

**THE UNIVERSITY OF HULL**

**Psychological Factors that Influence Patient Participation in Cancer  
Clinical Trials**

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By

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## **ABSTRACT**

The accrual of patients to cancer clinical trials has been noted by a number of authors as a significant problem. Research to date has examined a range of patient and physician related factors that may account for the low accrual rate. Patient refusal as a reason for non-participation has been found by previous research to account for a significant proportion of patients who are not entered onto a trial. This project aimed to explore the differences in attitudes and psychological variables between patients who refused a clinical trial and those who consented.

A cross sectional, single point, postal questionnaire design was employed. Patients who were medically eligible for current phase I, II or III cancer chemotherapy clinical trials received a series of self-report questionnaires. These assessed personality, mood status, emotional expression and health locus of control, and patients' attitudes to research and hypothetical clinical trials. Follow up semi-structured interviews were held with a sub-sample of participants.

During the data collection period, 48 patients were identified as eligible for clinical trials. Of these, 95.9% consented to a trial. The results query previous findings that patient refusal is a significant problem in accrual to trials. Thirty-one patients (63%) returned the questionnaires and of these, none refused entry to a clinical trial. Statistical analyses showed that patients' attitudes to research were related to their willingness to enter hypothetical clinical trials. An effect of personality and health locus of control on patients' perception of choice when offered a trial was found. Qualitative analysis revealed that the decision to enter a clinical trial was not difficult for patients, as had been previously proposed. Recruitment and methodological difficulties are discussed.

## **CHAPTER ONE : INTRODUCTION**

### **1.1 The Randomized Controlled Clinical Trial**

The systematic use of research evidence to improve health care has been promoted by the National Health Service (NHS) through its Evidence-Based Medicine initiative (NHS Executive, 1996). The National Research and Development Directorate have established criteria by which the strength and quality of evidence may be judged (Bandolier 36, 1997). The highest level of evidence of treatment efficacy is obtained from systematic reviews of randomized controlled trials (RCTs). The single RCT provides the next level of evidence in the hierarchy. Hence, in the field of oncology the effectiveness of new treatments is frequently determined by randomized controlled clinical trials. These trials aim to quantify the degree of therapeutic effect and eliminate distorting biases (Tobias & Souhami, 1993).

The recruitment of patients to RCTs is a long-standing difficulty. It has been estimated that less than 3% of cancer patients actually receive treatment as part of a clinical trial (Benson et al., 1991), although more recent studies suggest this has increased to 12% (Twelves et al., 1998; Spiro et al., 2000). The proportion of patients entered onto RCTs is thus far from satisfactory. Such low rates of recruitment compromise the rigorous scientific testing of a new treatment, which in turn leads to slow development and delayed availability (Cook-Gotay, 1991). In addition, low recruitment rates can result in small, selective patient subgroups, which may limit the application of results to the

rest of the population with the disease (Jack et al., 1990; Quoix et al., 1986). It is clear that maximizing recruitment to cancer clinical trials is of critical importance.

The literature examining the question of why patients do not enter cancer clinical trials has been approached from a wide range of angles and from a variety of disciplines. Research to date has demonstrated that characteristics of the trials themselves, the physicians and of the patients all influence trial participation (Cook-Gotay, 1991). This review aims to critically examine the literature on patient-related factors that influence recruitment to cancer clinical trials. It will place particular emphasis on research that explores the relevance of psychological factors.

Firstly, a more detailed explanation of the nature and purpose of clinical trials is required.

### **1.2 Cancer Clinical Trials – Phase I, II & III**

In oncology, the evaluation of a new drug involves the progression from phase I trials through to phase III. Determination of the safety and effectiveness of the new treatments is the aim of the trials (Schwartzmann et al., 1991). Phase I studies first try the new agent in patients with the aim of determining maximum tolerated dose and the toxicity profile in humans (Neal & Hoskin, 1997). Phase I trials are offered to patients for whom there is no other recognized treatment and less than 4% will achieve an objective response, whilst there is a high chance of unwanted side-effects (Estey et al., 1986). Phase II studies seek anti-tumor activity based on doses and schedules from the

phase I study. Again, treatment is offered to patients for whom conventional therapy has failed or there is no effective recognized treatment (Neal & Hoskin, 1997). Phase I and II trials place physical and psychological demands on the patient, which lead to greater pressure, stress and uncertainty compared with conventional treatment (Hope-Stone et al., 1997). Phase III trials compare the new agent with the best existing standard treatment. If there is no standard treatment a placebo is used. These trials require a large number of participants.

Therefore, a clinical trial is not a unitary concept, although a shortcoming of research in this area is the failure to distinguish between different types of trial.

### **1.3 Trials – Who Enters?**

Differences have been demonstrated between patients who participate in clinical trials and those who do not. In a review of the literature, Cook-Gotay (1991) states that patients entered onto protocol were in better condition, younger, heavier, of higher socioeconomic status and had better performance status. The author could not find evidence for differences in sex, race, marital status, religion or medical insurance coverage.

Elderly patients are under represented in cancer clinical trials (Walker et al., 1998). There is also substantial evidence that elderly patients are not given biological optimal treatment for their disease, which may be due to oncologists not giving aggressive treatment on compassionate grounds (Walker et al., 1998). However, a study of 80

women with breast cancer showed older and younger women's views to be very similar. Receiving the most effective treatment was equally important for both groups, regardless of time in hospital, side-effects and distance to travel (Walker et al., 1998).

It is important to note that many patients are not medically eligible for clinical trials. Medical ineligibility of a majority of cancer patients may account for the low participation rate. A review of the literature on accrual to cancer clinical trials showed that between 12 and 44% of patients are eligible for entry (Cook-Gotay, 1991). This has been supported by more recent work (e.g. Spiro et al., 2000). Hence, medical ineligibility cannot account solely for the low proportion of patients entering RCTs. It has been shown that patient refusal is also an important factor. Spiro et al. (2000) state that 73.5% of their eligible lung cancer patients refused trial entry. Quoix et al. (1986) found that 20% of eligible lung cancer patients were not entered for non-medical reasons. Other researchers have demonstrated similar figures. Cook-Gotay (1991) highlights patient refusal as a reason for non-participation as ranging from 15 to 32%.

### *Summary*

*Accrual of patients to clinical trials is a problematic issue. There may be differences between those who enter and those who do not, and some groups are under represented. Although not all patients are medically eligible for trials, patient refusal is a significant factor in the low participation rate.*



The research relevant to the question of “why do patients refuse? ” is reviewed in the following sections. To begin, individuals’ general concepts of clinical trials and medical research will be examined.

#### **1.4 Attitudes Towards Clinical Trials**

Research to date has noted that patients make their decisions within a social setting, and so it is important to consider non-patients’ attitudes towards trials as well as those of patients. Lay adults have reported favourable attitudes to the concept of clinical trials. In addition, individuals indicate their willingness to participate. Four hypothetical trials were presented to 1022 non-patients and two thirds said they would be willing to take part (Kemp et al., 1984).

It has been argued that these positive attitudes towards clinical trial research do not differ between the general public and patients (Casseileth et al., 1982). In a self-administered questionnaire survey of the general public (n=107), cardiology patients (n=84) and cancer patients (n=104), it was found that most (71%) believed that patients should serve as research subjects. The responses did not differ by demographic variables or subgroup. Increased scientific knowledge and potential benefits to others were cited as reasons in support of this belief. Seventy percent of the respondents thought the doctor had prior knowledge of the efficacy of the drug, which suggests that many did not understand the trial’s underlying principle.

Other research has found that many people do not have an accurate understanding of clinical trials. Focus groups with women in the community and breast cancer patients revealed that most did not understand the need for trials, the manner in which they were conducted, the use of placebos or randomization. While trials were seen as a benefit to future generations, they were not thought to benefit the individual, for whom they were considered a gamble and a last resort (Ellis & Butow, 1998).

It appears that there is an important difference between thinking about oneself and anonymous others (Casseileth et al., 1982). It was demonstrated that participants were more self-concerned and less altruistic when asked about their own treatment. Evidence for this was also provided by a survey of patients who had already given informed consent for a chemotherapy clinical trial. 'Helping doctors through research' was one of the least important reasons for these patients (Penman et al., 1984).

Research indicates that while both patients and the general population believe they should and would participate, it remains the case that many do not. The use of hypothetical trial descriptions in research may at least in part explain this discrepancy. It is questionable whether patient decision-making about actual trials is the same as hypothetical decision making. The latter situation has no implications for the individual's future, while the former has many. There is no literature comparing the two.

Patients' general attitudes towards medical care and research have been shown to influence how they perceive the manner and content of information disclosure for the trial into which they were enrolled (Verheggen et al., 1996). It may follow that prior attitudes influence a patient's decision to participate. In a review of the literature on decision-making issues for patients in clinical trials, Bujorian (1988) argues:

*"Patients often have a bias either towards or against clinical trials.....Patients may make hasty decisions based on their biases."*

For some, the trial offers a source of hope, but others fear experimentation. This view is in accordance with many anecdotal accounts of patient decision-making. However, Bujorian does not make it clear which research papers her conclusions are drawn from. Further research is required that examines a patient's attitudes and beliefs about clinical trials and how these impact on their decision about participating.

### *Summary*

*Patients and non-patients express positive views of clinical trials, although many may not have an accurate understanding of them. Hypothetical trial decision-making is likely to be different from a patient's decision-making about a real trial. Authors express the idea of a prior bias that influences a patient's decision, but this has little empirical support.*

This review will now consider the research that directly focuses on reasons for participation and refusal.

### **1.5 Specific Motivations and Barriers to Participation**

Authors have drawn attention to the fact that the proportion of patients excluded from protocols and the reasons for this are rarely documented (Antman et al., 1985; Lennox et al., 1979). More recently, a number of studies have addressed this issue by directly asking patients about their reasons for refusing or agreeing to participate.

A survey was conducted of 4281 individuals aged over 60 years who were enrolled into a hypotension trial. The findings revealed that contribution to science (96%), improving the health of others (96%) and improving one's own health (93%) were the most important reasons for joining the trial (Schron et al., 1997). In a survey of individuals eligible for clinical drug trials conducted by a contract research organization (CRO), financial compensation, improvement of health and contribution to science were the main motivations for participation (Cunny & Miller, 1994).

Research focusing on cancer clinical trials has revealed similar motivating factors. 'Others will benefit' and 'trust in the doctor' were cited as the main reasons for participation by 147 patients who accepted entry to a cancer RCT (Jenkins & Fallowfield, 2000). In an earlier study, interviews were conducted with 144 patients currently enrolled in phase II or III cancer clinical trials. The primary motivations for participation were benefits outweighing risk, trust in the hospital, trust in the physician,

beliefs it would fight illness, belief that the illness would get worse without it and the information provided by the physician (Penman et al., 1984).

These studies highlight the importance of altruistic motives and trust in the doctor for patients that agree to participate. Llewellyn-Thomas et al. (1991) argue that patients who participate in trials are more susceptible to the doctor's enthusiasm. However, it may be argued that the concept of social conformity is the underlying factor here, where patients that participate in a trial wish to give a "yes" response that will please the doctor.

Social desirability may also play a role when patients are asked to state their reasons for participating. A 'desire to help others' may be perceived as a socially desirable response rather than more 'selfish' reasons such as 'improving my own health'.

It has been noted that during illness people need to feel their needs are of top priority and the random assignment to a treatment program is not consistent with this (Schain, 1994). Schain highlights the importance of whether a person is primarily altruistic or self-protective. An altruistic individual who gains gratification from contributing to scientific knowledge is more likely to participate. However, an individual who has a strong sense of autonomy and believes the function of medical care is to make the patient well again is unlikely to participate. While these observations are interesting, the author provides no evidence to support her views.

Barriers to patient participation have been named as: scheduling and family conflicts, and the amount of time required (Devris et al., 1989). This research was not specific to cancer clinical trials. Another study focused on 68 individuals who were eligible for clinical drug trials, who considered participating, but did not. They cited schedule conflicts, risks involved and potential discomfort of the procedure as reasons for their refusal (Cunny & Miller, 1994). However it is unclear whether these individuals were healthy or suffering from disease. The authors did not state the type of drugs being tried or whether the trials were phase I, II, or III. The survey did use individuals involved with real protocols, but it is not clear how these results can be generalized to a population with cancer who must consider lifesaving treatment options. In addition, the survey was distributed by a Contract Research Organisation (Pharmaco-LSR) employee, which may have introduced bias into the results.

Barofsky and Sugarbaker (1979) used standardized interviews to compare patients who had completed one of three sarcoma clinical trials (n=48) with those who had declined or dropped out (n=32). It was found that both groups gave reasons that were related to self-interest, but for those who refused participation, the aversive aspects of the treatments were more important. The authors found no differences in socio-demographic variables or in psychosocial problems between the groups. They conclude that treatment-related factors were the major determinants of willingness to participate in the trials and state that:

*“Patients were not, for the most part, non-participants for trivial or for psychological reasons”*

However, this conclusion lacks supporting evidence as no standardized psychological scales or instruments were used.

This study highlights some of the methodological weaknesses in this area of research. Here the ‘non-participation group’ included: patients who were not willing to be randomized into a protocol, patients with recurrent disease who refused further therapy, patients who withdrew from further therapy and patients who withdrew from the protocol after beginning treatment (for example, because they found their reaction unacceptable). This would appear to be a heterogeneous group. The authors saw no reason to separate these patient populations, but did not provide statistical evidence to support this judgement, probably due to an already small sample size. It may be the case that very different reasons and decision-making processes were present in these different subgroups.

The authors recognized that the best time to interview patients was after they had completed treatment, or refused to enter or withdrawn from the trial. However this was not possible for approximately half the patients. These patients were interviewed by phone up to a few months later. This brings the validity and reliability of their responses into question. After this time lapse patients may not have been able to accurately recall their thoughts and reasons for the decisions they made. Research in

this area varies widely in terms of when in the trial process it is conducted. Evidence from qualitative studies suggests that a trial is a dynamic process where perceptions and views change as the trial progresses (Cox, 1999). It is thus difficult to make direct comparisons between studies that are conducted at different time points.

Finally, a piece of research in this area that has included a psychological measure is that of Lovegrove et al. (2000). They approached 150 women who were regular attendees at a clinic for those at high risk of breast cancer. The women had been offered participation in a 5-year Tamoxifen trial. This drug was being tried as a prophylactic agent against primary breast cancer in women at high familial risk of the disease. The trial was double-blind and placebo controlled. One hundred and six women agreed to enter the study, of which approximately 50% had agreed to the Tamoxifen trial and 50% had declined.

The women who were in the trial were significantly older than those who were not. Socio-economic status was not related to participation. More women in the trial (40%) gave an altruistic reason (for example, wanting to help future generations) than those not on the trial (7.5%). The participants completed the Multi Dimensional Health Locus of Control scale (MDHLC). Scores on this measure were not related to participation, despite predictions that higher scores on internal locus of control would be found in those electing not to join the trial. Those who declined the trial were more aware of lifestyle factors that influence the development of cancers and found the information given about the trial drug more difficult to understand.



Lovegrove et al. (2000) used patients who were currently asymptomatic and were offered participation in a trial of a preventative agent. This population may differ greatly from those diagnosed with cancer and work of this nature is still required on treatment trials. Also, it should be noted that the questionnaires were filled in retrospectively to entering or not entering the trial and may have been influenced by experiences since the women made their decision.

### *Summary*

*Patients identify a range of reasons for their decision. Some of these are logistical and others are related to their beliefs. The area is plagued with methodological difficulties. Sample sizes are small and heterogeneous. Patients are interviewed at different time points in the trial, making it difficult to directly compare findings. The phase of the trial used may not be stated or different phases are used and treated as one. Research has focused on symptomatic patients, asymptomatic patients, prevention trials and treatment trials. Making comparisons and drawing conclusions from the findings is thus problematic.*

The following section will examine the literature on the decision-making process in patients and its impact on clinical trial participation.

### **1.6 Decision-Making and Desire for Information**

The need for health care professionals to provide information to patients so that they may participate in informed decision-making about their care has been recognized over

the past 10 years (Sutherland et al., 1989). Patients' desire for information and participation in decision-making has been investigated by several studies. Generally, conflicting results have been found.

Many studies have shown that patients receive little information about their disease, tests and medication and that they would prefer to receive more (e.g. Faden et al., 1981). A strong association has been demonstrated between preference for information and participation in decision-making, especially in younger patients (Cassileth et al., 1980). Patients who are more highly educated have been found to want to participate in decision-making (Hack et al., 1994; Degner et al., 1997). However, sociodemographic factors have been shown to have no effect on preference by other studies (Ramfelt et al., 2000).

In one study, questionnaires about aspects of decision-making were administered to 210 patients with hypertension (Strull et al., 1984). Patients were found to prefer more information about hypertension (41%), whereas clinicians underestimated patient desire for discussion about their therapy. However, patients reported playing a passive role in actual decision-making, with 63% leaving the decision entirely up to the physician.

Hence, while patients require information and discussion with clinicians, they may actually play a limited role in decision-making regarding their treatment. The generalization of this study to cancer is of course questionable, although research on cancer populations has produced similar results. For example, Ramfelt et al. (2000)

studied 86 patients with newly diagnosed colorectal cancer and found that 62% preferred a collaborative role and 28% a passive role in treatment decision-making. When it came to their actual treatment decision, just 44% of the patients obtained their preferred role.

Sutherland et al. (1989) administered the Health Opinion Survey, the Information Seeking Questionnaire and the Preference for Decision-Making Questionnaire to 52 outpatients requiring post-surgery treatment for cancer. A positive association between information seeking and preference for participation in decision-making was found. Once again, patients concurrently felt that the physician should take primary responsibility in decision-making.

It is thus suggested by a number of studies that there is only a weak link between preferred and actual participating roles. It appears that patients' preferences for decision-making are related to factors other than their desire to be behaviourally involved. Sutherland et al. (1989) suggest that patients actively seek information to satisfy an aspect of 'psychological autonomy' and that this does not necessarily involve decision-making. They note Katz's (1984) definition of psychological autonomy as:

*"The capacity of a person to become informed so that he/she may exercise the right to self-determination."*

Patients express their autonomy by 'deciding not to decide' and passing responsibility to the physician.

Interestingly, research has shown that patients who play an active-role in decision-making have better outcomes. Women with early-stage breast cancer had less anxiety and depression if given a choice of treatment than those who had no choice (Fallowfield et al., 1990).

Qualitative investigations have produced findings consistent with the questionnaire-based research (Cox & Avis, 1996). Cancer patients believed that the doctor was the best person to decide on the most appropriate treatment for them. They wanted to give control to the doctors and for them to take responsibility for decision-making. This appeared to be based on respondents' feelings they did not possess the background knowledge to make such a decision.

There is an absence of research that investigates the relationship between decision-making preferences and clinical trial participation. A recent study (Llewellyn-Thomas et al., 1991) looked at whether patients who differed on clinical trial entry decision also differed in their attitudes towards decision control and the benefits associated with the trial arms. Sixty patients with a diagnosis of colon or rectal cancer participated. Twenty-five reported they would participate if faced with the choice, and 35 refused. Between group differences were noted, namely that those who would refuse participation reported lower scores for survival preference (that is, they were less

willing to tolerate short term toxicity for possible long term improved survival). This is consistent with other research that has found that aversive aspects of the trial itself were cited as reasons for refusal to enter (Barofsky & Sugarbaker, 1979).

Those participants who were less willing to give away decision-making to the physician were more likely to refuse trial participation. The authors concluded that it is possible that patients who agree to clinical trials are more susceptible to the physician's enthusiasm for the trial. This has important ethical implications for the process of obtaining informed consent and raises questions about the personality and coping styles of those enrolled in trials. Coping has been divided into active, distractive and avoidant (Weisman & Worden, 1976) and has implications for behaviour such as information seeking, and so in turn may affect a patient's decision.

Llewellyn-Thomas et al. (1991) demonstrated a link between a high desire for involvement in treatment decision-making and the lower likelihood of participation in clinical trial. It is noteworthy that 77% of the refusers cited 'aversion to randomization' as their primary reason. Randomization means that patients cannot predict or control the exact treatment they will receive. This may be intolerable to patients with a high need for control and decision-making. Research is needed that looks at the health locus of control and health beliefs of patients who are offered entry to a clinical trial.

The study by Llewellyn-Thomas et al. (1991) has the merit of using cancer patients. However, the patients were not eligible for a clinical trial and so the researchers used a

hypothetical trial situation. Once again thinking about a hypothetical trial may yield different results from considering a 'real' trial.

### *Summary*

*Patients express a wish to have more information about their disease and to play an active part in decisions about their treatment. However, they concurrently feel that the 'doctor knows best' and should make the final decision, perhaps as they do not possess enough background knowledge themselves. Patients with a high desire to participate in decision-making may be less likely to enter a clinical trial. It appears that decision making in medical care and especially that involving clinical trials is relatively poorly understood.*

Central to the decision-making process is the issue of informed consent. Research investigating the impact of the informed consent process will be briefly reviewed.

### **1.7 Informed Consent**

The informed consent process within the therapeutic research setting dates back to only the past 50 years (Daugherty, 1999). The concept generally refers to a patient's right to make an informed choice regarding their health care. This must involve disclosure of the type of research, full disclosure of information about the trial, the risks and benefits, the unproven nature of the research, the alternatives to participation and the subject's right to withdraw without detrimental effects to their care. It is also implicit that the

patient should understand this disclosure. The content and comprehension of information may be an important influence on a patient's decision-making.

The general conclusion from the literature is that the aims of informed consent are not met. In recent years concerns have arisen about the quality of written consent documents. In an analysis of the readability of five different surgical consent forms, it was found that all five were equivalent to undergraduate or graduate student material (Grundner, 1980). A larger study of nearly 100 consent forms, nearly 50% of which pertained to cancer clinical trials, found that consent forms were becoming increasingly lengthy and unreadable and did not improve patients' understanding (LoVerde et al., 1989). This appears not to have changed in more recent years, with the readability of consent forms for cancer research protocols still found to be at a level equivalent to at least 2 years of college education (Grossman et al., 1994). The authors concluded that consent forms provide no meaningful written information to patients considering research participation.

Research examining patients' use of consent forms supports this view. In a survey of 100 breast cancer patients after they had signed written consent documents, it was found that the documents had little impact on patients' decisions or knowledge (Muss et al., 1979). Within one day of signing consent forms, 200 cancer patients showed major deficits in their recall of the purpose, nature, implications and risks of the therapy. Forty percent could not recall the purpose or nature of the procedure (Casseilth et al.,

1980). Similarly, a more recent study (Cox & Avis, 1996) found that patients had poor recall of the information given when being asked to participate in the trial.

Hence, the research shows that patients have poor recall for the content of consent forms. It is possible that at the point of presentation, patients have limited ability to understand and process the information and that this later leads to difficulties with recall. If this is so, this suggests that patients make their decisions on little and poorly understood information and that fully informed consent is not obtained. This may support the view that patients have pre-existing views about clinical trials which are the major determinant of their decision.

Patient interpretation of the consent form has been shown to affect participation in a hypothetical trial (Sutherland et al., 1990). Fifty cancer patients were asked to identify the information on a consent form that would be important if they were deciding whether or not to participate. Patients who refused to participate focused on the risks of the trial only (70%). In comparison, only 33% of patients who indicated that they would participate focused entirely on risks. Patients also made incorrect interpretations of some of the statements made on the consent forms. The authors concluded that many decisions regarding entry to clinical trials are made on the basis of incomplete or inaccurate information as patients misunderstand what is presented to them.

The amount and type of information that should be given to patients with cancer when seeking their consent is greatly debated (Shaffer, 1982; Brewin, 1982). A balance is



required between respect for the patient's autonomy and active participation in decisions about their medical health care, and the potential anxiety and increased confusion that may result from too much disclosure (Grundner, 1980). There are a limited number of studies looking at the implications of different methods of consent for cancer clinical trials. One study used a randomized method to compare total disclosure of all relevant information with an individual approach at the discretion of the doctor (Simes et al., 1986). Fifty-seven patients who were candidates for cancer clinical trials agreed to participate. Total disclosure led to a better understanding of the treatment, research and side effects. It also led to increased anxiety and less willingness to enter randomized treatment.

### *Summary*

*Patients may not understand the details of the trial being offered to them. They have been shown to have poor recall of the information provided during the informed consent process. Those patients who focus on the risks of the trial may be less likely to enter. Overall, many questions remain unanswered about the impact of informed consent on patients' decisions about clinical trials. It appears that patients have different needs regarding the amount and type of information they receive. Taking a more individualized approach may improve accrual rates.*

Personality is an intensively researched area in oncology. A brief overview of this complex and controversial area will be the aim of the following section.

