0 (0%)
Doctor relinquishes decision-making to randomisation	29 (85%)	5 (15%)	0 (0%)
Effects on doctor-patient relationship	29 (83%)	5 (14%)	1 (3%)
Patient factors			
Patients express treatment preference	3 (9%)	23 (66%)	9 (26%)
Eligible patients refuse to join the trial	2 (6%)	21 (60%)	12 (34%)

There was a lack of time available for clinical trials such as for the explanation of the trial, obtaining informed consent and completing documentation. Closely associated with this was the lack of resources available locally to support participation in clinical trials. While sixteen centres (46%) found that explaining random allocation to adjuvant therapy was time consuming, this could be explained by the difference in treatment in each arm of the trial. Seven centres (21%) referred to the difficulty of recruitment because of the poor consent information. Eligible women's refusal to join the BASO II trial is an issue, either women deciding to choose their treatment, or women recognising the clinician's uncertainty regarding the trial could explain this. Only six centres (17%) identified the doctor-patient relationship effecting recruitment.

Media publicity on breast cancer and clinical trials did not appear to have greatly affected recruitment of patients, only five respondents identifying this as a factor.

3.3 Phase 2: Interviews with selected breast screening centres

The aim of this phase was to identify actual and potential barriers to recruitment. Each centre recruiting women to the BASO II trial that had completed a questionnaire was classified as good, medium or low recruiter based on their own estimation of the proportion of women recruited in their centre. From these, fourteen centres were selected for follow-up to include good, medium and low recruiters according to their own estimates; the reason for examining these was to see if there were differences between good and low recruiters and identify any. The centres were chosen to reflect different regions in the UK including Scotland & the North East; Trent; North West and North Wales; South West and South Wales; and South East and South coast, they included urban and rural and north and south.

Table 3.3 Breast screening centres recruitment: self-assessment of recruitment level (based on proportion (%) of eligible women recruited) versus actual recruitment (BASO II database April 1997).

Centre	Self-assessment	Assessment according to BASO II database
1	Medium (50%)	Medium
2	Good (75%)	Good
3	Medium (50%)	Good
4	Medium (50%)	Low
5	Good (84%)	Good
6	Good (80%)	Good
7	Low (0%)	Low
8	Low (0%)	Low
9	Medium (50%)	Low
10	Low (15%)	Low
11	Good (80%)	Medium
12	Low (10%)	Medium
13	Low (10%)	Medium
14	Low (15%)	Medium

This self-assessment was compared with the centre's actual recruitment according to the trial database (Table 3.3). Half the centres matched their self-assessment scores with the BASO database, 4 centres underestimated and 3 overestimated their recruitment. None of the centres had over or under estimated by more than two points, therefore the centres registered for the trial did appear to have insight regarding their own recruitment rates.

Method

Semi-structured interviews were chosen to explore factors affecting recruitment to clinical trials with these multi-disciplinary teams. The interview schedule was developed using issues raised in the questionnaire (Appendix C). The duration of the interviews ranged from 45 minutes to 120 minutes.

Results from interviews with multi-disciplinary teams

The teams described themselves as trialists, in that they believed that clinical trials were needed to resolve questions about optimum treatment for breast cancers, and acknowledged that the BASO II trial to be answering an important question. One of the propositions had been that centres might have had difficulty obtaining reliable pathology reports as an explanation as to why eligible women for the trial were not being identified; however, the units disagreed. All the centres visited were confident that they had reliable systems for identifying women, usually at the multi-disciplinary team meeting.

The interviews confirmed the questionnaire finding that refusal by eligible women to take part in the trial had been the main reason for failure to recruit. The reported reasons for refusal were preference for a particular treatment; anxieties about randomisation; and concern about allocation to an 'unnecessary' treatment, usually

radiotherapy. 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 six weeks for treatment.

Centres identified practical issues that helped or hindered recruitment, the most significant factors affecting recruitment to the BASO II trial related to gaining consent. The interview findings indicated that three issues accounted for this; there were variations in approach to 'selling the trial' to eligible women, the methods of obtaining consent, and patient preference. Following analysis, coding frameworks were developed and these are presented in Figures 3.1, 3.2 & 3.3, followed by a detailed exploration and presentation of the findings within each theme.

Selling the trial

The first theme was selling the trial and the resulting coding can be seen in Figure 3.1.

Figure 3.1: Selling the trial

Encouraging trials

Difficulties with design of trial

Backtracking of multi-disciplinary team

This theme reflects the interviewees' beliefs about the constraints and opportunities for 'selling' the trial to eligible women. Most of the centres acknowledged that BASO II is a simple trial yet there were some difficulties in explaining it to women.

Encouraging trials

The clinicians accepted the need to identify the optimum treatment for these cancers, and are concerned about under treatment and recurrence rates, and were committed to encouraging trials. Some centres used local audit information of recurrence rates, or other published studies to support the benefit for one or other arm(s) of the trial.

The 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 arms are not proven. A surgeon who said illustrated this:

As far as BASO II is concerned I take a very simple line... I tell them that they have a very favourable tumour, I tell them that all the lymph nodes are clear, I tell them with confidence - because we do look at margins very critically - that all the tumour has been removed and on those grounds I'm entirely happy that whatever option they get is perfectly reasonable and acceptable treatment. I don't know if it is, and that's why we are doing the trial ... I need to be very reassuring that you have a terribly good prognosis cancer, your glands are clear we know it's all been removed and I think you know those are all facts and they are absolutely true and they are hugely reassuring to the patient and I think if they have that information then the concept of them looking at whether or not additional treatments are necessary is easier to accept.

Difficulties with design of trial

However, some clinicians treated the idea of 'selling the trial' as pejorative, and questioned whether individualising the information given to women put them under too much 'pressure' and may not meet requirements for informed consent.

At the risk of insulting virtually all of our colleagues in the United Kingdom I think that nowadays, with the informed patients that we have, by and large the only

way that you can get somebody into the randomised control trial with a no treatment arm is to be less than honest in the discussion with them.

A consultant surgeon endorsed this:

...there's got to be some model that they've got that maybe we should be following or is it that they just don't bother to ask for informed consent?

One consultant surgeon, when asked what treatment he would advocate for his own wife, presenting with this tumour said:

We have discussed it...she'd probably have the lot. She'd probably have the mastectomy, chemotherapy and radiotherapy.

This clinician was clearly not in equipoise regarding this clinical trial and may influence recruitment by giving a subliminal message regarding his uncertainty, the women pick this up and they refuse to join the trial.

Backtracking by the multi-disciplinary team

A lack of consistency in the explanations given to women causes further difficulty in recruiting women to the BASO II trial, and clinicians acknowledged that some women do not perceive they are told a consistent story. A breast care nurse who said confirmed this:

We start off saying it's a package of treatment, wide local excision followed by radiotherapy, and that is equal to mastectomy... so if they [get randomised to] wide local excision alone, they're getting conflicting information.

Women have had the likely treatment plan explained to them prior to surgery; then following surgery the multi-disciplinary team has identified their eligibility for the trial;

this then requires clinicians having to 'backtrack' on the initial treatment plan. This backtracking undermines the apparent confidence clinicians previously expressed in the women's treatment plan, and introduces an element of doubt.

Smaller centres visited discussed the advantage of working in a small team. When there were only a few members of the multi-disciplinary team talking to eligible women about the trial there is a more consistent story.

Method of obtaining consent

The second theme identified was the methods of obtaining consent. The coding framework can be seen in Figure 3.2.

Figure 3.2: Methods of obtaining consent

Entering patients to BASO II

Eligibility issues

Factors affecting asking women

Organisational issues

Entering patients to BASO II

Where centres are positive when explaining the trial, they find recruitment straightforward. Entering patients proved to be more difficult in some centres because of other factors including local surgical practice or the effort of recruiting women relative to the clinical workload.

Eligibility issues

Local policies had an impact on trial recruitment these included axillary node sampling, acceptable margins around the tumour (some centres pay no attention to margin histology), and size of tumour.

The criteria [for the BASO II trial] is quite stringent ... it specifies the exact lymph nodes, exact size [of tumour], not all Ductal Carcinoma In Situ [DCIS]...a lot to fulfil before they're even eligible to go on the trial.

In some of the centres visited, they did not routinely undertake axillary node sampling; therefore if an eligible woman for the trial were identified, then further surgery would have to be done to ensure that the axillary nodes were negative. Other centres had made a decision locally, only to include women who had a tumour that was 1cm or less.

Extra staff was thought to improve recruitment through offering more time to discuss the trial, better follow up and having someone responsible for bringing eligible patients to clinicians attention. This was illustrated by a consultant surgeon and endorsed by others:

Clinics tend to be overbooked, and so to take half an hour, or an hour to sort someone out to discuss it [the trial], and randomise them, and remember where the forms are, and various things, is very difficult.

Factors affecting asking women

The time at which women were approached to enter the BASO II trial affected recruitment because this was at the result clinic, usually a stressful time for women as summarised by a breast care nurse who said:

Patients arrive very, very stressed. They often haven't slept...what they feel, is that we are going to tell them whether they are going to live or die...Then they're

given this really good news [a small, well-differentiated tumour and] then they're on a high...and actually getting them to listen and concentrate is very difficult.

Eligible women may be anxious for other reasons including those with existing mental health problems, or have home, work or caring difficulties; these women were usually identified by the multi-disciplinary team and were not approached to participate.

There was a general feeling that the longer women had to think about the trial the less likely they were to participate. In one of the centres visited the local research ethics committee required that women be given 24 hours to consider the trial before being randomised. In addition, if there was no system in place for following up the request the problem was compounded.

Organisational issues

Organisational issues, which could enhance the running and recruitment of patients to clinical trials, were raised, for example clinics specifically for trial recruitment; sufficient number of staff including data managers, and research and trials nurses. Funding that came with other clinical trials had been used in some centres to employ additional staff for the BASO II trial.

Local and regional support for clinical trials was thought to influence recruitment in a number of ways. The development of regional trials meetings in the United Kingdom, for example the Scottish Cancer Therapy Network, the All Wales Breast Group and the Yorkshire Group, were seen as helpful in sharing advice on recruitment, to compare recruitment rates and discuss clinical trials.

Patient preferences

The third theme was patient preference; the coding framework can be seen in Figure 3.3.

Figure 3.3: Patient preference

Concerns about treatment

Don't like clinical trials

Choice about treatment

Lack of continuity

Concerns about treatment

Factors identified by multi-disciplinary teams included the concern that clinicians do not apparently know the best treatment for this breast cancer; women having a treatment preference; and women not wanting to take part in clinical trials. It was felt that lack of continuity with staff contributed to these.

Choice about treatment

In all the centres visited, the multi-disciplinary teams referred to women wanting or expecting a specific treatment. Women's preference for a particular treatment varied, for example those women who live in rural areas at a distance from a centre, being randomised to an arm that included radiotherapy would have implications.

A woman seen recently, eligible for the trial ... she lives an hour and a half from here [and a couple of hours from the radiotherapy unit]. For her to go and have radiotherapy would be quite a challenge ... she'd stay in [hospital] for 5 days ...

home at weekends ... It's going to make a profound difference to their [the woman's and her family] lives for the next couple of months.

In centres covering farming communities, women sometimes chose to have a mastectomy, rather than joining the trial and encountering the chance that they are randomised to the radiotherapy arm of the trial. Because of work and home commitments, these women could not afford the time away from the farm.

Some women were perceived by the multi-disciplinary teams to be concerned about under treatment:

They [the women] want everything; they feel they're going to die. The biggest reason for refusal [to enter the trial] is that they're frightened they will get no treatment.

These women might be concerned about receiving less than the standard treatment.

There was discussion regarding those women who find the teams uncertainty regarding the best treatment for this tumour:

They're [the women] not quite so confident in what you are doing ... some patients say, "Why do you need a trial? Surely you know what you are doing?"

Don't like clinical trials

Some women find the clinician's uncertainty difficult to comprehend. This is closely associated with women's concerns regarding clinical trials – some just do not like them:

Mostly they [the women] think ... being in a trial ... [makes them] feel like a guinea pig ... they just don't like the concept.

Some women do not like the idea of random allocation:

They [the women] would rather choose their treatment, than the trial choose it.

Summary of multi-disciplinary team interviews and feedback to participating centres

The findings from all 14 interviews with the multi-disciplinary teams were summarised. General feedback was sent to each of the centres together with recommendations specific to that centre and suggestions on how recruitment could be enhanced in that centre. Feedback to the centres did not include this information on 'patient preferences' because this theme was based on what the multi-disciplinary teams thought the women wanted or was concerning them.

Although there were local and regional differences in policy regarding informed consent, the following general measures were suggested:

- a) Ensure a consistent approach within each centre for explaining the trial; this could be achieved by minimising the number of different staff discussing the trial with women.
- b) The evidence suggested that surgeons have the best success rate in obtaining consent.
- c) It was necessary for the clinicians to give a positive message about participation in randomised trials and that the clinician really does not know which treatment arm is best (ie and that they are in equipoise).
- d) Some centres had prepared their own posters and leaflets for display, about clinical trials, in patient areas. This introduces the possibility of participation in a clinical trial at an early stage, when diagnosis is first discussed.
- e) Each centre needs to have one person responsible for contacting eligible women with whom the trial has been discussed, when they have been given time to consider. This could be by a telephone call 24 hours after the appointment.

Information on the general and specific feedback is in Appendix H.

3.4 Retrospective and prospective audit at selected centres

Retrospective audit was undertaken using multiple methods including: analysis of nursing records; medical and pathology records; and the trial database to identify the number of eligible women for the trial, the women actually recruited to the trial and, where recorded, the reasons for women not participating in the trial.

Table 3.4 Retrospective audit (1.7.97 – 31.12.97) of 14 breast screening centres: numbers of women seen and numbers of women actually recruited to the BASO II trial.

Centre	Numbers eligible women seen	Numbers recruited to the trial
1	11	3
2	9	4
3	14	5
4	9	0
5	14	7
6	22	11
7	2	1
8	10	1
9	0	0
10	5	0
11	3	1
12	6	1
13	6	0
14	12	2
Totals	123	36

Retrospective audit

During the 6-month period, 1 July to 31 December 1997, a total of 123 eligible women were identified in 13 of the centres. Of these, 36 (29 %) women were entered to the trial, and 87 (71 %) refused to participate. Patient refusal continues to be the main reason for low recruitment.

The best recruiters are recruiting 50% of eligible women seen. The more women seen in practice (ie the larger breast screening units), the more likely they are to be recruiting larger numbers of women. It could be argued that the larger units are more likely to be

made up of specialist teams (Department Of Health 1995) and more committed to clinical trials and therefore more effective at recruiting patients to these trials.

Some of the centres maintained excellent records, which included details of trials the women had been informed of and approached to participate in, and if they refused, their reasons. Table 3.5 identifies the reasons for choosing not to participate.

Table 3.5 Retrospective study 1 July – 31 December 1997: Where recorded reasons given for non-participation by eligible women

Women's reason for refusal	Numbers
<i>Patient had a treatment preference:</i>	
• Did not want radiotherapy	8
• Wanted radiotherapy (concern about under treatment)	7
• Wanted Tamoxifen	3
• Did not want Tamoxifen (concern about side effects)	2
• Did not want to travel for treatment (therefore did not want radiotherapy)	2
• Declined randomisation	1
• Wanted to return to work (therefore did not want radiotherapy)	1
<i>Tamoxifen commenced prior to explanation of trial:</i>	
• Tamoxifen commenced prior to follow up appointment	2
<i>Did not like the clinical trials</i>	
• Did not want computer to decide treatment	1
<i>Personal reasons</i>	
• Psychological problems	2
• Family commitments	2
• Personal reasons	1
• Family objected to the trial	1
<i>Not approached to participate</i>	
• Overlooked or not approached	7
• Private patient	2
<i>Other reasons</i>	
• No reason recorded	8
• Patient did not attend follow up appointment	1
• Patient unable to understand the purpose of the trial (in spite of explanation)	1

Women's main reasons for refusal to the BASO II trial were either they had considered the treatment options and had a personal preference, or there were practical reasons such as having to travel for treatment, work or family commitments. Some decisions were clinically related reasons such as being overlooked by the multi-disciplinary team and not approached to join the trial; and Tamoxifen commenced prior to being offered the trial. In one centre recruiting to BASO II trial, following analysis of their pathology database 27 possibly eligible cases (grade 1, less than 2cm tumours) were excluded from the trial because some surgeons did not sample lymph nodes.

Prospective audit

The aim of the prospective audit was to:

- I. Identify the proportion of eligible women seen, the numbers actually recruited to the trial, and for those women who refused to be entered their reasons for refusal.
- II. To see if recruitment to the trial was improved following the general and specific feedback given to each centre after the multi-disciplinary interviews.

A prospective audit form was designed and sent to the 14 centres selected to assess the proportion of patients eligible, acceptance rates and the reasons for patient refusal (Appendix G). All new referrals, seen over a 6 month period, were to be assessed. A prospective audit was undertaken over a 6-month period from 1 May to 31 October 1998 at the 14 centres. Only 8 of the 14 centres completed the prospective audit forms, a reminder were sent and offers of help made, though no information was forthcoming from 6 centres. In addition, the BASO database was accessed to identify whether recruitment to the trial increased following the general and specific feedback given to the centres following the interviews.

Table 3.6 Prospective audit: Comparison of the number of eligible women to the number recruited (1 May to 31 October 1998)

Centre	Number eligible	Number recruited
2	9	4
3	9	0
5	11	6
8	5	1
11	1	1
12	2	1
13	6	2
14	7	2
Totals	50	17

During the six-month period, in the 8 centres returned the prospective audit data, a total of 50 women were identified as eligible for the trial. The numbers eligible compared with the numbers of women recruited in these centres are summarised in Table 3.6. Of these, 17 (34%) were recruited. Centre 3 had seen 9 eligible women, but was unable to recruit because there was no staff available to spend the time explaining the trial to the women. The 33 (66%) women who refused to be randomised to the trial provided their reasons for refusing, and these are summarised in Table 3.7. Some women identified more than one reason for non-participation.

Table 3.7 Prospective study: Women's reasons for refusing to participate in the BASO II trial, n = 49*

Reason for refusal	Number
Did not want radiotherapy	9 (18%)
Organisational factors (no staff available)	9 (18%)
Concerned about under treatment	8 (16%)
Inconvenience about radiotherapy eg's cost, travel, accommodation	6 (12%)
Preference for radiotherapy	5 (10%)
Radiotherapy would interfere with domestic responsibilities, job, holidays	2 (4%)
Preference for Tamoxifen	2 (4%)
Did not want Tamoxifen	2 (4%)
Concern about random allocation	2 (4%)
Eligibility for trial overlooked	2 (4%)
Conflicts with expected treatment	1 (2%)
Prefer no treatment	1 (2%)
*NB Some women identified more than one reason for not participating in the trial	

The BASO database was accessed and recruitment for the 6-month period across all 14 centres was 39 women. Comparisons were made between the retrospective and prospective reasons for refusal; direct comparisons were difficult because only 8 of the 14 centres returned data. Reason for refusal were that women had a treatment preference or for practical, or there were clinically related reasons. These match the findings of the retrospective study, demonstrating the multi-disciplinary teams' awareness of the issues influencing women's decisions.

Table 3.8 Comparison of numbers women recruited to BASO II using the retrospective and prospective audits

Centre	Retrospective audit 1.7.97. - 31.12.97.		Prospective audit 1.5.98. - 31.10.98.	
	Nos. eligible	Nos. recruited	Nos. eligible	Nos. recruited
2	9	4	9	4
3	14	5	9	0
5	14	7	11	6
8	10	1	5	1
11	3	1	1	1
12	6	1	2	1
13	6	0	6	2
14	12	2	7	2
Totals	73	21*	50	17**

*28% recruited

**34% recruited

The original aim of this research was to increase recruitment to the BASO II trial, by recommending adjustments to local protocols. Recruitment increased from 28% to 34%; if centre 3 was excluded on the grounds that they had no staff available to discuss the BASO II trial to eligible women, the percentage of women recruited is increased to 41%. Though recruitment has been improved it is difficult to draw conclusions from this phase of the study, on the reasons for this increased recruitment. The possible explanations are firstly, that feedback to each of the 14 centres led to an increase in the number of women recruited to the BASO II trial. Secondly, that the effect of an interest being taken in the BASO II trial led to an increase in the number of women randomised to this trial. Thirdly, that the interviews at each of the 14 centres served as a reminder to the multi-disciplinary teams of the importance of the BASO II trial.

In the majority of cases those units, which were good recruiters at the start of the study, have continued to be good recruiters. There was some improvement among the medium to low recruiter units, particularly in one centre, which following the multi-disciplinary team interview, moved from being a low to a good recruiter.

3.5 Phase 3: Focus group and individual interviews with women approached to participate in the BASO II trial

Method

Focus groups were the chosen method because they encourage individuals to participate who might be reluctant to be interviewed, or feel they have nothing to contribute. Compared to an interview, the participants can interact with each other, rather than with the facilitator, emphasising the women's' perspective rather than the researcher's. They were all tape recorded and lasted between one and three quarter and two hours.

Four centres recruiting women to the BASO II trial were approached to participate in this stage of the research and this included centres that were good, moderate and low recruiters to this trial. A total of four focus groups and three individual interviews were held with 21 women entered to the BASO II trial. A further eleven individual interviews were undertaken with women who had been invited to participate in the trial but had refused. One woman sent a letter stating her reasons for not joining the trial.

This phase of the research enabled the researcher to examine whether the women's reasons for participating or not in the trial matched those arising in the interviews with the multi-disciplinary teams.

Table 3.9 Characteristics of women (n = 33) in the BASO II focus group and individual interviews.

Age in years	Number
40-49	1
50-59	18
60-69	11
>70	3
Marital status	Number
Married	27
Widowed	0
Single	2
Cohabiting	1
Divorced	3

Of the women approached to take part in this phase of the study who had chosen not to participate in the trial, thirty-six women did not respond to the invitation to take part in this phase of the project; ten women replied stating that they did not want to participate, a further two women were unable to attend because of other commitments.

