Perspective and attitudes of patients participating in randomized trials

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FINAL APPROVAL OF SCHOLARLY PROJECT
For the Degree of Master of Science in Biomedical Sciences
Concentration in Physician Assistant Studies

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Title of Scholarly Project: Perspective and attitudes of patients participating in randomized trials

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Perspective and Attitudes of Patients Participating in Randomized Trials

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Acknowledgments

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Chapter 1

Introduction

Good health is the greatest gift that any human being can enjoy. Medicine has made tremendous progress over the years (Weatherall, 2000). This progress would not have been possible without the development of new treatment, diagnostic protocols, and drugs that are more effective (Trenius, 2000). The human genome project has opened the doors for infinite number of newer drugs to be developed (Trenius, 2000). This of course would increase the need for more animal experimentation and clinical trials (Trenius, 2000).

Increased longevity does not come without a price (WHO, 1997). The ideal vision for everyone may be to lead a physically and mentally healthy life well into old age (Illed, Wedel and Wiliielmsen, 2003). However, every year millions die prematurely or are disabled by diseases and conditions that are largely preventable (Illed, Wedel and Wiliielmsen, 2003). Longevity in itself could become a punishment as well as a boon (WHO, 1997). A large part of the price to be paid is in the currency of chronic diseases like heart disease, stroke, and cancer seen prevalent in adult and elderly population (WHO, 1997). With an increasing need to prevent and cure diseases, there is an increased need to test and compare the newer treatment regimens being developed (WHO, 1997). For some patients clinical trials offer the only hope (WHO, 1997). Yet, all too often, the very best treatment comes too late and offers too little (WHO, 1997).

The first large clinical trial was conducted in 1946, which evaluated the efficacy of streptomycin for pulmonary tuberculosis (Devereaux and Yusuf, 2003). The 1950’s saw the emergence of chemotherapeutic revolution for the treatment of cancer (Devereaux
and Yusuf, 2003). Pharmaceutical companies tried to establish their credibility by packing their advertising literature with citations of studies performed (National Institutes of Health, 2003). The first randomized controlled clinical trial for cancer patients was done in the mid-1950’s (Gehan, 1979). Since then tremendous progress has been made in the field of cancer research (Gehan, 1979). With clinical studies for breast cancer, like the Tamoxifen trial, the prevention of breast cancer is finally becoming a reality (Illed, Wedel and Wiliielmsen, 2003).

According to Meldrum (2000), we now practice evidence-based medicine. This helps to deliver quality health care and reduces the need for the use of unwanted resources thereby achieving cost control (Meldrum, 2000). The need for scientific evidence has tremendously increased the need to conduct flawless clinical trials (Meldrum, 2000). Clinical trials offer the tool to assist in making precise clinical decisions, but not to replace clinical judgment (Meldrum, 2000).

The ethical dilemma in conducting clinical trials is based on the risk-benefit ratio of the new therapy (Klein, 1979). Everyday new and more sophisticated drugs are being invented (Klein, 1979). New drugs have to go through the three classic phases of clinical study beginning with clinical pharmacology also known as Phase I of the clinical trials (National Institutes of Health, 2003). Researchers test a new drug or treatment in a small group of people (20-80) for the first time to evaluate its safety, determine a safe dosage range, and identify side effects (National Cancer Institute, 2003). Phase II is efficacy screening and role delineation (National Cancer Institute, 2003). Study drug or treatment is given to a larger group of people (100-300) to see if it is effective, and to further evaluate its safety (National Cancer Institute, 2003). Of these, Phase III is
primarily designed to answer questions of clinical efficacy (National Cancer Institute, 2003). Here the study drug or treatment is given to large groups of people (1,000-3,000) to confirm its effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow the drug or treatment to be used safely (National Institutes of Health, 2003). By identifying treatments with less morbidity, clinical trials have contributed to improving the quality of life of patients (National Institutes of Health, 2003).