## 1.8 Personality

Some writers have suggested a cancer-prone personality that is characterized by abnormal suppression of negative emotions and the inability to express anger (e.g. Watson et al., 1984; Copper and Faragher, 1993). However, research also indicates that emotional repression is a reactive rather than causal phenomenon in cancer patients (Kreitler et al., 1993).

Cancer patients have been shown to have high ratings on the 'Lie' or 'social conformity' scale of the Eysenck Personality Questionnaire (Greer & Watson, 1975). This scale had been implicated in survival (Ratcliffe et al. 1995). Patients who score highly on 'social conformity' may be more willing to please the doctor by entering the trial. Also using the Eysenck Personality Questionnaire, Lloyd et al. (1984) studied 40 patients with malignant lymphoma. Those who scored highly on the 'Neuroticism Scale' expressed greater dissatisfaction with the information and communication provided about their treatment. The authors suggested that personality assessment should be part of studies looking at patient-doctor communication.

It can be seen that personality style may affect the way in which patients perceive the trial and their options, and in turn affect their decision regarding trial entry. The personality characteristics of individuals who enter clinical trials are a neglected area of the literature.

Cami et al. (1989) compared a group of 62 healthy male university students who participated in phase I clinical trials with a control group with similar sociocultural characteristics. Higher 'Extraversion' and 'Psychoticism' scores on the Eysenck Personality Questionnaire were found in the trial participants. There were no differences in the L-Scale. Hence, the results indicated a greater degree of impulsivity and sociability in the trial participants. E and P correlate positively with sensation seeking (Furnam, 1994) and therefore the authors conclude that volunteers may have a greater tendency to risk-taking behaviour. Sensation-seeking may be an important personality characteristic involved in decision-making concerning clinical trials.

In addition, lower 'Neuroticism' scores were found in the volunteer group, which suggests a lower susceptibility to stress situations. Individuals who scored highly on the 'Neuroticism' scale would be predicted not to participate in phase I trials. The authors conclude that the personality characteristics of individuals who enter phase I trial may influence the psychodynamics of the drug under investigation.

These conclusions are not necessarily applicable to cancer treatment clinical trials. This research focused on healthy male, university volunteers who were involved in phase I trials. The personality of patients who consent to, or refuse to enter, cancer clinical trials (phases I-III), has not yet been investigated.

## *Summary*

*The literature on cancer and personality is an extensive area, but it remains a neglected area of the research focusing on clinical trial participation. It is not possible to draw conclusions from the research to date.*

### **1.9 Family Factors**

A further field of research that has been largely neglected by the clinical trials literature is the impact of the family on a patient's decision. The family is usually the most important source of psychological support for the cancer patient (Holland, 1996). Tabak (1995) describes how patients' decisions about their treatment are not made independently. In a study of cancer patients' activities that precede a decision to agree to or refuse experimental treatment, Tabak (1995) states that:

*"Cancer patients speak of consulting extensively with friends and family, in addition to the doctor, before making up their minds."*

Patients often need reassurance from family and friends, although the final decision is theirs (Penman et al., 1984). However, this support has been found to be an excessive pressure to accept experimental treatment for some patients (Perri, 1981). Families may wish to leave "no stone unturned" (Holland, 1982).

The influence of family members' views on experimental treatment and their impact on the patient's decision-making has not been systematically studied.

## **1.10 Health Models**

Several theories and conceptual models have been developed that aim to predict the health behaviour of individuals. These may be used to explain the behaviour of patients faced with a decision regarding a clinical trial.

The Health Belief Model (HBM) initially developed by Rosenstock (1966) and later by Becker and Maiman (1975) was first used to predict preventative health behaviours. It has more recently been applied to a wide range of health-related behaviours. The model predicts that behaviour is the result of a set of core beliefs that have been redefined throughout the person's life. The probability that a person will perform a particular health-related behaviour is influenced primarily by four core beliefs: the perceived seriousness of the disease, the perceived chance of getting disease, the perceived benefits of the behaviour and the costs and barriers of action. It also suggests a stimulus, a 'cue to action', is needed to trigger the decision-making process.

Four common concepts of the HBM and three other theories of health-related behaviour and how these may be applied to clinical trial participation have been described (Morrow et al., 1994):

*Probability* is the perceived likelihood of having the medical condition and of an expected outcome. Probability factors that may be important in the enrollment of patients in clinical trials include the individual's perception of the disease and the ability of the intervention to cure it.

*Severity* refers to the individual's perception of the severity of the disease or side effects. Severity factors important in the enrollment of patients into clinical trials include the patient's willingness to make trade-offs between survival and quality of life.

*Effectiveness* refers to the patient's perception of the probable success of the treatments in the trial. Their personal beliefs, altruistic motives, fears that the condition will worsen and desire to get the best care possible are all effectiveness factors that may affect participation.

Finally, *Perceived cost* is the sum of perceived barrier factors. These may include the patient's attitudes to randomization and research in general, and their degree of preference to participate in medical decisions. Other logistic costs may be of influence here, such as travelling time, cost and inconvenience.

Morrow et al. (1994) noted the confusion between accrual to randomized cancer control trials and randomized cancer treatment trials. The former deals with prevention, screening and detection and the latter with treatment, cure and side effects. The four concepts described above apply differently to each. Severity and probability have minimal influence to treatment clinical trials, where as cost and effectiveness play a much greater role.

Research that has directly applied the models of health behaviour to cancer treatment clinical trials is limited. However, an extended form of the HBM was used to explain participation behaviour in clinical trials by Verheggen et al. (1998). The authors present a model of explanation for trial participation. A measurement of the influence of important others and of the patient's locus of control were incorporated in the model.

The survey comprised a sample of 198 patients who were approached and asked to participate in a clinical trial. They were derived from different departments: surgery, dermatology, ENT, internal medicine, urology, cardiology, radiology, anesthesiology, orthopaedics and pulmonology, giving a total of 26 clinical trials. Data were collected through personal interviews from those patients who agreed and those who declined participation.

A distinction was made between 'Old cases' (those with health problems dating back more than 3 months) and 'new cases' (those with no prior health problems until developing symptoms in the 3 months before the trial). Motivation for trial participation differed between these two groups. The 'new cases' tended to participate if they expected to run low risks and get better treatment in the trial and if they worried about their health. The 'old cases' were more motivated by getting treatment as quickly as possible and by the hope for higher personal comfort in the trial, rather than the expectation of better medical treatment.

The results of the locus of control analysis showed that patients who felt powerless on health matters as shown by a high score on the chance scale, had lower expectations of personal comfort in the trial and hence were less likely to participate. In contrast, patients with a high score on external locus of control, indicating a high reliance on the physicians to solve their medical problems, had a higher chance of trial participation.

The authors conclude that patients make a decision about a clinical trial by making a personal balance account. They weigh up the beliefs for and against it. The physical and emotional value patients hope to gain from participation, compared with the standard treatment, minus the trial risks and cost, form this personal balance account. This was found to depend upon the amount a patient felt physically threatened by their illness, how they regarded their illness and their opinions on medical care.

However, it is notable that the response rate to the survey in the non-participants was significantly lower than in the participants. This appears to be a significant problem in research in this area and questions the representativeness of samples of patients who decline entry to clinical trials. It was also not clear which 'locus of control' scale was used and no evidence of its reliability and validity are given. The HBM is criticized as being highly abstract. It uses concepts that are difficult to define (Gillam, 1991) and measure, and assumes individuals are rational information processors (Ogden, 1996).



## *Summary*

*A patient's decision-making regarding a clinical trial may be conceptualized in terms of the Health Belief Model, where the patient makes a personal balance account based on their beliefs about their illness and the gains and risks of the trial. Research in this area has shown that patients with a high external locus of control are more likely to enter a trial. However, health models have been criticized on theoretical grounds.*

### **I.11 Individual Experience of Clinical Trials**

Cox (1998) highlights the absence of work that addresses the experience of experimental treatment of cancer from the viewpoint of patients themselves. Most work to date is quantitative in nature and conducted at the beginning of the trial, which leads to neglect of how the individual adapts to, makes sense of and ultimately reflects on the whole trial experience. Patients involved in clinical trials may provide unique insights into the whole trial experience which may be used to improve the way trials are conducted, right from the informed consent process to ending the trial and aftercare. Cook-Gotay (1991) suggests that work should focus on the patients' motivations, understandings and perspectives of the trial. There are a limited number of studies that use a qualitative methodology.

A pilot study (Cox & Avis, 1996) aimed to give greater attention to patients' experiences of clinical trial participation. The informed consent process, reasons behind decision-making concerning participation and the impact of participation on the patients' lives were explored. The study reports the views of 7 patients as they

progressed through an anti-cancer drug trial. Six patients were enrolled on phase II trials and one on a phase I trial. Semi-structured interviews were conducted on three occasions throughout the trial process.

The participants gave hope, a desire to help others, feeling they had no other choice, family pressure and a wish to take part in the research as reasons for participating. The authors highlight concepts of *hope* and *choice* as needing further inquiry in terms of what they actually mean to patients. They note the inherent conflict in the process of accrual to clinical trials where a patient is being asked to make a choice in a situation where they feel they have little knowledge and control, and where they perceive they have no choice.

The results need to be interpreted with caution due to the small sample size. However, other research has shown that patients perceive the trial as their only option (Cobb et al., 1954). More recent research has used larger samples and two studies that are of particular interest are described below.

Using Grounded Theory, Stetz (1993) interviewed 24 patients with advanced liver disease over a 6 month period, before, during and after receiving experimental treatment for cancer. Sixteen spouses were also interviewed. Stetz described the primary psychosocial process of individuals involved in experimental treatment as 'survival work'. That is, behaviourally and cognitively choosing life over death, or choosing treatment as opposed to letting the disease take its course. Reasons for engaging in

'survival work' were feeling there was no other option, fear of dying, desire to survive, a need to do something, believing the treatment would work and being offered the opportunity to try something. At the time of decision-making, patients and spouses gathered information to help or support their choice.

The actual treatment period was experienced as 'suspended time' both behaviourally and psychologically. During this time patients were alert to signs of their disease and the effects of treatment. Finally, after the trial had ended, 'carrying on' was the main process for patients and their spouses. They needed to carry on with life without the hope that the treatment was a cure and they desired to live as normally as possible.

Cox (2000) used semi-structured interviews to obtain the views of 55 patients offered participation in a phase I or II clinical trial. Patients were interviewed at 4 points during the trial process. The research focused on their recruitment experiences, decision-making, reasons for participation, experience of the trial and the meaning of the trial. Patients also completed 2 quality of life measures; the Hospital Anxiety and Depression Scale (HADS) and the European Organisation for Research and Treatment of Cancer (EORTC). At follow up, the sample size had reduced from 55 to 27 patients.

There were no statistically significant findings from the questionnaire data. However, the interview data gave important insights. At the recruitment stage the trial offered hope for some patients, a chance to help themselves and to help others. Eighty percent wanted the professionals to present them with the information and advise them what to

do. Accepting seemed the right thing to do as it was what the doctor had offered. Reasons for accepting were similar to those found in earlier studies: wanting to help others, desire to be in expert hands, feeling they had no choice and they had nothing to lose.

An increasing sense of being burdened (e.g. side-effects, trips to hospital) by the trial was identified as patients progressed through the trial. Similar to Stetz's notion of 'suspended time', patients felt their life was on hold for the trial duration. However, the trial also gave patients a sense of purpose, which enabled them to continue. At trial conclusion, patients viewed participation as a positive thing despite being disappointed by the clinical outcome. Cox (2000) concluded that:

*"...Trial participation...is a dynamic process, that has different meaning and impact according to the stage of trial involvement the patient is experiencing."*

These two studies show that clinical trials are a process that begins when the trial is offered to the patient and continues even after the trial has ended. The qualitative data provide support for many of the quantitative studies described earlier. The findings highlight the importance of concepts such as hope, desire to help others and the trial being the only option. These insights may be useful in improving communication with patients and their care. Steltz concludes that the findings imply that clinically, cancer nurses can assess and support the 'survival work' of patients and their relatives. By

being aware of the experience of a clinical trial, nurses can help the patient adjust to the uncertainties of the disease and treatment.

It is noteworthy that 58% of patients in the study by Cox (2000) said that the offer of the trial generated uncertainty. This draws attention to the confusion many patients experience at this time. A personal account of being offered entry to a clinical trial remarks on the great stress and bewilderment inherent to the situation (Thornton, 1992):

*“I cannot understand how a woman can properly judge the proposal that has been put to her....”*

The author comments on the feelings of isolation and overwhelming nature of the decision:

*“...To ask your average woman-in-the-street to have to decide whether or not to take part at the moment she has just been told she has a carcinoma would seem to be asking just too much.”*

Although this is an account of just one patient’s views, Thornton draws attention to the fact that being offered a trial can be an immensely stressful and unwanted experience. As in other research, she describes how she hoped to have her treatment decided by a confident physician, and was instead left to decide for herself. The majority of research to date has focused on patients who have agreed to participate and speaks of the hope it

offers them. No qualitative studies have explored trial refusers' experience of being offered the trial or how they later feel about their decision. Studies that do include patients who have refused the trial are limited and only ask for surface reasons for refusal. We know very little about the motivations, concerns, coping, emotional status or views of these patients.

Thornton also draws attention to the fact the patient must make decisions about their treatment at a time when they have just received possibly devastating news. Cancer is one of the most feared diseases of all (Cox, 1984). For many, the word cancer means death, disfigurement and physical dependence (Holland, 1996). Hence, patients are likely to have difficulties coping with the situation. It is important to understand the psychological reactions of patients in order to understand their decision-making at this time. This leads us to a brief consideration of the literature on the psychological impact of cancer diagnosis.

### **1.12 Psychological Reactions to Cancer**

The period following diagnosis is characterized by great emotional distress. Anxiety and depression are the predominant symptoms and these may be within the morbid range on psychiatric interview (Lloyd et al., 1984). Emotional reactions to an abnormal mammogram have been found to be shock, followed by numbness and disbelief as medical investigations proceed. Patients have high anxiety at this point and then a diagnosis of breast cancer leads to rage, sadness and despair (Massie & Holland, 1989). The diagnosis of a recurrence results in the same emotional reactions of terror, shock

and disbelief as the woman is thrown “back to the beginning”, yet this time with the added burden of “preparing for the inevitable” (Payne et al., 1996). The patient has to decide if she can commit to treatment that will cause discomfort.

Anxiety and depression have been found to peak after breast cancer diagnosis and gradually decline over the next year (Vinokur et al., 1990). It is difficult to establish what is ‘normal’ sadness and worry in these patients. Studies report a point prevalence of depression in cancer patients ranging from 1.5% to 50% (Colon et al., 1990; Fras et al., 1967). The general consensus is that one in four patients suffer from depression (McDaniel et al., 1995). Similarly, 20 to 25% of patients experience anxiety at a clinical level (e.g. Cella et al., 1993). Decision-making problems are common (Ibbotson et al., 1994). Consequently, the mood status of the individual may have important implications for the clinical trial proposal.

There are individual differences in the way patients respond to diagnosis. Developmental life-cycle stage may determine the response. Older people have been found to be less distressed following the diagnosis of cancer than younger people. For example, Harrison and Maguire (1995) assessed 520 patients aged between 18 and 75, within 8 weeks of diagnosis of a range of cancer types. A point prevalence of anxiety and depression disorders was found to be 17.1%. These cases were significantly younger.

Similarly, Cassileth et al. (1986) also found highly significant age differences for scores of anxiety, depression and general positive affect in 1278 patients with cancer. Similar results have been found in groups of patients with breast cancer, colorectal cancer (Mor et al., 1994), and gynaecological cancer (Paraskavaidis et al., 1993). In the latter of these studies higher levels of anxiety or depression on the Hospital Anxiety and Depression Scale were associated with greater dissatisfaction with the information received.

A woman's coping abilities may affect her response. Avoidant coping and denial have been associated with greater distress in women with breast cancer (McCaul, 1999). Greater emotional expressiveness has been associated with improved adjustment (e.g. Classen et al., 1996). Social, cultural, financial, familial factors and degree of emotional support all influence adaptation to cancer (Rowland & Massie, 1996).

### *Summary*

*Depression and anxiety are commonly found in cancer patients and are more severe immediately after diagnosis. A patient's emotional reaction may depend on their coping abilities and a variety of other social and personal factors. A decision regarding a clinical trial is made during an emotionally stressful time.*

### **1.13 Psychological Factors and Prognosis**

A further field of research is that concerned with psychosocial predictors of cancer course and survival. A complete review of this area is beyond the scope of this review.



However, the relevant studies will be described. Psychosocial factors may influence patient participation in clinical trials, which may lead to unrepresentative trial groups. These groups may or may not have a greater chance of survival.

Patients with good quality of life scores are associated with a better response to chemotherapy (e.g. Coates et al., 1992) and with prolonged survival in patients with advanced disease (e.g. Earlam, 1996). A 'fighting Spirit' and emotional expressiveness (Greer, 1991), denial (Schulman et al., 1993), and outgoing personality (Stavraky et al., 1988) have all been associated with longer survival time (Butow et al., 1999). It is important to note that these relationships have not been shown to be causal.

Ratcliffe et al. (1995) found that high depression scores on the HADS and high L-scores on the Eysenck Personality Inventory (EPI) at diagnosis were independent prognostic factors for death at 5 years in 63 patients with lymphoma who received chemotherapy.

Walker et al. (1999) studied 96 women with advanced breast cancer. High HADS depression and anxiety scores were independent predictors of poor response to chemotherapy.

In a recent study, Watson et al. (1999) investigated the effect of psychological response on outcome at 5 years in 578 women with early stage breast cancer. A high score on the depression category of the Hospital Anxiety Depression Scale (HADS) was associated with an increased risk of death, as was a high level of hopelessness and helplessness.

Emotional control as measured by the Courtauld Emotional Control Scale (CEC) did not have an impact on survival.

It can be seen that patients' mood, coping and personality may influence survival. If these variables influence patients' participation in clinical trials, they have important implications for the generalization of the trial findings.

However, research in this area is inconsistent and contradictory in its findings. Many research findings have failed to support any link between psychosocial factors and response or survival. Tross & Herndon (1996) found no evidence of the contribution of psychological factors to survival in 280 women with stage II breast cancer. Other studies have also failed to find an association (e.g. Jamison et al., 1987).

### *Summary*

*The link between survival and psychological factors has produced contradictory findings. Studies suffer from methodological problems such as short follow-up periods, small sample sizes, failure to control for prognostic medical variables, and use of unreliable psychometric scales. Yet despite these shortcomings, the associations demonstrated are important considerations for the clinical trial literature.*

## **Summary of the Literature Review**

The research on patient-related factors that influence accrual to cancer clinical trials has produced varied results. Differences have been demonstrated between patients who enter and those who refuse clinical trials. We know more about the characteristics of those who agree to enter, than those who refuse. This remains a neglected area.

This review has highlighted the importance of patients' beliefs about the trial, the trial's benefits and costs, decision-making preferences and patients' own health in general. It has speculated that factors such as personality, family views and coping may also be important. The decision-making process has been shown to be complex and subject to individual differences.

Research has moved towards viewing the trial as a dynamic process that has different meaning for different individuals. A patient's decision regarding a trial needs to be viewed in the context of their emotional status at that time.

There are few research studies looking at the impact of psychological factors, and to a large extent the contribution of psychological theory has been excluded or dismissed. Psychological problems are common and sometimes severe in patients with cancer (Lloyd et al., 1984) and yet the impact of these on a patient's decision regarding a clinical trial has not been investigated.

Finally, there are many methodological problems throughout the literature. Samples may mix patients with different types of cancer, and those with newly diagnosed and recurrent disease. Research has examined phase I, II and III trials, all of which have different implications for the participants and so are not always directly comparable. Samples are often small and characterized by low response rates, especially in the patient groups who decline entry to the trial. There is also a deficiency of standardized psychometric scales used in the research and most studies fail to report any reliability and validity statistics of those that have been constructed. Finally, research has often used participants for whom the decision and problem are not highly salient. The use of hypothetical scenarios has been criticized on grounds of validity by other authors and it is important that future research addresses this problem.

This research aims to overcome methodological weaknesses of previous research by focusing only on chemotherapy phase III trials. Surgical and preventative trials will be excluded and the research will focus on newly diagnosed patients. It aims to explore both the views of patients who consent and those who refuse to enter a clinical trial. The research will investigate the validity of using hypothetical trial scenarios as a measure and will address the lack of research considering psychological factors by using established psychometric scales.

## **AIMS AND HYPOTHESES**

This study aims to examine the impact of various psychological factors on cancer patients' decision to accept or decline a clinical trial. It also aims to examine the influence of relatives' attitudes on this decision.

### **1. General Attitudes**

#### **Research Hypothesis**

Prior attitudes towards clinical trials (as measured by a 13-item, 5-point Likert scale questionnaire) will affect a patient's decision to enter or refuse a clinical trial.

#### **Null Hypothesis**

Prior attitudes towards clinical trials (as measured by a 13-item, 5-point Likert scale questionnaire) will not affect a patient's decision to enter or refuse a clinical trial.

### **2. Predictions of Own Behaviour**

#### **Research Hypothesis**

'Willingness to participate' in a cancer clinical trial (as measured by 4 hypothetical scenarios, on 5-point Likert scales) will affect a patient's decision to enter or refuse a clinical trial.

## **Null Hypothesis**

'Willingness to participate' in a cancer clinical trial (as measured by 4 hypothetical scenarios, on 5-point Likert scales) will not affect a patient's decision to enter or refuse a clinical trial.

### **3. Emotional Expression**

#### **Research Hypothesis**

There will be a difference in the level of emotional expression (as measured by the Courtauld Emotional Control Scale) between patients who refuse clinical trial participation and those who consent to a trial.

#### **Null Hypothesis**

There will not be a difference in the level of emotional expression (as measured by the Courtauld Emotional Control Scale) between patients who refuse clinical trial participation and those who consent to a trial.

Emotional expression is not hypothesized to affect decision making, rather it is a factor that has been implicated in survival. Differences that exist between trial participants and those who refuse to participate may bias the trial's results. Emotional expression may need to be controlled for in cancer clinical trial research

#### **4. Personality Styles**

##### **Research Hypothesis**

Personality style (as measured by the Eysenck Personality Questionnaire – short form) will affect a patient’s decision to enter or refuse a clinical trial.

##### **Null Hypothesis**

Personality style (as measured by the Eysenck Personality Questionnaire – short form) will not affect a patient’s decision to enter or refuse a clinical trial.

#### **5. Mood Status**

##### **Research Hypothesis (A)**

Level of depressed mood (as measured by the Hospital Anxiety Depression Scale) will affect a patient’s decision to enter or refuse a clinical trial.

##### **Null Hypothesis (A)**

Level of depressed mood (as measured by the Hospital Anxiety Depression Scale) will not affect a patient’s decision to enter or refuse a clinical trial.

##### **Research Hypothesis (B)**

Level of anxiety symptoms (as measured by the Hospital Anxiety Depression Scale) will affect a patient’s decision to enter or refuse a clinical trial.

### **Null Hypothesis (B)**

Level of anxiety symptoms (as measured by the Hospital Anxiety Depression Scale) will not affect a patient's decision to enter or refuse a clinical trial.

## **6. Health Beliefs**

### **Research Hypothesis**

Health locus of control (as measured by the Multidimensional Health Locus of Control Scale) will affect a patient's decision to enter or refuse a clinical trial.

### **Null Hypothesis**

Health locus of control (as measured by the Multidimensional Health Locus of Control Scale) will not affect a patient's decision to enter or refuse a clinical trial.

## **7. Relatives' General Attitudes**

### **Research Hypothesis**

Relatives' prior attitudes towards clinical trials (as measured by a 13-item, 5-point Likert scale questionnaire) will affect a patient's decision to enter or refuse a clinical trial.



### **Null Hypothesis**

Relatives' prior attitudes towards clinical trials (as measured by a 13-item, 5-point Likert scale questionnaire) will not affect a patient's decision to enter or refuse a clinical trial.

## **8. Predictions of behaviour**

### **Research Hypothesis**

Relatives' 'willingness to participate' in a cancer clinical trial (as measured by 4 hypothetical scenarios, on 5-point Likert scales) will affect a patient's decision to enter or refuse a clinical trial.