As previously stated, in one centre access to the women was not possible because the completed Local Research Ethics Committee forms had not been submitted by the surgeon (see chapter 2). The response from women to take part in this phase of the research was disappointing and possible explanations for this are discussed in chapter 5. Some women who agreed to participate in the research stated that they did not want to take part in a focus group discussion, and individual interviews were offered as an alternative.

The aim of the focus groups and individual interviews were to find out when women first became aware of the trial, and what they thought the trial might entail; their decision-making process regarding participation or not; their subsequent experience of the trial;

their personal experience of breast cancer; and how the trial organisers might improve recruitment to the trial.

Results from the focus groups with women who entered the BASO II trial

Following analysis of the transcripts the following themes were identified: decision-making, concerns and contraindications, and the trial experience. The first theme identified was decision-making and the coding framework for this is provided in Figure 3.4.

Figure 3. 4 Decision-making

Altruism

Motivation

Decision-making

Women's reasons for deciding to participate in the BASO II trial varied but can be divided into the two themes of altruism and motivation.

Altruism

There was an acknowledgement by many of the women of the importance of clinical trials in the development of healthcare, which may benefit them but is more likely benefit future generations.

It gives it a meaning ... you feel that somebody else is going to benefit from what they've [the trial organisers] learnt from you.

This was very different to the groups and interviews held south of the border. A recurrent theme that ran through focus groups held in Scotland was the theme of giving something back to the NHS and society as a whole:

... they'll never eradicate cancer...but anything that can help alleviate it in some way, or to make it easier for people, can only be good.

Motivation

Women chose to participate in clinical trials for different reasons. It was noticeable in the focus groups that there was discussion about how and who had approached them from the multi-disciplinary team. This had had a significant effect on recruitment for example one woman commented on how persuasive one of the clinical oncologists was:

...he actually, kind of, persuaded me to [to join the trial] because the things I had [a small, node negative, well-differentiated tumour], he said, "You are a good case to be on the trial".

Although the oncologist had been influential, this woman had not felt pressurised to join the trial; the decision to join the trial had been hers. In comparison, at another centre a woman had been entered to the trial but then refused the randomised therapy. This woman spoke about the research nurse at this centre, and how helpful she had been, providing information and answering all her questions. Up to this point she was prepared to join the trial - she was then asked to see a doctor:

...I felt very cheated at this interview...[they] hadn't told me why [I need to meet the doctor]; and there was me thinking it was something about me, and it seemed it was all set up for me to be on this trial [the BASO II]. So I wasn't best pleased,...he gave me a leaflet and tablets [Tamoxifen]...and then he rushed off to some meeting.

It became apparent that following the meeting and discussion with the research nurse, the woman was randomised to the trial, before meeting the doctor, without her knowledge. She became aware of this fact when she met the doctor and was told which treatment option she had been randomised to. Following her encounter with the doctor, she did not take the medication. Instead, she went to the local university library and read articles in the medical and nursing press on breast cancer and how to treat it; she also sought independent advice from a number of cancer charities about treatment options. Although she was randomised to the BASO II trial, she was not compliant and did not continue with the Tamoxifen. This woman's anger at not being fully informed means that she was lost to the BASO II trial, she has told other people of her experience, and her experience may affect her attitude and relationship with other multi-disciplinary teams and other clinical trials.

The clarity and amount of information provided to women varied considerably from a clear and detailed description of the trial, the different treatment options and side effects associated, through to vague explanations with no written information.

The women referred to how defenceless they felt when approached to join the trial. Within a few weeks they have discovered a breast lump, been through a series of investigations, undergone surgery and find themselves in an outpatients department, waiting for the results from the pathology report. At this hospital appointment, these women are then told that they have breast cancer but that it is a small, well-differentiated tumour, with a good prognosis. However, these women are in a state of shock:

...you're so vulnerable...my first feeling was sheer disbelief...the person talking to you is wanting to help you, so you are ...very willing to agree to anything they

suggest...so you think you will be pleasing the person [a member of the multi-disciplinary team] if you say “Yes” [to join the trial].

Presentation of the trial to women requires care and sensitivity, from the multi-disciplinary team; whilst acknowledging that women eligible for this trial have a good prognosis, these women are overwhelmed by the word ‘cancer’.

Prior to agreeing to join the trial most women consulted others about the trial, including family, friends and other health care workers.

...I spoke to my doctor [GP]...and she said it’s totally ethical, so they must believe you’ll be all right with nothing [if randomised to the no treatment arm] or else you wouldn’t be offered nothing. [It’s] totally ethical...they can’t do anything if there’s danger ... [and] I believed her.

Although women ultimately made the final decision whether to participate or not, they needed to talk about the trial, obtain other people’s opinions, before making the choice to join the trial and be randomised to one of the treatment options.

Centres of excellence

The women who participated in the focus groups referred to the reputation of the hospitals attended:

You’re at a teaching hospital...I came to this hospital because it is the best there is...you’ve got to expect to take part in a few researches [sic], ... I would like to put something back ... I don’t mean that’s extremely noble or anything ... if we don’t, who will?

This is closely associated with altruism and women's motivation for joining the trial. The women who participated in this phase of the research discussed the reputation of the both the hospital and individual members of the multi-disciplinary teams:

I was going to take the joys of coming to a centre of excellence. They're [the multi-disciplinary team] marvellous, absolutely marvellous.

Where the clinicians had a national and international reputation the women knew and identified this as a reason for being referred to the hospital. It was evident that many of the women had been approached to join other clinical trials, and some were participating in a number of other trials.

I've got other research things to do...When I was having my operation ... they said would I take part in the research [by] having a drip. ... then, they came back again and asked if I would take part in another trial ... and I have to fill in forms.

These women expected to be approached and be asked to sign up for different clinical trials. In one of the good recruiting centres the women discussed the perceived benefits of participating in a clinical trial, including the extra care available to them because of the trial:

... [my reason for joining was] that you'd be very carefully monitored, and that did have a lot of bearing on my decision.

...I'm happy that I'm here, a [hospital check up] every three months...I must admit that I feel hopeful, and [that] I'll never get it [breast cancer] again.

...because you're on the trial you get everything; they're always [there] on call for you.

It was not only the women participating in the BASO II trial who saw the benefit of joining a clinical trial:

...one of my sisters said “You shouldn’t do it [join the trial]...it’s too risky”,...she was very much against it ... [But] my husband was there, and he was saying if you come every three months you’ll be checked up ... somebody’s always watching you, looking after you.

When compared with the findings from the multi-disciplinary team interviews, these women were sold the trial, they were enthusiastic about being part of the trial and because of the extra care they would be receiving from the multi-disciplinary team. Yet only one of the centres visited explicitly said to the women that they would receive additional benefits from participation in the BASO II trial; the women interviewed stated they had been told they would have the security of additional screening that came with being part of a clinical trial. For many women this was the prime reason for joining the BASO II trial. The provision of an improved care regime for trial participants was not emphasised outside this one centre.

The second theme identified was concerns and contraindications, the coding framework is provided below in Figure 3.5.

Figure 3.5: Concerns & contraindications

Effects of treatments

The clinic environment

Cost to women

Concerns and contraindications

The women talked about how helpless they felt while waiting to receive the results of their biopsy or surgery; the overwhelming thing on their mind was “Have I got cancer?” and “Am I going to need further treatment?”

...I wanted information, I knew the doctor's time was very valuable ... I would have liked to know what the treatment would have been if I hadn't been on the BASO II trial...It would have given me a decent starting point ... I would have felt they [the multi-disciplinary team] were on my side.

In spite of the women's high anxiety levels at these outpatient clinics, they still wanted and needed to be fully informed of what type of breast cancer they had, what the treatment options available were, and the opportunity to discuss these with someone.

Effects of treatments

Before making the decision to join women considered the consequence of the different treatment options. There were concerns expressed about under-treatment and that they may not be receiving what they saw as the standard treatment:

... I think, if they'd come back [following randomisation] and said you're [on] nothing, I don't think I could have taken that ... I couldn't have taken nothing.

Wide local excision is a surgical treatment, but this woman was unable to contemplate this treatment alone, she saw this as under-treatment. In the same focus group was a woman who had been randomised to wide local excision alone – the researcher was concerned about whether this woman might feel that she had been under-treated; there was discussion among the group and she was happy with receiving wide local excision alone.

Reference was made to the side effects of some of the treatments and these were much talked about in each of the focus groups held. For example, those women taking Tamoxifen chatted about the side effects experienced:

... the night sweats are the worst ... I lie there and I try to get to sleep. The water running off you ... I thought there might come a point when I could sleep through [the night] ... but you can't ... the loss of sleep is a big problem.

The women not only talked about their problems, but also their strategies for dealing with each of the side effects experienced:

... I've got a spare pair of pyjamas on the floor beside my bed. I get up, change my pyjamas, [and] I get back into bed [and go back to sleep again].

In one centre, some of the women had been told, by one of the breast care nurses, about a product on the market that might improve their night sleep:

... you can buy this nightdress, which is very expensive. It's from Ireland only and it's special material ... Another lady ... she was up six, seven times [a night] ... [but] since she started wearing it, she can sleep say [from] 11.30 [pm] until about 5 [am] o'clock.

As referred to earlier, many of these women were taking part in other clinical trials, one of which was a homeopathic treatment, to help manage the side effects of Tamoxifen.

The women on this treatment found it effective and they told other members of the group where they could find information about this trial.

There were opinions expressed about radiotherapy; one woman was concerned about the side effects and the perceived disadvantages of receiving radiotherapy.

[My husband] came back with these [Cancer Guidance Sub-Group of the Clinical Outcomes Group 1996]... There was no significant difference between those who'd been on the radiotherapy and those who hadn't...[I'd also read that] once you'd had radiotherapy, that was it [If I got recurrence, I couldn't receive more radiotherapy] ... [I'd] rather save [radiotherapy] ... for if it [breast cancer] comes back.

Some women had contacted other organisations at initial diagnosis and had obtained information on different treatment options for this form of breast cancer, and this was useful for evaluating the treatments and making the decision to join the trial. All the women who participated in these groups were asked about information available for them to take home – they had little or no recall of written information given to them regarding the BASO II trial.

The clinic environment

The women also talked about the effect of attending the outpatient clinics. Delays in these clinics had a profound impact on them:

The time that really bothered me, was the time I came back to get my results, and my appointment was 3 o'clock and I get taken in at five past four ... [I was] almost hysterical by that time ... really, it was quite traumatic.

The women's anxiety levels are so high because in the time that they are waiting for the result of their biopsy or surgery, they are convinced that they have breast cancer and are going to die. Therefore any delay makes the experience even more traumatic.

These delays occurred in other clinics:

Actually, the worst thing about having the whole thing...is sitting in that damned waiting room for your appointment, for your check ups.

You can wait up to two hours and you go in, they examine you, and [then] they're gone [the doctors].

Some women devised strategies to try and overcome these delays:

I ask for the first appointment so that I could get home a bit quicker.

By having the first appointment, women were less likely to encounter extra waiting. The clinic environment also had a bearing on the women's experience of the trial; some of the clinics were very cramped:

The [clinic], the fact that it's, I mean, just a Portakabin, it's like a rabbit warren.

...it's not a large enough room...you're sitting with your knees touching.

But at least we can talk; but the men...they'll be upstairs...sitting in reception, they just don't know what to do.

I sat for over an hour in one of these cubicles, and you couldn't see anyone...and you felt so isolated...he [husband] was sitting somewhere else, feeling equally isolated...it was stressful.

Another occurrence was women waiting to be seen by the multi-disciplinary team when they have no clothes on:

...you've got to go through and get undressed; you don't get dressed again. So you are sitting...in a state of undress...hanging out, all over the place shall we say.

The cost to women

There were costs associated with participating in this clinical trial and they were not only financial costs, and included time spent attending hospital appointments and the cost (and time) of travelling to hospital for radiotherapy treatment, as well as emotional costs.

I've got to come quite a distance...by the time you've paid all your train fares, it's about a tenner.

...the last time [my appointment] was 3 o'clock, and I drove up. By the time I'd walked back to my car and got into the traffic, I didn't get home until half past seven.

Some women were dependent on hospital transport to get them to and from home for their hospital appointments:

It was time consuming, you're away...early in the morning and you didn't know what time you were going to go home. ...There could be another two people in that car, who were going to different hospitals, so you were stuck.

In one of the centres women were given different days for their mammograms and other appointments despite having the same multi-disciplinary team responsible for their care:

I had [sic] to go for a check-up tomorrow and my mammogram is on another day...it's two days I've got to come in...another appointment, and it's another day off work.

This meant extra financial and emotional costs to women including time and travel. The third theme identified was trial experience and the coding framework is to be found in Figure 3.6.

Figure 3.6: Trial experience

Negative

Positive

Trial experience

Negative

A recurring theme throughout all the focus groups and individual interviews was that there was no written information available about the trial.

...I'd like a little more detail...what the study will involve...There should be pros and cons, and some explanation of the benefit if you do take part. What you can be doing for others...that's what we want to know.

The media was seen as having a negative effect for women with breast cancer:

...the mania of the media...trying to frighten us...all the statistics quoting so many will be dead in five years...they don't mention the survivors. It's the one's that don't make it that they...put in the papers.

Women felt that there should be a more balanced representation of breast cancer and its implications in newspapers, on television and the radio.

In all the focus groups held the women talked about the lack of continuity with doctors:

I've seen someone different every time...every time you go, they've [the doctor] got to read up on your notes...it's not like going to your own doctor, he knows what's wrong with you.

There were discussions about axillary nodes; women were not sure why these were removed, nor the rationale for the number of axillary nodes removed:

...I want to know about 'nodes'...I'd read about taking the nodes out and I didn't know anything about them...How many are they likely to take out?

It became apparent that each woman had had different numbers of axillary nodes removed, anything from five to twenty-one nodes. This was another example of women wanting to be fully informed about all aspects of their care and treatment. Other negative aspects of the trial have been referred to earlier.

Positive

In the questionnaires to the BASO nominated surgeons and the interviews with the multi-disciplinary teams there was a reference to women's concerns about randomisation, however this was not an issue expressed by any of the women interviewed regarding this trial. The only reference to randomisation was by a woman who was disappointed because she felt the computer had not chosen her:

And then she [the breast care nurse] phoned up and said "You haven't been chosen...for the radiotherapy".

This woman felt that she had lost something in comparison to other women randomised to the radiotherapy or Tamoxifen arm of the trial; this could be associated with concern about under-treatment.

With the exception of one, all the women were given time to think about the trial and whether they wanted to participate. One woman felt being given time to consider trial participation by the multi-disciplinary team was because they did not want her to join the trial:

*I offered [to join the trial] and she said, "No, we don't want to hear right away".
... They were saying "What do you want to do?" and I was offering [to join the
trial], but they were saying, "No, you don't. Go home and think about it". Even
when I 'phoned up and said I'm going to do it, she didn't seem as though [she
wanted me on the trial].*

This is an interesting contrast - the multi-disciplinary teams want women to join the trial, but also want to give sufficient time for them to consider, before opting to join the trial.

The women did value the individual care and attention they received as a result of being part of the trial.

*They make you feel that you're the only person there and they're looking after
you...you're not one of the crowd...they spend time...and make you feel that bit
special.*

*I think it's a great peace of mind to think...I can 'phone up...it's just the feeling of
relief...they look after you.*

These comments are closely associated with the women's need for continuity with the multi-disciplinary team; more junior doctors were unable to provide this because of medical rotation. The breast care nurses and research nurses were seen as key people who provided stability:

*...it's nice...to have somebody like that [who] you can identify with...Not so
much the doctors...they do the big stuff...she [the nurse] sort of does the
mothering...you know, the care.*

...they [the breast care nurses] are the familiar face, that you see each time you come.

The nurses had a role in clarifying what the clinicians had said to women about the trial:

...[the clinicians said] go into one of the rooms and we'll get [the breast care nurse] to see you...she sort of explained it [the trial] and other things [to me].

In spite of the women's anxiety when waiting for their results in the clinic, and how that this affected how much information they were able to take on board regarding the trial.

Women said that the explanations given were good:

...I didn't think it was too technical, I mean it was put in layman terms. Anything that I was told, I understood.

However, in only one of the centres did the women refer to the multi-disciplinary team actually discussing the benefits of taking part in a clinical trial. Finally, throughout the groups the women emphasised the importance of attending a hospital that was seen as a centre of excellence, including supportive staff.

Summary of the main findings from the women randomised to the BASO II trial

Although an individual made each of the quotes used, each quote represents a common experience. It was not possible to record the universality of a particular finding because of the use of group interviews. The following points are the most important factors identified by the women who were entered to the BASO II trial:

- When explaining the BASO II trial to women for the multi-disciplinary team to be explicit about the benefits of participating in a clinical trial eg access to centres of excellence, knowledgeable staff, additional screening and contributing to the development of better treatment and care.

- For the multi-disciplinary team to recognise how anxious women are when attending the results clinic, and their difficulty in understanding and remembering additional information.
- The need for information (oral, written and visual) about clinical trials, the BASO II trial and the different treatment options available to women, that can be taken away, and understood later.
- The cost incurred by women for participating in the trial eg side effects of treatments, travelling for treatment and appointments, and the time commitment.

Individual interviews with women who refused to participate in the BASO II trial

Initially, focus groups were planned for women who had refused to participate in the trial. However, none of the women approached were willing to be interviewed with other women present. Therefore, seven one-to-one interviews were undertaken, plus one woman wrote a detailed letter with her reasons for not participating in the trial. The information was transcribed, analysed and three themes were identified. These were women's attitudes, the cost to women, and their thoughts of this clinical trial. The coding framework is summarised in figures 3.7, 3.8 & 3.9. The first theme identified was women's attitudes.

Figure 3.7: Women's attitudes

The optimists

Responsibility to society

The pessimists

Women's attitudes

It was evident when examining the data from this group of women that they fell into two distinctive groups regarding their personal thoughts regarding breast cancer; they were either optimists or pessimists.

The optimists

The women who saw themselves as optimists talked about how important their and others, attitude was on their future health:

You are a bit emotional, because it's a shock initially...but then you have to think to yourself...I've got to get on with this... If you look at other people [people who talk about their experience on television]...they've all had a positive attitude... How can you have anything else really, if you're sensible?

This woman spoke at length about how a negative attitude affected an individual's health, as well as impacting on others.

Responsibility to society

These women had a strong sense of responsibility and recognised the importance of clinical trials, and their role in developing improved treatments for breast cancer. This is illustrated by a woman who was optimistic about her future, felt her prognosis was good, and that her risk of recurrence was minimal and yet:

I felt a bit guilty. I still feel a bit guilty, that unless people do take part in trials, we will never progress...but I felt it was too big a thing to ask.

This woman acknowledged that it had been her choice not to participate in the BASO II trial, she was disappointed with her decision; but she felt very strongly that she could not have coped with randomisation to the radiotherapy arm of the trial. This feeling of

responsibility was evident among other women who were as confident about their future regarding breast cancer:

I think they did say that you can change your mind at any time; you know, if you started with it [the treatment option chosen] and then you find that it was too much [you could withdraw]; but I wouldn't do that, if I started something, I'd have to finish it.

The pessimists

In comparison, there were women who were pessimistic about their risk of developing breast cancer again:

I'm thinking that I'll get it [cancer] somewhere else...it's lurking, ready to pounce...I'm going through the whole thing in my head... That's on bad days,...I'm on a bad day, I can't think about tomorrow.

This woman's fear of cancer permeated the whole interview, causing the researcher to speculate whether the woman saw the researcher more as a counsellor, than an interviewer. Another woman, when asked about how she felt about cancer said:

It's a black cloud, hanging over my head. I never get away from it...[I] pick up a magazine...[and] it's there. [It's] thrown in your face,... once you've had cancer, that's it, your days are numbered. It's going to come back...It's on my mind all the time, [I'm] tormented, tormented.

These women had not contacted or spoken to anybody about their concerns, neither their GP nor the breast care nurse, to talk about their fear of cancer. These women had not talked to their families about their fears; nor had they accessed other voluntary support services, such as CancerBACUP or Breast Cancer Care.

Women who were pessimistic about their future risk of cancer talked about whether they had made the wrong decision and that they might have been 'better off' if they had joined the trial:

I had mixed feelings ... when I was able to think straight ... I kept that paper where it said my cancer was a good type ... Should I have had radiotherapy? Should have I gone on the trial?

They had conflicting feelings as to whether they had opted for the 'right' treatment option that is not to participate in the BASO II trial.

Among this group of women there was a concern about receiving less than standard treatment.

...they were asking me to take part in an experiment [the trial] and I thought, "Oh, no". I mean, if I thought it was standard procedure, I could have said "Yes".

This anxiety about receiving less than standard treatment was supportive in the findings from the interviews with the multi-disciplinary teams. The next theme explores in more detail the cost of participating in clinical trials from the women's perspective.

Cost to women

The coding framework for this included:

Figure 3.8: Cost to women

Treatment options

Travel and time commitments

These women had thought carefully about the implications of trial participation and identified the personal costs to them; these costs were not only financial but also associated to personal health (including physical and emotional aspects).

Treatment options

A couple of women interviewed were concerned that had they joined the trial, they would have been overtreated:

... it was obvious that, as far as I could tell, the treatment in my case was not considered to be essential – otherwise I would have been recommended to have it.

This demonstrates how the women picked up cues, or reinterpreted what the clinicians had said to them regarding the trial.

...he [the oncologist] thought that there really wasn't any need for radiotherapy because he said the chances of my getting the cancer again were more or less the same as any other person... The thought of having anything else done to me that wasn't absolutely necessary [was unthinkable].

Closely associated with this is the women's concern about over treatment, plus the side effects associated with radiotherapy.

... initially, they'd mentioned radiation [radiotherapy]. I had in mind that I would have a lumpectomy followed by this radiation...I said to him, is it going to make a difference whether I have it or not? And he said, "I really don't know". And I thought...is there any point in putting myself through it, if it's not going to be of any benefit, and it might harm other tissue?

This illustrates how the clinicians may provide women with conflicting information. This woman was expecting to receive radiotherapy following a wide local excision, instead, when she next met a clinician she was asked to join the trial because he was uncertain of the most appropriate treatment for this breast cancer. This mirrors the concern raised in phase 2 with the multi-disciplinary teams.