### **Null Hypothesis**

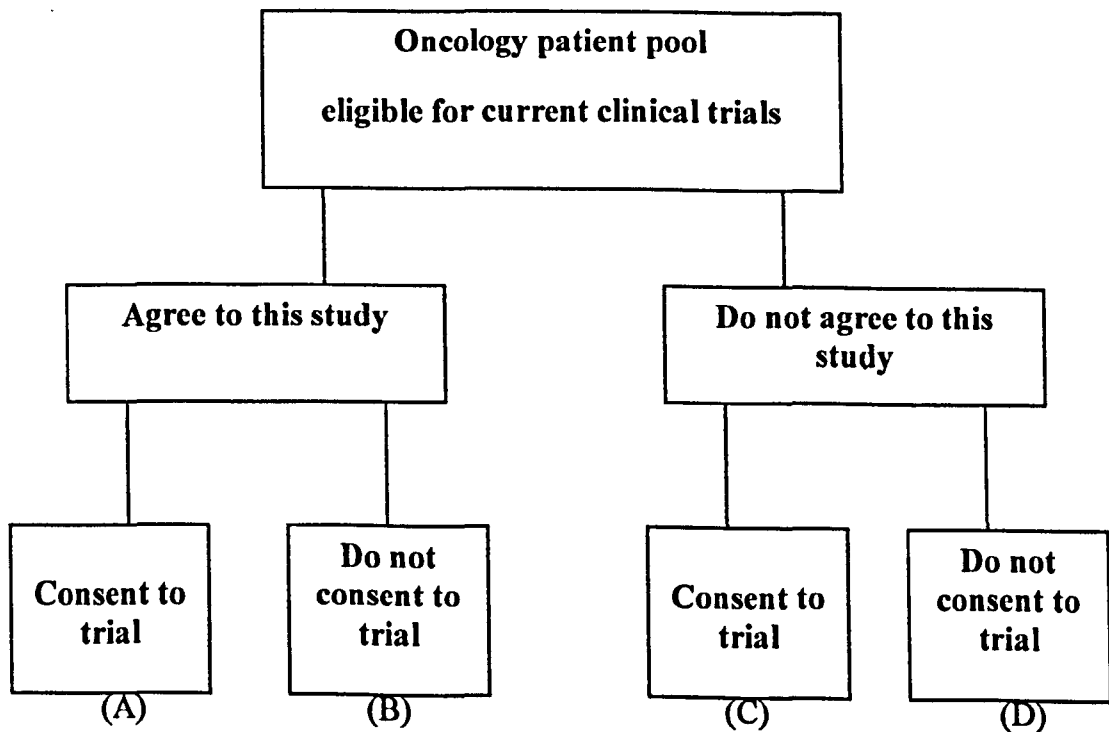
Relatives' 'willingness to participate' in a cancer clinical trial (as measured by 4 hypothetical scenarios, on 5-point Likert scales) will not affect a patient's decision to enter or refuse a clinical trial.

## CHAPTER II - METHODOLOGY

### 2.1 Original Design

This original aim of this research was to explore the differences between patients who consented to a cancer clinical trial and those who refused. It focused on cancer patients who were eligible for a clinical trial and asked them to complete psychological and attitudes measures. The measures examined patients' opinions about clinical trials and their views concerning their own participation if faced with the decision. The patients' current mood status, emotional expression, health beliefs and personality characteristics were also assessed by the measures. After completing the measures the patients were asked to enter the cancer clinical trial for which they were eligible. Their decision was recorded and used in this research. Figure 1 illustrates the original design.

**Figure 1. Original design of the research**



It is shown that patients who agreed to enter this study would form two groups, according to whether they consented to, or refused to enter the clinical trial proposed to them. This study aimed to focus on groups A and B and to compare the scores on the attitudes scales and psychological measures of these two groups.

A cross sectional, single measures point, postal survey design, was implemented. Both standardised, established self-report measures and newly designed questionnaires for this study were used. The measures that were selected aimed to detect differences between the two groups of patients. Their selection was based on the findings of previous research and/or aimed to address areas neglected by previous studies as highlighted in the literature review. Consideration was taken of the reliability and validity data of the measures during selection.

Questionnaires were sent immediately after the eligible referral was received by the Oncology Department, or in the case of in-patients, when a patient was considered eligible for a trial. This time point was chosen so that the patients received the questionnaires before being approached by their consultant about a cancer chemotherapy trial. This was considered necessary so that the trial information the patients received did not influence their responses to the questionnaires.

In a qualitative follow-up phase, an in-depth, semi-structured interview was offered to those patients who had returned the questionnaires, after they had received 3 cycles of treatment. This aimed to explore patients' recollections about their decision-making regarding the trial, their attitudes towards trials and research, and any changes that may have occurred since beginning their treatment. This time-point was chosen firstly as it

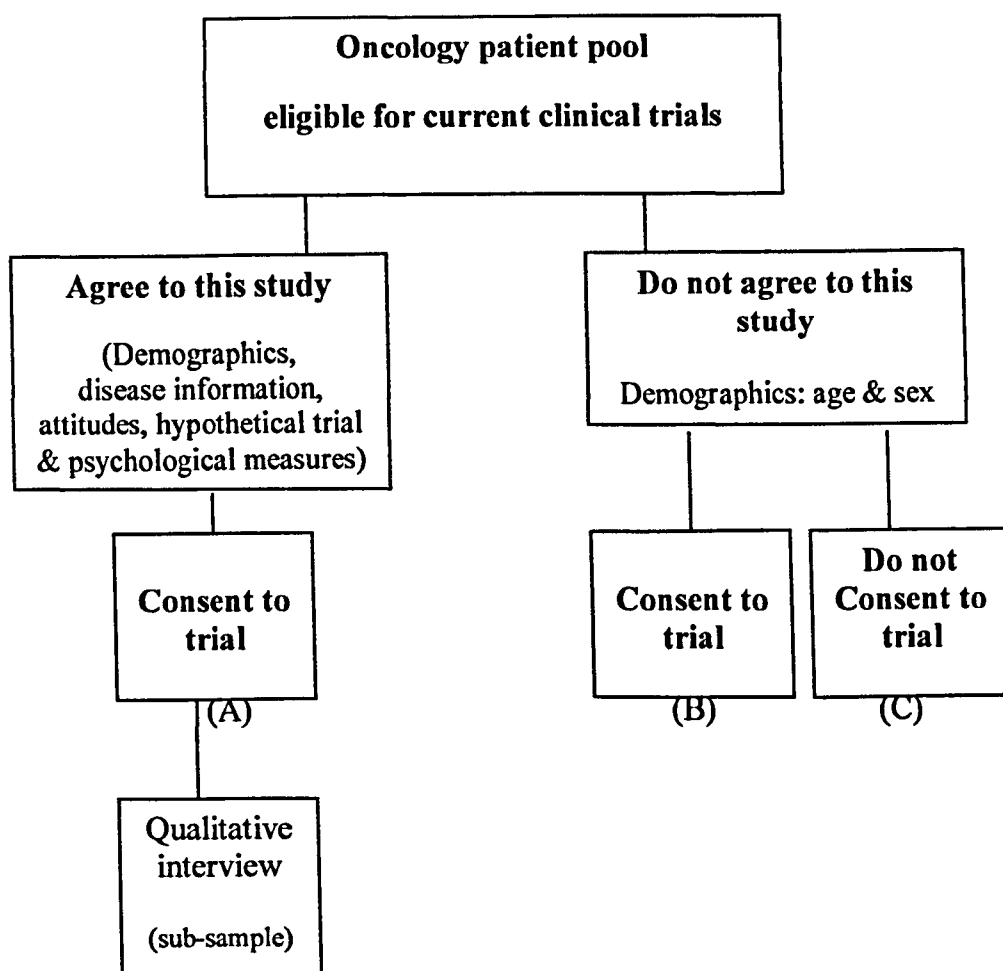
was felt that patients would have some experience of trial or non-trial treatments, but would still be close enough to have reliable recollections of when they made the decision. Secondly, the time constraints of the study meant that a longer period was not possible.

## **2.2 Modifications to Design**

The original design and aims of the research had to be modified due to the characteristics of the responders. It became apparent that the number of patients agreeing to this research and refusing clinical trials was going to be very low. In fact, the final sample contained no patients in group B (see figure 1). Therefore, a single group design was required.

The revised design, showing the data obtained from each group is shown in figure 2. The research aims were modified to explore the characteristics and responses on the measures of the patients within group A. The focus of the research became the characteristics of patients who consented to a cancer clinical trial and were willing to participate in this research project. This group was also compared with groups B and C on basic demographic information (See figure 2).

**Figure 2. Modified research design**



### **2.3 Participants**

Successive patients who fulfilled inclusion criteria (see Appendix I) to participate in current phase I, II or III cancer chemotherapy randomized clinical trials at an Oncology Department in the North East of England were asked to participate in this study. The initial plan was to only include patients eligible for phase III trials, however in order to increase the sample size patients eligible for phase I and II trials were included. Surgical trials were excluded in order to obtain an as homogeneous group of patients as possible. The time period from November 2000 to April 2001 was selected.

Participants were all over 18 years of age and were male or female. Each patient was asked to choose one relative or close friend to participate.

## **2.4 Measures**

### **Independent Variables**

#### **Demographic Details**

Participants filled in a short questionnaire asking for personal information. Their age in years and marital status were recorded. The number of years of education a person had completed and their occupation were also recorded. Participants were asked to state any other medical problems and stressful life events that had occurred in the last 6 months.

#### **Disease Related Information**

The medical records of the patients who participated in this study were consulted at the end of the data collection period. The number of months since the diagnosis of the cancer for which the patient was approached about a trial was recorded. The number of previous treatments and of diagnoses of cancer the patient had received were recorded. In addition, the number of months since the patient's first diagnosis of cancer was noted. A count of the number of previous trial treatments the patient had received was made.

## **Non-Responders**

The age and sex of patients who did not return their questionnaire packs were recorded. It was also recorded whether they refused or agreed to involvement in a subsequent clinical trial.

## **Dependent Variables**

### **Hypothetical Trial Scenarios (Appendix V)**

Previous research has used vignettes to assess patients' willingness to enter cancer clinical trials. However, the validity of these as a measure of whether or not patients will enter a trial has not been assessed. Research has indicated that most patients state that they would enter a trial, but statistically this is unlikely. No previous research has directly compared a patient's hypothetical decision with their real one. In this research vignettes were formulated to look at the correspondence between hypothetical choice and real choice.

Four descriptions of trials were developed through discussions with a Consultant Oncologist. The participant was told that these are possible situations sometimes faced by patients. They were asked to read each one and indicate how likely they would be to enter the trial on a 5-point Likert scale ranging from 'definitely agree' to 'definitely not agree'.

**Trial 1.** Focused on the situation where the standard treatment would not help. There was a new drug, which was randomized against placebo.

**Trial 2.** Focused on the new trial drug having more side-effects than the standard treatment.

**Trial 3.** Focused on the new trial drug having fewer side effects than the standard treatment.

**Trial 4.** Focused on the situation where there was no right or wrong treatment for the disease and two similarly effective treatments were included in the trial.

A score of 1 to 5 was obtained on each hypothetical trial. These scores were combined to give an overall 'willingness to participate' score, (the higher the score the less willing the patient was to enter the trials). Comparison of responses on the individual trials was expected to reveal the importance patients attached to side effects, the possibility of receiving no treatment (placebo) and differences in predicted effectiveness.

Research has indicated that relatives are an important source of support for cancer patients and that when considering a trial, patients consult with their relatives. As patients are unlikely to make their decision in isolation, this research aimed to assess the impact of relatives' views. Therefore, the chosen relative was also asked to complete a copy of the hypothetical trials measure (see Appendix XIV). They were asked to indicate whether they thought their relative should enter the trials on the same 5-point Likert scales. Their scores were combined to give a 'relative's willingness to participate' score.

### **Attitudes to Trials and Research Questionnaire (Appendix VI)**

The questionnaire was designed as a general measure of prior general attitudes towards medical research and cancer clinical trials. It addressed issues such as randomization,



double-blind trials, hope, chance of survival, benefit to others and the necessity of trials. This was included as authors have previously suggested that patients have biases towards clinical trials, and that patients make their decision based on these biases (e.g. Bujorian, 1988). Previously, research has not systematically addressed the impact of prior attitudes on a patient's decision about involvement in a subsequent clinical trial. This research aimed to compare patients' reported attitudes with their decision regarding a subsequent trial, and their expressed 'willingness to enter' the hypothetical trials.

The 13-item attitudes questionnaire was developed through reviewing the literature, discussions with the academic supervisor of the research, and through a research presentation and discussion with other postgraduate clinical psychology trainees.

Questions 1-10 focused on the issues noted above and patients were asked to indicate their responses on 5-point Likert scales. Lower scores indicated more positive attitudes to the value of clinical trial research. Scores from items 1-10 were combined to give an 'attitudes total score'.

Questions 11-13 considered the issues of who should make the decision to enter a trial and the influence of family members. These three items were not used in the 'attitudes total score', as they reflected neither a positive or negative attitude to trial research. Responses to these questions were considered independently.

The participating relative was also asked to complete the 'attitudes to trials and research questionnaire'. The relatives' version took the same format and questions were the

same, except for wording changes to questions 9-12 (see Appendix XV). These were changed to ask the relative to consider how they felt about the patient's participation, rather than their own. The relative was asked to complete this questionnaire as part of the exploration of the impact of their views on the patient's decision-making.

Again questions 1-10 were combined to give an 'attitudes total score'. This was compared with the total score obtained by the patient.

### **Hospital Anxiety and Depression Scale (HADS)**

**(Zigmond and Snaith, 1983) (Appendix VII)**

As described in Chapter One, depression and anxiety are common in cancer patients (McDaniel et al., 1995), and have been shown to influence response to chemotherapy (Walker et al., 1999). The mood status of patients who enter clinical trials versus those who refuse may have implications for the outcome and generalizability of the trial. Previous research has not assessed these patients on a measure of anxiety and depression.

The HADS was designed specifically for physically ill patients in the United Kingdom. Somatic items that are frequently associated with cancer are omitted so they do not affect the depression scores. It provides a measure of anxiety and depression and information on the clinical significance of the scores. This 14-item test asks patients to consider how they have been feeling over the last week and to rate statements that reflect common symptoms of anxiety and depression. The validity and reliability of this test for cancer patients have been demonstrated by many studies (e.g. Razavi et al., 1990; Grassi et al., 1993). Moorey et al. (1991) reported the internal consistency of the

two subscales as assessed by Cronbach's alpha to be 0.90 for depression and 0.93 for anxiety. Zigmond and Snaith (1983) assessed concurrent validity by comparison of HADS scores with 5-point psychiatric rating scales for 100 medical outpatients. The correlation coefficients were: anxiety  $r= 0.54$ , and depression  $r= 0.79$ . The scale takes approximately ten minutes to complete.

### **Eysenck Personality Questionnaire – Revised Short Form**

#### **(Eysenck and Eysenck, 1991) (Appendix VIII)**

A number of studies have investigated the relationship between personality and treatment response and survival in cancer (e.g. Ratcliffe et al. 1995). Again, previously the impact of personality on patients' decision-making about a clinical trial has not been investigated.

The Eysenck Personality Scales attempt to measure the major dimensions of personality – P (psychoticism), N (neuroticism), E (extraversion) and L (lie scale or social conformity). Various earlier personality questionnaires were developed to form the EPQ, which has since been revised. A short scale was devised to save time, which includes 12 items from each of the four dimensions listed above. The EPQ manual (Eysenck and Eysenck, 1991) provides full statistical details of the scale. Reliabilities for the 4 scales are shown as; P, 0.62; E, 0.88; N, 0.84 and L, 0.77 for males. Similar figures are quoted for females.

## **Multidimensional Health Locus of Control Scale**

**(Wallston et al., 1978) (Appendix IX)**

Research has suggested that patients with a high external locus of control are more likely to enter clinical trials (e.g. Verheggen et al., 1998). However, this is an inconsistent finding which requires further research to confirm differences between patients who consent and those who refuse clinical trials.

This MDHLC scale provides a measure of three dimensions of health locus of control:

**Internality**, the extent to which a person believes they have control of their own health, **Chance**, a measure of belief in external or chance factors determining their health, and **Powerful Others**, a measure of belief that others, particularly health professionals, have control over their health.

There are 18 items on the scale, which the person must rate on a 6-point Likert scale ranging from 'strongly disagree' to 'strongly agree'. Each of the three scales are scored between 6 and 36. The scale takes approximately 5 minutes to complete.

Wallston et al. (1978) believed that a person's beliefs about personal control affect the decisions they make about their health. A person who scores highly on Internality is more likely to regard their health as within their control.

The alpha reliabilities for each of the three scales ranged from 0.673 to 0.767 (Wallston et al., 1978). Internality and powerful others were statistically independent, internality and chance were negatively correlated and powerful others and chance were positively

correlated. Health status was positively associated with internality, negatively associated with chance and was not related to powerful others.

### **Courtauld Emotional Control Scale (CECS)**

**(Watson and Greer, 1983) (Appendix X)**

The suppression of negative emotions has been suggested as a focal characteristic of the cancer-prone personality. Emotional expression has been associated in survival by some writers (e.g. Greer, 1991), and thus differences in emotional expressiveness between patients who consent to a trial and those who refuse may have important implications.

The CEC is a questionnaire measure of the extent to which patients suppress negative emotions or show emotional control. There are three sections corresponding to the three moods: anger, anxiety and depression. In each section there are seven statements which the respondent must rate on a 1-4 point scale of frequency.

Adequate test-retest reliability has been shown (anger 0.86, depression 0.89, anxiety 0.84 and total score 0.95) and internal consistency (alpha coefficients 0.86, 0.88 and 0.88). All three sections show significant positive correlations with each other, providing evidence for the validity of the scale as a measure of the emotional control construct (Watson and Greer, 1983).

## **Qualitative Measures**

### **Semi-Structured Interview Questions**

#### **(Appendix XVI)**

Qualitative methodology has been suggested by other writers as the way to access patients' true feelings and experiences of cancer clinical trials (e.g. Cox 1998). The open-ended questions for the follow-up interviews were developed through discussions with a trials nurse, oncologists and a researcher who has previously conducted a number of qualitative studies on patients' experiences of cancer clinical trials. The questions were not designed to explore patients' trial experiences, rather they aimed to retrospectively investigate the decision-making process that the patient went through when the trial was proposed to them. They aimed to explore patients' attitudes before the trial and whether these had changed, their hopes and fears, how they made their decision, the influence of their family and whether this research study had influenced their decision. It was recognised that by providing information about trials and making patients think about the possibility of being entered, they may have been more receptive when faced with the 'real' trial.

## **2.5 Procedure**

### **Ethical Approval**

The Local Research Ethics Committee granted ethical approval for the project in July 2000. The Research and Development Consortium also granted local trust approval before data collection began.

## **Recruitment**

Referrals between November 2000 and April 2001 were screened by the Consultant Oncologist. One NHS trust area in the North of England was used. Patients who were eligible for current phase I, II or III clinical trials were identified. Names were passed to the trials nurse who dispatched a pack containing the patient information sheet, consent form, attitudes questionnaire, hypothetical trial scenarios, HADS, EPQ-Short Form, MDHLC and the CECS (see Appendices II-X). The pack also contained the relative's questionnaires (see Appendices XI-XV) and a prepaid envelope for return. Completion and return of the packs was completely voluntary.

The patient information sheet (see Appendix II) described the purpose of the study, why the patient had been chosen and a brief description of the nature of clinical trials. This description was included after 4 exploratory interviews revealed that patients were not sure what was meant by 'a clinical trial'. It was stressed that the study was not asking patients to enter a trial, rather it was an investigation of their views. The information sheet also emphasised that participation was voluntary and separate to patients' medical care. The consultant would not be contacted about their results and all the information was confidential. Instructions for filling in the pack and its return were included and it was stated that the patients would be contacted again in 3 months to participate in a further interview. It was emphasised that the patient did not have to agree to the second interview.

If the questionnaires were not returned in 10 days, the trials nurse was consulted about the medical status of the patient. If the patient was deemed 'well enough' by the trials nurse a telephone call was made to the patient asking them if they had received the

questionnaire pack. Patients who had, but did not wish to return them were asked if they were willing to give a reason for this. Patients who did intend to return them were asked to do so as soon as possible. All patients were thanked for their time.

A patient's decision regarding the cancer treatment trial offered to them was recorded. If a patient had entered a trial, the name of that that trial was recorded. This information was obtained from the clinical trials nurse.

### **Follow-up Interviews**

The trials nurse was consulted before any attempt was made to contact patients again. Those who had died, were currently in-patients or were deemed too ill to participate, were excluded from the follow-up sample. Of the remaining patients, telephone contact was made with those who had volunteered for this study after 3 cycles of their treatment. They were asked if the researcher could visit them at home, or arrange to meet them at the oncology outpatient clinic for an interview. It was explained that the interview would take 45 minutes to 1 hour and was about how they decided to enter the trial and their experiences. It was again stressed that this was purely voluntary and they were under no obligation to agree.

The patients who agreed were visited within the following week at a time convenient to the patient. The original patient information sheet was given again to patients and attention was drawn to the researcher's name and the person to contact for further information. Patients were reminded that they did not have to answer any questions if they did not wish to and that they could withdraw from the interview at any time. Interviews were recorded using a dictaphone.



## **2.6 Statistical Analysis**

The data were analysed using SPSS for Windows Version 9.0. The research supervisor and a statistician were consulted for advice on appropriate statistical analyses. Due to the nature of the data collected an exploratory approach was taken. The following analyses were conducted:

- To assess the appropriateness of parametric or non-parametric analysis, the distribution of the variables were examined and the normality of the distributions were tested using the Kolmogorov-Smirnov test.
- A Hierarchical Cluster Analysis was performed on the attitudes questionnaire to identify groups of questions measuring different themes.
- A Hierarchical Cluster Analysis was performed on the attitudes questionnaire to identify particular groups of patients with similar views.
- The clusters identified by the second Hierarchical Cluster Analysis were used as independent variables. Independent T-Tests were performed on the normally distributed dependent variables. The Mann-Whitney U Test was used to analyse the dependent variables that were not normally distributed.
- A series of four questions were formulated in reference to the literature review and the data set investigated using appropriate statistical analyses for each.

- Content analysis was performed on the qualitative interview data. A second rater also completed the analysis.

## **CHAPTER THREE : RESULTS**

### **3.1 Recruitment**

During the data collection period from 14.11.00 to 20.04.01, forty-nine referrals of patients eligible for current phase I, II or III clinical trials were received by the two oncologists participating in this study. Questionnaire packs were dispatched to all forty-nine and thirty-one were returned, giving a response rate of 63%.

The distribution of the eligible participants over the data collection period was examined and is shown in table 1. The number of patients eligible for trials ranged from 4 to 12 per month. The fewest number of questionnaires were dispatched during December and the Christmas period. This was also the time of the lowest response rate. As is shown below the response rate ranged from 100 to 50 %.

**Table 1: Questionnaire packs sent and returned during November 2000 – April 2001**

Month	Questionnaires Sent	Questionnaires Returned (%)
November	12	7 (58)
December	4	2 (50)
January	6	6 (100)
February	9	5 (55)
March	12	8 (66)
April	6	3 (50)
<b>Total</b>	<b>49</b>	<b>31 (63)</b>

All (100%) of the participants (patients who returned their questionnaires) consented to the clinical trial proposed to them. Table 2 shows the relative rates of trial consent of the participants and non-responders (patients who did not return the questionnaires).

**Table 2: Participant and non-responder rates of trial consent**

	Consented to trial	Refused trial
Participants n=31	31	0
Non-responders n=18	16	2
<b>Total</b>	<b>47</b>	<b>2</b>

Only 2 of 49 patients (4.1%) refused clinical trial participation and both did not return their questionnaires.

An examination of the trials to which participants consented revealed that there were 9 current cancer chemotherapy clinical trials. These were grouped according to the phase of the trial (I, II or III). The number of participants in each phase of trial is shown in table 3. Data were unavailable on 3 participants.

**Table 3: Participant consent to trials by phase**

Phase	Number of Participants (%)
I	8 (28.5)
II	12 (43.0)
III	8 (28.5)
<b>Total</b>	<b>28 (100.0)</b>

### **3.2 Comparison of Participants and Non-Responders**

The age and sex of the non-responder and participant groups are show below in table 4. Statistical analyses showed that the groups were not statistically different on these variables. It was not considered ethically acceptable to consult records for further demographic information on the non-responder group.

#### **Sex**

Approximately equal numbers of male and female patients participated in this study. In comparison, it was noted that a high proportion of males existed in the non-responder group. However, Chi-Square analysis found no association between sex and whether or not a patient participated in this research (Chi-Square=2.0, df=1, p=0.157). Fisher's Exact Test was also not significant (p=0.23).

#### **Age**

The mean age of the participant group was 59.5 years (SD 10.1). The male participants had a mean age of 64.6 years (SD 8.5) and the females were younger by a mean of 10.4 years. The non-responder group was slightly older than the participant group, although this difference was not statistically significant ( $t=-0.342$ ,  $df=47$ ,  $p= 0.734$ ).

**Table 4: Comparison of age and sex of participants and non-responders**

		n	Mean Age (SD)	Mean Age (SD)
Participants (N=31)	Males	16	64.6(8.5)	59.5(10.1)
	Females	15	54.1(9.1)	
Non-responders (N=18)	Males	13	60.0(15.0)	60.7(13.7)
	Females	5	62.6(10.85)	

### 3.3 Demographics of Participants

#### **Marital Status**

As shown below 77.4% of the sample were married and 12.9 % divorced. A minority was single or widowed.

**Table 5: Marital status of participants**

Marital Status	Frequency	Percentage
Married	24	77.4
Divorced	4	12.9
Single	2	6.5
Widowed	1	3.2
<b>Total</b>	<b>31</b>	<b>100.0</b>

#### **Education**

The majority (48.4%) of the sample had completed education to the secondary level. A considerable proportion (35.5%) had education at the college level and 5 participants had been to university.

**Table 6: Education completed by participants**

	Frequency	Percentage
Secondary	15	48.4
Further	11	35.5
Graduate	3	9.7
Post-Graduate	2	6.4
<b>Total</b>	<b>31</b>	<b>100.0</b>

## Occupation

The occupations of participants were recorded as: 1= professional, 2= skilled, 3= semi-skilled, 4= unskilled manual. If a participant was retired they were classified according to their previous occupation and if they were a 'housewife' they were classified according to their spouse's occupation. Nearly half the sample were unskilled workers, 16.1 % were semi-skilled, 29% were skilled and a minority were in a professional occupation (see table 7).

**Table 7: Occupation of participants**

	Frequency	Percentage
Professional	3	9.7
Skilled	9	29.0
Semi-Skilled	5	16.1
Unskilled	14	45.2
<b>Total</b>	<b>31</b>	<b>100.0</b>

## Life events

Only three participants indicated that they had suffered additional, difficult life events in the last 6 months. All three noted financial difficulties, which were related to being unable to work.

### 3.4 Information on Disease

A count of the number of months since a participant's first diagnosis of cancer was made. The total number of times a cancer had been diagnosed on different occasions and the total number of treatment courses participants had been given (included surgical, radiotherapy and chemotherapy) were recorded. It was noted whether or not a

participant had enrolled in previous cancer clinical trials. The number of months since the diagnosis of the most recent cancer was recorded. The medical files of two participants could not be recovered.

### **Time since first diagnosis**

There was a range of 180 months (15 years) in the time since participants' first diagnosis of a cancer. Hence, some were newly diagnosed with a primary cancer and others experienced reoccurring disease. The results are shown in table 8.

**Table 8: Time in months since first diagnosis of a cancer**

	N	Minimum	Maximum	Mean	St.Deviation
Time (Months)	29	0.0	180.0	38.9	55.7

### **Number of cancers diagnosed**

Participants had been diagnosed with cancer between one and four times (inclusive of the cancer for which they were referred for the trial). The mean number of diagnoses was 1.93 (SD 1.1). Table 9 shows the frequency of the number of diagnoses. It can be seen that nearly half of the sample had been diagnosed with cancer for the first time.



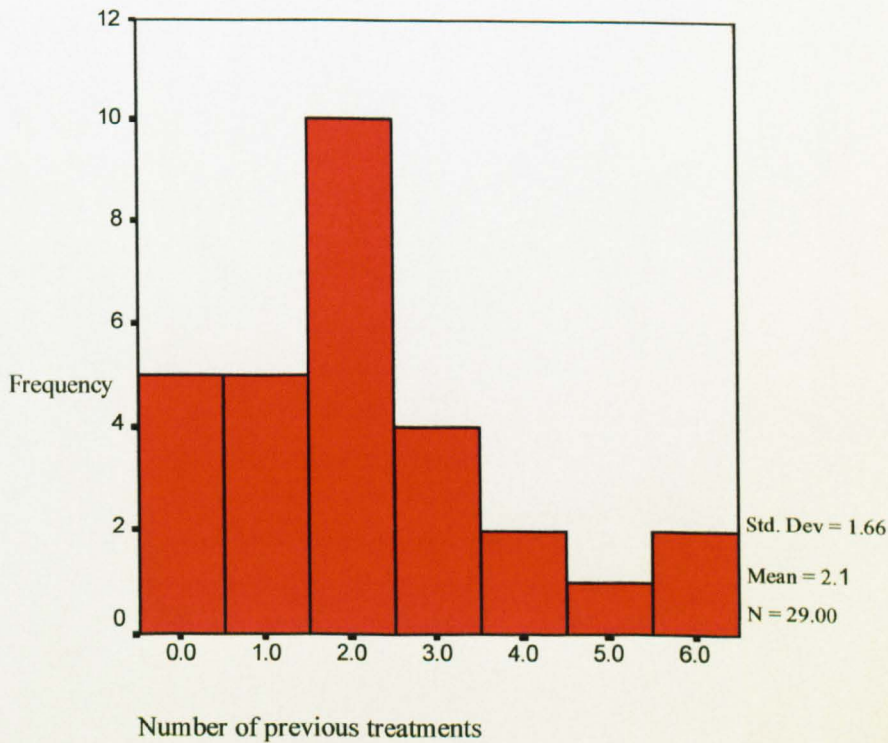
**Table 9: Frequency of cancer diagnoses**

Number of Diagnoses	Frequency	Percentage
1	14	48.3
2	6	20.7
3	6	20.7
4	3	10.3
<b>Total</b>	<b>29</b>	<b>100.0</b>

**Number of treatments received**

Five (17.9%) of the participants had not received any previous treatments for cancer. The modal number of previous treatments was 2. Therefore, although nearly half the sample had been diagnosed with only one cancer, many participants had received previous treatments. The frequencies are shown in figure 1.

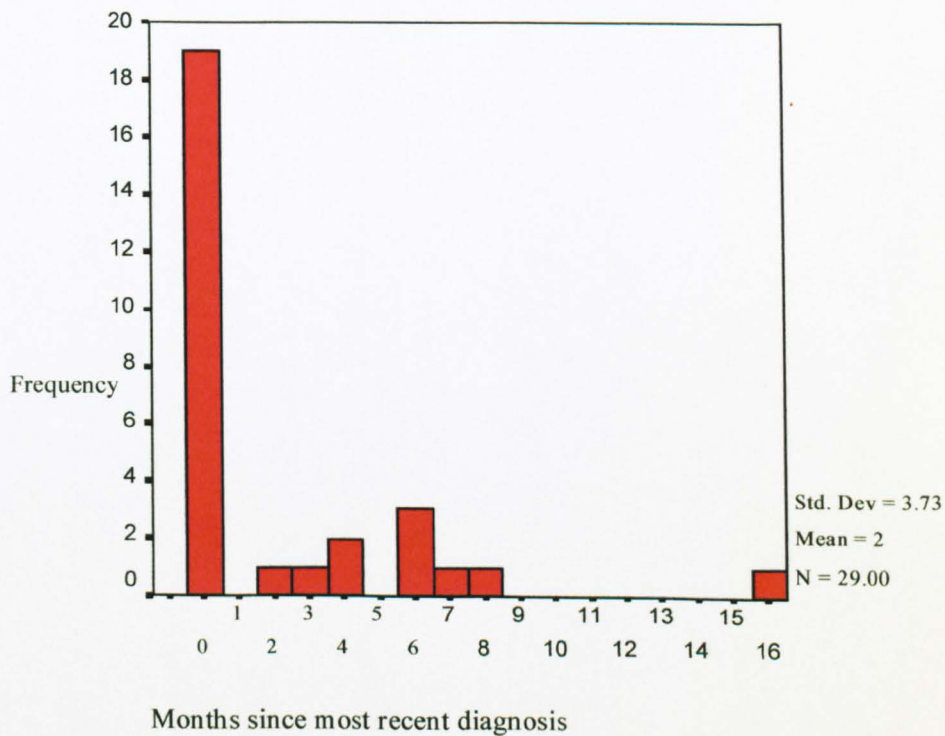
**Figure 1: Frequency of number of previous treatments**



### Time since most recent diagnosis

It is shown in figure 2 that approximately half the sample had been diagnosed with their most recent cancer (for which they were offered the trial) within the previous month. The mean time since diagnosis was 2.2 months (SD 3.7).

**Figure 2: Time since most recent diagnosis in months**



### Previous cancer clinical trials

None of the 29 participants had previously been treated in a cancer clinical trial.

### **3.5 Psychometric Measures**

The mean scores and standard deviations on each of the standardized psychometric scales are shown below in table 10. It can be seen that that some questionnaires were omitted by participants. The data on the HADS showed that the sample was not significantly depressed or anxious. The results from the psychometric scales are discussed in later sections.

**Table 10: Mean scores of the participants on the psychometric measures**

<b>Measure</b>	<b>n</b>	<b>Min. Score</b>	<b>Max. Score</b>	<b>Mean Score</b>	<b>St. Deviation</b>
HADS – Anxiety	29	2.00	14.00	6.76	3.0
HADS - Depression	29	1.00	14.00	5.31	3.23
EPQ –P	31	0.00	9.00	2.42	1.88
EPQ-N	31	0.00	12.00	5.06	3.08
EPQ-E	31	0.00	12.00	7.26	3.45
EPQ-L	31	1.00	11.00	5.74	3.16
MDHLC -Internal	30	11.00	33.00	21.63	5.72
MDHLC-Chance	30	13.00	14.00	20.03	5.07
MDHLC-Powerful Others	30	7.00	32.00	19.27	6.95
CEC – Angry	25	7.00	20.00	14.10	3.84
CEC- Unhappy	25	8.00	22.00	17.04	3.02
CEC-Anxious	25	12.00	23.00	17.72	2.98
CEC-Total	25	34.00	64.00	49.16	7.28

### 3.6 Demographic Information on Relatives

Twenty-eight relatives completed and returned the questionnaires. Their mean age was similar to that of the patient sample.

**Table 11: Age of relatives**

	Minimum	Maximum	Mean	St. Deviation
N=28	24.00	85.00	55.6071	13.5874

#### **Relationship to patient**

The majority of the participants chose their spouses to complete the questionnaires. A few chose a brother or daughter and only one participant chose to ask a friend (see table 12).

**Table 12: Relationship of relative group to patient participants**

Relationship	Frequency	Percentage
Partner	1	3.6
Husband	12	42.9
Wife	9	32.1
Brother	2	7.1
Daughter	2	7.1
Niece	1	3.6
Friend	1	3.6
<b>Total</b>	<b>28</b>	<b>100.0</b>

### **3.7 Statistical Analysis**

As is shown above all the participants consented to a clinical trial. Hence, the data could not be divided into two groups according to consent or refusal of a trial, as described in Chapter 2: Methodology. As it was not possible to use the data obtained to test the hypotheses, an exploratory approach to the data was taken.

#### **Distribution of data**

The distribution of the raw data of each of the dependent variables was examined. The Kolmogorov-Smirnov test was used to test the deviation from normality of each distribution.

The K-S tests for the attitudes total score, age, HADS anxiety, EPQ-E, EPQ-N, MDHLC internal, MDHLC powerful others, CEC-Angry, CEC-Anxious, and the CEC-Total score were not significant indicating that the distributions were normal.

A mathematical square root function was applied to the HADS depression scores, the hypothetical trial total scores, the EPQ-Lie scale scores and the CEC-Unhappy scores. After the application of this function, The K-S tests were not significant, indicating that the distributions were normal. The square root functions were used in the statistical analyses.

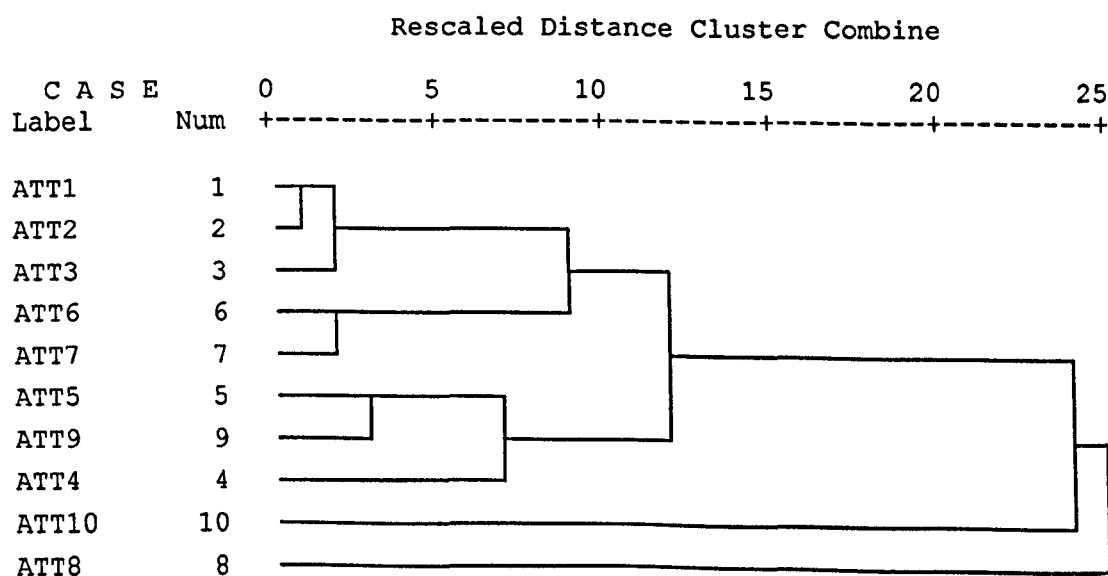
The K-S tests for the attitudes questions 1-13, the hypothetical trials 1-4, the MDHLC-Chance scale and the EPQ-P scale were significant, indicating that the distributions were not normal. The distributions for the attitudes questions 7 and 11 were negatively

skewed. All the other distributions that were not normal were positively skewed.

### Exploratory analysis of the attitudes questionnaire

Advice from a statistician was taken and a hierarchical cluster analysis was performed on the attitudes questionnaire (Appendix VI) to identify relationships between the question items. This measure was selected as it was considered to cover a wide range of aspects of trials and medical research, as opposed to the hypothetical trials, which were more constrained in their focus. As this was a new measure it was unknown whether it measured a single underlying construct or a number of different ones. Questions 1 to 10 were used in the analysis as these used the same scale. Questions 11 to 13 were excluded, as their scales did not range from positive to negative. This test does not rely on the normal distribution of the data. The results of the hierarchical cluster analysis are shown below in Figure 3.

**Figure 3: Dendrogram using average linkage (between groups)**



The analysis showed a close relationship between questions 1, 2 and 3. Examination of these questions (see Appendix VI) showed that they all referred to the potential benefit of research and clinical trials.

Questions 6 and 7 were also closely linked and these questions referred to prolonging life. Interestingly, question 4, which referred to the cure of cancer, was not closely linked to these items by the analysis.

Questions 5, 9 and 4 were linked by the analysis. It was more difficult to see the connection between these questions as they dealt with randomization, cure and whether or not patients should volunteer for research.

Overall, questions 1 down to 4 on the dendrogram were clustered together in one main group. Hence, the hierarchical cluster analysis of the attitudes questionnaire suggested that the majority of the questions were measuring the same construct.

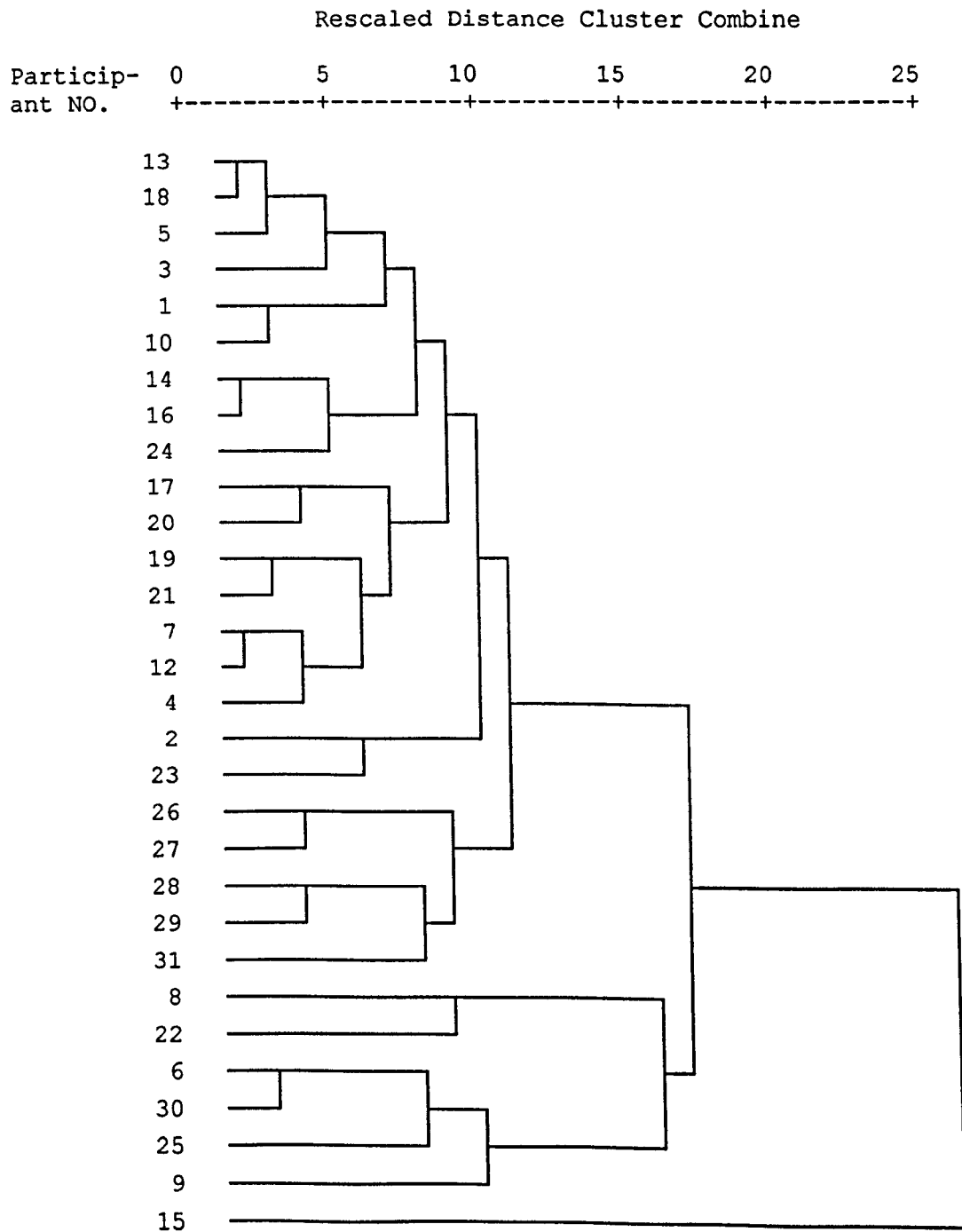
It also identified two questions (8 and 10) that were separate from this main cluster, but not linked together. Question 10 addressed a patient's views on double-blind methodology and question 8 asked whether patients received more help and support in a clinical trial. Participants' attitudes to these issues were shown to be different from their attitudes to the other questions.

### **Exploratory analysis of participants' attitudes**

Advice from a statistician was taken and a second hierarchical cluster analysis was performed on the attitudes questionnaire with the aim of identifying particular groups of

participants within the trial group. Therefore, this time the test clustered cases (participants) rather than variables (questions). Figure 4 shows the dendrogram results from the cluster analysis of the participants.

**Figure 4: Dendrogram using average linkage (between groups)**





An examination of the dendrogram identified two main clusters and one outlier. The first cluster is shown from participant number 13 to 31 (23 participants), the second from number 8 to 9 (6 participants) and the outlier is number 15.

The raw data from these groups were examined. Participant 15 emerged as having higher scores on the attitudes questions, indicating less positive views. The participant indicated that she was 'very uncomfortable' with randomization and double-blind methodology. This response was unique to her case in this study. The patient also indicated strongly that it was her choice and that the doctor was not the best person to decide. The participant felt ambivalent as to whether participation in a trial would help future patients and disagreed that a 'miracle' cure would be found.

### **Cluster 1**

In comparison, the largest cluster of participants showed positive views towards trials and research. Their responses were generally more mixed and less positive than the second cluster described below. Their responses indicated that they agreed that the trial would help future patients, that patients should volunteer, and that a cure would be found. The participants in this cluster were most likely to indicate that they were 'neither uncomfortable nor comfortable' with randomization and double-blind methodology. Half the group thought the doctor was the best person to make the final decision, five more were ambivalent about this statement and the remaining six disagreed with the statement.

### **Cluster 2**

The second cluster of six participants formed a highly positive group. They indicated

very positive attitudes to entering trials, strongly agreed that a trial would help others, that patients should volunteer, and that a cure would be found. All the participants in this cluster indicated they would be 'very comfortable' or 'somewhat comfortable' with randomization and double-blind methodology. Entering the trial would give this group 'a little' or 'a lot' more hope than receiving the standard treatment. All but one 'strongly agreed' that the doctor was the best person to make the final decision. They perceived themselves as having less choice than cluster 1 when asked to enter a trial.

### **Analysis of cluster differences**

For the purpose of further analysis, the two main clusters were considered to be two independent, unrelated groups, on the basis of their attitudes to clinical trials. Independent T-Tests were performed using the two main cluster groups to test the difference in means on the dependent variables. For all but one of these variables, Levene's test for equality of variances was not significant, indicating that the variances in the two groups were equal. The results of the effect of cluster on the dependent variables that met the parametric assumptions are shown in table 13.

Some participants did not complete all of the questionnaires. Consequently, scores from the HADS (2 participants), MDHLC (1 participant) and CEC (5 participants) were missing from cluster 1. The CEC scores were missing from 1 participant in cluster 2.

It is shown that just one result was statistically significant; the difference between the hypothetical trial scores. An examination of the data showed that cluster 1 had a higher mean hypothetical trial total score. This indicated less willingness to enter the trials than cluster 2. Hence, cluster 2, who had highly positive attitudes, had significantly

lower (more willing to enter) hypothetical trial scores.

The EPQ-Neuroticism score approached significance ( $p=0.077$ ). The second, highly positive cluster had higher EPQ-N scores, suggesting a relationship between attitudes and scores on this measure.

**Table 13: Independent T -Test results**

Variable	t	df	Mean Difference	Significance (2-tailed)
Hypothetical Trials (total Score)	2.326	27	0.404	0.028
<u>HAD:</u>				
-anxiety	0.147	25	0.214	0.884
-Depression	-0.129	25	-4.39	0.898
<u>EPQ:</u>				
-E	0.385	27	0.377	0.703
-N	-1.840	27	-2.558	0.077
-L	0.326	27	0.106	0.747
<u>MDHLC:</u>				
- Internal	-0.591	26	-1.515	0.559
- Powerful others	-0.848	26	-2.742	0.404
<u>CEC:</u>				
-Angry	1.017	21	2.011	0.321
-Anxious	1.261	21	1.789	0.221
-Unhappy*	1.450	20.399	1.456	0.162
-Total	-0.619	21	-2.344	0.543

\* Equal variances not assumed

It should be noted, that by carrying out 12 independent t-tests the probability of at least one Type-I error is greatly increased to 49%. In this case the Bonferroni Correction should be considered. When applied, this shows that significance should only be accepted when less than 0.0042. This correction has been criticised for being too conservative and hence increasing the probability of a Type-II error. However, the significant difference found should be interpreted with caution and not considered rigorous.

The Mann-Whitney U Test was used to assess differences between the two clusters on the cancer-related information, years of education and EPQ-P scores. This non-parametric test was selected as the distributions of these variables deviated significantly from normal according to the K-S test. The results of the Mann Whitney U Test are shown below in table 14.