It was evident that women attending teaching hospitals or hospitals linked to academic departments were more likely to be approached to participate in other clinical trials. Although this group of women had refused to join the BASO II trial, most of these women were involved in other clinical trials.

There were women concerned about under-treatment:

I've got a 9-year-old child, if I had not had radiotherapy, and I had developed cancer again, I would never have forgiven myself...if I did go into the trial and...have my name fed into the computer, and I wasn't going to have treatment, it would be a lot to live with.

All women were treated with wide local excision yet this woman felt very strongly that she needed something more, if she was to be 'safe' from the threat of breast cancer. By not participating in the trial she was able to choose her treatment and have radiotherapy.

Travel and time commitments

Some women, who were otherwise willing to join the trial, had decided not to participate in the BASO II trial because of the time and cost associated with travelling for the radiotherapy treatment.

...we talked it over, both me and [my husband], and we said it was an expensive thing [to pay for] out of the pension, to have to go to [the radiotherapy department 20 miles away]. We also enquired about an ambulance car, because I knew there was two more [women] that were going [for radiotherapy]...all three of us could go together. But they wouldn't put an ambulance car on.

This woman was prepared to participate in the BASO II trial but was lost to the trial because of the personal cost she and her pensioner husband would have incurred in travelling to and from the radiotherapy department. The researcher interviewed another woman, from the same unit, who was provided with an ambulance car to take her to and from the radiotherapy unit.

As highlighted earlier, some of these women had chosen to participate in other clinical trials:

I have to keep going to the hospital for blood tests, but they send a taxi for me, who would wait [while the tests were done].

This woman could not understand how one trial (the Faslodex trial) provided incentives to patients, such as transport to and from the hospital, which enabled women to participate in the trial, whilst other trials such as the BASO II trial did not.

Thoughts about the BASO II trial

The final theme identified from the transcripts were the women's thoughts of the BASO II trial; the coding framework was:

Figure 3.9: Thoughts about the BASO II trial

Negative

Positive

The women interviewed had both negative and positive thoughts regarding the trial and how they were approached.

Negative

There was evidence that women had received conflicting information from the clinicians:

I just had been told initially that ... for a lumpectomy you always had radiotherapy...I got all geared up to that, I know what I've got to do ... [then] being told I could go into a trial; it really brought me up with a jolt [because there were four different treatment arms].

Another woman who had attended the same hospital endorsed this view.

Women referred to the timing of when they were approached by members of the multi-disciplinary team to participate in the trial; this was at the 'results' clinic, when they were being told their result from histology report:

I was so nervous, so tense ... ready to run away ... I had to wait a while ... he [the clinical oncologist] was taking so much time to tell me what the cancer was,

what type ... the prognosis ... I was being put under more pressure because he was explaining [carefully and in detail]... I thought yes, I know all this, just tell me...eventually I just had to say to him, "Will you please tell me?" [he then said]... about the trial ... [and] I said "No, I've had enough, I want to go home and just try and get on with my life".

A woman from another centre who said supported this view:

He gave me something to think about, that I didn't really want to think about... I'm not really faulting the doctor; it's just the fact that he threw another spanner in the works...that you were totally not expecting.

These comments support the importance of the multi-disciplinary team making it clear that women may be approached to join clinical trials. This could be achieved verbally and through written and visual information about clinical trials and those taking place at that hospital.

None of the women interviewed had received written information on the BASO II trial.

As one woman said:

I think you need more information...they've got to explain everything you need to know fully [including complications of treatments]...I do feel these things are essential.

This written information could include details and side effects of each treatment. This would also provide women with information to show and discuss with their families and friends.

Finally, some women did not understand why they could not choose their preferred treatment option and still participate in the trial.

I therefore decided not to take part in the trial, as I could not 'randomly' select which side [treatment] I was going to have. I think they've got it wrong, that they don't give you a choice.

Positive

Even though these women had decided not to take part in the BASO II trial, they recognised that clinical trials were important and necessary if treatments for breast cancer were to improve. The majority of the women interviewed believed that the multi-disciplinary team had involved them in the decision-making process.

...they were very good at saying, "I'm sure you will have some questions later on...do feel free [to call us]."... They've always given you the option; they've been very good at that.

One woman had followed this advice and had contacted different members of the multi-disciplinary team on several occasions to discuss aspects of the BASO II trial and different treatment options, before deciding that the trial was not what she wanted.

With the exception of a few points, these women thought they had received a good service and the best treatment.

...I am full of admiration...within the space of a couple of months...it was all done and dusted...Every six months I go back...which I find very reassuring...I think we have a first class service...if I've got any problems, you can 'phone...any time, if I'm feeling worried or just want reassuring, they are very good.

Summary of the findings from the interviews with women who refused to join the BASO II trial

The following points repeat some of the main factors raised by the women who joined the trial.

- For the trial the multi-disciplinary team to recognise how anxious women are at the 'results' clinic, and their difficulty in understanding and remembering any verbal information given.
- Conflicting information from the multi-disciplinary team, for example prior to surgery being told standard treatment is wide local excision with radiotherapy, but at the 'results' clinic told about the uncertainty of the best treatment and offering them the BASO II trial.
- The need for information (oral, written and visual) about clinical trials, the BASO II trial and the different treatment options available to women, that can be taken away, and understood later.
- The costs of trial participation for women eg side effects of treatments, travelling for treatment and appointments, and the time commitment. The use of incentives such as hospital transport or taxis to and from the hospital.

3.6 Discussion of key findings

The purpose of this study was to identify the factors affecting the accrual of women to clinical trials; this was achieved by examining entry to a randomised trial in breast cancer, the BASO II trial, from a number of different perspectives. Factors affecting accrual were divided into the categories identified in the summary of the literature review these were: trial, clinician and patient related.

Trial related factors

Once involved in a clinical trial clinicians need to be reliably and regularly informed of how the trial is progressing including general recruitment, recruitment to the different arms and comparison between centres and regions. The content of the current newsletter sent to clinicians recruiting to the BASO II trial is felt to be helpful but its production is too erratic.

All the centres visited stated they were committed trialists with no difficulty identifying eligible women for this trial, albeit with variations in actual recruitment rates. There were some good models of local and regional support groups for clinicians, where they were able to 'get together' and discuss different clinical trials. This allowed less experienced clinicians to be supported by more experienced clinicians.

Any information the BASO II trial must be available to all women, which includes information explaining the trial in greater detail and the implications of participating in an accurate and straightforward manner (Cox 1999). Not having this information is unethical, and were the same protocol for the BASO II trial to be submitted for MREC today, it would not receive approval. Some centres have undertaken the development of trial information independently, and this good practice could be shared with all centres involved in the trial. Trial organisers (Bradburn et al 1995; Consumers in NHS Research Support Unit 2000) are now seeking some patient's views as their insights can provide valuable information to healthcare researchers.

Women need to be aware that they may be approached to participate in clinical trials, the multi-disciplinary team need to explain that women may be asked to join a clinical trial, from the moment they first visit hospital. This could be achieved by the use of posters and information leaflets, for example in the outpatient department with

information about what clinical trials are, examples of clinical trials available at the hospital, the different treatment options and their side effects. All this information should be available for women to take away. Women suggested the development of well-resourced information centres in the hospital where they could access and retrieve information about clinical trials and different treatment options.

Clinician related factors

The BASO II trial was seen by most multi-disciplinary teams as a simple and straightforward trial yet for some teams, explaining the different treatments to eligible women was not easy. There appears to be an interaction between the clinician's views regarding treatment options, ethical considerations, and the way they explain the trial. It has been argued that a state of 'theoretical equipoise' is neither realistic nor required ethically (Freedman, 1987) and that the individual clinician need not be in equipoise, so long as the expert clinical community is in a state of uncertainty about a treatment ie 'collective equipoise'; this is even if the clinician has a preference for one treatment on for instance the basis of a hunch, audit data or small-scale study.

In recruitment to the BASO II trial, the problem arises in convincing women to accept the perspective of collective equipoise, since it involves encouraging women to adopt the perspective of the clinical community rather than the individual clinician's perspective. Those clinicians who try to adopt the perspective of collective equipoise appear to be reluctant to 'sell the trial' to women, when compared to their colleagues in theoretical equipoise. When approaching women, these clinicians appear unable to genuinely embrace collective equipoise – their concern about the trial is transferred to the patients, and as a result women are not encouraged to participate. This was confirmed by the findings from the three different phases. This is contrary to Freedman

consideration for people unable to read, and in appropriate translations. These could be made available in outpatient clinics and/or an information centre.

There needs to be a system for identifying, approaching and recording which trial women are eligible for; whether they have had the trial explained; the women's decision; when the women were randomised and to which arm. For those women who are given time to consider participation there needs to be a system for ensuring that they are contacted to find out their final decision. In order for this to be achieved, there must be sufficient staff including clinicians, data managers, research nurses and trial managers. As discussed earlier the NHS has an obligation to recognise and value these staff, in particular clinician involvement in clinical trials.

The women who joined the BASO II trials genuinely felt they were 'giving' something back to society (Cassileth et al 1982); but this is rarely mentioned by those staff recruiting eligible women to the trial (Lawrence 1993). Centres can make it easier for patients to participate by carrying out any treatments or check-ups at a centre close to the patient's home and/or place of work, and by arranging treatments and check-ups for the same day. Trial organisers could provide incentives for women by providing help with transport to and from hospital treatments and appointments, or travel expenses where required.

3.7 Summary and conclusion

The findings from the three different phases examining the BASO II trial have been presented. There are similarities and differences between the consultant surgeons, the multi-disciplinary teams and women's perspectives. For instance the similarities are that: women do have treatment preferences; the time when women are first approached

to join the trial is not good because they are very anxious at 'results clinic', and the women do pick up any uncertainty displayed by the multi-disciplinary team. The differences are numerous but mainly relate to practicalities such as insufficient staff and time available for recruiting women (for the clinicians and multi-disciplinary teams); and the commitments associated with trial participation (for the women).

The next chapter moves on to examine the different phases of the IBIS trial.

CHAPTER 4 THE INTERNATIONAL BREAST CANCER INTERVENTION STUDY

- 4.1 Introduction
- 4.2 Questionnaire regarding the IBIS trial
- 4.3 Interviews with selected multi-disciplinary teams
- 4.4 Retrospective and prospective audits
- 4.5 Focus group and individual interviews with women
- 4.6 Discussion of key findings
- 4.7 Summary and conclusion

CHAPTER 4 THE INTERNATIONAL BREAST CANCER INTERVENTION STUDY (IBIS)

4.1 Introduction

The aim of this chapter is to present the results from this research to identify factors that affect the accrual of women into the International Breast Cancer Intervention Study (IBIS). The chapter starts by placing the research in context and then moves on to present three phases. Phase one presents the results from a survey of clinician opinion; phase two includes in-depth interviews with multi-disciplinary teams, and a retrospective and a prospective audit, with selected centres. The final phase represents the results from women approached to participate in the trial, including women who agreed to enter the trial and those who did not. The chapter concludes with a discussion of the findings.

Background to the International Breast Cancer Intervention Study (IBIS)

IBIS is an international, preventative trial, co-ordinated by the Imperial Cancer Research Campaign (ICRF) and the Cancer Research Campaign (CRC), to evaluate the reduction in incidence and mortality from breast cancer associated with taking Tamoxifen daily for five years.

Study populations

This is an international study but this case study focuses on UK recruitment only. The first phase of this research was the identification of all the BASO nominated breast surgeons through the 'Quality Assurance Guidelines for Surgeons in Breast Screening' (NHSBS & BASO 1996). There are 118 surgeons nominated by the BASO, each surgeon is responsible for the collection of relevant data on breast screening at each

screening unit and is the person in a breast unit to whom most women seeking advice on family history and risk from breast cancer are referred.

4.2 Phase 1: Questionnaire to BASO nominated surgeons regarding IBIS

Method

The questionnaire 'Factors affecting accrual to IBIS' were sent to the 118 British Association of Surgical Oncology nominated surgeons, and to a further four centres recruiting women to IBIS, but who were not screening units for BASO (Appendix B). The first phase involved the collection of data by means of a self-completed questionnaire; this provided the base line for information regarding accrual to clinical trials. A questionnaire was sent in August 1998 asking the surgeons for their views on clinical trials, the number of clinical trials of adjuvant treatment currently offered at their centre, their experiences of joining IBIS, or their reasons for not joining. Surgeons who were randomising patients into the IBIS trial at the time were asked further questions about their method for identifying and approaching eligible women, the difficulties they experienced in entering eligible women into the trial, and for an estimation of their recruitment rate during the previous 12 months. Eighty questionnaires were returned (response rate of 66%) the analysis of the questionnaires is in Appendix I.

Results from IBIS questionnaire

Clinicians views about clinical trials

Six clinicians had not heard of IBIS prior to receiving the questionnaire. In August 1998, nineteen centres were registered to recruit women to IBIS. Forty-five (58%) clinicians that responded to the questionnaire experienced significant pressure from the clinical community to participate in randomised controlled clinical trials (RCTs).

However, fifty-nine (80%) felt that they were given more acknowledgement for their clinical work than for their contribution to scientific knowledge. Thirty-one clinicians (39%) stated that having to explain the details of a clinical trial discouraged them from approaching women. Interestingly, fifty (67%) of the clinicians, when faced with a controversial treatment decision were more comfortable when the decision was taken within the context of a clinical trial. Less than half the respondents (47%) were disappointed if an eligible patient chose not to participate in a clinical trial.

More than half the respondents (55%) were reluctant to participate in a trial that had a treatment arm that involved less treatment than standard practice. The same number (54%) were more likely to rely on published data than their own clinical data when there was conflicting information.

Factors affecting centres registering to join IBIS

The centres experienced little difficulty in obtaining information about IBIS, only fourteen (19%) experienced some difficulty or were prevented joining the study because of conflicting trials. This could be because this is a preventative study and unusual. Eighteen clinicians had experienced some difficulty or have been prevented from participating in IBIS as a result of adapting local practice to fit the trial protocol; this is associated with the design of the study.

Seventeen centres had been prevented or had experienced some difficulty in obtaining approval from local research ethics committee for this study. Eighteen (29%) had also experienced problems with the number of eligible women seen at the centre. Twenty centres not registered for IBIS stated that this was because Tamoxifen should not be given to well women unnecessarily.

Table 4.10 Factors causing difficulties to units in joining IBIS (n= 70)

Factor	Frequency of response			
	No difficulty	Some difficulty	Prevented from joining IBIS	Missing data
Making ethics application	40 (70%)	15 (26%)	2 (4%)	13
Obtaining ethics approval	43 (78%)	10 (18%)	2 (4%)	15
Number of eligible women seen	45 (72%)	14 (22%)	4 (6%)	7
Conflicting trials	54 (84%)	5 (8%)	5 (8%)	6
Adapting local practice to protocol	43 (71%)	16 (26%)	2 (3%)	9
Scientific design of IBIS	45 (74%)	9 (15%)	7 (11%)	9
Relevance of trial to practice	43 (72%)	12 (20%)	5 (8%)	10
Obtaining information on IBIS	51 (79%)	10 (15%)	4 (6%)	5

Less than 10% of clinicians saw IBIS as not relevant to their clinical practice. Obtaining trial information was good. What is interesting to note is that 16% stated they experienced some difficulty or were prevented from joining IBIS because of conflicting trials, when there are no conflicting trials.

For these centres other difficulties associated with joining the trial were: women do not like placebo arms in clinical trials; lack of resources locally to support clinical trials; not having a local family history clinic; clinicians refer women eligible for this trial to a clinical geneticist or other centres recruiting to the IBIS trial; their concerns about the side effects of Tamoxifen; do not agree with the trial; no funding for mammography in

the under 50 year age group; time commitment of entering women to the trial; and discouraged by the IBIS Coordinating centre in London.

Factors affecting entering women to IBIS

The people most responsible for identifying eligible women were either the surgeon or the clinical geneticist. The surgeon and the breast care or genetics nurse were responsible for explaining the study to women and obtaining their consent. In terms of resources 79% of centres had a breast care nurse, 47% had a data entry clerk, and 37% had a research registrar.

Table 4.11 Factors causing clinicians difficulty in recruitment of women into IBIS (n=19)

Factor	Frequency of response	
	Has caused some difficulty	Has prevented entering patients
Clinician factors		
Explaining the random allocation to patients	9 (47%)	10 (53%)
Extra time required to explain trial to women	9 (47%)	10 (53%)
Poor design of consent information	15 (79%)	4 (21%)
Relinquish decision-making to randomisation	18 (95%)	1 (5%)
Effects on doctor-patient Relationship	18 (95%)	1 (5%)
Patient factors		
Women express treatment preference	8 (42%)	11 (58%)
Eligible women refuse to join the trial	1 (5%)	18 (95%)

Explaining random allocation and the time required to explain the trial to women

continues to be an issue with more than half of the clinicians (53%) stating that this prevented them from recruiting eligible women to IBIS. 95% stated that they experienced some difficulty in entering women because women have already decided that they did not want to participate in the trial, therefore why do women attend clinic if they do not want to participate? It is interesting to note that 53% of women express a treatment preference because Tamoxifen is not available, as a preventative treatment for women with a family history of breast cancer, but double mastectomy is an option for some women.

65% of centres recruiting women to IBIS stated that media publicity had affected recruitment of eligible women to this trial. This questionnaire was administered after the early release of findings from the United States of America Breast Cancer Prevention Trial (NSAPB-P1 trial) - which reported a 45% reduction in the incidence of breast cancer, from 1 in 130 to 1 in 236 women, due to Tamoxifen (National Cancer Institute 1998a). Other reasons identified as affecting recruitment were women requesting bilateral mastectomies and publicity from the ICRF.

Estimation by centres of recruitment rates

Estimation of the numbers of women who had been entered into IBIS varied widely, with a range from 2 to 501. The ICRF keep a trial database and the number of women entered to the trial, centre-by-centre, month-by-month. The nineteen centres recruiting women to this trial are informed of their own as well as other centres recruitment via an IBIS trial newsletter. The proportion of eligible women seen by centres and entered into the trial ranged from 10 to 95%; and 77% of these centres thought they would recruit more women to the study over the next 12 months.

Major benefits and drawbacks of participating in IBIS

The main benefit seen by the clinicians was to answer the question as to whether Tamoxifen benefits women with a family history of breast cancer. They thought the trial provided reassurance to some women through the additional screening provided by the trial. Clinicians felt that their involvement in clinical trials was important, contributing to professional knowledge as well as benefiting women. The major drawback of the trial was the lack of resources available locally for clinical trials including clinic time, staff and facilities. Other points raised were concerns regarding the side effects of Tamoxifen, women's concern regarding randomisation, and whether there was to be continued funding for this trial.

4.3 Phase 2: Interviews with multi-disciplinary teams

Method

There was a need to explore the issues raised by the questionnaire in more detail from the perspective of the multi-disciplinary teams; in order to gain an understanding of the problems experienced by them when recruiting women to clinical trials. Semi-structured interviews were chosen to explore factors affecting recruitment to clinical trials with these multi-disciplinary teams. The interview schedule was developed using some of the issues raised in the questionnaire. The duration of the interviews was from 45 minutes to 120 minutes. The aim of these interviews was to identify the actual and potential barriers to recruitment to IBIS, and the factors that enhanced recruitment.

The researcher classified each centre that had completed a questionnaire as a good, medium or low recruiter based on the number of women recruited in their centre. From these, six centres recruiting women to IBIS were selected for further follow-up. In the six centres, members of the multi-disciplinary team were interviewed using a semi-

structured interview schedule (Appendix D), in either an individual or group setting. The interview schedule was developed from issues raised in the questionnaires and used as a guide in the interviews. The semi-structured schedule ensured that the information required by the researcher could be obtained, whilst providing the interviewees with the opportunity to expand or illustrate issues that arose.

The interviews were arranged by contacting the consultant surgeon at each of the selected centres; this letter provided information about the study and the purpose of the interview. All those contacted agreed to participate and arrangements were made to interview them in their work environment, at their convenience. Every effort was made to conduct the interviews in private and uninterrupted, and this was achieved. The interviews lasted between fifty minutes and one and half-hours and were tape-recorded.

All the data were collected prior to analysis. The interview tapes were professionally transcribed and these transcripts were checked and corrected against the audiotapes for accuracy. Following familiarisation, the transcripts were analysed and the main themes identified. The data were coded and analysed, this produced recurrent themes and issues across the six centres. The aim of the analysis was to accurately describe what was occurring and to reconstruct the data into a form, which could be used.

Results from interviews with the multi-disciplinary teams

Initially three broad themes were identified in the data: selling the trial, practicalities of the trial and the women's issues. Two other researchers read the transcribed interviews and checked the validity of the findings. The reduction of the interviews into themes provides an overview of the factors affecting recruitment of women to IBIS from the multi-disciplinary perspective with their recommendations on how this might be improved. Three themes were identified: selling the IBIS trial; practicalities of the trial;

and women's issues and summarised in figures 4.10, 4.11 and 4.12.

All of those interviewed stated that they were committed trialists and clinical trials were seen as being the way forward in determining the effectiveness of treatments and the development of new treatments. One consultant surgeon stated that he knew that the staff in the department and colleagues around the United Kingdom valued the recruitment to clinical trials which took place locally; however, this work was not valued by local NHS managers, even with the increasing emphasis on research and development.

I saw IBIS as a good piece of research that I could start and finish in my professional lifetime as a consultant;...I was interested in... prevention...[it] was a useful thing to do...Unless we continue to do clinical trials we'll just stand still, and standing still isn't good enough, because women still die of breast cancer.

Another surgeon said:

Well, there is ... nothing else on the horizon to prevent breast cancer that's why it's important. All the other... [clinical trials] are involved in the treatment of the cancer so if you can do something to prevent it, it's a pretty sensible thing.

A clinical geneticist supported this view:

I think the evidence, from the use of Tamoxifen in affected women...would indicate that it benefits those affected women. It [Tamoxifen] reduces their risk of recurrence or another tumour forming...from a scientific basis, it's worth looking at. I think it's reasonable to investigate its potency in high-risk women who have never had a tumour. As a woman, I think anything that reduces a woman's risk of developing a breast cancer is worth looking at, but I think it's very important to look at the toxicity and other problems associated with giving a

drug to perfectly well, asymptomatic women; and so from that point of view a trial like this is reasonable for fully informed women.