Again, some data were missing. In cluster 1, one participants' MDHLC chance score was missing and the disease related information was not available on 2 participants. Otherwise the data set was complete.

**Table 14: Results of Mann Whitney U Analysis**

Variable	Mean Rank cluster 1	Mean Rank cluster 2	Mann Whitney U	Sig.
Months since First diagnosis	14.23	11.08	45.5	0.376
Months since this diagnosis	13.00	15.17	50.0	0.457
Number diagnoses	13.88	12.25	52.5	0.622
Number treatments	13.57	13.25	58.5	0.926
Years education	15.83	11.83	50.0	0.297
EPQ-P	14.50	16.92	57.5	0.527
MDHLC -Chance	13.95	16.50	54.0	0.499

The differences between the two clusters on these dependent variables were not statistically significant. It should be considered that by using a non-parametric test the probability of a type II error has been increased due to reduced statistical power. The two clusters show a mean difference of 23 months (but only 3.15 ranks) on the 'time since first diagnosis' variable. This may suggest that a longer length of disease (cluster 1) leads to less positive attitudes. However this difference was not statistically significant according to the Mann Whitney U Test.

The increased probability of a type II error needs to be balanced again against the increased probability of a Type I error caused by using 7 Mann Whitney U Tests. Again, the Bonferroni Correction needs to be considered.

### 3.8 Further Exploratory Analyses

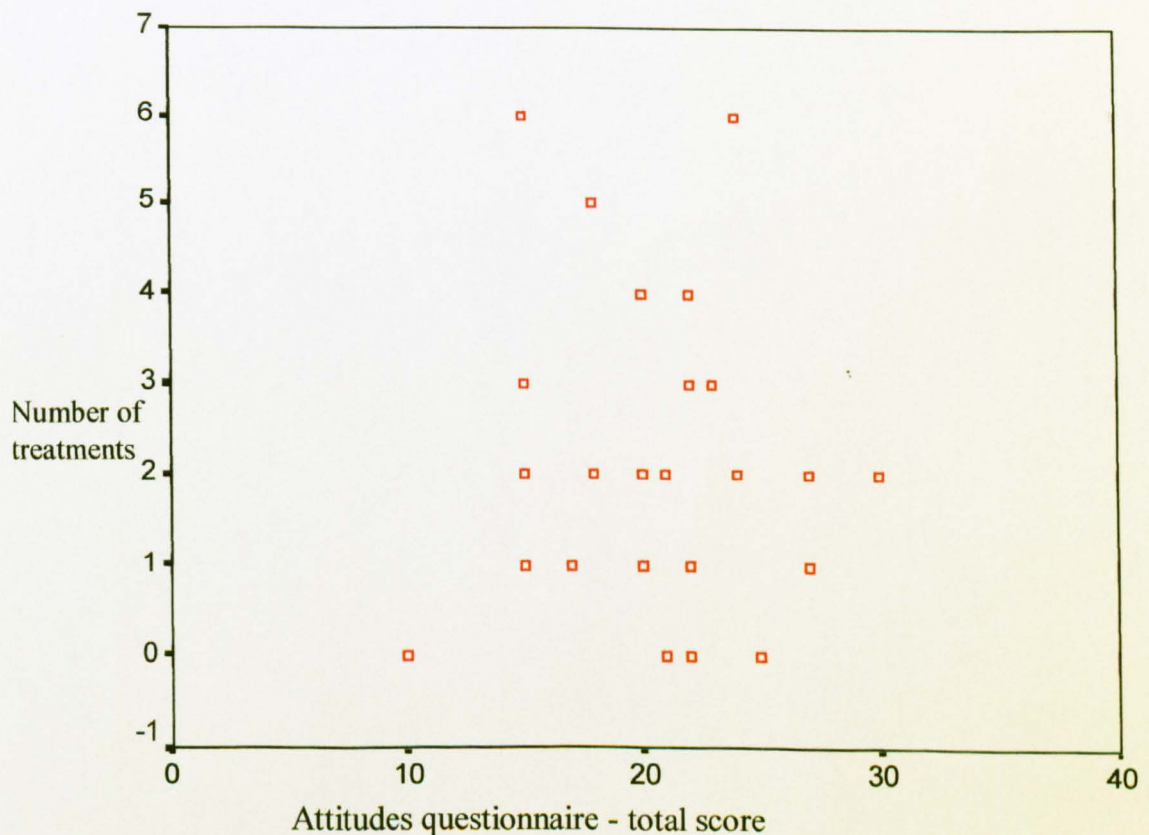
A series of four questions were formulated with the aim of making exploratory analyses of the relationships between the variables. The four questions chosen were based on themes from the literature review and from the qualitative interviews.

#### Question 1

**Does the number of previous treatments affect participants' attitudes ?**

Spearman's Rho correlation coefficient was used as the data violated parametric assumptions. The correlation between number of treatments and participants' attitudes as measured by the attitudes total score was not statistically significant. The relationship is illustrated in figure 5.

**Figure 5: Scatterplot illustrating the relationship between number of previous treatments and participants' attitudes questionnaire total score**

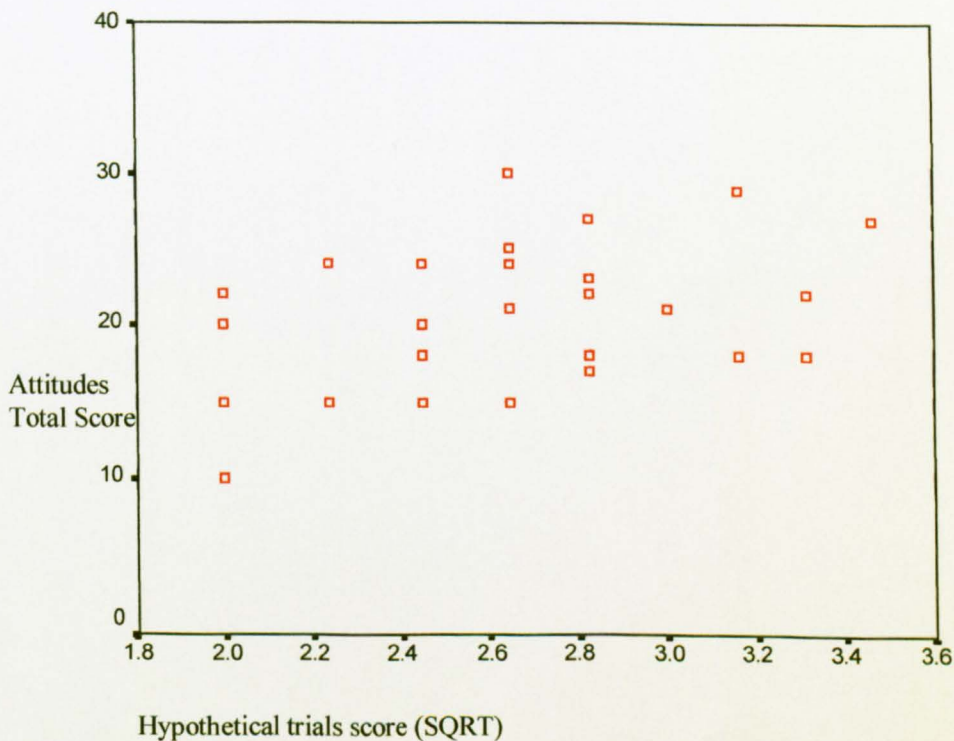


**Question 2**

**Are participants' scores on the attitudes questionnaire related to 'willingness to enter' as measured by the hypothetical trials?**

A statistically significant positive correlation was found between the attitudes score and participants' willingness to enter the hypothetical trials (Pearson=0.396,  $R^2=0.157$ ,  $p=0.027$ ). Participants with more positive views were more willing to enter the hypothetical trials. Figure 6 illustrates this relationship. However, the  $R^2$  value shows that only 15.7% of the variance in hypothetical trial scores can be accounted for by the attitudes score.

**Figure 6: Scatterplot illustrating the relationship between attitudes and willingness to enter hypothetical trials.**



### **Question 3**

**Is a participant's perception of choice related to personality and locus of control measures?**

For the purpose of this analysis participants were divided into three groups according to their responses to question 11 on the attitudes questionnaire: "If my doctor asked me to participate in a clinical trial, I would feel I had no other choice". The groups were as follows:

**Group 1 (n=6) :** Participants who indicated that they 'strongly agree' or 'agree',

**Group 2 (n=7) :** Participants who indicated that they 'neither agree' or 'disagree',

**Group 3(n=17):** Participants who indicated that they 'strongly disagree' or 'disagree'.

This question was chosen as a measure of 'choice' as it was considered to reflect the patient's perception of a doctor offering them a clinical trial. It was considered to be a measure of the how much the patient would feel pressurised and whether they could see the possibility of alternatives. The concept of 'choice' is a very complex variable and this is only a very narrow and limited measure of this.

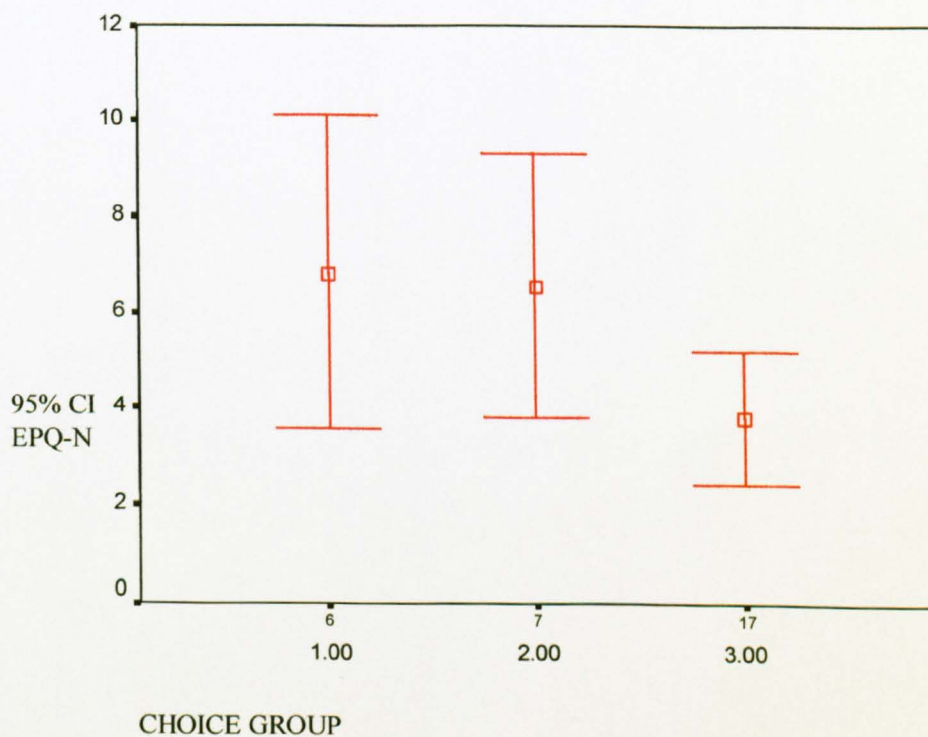
One way analysis of variance was used for the variables that met parametric assumptions. The Kruskal Wallis test was used for the remaining variables.



### Personality (Eysenck Personality Questionnaire, EPQ)

One way analysis of variance found a statistically significant effect of 'choice' on the EPQ – Neuroticism scale ( $F=3.683$ ,  $df=2,27$ ,  $p<0.05$ ). Figure 7 shows the mean EPQ-N scores with 95% confidence intervals for each of the choice groups. It is shown that group 1, who perceived themselves as having the least choice if asked to enter a trial, had the highest EPQ-N scores. Group 3, who saw themselves as having the most choice, had the lowest EPQ-N scores. Group 2, who neither agreed nor disagreed with the statement, had a mean EPQ-N score that fell in between the two other groups.

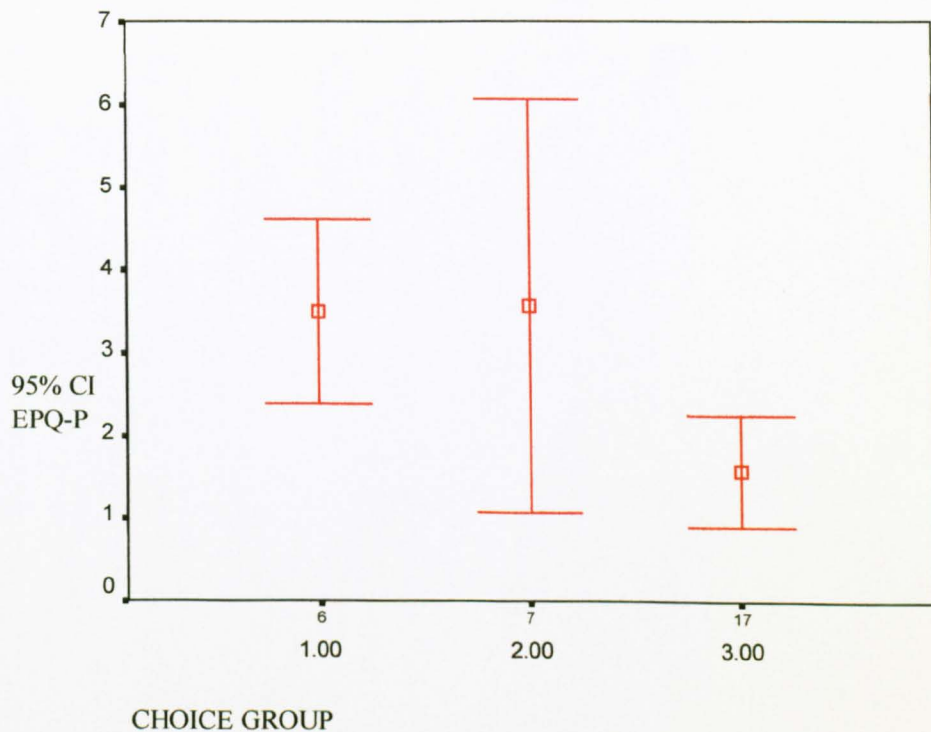
**Figure 7: Mean and 95% confidence intervals of EPQ-Neuroticism scale scores for each of the 'choice' groups**



A significant effect of choice was found on the EPQ-Psychoticism scale using the Kruskal Wallis test ( $\text{Chi-Square}= 8.451$ ,  $df=2$ ,  $p<0.05$ ). Figure 8 shows the mean EPQ-P scores with 95% confidence intervals for each of the choice groups. Group 3

(highest perception of choice) is shown to have the lowest EPQ-P scores. Groups 1 and 2 have similar mean scores, but group 2 has a larger range within 95% confidence interval of the mean.

**Figure 8: Mean and 95% confidence intervals of EPQ-Psychoticism scales scores for each of the 'choice' groups.**



Choice did not have a significant effect on the EPQ-Extraversion or EPQ- Lie scales.

### **Locus of Control (Multidimensional Health Locus of Control Scale, MDHLC)**

A statistically significant effect of choice on the Internal scale of the MDHLC was found ( $F=3.412$ ,  $df=2,26$ ,  $p<0.05$ ), and on the Powerful Others scale ( $F=7.989$ ,  $df=2,26$ ,  $p<0.005$ ).

Figure 9 shows that group 1 (lowest perception of choice) had the highest scores on the Internal locus of control scale. In general, as perception of choice increased, scores on the Internal scale decreased (locus of control became more external).

**Figure 9: Mean and 95% confidence intervals of MDHLC Internal scale scores for each of the ‘choice’ groups**

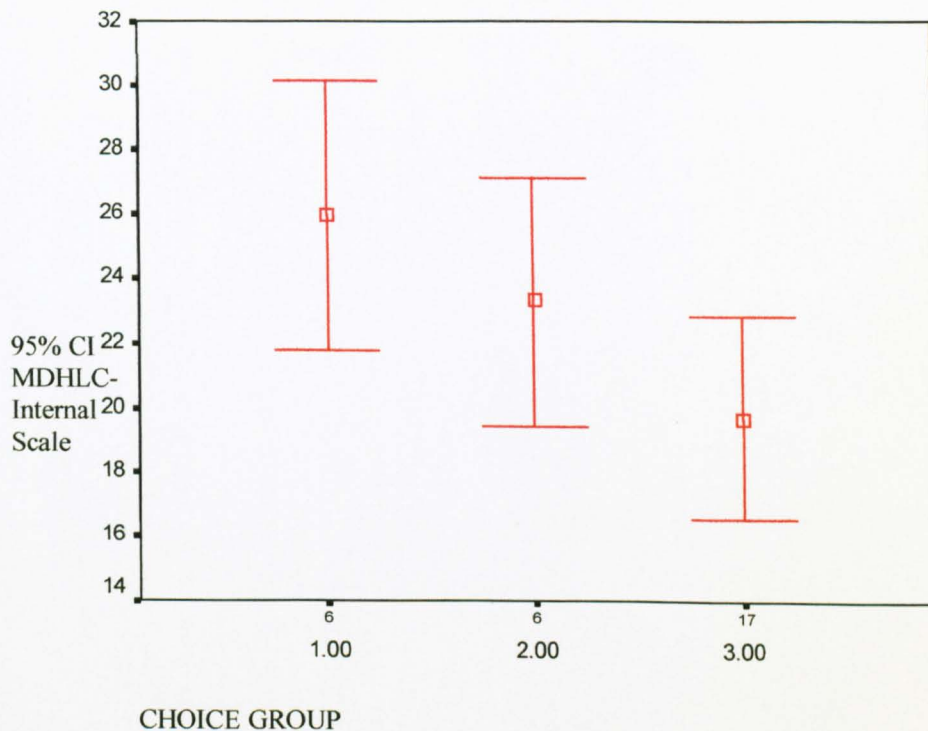
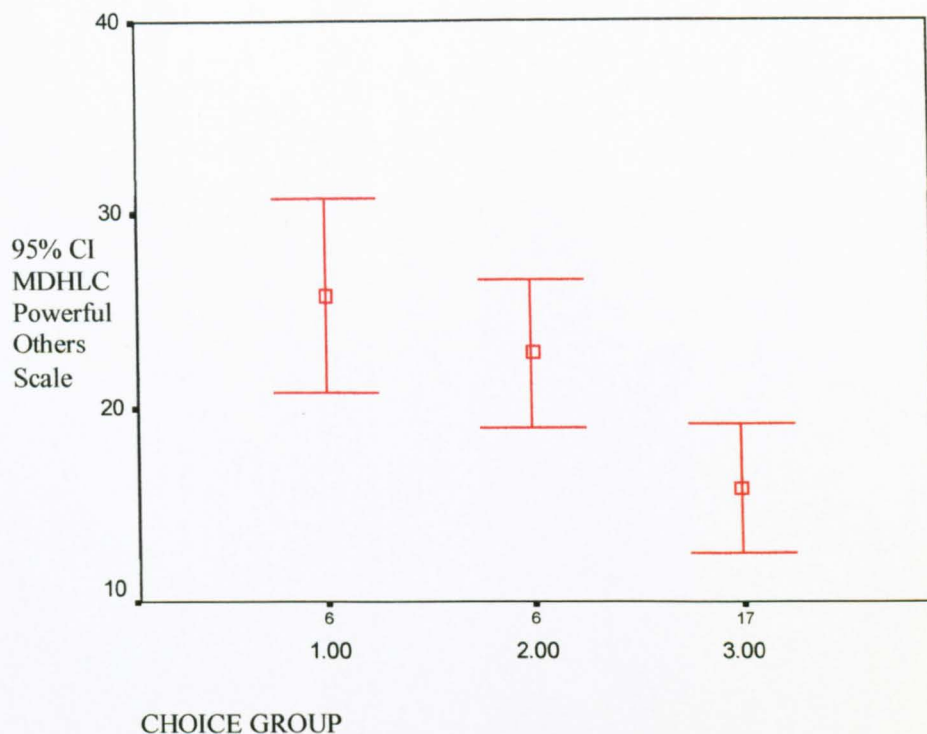


Figure 10 shows the mean and 95% confidence intervals for the MDHLC Powerful Others scales. It is shown that as perception of choice increased over the three groups the scores on the Powerful Others scale decreased.

Choice was found not to significantly affect scores on the Chance scale of the MDHLC using the Kruskal Wallis test (Chi-Square= 5.061, df=2, p=0.08).



**Figure 10: Mean and 95% confidence intervals of MDHLC Powerful Others scale scores for each of the ‘choice’ groups.**



#### **Question 4**

**Are participants’ and their relatives’ attitudes and willingness to enter trials scores related?**

The majority (96.7%) of participants indicated that they would take into account the views of their family in response to Question 12 (“If you were asked to participate in a clinical trial how much would you take the views of your family/friends into account”). Thus, this population’s views were considered important. Table 15 shows the mean total attitudes score and the mean total hypothetical trials score of the participant and relative groups. Only those participants who had a relative who completed the questionnaires were included.

**Table 15: Mean attitudes total score and hypothetical trial total score for participant and relative groups**

	Mean (SD) attitudes total score	Mean (SD) hypothetical trials total score
Participants (n=27)	21.40 (4.25)	7.39 (2.1)
Relatives (n=27)	21.03 (3.86)	7.25 (2.41)

It is shown that the scores for the two groups were very similar. Pearson Correlation was used to examine the relationship between each participant and their chosen relative's views. The correlation coefficients on both the measures were not significant. Therefore, while the two groups were similar in their views, this was not so on a case by case basis.

### **3.9 Qualitative Findings**

A convenience sample of the first four participants to complete three cycles of treatment during February 2001, who were considered physically well enough by the trials nurse, were approached for interview. All four agreed and were visited by the researcher at their homes. The sample consisted of one male and three females. The mean age of the sample was 56.5 years (SD 11.1).

Content Analysis was performed on the semi-structured interview data. Three main categories were pre-determined in the analysis as these were the focus of the original interview questions. As the questions would have influenced the participants' responses, it was felt artificial to claim that these emerged from the data. The categories were Attitudes, Decision-Making and Disease/Treatment Experiences. In each of these, further sub-categories emerged from the data.

A second person was also asked to perform the analysis. The second rater was a male non-psychologist, with a background in special education teaching and previous experience of using qualitative methods. He was not familiar with the background literature or aims of this study. The second rater's categories differed from the first rater. The second rater identified main emotional and behavioural themes. In contrast, the first rater focused more on the trial process. The second rater's themes were considered to run through the sub-categories identified by the first rater. The themes are presented at the end of each category. The results of the content analysis are presented below.

## **1. ATTITUDES**

### **SUB-CATEGORIES:**

#### **Pre-held views**

All four participants in this study reported holding positive views towards medical research in the past. They described it as “a good way of finding new treatments” and it being needed in society.

More specifically, when asked about clinical trials participants remained positive in their opinions. Three of the participants had been involved in some form of research in the past. However, they did not draw a distinction between chemotherapy clinical trials, newly available tried treatments, and their x-rays being shown to medical students. To the participants the basis of ‘research’ was common to all of these and they felt comfortable with it.

One of the participants had no previous experience of clinical trials or medical research. He described how it was “all new to me”, but nevertheless he still thought he held a positive view of such treatments. He believed that he had a limited understanding of clinical trials before being asked to enter one, and that he was still unclear about many issues.

#### **Impact of this research project**

Three out of the four participants could remember reading the information and filling in the questionnaires. However, they could not remember the actual questionnaires or their responses. One participant thought that the project had made her think more about

trials in a general sense. All four participants said that the research had not influenced their decision about the clinical trial. In general, the participants did not seem to have made a connection between the two. Two participants thought the hypothetical trial scenarios were different from making the real decision, but were unsure how.

### **THEMES:**

**Information seeking:** The theme of being interested in research and actively seeking information to aid understanding, e.g. via the Internet, was identified. Interest in this research project formed part of this information seeking theme.

**Confusion:** The theme of confusion about how the trial fitted into the wider picture of research and science emerged. Lack of understanding of trials and their purpose, and of the relevance of this project was found.

## **2. DECISION-MAKING**

### **SUB-CATEGORIES**

#### **Trial proposal**

All participants could recall being asked about the trial and could give brief details about the protocol. All four knew that participation was voluntary and that they had a choice between saying yes or no. One participant knew there was no alternative treatment, but two didn't know what would have happened if they had said no. One



participant knew that she would be treated, but knew nothing of the alternative treatment. Consequently, all four felt there was no 'real choice':

*" I don't think there was an alternative. I don't seem to remember...I was that shocked at the cancer.....I didn't really listen to what he was saying, apart from the fact that there was this treatment that was a trial....I was more thinking of that than any other offer."*

All participants described making their decision quickly, usually between 15 and 45 minutes after first being asked. One participant made her decision spontaneously, she said "it never entered my mind to say no". The participants expressed trust in the doctor and their expert opinion. After leaving the hospital all four discussed the trial with family members, mainly with the purpose of checking that they were comfortable with the treatment. For some family members it was "another road to go down" and they felt that "there was nothing to lose". However, while participants wished to check out their family's views, they also felt that no one could have changed their mind.

### **Motivations**

Participants' reasons for entering the trial fell into the two main categories of 'helping themselves' and 'helping others in the future'.

*Helping themselves:* The participants expressed the idea that the treatment would somehow do them good. It offered them hope for stopping tumour growth, prolonging life, but interestingly, not cure. None of the participants thought this trial would cure them. Two expressed having "nothing to lose" and:

*“As long as it’s not making me worse....or feeding the complaints, I’m all right with it.”*

For one participant, the fact that the treatment was experimental made it possibly a superior treatment:

*“With science and medical advances...the trial is more up to date, and so has more hope in it.”*

*Helping others in the future:* participants expressed concern and pleasure that the research would be used to help others in the future. However, such altruistic motives were mentioned less than those pertaining to the participants’ own lives.

To all four participants it did not matter that the chemotherapy they were receiving was experimental. It was not an issue of importance to them. To them it was a *treatment* foremost and it offered the best hope of life. The choice to enter the trial was not a difficult decision to make for all four participants. One described it as “automatic”. Another said:

*“If there’s not much chance with the normal treatment, and they hope this is better, well that’s it.”*

This links with earlier descriptions of the lack of choice these participants felt they had realistically.

For one participant, being part of the trial fitted in with her self-concept as someone who helped others:

*“I’m doing a bit of good. I’m always doing things for other people. It’s always for someone else...this is just something else I have taken on.”*

### **Barriers**

The four participants interviewed could not recall any particular worries about the trial. They seemed to have calmed any concerns they may have had with the knowledge that they could discontinue the trial at any point. This was a very important aspect for them:

*“ ...You can stop treatment anytime you like, you are not forced to go ahead and have it.”*

*“If it’s not working they will change it, ... so I wasn’t putting myself in a corner.”*

### **THEMES:**

- Hope:** The focus on positive aspects of the trial and what it offered to the participant emerged as an overall theme of this category.
- Nothing to lose:** The theme of being forced by circumstances into the decision was identified. From the time of proposal, to consulting with others, to making the decision, this factor was evident in participants’ responses.

### 3. DISEASE/TREATMENT EXPERIENCES

#### SUB-CATEGORIES

##### Impact of disease

On diagnosis all participants described shock and horror that the cancer had returned or occurred:

*“Four years down the line, I thought I was OK. I only had a year to go, to get the all clear. You have the carpet ripped from under you.”*

*“...He said ‘cancer’ straight away, well, it terrifies you.”*

Differences were evident between the participants when they were asked about how the cancer had changed their lives. One participant described “making the most of each day” and striving to maintain as normal as life as possible. She had tried to continue to do the things she had before, even if she had to come home earlier or not travel as far. She thought that it hadn’t changed her as a person:

*“We worry, naturally, but you don’t let it get you down.”*

Another described in detail and with dismay the differences in his everyday life. These ranged from being unable to do domestic chores to not being well enough to go on holiday. For this man the cancer was something he did not deserve and it had devastated his plans for his retirement years.

Three of the participants thought that cancer had changed their personalities. One described becoming depressed and irritable, where as before she was an easy-going cheerful individual. One said:

*“I’m a different person altogether. I’m not me as I was before. Before I was bubbly. I can be nasty to my wife, she only has to make the slightest mistake.”*

Even within this small group, different responses emerged (both emotional and practical) to having cancer.

#### **Experience of clinical trial treatment**

All four participants described distressing physical side effects from the trial chemotherapy. All four said that they expected these and thought the effects would be similar in any non-experimental treatment. However, one participant mentioned feeling like a “guinea pig” at the start of her trial when she suffered severe side effects. Three of the participants had considered discontinuing the trial due to the side effects and at these times they called on relatives and professionals for help and advice. For these participants the hope that it would get easier helped them to continue.

Three participants described changes to their life-style as a direct result of the treatment. Being too unwell to work, go on holiday or socialize were important losses for them.

In retrospect, none of the participants felt they had any misconceptions about what the trial would be like. Likewise, none of their views and attitudes towards clinical research had been changed by the trial. All four participants said that they would volunteer for a

trial if given the choice again. Although, one participant thought she may decline if the trial involved “a lot of risk” in terms of adverse effects. Again, the experimental nature of the treatment was not relevant to participants on a day to day basis. It was just a treatment.

### **The future**

All the participants expressed hope and optimism that the trial chemotherapy was working and predicted (although tentatively) positive outcomes. One participant predicted that after the trial he would be feeling:

*“Hopefully full of vigour. I’m having a scan in a month, I hope it shows it’s shrinking. The pains gone, I don’t think it’s growing anymore.”*

All the participants were highly focused on their next scan which would tell them if the trial was having any effect on their disease. This was a point of great anticipation and anxiety. The success of the trial was the most important aspect of their future.

### **THEMES:**

**Anger and resentment:** The theme of intense and distressing emotional reactions to participants’ experiences was evident throughout this category.

**Worry:** The theme of great concern about the impact of the disease and its treatment on health, relationships and quality of life emerged.

**Moving on:**

The theme of actively coping with adversities, (e.g. using humour, support and recreation) and looking towards the future was found in this category

### **Summary of Qualitative Findings**

The categories and themes identified in the analysis are shown in figure 11. Participants reported positive views of clinical trials and research, and that these had not been changed by their experiences. Their decision to enter the trial was not difficult and they did not consider refusing. They were unclear about the alternatives. To these four participants the trial was a treatment, first and foremost. They hoped it would help them to live longer, but thought it would probably not cure them. The diagnosis of cancer and having chemotherapy had changed the lives of all the participants. In the longer term, individual differences in coping were evident. All were hopeful for the future and did not regret entering the trial.

**Figure 11: Main categories, sub-categories and themes identified by the analysis.**

<b>Main categories</b>	<b>Sub-categories</b>	<b>Themes</b>
<b>ATTITUDES</b>	Pre-held views Impact of this project	Information-seeking Confusion
<b>DECISION-MAKING</b>	Trial Proposal Motivations Barriers	Hope Nothing to lose
<b>DISEASE/ TREATMENT EXPERIENCES</b>	Impact of disease Experience of trial treatment The future	Anger & Resentment Worry Moving on



## **CHAPTER FOUR : DISCUSSION**

### **4.1 Discussion of Main Findings**

The research found that 95.9% of eligible cancer patients consented to the chemotherapy clinical trial proposed to them. This is strikingly different from other recent studies. For example, Spiro et al. (2000) found that only 26.5% of eligible patients consented to the trial. A review of the literature has found patient refusal as a reason for non-entry to range from 15 to 32% (Cook-Gotay, 1991). The apparent refusal rate of 4.1% found in this research was highly unexpected.

The possibility that patients who refused a trial may also refuse to take part in this research project was considered during the design phase of the project. However, the potential problem that so few would refuse trial entry was not foreseen. It must be questioned why such a high consent rate occurred on this occasion.

The high rate of consent may be a characteristic of the oncology department studied. Increased accrual rates have been found in centres participating in national cancer programs (Cook-Gotay, 1991) and the centre used in this study was involved in a number of multi-centre trials. However, the original impetus of this research was the Head of Department's observation of a difficulty in recruiting eligible patients to clinical trials. During subsequent discussions the hospital appeared to be a typical example of a national problem.

Another possible explanation was that this research influenced patients' decisions. By introducing the idea of a trial, patients may have been more open to further consideration, a phenomenon known in social psychology as the 'foot in the door effect'

(Synder & Cunningham, 1975). Indeed, the information sheet contained a paragraph explaining the nature of clinical trials (See Appendix II). This was included as preliminary discussions with patients revealed that they were unsure what a clinical trial was. If lack of understanding is a reason for refusal, this research may have influenced the accrual rate. While we know that patients have poor understanding and recall of the trial information provided (e.g. Casseilth et al., 1980), no study has yet systematically investigated the role of this on clinical trial participation. It is therefore unclear whether or not this research influenced patients' decisions.

This research may have made patients more likely to consent in a general, indirect way. Patients may have been less worried by the trial proposal as they had already been exposed to an information sheet, consent form and to the general process of research. Although it may be argued that this was a completely different type of research, the qualitative findings showed that participants considered research as a unitary concept and did not differentiate between different forms. Hence, exposure to 'research' may have influenced the consent rate.

Other reasons for the high participation rate pertain to hospital influences. It may be that staff were more active in their recruiting, as they knew a research project was in progress.

Characteristics of the trials and the eligible patients may have influenced the consent rate. Post hoc examination of the inclusion criteria for the clinical trials revealed that a number required patients with advanced or metastatic (secondary tumours at a distance from the primary site of cancer) disease. Some trials required patients who had

inoperable cancer or for whom first line chemotherapy had failed. It is a possibility that the trials involved in this research required patients who had few alternatives and this caused the high consent rate. Previous research that has quoted lower consent rates may have focused on trials with different inclusion criteria.

It is also a possibility that patient refusal is not the main problem in accruing eligible patients for trials at this centre or elsewhere. Less than 3% of cancer patients are estimated to receive treatment as part of a clinical trial (Benson et al., 1991). This study suggests that this is not due in the main to patient refusal and that low participation rates may be due to other factors. These include: patient ineligibility (e.g. Lee et al., 1980; Lee & Breaux, 1983), lack of physician time and research staff (Smith & Goodare, 1995), patients' logistical reasons (Cook-Gotay, 1991), physicians' difficulties in obtaining informed consent (Taylor & Kelner, 1987*a*), physician reluctance to discuss controversies of treatment with patients (Taylor et al., 1984) and physicians' concerns about the impact of randomization on the doctor-patient relationship (Taylor & Kelner, 1987*b*).

It is interesting that the two patients, who refused clinical trial participation, also chose not to consent to this research project. Cox (1999) has reported similar findings. Although conclusions cannot be drawn from only two patients, it may be the case that these patients are reluctant to take part in research in general, rather than just the clinical trial. They may hold negative views about research that extend beyond the clinical trial. This means that studies that aim to investigate the views of patients who refuse to enter clinical trials will have difficulty in accruing their sample.

Finally, it is also a possibility that the consent rate of 95.9% found by this research is not reliable, due to recruitment difficulties. This is discussed later in section 4.2.

The hypotheses and planned statistical analyses aimed to compare patients who refused with those who consented. All the participants who consented to this research also consented to the clinical trial, and consequently the original research hypotheses were rendered unanswerable. Advice from a statistician and the research supervisor were sought. A large number of approaches were possible and an exploratory one was selected. It was decided to examine the group of participants in terms of their attitudes to medical research and clinical trials to see if they were a unitary whole or whether differences existed between them.

The hierarchical cluster analysis of the attitudes questionnaire identified two main groups of participants. Cluster 1 showed a mixture of positive and negative responses to the attitudes questionnaire. Cluster 2 showed highly positive attitudes. The cluster analysis also identified one participant whose responses were different from the other two groups. Examination of this participant's scores revealed mainly negative views towards medical research. Interestingly, this patient still entered a trial.

The two main clusters significantly differed on their responses to the hypothetical trials. The more positive group indicated that they were more willing to enter the trials. No significant differences were found on any of the psychological scales, number of years education, or on the disease related information. It can be concluded that patients' prior beliefs and views predict how they believe they would respond given the choice of

entering a clinical trial. This gives some support to the view that a pre-held bias determines whether or not a patient will enter a clinical trial (Bujorian, 1988).

However, it is acknowledged that hypothetical trials have questionable validity and their use has been criticised here and by other authors. It was an original aim of this research to investigate the validity of these measures. Unfortunately, it is not possible to draw conclusions due to the absence of data from patients who refused to enter a trial. It is interesting that the patient identified by the cluster analysis, who had negative views and expressed the lowest willingness to enter the hypothetical trials, still entered the trial proposed to her. This queries the validity of the measures. In addition, the qualitative analysis showed that patients thought the hypothetical trials were different from the real decision.

The difference between the two clusters on the EPQ-Neuroticism scale approached significance. This suggested that cluster 2, who expressed highly positive attitudes, were a group that were more prone to worry, depression and 'emotionality'.

It was noted that cluster 2 (highly positive attitudes) had a mean time since first diagnosis of 22 months. This was lower than cluster 1 (mixed attitudes), who had a mean of 45 months. This difference was not statistically significant, but does suggest a trend of a longer duration of disease being related to less positive attitudes. This is not statistically supported, or indeed necessarily a causative relationship.

Further exploratory analysis of the data aimed to explore patients' perception of choice (as investigated by question 12 on the attitudes questionnaire) and how this related to

other variables. Choice was identified in the literature review as an important concept for patients.

Participants were divided into three groups according to their response to question 12 (see appendix VI). The analysis showed that participants' perception of their amount of choice when faced with the decision was related to scores on the Eysenck Personality Questionnaire – Neuroticism Scale. The group who viewed themselves as having the highest degree of choice had the lowest EPQ-N scores. The Neuroticism or emotionality scale considers an individual's proneness to worry and depression. The higher the score the more likely the person is to be a worrier, suffer from depression, sleep badly and have a preoccupation with things that may go wrong. Hence, in this study cancer patients with higher degrees of these characteristics perceived themselves as having no other choice when asked by their doctor to enter a trial.

Differences were also found between the three groups on the EPQ-Psychoticism scale. Psychosis is considered to be the 'pathological exaggeration of high degrees of some underlying trait of Psychoticism' (Eysenck and Eysenck, 1991). The scale is also termed 'tough-mindedness'. A high scorer on this scale would be a solitary person, who lacks empathy and care for others, has a disregard of danger and is cruel. The EPQ-P mean scores of each group were not more than one standard deviation above the mean of the standardisation group, and so were not abnormally high. The analysis showed that the group with the lowest scores on this 'tough-mindedness' scale saw themselves as having the highest degree of choice if asked by their doctor to participate in a trial.

The P and N scales were significantly positively correlated in this sample. It may be the case that patients who feel the most compelled to do as their doctor has asked and cannot see alternative choices, are those who have higher degrees of anxiety and emotionality and less empathy, care for others and sensitivity.

However, other variables may account for the reported differences. In the normative data presented in the manual (Eysenck and Eysenck, 1991) the EPQ-P scores for the 51-60 year age group are lower than for the 61-70 age group. Choice group number 3 had a mean younger age than the other two groups and fell into the former age band, while groups 1 and 2 fell into the latter. We would therefore expect group 3 to have lower scores. In addition, group three contained a higher percentage of females, who again have lower EPQ-P scores according to the normative data. Hence, it may be that younger females perceive themselves as having the higher degrees of choice than older males.

This does not apply to the EPQ-N scale findings, as females (and hence group 3) would be expected to have higher N-scores according to the normative data. In addition, N scores are affected by age in the opposite direction than the one observed in relation to 'choice'. This finding is thus more robust than the EPQ-P findings.

On the Multi Dimensional Health Locus of Control scale statistically significant differences were found between the three groups. The relationship was observed that as perception of choice increased, scores on the Internal scale decreased. The Internal scale measures the degree to which a person sees herself as in control of her own health. It was found that a person who saw her health as controlled by internal factors was

likely to see herself as having little choice when asked by her doctor to enter a trial. This finding is perhaps unexpected. It is in contrast to previous findings that patients with a high internal locus of control showed less reliance on their doctor's advice and were less likely to enter a trial (Verheggen et al., 1998). The two studies are, of course, not directly comparable as they use different scale and concepts.

Statistically significant differences between the choice groups were also found on the Powerful Others scales of the MDHLC. The trend was observed that as perception of choice increased, the scores on the Powerful Others scale decreased. This scale is a measure of a person's belief in others' (particularly doctors') control over their health. The finding that patients, who have a high belief in others' control over their health, regard themselves as having no other option when asked by their doctor to enter a clinical trial is perhaps expected. It can be concluded that the doctor may easily influence these patients, and this has implications for informed consent, where it is essential the patient is making an informed choice of their own.

It is again possible that other uncontrolled variables are responsible for the observed differences. Data are not provided for this scale according to age or sex. It is noted that group 3 had a particularly low Internal score when compared with the data provided by Watson et al. (1978). This may be a distorted view produced by a small sample size.

This research considered the views of an important relative of the patient. Previous research has suggested that cancer patients consult with their relatives before making a decision regarding treatment (Tabak, 1995). Research has also shown that family members may put excessive pressure on the patient to accept experimental treatment



(Peri, 1981). It may be hypothesised that relatives' scores on the hypothetical trials would reflect greater willingness to enter, than the scores of the patients themselves. The relatives' attitudes to trials may be predicted to be highly positive, reflecting a desire for the patient to enter 'no matter what'. However, the results did not support this. The patient and relative groups showed very similar mean scores on the hypothetical trials and attitudes questionnaire total score, suggesting no difference in their overall views.

The majority of patients (96.7%) indicated that they would take their family's views into account, but the correlation between each patient's and their relative's scores was not significant. This showed that within a couple or family there may be different views. Examination of the data showed that the score differences were in both directions; in some cases the relative was more positive and vice versa. It emerged from the qualitative data that while the patients talked to their relatives, with the wish to ensure that the relative felt comfortable with the trial, they also felt concurrently that no one could have changed their mind. It appears that for patients the decision is more of a personal one than previously suggested.

It was a foreseen problem that couples would consult each other when completing the questionnaires. The fact that their views were not correlated suggests they did not, and this increases the validity of the scores.

Qualitative methodology has been proposed as an appropriate and desirable methodology for investigating patients' perspectives of cancer clinical trials (Cox, 1998). The qualitative results of this research revealed important insights into the

experience of being diagnosed, deciding to enter a trial and of trial treatment. These contribute to the existing literature. The four patients interviewed discussed very similar issues and consistent themes emerged from them in the analysis. The most salient findings will be now be discussed.

An important and new finding was that entering the trial was not a difficult decision for the patients and that they did not consider refusing. The patients were not fully aware of the alternatives, or in some cases, even if there was one. This may at least in part explain the 95.9% consent rate found in this study. The decision to enter a trial has been conceptualised by previous research and assumed at the start of this study to be difficult for patients. It appears that this is not the case. The trial was a *treatment* for these patients, it did not matter whether it was experimental or standard, and they did not consider refusing. They did not think about its experimental nature in any depth. Patients who refuse a trial may consider the experimental nature important, but it was not possible to interview these patients. The qualitative results are based on a highly selective group of patients and important insights would have been gained from patients who refused trial entry.

Patients did not distinguish between different types of research. They considered new treatments, blood tests for research and x-rays being shown to medical students, as much the same thing. This suggests that the patients did not fully understand the nature of the clinical trial, despite information sheets from both this research and the trial. Given their lack of knowledge of alternatives, it would seem that the view that patients make their decisions on incomplete and inaccurate information (Sutherland et al., 1990) is supported.

The results supported previous findings that the desire to help others and to survive were the important motivations for entering the trial (Cox and Avis, 1996; Stetz, 1993). Similar themes of 'nothing to lose' and 'having to try something' emerged. It was noted by the researcher during the interviews that the patients described the desire to help others less frequently than helping themselves. For these patients the primary motivation for entering the trial was not an altruistic one. Comments patients make about helping others may at times be socially desirable responses.

Cox and Avis (1996) noted that patients perceive they have no choice when offered a trial. The findings of this research question this view. All four patients knew explicitly that it was their choice to enter, that they could say yes or no, and that participation was voluntary. However, this did not equate to the patients having to make a decision between two or more alternatives. They knew they had a choice in theory, but this was not a 'real choice' for them. There appears to be a difference between 'knowing' and 'feeling' that they actually had a choice.

The findings showed that patients made their decision during a time of emotional shock and feelings of horror. This is consistent with previous research (e.g. Thorton, 1992). However, the trial proposal was not seen as unwanted by patients; it was in fact received with relief that something was being offered.

## **4.2 Discussion of Methodological Issues**

### **Recruitment**

This research suffered profound, unforeseen recruitment problems. Despite early predictions of fulfilling the number of participants needed to meet the power calculation ( $N = >120$ ), when data collection began it became apparent there were fewer eligible patients than predicted. There were less clinical trials being conducted, which required fewer participants, than the researcher had originally been told to expect. A second consultant oncologist within the department was approached for permission to include his patients in the study. The oncologist consented, but was unable to offer assistance in the identification of the patients for the study.

Two further centres were approached in geographically distant regions. One declined due to existing research demands on patients. The other agreed, but despite considerable efforts by the researcher, the application for ethical approval in that region could not be submitted within the time constraints of the study.

The process of recruitment also suffered considerable difficulties. Initially, the questionnaires were planned to form part of an interview held in the clinic when the patient came to see the consultant, before they were offered a trial. Preliminary discussions with experienced oncologists, nurses and with a small number of patients indicated this as a suitable environment and time point. However, during the early stages of data collection an interview had to be discontinued due to patient distress. It was felt that this was not the time to be placing unnecessary pressure on patients and perhaps placing them in a situation where they felt they could not refuse participation.

It was also apparent that a patient's only focus was on what the doctor was going to tell them and that they were too anxious to accurately complete the questionnaires. Hence, due to ethical considerations, the design was reconsidered with the research supervisor and consultant oncologist. It was decided to change the design to a cross-sectional, postal questionnaire (see Chapter II: Methodology), so that patients could participate in their homes when feeling less anxious. Patients who did not want to participate would not feel pressurised to consent. It was acknowledged that this would probably lead to a lower response rate.

These changes were proposed to the Local Research Ethics Committee and ethical consent was granted one month later. This shortened the planned data collection period.

Once data collection began further difficulties in recruitment were experienced. The researcher was relying on a busy clinical trials nurse to identify and dispatch the prepared questionnaire packs. The trials nurse was in turn dependent on the consultants' secretary to give her the referrals for screening before they were sent off for appointments to be arranged. This proved to be impossible as the administration staff frequently forgot. The procedure was changed so that the trials nurse met regularly with the two consultants to identify eligible patients. This was found to be the best method, but was unfortunately different from the original proposal where the oncologists themselves would identify patients as soon as referrals were received, and then alert the trials nurse to send out the questionnaire pack. The recruitment process employed was unsatisfactory due to its reliance on the nurse's memory and time. It is possible that it led to many appropriate referrals slipping through unnoticed.

It is apparent that the 95.9% consent rate to clinical trials is a highly unreliable figure. It is unknown how many patients were asked to enter a clinical trial, but did not receive a questionnaire pack.

There was also no way of ensuring that patients completed the questionnaires before they were approached about the trial. They would have received the questionnaires before being approached, but it was not checked when the pack was returned, due to practical and communication difficulties. Patients' responses may have been contaminated by their decision to enter the trial.

The telephone calls to patients who had not responded 10 days after the questionnaire pack had been dispatched had to be discontinued. This was due to unavailability of the trials nurse for consultation regarding the patients' medical status at appropriate times. Data concerning patients' reasons for not responding were therefore not available. This is unfortunate, as insights may have been gained from these patients.

The literature review found shortcomings in previous research. Studies were criticised on the grounds that their samples included patients with new and recurrent disease, in phase I, II, and III trials and with different types of cancer. This research failed to rectify these shortcomings. It was initially planned to use only phase III clinical trials, but this had to be extended to include phase I and II given the lack of eligible patients. Again, it was planned to recruit only patients with newly diagnosed disease, but the sample was extended to those with recurrent disease to increase numbers. However, the majority of patients were newly diagnosed with the cancer for which they were offered the trial. It was not possible to focus on one type of cancer, again due to problems in

recruiting eligible patients. This research did exclude surgical clinical trials and all the patients recruited were offered a chemotherapy clinical trial. However, post hoc analysis of the trials revealed that one was a trial of a vaccine for patients who were currently disease free (see Appendix I). It can be concluded that the sample in this research was a highly heterogeneous group in terms of disease and treatment related variables.

Differences between responders and non-responders may exist. This is a problem inherent to all research where participation is voluntary. It is a particular difficulty associated with postal questionnaires, which often have low response rates. However, a reasonably high response rate of 63% was obtained in this study, which increased the representativeness of the views expressed. It may be that patients with positive views about research were more likely to enter this project and report positive views about clinical trials. This study is likely to have obtained a skewed picture of trial participants' opinions.