Whilst this clinician was enthusiastic about IBIS she was cautious and concerned about the toxicity of Tamoxifen in well women.

The multi-disciplinary teams interviewed talked about the difficulties encountered with sharing their enthusiasm for the IBIS trial with women.

Patients in this country don't like the idea that the doctor doesn't know what the best treatment for them is, they still expect you to tell them what is best for them... and we, as doctors probably don't have enough time to sit down and explain why it is that we don't know the answers to everything.

This reflects the literature on uncertainty and time constraints, discussed previously (Taylor, 1984; Taylor and Kelner 1987; Taylor, Feldstein et al. 1994).

Selling the IBIS trial

The first of the three themes identified was selling the trial to women; the framework is highlighted in figure 4.10.

Figure 4.10 Selling the IBIS trial

Systems

Informed consent

Equipoise

Vulnerable women

Although there are criteria and protocol laid down by the trial designers there were different systems in place in each of the centres to support the trial.

Systems

Three of the centres appeared to have good systems in place to support the recruitment of women to IBIS, such as staff dedicated to this trial only; using risk levels to assess eligibility, via the telephone, prior to the women attending clinic; holding more than one clinic for IBIS per week; follow up of women who did not keep their clinic appointment; and in one centre a system for informing GPs about the outcome of every mammography. As one consultant surgeon said:

I think the reason it's [IBIS] been successful here is ... a) I wanted to do it b) it (the trial) provided me with a nurse to help run it ... I didn't have to have that run in period, when I had to recruit patients into clinical trials; before I'd got enough money in the pot to appoint somebody; and then have to continue having that nightmare headache of... "I haven't got enough money to pay you next month, can we get some more patients?"

This comment makes one wonder whether this centre had the women's interest at heart or if the centre were more interested in the money associated with the trial.

Some centres ran three clinics per week specifically for recruiting women to the trial. These centres had the resources necessary to run these, such as clinic availability, time and staff to support the trial. This centre had two research nurses solely responsible for the running and co-ordination locally of IBIS. In these centres the interviewees saw the trial as an important trial, and they were committed to recruiting all eligible women. This

commitment is demonstrated by the following comment:

... we cannot run IBIS clinic in the same way as you run a symptomatic clinic ... firstly, because they are healthy patients and they have more questions to ask, more worries; and secondly, you cannot explain the ins and outs of a trial in two minutes; and thirdly, I felt that the women are going to have adequate time [for] questions [to be] answered ... if you want really to run an efficient trial we know that you need the clinician committed, and you need a nurse ... somebody who understands about the drug you are using, so they take the patient away and explain to them what's going to happen. Clerical staff [are also] important ... It just needs a general level of commitment, and you cannot get people to show this commitment when they are under pressure.

This centre gave more time to this trial and the women enrolled on the trial, than they do to other breast cancer clinical trials. The research nurse and data manager gave more time to the trial than they were paid for, for example:

...everytime a women comes for follow-up we write to her GP and say she's had her 6 months follow up everything's fine or whatever's happened and we include a sheet reminding them what IBIS is all about.

This centre, as well as providing additional information, above and beyond the requirements of the trial, also used the opportunity to remind GPs about the trial, with the aim of recruiting more women to IBIS. Interestingly, this centre was a good recruiter to IBIS, but were poor recruiters to the BASO II trial (see chapter 3).

Other centres acknowledged the cost of running clinical trials and had sought means of obtaining additional funding in order to support the IBIS trial and infrastructure:

... our extra funding comes from the [local] cancer trust.

Some centres had experienced difficulties setting up and running the trial locally:

... looking back at records to do with IBIS ... there were difficulties ... liaising with the other services that you need for the study ... trying to work out about storage of drugs ... where to hold the clinic ... where there would be access to breast surgeons ... it took quite a lot of arranging.

This reflects the importance of support and commitment of other staff and services in the trust in order to ensure successful recruitment locally.

Informed consent

Issues were raised by some centres regarding the ethics of research, that is the conflict between the needs of the women versus the needs of society and of women in the future. Some of the staff interviewed for phase 2 were also responsible for recruiting women to IBIS and they had personal experience of breast cancer; this information was known by the other centres recruiting to this trial, and was referred to during the interviews with other multi-disciplinary teams and in personal communications. During these interactions it was suggested that this centre were good recruiters, because the nurse concerned was driven by her personal encounter of breast cancer. If this were the case, the personal ethics of the nurse concerned could be called into question.

Four of the multi-disciplinary teams interviewed referred to and emphasised the importance of informed consent. Some of these multi-disciplinary teams discussed this in greater depth and described how they ensured that they obtained fully, informed consent from the women, prior to enrolling them onto the trial.

I think before they come they've [the women] made the decision in their own minds; my job is to make sure that when they come, ... that it was an informed decision. So I sort of set aside the fact that I think they've made the decision ...

[I] give them all the information; you see some of them wavering at that point. But others say, "That's fine. I've thought about all this, I've read the paperwork, I'm yours" and they go and have the mammogram, or whatever, and they're on the trial that afternoon.

The centres that were good recruiters to this trial did not discuss issues of informed consent with the researcher; this was only discussed when raised by the researcher. For example, one of the good recruiting centres only referred to informed consent when discussing recruiting people with a learning disability, but not for other women.

In the centres visited, only one centre experienced a conflicting local trial, and in this centre the multi-disciplinary team were entering women to the IBIS trial that had a higher risk of breast cancer than required by the trial protocol. There were considerable differences in centre estimations regarding the number of eligible women recruited to the trial ranged from 15-100%. It was not possible for the researcher to verify the accuracy of these estimates. The one centre that stated that they achieved 100% recruitment achieved this by screening women, over the telephone, prior to inviting them for a clinic appointment; this appeared an effective use of the trial team and women's time.

Equipoise

Those centres that were good recruiters referred to the issue of equipoise covertly.

One consultant surgeon talked about the importance of the trial:

... I think nobody should talk to patients or volunteers about study if they don't believe in the study themselves because ... if you start just to sell the study because you want to have numbers in it, I think they [the women] sense it. If you really...believe that it is a good a study, [that] you are doing a good work,

then you are enthusiastic about it, you are open about it ... I mean they know ... When I approach them ... I say [this is] the information, go and think about it, it won't actually benefit me in the slightest whether you take part or not. I mean at the end of the day this is a study for the women ... don't feel that you are doing me a favour by taking part. ... if you believe in the study, the patients feel how sincere you are about what you're saying ... you're doing it for their benefit.

This surgeon felt that Tamoxifen was a low risk drug with few side effects for women. He emphasised that centres should not participate in a clinical trial unless they genuinely believe in its importance (Maslin-Prothero et al 1999). This issue of equipoise was raised in the previous study (chapter 3); yet, this was the centre that was a good recruiter to IBIS, but a low recruiter to the BASO II trial. In contrast, the following quote comes from a centre that was a high recruiter to the BASO II trial (chapter 3), but a low recruiter to IBIS.

... there is something in the interaction between doctor and patient, that the patient looks out for some cues or some non-verbal thing, and the patient picks up on this and decides for herself whether or not that doctor's actually encouraging her to take part in the trial. Even though he has just stuck to the facts... I think the patients, by and large, may not hang onto their relative risk as an indicator...they actually hang on to what the doctors telling them, whether verbal or otherwise. If you don't want to enter this trial we have a facility where you can be seen up to the age of 50, or in certain cases up to the age of 60, with closer surveillance [ie family history clinic]. I've stuck to the facts; other centres may not be able to say that.

This view could be explained by a number of factors: this centre did not actively seek out women to participate in IBIS by advertising in the local press or on the local radio;

the staff at this centre speculated whether they gave women a subliminal message, that is they were keen for older women to enter the trial, but not younger women, because of their concerns about giving Tamoxifen to young, well women.

... we mention to them that Tamoxifen has been used for over 30 years in the treatment of adjuvant therapy for known breast cancer patients; but what we're asking for is a sort of a mental leap to get them to take it as a prophylactic, and not as a treatment drug, and that the toxicity and side effects in premenopausal women is, to be honest, unknown. So we make that clear...and leave it to them to decide whether or not they want to be part of it [IBIS] ... there's a difference between somebody in a study where they're going to get a treatment anyway...and somebody where you're asking them to take a drug in prevention ... they [must] understand it [the trial] completely.

There were centres that felt this trial did not have a high enough relative risk level (Claus tables). This point was emphasised by an interview with a clinician that refused to randomise women to IBIS, because they felt strongly that the criteria for selecting younger, eligible women were too lenient.

One of the surgeons acknowledged the role of the family history clinic in providing additional support for women with a history of breast cancer. But there was concern regarding confirming a genuine family history of breast cancer; there was no system in place for verifying information provided by women. This unease was highlighted in another centre where they were identifying women and recruiting women to IBIS with a higher risk level than the criteria for recruitment to the trial, because they saw the selection criteria for the IBIS trial as too broad.

Vulnerable women

A number of the centres referred to the vulnerability of women.

Interviewer: You've talked about the importance of giving these women ... all the information that there is - do you find that at any time there are women you actually don't approach about the trial, and if so what are the reasons?

Well, I could, from a genetic clinic point of view. There might be women that we've seen, whom we know are post bereavement...or [have] a close relative with breast cancer ... who might be emotionally vulnerable; and it wouldn't really be correct to ask them to think of such an important decision at that time ... [that is] somebody that we felt wasn't able to fully understand and make an informed decision. Perhaps for any reason, whether it's emotional or cognitive or whatever.

A genetics nurse, at another centre endorsed this:

... it can be a stressful time in their lives as well, 'cause ... most of them will have recently seen relatives going through breast cancer ... it's been quite difficult time for them, probably.

Practicalities affecting recruitment to IBIS

The second theme identified related to practicalities of the trial and the coding framework is in Figure 4.11.

Figure 4.11 Practicalities of the trial

Support from colleagues

Infrastructure

Support from colleagues

There was a reference by the centres interviewed, to the importance of obtaining support for the trial from other colleagues in the hospital. One of the centres referred to the radiographers (responsible for the mammograms), and it was thought that they were not as committed to the trial as other members of the multi-disciplinary team:

... it's the time... because we don't have anybody specifically for research studies, so it comes out of our time and it's difficulty arranging clinics when you've got to sort out about mammography. It's extremely difficult for us to do that ... I mean I'd love to recruit more women onto it [IBIS] but we just don't seem to have the ... resources.

Communication between different members for the multi-disciplinary teams was seen as essential; a number of the centres had developed effective strategies for sharing information between the team members regarding individual women and the trial.

There were also examples of good record keeping such as one centre kept the details of women who had enquired about the trial but were too young to join the study. This centre kept details of these women and contacted them when they reached an age where they were now eligible for the trial, to see if they were still interested in joining.

In addition, there was a feeling that hospital managers in the Trusts did not value the recruitment of people to clinical trials.

Interviewer... Do you feel you get support from, not just from your boss for being involved in clinical trials, but from the NHS? Do you feel it's valued and appreciated?

I think it's an extremely difficult question to answer ... how would you measure that? In the NHS you don't... get Brownie points for things like [this] ... I think [it

is] a general trend in the NHS, and none of us, nurses and doctors alike, get enough support and back patting, and feather stroking... I am still expected to do all the other things I do.

This response reinforces points raised by the clinicians that completed the questionnaire in phase 1 of this case study, regarding the lack of recognition by NHS managers of clinician involvement in research.

There was a sense of a lack of time to devote to this trial. This can be illustrated in one centre where they only had a clinic for the trial once every two months. In addition the women at this centre had to travel over a mile to another hospital site for mammograms. There were insufficient resources locally to support more frequent clinics.

It's only held every two months [IBIS clinic], so we can only fit a certain number of women into it ... I think that slows down our recruitment; because we have quite a few women that want to come into the study, but we've just been unable to see them quickly enough.

Because of the length of time between clinic appointments, women had a couple of months to make the decision about joining the trial; this could be a one reason why this centre was a poor recruiter.

... I get the impression if they don't join that afternoon then we're probably not going to get them ... and maybe that's the last we hear of them.

There was a sense that the longer women are given to think about the trial, the less likely they are to join (see also chapter 3). The length of time given women to consider participation varied from centre to centre from immediately to over 8 weeks. In other

centres women were randomised immediately, unless the women asked for more time to consider the trial. One of the good recruiting centres gave women the option of more time to think about joining the trial, although a mammogram was already arranged for their next hospital visit. It could be argued that this is an additional enticement or incentive for women to join the trial, because women are persuaded by the chance to be screened with a mammogram at their next hospital visit.

Infrastructure

The importance of local and regional infrastructure to support clinical trials has been mentioned earlier. Some centres gave more time to the study per week than was actually allocated by hospital managers. In the centre where there were staff whose sole responsibility to this one trial; one of the research nurses were seen as being the key to good recruitment; illustrated by the following quote from another centre:

In [this other] centre [they]... have far more hours available ... she [the research nurse] goes and speaks to, ... practice nurses, and so on. I don't have the time to do that ... We've decided she's actually got a pit outside the hospital that she drops them into as they go past (laughter)... IBIS is the only thing she does.

Three of the centres visited ran separate family history clinics. The responsibility for the co-ordination of these family history clinics varied between centres, but it was usually either a clinical geneticist or surgeon. One breast care nurse felt that the existence of a family history clinic locally was a demotivator to recruiting women to IBIS, because there was an alternative choice for women with a family history of breast cancer. The existence of family history clinics appeared to be down to the enthusiasm of local staff, who developed and maintained these clinics. The growth in the number of family history clinics in the United Kingdom has led to centres revisiting their criteria for eligibility; in some instances women are now being discharged from these family history

clinics as under the new criteria these women no longer fit the more stringent criteria.

Another of the centres provided flexible appointment times in order to meet the needs of individual women. Appointments were arranged either first thing in the morning, or during lunch times, in order to accommodate women enrolled on the trial, but had other responsibilities such as work, or caring for dependants, and were unable to attend at the usual clinic times.

... if anybody phones up today and says "I can't make it next Friday but I can make it on Wednesday", and we can fit them in, we just move the drugs and notes into the next pile so they're all there ready.

The backup and support provided by IBIS co-ordinator, based at the ICRF in London appeared to be good at supporting the centres visited and this was appreciated:

Yes ... [it is] easy to communicate with London. There's always somebody there that you can talk to, if you are concerned about anything.

The availability of someone to discuss issues or to give advice was seen as important by all of the centres.

Women's issues

The final theme was related to women's issues and these are summarised in figure 4.12.

Figure 4.12 Women's issues

Cost to women

Uncertainty

Articulate women

Additional care

The majority of women who telephone and enquire about the trial, either to the London office or at the local centres, were not eligible for the trial. Some centres screened women over the telephone, to ensure their eligibility for joining the trial, prior to inviting them to attend IBIS clinic locally. In the centres where they undertook this screening, the women whom then attended the clinic were more likely to be recruited to the trial.

Cost to women

The multi-disciplinary teams perceived that there was a cost to women, being involved in the trial. First, there was a financial cost, especially for those women who traveled great distances to attend the clinic; unlike some trials, women on the IBIS trial receive no remuneration for travel costs. Some women were travelling distances of more than several hundred miles in order to attend their nearest IBIS clinic.

...there is geography to take into account because ... there are women that we see, who are suitable but, who live [more than 120 miles away] ... it's not reasonable to ask them to come down ... there are women who do travel because they've asked to.

Some centres had developed additional systems of support to enable women who wanted to be in the trial, but had problems getting to and from clinic; a data manager set up a system for sharing lifts to clinic:

[She] devised ... an amazingly good system where ... all the names and addresses [of women on IBIS] are circulated to the other members ... so

they know the people who live locally and sometimes they do lift sharing ... It's all very well organised.

Another centre would arrange appointments to take into account either where women were travelling from, or their work commitments:

... the clinic doesn't start until half past ten ... [but if] a patient could get here at half past nine, [the research nurse] comes in [early] so that a patient could be seen on her way to work. So yes, we are very ... flexible.

... the ones that live a long way away, but work [near our centre]; we give them peculiar [appointment] times ... and then they'll come back and have their mammograms on a different day.

These special arrangements were for the women's convenience, not the multi-disciplinary teams. There were other costs to women associated with the trial including the time spent travelling to and from clinic appointments; waiting in clinic; compliance issues such as taking medication daily for 5 years; plus side effects experienced as a result of the medication.

... [There] are women who've got members of their family, most of whom will have had Tamoxifen at some stage or other, and 50% of them ... will get side effects of some kind or another. I mean there's a drug [Tamoxifen] that has a really very poor side effect profile ... they're healthy women and ... some healthy women don't like taking tablets, and that's a unique thing with IBIS.

The support and encouragement of partners and family was seen as important. The more anxious the women were, the more likely they were to drop out of the trial, although the rate was low, approximately 10 percent. The careful selection and

screening of women, prior to entering them to the trial could explain the women's compliance.

Uncertainty

At the time of the interviews with the multi-disciplinary teams, there was a great deal of uncertainty as to the future of IBIS. Many women were approaching the end of their 5 years on the trial, and the centres were unsure about the future of the trial and whether there was to be any further follow-up of women who have completed the trial.

... bearing in mind some women started four years ago there's ... the implication of the follow up at the end of five years. They have to be discharged and, having got used to coming every six months that's going to be quite difficult for them.

One research nurse referred to this uncertainty:

Interviewer: You must have some women who are coming to the end of the trial?

We have, our first one comes in February. We're not 100% sure at the moment, we think we're going to follow them up a year later, so that'll be at 6 years and we're not really sure what's going to happen after that.

This ambiguity created anxiety for the women enrolled on the trial, and the staff responsible for the women's care, particularly those whose sole responsibility was IBIS; they were unable to keep the women fully informed regarding the future of IBIS. If women were to be followed up, on completion of the trial it would have cost implications for either the trial organisers or the hospitals, as to who would cover the cost of staff, clinic time, mammograms etc.

Additional care

Some of the centres provided added 'extras' for those women enrolled in the trial. One of the breast care nurses suggested:

... if you're in a centre where there's no family history clinic then... [the trial is] probably your only way of accessing care [and screening].

There was an acknowledgement that women were using the trial as a way of receiving free screening and 18 monthly mammograms; for those centres that highlighted this bonus to potential recruits, this made recruiting women to IBIS easier. One of the centres that were good recruiters also wrote to women and their GPs informing them of the outcome of their mammogram, the aim was to reduce women's concerns.

Only some of the centres visited had access to clinical geneticists, and their involvement and activity in the trial varied from centre to centre; in some centres the clinical geneticists would attend every clinic, whilst others could be consulted as required, to advise on women with an apparent higher risk.

The relationship between the staff and women entered to the trial was seen as very important.

... our drop out rate is probably less than most peoples, and, I think that is because we are really nice to the patients. I mean ... they ring up, and we go out of our way to accommodate them. [Our research nurse] will ring people from [her] home in the evening.

... you know they see the same face and they can trust you... the fact that you are at the end of a telephone, and you will actually come back to them. I always say to them, you can leave a message on the answerphone. I only work part

time but [the data manger] will take the messages.

This special relationship was still available to women, even if they came off the study:

We follow the patients up, I don't think they should just suddenly be dropped. I think they should have support, and that is why we still carry on seeing them ... just because they're not part of the study any more... there's always ... this worry at the back of their mind, that they're going to get breast cancer... we should carry on seeing them at least once a year.

This extra care is laudable, however it has resource implications for those centres providing this additional service, beyond the remit of the trial.

Articulate women

Several centres referred to the case of articulate women; a consultant surgeon referred to the difficulty of recruiting well-educated women to IBIS because they were too well informed. This point was also raised in another centre where another surgeon felt that many well-educated, informed women chose to attend the IBIS clinic for the sole purpose of questioning and challenging the multi-disciplinary teams, and then refuse to participate in the trial. The suggestion was that these women had already decided that they did not want to take part in the trial, but wanted an opportunity to confront the doctor's authority.

Other centres also discussed the issue of eloquent women, however their perception of these women was very different. These centres felt that this group of women were highly motivated and 'pushed' the multi-disciplinary team to allow them to sign up for the trial. This is illustrated by the following comment:

... they have informed themselves you see, ... a better, well-educated group

because they have decided for themselves they want to be a part of this [the IBIS trial]. They haven't just read the headlines, they've read the small print; and the pros and cons have been weighed carefully, and obviously talked over with their spouses or their partners and ... [they say] "I want to be part of this trial". Now that, to me, is an ideal person. I think one of the ... main benefits we've had from the NSABP trial, is that subgroup of patients coming forward having seen the data, and having decided for themselves, and understanding the data that those figures are good enough for them to be a part of a trial.

In one of the good recruitment centres all eligible women were offered the trial. Enthusiastic women could be seen as a trialists delight, but centres are dependent on the honesty and reliability of information given to them by prospective recruits.

Well, the problem really is that of verifying because we take women at their word that they have [a] breast cancer risk; but we've both had the experience of women who say, for example, that their grandmother may have had cancer at the age of 35 [and a mastectomy] and lived onto the age of 74. [But] mastectomies were performed in those days for other things besides from breast cancer; and [the] verifying of these cases is extremely difficult and ... makes the interpretation of their family history very, very difficult.

Summary of the multi-disciplinary team interviews

The interviews with the multi-disciplinary teams raised three main themes regarding the recruitment of women to IBIS: selling the trial, practicalities of the trial, and women's issues. The key issues appear to be:

- All the centres visited were committed to the recruitment of patients to clinical trials.
- The importance of mechanisms that support trials, these include sufficient staff and

clinic time, and the commitment of colleagues and local NHS managers.

- The cost to women if they entered the IBIS trial.
- The enthusiasm of women who want to join IBIS and see the trial as a means of reassurance, with the free screening provided by the trial.
- The multi-disciplinary teams uncertainty about recruiting younger women to IBIS.

The next stage of the project was to examine recruitment to the trial by undertaking a retrospective and prospective audit.

4.4 Retrospective and prospective audit

Method

The retrospective and prospective audit was to identify the number of women eligible for recruitment to the trial. The aim was to use the retrospective audit to establish the numbers of women recruited to the trial; it was not possible to ascertain the numbers of eligible women in this trial because women are referred by the IBIS co-ordinating centre in London. Comparisons were made between the retrospective and prospective audits to see if recruitment to the trial was increased.

Retrospective audit

A retrospective audit of 6 months recruitment was undertaken to identify all the women recruited to IBIS. During the 6 month period 1 July - 31 December 1998, prior to the interviews in the seven centres with the multi-disciplinary teams, a total of 190 women were recruited and entered to the trial from all seven centres.

Table 4.12: Numbers of women recruited to IBIS by Centre (1 July to 31 December 1998)

Centre	Number of women recruited
A	70
B	38
C	8
D	11
E	1
F	48
G	14
Total	190

In addition, some of the centres maintained excellent records, which included details of: who approached women to participate in the trial, and if women refused, their reasons for choosing not to participate in IBIS.

Prospective audit

Coincidentally, following the interviews with the multi-disciplinary teams, a national recruitment facilitator was appointed in April 1999. The aim of this appointment by the trial organisers was to boost recruitment in order to meet the international trial recruitment target of 7000 women entered to the trial by the end of 1999. The decision was made by the research team to examine recruitment to the trial before and after, in the seven centres, to see if national recruitment facilitator improved entry to the trial. The person appointed to the position was from one of the centres in phase 2 of this study and had the highest recruitment rate world wide. This new post was not advertised nationally and there was no competition for the position; the job provided the appointee with 2 days a week to focus on nation-wide recruitment to the trial. The national recruitment facilitator was entitled to expenses, but there was no secretarial or

other support to facilitate her in this new role.

A prospective audit was undertaken in the seven centres to examine if recruitment increased following this appointment. In the six-month period 1 July – 31 December 1999, in the seven centres a total of 128 women were recruited to IBIS. This was a reduction in the numbers of women entered when compared with the previous years figures (Table 4.12) in spite of the national recruitment facilitator post.

Table 4.13 Comparison of numbers of women recruited (retrospective versus prospective audit)

Centre	1 st July 1998- 31 Dec 1998	1 st July 1999- 31 Dec 1999	Difference
A	70	47	-23
B	38	36	-2
C	8	3	-5
D	11	11	0
E	1	7	+6
F	48	20	- 28
G	14	4	- 10
Total	190	128	- 62

There are a number of factors that might account for this reduction. The trial was to stop recruiting at the end of December 1999 and yet there was a great deal of uncertainty regarding the future of IBIS, with talk of extending trial recruitment for another six months. The seven centres examined may have started to wind down recruitment of women to the trial when it became evident that world wide recruitment would not achieve its aim of 7000 women randomised to IBIS by the end of 1999. And, whilst the national recruitment facilitator was an excellent recruiter in her own centre, no consideration was given to how other centres recruiting to IBIS might feel about this individual advising them on how to enhance their recruitment in their centre, and others

might disagree with her methods for enhancing recruitment.

The next section presents the findings from the women's perspective and includes their perceptions of IBIS and why they chose, or refused, to participate in the trial.

4.5 Focus groups and individual interviews with women

Method

Focus groups were the chosen method because they can encourage individuals to participate in a discussion that might be reluctant to be interviewed on an individual basis, or feel they have nothing to contribute. Compared to an interview, the participants can interact with each other rather than with the facilitator, with an emphasis on the women's' perspective rather than the researcher's. For those women who did not want to be a member of a focus group, individual interviews were undertaken. All the focus groups and individual interviews were tape recorded and lasted between two and two and a quarter hours.

Four of the seven centres involved in phase 2 of this study were approached to participate in the third phase, and included centres that were good, moderate and low recruiters to the trial. Having secured Multi-centre Research Ethics Committee (MREC) approval, the researcher went through the process of obtaining Local Research Ethics Committee (LREC) approval at each of the centres; this was a time consuming but necessary process.

The aims of the focus groups and individual interviews was to: identify how women had heard of the trial, the information received regarding the trial, the women's view of the service received, and suggestions on how the trial experience might be improved. A

total of seven focus groups and two individual interviews were held with women who were entered into IBIS - consisting of forty-nine women. A further seven individual interviews were undertaken with women who had enquired but subsequently decided not to participate in the trial.

As with all research, there were women who were approached to take part in this phase of the research but did not partake. A total of fifteen women did not respond to the researchers invitation to take part in one of the focus groups held. A further twenty-one women wrote to the researcher stating why they were not participating in the focus groups. Their reasons are found in table 4.14.

Table 4.14 Where provided, reasons given by women for not attending focus groups (n=21)

Reason	Number
No reason	8
Depending on a lift with someone else	4
Too far to travel	2
Work commitment	2
Hospital appointment	1
Child care commitment	1
No longer on the trial	1
Holiday	1
Illness in family	1

None were asked to explain why they could not attend the focus group, yet they chose to provide me with an explanation; this demonstrates the difference between the BASO II and IBIS women with regards to personal motivation and drive. Of these, eight women gave no reason, thirteen women were unable to attend due to other commitments and they gave an explanation. Information regarding the focus group members is included in table 4.15.

Table 4.15 Characteristics of women involved in the IBIS focus groups and interviews (n =56)

Age in years	Number
40-49	6
50-59	36
60-69	14
>70	0
Marital status	Number
Married and cohabiting	42
Widowed	6
Single	3
Divorced	5

Focus groups and interviews with women entered to IBIS

Five of the focus groups took place on study days organised in Breast Cancer Awareness month (in October 1998 and October 1999). Following analysis of the transcriptions three themes were identified: decision-making; concerns and contraindications; and trial experience.

Decision-making

Following analysis the theme decision-making was identified and the coding framework is in Figure 4.13.

Figure 4.13: Decision-making

Motivation

Altruism

Screening

The women who chose to participate in the focus groups appeared to be highly motivated individuals. They were proactive and yet it was apparent that the women were either optimistic or pessimistic regarding their perceived risk of developing breast cancer.

Motivation

Women's reasons for participating in the trial varied; the initial motivation was a high level of personal need because of a family history of breast cancer. The women expressed a concern regarding the number of deaths per year from breast cancer in the United Kingdom (when compared to other developed countries), the absence of NHS breast screening (such as mammography) for women under 50 and over 65 years, plus the difficulty of accessing expert screening and advice from GPs.

My sister died of breast cancer. Two young children, and an aerobics instructor. [She] ended up riddled with cancer [she had seven operations over a five year period].

... having got a family history [of breast cancer], which is absolutely unbelievable - aunt, mother, grandmother, cousin – you name it, we've got it.

Closely associated with this is the lack of family history clinics in some areas of the United Kingdom.

Women referred to the fact that they stood a 50% chance of receiving Tamoxifen, as being a prime reason for participating in this trial. One woman referred to having to 'push' the multi-disciplinary team to include her in the IBIS trial. Endometrial cancer is

one of the side effects of Tamoxifen, so women who had had hysterectomies stated that this made the decision to join the trial easier.

Altruism

There was considerable evidence of women's unselfish volunteering to participate in a preventative trial when they are well.

...certain things, you think, that are your duty to do...your contribution to society.

...research into things to try and help others, that was my main idea and to see if I could glean any more information for myself because you live with the fear all the time...of contracting [breast cancer].

This was explained by their very personal experiences of breast cancer such as making it safer for daughters, granddaughters and sparing family the angst of seeing them sick and dying - as I saw my grandmother, mother, sister die.

Because of my family history, I felt that participation in such a trial could help treatment for this and future generations ie my daughter.

The fact that this was a preventative trial was seen as very important because the majority of clinical trials are treatment trials. The women saw clinical trials as giving the answers and this mirrors the clinician perceptions of why clinical trials are important. It was evident that a number of the women participating in this phase of the research worked in healthcare settings as nurses, doctors, medical secretaries and receptionists. These women might have adopted the view of their clinical community, where they worked.

Screening

What 'sold' the IBIS trial to women was the opportunity to receive regular screening, with access to hospitals, seen as centres of excellence, and the experts working there. The screening was seen as being more beneficial than the 50% chance of receiving a treatment.

...from a bit of a selfish point of view, if somebody is going to check you...it was reassuring...it's the only way you hopefully hear things. We were getting a bit of reassurance.

The additional screening, provided by the trial, gave women peace of mind and reassurance, not only for themselves, but also for their families. The screening was perceived as preferential treatment, a perk, to participating in a clinical trial. This was more evident in those women who had other health problems identified as a result of the six monthly screening provided by IBIS. This could be argued as not directly affecting recruitment, but it is associated with women's commitment and compliance, encouraging women to stay on the trial. The women who had experienced other health problems appreciated being referred to appropriate health professionals promptly.

I've got this awful fibroid...and it started giving me problems...I rang [the research nurse] ... Within three weeks I saw [a gynaecologist] ... if I hadn't [been on the trial] I would have waited three months.

I told [the research nurse] exactly what the problem was, and ten minutes later I had an appointment to see [the surgeon] the following morning...What other specialist would run around like that?

1st April, I found this [breast lump] myself...I was hysterical...I phoned [the data manager]...she said come straight over. I mean it's wonderful, isn't it? Anybody

else...says, "I'll get you an appointment"...[but instead I was seen immediately] I went straight over at 11 o'clock, that morning.

Across all the centres visited women considered that they received specialist treatment, regardless of whether the centre was a good, moderate or low recruiter.

Concerns and contraindications

The findings from this theme are encapsulated in figure 4.14.

Figure 4.14: Concerns and contraindications

Side effects of treatment

Clinic environment

Cost to women

Whilst the first theme identified why women chose to participate, and the perceived benefits of the trial, the women did have concerns about aspects of the trial.

Side effects of treatments

Prior to entering IBIS women were given considerable information from the trial organisers regarding the side effects of Tamoxifen. In all the focus groups and one-to-one interviews women referred to the side effects they had experienced since commencing the trial, such as weight gain, night sweats, hot flushes and nail splitting. In each of the focus groups held women tried to 'guess' whether they were receiving Tamoxifen or the placebo. Most of the women interviewed experienced very similar side effects, yet not all of them would have been on Tamoxifen. The side effects

experienced could be explained by the fact that all the women spoken to were over the age of 40 years, so they may be presumed to be approaching their menopause and a time when many women experience weight gain and other physical factors associated with reduced activity and growing older.

Well, is it because I'm the age I am...or am I on Tamoxifen? I mean, you don't even know if you're on it or not.

Or could these side effects be explained by the placebo effect, which appears to have an effect on both imagination and individual health (Walker, Hays & Eremin, 1999a; Walker, Heys et al. 1999b). All the women who participated in the focus groups and individual interviews expressed a wish to know whether they had been on Tamoxifen or the placebo.

Debates occurred between women who had been on the trial for more than 4 years and those who had recently joined, regarding hormone replacement therapy. Initially, women on hormone replacement therapy were excluded from the IBIS trial because it was contraindicated in conjunction with Tamoxifen. However, the criteria for the trial have changed over the years, and hormone replacement therapy is now considered safe. This apparent contradiction led to some confusion and concern among the women.

Finally, some women experienced reluctance on the part of other family members regarding their participating in the IBIS trial.

...[my] daughters weren't so keen...They don't like the idea of me popping a pill every day [for the next 5 years].

My husband wasn't too keen on the idea. When he read [the trial information] it

could possibly have complications.

[My] brother-in-law said [if you go on Tamoxifen] “You’ll lose your sex drive, you will get fat”.

The majority of women were very determined that this trial was something they wanted to do, it was their decision and nobody else’s.

I didn’t discuss it [the trial] with anybody...I made the decision very quickly; this is for me, get on with it...Is there anything worse than breast cancer here? No, therefore [I signed up].

I had already decided from the time I saw I could do it [join the trial]...nothing was going to stop me.

I really did think about it, it was my decision.

This matches with the results from multi-disciplinary team interviews, where it was felt that many women had already made up their mind to join the trial, before arriving for their initial clinic appointment.

Clinic environment

Where the clinics take place was important to the women spoken to. Some centres had excellent facilities, which were valued by the women.

It all seems very casual and relaxed and comfortable. [And yet] I’m sure they are all very busy.

...it’s almost like a club.

However, in one centre, the clinic had recently moved from a breast screening unit to a general outpatients department.

The new place [clinic] is horrendous... There's a chest clinic, psychiatric clinic and everything else in one room, and I can't see that that's going to be really acceptable.

The atmosphere in this clinic had changed from being quiet, relaxed and friendly, to noisy and chaotic, with lots of people, and 'children running around'. This dissatisfaction with the new clinic appears to be related to how the women enrolled on the IBIS trial emphasised that they were well-women, and partners, not patients in this clinical trial. In another centre, the clinic was held in a Portakabin, which was very cramped.

...those little mobile huts. [It's like a] little rabbit warren.

The women found this environment disconcerting and unsatisfactory; staff at this centre were aware of the effect the environment had on all women, and money was being raised to build a new clinic, specifically for screening and women with breast disease. It could be argued that this factor is not connected with trial recruitment, but it does have an effect on their experience of the trial and may influence compliance.

All the women referred to the importance of the staff involved in the trial in making their experience of IBIS a positive one.

You're made to feel very welcome and that they appreciate what you are doing. ... They give the impression, nothing else is happening, [they are there] just for you.

It's absolutely first class service; you wouldn't get it if you paid privately.

*...I think (the breast care nurse is) the one...the only one I seem able to relate to
... you could ring her up at any time.*

The women commented on the lack of continuity with doctors, the majority of them were aware that doctors (particularly more junior doctors) rotated through different clinical settings. It could be argued that this is not directly linked to factors affecting recruitment, but it is a trial retention issue; knowing the multi-disciplinary team and seeing a familiar face at clinic appointments encouraged these women.

The women appreciated that the medical staff experienced others demands on their time, and that they do not have the time to spend with each woman, answering their questions. But, they stated that it was important the doctors did not lose sight of the women, their contribution to the trial and what concerned them. Simple things were important to the women's experience, such as the doctors wearing name badges, and introducing themselves to women. Closely associated with this was the recognition that although there may be delays in clinic that were unavoidable, women still wanted to be kept informed. These women realised that a long wait in clinic might be because another woman has a problem, such as a breast lump, and therefore were understanding and appreciative, but needed to be kept informed. The next section builds on this theme by exploring the cost to women in greater depth.

Cost to women

There were personal costs to women, associated with attending IBIS clinics, these include such things as time spent travelling to and from clinic, the cost of travelling to clinic appointments (some women have over 300 mile round trips), taking time off paid work, organising and payment for care of children and other dependants, whilst they attend hospital clinic.

I have to drive three quarters of an hour...every time and then [there is] car parking...That could put people off who were really pushed [financially]... If you live where I do, there's no such thing as public transport.

...it's a long journey...three quarters of an hour journey [from home to nearest town]...an hour and twenty minutes on the train and then [I] have to get a cab, or try and get a bus [to the clinic].

There were some women who were booked to have their mammograms on a different day to their appointment with the multi-disciplinary team. This arrangement was inconvenient for most women, but more so for those women who had to travel any distance to attend IBIS clinic.

There are other commitments associated with IBIS, such as remembering to take a tablet daily for five years. One woman, who has now completed the trial, talked about the difficulty she experienced every day and the only way she could swallow her tablet was to break it up and put it on her toast and marmalade. She said she would never be able to take a tablet again.

Women also talked about the worry they experienced prior to each hospital visit, especially when a mammogram is scheduled.

[I] worry before hand, especially if a mammogram is scheduled. [Then] incredible relief afterwards.

For the women who were contacted with the results of their mammogram this was a bonus. Some women expressed concern about being tested for other things, which when they asked what the tests were for the multi-disciplinary team did not appear to

know, or were vague. Results from these 'other' tests were never given. The uncertainty of the multi-disciplinary team could be explained by the turn over of clinical staff, and they do not know what or why certain tests are being undertaken.

Trial experience

An outline of this theme is to be found in Figure 4.15.

Figure 4.15: Trial experience

Positive

Negative

This theme really pulls the women's experience of participating in the IBIS trial together, and develops some of the categories referred to earlier.

Positive experience

Overall, the women valued the extra care and screening they received as a result of being a part of this clinical trial. Women referred to being chosen for the study, participating in the trial was something special, a privilege. The women also discussed how the IBIS trial felt different to other clinical trials because it was a preventative trial and they felt they were participants, not patients.

The key to the women's trial experience was the person they saw as responsible for coordinating IBIS in their local centre - this invariably was a breast care nurse, research nurse or data manager.

One of the best things they did was to get [the research nurse] in, because she is absolutely brilliant; and she is so dedicated.

These individuals provided a familiar face, as well as a high level of empathy for women on the trial, someone to contact if they had worries or concerns. By having a key person in each centre, this removed the women's need to 'know' the doctor.

The newsletter provided by the trial organisers was appreciated, as well as being interesting and informing women, it provided them with another source of information and support. Some women sent their newsletters to relatives in other parts of the world including Australia, Canada and the United States of America.

I sent mine to my sister in Australia, and she's subsequently started on the [IBIS] trial.

The women also valued the opportunity to get together with other women on the trial, for example the study days held in two of the centres, in association with Breast Cancer Awareness month. The women also referred to the focus groups (held by the researcher) and how they provided an opportunity to discuss issues with other people who understood what they were experiencing. Other researchers who have used focus groups as a means of collecting data support this view.

Negative experience

But everything was not perfect. When the focus groups were first started in October 1998, some women had been on the trial for over four years and they were uncertain of what the future held for them as individuals. As the focus groups progressed, women were completing their five years on the trial. These women referred to a feeling of being exposed to the risk of breast cancer, now that the screening associated with the trial was discontinued, and how they felt abandoned by the trial organisers (Cox 1999). In the women's eyes, the trial organisers had not thought through to the end of the trial, and had failed to consider the needs of the IBIS trial participants.

...are you going to abandon me now?

These women felt they were entitled to some degree of aftercare. This follows the same concern raised in the interviews with the multi-disciplinary teams. Not all areas in the United Kingdom have access to a family history clinic, plus many of these women would not fulfill the increasingly stringent criteria of these clinics where they exist.

There were pragmatic points raised by the women including: delays in clinic; the change of doctors; the financial costs of travelling; side effects of treatments; wanting to know if they were on Tamoxifen or the placebo; and not being able to donate blood.

...you know it is going to be busy [the clinic] and [I] think, well, I'm here for a couple of hours...it's no good going there and thinking you'll be out [in half an hour].

Finally, the women who were involved in IBIS could not understand why there was a difficulty recruiting to this trial, and why more people did not know about the trial. They frequently referred to their own GPs lack of awareness and knowledge.

My GP didn't even know about the [IBIS] scheme.

I'm surprised that GPs don't know about it. I think that could be improved.

There was an acknowledgement that GPs could not be expected to know about every clinical trial, but they felt GPs should be more knowledgeable and the women felt the responsibility for information giving, to the clinical community and eligible women, fell with the trial organisers.

Summary of the main factors identified by women in the IBIS trial

Three main themes were identified from the transcripts of these focus groups: decision-making, concerns and contraindications, and trial experience. From these the key factors appear to be:

- How women perceive their own risk from breast cancer to be.
- The costs associated with trial participation eg time, effort, travel, financial and the side effects of treatments.
- The self-motivation of these women, which appears to be driven by the additional care and free screening provided by the trial.
- The importance of the staff and clinic environment in making the trial experience more positive.

The next section examines those women who chose not to join the IBIS trial.

Interviews with women who chose not to be entered to the IBIS trial

A total of seven women were interviewed, who after approaching either the ICRF in London or their nearest local centre for information about the IBIS trial, chose not to join the trial. The original research proposed that focus groups are undertaken with all these women; but this was not feasible if we were to obtain a national perspective, therefore individual interviews were held. Following analysis there were three themes identified: the women's personal view of breast cancer; the cost of participating in the trial; and their thoughts of the IBIS trial summarised in Figure 4.16, 4.17 and 4.18.

Women's views of breast cancer

Figure 4.16: Women's views of breast cancer

The optimists

The pessimists

The women appeared to fall into two groups, there were either optimistic and felt their chances of developing breast cancer was the same as any other woman's, or they were pessimistic and convinced they were going to develop breast cancer.

The optimists

Some of the women interviewed were very positive about their personal risk of breast cancer and did not see the point of worrying themselves unnecessarily. As one woman stated:

Why trouble trouble, 'til trouble troubles you?

These women felt that although they had a family history of breast cancer that they did not think that they had a high enough risk. One of these women regularly attended a local family history clinic, receiving screening and therefore did not need the security of screening associated with the trial, and available to women who are entered to the IBIS trial.

The pessimists

In comparison, these women were driven by their anxiety, they were fearful about contracting breast cancer and saw participating in the IBIS trial as a constant reminder of their family history.

One woman commented on how the fear of breast cancer drove other women to try anything, and cited her own mother had had a primary breast cancer, followed by contralateral breast cancer, and was treated with mastectomy for both occurrences.

She said:

...my mother went completely bananas with her diet after [breast cancer]; she went to extremes...[and] followed every quack's peculiar, quirky bit of

information...about how she could prevent any more cancer occurring.

Reference was made to a personal friend, a consultant surgeon, with a family history of breast cancer, who had chosen to have a bilateral mastectomy:

...not because she had breast cancer, but because she felt the risk [of breast cancer]...was really high, she did it as a preventative thing...[Personally] I find that extreme.

There was a reference to Tamoxifen, made by another women who said:

...I would be wasting my time [on the trial], if I wasn't on Tamoxifen.

These women felt that there was very little they could do to prevent breast cancer occurring:

...it's all in the lap of the Gods really.

Cost to women of participating in IBIS

Figure 4.17: Cost to women of participating in the IBIS trial

Side effects of treatments

Commitment

There were perceived costs to the women for participating in the in IBIS and these deterred them from joining the trial.

Side effects of treatments

All the women interviewed expressed concern about the side effects, not only of the medication, but also the screening associated with the trial such as mammograms. The

main concern was about the taking of Tamoxifen by healthy women, and the unknown long-term effects of taking the drug. There was disquiet about some of its specific side effects; one of the women had a long history of migraine:

And I thought, no thank you, I have just got my migraine under control, there is no way I am going to risk getting those back.