On the variables of age and sex there were no statistically significant differences between the responders and non-responders. This suggests that the responder group was representative of the population on some variables.

The sample had a mean age of 59.5 years (SD 10.1) and contained approximately equal numbers of males and female participants. The majority was married and had completed education to the secondary level, although considerable numbers had further education. Approximately half (45%) of the sample, were in, or retired from, an unskilled occupation. It is difficult to say if this sample is representative of the clinical

trial population or if it is related to local socio-economic factors. The findings may be limited in their generalizability to the rest of the population. It would have been advantageous to use a number of centres in different geographical areas to overcome this difficulty.

The design selected was a cross-sectional postal questionnaire. As already discussed, postal questionnaires suffer from low response rates leading to problems in generalizing from the results. In addition, it was found that some participants incorrectly or incompletely filled in the questionnaires, leading to missing data. There was no way of checking that they understood the questions, so respondents may have interpreted them in different ways. Participants may also have asked the views of others before answering. It is questionable whether we measured the participants' views or those of their friends and family.

The cross-sectional design was appropriate to the research hypotheses. The researcher was interested in patients' attitudes, emotional status, coping and personality at a particular point in time and how these factors affected their decision regarding a clinical trial. This would not have allowed causal relationships to be established, but would have allowed comparison of those who consented with those who refused a clinical trial. This design was also appropriate to the time limits of the data collection period.

### **Statistical Analyses**

This research suffered from the problems of a small sample size and the existence of only one group of participants, rather than two as planned. The data obtained could not be used to answer the research hypotheses. It was necessary to adopt an exploratory



approach and to look at the characteristics of the group of patients who consented to a cancer clinical trial.

It is acknowledged that the reported results are only a small proportion of the potential number of analyses of the relationships between the variables. It was considered important to select questions that related to the early aims of the study and the findings of the literature review; for example, to look at the concept of choice, the influence of relatives and health locus of control. It is acknowledged that by completing a series of Independent T-tests, Mann Whitney U Tests and correlations that statistically significant results would be found according to chance. The likelihood of making Type I errors was increased and to avoid this the Baroffsky Correction was suggested. None of the significant results remained so once this correction was applied. In fact, many of the results observed were only significant at the 95% confidence level. Consequently, the results of the statistical analyses cannot be considered robust and need to be interpreted with caution.

The use of non-parametric statistical analyses, which are less powerful and so less likely to detect an effect of the independent variable on the dependent variable, increased the likelihood of a type II error. Some relationships may have overlooked.

Qualitative methodology and analysis were also used in this research. The aim was to combine the two research positions to give a more complete picture of patients' experiences. A semi-structured interview was used, with pre-determined, open-ended questions. During these interviews every care was taken to follow up the issues brought up by the participants and to obtain a picture of their reality, whilst providing some

structure to the interview. It was not a necessity to adhere rigidly to the interview questions.

Qualitative research is often criticised as subjective and influenced by the researcher's own biases. In this research it is acknowledged that the prior views of the researcher did intrude on the interviews in terms of the questions selected. However, it was made clear in the results chapter that the initial three categories into which the responses were placed were predefined, and did not emerge from the data. It is felt that the sub-categories that emerged within these were dependent on the participants' responses and were not merely a reflection of the researcher's interests. The use of another individual to categorise the data who was not familiar with the relevant literature increased the validity and reliability of the findings. The second rater approached the data differently and identified themes that ran through the researcher's sub-categories.

Content analysis was selected as it potentially allowed the emergence of similarities and differences between patients' experiences. By creating categories, important themes were observed that were common to the patients and were useful in explaining other findings of the research. However, it is acknowledged that by breaking up the data in this way the complete experience of each individual may have been lost.

The qualitative findings of this research are based on only four patients, all of whom consented to a clinical trial. They cannot be considered representative of the whole population and so the results cannot be generalized. Previous qualitative projects have also focused on patients who have consented to trials and not those who have refused

(e.g. Cox, 1999). This deficiency in the literature was identified in the review and it is unfortunate that this project could not rectify this.

## **Measures**

The attitudes questionnaire was designed by the researcher for this study. Without a comparison sample, it is difficult to say whether this measured underlying beliefs that are related to trial consent or refusal. Also without a 'normative' sample, it is not possible to consider whether this group were highly positive or whether their attitudes were same as those of the general population. However, patients showed a variety of responses and by hierarchical cluster analysis it was possible to identify two groups of patients according to this questionnaire.

The hierarchical cluster analysis also showed that the majority of the questions were measuring the same construct. It is felt that the questionnaire did measure prior views of research and trials in general, although further research using this measure would be needed to confirm this. The use of the 'total score' in the analysis as an overall measure of attitudes may have led to the neglect of important differences on the individual questions.

The hypothetical trial scenarios were designed for this study by a consultant oncologist and the researcher. As detailed in the methodology section, they were designed to measure a patient's willingness to enter different types of trials. For each trial, different factors were important, such as side effects, predicted effectiveness and the absence of another treatment option. However, it is questionable whether patients understood the differences between the scenarios. The scores on all four scenarios were highly

correlated with each other (see Appendix XVII) and so it was decided to use the 'total score' in the analyses, as a measure of willingness to enter trials. The normal distribution of this variable also allowed the use of parametric statistics, which increased the power of the analysis. However, by using this total score it is possible that differences between the scenarios were overlooked.

The hypothetical trial total score and the attitudes questions total score were significantly correlated, which supports the view that they were measuring some underlying trait or view point. It cannot be concluded how these relate to behaviour.

#### **4.3 Summary and Conclusions**

This research set out to explore the differences between cancer patients who consented to a clinical trial and those who refused. However, this comparison was not possible. Recruiting difficulties were experienced and the final sample consisted only of patients who had consented to a cancer clinical trial. As in previous research, this meant that patients who refused to enter were not included. This group remained an elusive proportion of patients. The high consent rate demonstrated in this study casts doubt on patient refusal as a significant problem in cancer clinical trial research.

Two groups of patients could be identified according to their attitudes towards research and these groups differed on their willingness to enter hypothetical trials. It appears that these two questionnaires were measuring patients' underlying views. However, it is not possible to say whether patients who refused a clinical trial would report less positive views.

A patient's rating of their amount of choice if asked to enter a trial was related to their personality and health locus of control. Although the concept of choice is complex and this research addressed a very limited part of this, the findings have important implications for the process of informed consent.

The qualitative findings of this project showed that patients did not know of the alternatives to the trial. The research also showed that patients who are more prone to worry and depression are likely to be unable to see that they have alternative choices. In the situation of being offered a clinical trial they are easily influenced by their Doctor. The results also showed that patients who place the responsibility of their health in professionals also perceive themselves as having no choice if offered a clinical trial. These patients are easily influenced by the doctor.

The findings also suggested that patients with a high internal locus of control perceived themselves as having no choice if offered a trial by their doctor. As discussed earlier this finding was inconsistent with previous research. This finding highlights the complexity of the issue of choice. It may be the case that by choosing to enter a trial patients feels they are actively making a choice and that they are actively doing something to fight their disease. Even if they were not aware of alternatives, the patient considers that they are still making a choice. This is consistent with the qualitative findings which showed that patients knew they had a choice, felt they had made one, but concurrently did not know of the alternatives. In this situation making a 'choice' did not mean deciding between two or more alternatives.

Informed consent requires that the patient is making a fully informed choice. This research suggests that the informed consent process needs to be tailored to individual needs and the personality and beliefs of the patients taken into account. The doctors and research staff need to be aware that their opinion is highly influential on some patients' decisions. These patients need help to weigh up their choices. More emphasis on the actual alternative treatments needs to be made and it be confirmed that the patient is aware of them, even if the alternative is no treatment. Patients need more time to consider the implications of the trial and the alternatives.

Finally, the qualitative findings of this study added insights into patients' experiences and concepts of clinical trials and their decision to enter.

It is clear that the experience of a clinical trial is highly subjective and has many different meanings for patients. A patient's decision appears to be dependent on a large number of factors, which include the characteristics of the trial itself, the doctor's attitudes and opinion, and the patient's medical status. The psychological characteristics and attitudes of the patient are likely to form just one part of an interaction between many influences.

It is concluded that future research needs to specifically address the issue of how to include patients who refuse a clinical trial. It is important to explore the characteristics and viewpoints of these patients, using both qualitative and quantitative methodologies.

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## APPENDIX I

### INCLUSION CRITERIA FOR CLINICAL TRIALS

**AIM HIGH** - *A phase II study of observation vs low dose extended duration interferon alpha- 2a in high risk resected malignant melanoma.*

- Patients with histologically proven malignant melanoma and high risk of recurrent metastatic disease with either:

histologically proven metastatic melanoma in regional lymph nodes after therapeutic radical regional node dissection at initial presentation,

*or*

histologically proven metastatic melanoma in regional lymph nodes after therapeutic radical regional node dissection at subsequent recurrence,

*or*

Non-nodal superficial regional recurrence (local or in-transit disease),

*or*

Primary tumours 4 mm or more Breslow thickness without any detectable focus of metastasis.

- Fit to receive interferon if allocated.
- Less than 12 weeks since resection.
- Healed surgical wound.
- Clinically disease free.
- No history of malignant disease.
- Not pregnant or lactating.
- No previous biological therapy.
- Not on steroids or immunosuppressive therapy.
- Written informed consent.

**BBR** – *A phase II trial of BBR3464 in patients with gastric or gastric-oesophageal adenocarcinoma who have failed first line chemotherapy.*

- Patients with histologically or cytologically proven inoperable, locally advanced or metastatic gastric or gastro-oesophageal adenocarcinoma who have failed first line treatment.



## APPENDIX I (CONTINUED)

- Aged at least 18 years.
- Life expectancy of at least 3 months.
- WHO performance status of 0-1.
- Patients must have measurable disease as measured by x-ray or CT scan.
- Carbon Monoxide Diffusion capacity must be at least 50% of predicted value.
- Recovery from acute toxicities.
- Written consent from the patient prior to the study.
- Patient must be able to co-operate with the treatment and comply with the requirements of the study protocol for the duration of the trial.
- Patients with brain metastases are eligible provided they have stable symptoms and a stable dose of steroid within one month of receiving the study drug and are able to give informed consent.

### **FOCUS** – *A randomised phase II trial to assess the role of irinotecan and oxaliplatin in advanced colorectal cancer*

- Histologically confirmed adenocarcinoma of the colon or rectum.
- Inoperable metastatic or locoregional disease (synchronous or recurrence).
- No previous chemotherapy for established metastatic disease.
- Measurable or evaluable disease.
- Adequate bone marrow, renal and hepatobiliary function.
- WHO performance status 0, 1 or 2 and are considered fit to undergo all possible treatments.
- Not pregnant and are using adequate contraception.

### **GEMCITABINE**– *A phase I/II study of chemo-radiotherapy using gemcitabine (2FdC) as a radiosensitiser for brain metastases from adenocarcinomas.*

- Histological/cytological diagnosis of adenocarcinoma predating, antedating or synchronous to the brain metastases for which gemcitabine is an accepted therapeutic agent.
- Performance status equal to or less than 2.
- Able to co-operate with intended RT treatment.
- Ability to understand the trial requirements and give informed consent.

## APPENDIX I (CONTINUED)

- No concurrent or metachronous or antedating malignancy of other organs except of basal cell carcinoma of the skin and in-situ carcinoma of the cervix, both adequately treated.
- Adequate haematological, renal and liver functions for chemotherapy.
- No age limit
- No surgical procedures to the brain
- Stable on steroids
- Metastases measuring 2x2x2cm or more on staging CT scan.
- Signed consent form.

**ISIS** – *A phase III prospective, randomised, open-label trial of chemotherapy with carboplatin and paclitaxel, vs carboplatin and paclitaxel in combination with isis 3521, in antisense previously untreated, non-small cell lung cancer.*

- Patient is  $\geq 18$  years old.
- Patient is using an effective form of contraceptive.
- Patient has histologically or cytologically confirmed diagnosis of non-small cell lung cancer.
- Patient has Stage IV disease or Stage IIIB with malignant pleural or pericardial effusion.
- Patient has either:

At least one unidimensional measureable lesion,

*or*

Non-measureable, evaluable disease.

- Patient has signed consent form.
- ECOG is  $\leq 1$ . Patient is able to perform light housework/officework (if not ECOG =2).
- Serum creatine is  $\leq 1.5$ mg/dL; Serum bilirubin  $\leq 1.5$ mg/dL.
- Serum aspartate aminotransferase concentration  $< 3 \times$  ULN.
- ANC is  $\geq 1500/\text{mm}^3$ ; platelet count  $\geq 100,000/\text{mm}^3$ ; haemoglobin is  $\geq 10.0$  g/dL.

**MTA DOX** – *A phase I, dose-escalating study of MTA and Doxorubicin administered every 21 days in patients with locally advanced or metastatic cancer.*

- Histologic or cytologic diagnosis of locally advanced or metastatic cancer.

## APPENDIX I (CONTINUED)

- Previous chemotherapy is permitted.
- No other chemotherapy for 4 weeks before enrolment in the study.
- Performance status 0 to 2 on the WHO scale.
- Evidence of locally advanced or metastatic disease. Can be measurable, evaluable or non-measurable.
- Life expectancy of at least 12 weeks.
- Prior radiotherapy allowed to 25% of bone marrow producing areas.
- Patient compliance and geographic proximity that allow adequate follow-up.
- Adequate organ functioning.

**RFA** – *A phase II study of combination primary chemotherapy (Campto-5FU/FA) followed by RFA (radiofrequency ablation) for patients with low volume inoperable liver metastases from colon cancer.*

- Patient with metastatic colorectal cancer isolated to the liver who is classified as inoperable due to anatomical or performance status considerations.
- Histological diagnosis of colorectal cancer.
- Accessibility of lesions to an RFA probe.
- Patients have received prior chemotherapy, which has been discontinued for 4 weeks prior.
- Histology of liver metastases for metachronous lesions . 2 years post surgery.
- Number of lesions  $\leq 6$ . With any single lesion maximum diameter  $\leq 3.5$ cm.
- Performance status (WHO) score 1 or 0.
- Life expectancy longer than 3 months.
- Liver function (Bilirubin  $< 1.5 \times$  ULN transminases  $< 5 \times$  ULN)
- Renal function (serum creatinine  $\leq 135$  umol)
- Haematological function (ANC  $\leq 2 \times 10^9/L$  and platelets  $\leq 150 \times 10^9/L$ )
- Normal coagulation profile.
- Lesions demonstrated by ultrasound or Fluroscopy.

**THERATOPE®** – *A multi-centre phase III, randomised, controlled study of Theratope vaccine for metastatic breast cancer.*

- Previously diagnosed (histologically or cytologically confirmed ) breast cancer.

## APPENDIX I (CONTINUED)

- Has received between 4-8 cycles of first line chemotherapy for metastatic disease.
- Has either (a) no evidence of disease or (b) non-progressive disease following first line chemotherapy.
- Has a neutrophil count  $\geq 1.0 \times 10^9/L$ ; platelet count  $\geq 75 \times 10^9/L$ ; haemoglobin  $\geq 9$  g/dL.
- Has performance status of  $\leq 2$  on the ECOG scale.
- Is female and at least 18 years old.
- Is considered reliable and has signed the consent form.
- Is accessible for treatment and follow-up.

**TULARIK** – *A phase II, two arm, open label study of T138067-sodium in breast cancer patients who have failed up to two prior regimes for locally advanced breast cancer.*

- Pathologic diagnosis of breast cancer. Locally advanced or metastatic disease.
- Any amount of prior adjuvant chemotherapy.
- Any chemotherapy or major surgery must be completed at least 4 weeks before study treatment.
- Patients must have recovered from the acute side effects of radiotherapy.
- Patients must have bi-dimensionally measurable disease amenable to radiologic imaging techniques.
- Female, at least 18 years of age.
- Karnofsky performance status of 70 or greater.
- Estimated life expectancy of at least 12 weeks.
- Must be using effective contraception.
- Able to comply with study procedures and follow up procedures.
- Patient signed consent form.
- Patients must have adequate organ function.

## APPENDIX II

### PATIENTS' INFORMATION SHEET

#### PEOPLES' VIEWS ON CANCER CLINICAL TRIALS

You are being invited to take part in a research study. The following information tells you why the research is being done and what it will involve. Please take time to decide whether or not you wish to take part.

#### What is the purpose of this study ?

We are interested in what people think about clinical trials. We would like to work out what makes some people want to enter a trial and what makes others not want to.

**This study is NOT asking you to enter a clinical trial, we are just interested in your opinions.**

#### What is a Clinical Trial?

A clinical trial is a study that tries to test whether a new treatment is better than an existing treatment. Although treatments for cancer have improved; we still do not know all the answers. Clinical trials are the means by which we find those answers. Involvement by patients in clinical trials is purely voluntary. In a trial a patient is randomised (selected by chance) to have either the standard treatment (which may be nothing) or the new treatment.

#### Why have I been chosen ?

You have been chosen because your cancer is newly diagnosed. Up to 200 other patients will also be studied over the next year. We are also asking your relative/friend to help with the study.

#### Do I have to take part ?

It is up to you whether or not you take part. If you do take part you must sign the consent form included in this pack. You can withdraw from the study at any point.

Your decision will not effect the standard of care you receive.

The study is separate to your medical care and your consultant will not be contacted about your individual results.

#### What should I do now ?

1. Some of the questionnaires in this pack are for you and there are also a small number for one of your relatives or friends to fill in.

## APPENDIX II (CONTINUED)

2. The ones for your relative/friend are on blue paper and are marked "relative/friend" in the top left corner. Please choose someone whom you are close to (possibly the person who attends your hospital appointments with you). Your relative/friend will have an information sheet like this one telling them what to do.
3. After reading this information sheet please sign the consent form.
4. Then fill in the questionnaires included in this pack. There are 7 all together. This will take about 35 minutes in total, but you don't have to do them all at once. It is important that you do this before your first clinic appointment.

Only put your name on the sheet entitled "personal Information". DO NOT put your name on any other of the questionnaires.

Please read the instructions on the top of each of the questionnaires carefully and answer all questions. Please note, the pink questionnaire has questions on the back too !

Please do not confer with your relative while filling them in. You are welcome to share answers afterwards!

5. You should put your and your relative's completed questionnaires in the envelope and bring it to your first clinic. Alternately, return them in the pre-paid envelope.
6. We will contact you again in approximately 3 months to ask you to participate in a further interview. If you have agreed to participate in the study today you do not have to take part in the second interview.

### **Will my taking part be kept confidential ?**

All information collected about you will be kept strictly confidential. All information that leaves the hospital will have your name removed from it.

### **What will happen to the results of the research study ?**

The results of this study are likely to be published after the summer of 2001. You will not be identified in any report or publication. We will send you a copy of the results if you wish.

### **Who has reviewed this study ?**

This study has been reviewed and passed by the Hull and East Riding Local Research Ethics Committee.

## **APPENDIX II (CONTINUED)**

### **Who should I contact for further information ?**

Professor M. Lind.  
Department of Academic Oncology  
Princess Royal Hospital  
Salhouse Road  
Hull

### **THANKYOU FOR TAKING PART IN THE STUDY**

You will be given a copy of this information sheet and a signed consent form to keep.

14.09.00, Version 3

**APPENDIX III**

**PATIENT CONSENT FORM**

Patient identification number for the study

**Title of Project: Psychological Factors that Influence Patient Participation in Cancer Clinical Trials.**

**Name of researcher: Cheryl Jane Davis, Trainee Clinical Psychologist**

1. I confirm that I have read and understood the information sheet dated 14.09.00 (version 3) for the above study.
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.
3. I understand that sections of my medical notes may be looked at by the above named researcher. I give my permission for this.
4. I agree to take part in the above named study.

\_\_\_\_\_  
Name of Patient

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Name of person taking consent  
(if different from researcher)

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Researcher

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature



**APPENDIX IV**

**PATIENT DEMOGRAPHIC INFORMATION**

Participant number

**PERSONAL INFORMATION**

Name \_\_\_\_\_

Date of birth \_\_\_\_/\_\_\_\_/\_\_\_\_

Occupation \_\_\_\_\_  
(if housewife, what is the occupation of your husband?)  
(if retired, what was your job previously?)

**Marital status:**

(Please tick)                      Married  
                                            Divorced  
                                            Single  
                                            Widowed

At what age did you leave school? \_\_\_\_\_

Have you any other medical problems? (Please tick)                      Yes                      No

If yes please give brief details:

\_\_\_\_\_

Have you had any other major problems/events in the last 6 months?  
(For example, unemployment, relationship break-up, financial problems etc.)

(Please tick)                      Yes  
                                            No

If yes, please give brief details:

\_\_\_\_\_

## **APPENDIX V**

### **HYPOTHETICAL TRIALS – PATIENT VERSION**

This booklet contains descriptions of 4 situations sometimes faced by patients.

These situations have been made up by us, but are based on previous real-life cases.

Please read each one carefully and imagine that the situation is real.

Circle the answer which best describes what you think you would do if faced with the decision.

**APPENDIX V (CONTINUED)**

***1***

Your consultant tells you that the standard treatment for your disease will **not** help. However, there is a new drug, which may help.

The consultant tells you about a clinical trial in which you would either receive:

no treatment

or

the new drug.

It would be decided by chance which of these you would receive. You would have an equal chance of receiving either one.

After a full explanation of the trial by the consultant would you agree to enter ?

**1**  
definitely  
agree

**2**  
probably  
agree

**3**  
not sure

**4**  
probably  
not  
agree

**5**  
definitely  
not  
agree

**APPENDIX V (CONTINUED)**

**2**

Your consultant explains to you that the standard treatment for your disease is **drug A**. There is also a new (experimental) treatment that may be helpful, **drug B**.

**Drug A** has very few side effects.  
**Drug B** has a lot of side effects.

There is a clinical trial where it will be decided by chance whether you receive **drug A** or **drug B**.

After a full explanation of the trial by the consultant would you agree to enter ?

<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>
<b>definitely</b>	<b>probably</b>	<b>not sure</b>	<b>probably</b>	<b>definitely</b>
<b>agree</b>	<b>agree</b>		<b>not</b>	<b>not</b>
			<b>agree</b>	<b>agree</b>

**APPENDIX V (CONTINUED)**

**3**

Your consultant explains to you that the standard treatment for your disease is **drug A**. There is also a new (experimental) treatment which may be helpful, **drug B**.

**Drug A** has a lot of side effects.  
**Drug B** has very few side effects.

There is a clinical trial where it will be decided by chance whether you receive **drug A** or **drug B**.

After a full explanation of the trial by the consultant would you agree to enter ?

**1**  
definitely  
agree

**2**  
probably  
agree

**3**  
not sure

**4**  
probably  
not  
agree

**5**  
definitely  
not  
agree

**APPENDIX V (CONTINUED)**

**4**

Your consultant explains to you that there is no right or wrong treatment for your disease.

There are 2 treatments that are thought to be similarly helpful.

They have similar side effects.

There is a clinical trial where you will receive one of these treatments. Which one you receive will be decided by chance.

After a full explanation of the trial by the consultant, would you agree to enter ?

**1**  
definitely  
agree

**2**  
probably  
agree

**3**  
not sure

**4**  
probably  
not  
agree

**5**  
definitely  
not  
agree

## APPENDIX VI

### ATTITUDES TO TRIALS AND RESEARCH QUESTIONNAIRE – PATIENT VERSION

Please read each of the following questions and put a circle around your answer. If none of the options describes how you feel, just choose the closest one. Please answer all questions.

We are interested in your *opinions*. There are no right or wrong answers.

1) In general, my view of medical research using patients is:

1	2	3	4	5
very positive	positive	neutral	negative	very negative

2) To develop new treatments for cancer, I think clinical trials are:

1	2	3	4	5
very necessary	somewhat necessary	neither needed or not needed	somewhat unnecessary	very unnecessary

3) How much do you agree with this statement ?

“A patient’s participation in a clinical trial for a new cancer treatment would help future patients”

1	2	3	4	5
strongly agree	agree	neither agree or disagree	disagree	strongly disagree

APPENDIX VI (CONTINUED)

4) How much do you agree with this statement ?

“One day a ‘miracle’ cure for cancer will be found”

1	2	3	4	5
strongly agree	agree	neither agree or disagree	disagree	strongly disagree

5) How much do you agree with this statement ?

“Patients should volunteer for clinical trial research”

1	2	3	4	5
strongly agree	agree	neither agree or disagree	disagree	strongly disagree

6) How would participating in a trial, rather than receiving the standard treatment effect your hope of being cured ?