Another issue that discouraged the women from entering the trial was their personal experience of the menopause; most of these women interviewed had been through the menopause and did not want to have similar symptoms again, such as vaginal bleeding, hot flushes and night sweats. One woman was still experiencing problems with the menopause and felt this was affecting her effectiveness at work:

...I've been on hormone replacement therapy for quite a while...My GP has tried to reduce the dose,...[and] I've been struggling with that 'cos I've got menopause problems again...The side effects of Tamoxifen actually mimic the menopause...[and] I thought I can't be doing with that.

Women also referred to the commitment of taking a tablet daily for five years. Three of the women, who had refused to join the IBIS trial, stated that they did not think they could make that long and big a commitment.

Commitment

Four of the women interviewed talked about the time spent attending clinic appointments. This was the number of clinic appointments and the time spent waiting for mammograms or to be seen by the multi-disciplinary team. It was evident that some women had misunderstood the commitment required by the trial organisers, and the women had not sought clarification.

One woman attended a family history clinic at the same hospital where she would have been attending IBIS clinics; there had been a change in practice, where mammograms and appointments with the multi-disciplinary team were held on different days. Similar practice has been introduced in other centres in the United Kingdom and this practice may exclude other women from entering IBIS, or on those already entered onto the trial. This emphasises the importance of a co-ordinated approach between different departments eg radiographers and clinicians negotiating, and working together to increase efficiency and effectiveness and reduce the inconvenience to women.

This issue has been raised by those women already entered to IBIS, and was identified as an issue for four of the women interviewed. For some of these women attending clinic appointments would involve a 120-mile round trip. For one woman there was a hospital near her home recruiting to IBIS but had not been notified of this option. An additional concern was parking facilities at hospitals, not only the cost of parking, but trying to find a place to park; this was a point also highlighted by women already on the trial.

Thoughts of the trial

Figure 4.18: Thoughts of the IBIS trial

Positive aspects

Negative aspects

This draws together the different women's overall thoughts of the trial including positive and negative aspects, and how the trial co-ordinators might improve recruitment.

Positive aspects

All the women interviewed had heard about the trial through the media, this included local and national newspapers, women's magazines, and local and national radio stations. It was the women who made the initial contact either with the ICRF in London or with the trial co-ordinator for their area.

Regarding the written information received telling the women about the trial; overall they felt the information was satisfactory. There was a belief that the information could be improved by reducing the amount sent out to women initially and simplifying the explanations.

When the women contacted the local co-ordinators and discussed the trial, they considered that the staff explaining the trial were clear and had got the details of the trial across. None of the women felt they were pressurised to join the trial.

...I think that they did all the sale that they possibly could. So in terms of planning the product....they did all they could have done in a sensitive, caring, professional way...I wouldn't want a mega, pushy sales drive.

This woman refers to the explanation of the IBIS trial as a sales pitch, which mirrors the clinician interpretation of how they get their message across.

Negative aspects

The women interviewed were invited to suggest how the trial experience might be improved. There was a consensus that there was too much information, and for some women this literature was pitched at too high a level. There was a suggestion that the trial team could include some information on the likelihood of developing side effects from any medication for example the percentage of women who experience migraines.

Even though these women chose not to participate in the IBIS trial they were surprised that their GPs were unaware of the trial, and that information about the trial was not to be found in local health centres or hospital waiting rooms. The women a number of suggestions about raising the awareness of people through advertising the trial in education establishments such as colleges of further education and universities, as well as in local and national media outlets.

Summary of factors affecting women who refused to join IBIS

There were three themes identified from the transcripts: the women's personal views of breast cancer, the cost of participating in the trial, and their thoughts of the IBIS trial.

From these the following key factors were identified:

- The costs of participating in the trial that are the side effect of treatment, travelling to and from the appointments, and the time commitment.
- The women have perceived risk of getting breast cancer.
- None of these women interviewed had been to the trial centre and talked about the trial with a member of the multi-disciplinary team, but they had spoken to a member of staff on the telephone.

The next section pulls all the findings from the IBIS study together.

4.6 Discussion of key findings

Using the criteria developed in chapter 1 the main findings from this study can be grouped under: trial related factors, clinician related factors and patient related factors.

Trial related factors

All the multi-disciplinary teams stated that they were committed trialists and felt this was a relevant and important trial because it was a preventative trial; but they felt there was

a lack of recognition as to the importance of participating in clinical trials for the Trust manager's perspective. Resources were essential if the multi-disciplinary teams were to be effective at recruiting eligible women; the most successful recruiters to IBIS had extra staff and additional systems in place to support the running of the trial and the women entered. For the women participating in the trial their experience had been positive; in their opinion the trial represented five years of freedom from anxiety because of the screening.

Any information about the trial needs to include a statement of the trial objective and future usefulness, a full and balanced presentation of the benefits and risks of participation, and detail of the commitment to the trial evident in order that women with dependants, work obligations, or living at a distance from the centre could make an informed decision whether to join the trial or not.

Clinician related factors

There was reluctance by some centres to promote IBIS strongly, because the staff do not want to be seen as coercing women to participate in the trial. Some clinicians and multi-disciplinary teams have concerns about giving Tamoxifen to younger women that the criteria should be for older women with a higher risk. The women may pick up on the multi-disciplinary team's unease and therefore choose not to join the trial (Gotay 1991; Tobias & Souhami 1993).

Patient related factors

The local co-ordinator of IBIS in each centre played a key role by being a primary source of information, being approachable and supportive to the women during the course of the trial. There was uncertainty for both the staff and women as to what would happen to the women on completion of the 5 years of the IBIS trial. The local co-

ordinators for IBIS were key to the trial participants and held in high personal and professional regard by women, these co-ordinators rather than the doctors had addressed most queries.

The women entered in the trial saw themselves as well women, in charge of their own lives and able to make informed decisions. To the women a prime motivation for joining the trial was the free screening provided by the trial, but this benefit only became apparent to them at the initial hospital appointment, where they discussed the trial. Not all women had access to a family history clinic where they could access screening.

Other reasons for joining the trial were following the experience of relatives who had died following breast cancer and a hope that the results of the study would make it safer for daughters, granddaughters and future generations. From the women's point of view they do have a choice about whether to participate in the trial or not. Their decision appears to be based on their own personal outlook regarding breast cancer. Many of these women had cared and observed relatives dying from breast cancer, and this has shaped their view. The women appear to fall into two groups – optimists and pessimists, however, it is not straightforward that is with the pessimists joining the trial out of fear, and the optimists waiting to see what happens.

None of the women randomised to the IBIS trial thought that the side effects associated with the medication was as bad as their risk of breast cancer. For those women who had chosen not to participate in the trial their decisions were more complex; there was a fear of breast cancer and a difficulty in confronting this fear. Many of these women did not want to risk the side effects associated with taking Tamoxifen. Some of them were unsure about the benefits of clinical trials. There were other issues relating to the practicalities of participating in the trial including too far to travel for appointments, too

frequent appointments and the costs associated with these.

4.7 Summary and conclusion

This chapter has reported on IBIS, a preventative trial. The findings from the three phases of the project have been presented. There are some interesting similarities and differences between the different groups accessed; their opinions converge in relation to women joining IBIS to access free screening; the costs to women of participating in the trial; and finally, women thoughts of the IBIS trial organisation. The differences were greater with the key points being: eligible women continue to refuse to join the trial; lack of time and availability of staff to support the trial; the difficulty of explaining random allocation to women; and the low numbers of eligible women seen in practice.

In the final chapter the thesis as a whole will be discussed, including its contribution to new knowledge and recommendations for improving recruitment to clinical trials from the clinicians, the multi-disciplinary teams and women perspectives.

CHAPTER 5 DISCUSSION AND CONCLUSION

- 5.1 Introduction
- 5.2 Recommendations
- 5.3 Methodological considerations
- 5.4 Key findings and their contribution to new knowledge
- 5.5 Areas for future research
- 5.6 Summary and conclusion

Chapter 5 Discussion and conclusion

5.1 Introduction

The first aim of this chapter is to set out the factors recognised in this thesis as influencing the recruitment and randomisation to trials, the second to use this knowledge to make recommendations on how recruitment to clinical trials might be improved. In doing this the project as a whole will be examined by revisiting the aims of the research, examining how the thesis has met these, discussing the key findings and their implications and considering their contribution to existing knowledge. The strengths and weaknesses of the research are assessed, with suggestions for further work.

The thesis began with a literature review of issues related to the recruitment to clinical trials. Three factors were identified as inhibiting the clinical trial process; these are the trial design factors, clinician related variables and patient-related factors. This review acknowledged the existing work but recognised that there had not been a detailed examination of recruitment to a defined clinical trial from the combined perspectives of surgeons, clinical multi-disciplinary teams and patients. To investigate this gap in knowledge this thesis used a combination of quantitative and qualitative methods to explore these different perspectives. The results from this multiple methods approach have corroborated the general findings from previous research on this subject as well as generating new knowledge.

Update on the two breast cancer trials

On 31 October 2000 the BASO II trial stopped recruiting women to the trial. A total of 1162 women were randomised. Preliminary analysis of the data suggests that for these

tumours wide local excision alone is the treatment of choice. The IBIS trial is stopping recruitment at the end of December 2000; analysis will not be possible for a further 5 years.

5.2 Recommendations for improving recruitment to breast cancer clinical trials

Trial design

- Better selection of trials with rejection of less important ones. A trial must address a relevant issue with a high probability of confirming or changing practice.
- The design of trials to be kept as simple as possible.
- A clear recruitment plan, which includes both trial staff and potential patients in the planning and implementation of the trial.
- Flexibility in recruitment strategies. This will allow the participation of more clinicians and increase the relevance of trial results to widespread clinical practice, ie not confined to research groups.

Clinician/multi-disciplinary team factors

- Participation in clinical trials by multi-disciplinary teams should be an expected component of their practice. Participation helps to maintain clinical competence as a part of continuing education. Failure to participate in clinical trials should require justification.
- Adequate funding of clinical trials to meet the staffing requirements and the needs of the defined study population.
- Financial incentives for recruiters.
- Education programmes for managers, clinicians and the trial team public on

communication, clinical trials etc. To be funded by grant bodies.

- Information on the women approached to join clinical trial, and other details to be recorded on the new BASO database.
- Funders of routine healthcare, for example NHS managers must be informed that evidence-based practice resulting from good clinical research is usually more cost effective than traditional practices, or the uncritical adoption of unproved treatments.

Patients

- Financial incentives for trial participators to cover costs eg for fares to hospital appointments/treatments, to cover cost of childcare etc.
- The use of sites and facilities that enable access to the trial for trial participators, for example for women to attend hospitals for treatment and appointments near to their home or work.
- Availability of women, who have participated in clinical trials, who are willing to talk to potential patients about their experience of breast cancer and their experience of trial participation.
- Use of media and the set up information centres in clinical areas to educate and inform people about clinical trials, where people can access information regarding clinical trials, their specific illness, for example posters, leaflets, CD ROM and access to the Internet.
- Improvement of the clinic environment to include making the clinic environment more comfortable; reduced waiting time in clinic; some way of informing women about how long they have to wait in clinic; and organising treatments and appointments on the same day.

Where possible to allow women to choose their treatment option, and to be included in a study.

5.3 Methodological considerations for research on this topic

Impact

Since commencing this research, specific Internet sites that highlight relevant research and literature have been set up. These include the United Kingdom Co-ordinating Committee on Cancer Research (UKCCCR) register Internet site (this holds the details of over 500 randomised controlled clinical trials); the National Research Register database held by the NHS Research & Development Directorate (details include 50,000 NHS research projects, of which 2662 are related to cancer); the Current Science meta-register of randomised controlled trials (has details on clinical trials in medicine); and the Cochrane Cancer Network part of the international Cochrane Collaboration, which carries out reviews of clinical trials. This group is proposing to collaborate with Cancer British Association of Cancer United Patients (CancerBACUP) to devise patient orientated summaries of these reviews.

Other work has also been published in the area of clinical trials and recruitment (see chapter 1 literature review). This means that there is a growing body of work in this area, developing a knowledge base on recruitment to clinical trials. This thesis builds on this work by providing new insights to recruitment using two breast cancer trials as case studies.

Gaining access to the selected trials

Gaining access to the different populations under study has been a difficult and time-consuming activity. This research was very dependent on the co-operation of local

clinicians and their colleagues to provide access to multi-disciplinary teams, information and patients. Ethical approval had been obtained from MREC, yet some LREC committees wanted to make changes to the patient information and consent forms, contrary to protocol. Other researchers (Lux et al. 2000) have identified these difficulties.

Practical difficulties

When approaching women to take part in the focus group interviews there was a poor response from those women entered to the BASO II trial (in comparison to those entered to IBIS); one possible explanation is that the BASO II women have had breast cancer and they now want to put this experience behind them. Being contacted by a researcher who wants to meet you, to talk in detail about your thoughts regarding breast cancer and clinical trials would be an unwanted intrusion, a reminder of breast cancer. The researcher did take the opportunity to explore possible explanations with focus group participants, as to why they thought other women chose not to be interviewed. These women could understand that others might be not want to discuss their personal experience of breast cancer and share their thoughts and feelings with other women. The women who chose to take part in the focus groups spoke about how beneficial the encounter was, providing them with an opportunity to talk about their personal experience, as well as the opportunity to talk to other women.

In contrast, there was an over recruitment of women randomised to the IBIS trial, because so many of the women approached to participate in the focus groups wanted to take part. This could be explained by a number of factors, on two of the occasions the focus groups took place on the same day as seminars associated with Breast Cancer Awareness month; therefore the women were going to be present at the venue

where the planned focus groups would take place. The women randomised to IBIS trial were more vocal and articulate than those interviewed for the BASO II trial, and they were not afraid of expressing their opinions. Also, those women who were unable to attend the focus group discussions wrote to the researcher and provided reasons for their non-attendance (see chapter 4).

Data collection

The process of collecting data from the 14 centres randomising women to the BASO II trial was complex, involving scrutiny of pathology databases and individual patient records. Ethical approval had been gained but under the latest Data Protection Act (1998) implemented in 2000, accessing these records would be very difficult and therefore, it is unlikely that the same method could be used today.

5.4 Key findings and their contribution to new knowledge

This is a clinical, pragmatic piece of research that examined the experience of recruiting women to two breast cancer trials. When matching the similarities between the findings from the three groups accessed ie clinicians, multi-disciplinary teams and women the following were identified: adapting local practice to meet the requirements of the trial; the time it takes to explain the trial to eligible women; eligible women refuse to participate in the trial; women have a preferred treatment; selling the trial to women; lack of time and staff; accessing centres of excellence; the cost of participation for women; and women's high motivation. From these the research identified factors and strategies that influence recruitment practice.

Implications for practice

Design of trials

Any clinical trial takes considerable time and resource to establish and run. Only important clinical questions should be asked and the subsequent research must be designed to address well-defined questions efficiently and effectively (Mossman 2000). There is a requirement for trial design to be simple and flexible ie simplifies treatments, simplify data requirements, collect less information and simplify entry criteria (Peto & Baigent 1998). It is the responsibility of the commissioners of research and the trial organisers to ensure that clinical trials are relevant to clinical care, that the eligibility criteria reflect the patient population and that findings be widely disseminated in order that they impact on routine clinical practice throughout the health services (Yusuf, Held et al. 1990; Swanson and Ward 1995; Farrell 1998). This could be achieved by developing trials that interest the public and address questions they see as relevant and are understandable; by involving the public at the design stage this may be accomplished (Chalmers 1998; Cockburn et al 1998; Consumers in NHS Research 2000; Gott et al 2000).

Ease of recruitment

Since the commencement of this thesis the Arimidex, Tamoxifen, Alone, or in Combination (ATAC) trial of adjuvant hormone therapy was established, recruited (n=5000) and completed within two years, the most successful recruitment to a breast cancer clinical trial ever. One of the consultant surgeons interviewed for this thesis in 1998 said:

ATAC is delightful. It is properly funded and it's dead easy. Both these things combined make it a very, very attractive. There are loads of patients who are eligible. It's not very complicated to explain the two treatments are quite similar

and one can genuinely argue that there's not much difference. Zeneca [who funded the trial] have been extremely smart with ATAC.

One of the chief investigators in the ATAC trial has sent a questionnaire to clinicians recruiting to the ATAC trial to ascertain why this breast cancer trial was so successful in comparison to others. The questions are financial inducements, consumer support, trial protocol, infrastructure, treatments, no other similar trial, and the design of the trial. The results from the questionnaires are not yet analysed or published, but will be important.

It may be argued that the success of the ATAC trial is simply because of the financial inducement to units, associated with each patient. This thesis has however highlighted the importance of incentives for both clinicians and patients. If this is so part of this thesis is negated, since it follows that whatever conclusions have been made regarding factors for recruitment the overwhelming factor is the desire of the clinician to enter the patient. That is not to say that the approach to women is unethical in the situation of incentives to the clinician; the explanation is that many women are keen to join clinical trials (see chapters 3 and 4) and will do so if approached. Incentives for clinicians will give a higher approach rate and recruitment.

Approaching eligible women

The thesis has demonstrated the importance of how patients are approached to participate in clinical trials as this affects uptake. Asking a patient face-to-face to consider joining a clinical trial will frequently result in greater participation, but this can have ethical implications (Taylor et al. 1984; Freedman 1987; Moore et al 1990). It can be very difficult for patients in a relative position of powerlessness, to decline to take part in a clinical trial (Illich 1977; Oakley 1981). Approaching a woman who has just

been diagnosed with breast cancer may result in a refusal to join the trial because they are unable to manage the diagnosis, understand what the trial entails, and enter the trial at the same time (Degner & Sloane 1992; Thornton 1992; Maslin 1994). At this stage women want information about the stage of the disease, likelihood of cure and treatment options (Luker et al 1995; Bilodeau & Degner 1996). These difficulties may be resolved by a strategy of only recruiting patients at a second or subsequent visit to the outpatient clinic; enabling the patient to establish a relationship of trust with the clinical staff, to accept the diagnosis, and allow the patient time to consider the trial.

Lack of time

Recruiting individuals to clinical trials requires time and effort, which demands adequate resources. Clinicians in both the BASO II and IBIS trials studied in this thesis referred to the lack of time available to explain trials to patients as a hindrance, a factor identified by others (Taylor et al. 1984; Jenkins, Fallowfield et al. 1999). Data managers, research nurses, trials nurses are key people, who make an essential contribution to the maintenance of clinical trials by supporting patients and other members of the multi-disciplinary team; sufficient funds are necessary to create and maintain these positions.

Improved communication

Members of the multi-disciplinary team provide information in different ways, and they need to be flexible, willing and able to adapt their approach to meet the needs of individual patients. A number of studies on improving the communication skills of multi-disciplinary teams have been undertaken (Maguire et al 1984; Maguire 1990; Fallowfield et al. 1998; Maguire 1999). The answer may lie in introducing the relevance and skills of communication, research and clinical trials to healthcare professionals

earlier in their education and training, as well as postgraduate level (Cockburn et al 1998; Doyal & Gillon 1998). These subjects exist in the curricula, but there is a long lead-in time until these healthcare professionals are in a position where they can make a difference.

Doyal and Gillon (1998) propose a core curriculum that covers the main professional and legal obligations, taught by a senior academic in ethics and law "... with relevant professional and academic expertise." (Doyal and Gillon 1998 p 1624). They were referring to medical students, but this is relevant to all healthcare professionals as all healthcare professionals should expect to be involved in recruiting patients to clinical trials (Segelov, Tattersall et al. 1992). Any curriculum would need to include good communication; informed consent and refusal of treatment; the clinical relationship; truthfulness; trust; and medical research. These modules need to be evidence-based, providing the skills necessary to inform women adequately of clinical trial participation, demonstrating concern and empathy.

An informed public

Some (Baum 1993; Thornton 1994; 1997) have proposed establishing a network of informed women, an interest group who demand randomised control trials and the evaluation of new treatments for breast cancer, rather than individualistic, anecdotal, or uncontrolled treatments; this would use a card, similar to the organ donor card, carried by people who wish to be considered for future trials (Lindley 1998; Twentyman undated cited by Bryan 2000). The National Cancer Institute in the USA has a programme to educate the general public about clinical trials (National Cancer Institute 1998b).

In order for patients to be able to make an informed decision they need to understand that they may be approached to join a clinical trial and what clinical trials entail.

Information of this kind is available in the Cancer British Association of Cancer United Patients (BACUP) booklet 'Understanding clinical trials' (BACUP 1996) which has specific information about different clinical trials. With information on the Internet there is the potential for trial participants to have direct access to information. In some centres this use of technology is actively encouraged, for example the CRC Institute for Cancer Studies in Birmingham allows patients to access the CRC CancerHelp site while waiting in outpatients departments (Bryan 2000). Any information needs to be prepared to ensure patient understanding and comprehension (Daugherty et al 1995).

The results of completed clinical trials should be more freely available to patients by either informing trial participants individually on completion (Thornton 1993; Cockburn et al 1998; Cox 1999) and by making the results available on the Internet. All those who have participated in this thesis have been kept informed of the findings; this includes the multi-disciplinary teams, the women interviewed and the NHS funders. Dissemination of results demonstrates to staff and patients the importance of their contribution.

Another approach is to involve consumers at all stages of design, conduct of trials, and the UKCCCR and NHS (NHSE 1996; Department of Health 1998b, 1999, 2000; Hanley 1999; Hanley, Bradburn et al. 2000) have endorsed informal discussion - this approach. A Consumer Liaison Group has been set up to provide a forum for joint working and exchange of information between leading cancer charities and the UKCCCR (Consumers in NHS Research Support Unit 2000). There were no consumers on the trial committees for either the BASO II or IBIS trials.

Better care?

When approached to participate in research, all research subjects should be informed and reassured that refusal to participate in a clinical trial would not affect their treatment. However there is a suggestion that the patient receives better care as a result of participating in randomised control trials (Kemp et al 1984; Freedman 1990; Benson et al 1991; Stiller 1994) through closer follow-up by and experts, and extra investigations. The women randomised to the BASO II and IBIS trials saw trial participation as an advantage through what they described as better care and access to the multi-disciplinary team, particularly nurses who can be telephoned for advice; this view is supported by others (Kardinal & Cupper 1979; Cox 1999). Lilford (undated, cited by Bryan, 2000) has argued that this offer of improved care may be misleading; instead he suggests that patients should be treated according to established protocols. Many healthcare professionals would endorse his observation; because offering and providing 'better care' to trial participants would be seen as unethical.

5.5 Areas for future research

There are a number of directions for future research, which would build on the research in this thesis:

- To undertake a comparative study to examine whether incentive payments make a difference to the recruitment of patients to clinical 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.

5.6 Summary and conclusion

In this thesis I have attempted to answer some important questions in relation to recruitment to breast cancer clinical trials using a multi-method approach that reflects the different perspectives of those individuals researched. The findings contribute to the debate and knowledge of the recruitment of women to breast cancer clinical trials in a number of ways. Firstly, by including the views of all the key stakeholders concerned with breast cancer clinical trials. Secondly, by highlighting the factors affecting recruitment to these two breast cancer clinical trials. Thirdly, by making recommendations on methods to enhance recruitment.

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Appendix A

Questionnaire regarding BASO II trial for BASO nominated surgeons

1

Section A Background Views about Clinical Trials

All BASO Nominated Surgeons should answer this section.

Name & place of work.....

- 1 Do you suffer significant pressure to participate in randomised clinical trials?
 A Yes
 B No

- 2 In your setting, are clinicians given more acknowledgement for:
 A clinical work with patients?
 B contributing to scientific knowledge?

- 3 Do you find that the thought of having to spell out all the details of a trial to eligible patients discourages you from approaching them to participate?
 A Yes
 B No

- 4 When faced with a controversial treatment decision, do you feel most comfortable when:
 A You make the decision outside of a clinical trial?
 B The decision is made for you by the trial protocol?

- 5 When an eligible patient chooses not to enrol on a trial that you have suggested, do you:
 A Often feel disappointed?
 B Seldom feel disappointed?

- 6 Are you reluctant to participate in a trial that may randomise the patient to a treatment arm that involves less treatment than your standard practice?
 A Yes
 B No

- 7 When published data and clinical experience conflict, are you more likely to rely on:
 A Your clinical experience?
 B Published data?

- 8 Prior to receiving this questionnaire had you heard about the BASO II trial?
 A Yes
 B No

- 9 Are you currently participating in multi-centre breast cancer treatment trial of adjuvant therapy (radiotherapy or systemic) other than BASO II?
 A Yes
 B No
 If yes, how many other such trials?

N.B. If you answered no to question 8, then you need not complete the questionnaire any further. Please return questionnaire in pre-addressed envelope.

Section B Factors affecting joining BASO II trial

This section should be answered by **all BASO Nominated Surgeons**, it relates to difficulties that your centre has experienced in registering to join BASO II.

Please place a tick in the relevant box.

The following factor:	has presented no difficulty in joining BASO II trial	has presented some difficulty in joining BASO II trial	has prevented me joining BASO II trial
10 Getting the information about the BASO II trial			
11 Participation in conflicting breast cancer treatment trials			
12 Adapting local practice to fit the trial protocol			
13 Obtaining pathology reports complying with trial criteria			
14 Making the application to the local ethical committee to obtain approval			
15 Obtaining approval from local ethics committee			
16 The scientific design of the study			
17 Number of eligible patients seen in practice			
18 Relevance of the design of the trial to my practice			

19 Any other difficulties you have experienced in joining BASO II trial?

- 20 If you have decided not to enter BASO II is it because you have decided to:
- A Give radiotherapy to all patients who would be eligible for BASO II?
 - B Give Tamoxifen to all patients who would be eligible for BASO II?
 - C Not give radiotherapy to any patients eligible for BASO II?
 - D Not give Tamoxifen to patients eligible for BASO II?

N.B. If you have not registered to join BASO II then you need not complete the questionnaire any further. Please return the questionnaire in the pre-addressed envelope. Otherwise, please continue to the next section.

Section C Factors affecting entering patients to BASO II trial

We are very glad that you are a **Nominated Surgeon** working at a centre that has registered to take part in BASO II trial. This section relates to your experience of entering eligible patients in BASO II trial.

21 Who identifies eligible patients for BASO II at your centre?
(Please indicate whichever responses apply)

A	Surgeon	<input type="checkbox"/>
B	Pathologist	<input type="checkbox"/>
C	Clinical oncologist	<input type="checkbox"/>
D	At a multi-disciplinary meeting	<input type="checkbox"/>

22 Who explains the BASO II trial to eligible patients at your centre?
(Please indicate whichever responses apply)

A	Surgeon	<input type="checkbox"/>
B	Breast Care Nurse	<input type="checkbox"/>
C	Clinical Oncologist	<input type="checkbox"/>
D	Other (Please specify)	<input type="checkbox"/>

23 Who approaches eligible patients at your centre to ask for the consent to enter them into the BASO II trial?
(Please indicate whichever responses apply)

A	Surgeon	<input type="checkbox"/>
B	Breast Care Nurse	<input type="checkbox"/>
C	Clinical Oncologist	<input type="checkbox"/>
D	Other (Please specify)	<input type="checkbox"/>

24 Are any of the following resources available locally for the support of a multi-centre clinical trial?
(Please indicate whichever responses apply)

A	Data Entry Clerk	<input type="checkbox"/>
B	Breast Care Nurse	<input type="checkbox"/>
C	Research Registrar	<input type="checkbox"/>
D	Other (Please specify)	<input type="checkbox"/>

25 Has media publicity of adjuvant breast cancer treatments affected the recruitment of eligible patients to the BASO II trial at your centre?

A	Yes	<input type="checkbox"/>
B	No	<input type="checkbox"/>

If yes, in what ways has media publicity affected recruitment?

The following questions relate to difficulties that have been experienced at your centre in entering eligible patients into the BASO II trial.

Please place a tick in the relevant box.

The following factor:	has presented no difficulty in entering patients	has presented a difficulty in entering some patients	has prevented me from entering any patients
26 Time needed to explain the trial to eligible patients			
27 Explaining random allocation to eligible patients			
28 Eligible patients express a preference for a treatment			
29 Poor design of informed consent information			
30 Eligible patients refusing to join			
31 Relinquishing my decision making to randomisation			
32 Concern about the impact of the trial on the individual doctor patient relationship			
33 Eligible patients change their mind after randomisation			

Any other factors that have caused difficulties in entering eligible patients?

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Section D Estimation of recruitment rates

34 Estimate the total number of patients entered into the BASO II trial from your centre by 1 January 1997.

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35 Estimate what proportion of eligible patients have been entered into BASO II trial from your centre since registering to join the trial?

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.....

36 Estimate your likely recruitment to the BASO II trial over the next twelve months

- A I am likely to enter **more** patients than in previous years
- B I am likely to enter **fewer** patients than in previous years

Section E Benefits and drawbacks of BASO II trial participation

37 What do you consider to be the three major benefits in participating in the BASO II trial on a clinical, personal and professional level?

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38 What do you consider to be the three major drawbacks in participating in BASO II trial on a clinical, personal and professional level?

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Thank you for taking the time to complete this questionnaire. Please can you return the questionnaire in the pre-addressed envelope.

Appendix B

Questionnaire regarding IBIS for BASO nominated surgeons

Factors Affecting Accrual into International Breast Cancer Intervention Study (IBIS)

Please return completed questionnaire to:

Siân Maslin-Prothero, B55a, B Floor, Medical School, QMC, Nottingham, NG7 2UH

Section A Background Views about Clinical Trials

This section should be answered by **all Nominated Surgeons**.

Name

- 1 Do you suffer significant pressure to participate in randomised clinical trials?
 A Yes
 B No

- 2 In your setting, are clinicians given more acknowledgement for:
 A clinical work with patients?
 B contributing to scientific knowledge?

- 3 Do you find that the thought of having to spell out all the details of a trial to eligible patients discourages you from approaching them to participate?
 A Yes
 B No

- 4 When faced with a controversial treatment decision, do you feel most comfortable when:
 A You make the decision outside of a clinical trial?
 B The decision is made for you by the trial protocol?

- 5 When an eligible patient chooses not to enrol on a trial that you have suggested, do you:
 A Often feel disappointed?
 B Seldom feel disappointed?

- 6 Are you reluctant to participate in a trial that may randomise the patient to a treatment arm that involves less treatment than your standard practice?
 A Yes
 B No

- 7 When published data and clinical experience conflict, are you more likely to rely on:
 A Your clinical experience?
 B Published data?

- 8 Prior to receiving this questionnaire had you heard about the IBIS trial?
 A Yes
 B No

- 9 Are you currently participating in multi-centre breast cancer treatment trial of adjuvant therapy (radiotherapy or systemic) other than IBIS?
 A Yes
 B No

If yes, how many other such trials?

N.B. If you answered no to question 8, then you need not complete the questionnaire any further. Please return questionnaire in pre-addressed envelope.

Section B Factors affecting joining IBIS

This section should be answered by **all Nominated Surgeons**, it relates to difficulties that your centre has experienced in registering to join IBIS.

Please place a tick in the relevant box.

	The following factor:	has presented no difficulty in joining IBIS	has presented some difficulty in joining IBIS	has prevented me joining IBIS
10	Getting the information about the IBIS			
11	Participation in conflicting breast cancer treatment trials			
12	Adapting local practice to fit the trial protocol			
13	Obtaining pathology reports complying with trial criteria			
14	Making the application to the local ethical committee to obtain approval			
15	Obtaining approval from local ethics committee			
16	The scientific design of the study			
17	Number of eligible patients seen in practice			
18	Relevance of the design of the trial to my practice			

19 Any other difficulties you have experienced in joining IBIS?

20 If you have decided not to enter IBIS is it because you have decided to:

- A Give Tamoxifen to all patients who would be eligible for IBIS?
- B Not give Tamoxifen to patients eligible for IBIS?

N.B. If you have not registered to join IBIS then you need not complete the questionnaire any further. Please return the questionnaire in the pre-addressed envelope. Otherwise, please continue to the next section.

Section C Factors affecting entering patients to IBIS

We are very glad that you are a **Nominated Surgeon** working at a centre that has registered to take part in IBIS. This section relates to your experience of entering eligible patients in IBIS.

21 Who identifies eligible patients for IBIS at your centre?
(Please indicate whichever responses apply)

- A Surgeon
- B Pathologist
- C Clinical Oncologist
- D At a multi-disciplinary meeting

22 Who explains IBIS to eligible patients at your centre?
(Please indicate whichever responses apply)

- A Surgeon
- B Breast Care Nurse
- C Clinical Oncologist
- D Other (Please specify)

23 Who approaches eligible patients at your centre to ask for the consent to enter them into IBIS?
(Please indicate whichever responses apply)

- A Surgeon
- B Breast Care Nurse
- C Clinical Oncologist
- D Other (Please specify)

24 Are any of the following resources available locally for the support of a multi-centre clinical trial?
(Please indicate whichever responses apply)

- A Data Entry Clerk
- B Breast Care Nurse
- C Research Registrar
- D Other (Please specify)

25 Has media publicity of adjuvant breast cancer treatments affected the recruitment of eligible patients to IBIS at your centre?

- A Yes
- B No

If yes, in what ways has media publicity affected recruitment?

.....

26 The following questions relate to difficulties that have been experienced at your centre in entering eligible patients into IBIS.

Please place a tick in the relevant box.

	The following factor:	has presented no difficulty in entering patients	has presented a difficulty in entering some patients	has prevented me from entering any patients
27	Time needed to explain the trial to eligible patients			
28	Explaining random allocation to adjuvant therapy to eligible patients			
29	Eligible patients express a preference for a treatment			
30	Poor design of informed consent information			
31	Eligible patients refusing to join			
32	Relinquishing my decision making to randomisation			
33	Concern about the impact of the trial on the individual doctor patient relationship			
34	Eligible patients change their mind after randomisation			

35 Any other factors that have caused difficulties in entering eligible patients?

.....

Section D Estimation of recruitment rates

34 Estimate the total number of patients entered into IBIS from your centre by 1 January 1998.

.....
.....

35 Estimate what proportion of eligible patients have been entered into IBIS from your centre since registering to join the trial?

.....
.....

36 Estimate your likely recruitment IBIS over the next twelve months

- A I am likely to enter **more** patients than in previous years
- B I am likely to enter **less** patients than in previous years

Section E Benefits and drawbacks of IBIS

37 What do you consider to be the three major benefits in participating in IBIS on a clinical, personal and professional level?

.....
.....
.....

38 What do you consider to be the three major drawbacks in participating in IBIS trial on a clinical, personal and professional level?

.....
.....
.....

Thank you for taking the time to complete this questionnaire. Please can you return the questionnaire in the pre-addressed envelope.

Appendix C

Interview schedule with multi-disciplinary teams regarding the BASO II trial

BASO II Interview Checklist

Who made the decision locally to join the BASO II trial?

As far as you are aware, were there any difficulties in obtaining local agreement to join the BASO II trial?

How did you decide which arms of the BASO II trial to randomise patients into?
Were there any difficulties with this decision?

What would be the standard treatment for women eligible for the BASO II trial at this centre?

Do you think that there is genuine uncertainty about the best form of treatment/adjuvant therapy for these women?

In your opinion, do your colleagues share your enthusiasm for the trial?

RECRUITMENT

There is evidence that less than half the eligible patients get recruited into breast cancer trials, what general explanations do you have for this fact?

Patients, clinical, trial

How does this apply to BASO II in your experience?

What proportion of eligible patients do you think you are recruiting from this centre for BASO II?

Do you think that this could be improved?

IDENTIFYING ELIGIBLE WOMEN

What is your usual procedure for identifying women eligible for BASO II.

In your view, are there any difficulties with the way in which eligible women are identified at this centre?

Do you think that there are women who might be eligible for BASO II who are not being identified? If so, what would help to avoid this happening?

Are there competing clinical trials for women who are eligible for BASO II. If so, how is this resolved?

Do you obtain suitable pathology reports?

APPROACHING ELIGIBLE WOMEN

What reasons prevent you from asking an eligible woman to participate?

Do general health, psychological concerns, likely cosmetic result, pathology report etc influence whether you approach someone to participate?

Does the extra time and effort required to ask patients to participate in a clinical trial ever put you off approaching an eligible woman to ask her to participate in BASO II.

Who usually approaches eligible women and explains the trial to them?

In your experience, are some women harder to ask to participate in clinical trials than others? What characteristics?

Do you derive pleasure from recruiting women into clinical trials?

What sort of concerns do you find that women have about the BASO II trial?

In general, how do you respond to women who are unsure whether to participate in the BASO II trial?

What reasons do women give who do not wish to take part in the BASO II trial?

Appendix D

Interview schedule with multi-disciplinary teams regarding IBIS

IBIS – interviews with multi-disciplinary teams

THE TRIAL

- Who made the decision locally to join the IBIS trial?
- As far as you were aware, were there any difficulties in obtaining local agreement to join IBIS?
- Do you have an identified Breast Family History clinic, separate from other clinics, at this centre?
- Do you think there is genuine uncertainty about the efficacy of hormonal agents in reducing the chances of breast cancer in these women?
- In your opinion, is this an important trial for the improvement of treatment/care for women a family history of breast cancer?
 - How would you rate its significance – high, medium, low?
 - Do your colleagues share your enthusiasm for the study?
 - Are there any aspects of the study that you do not like/think appropriate eg side effects, particularly in young women?

RECRUITMENT

- There is evidence that less than half of all eligible women get recruited into breast cancer trials - what general explanations do you have for this?
- What factors do you find make it difficult to recruit women into clinical trials?
 - What factors make it difficult to recruit women to IBIS?
 - If not, why not?
- What proportion of eligible women for IBIS seen at this centre do you think you are recruiting?
- Do you think this could be improved?

IDENTIFYING ELIGIBLE WOMEN

- What is your usual procedure for recruiting women for IBIS eg radio, newspapers?
 - Do you have ethical concerns about any approaches adopted?
- What is your usual procedure for identifying eligible women for IBIS?
 - Are eligible women identified prior to coming to clinic?
 - What reasons make women ineligible (in your opinion)?
- In your view, are there any difficulties with the way in which eligible women are identified?
- The approach taken locally to recruit (including method & ethical stance) are there still women eligible for IBIS who are not being identified

- If so, what would/could avoid this happening?

APPROACHING ELIGIBLE WOMEN

- Who usually approaches women and explains the trial to them?
- Are there any reasons that would prevent you from asking eligible women to participate?
- Has the trial set a high enough relative risk level (Claus tables)?
- Do general health, psychological concerns etc influence whether you approach someone to participate?
- Does the extra time and effort required to ask women to participate in a clinical trial ever put you off approaching eligible women and asking her to participate in IBIS?
- In your experience, are some women harder to ask to participate in clinical trials than others are?
 - If so, what are the characteristics?
- Do you gain a sense of satisfaction from recruiting women to clinical trials?
- What concerns to women have about IBIS?
- How long are women given, who are unsure, whether to participate (or not) in IBIS?
- What reasons do women give for not participating in IBIS?
- What is going to happen to women at the end of the trial?

Focus groups

- Jack Cuzick has written to you about women from your centre participating in some group interviews.
- Is your centre interested in taking part in this part of the study?
- MREC approval is being sought for these group interviews.
- Who do I need to contact locally to arrange these interview
- Is there a place where these group interviews could be conducted?
- Have you got any questions you would like to ask me?

Thank you for taking part in this interview. If you are interested I will send you a copy of the report when it is completed.

Appendix E

Focus group topic guide

Focus group guidelines

Introduction, importance of being honest
Confidentiality, audio taping, procedure
Names and when you joined the trial

Initial approach

“Tell me all the things that happened from when you first became aware of the trial up until when you signed up?”

Prompts

How were you first made aware/what initial information did you receive/who from?
What did you see as the benefits of the trial to you? Generally?
What information given you by hospital staff: verbal, written?
Where personal/general benefits apparent as you heard and learned more? If so, what?

Personnel encountered: reactions to them, their manner, and their role

Anything surprising/confusing?
Any omissions?
How well did you understand the nature of the trial?
Initially
Subsequently
Did anyone check you understood what the trial was about?

How do you feel about clinical trials in general?

Decision process

“Tell me all the factors taken into account”

Probe

Treatments/care offered
Anyone else consulted? Who?
Did you get back-up information from any other sources? What?
Family, work commitments
Travel commitments

At what stage did you decide to join the trial?
What was the single, most important factor?
Any remaining doubts at the time?

Expected advantages/benefits in joining the trial?
Expected disadvantages/reservations?

How long did the decision take? Why?
Was any of the hospital staff instrumental in your decision? Which and why?
Was there a deadline?
Was the decision easy or difficult?

How did you inform the hospital of your decision?
What were your expectations at that point?

Subsequent experience

"Tell me what your experience of the trial has been during the time you have been on it".

Prompts

Good points/benefits.

Drawbacks/reservations.

Level of satisfaction, mark out of 10.

Ensure the following are covered:

Type of care/treatments received

Quality of treatments/care

Evaluation of personnel: doctors, nurses, receptionists Professional expertise, patient handling (no names just examples of behaviour).

Appointment frequency

Continuity – do you see the same people? Does it matter?

Time available for each appointment sufficient, rushed?

Hospital buildings/provision. Any influence?

Any information received since joining trial?

IBIS – newsletter, evaluation?

If no information received reactions?

Have you ever wanted to ask questions?

What did you do?

Nature/quality of response.

IBIS groups only:

Media coverage last April (1998)?

What heard/seen? Source?

Reactions.

Personal attitudes regarding cancer experience/level of risk

BASO II groups

When was your initial diagnosis?

How did you feel and react?

Collect different experiences

How do you feel about cancer now?

How do you feel about your level of risk of cancer now? Better/worse?

How often do you think about breast cancer?

What would be the most valuable thing you could say to somebody who has just been diagnosed with breast cancer?

IBIS groups

How do you feel about your level of risk from breast cancer?

Collect different reactions

How often do you think about it?

Are you optimistic or pessimistic on balance?

What would the optimists say to the pessimists, to make them feel more positive?

Summary

How has experience of the trial compared with initial expectations: In what ways better/worse?

Was the decision to join the right one or not?

Thought bubble: “The one thing you would most like to say to the trial team...”.

Audit on flipchart:

What did the trial team get: right, wrong, and how might they improve the trial?

Final words of advice to those setting up future trials

Complete demographic information sheets

Thank you

Appendix F

BASO II prospective study form

Factors Affecting the Accrual of Patients into Clinical Trials
BASO II – Grade 1 – Node Negative - Size ≤2.0 cms
Please complete one form for each woman identified as eligible.

	Question	Possible Answers		No	Yes
1	Is the patient eligible for BASO II		→		
2	Was Trial discussed		→		
				→ Q3	→ Q4
3	If NO, reason(s) why they were not approached to participate in the BASO II Trial: (Please tick all that apply)				
A	Eligibility for BASO II Trial overlooked		→		
B	Patient factors (eg psychological):	Anxious	→		
		Depressed	→		
		Psychotic	→		
		Unable to understand options	→		
C	Organisational factors (eg no one available to talk to patient about the trial)	Clinical oncologist	→		
		Surgeon	→		
		Breast care nurse	→		
		Other (please specify)	→		
4	<i>If the answer to Q2 was YES, was the patient randomised?</i>		→		
				→Q5	End
5	If NO, reasons for patient refusal to participate (please tick all that apply)		→		
A	Concerned about under treatment		→		
B	Concern about random allocation		→		
C	Other		→		
D	Patient did not want to have:	Radiotherapy	→		
		Tamoxifen	→		
F	Conflicts with expected treatment (explained at a previous visit)		→		
G	Patient had Treatment preference for:	Radiotherapy	→		
		Tamoxifen	→		
		No treatment	→		
H	Radiotherapy would interfere with:	Domestic responsibilities	→		
		Occupational commitments	→		
		Holidays	→		
I	Radiotherapy would cause:	Additional expense of travelling	→		
		Additional expense of staying for treatment	→		
		Inconvenience of travelling	→		

Appendix G

Analysis of BASO II questionnaires

Results from BASO II questionnaire

118 questionnaires were sent to BASO nominated breast screening surgeons in February 1997. 80 complete questionnaires were returned a 68% response rate. Of these 39 (49%) were registered for the BASO II trial.