1	2	3	4	5
much more hope	a little more hope	neither more or less hope	a little less hope	much less hope

7) How do you think participating in a clinical trial would effect a patient's chance of survival compared with the standard treatment?

1	2	3	4	5
strongly increase	somewhat increase	neither increase or decrease	somewhat decrease	strongly decrease



APPENDIX VI (CONTINUED)

8) How much do you agree with this statement ?

“Patients receive more help and support if they participate in a clinical trial”

1	2	3	4	5
strongly agree	agree	neither agree or disagree	disagree	strongly disagree

9) Clinical trials are ‘randomised’.

This means the patients who volunteer could receive any one of the treatments in the trial. They cannot choose which one.

How comfortable would you feel about this ?

1	2	3	4	5
very comfortable	somewhat comfortable	neither comfortable or uncomfortable	somewhat uncomfortable	very uncomfortable

10) A clinical trial may be ‘double blind’.

This means that neither the doctors or yourself would know which treatment you were receiving.

How comfortable would you feel about this ?

1	2	3	4	5
very comfortable	somewhat comfortable	neither comfortable or uncomfortable	somewhat uncomfortable	very uncomfortable

APPENDIX VI (CONTINUED)

11) How much do you agree with this statement ?

**“If my doctor asked me to participate in a clinical trial. I would feel that I had no other choice”**

1	2	3	4	5
strongly agree	agree	neither agree or disagree	disagree	strongly disagree

12) If you were asked to participate in a clinical trial how much would you take the views of your family/friends into account ?

1	2	3	4	5
a lot	somewhat	a little	not at all	don't know

13) How much do you agree with this statement ?

**“The doctor is the best person to make the final decision”**

1	2	3	4	5
strongly agree	agree	neither agree or disagree	disagree	strongly disagree

## APPENDIX VII

### HOSPITAL ANXIETY AND DEPRESSION SCALE

Doctors are aware that emotions play an important part in most illnesses. If your doctor knows how you feel he will be able to help you more.

This questionnaire is designed to help your doctor to know how you feel. Read each item and place a firm tick in the box opposite the reply which comes closest to how you have been feeling in the past week.

Don't take too long over your replies: your immediate reaction to each item will probably be more accurate than a long thought out response.

**I feel tense or wound up:**

Most of the time  
A lot of the time  
Time to time, occasionally  
Not at all

**I feel as if I am slowed down:**

Nearly all the time  
Very often  
Sometimes  
Not at all

**I still enjoy the things I used to enjoy:**

Definitely as much  
Not quite so much  
Only a little  
Hardly at all

**I get a sort of frightened feeling like 'butterflies' in the stomach:**

Not at all  
Occasionally  
Quite often  
Very often

**I get a sort of frightened feeling as if something awful is about to happen:**

Very definitely and quite often  
Yes, but not too badly  
A little, but it doesn't worry me  
Not at all

**I have lost interest in my appearance:**

Definitely  
I don't take as much care as I should  
I may not take quite as much care  
I take just as much care as ever

**I can laugh and see the funny side of things:**

As much as I always could  
A lot of the time  
Definitely not so much now  
Not at all

**I feel restless as if I have to be on the move:**

Very much indeed  
Quite a lot  
Not very much  
Not at all

**Worrying thoughts go through my mind:**

A great deal of the time  
A lot of the time  
From time to time, but not too often  
Only occasionally

**I look forward with enjoyment to things:**

As much as I ever did  
Rather less than I used to  
Definitely less than I used to  
Hardly at all

**I feel cheerful:**

Not at all  
Not often  
Sometimes  
Most of the time

**I get sudden feelings of panic:**

Very often indeed  
Quite often  
Not very often  
Not at all

**I can sit at ease and feel relaxed:**

Definitely  
Usually  
Not often  
Not at all

**I can enjoy a good book or radio or TV programme:**

Often  
Sometimes  
Not often  
Very Seldom

## APPENDIX VIII

### EYSENCK PERSONALITY QUESTIONNAIRE- REVISED, SHORT SCALE

INSTRUCTIONS: Please answer each question by putting a circle around the 'YES' or 'NO' following the question. There are no right or wrong answers, and no trick questions. Work quickly and do not think too long about the exact meaning of the questions.

PLEASE REMEMBER TO ANSWER EACH QUESTION

- |    |                                                                                                           |        |
|----|-----------------------------------------------------------------------------------------------------------|--------|
| 1  | Does your mood often go up and down?                                                                      | YES NO |
| 2  | Do you take much notice of what people think?                                                             | YES NO |
| 3  | Are you a talkative person?                                                                               | YES NO |
| 4  | If you say you will do something, do you always keep your promise no matter how inconvenient it might be? | YES NO |
| 5  | Do you ever feel 'just miserable' for no reason?                                                          | YES NO |
| 6  | Would being in debt worry you?                                                                            | YES NO |
| 7  | Are you rather lively?                                                                                    | YES NO |
| 8  | Were you ever greedy by helping yourself to more than your fair share of anything?                        | YES NO |
| 9  | Are you an irritable person?                                                                              | YES NO |
| 10 | Would you take drugs which may have strange or dangerous effects?                                         | YES NO |
| 11 | Do you enjoy meeting new people?                                                                          | YES NO |
| 12 | Have you ever blamed someone for doing something you knew was really your fault?                          | YES NO |
| 13 | Are your feelings easily hurt?                                                                            | YES NO |
| 14 | Do you prefer to go your own way rather than act by the rules?                                            | YES NO |
| 15 | Can you usually let yourself go and enjoy yourself at a lively party?                                     | YES NO |
| 16 | Are <i>all</i> your habits good and desirable ones?                                                       | YES NO |
| 17 | Do you often feel 'fed up'?                                                                               | YES NO |
| 18 | Do good manners and cleanliness matter much to you?                                                       | YES NO |
| 19 | Do you usually take the initiative in making new friends?                                                 | YES NO |
| 20 | Have you ever taken anything (even a pin or a button) that belonged to someone else?                      | YES NO |
| 21 | Would you call yourself a nervous person?                                                                 | YES NO |
| 22 | Do you think marriage is old-fashioned and should be done away with?                                      | YES NO |
| 23 | Can you easily get some life into a rather dull party?                                                    | YES NO |
| 24 | Have you ever broken or lost something belonging to someone else?                                         | YES NO |
| 25 | Are you a worrier?                                                                                        | YES NO |
| 26 | Do you enjoy cooperating with others?                                                                     | YES NO |
| 27 | Do you tend to keep in the background on social occasions?                                                | YES NO |
| 28 | Does it worry you if you know there are mistakes in your work?                                            | YES NO |
| 29 | Have you ever said anything bad or nasty about anyone?                                                    | YES NO |
| 30 | Would you call yourself tense or highly strung?                                                           | YES NO |
| 31 | Do you think people spend too much time safeguarding their future with savings and insurance?             | YES NO |
| 32 | Do you like mixing with people?                                                                           | YES NO |
| 33 | As a child were you ever cheeky to your parents?                                                          | YES NO |
| 34 | Do you worry too long after an embarrassing experience?                                                   | YES NO |
| 35 | Do you try not to be rude to people?                                                                      | YES NO |
| 36 | Do you like plenty of excitement and bustle around you?                                                   | YES NO |
| 37 | Have you ever cheated at a game?                                                                          | YES NO |
| 38 | Do you suffer from nerves?                                                                                | YES NO |
| 39 | Would you like other people to be afraid of you?                                                          | YES NO |
| 40 | Have you ever taken advantage of someone?                                                                 | YES NO |
| 41 | Are you mostly quiet when you are with other people?                                                      | YES NO |
| 42 | Do you often feel lonely?                                                                                 | YES NO |
| 43 | Is it better to follow society's rules than go your own way?                                              | YES NO |

**APPENDIX VIII (CONTINUED)**

- |    |                                                                     |        |
|----|---------------------------------------------------------------------|--------|
| 44 | Do other people think of you as being very lively?                  | YES NO |
| 45 | Do you always practice what you preach?                             | YES NO |
| 46 | Are you often troubled about feelings of guilt?                     | YES NO |
| 47 | Do you sometimes put off until tomorrow what you ought to do today? | YES NO |
| 48 | Can you get a party going?                                          | YES NO |

**PLEASE CHECK THAT YOU HAVE ANSWERED ALL THE QUESTIONS**

## APPENDIX IX

### MULTIDIMENSIONAL HEALTH LOCUS OF CONTROL SCALE

This is a questionnaire designed to determine the way in which different people view certain important health-related issues. Each item is a brief statement with which you may agree or disagree. Beside each statement is a scale which ranges from strongly disagree (1) to strongly agree (6). For each item we would like you to circle the number that represents the extent to which you disagree or agree with the statement. The more strongly you agree with a statement, then the higher will be the number you circle. The more strongly you disagree with a statement, then the lower will be the number you circle. Please make sure that you answer every item and that you circle only one number per item. This is a measure of your personal beliefs: obviously there are no right or wrong answers.

Please answer these items carefully, but do not spend much time on any one item. As much as you can, try to respond to each item independently. When making your choice, do not be influenced by your previous choices. It is important that you respond according to your actual beliefs and not according to how you feel you should believe or how you think we want you to believe.

		Strongly Disagree					Strongly Agree
1	If I get sick, it is my own behaviour which determines how soon I get well again.	1	2	3	4	5	6
2	No matter what I do, if I am going to get sick, I will get sick.	1	2	3	4	5	6
3	Having regular contact with my doctor is the best way for me to avoid illness.	1	2	3	4	5	6
4	Most things that affect my health happen to me by accident.	1	2	3	4	5	6
5	Whenever I don't feel well, I should consult a medically trained professional.	1	2	3	4	5	6
6	I am in control of my health.	1	2	3	4	5	6
7	My family has a lot to do with my becoming sick or staying healthy.	1	2	3	4	5	6
8	When I get sick, I am to blame.	1	2	3	4	5	6
9	Luck plays a big part in determining how soon I will recover from an illness.	1	2	3	4	5	6
10	Health professionals control my health.	1	2	3	4	5	6
11	My good health is largely a matter of good fortune.	1	2	3	4	5	6
12	The main thing that affects my health is what I myself do.	1	2	3	4	5	6
13	If I take care of myself I can avoid illness	1	2	3	4	5	6
14	When I recover from an illness, it's usually because other people (for example doctors, nurses, family, friends) have been taking good care of me.	1	2	3	4	5	6
15	No matter what I do I'm likely to get sick.	1	2	3	4	5	6

**APPENDIX IX (CONTINUED)**

16	If it's meant to be, I will stay healthy.	1	2	3	4	5	6
17	If I take the right actions, I can stay healthy.	1	2	3	4	5	6
18	Regarding my health, I can only do what my doctor tells me to do.	1	2	3	4	5	6

## APPENDIX X

### COURTAULD EMOTIONAL CONTROL SCALE

Listed below are some of the reactions people have to certain feelings or emotions. Read through the items on each list and, by circling an appropriate number on the scale indicate how far each describes the way you generally react

For example: In reaction A, if you think you 'almost never' keep quiet when you feel angry or annoyed, then you would circle 1.

Please circle a number for every reaction from A through U. Work quickly and circle one number on each line.

WHEN I FEEL ANGRY (VERY ANNOYED):		almost never	sometimes	often	almost always
A	I keep quiet	1	2	3	4
B	I refuse to argue or say anything	1	2	3	4
C	I bottle it up	1	2	3	4
D	I say what I feel	1	2	3	4
E	I avoid making a scene.	1	2	3	4
F	I smother my feelings	1	2	3	4
G	I hide my annoyance	1	2	3	4

#### WHEN I FEEL ANXIOUS (WORRIED):

H	I let others see how I feel	1	2	3	4
I	I keep quiet	1	2	3	4
J	I refuse to say anything about it	1	2	3	4
K	I tell others about it	1	2	3	4
L	I say what I feel	1	2	3	4
M	I bottle it up	1	2	3	4
N	I smother my feelings	1	2	3	4

#### WHEN I FEEL UNHAPPY (MISERABLE):

O	I refuse to say anything about it	1	2	3	4
P	I hide my unhappiness	1	2	3	4
Q	I put on a bold face	1	2	3	4
R	I keep quiet	1	2	3	4
S	I let others see how I feel	1	2	3	4
T	I smother my feelings	1	2	3	4
U	I bottle it up	1	2	3	4

Please check that you have circled one number on each line and that you have circled a number for every reaction, from A through to U.

Thank you.



## APPENDIX XI

### RELATIVE/FRIEND'S INFORMATION SHEET

#### PEOPLES' VIEWS ON CANCER CLINICAL TRIALS

You are being invited to take part in a research study. The following information tells you why the research is being done and what it will involve. Please take time to decide whether or not you wish to take part.

##### What is the purpose of this study ?

We are interested in what people think about clinical trials. We would like to work out what makes some people want to enter a trial and what makes others not want to.

**This study is NOT asking your relative to enter a clinical trial, we are just interested in your opinions.**

##### What is a Clinical Trial?

A clinical trial is a study that tries to test whether a new treatment is better than an existing treatment. Although treatments for cancer have improved; we still do not know all the answers. Clinical trials are the means by which we find those answers. Involvement by patients in clinical trials is purely voluntary. In a trial a patient is randomised (selected by chance) to have either the standard treatment (which may be nothing) or the new treatment.

##### Why have I been chosen ?

Your relative has been chosen because their cancer is newly diagnosed. Up to 200 other patients will also be studied over the next year. We are also asking a relative or friend who is close to the patient to help us with the study.

##### Do I have to take part ?

It is up to you whether or not you take part. If you do take part you will be asked to sign a consent form. You can withdraw from the study at any point.

Your decision will not effect the standard of care your relative/ friend receives.

The study is separate from their medical care. The consultant will not be contacted about your or your relative's individual results.

##### What will happen to me if I will take part ?

- 1 Your questionnaires are on blue paper.
- 2 After reading this information sheet please sign the consent form

## APPENDIX XI (CONTINUED)

- 3 Then complete the questionnaires. There are 3 in total. This will take about 15 minutes in total, but you don't have to do them all at once. It is important that you fill them in before your relative's first clinic appointment.

Only put your name on the questionnaire entitled "personal information". DO NOT put your name on the others.

Please read the instructions on the questionnaires carefully and answer all questions.

Please do not confer with your relative while filling them in. You are welcome to share answers afterwards!

3. You should put the completed questionnaires in the envelope and give it to your relative for them to take to the clinic where they will be collected by a clinical trials nurse. Otherwise, they may post them back to us in the pre-paid envelope.

### **Will my taking part be kept confidential ?**

All information collected about you will be kept strictly confidential. All information that leaves the hospital will have your name removed from it.

You will be given a participant number.

### **What will happen to the results of the research study ?**

The results of this study are likely to be published after the summer of 2001. You will not be identified in any report or publication. We will send you a copy of the results if you wish.

### **Who has reviewed this study ?**

This study has been reviewed and passed by the Hull and East Riding Local Research Ethics Committee.

### **Who should I contact for further information ?**

Professor M. Lind.  
Department of Academic Oncology  
Princess Royal Hospital  
Salthouse Road  
Hull

## **THANKYOU FOR TAKING PART IN THE STUDY**

You will be given a copy of this information sheet and a signed consent form to keep.

29.08.00, version 2

**APPENDIX XII**

**RELATIVE/FRIEND'S CONSENT FORM**

Relative/friend identification number for the study

**Title of Project: Psychological Factors that Influence Patient Participation in Cancer Clinical Trials.**

**Name of researcher: Cheryl Jane Davis, Trainee Clinical Psychologist**

1. I confirm that I have read and understood the information sheet dated 29.08.00 (version 2) for the above study.
  
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without legal rights being affected.
  
3. I agree to take part in the above named study.

\_\_\_\_\_  
Name of relative/friend                      Date                      Signature

\_\_\_\_\_  
Name of person taking consent  
(if different from researcher)                      Date                      Signature

\_\_\_\_\_  
Researcher                      Date                      Signature

**APPENDIX XIII**

**RELATIVE/FRIEND'S DEMOGRAPHIC INFORMATION**

Participant number

**PERSONAL INFORMATION**

Name \_\_\_\_\_

Date of birth        /        / \_\_\_\_\_

Occupation \_\_\_\_\_  
(if housewife, what is the occupation of your husband?)  
(if retired, what was your job previously ?)

**Marital status:**

(Please tick)                      Married  
                                            Divorced  
                                            Single  
                                            Widowed

**What is your relationship to patient?**

(Please tick)

- Partner**
- Husband**
- Wife**
- Brother**
- Sister**
- Son**
- Daughter**
- Aunt**
- Uncle**
- Niece**
- Nephew**
  
- Friend**

## **APPENDIX XIV**

### **HYPOTHETICAL TRIALS – RELATIVE/FRIEND'S VERSION**

This booklet contains descriptions of 4 situations sometimes faced by patients.

These situations have been made up by us, but are based on previous real-life cases.

Please read each one carefully and imagine that the situation is real.

Circle the answer which best describes what you think your relative should do if faced with the decision.

**APPENDIX XIV (CONTINUED)**

***1***

Relative/friend

Your consultant tells you that the standard treatment for your relative's /friend's disease will **not** help.

However, there is a new (experimental) drug which may help.

The consultant tells you about a clinical trial in which your relative/friend would either receive:

no treatment

or

the new drug

It would be decided by chance which of these they would receive. They would have an equal chance of receiving either one.

After a full explanation of the trial by the consultant, do you think your relative/friend should enter?

1  
definitely  
yes

2  
probably  
yes

3  
not sure

4  
probably  
no

5  
definitely  
no

APPENDIX XIV (CONTINUED)

2

Relative/friend

Your consultant explains to you that the standard treatment for your relative's/friend's disease is drug A. There is also a new (experimental) treatment which may be helpful, drug B.

Drug A has very few side effects.  
Drug B has a lot of side effects.

There is a clinical trial where it will be decided by chance whether your relative/friend receives drug A or drug B.

After a full explanation of the trial by the consultant, do you think your relative/friend should enter?

1  
definitely  
yes

2  
probably  
yes

3  
not sure

4  
probably  
no

5  
definitely  
no

APPENDIX XIV (CONTINUED)

3

Relative/friend

Your consultant explains to you that the standard treatment for your relative's/friend's disease is **drug A**. There is also a new (experimental) treatment which may be helpful, **drug B**.

**Drug A** has a lot of side effects.  
**Drug B** has very few side effects.

There is a clinical trial where it will be decided by chance whether your relative/friend receives **drug A** or **drug B**.

After a full explanation of the trial by the consultant, do you think your relative/friend should enter ?

1  
definitely  
yes

2  
probably  
yes

3  
not sure

4  
probably  
no

5  
definitely  
no



APPENDIX XIV (CONTINUED)

4

Relative/friend

Your consultant explains to you that there is no right or wrong treatment for your relative's/friend's disease.

There are 2 treatments that are thought to be similarly helpful.

They have similar side effects.

There is a clinical trial where your relative/friend will receive one of these treatments. Which one they receive will be decided by chance.

After a full explanation of the trial by the consultant, do you think your relative/friend should enter ?

1  
definitely  
yes

2  
probably  
yes

3  
not sure

4  
probably  
no

5  
definitely  
no

## APPENDIX XV

### ATTITUDES TO TRIALS AND RESEARCH QUESTIONNAIRE – RELATIVE/FRIEND'S VERSION

Please read each of the following questions and put a circle around your answer. If none of the options describes how you feel, just choose the closest one. Please answer all questions.

We are interested in your *opinions*. There are no right or wrong answers.

1) In general, my view of medical research using patients is:

1	2	3	4	5
very positive	positive	neutral	negative	very negative

2) To develop new treatments for cancer, I think clinical trials are:

1	2	3	4	5
very necessary	somewhat necessary	neither needed or not needed	somewhat unnecessary	very unnecessary

3) How much do you agree with this statement ?

“A patient’s participation in a clinical trial for a new cancer treatment would help future patients”

1	2	3	4	5
strongly agree	agree	neither agree or disagree	disagree	strongly disagree

APPENDIX XV (CONTINUED)

4) How much do you agree with this statement ?

“One day a ‘miracle’ cure for cancer will be found”

1	2	3	4	5
strongly agree	agree	neither agree or disagree	disagree	strongly disagree

5) How much do you agree with this statement ?

“Patients should volunteer for clinical trial research”

1	2	3	4	5
strongly agree	agree	neither agree or disagree	disagree	strongly disagree

6) How would participating in a trial, rather than receiving the standard treatment effect your hope for your relative/friend being cured ?

1	2	3	4	5
much more hope	a little more hope	neither more or less hope	a little less hope	much less hope

7) How do you think participating in a clinical trial would effect a patients' chance of survival compared with the standard treatment?

1	2	3	4	5
strongly increase	somewhat increase	neither increase or decrease	somewhat decrease	strongly decrease

APPENDIX XV (CONTINUED)

8) How much do you agree with this statement ?

**“Patients receive more help and support if they participate in a clinical trial”**

1	2	3	4	5
strongly agree	agree	neither agree or disagree	disagree	strongly disagree

9) Clinical trials are ‘randomised’.

This means the patients who volunteer could receive any one of the treatments in the trial. They cannot choose which one.

**How comfortable would you feel if your relative/friend entered a trial like this ?**

1	2	3	4	5
very comfortable	somewhat comfortable	neither comfortable or uncomfortable	somewhat uncomfortable	very uncomfortable

10) A clinical trial may be ‘double blind’.

This means that neither the doctors or the patient would know which treatment the patient was receiving.

**How comfortable would you feel if your relative/friend entered a trial like this ?**

1	2	3	4	5
very comfortable	somewhat comfortable	neither comfortable or uncomfortable	somewhat uncomfortable	very uncomfortable

APPENDIX XV (CONTINUED)

11) How much do you agree with this statement ?

**“If my doctor asked my relative/friend to participate in a clinical trial. I would feel that they had no other choice”**

1	2	3	4	5
strongly agree	agree	neither agree or disagree	disagree	strongly disagree

12) If your relative/friend were asked to participate in a clinical trial how much would you like them to take your views into account?

1	2	3	4	5
a lot	somewhat	a little	not at all	don't know

13) How much do you agree with this statement ?

**“The doctor is the best person to make the final decision”**

1	2	3	4	5
strongly agree	agree	neither agree or disagree	disagree	strongly disagree

## APPENDIX XVI

### FOLLOW-UP INTERVIEW QUESTIONS

1.

Did you know anything about clinical trials before we approached you?  
What were your opinions?  
Did this study make you think about trials?  
Did this study influence your decision?

Did your opinions change when you were asked about the real trial?  
What are your opinions now?  
Looking back do you think you had any misconceptions about trials?

Was there anything that went through your mind that you dismissed as being 'silly' or not important?

2.

Do you remember the hypothetical trials we gave you?  
How did you make your decision?  
Was it different when it came to the real trial?.....How?

3.

How did you see your disease at that time?  
How did you feel about being faced with a decision like that?  
Should the patient have to decide?  
Did you feel the decision should be yours?  
Did it feel like a choice?

4.

What did the trial offer you?  
How much did you believe it would be a cure?  
What were your fears about the trial?  
Do you worry you've made the wrong decision?  
How do you predict feeling after the trial has ended what may you be thinking?

5.

Remembering yourself before the cancer, how are you different?  
How has your attitude towards life and illness changed?  
Would you volunteer for research again?

6.

Thinking about your family....  
Did you discuss the trial with them, (prompt – what was their opinion)  
Was that helpful?  
How much did they influence your decision?  
Were your opinions alike at the start?  
Did they have any misconceptions about trials?

## APPENDIX XVII

### HYPOTHETICAL TRIAL CORRELATIONS

		1	2	3	4
Spearman's rho	1 Correlation	1.000	*.372	*.404	** .549
	Coefficient				
	Sig. (2-tailed)	.	.039	.024	.001
	N	31	31	31	31
	2 Correlation	*.372	1.000	** .717	*.393
	Coefficient				
	Sig. (2-tailed)	.039	.	.000	.029
	N	31	31	31	31
	3 Correlation	*.404	** .717	1.000	*.448
	Coefficient				
	Sig. (2-tailed)	.024	.000	.	.011
	N	31	31	31	31
	4 Correlation	** .549	*.393	*.448	1.000
	Coefficient				
	Sig. (2-tailed)	.001	.029	.011	.
	N	31	31	31	31

\* Correlation is significant at the .05 level (2-tailed).

\*\* Correlation is significant at the .01 level (2-tailed).