Section A	Background Views about Clinical Trials	No.	Percentage
1	Do you suffer significant pressure to participate in randomised clinical trials?		
	A Yes	46	58%
	B No	33	42%
	Missing data = 1		
2	In your setting, are clinicians given more acknowledgement for:		
	A clinical work with patients?	63	88%
	B contributing to scientific knowledge?	9	12%
	Missing data = 8 (3 ticked all options, 5 did not complete)		
3	Do you find that the thought of having to spell out all the details of a trial to eligible patients discourages you from approaching them to participate?		
	A Yes	37	46%
	B No	43	54%
4	When faced with a controversial treatment decision, do you feel most comfortable when:		
	A You make the decision outside of a clinical trial?	26	35%
	B The decision is made for you by the trial protocol?	49	65%
	Missing data = 5 (1 ticked all options, 4 did not complete)		
5	When an eligible patient chooses not to enrol on a trial that you have suggested, do you:		
	A Often feel disappointed?	42	55%
	B Seldom feel disappointed?	35	45%
	Missing data = 3 did not complete		
6	Are you reluctant to participate in a trial that may randomise the patient to a treatment arm that involves less treatment than your standard practice?		
	A Yes	44	56%
	B No	34	44%
	Missing data = 2 (1 ticked all options, 1 did not complete)		
7	When published data and clinical experience conflict, are you more likely to rely on:		
	A Your clinical experience?	29	41%
	B Published data?	42	59%
	Missing data = 9 (2 ticked all options, 7 did not complete)		
8	Prior to receiving this questionnaire had you heard about the BASO II trial?		
	A Yes	77	96%
	B No	3	4%
9	Are you currently participating in multi-centre breast cancer treatment trial of adjuvant therapy (radiotherapy or systemic) other than BASO II?		
	A Yes	63	81%
	B No	15	19%
	Missing data = 2 did not complete		
	If yes, how many other such trials?	0-12	

Section B

Factors affecting joining BASO II trial

	The following factor:	has presented no difficulty in joining BASO II trial		has presented some difficulty in joining BASO II trial		has prevented me joining BASO II trial	
		No.	%	No.	%	No.	%
10	Getting the information about the BASO II trial Missing data = 0	66	89%	5	7%	3	4%
11	Participation in conflicting breast cancer treatment trials Missing data = 1 not completed	45	63%	19	26%	8	11%
12	Adapting local practice to fit the trial protocol Missing data = 1 not completed	44	60%	19	26%	10	14%
13	Obtaining pathology reports complying with trial criteria Missing data = 1 not completed	63	87%	9	12%	1	1%
14	Making the application to the local ethical committee to obtain approval Missing data = 2 not completed	45	63%	24	33%	3	4%
15	Obtaining approval from local ethics committee Missing data = 3 not completed	46	65%	21	30%	4	5%
16	The scientific design of the study Missing data = 2 not completed	57	79%	12	17%	3	4%
17	Number of eligible patients seen in practice Missing data = 0	52	70%	20	27%	2	3%
18	Relevance of the design of the trial to my practice Missing data = 2 not completed	56	78%	12	17%	4	6%

19	Any other difficulties you have experienced in joining BASO II trial?	No.	%
	Yes	24	35%
	No	44	65%
	Missing data = 6 not completed		

Difficulties in joining the BASO II trial including: lack of time to participate in more trials (9); lack of research infrastructure (6); patients not keen to join trials (6); 2x2 randomisation can be difficult for patients to understand (4); give radiotherapy to all women (3); axillary node biopsy not routinely undertaken (2); clinical oncologists not complying with protocol; no patient information leaflets; no agreement among multi-disciplinary members.

20	If you have decided not to enter BASO II is it because you have decided to:	No.	%
	A Give radiotherapy to all patients who would be eligible for BASO II?	12	19%
	B Give Tamoxifen to all patients who would be eligible for BASO II?	12	19%
	C Not give radiotherapy to any patients eligible for BASO II?	1	2%
	D Not give Tamoxifen to patients eligible for BASO II?	1	2%

Section C Factors affecting entering patients to BASO II trial

		Number	Percentage
21	Who identifies eligible patients for BASO II at your centre? (Please indicate whichever responses apply)		
	A Surgeon	20	56%
	B Pathologist	0	100%
	C Clinical oncologist	4	11%
	D At a multi-disciplinary meeting	21	58%
	Missing data = 0		
22	Who explains the BASO II trial to eligible patients at your centre? (Please indicate whichever responses apply)		
	A Surgeon	31	86%
	B Breast Care Nurse	19	53%
	C Clinical Oncologist	14	39%
	D Other	3	8%
	Missing data = 0		
23	Who approaches eligible patients at your centre to ask for the consent to enter them into the BASO II trial? (Please indicate whichever responses apply)		
	A Surgeon	29	81%
	B Breast Care Nurse	4	11%
	C Clinical Oncologist	12	33%
	D Other	2	6%
	Missing data = 0		
24	Are any of the following resources available locally for the support of a multi-centre clinical trial? (Please indicate whichever responses apply)		
	A Data Entry Clerk	9	25%
	B Breast Care Nurse	28	78%
	C Research Registrar	3	8%
	D Other	7	19%
	Missing data = 0		
25	Has media publicity of adjuvant breast cancer treatments affected the recruitment of eligible patients to the BASO II trial at your centre?		
	A Yes	3	9%
	B No	32	91%
	Missing data = 1 not completed		

The following questions relate to difficulties that have been experienced at your centre in entering eligible patients into the BASO II trial.

	The following factor:	has presented no difficulty in entering patients		has presented a difficulty in entering some patients		has prevented me from entering any patients	
		No.	%	No.	%	No.	%
26	Time needed to explain the trial to eligible patients Missing data = 1 not completed	19	54%	16	46%	0	0%
27	Explaining random allocation to eligible patients Missing data = 1 not completed	7	20%	28	80%	0	0%
28	Eligible patients express a preference for a treatment Missing data = 1 not completed	3	8%	23	66%	9	26%
29	Poor design of informed consent information Missing data = 2 not completed	27	79%	7	21%	0	0%
30	Eligible patients refusing to join Missing data = 1 not completed	2	6%	21	60%	12	34%
31	Relinquishing my decision making to randomisation Missing data = 2 not completed	29	83%	5	15%	0	0%
32	Concern about the impact of the trial on the individual doctor patient relationship Missing data = 1 not completed	29	83%	5	14%	1	3%
33	Eligible patients change their mind after randomisation Missing data = 3 not completed	16	48%	15	46%	2	6%

Any other factors that have caused difficulties in entering eligible patients?

8 stated other factors these were:

Just received ethical approval; limited number of eligible women seen; women seek advice from other colleagues who recommend Tamoxifen; women unable to grasp randomisation and clinician uncertainty (2); pressure of clinics; and performing axillary node testing (2) for tumour less than 5cms.

Section D Estimation of recruitment rates

34 Estimate the total number of patients entered into the BASO II trial from your centre by 1 January 1997.
0-49 patients

Missing data = 6 not completed

35 Estimate what proportion of eligible patients have been entered into BASO II trial from your centre since registering to join the trial?
0-84%

Missing data = 5 not completed

36 Estimate your likely recruitment to the BASO II trial over the next twelve months

		No.	Percentage
A	I am likely to enter more patients than in previous years	27	79%
B	I am likely to enter fewer patients than in previous years	3	9%
	I am likely to enter the same number of patients	4	12%

Missing data = 2 not completed

Appendix H

General and specific feedback to centres following interviews with multi-disciplinary teams recruiting to the BASO II trial

Findings from interviews with multi-disciplinary teams

Overall, the clinicians interviewed acknowledged that the British Association of Surgical Oncology II trial is answering an important clinical question.

The refusal of eligible women to take part in the trial remains the main reason for failure to recruit. The main reported reasons for refusal were:

- preference for a particular treatment;
- anxieties about randomisation;
- and concern about allocation to an 'unnecessary' treatment, usually radiotherapy.

The only evidence to suggest that differences in the characteristics of eligible women could account for variation in recruitment rates between centres is that those with a large rural population find that women in outlying areas are less willing to accept random allocation to radiotherapy.

The findings indicate that two issues could explain differences in recruitment between centres:

1. Variations in approach to 'selling the trial' to eligible women and
2. the arrangements for obtaining consent.

1. Selling the trial

- a) The idea that the trial has to be 'sold' to eligible women occurred in many interviews. 'Selling the trial' is about communicating uncertainty regarding the benefits of the treatment arms of the trial at a time when women are thought to want security and certainty.

Although British Association of Surgical Oncology II is a simple trial, it was not regarded as a particularly easy trial to 'sell' because of differences between what each centre regarded as 'standard' treatment and the trial protocol, concerns about 'undertreatment', and a 'no treatment' arm.

Centres with high recruitment rate approached 'selling the trial' by providing a positive message regarding random allocation to treatment as a rational policy, clearly stating that the benefits of the additional treatments are not proven.

However, some centres expressed concern that the idea of 'selling the trial' put women under too much pressure to participate and did not allow for individual concern about 'undertreatment'

- b) A lack of consistency in the explanations given to women causes difficulty in 'selling the trial', especially when women do not perceive they have been given a consistent message. This can be the result of having been seen by different personnel on two occasions, or being given a definite treatment plan (eg surgery and radiotherapy as the standard) prior to identification as being eligible for British Association of Surgical Oncology II.

2. Practicalities affecting obtaining consent

- a) Policies for obtaining women's consent varied; some centres allow women to make a decision about trial participation immediately, while others are required to give patients 24 hours to consider before asking for a decision. There was a general perception that the longer women have to think about a trial the less likely they are to participate.
- b) Several centres did not have a follow-up system for contacting patients who had been asked but not consented to participation, which meant that eligible women who might have entered the trial were lost.
- c) The provision of local support was thought to positively influence recruitment to all trials in a number of ways. Extra staff could improve the chances of recruitment through (i) offering more time to discuss the trial; (ii) better follow up of patients who delay the decision to participate; (iii) having someone responsible for bringing eligible patients to clinicians' attention.
- d) The development of regional breast trials meetings was helpful in sharing advice on recruitment, comparing recruitment rates and discussing methods for improving recruitment to all trials.

Although there are local and regional differences in policy regarding informed consent, the following measures could help many centres to improve recruitment.

- Ensure a consistent approach for explaining the trial, minimizing the number of different clinicians who discuss the trial with women. The evidence suggests that surgeons have the best success rate in obtaining consent.
- Give a positive message about participation in randomised trials, ie that the clinician really does not know which arm is best.

- Displaying posters and leaflets about trials in patient areas. (Some centres had prepared their own trial posters for display in-patient waiting areas).
- Introduce the possibility of participation in a clinical trial at an early stage when diagnosis is first discussed.
- Have one person responsible for identifying and following up consent from eligible women after the trial has been discussed.
- Use an active procedure for following up consent for women who have been asked to participate and delayed this decision, such as a telephone call after 24 hours.

Specific feedback which might help individual centres to recruit

Centre 1 (medium recruiter)

- Ensure continuity of care for women. That is ensuring that all women seen will be offered a package of care where they might be invited to participate in a clinical trial, if they fit the trial protocol.
- Telephone or arrange another appointment to speak to those women offered the trial but wanted more time to think before deciding to participate in the trial.

Centre 2 (high recruiter)

- Telephone or arrange another appointment to speak to those women offered the trial but wanted more time to think before deciding to participate.

Centre 3 (high recruiter)

- Routinely undertake node sampling in all cases, as recommended in British Association of Surgical Oncology guidelines (18% of tumours of <1cm are node positive).
- Pathologist to flag those women suitable for British Association of Surgical Oncology II.
- Establish a clinic specifically for recruitment to clinical trials.

Centre 4 (low recruiter)

- Ensure continuity of care for women. That is ensuring that all women seen will be offered a package of care where they might be invited to participate in a clinical trial, if they fit the trial protocol.
- Routinely undertake node sampling in all cases, as recommended in British Association of Surgical Oncology guidelines (18% of tumours of <1cm are node positive).
- Pathologist to flag those women suitable for British Association of Surgical Oncology II.
- Telephone or arrange another appointment to speak to those women offered the trial but wanted more time to think before deciding to participate.
- Be more positive about the tumour ie it is small, node negative; and about the clinician not knowing the best treatment.
- There appeared to us to be a bias on the part of the radiotherapist inviting patients to participate in the British Association of Surgical Oncology II trial.

Centre 5 (high recruiter)

- Increase the size of tumour to 2 cms.

Centre 6 (high recruiter)

No recommendations.

Centre 7 (low recruiter)

- Increase the size of tumour to 2 cms.
- Ensure continuity of care for women. That is ensuring that all women seen will be offered a package of care where they might be invited to participate in a clinical trial, if they fit the trial protocol.
- Be more positive about the tumour ie it is small, node negative; and about the clinician not knowing the best treatment.
- All the clinicians need to be committed to recruiting women to the British Association of Surgical Oncology II trial, not recommending a preferred treatment such as radiotherapy.

Centre 8 (low recruiter)

- Be more positive about the tumour ie it is small, node negative; and about the clinician not knowing the best treatment.
- Ensure continuity of care for women. That is ensuring that all women seen will be offered a package of care where they might be invited to participate in a clinical trial, if they fit the trial protocol.

Centre 9 (low recruiter)

- Telephone or arrange another appointment to speak to those women offered the trial but given 24 hours (as required by the ethics committee) to think before being consented to participate in the trial.
- Make sure someone follows up those women given extra time to think about participating in the British Association of Surgical Oncology II trial eg a breast care nurse, trials nurse.
- Go back to the local ethics committee and request that they reconsider the 24 hour delay given for women to consider trial participation.
- Ensure continuity of care for women. That is ensuring that all women seen will be offered a package of care where they might be invited to participate in a clinical trial, if they fit the trial protocol.

Centre 10 (low recruiter)

- Ensure all the multi-disciplinary team are saying the same things to women. Be more positive about the tumour ie it is small, node negative; and about the clinician not knowing the best treatment.
- Establish a clinic specifically for recruitment to clinical trials.
- Appoint trials nurse to look after the trial.
- Ensure continuity of message ie that women are not told they will be having radiotherapy after they have had their surgery (ie before they have received the pathology results).

Centre 11 (medium recruiter)

- Be more positive about the tumour ie it is small, node negative; and about the clinician not knowing the best treatment.

Centre 12 (medium recruiter)

- Form an all Wales trials group; for support and encouragement.
- Be more positive about the tumour ie it is small, node negative; and about the clinician not knowing the best treatment.
- Develop a data manager/trials co-ordinator post; someone to follow-up those women given time to think about participating in the trial.

Centre 13 (medium recruiter)

- Be more positive about the tumour ie it is small, node negative; and about the clinician not knowing the best treatment.
- Develop a data manager/trials co-ordinator post; someone to follow-up those women given time to think about participating in the trial.
- Establish a clinic specifically for recruitment to *clinical trials*.

Centre 14 (medium recruiter)

- Telephone or arrange another appointment to speak to those women offered the trial but wanted more time to think before deciding to participate in the trial.

Appendix I
Analysis of IBIS questionnaires

Results from IBIS questionnaire

118 questionnaires sent to BASO nominated surgeons, plus a further 4 to centres recruiting to IBIS (but not screening centres for BASO). 80 questionnaires returned a 66% response rate.

Section A		Background Views about Clinical Trials	No.	Percentage
1	Do you suffer significant pressure to participate in randomised clinical trials?			
	A	Yes	45	58%
	B	No	33	42%
	Missing data = 2 not completed			
2	In your setting, are clinicians given more acknowledgement for:			
	A	clinical work with patients?	59	82%
	B	contributing to scientific knowledge?	13	18%
	Missing data = 8 (2 ticked all options, 6 did not complete)			
3	Do you find that the thought of having to spell out all the details of a trial to eligible patients discourages you from approaching them to participate?			
	A	Yes	31	39%
	B	No	48	61%
	Missing data = 1 not completed			
4	When faced with a controversial treatment decision, do you feel most comfortable when:			
	A	You make the decision outside of a clinical trial?	23	32%
	B	The decision is made for you by the trial protocol?	50	68%
	Missing data = 8 (2 ticked all options, 6 did not complete)			
5	When an eligible patient chooses not to enrol on a trial that you have suggested, do you:			
	A	Often feel disappointed?	37	47%
	B	Seldom feel disappointed?	41	53%
	Missing data = 2 did not complete			
6	Are you reluctant to participate in a trial that may randomise the patient to a treatment arm that involves less treatment than your standard practice?			
	A	Yes	43	55%
	B	No	35	45%
	Missing data = 2 did not complete			
7	When published data and clinical experience conflict, are you more likely to rely on:			
	A	Your clinical experience?	31	44%
	B	Published data?	39	56%
	Missing data = 10 (2 ticked all options, 8 did not complete)			
8	Prior to receiving this questionnaire had you heard about the IBIS trial?			
	A	Yes	74	92%
	B	No	6	8%
9	Are you currently participating in multi-centre breast cancer treatment trial of adjuvant therapy (radiotherapy or systemic) other than IBIS?			
	A	Yes	79	99%
	B	No	1	1%
	If yes, how many other such trials?		0-20	

Of the 80 clinicians who completed Section A, 6 had not heard of the trial and 4 clinicians were not registered for the trial; they did not complete the rest of the questionnaire.

Section B Factors affecting joining IBIS

The following factor:	has presented no difficulty in joining IBIS		has presented some difficulty in joining IBIS		has prevented me joining IBIS	
	No.	%	No.	%	No.	%
10 Getting the information about IBIS Missing data = 5 not completed	51	79%	10	15%	4	6%
11 Participation in conflicting breast cancer treatment trials Missing data = 6 not completed	54	84%	5	8%	5	8%
12 Adapting local practice to fit the trial protocol Missing data = 9 not completed	43	71%	16	26%	2	3%
13 Obtaining pathology reports complying with trial criteria	Not applicable		Not applicable		Not applicable	
14 Making the application to the local ethical committee to obtain approval Missing data = 3 not completed	40	70%	15	26%	2	4%
15 Obtaining approval from local ethics committee Missing data = 5 not completed	43	78%	10	18%	2	4%
16 The scientific design of the study Missing data = 9 not completed	45	74%	9	15%	7	11%
17 Number of eligible patients seen in practice Missing data = 7 not completed	45	71%	14	22%	4	6%
18 Relevance of the design of the trial to my practice Missing data = 10 not completed	43	72%	12	20%	5	8%

19	Any other difficulties you have experienced in joining IBIS trial?	No.	%
	Yes	27	47%
	No	31	53%
	Missing data = 12 not completed		

The difficulties were: women do not like placebo arms in clinical trials; lack of resources locally to support clinical trials; not having a local family history clinic; clinicians refer women eligible for this trial to a clinical geneticist or other centres recruiting to the IBIS trial; their concerns about the side effects of Tamoxifen; clinicians do not agree with the trial; no funding for mammography in the under 50 year age group; time commitment of entering women to the trial; and discouraged by the IBIS Coordinating centre in London.

20	If you have decided not to enter IBIS is it because you have decided to:	No.	%
	A Give Tamoxifen to all patients who would be eligible for IBIS?	0 (no)	100%
	B Not give Tamoxifen to patients eligible for IBIS?	19 (yes)	40%

Section C Factors affecting entering patients to IBIS trial

		Number	Percentage
21	Who identifies eligible patients for IBIS at your centre? (Please indicate whichever responses apply)		
	A Surgeon	15	79%
	B Breast care/Genetics nurse	10	53%
	C Clinical geneticist	13	68%
	D At a multi-disciplinary meeting	8	42%
	Missing data = 0		
22	Who explains the IBIS trial to eligible patients at your centre? (Please indicate whichever responses apply)		
	A Surgeon	12	63%
	B Breast Care/Genetics Nurse	11	58%
	C Clinical Geneticist	5	26%
	D Other	7	37%
	Missing data = 0		
23	Who approaches eligible patients at your centre to ask for the consent to enter them into the IBIS trial? (Please indicate whichever responses apply)		
	A Surgeon	12	63%
	B Breast Care/Genetics Nurse	5	26%
	C Clinical Geneticist	6	32%
	D Other	7	37%
	Missing data = 0		
24	Are any of the following resources available locally for the support of a multi-centre clinical trial? (Please indicate whichever responses apply)		
	A Data Entry Clerk	9	47%
	B Breast Care/Genetics Nurse	15	79%
	C Research Registrar	7	37%
	D Other	4	24%
	Missing data = 0		
25	Has media publicity of adjuvant breast cancer treatments affected the recruitment of eligible patients to the IBIS trial at your centre?		
	A Yes	11	69%
	B No	5	31%
	Missing data = 3 not completed		

The following questions relate to difficulties that have been experienced at your centre in entering eligible patients into the IBIS trial.

	The following factor:	has presented no difficulty in entering patients		has presented a difficulty in entering some patients		has prevented me from entering any patients	
		No.	%	No.	%	No.	%
26	Time needed to explain the trial to eligible patients Missing data = 0	9	47%	10	53%	0	0%
27	Explaining random allocation to eligible patients Missing data = 0	9	47%	10	53%	0	0%
28	Eligible patients express a preference for a treatment Missing data = 0	8	42%	11	58%	0	0%
29	Poor design of informed consent information Missing data = 0	15	79%	4	21%	0	0%
30	Eligible patients refusing to join Missing data = 0	1	5%	18	95%	0	0%
31	Relinquishing my decision making to randomisation Missing data = 0	18	95%	1	5%	0	0%
32	Concern about the impact of the trial on the individual doctor patient relationship Missing data = 0	18	95%	1	5%	0	0%
33	Eligible patients change their mind after randomisation Missing data = 1 not completed	4	22%	14	78%	0	0%

Section D Estimation of recruitment rates

34 Estimate the total number of patients entered into the IBIS trial from your centre by 1 January 1997.

20-501 patients

Missing data = 3 not completed

35 Estimate what proportion of eligible patients have been entered into IBIS trial from your centre since registering to join the trial?

10-97%

Missing data = 5 not completed

36 Estimate your likely recruitment to the IBIS trial over the next twelve months

		No.	Percentage
A	I am likely to enter more patients than in previous years	13	81%
B	I am likely to enter fewer patients than in previous years	3	19%

Missing data = 3 (1 ticked both options, 2 not completed)