Many patients participate in clinical trials thinking they might get better medical care (Cassileth, Lusk, Miller and Hurwitz, 1982). It becomes very important to assess the satisfaction of patients’ participation in a clinical trial especially when a newer therapy, which may cause pain and discomfort, is being tested (Cassileth, Lusk, Miller and Hurwitz, 1982).

According to Grimes and Schulz (2002), randomized clinical trials have become the gold standard, to avoid bias in the study. Patients generally are not aware of the treatment regimen they are assigned (Grimes and Schulz, 2002). It sometimes could be very frustrating, not knowing if you are on actual medication or just a placebo (Grimes and Schulz, 2002). Many times the researcher does not know the drug that is being offered to his or her patient, as all drugs tested or compared might be designed to look the same in a double blinded, placebo controlled clinical trial (Grimes and Schulz, 2002).

A randomized clinical trial is a relatively new tool and results reflect the average patient in the trial group (Yusuf and Devereaux, 2003). Patient satisfaction in a clinical trial is important, as they become advocates for future clinical trials (Yusuf and
Devereaux, 2003). Before participating in the trial a realistic view should be given, about what the trial could mean to them and to their health (Yusuf and Devereaux, 2003).

There is a lack of knowledge about patient’s attitudes, perspective, and their experiences in clinical trial participation. This study aims at the hypothesis that, there is no change in attitudes and perspective of subjects participating in randomized trials based on age, gender, annual income, and education level.
Chapter 2

Review of literature

Need for clinical trials

With the increasing need for more precise diagnostic, prognostic, and therapeutic methods, the design and conduct of clinical trials has vastly improved (Illed, Wedel, and Wiliielmsen, 2003). This has coincided with the need for so-called evidence-based medicine (Meldrum, 2000). Clinical research, until about 50 years ago was mainly based on observational and epidemiological methods (Illed, Wedel, and Wiliielmsen, 2003). According to Doll (1998), tremendous progress has been made in areas of conducting clinical trials since 1948. Before clinical trials, there were no set standards of care (Doll, 1998). Treatment for a specific disease varied from one textbook to another (Doll, 1998).

Fifty years ago, the trial of streptomycin in patients with pulmonary tuberculosis, published by the British Medical Research Council heralded the arrival of the randomized clinical trial into medical research (Medical Research Council, 1948). The 1950’s saw the emergence of chemotherapeutic revolution for the treatment of cancer (Devereaux and Yusuf, 2003). The first randomized clinical trial was conducted in the area of infectious diseases and then was expanded to preventive interventions (Gehan, 1979). This increased the need for larger clinical trials (Gehan, 1979). The polio vaccine trial randomized more than 400,000 children to active vaccine or placebo (Meldrum, 2000). In the last 20 years, changes in the design and outcome of clinical trials have seen a shift away from small trials towards larger simple ones (Hulley, Grady, and Bush 1998). The last two decades have seen exponential growth in the use of randomized
clinical trial in medical research (Sackett and Hoey, 2000). By 1998, more than 5000 reports of clinical trials was being published each year, and that figure increased to more than 12,000 a decade later (Sackett and Hoey, 2000). Now, more than 200 clinical trials are being published every week (Sackett and Hoey, 2000). These trials address important questions on reducing mortality, morbidity and major clinical outcomes (Yusuf, Collons, and Peto, 1984).

Demand for effective and high quality performance is a challenge for scientists, hospitals, pharmaceutical companies, authorities and finally the society has increased the need for larger and more effective clinical trials (Iiled, Wedel, and Wilielmsen, 2003). Tripathy (2003) stated the need for several modalities and areas of expertise for optimal patient management. The only way for overcoming barriers to multidisciplinary care should include incentives for collaborative and coordinated clinical trials across various disciplines (Sidney, Petitti, and Quesenberry, 1997). Tripathy also stated that the basis for medical decisions and recommendations, which must reflect outcomes and clinical trials, should be designed and interpreted with broad input (Tripathy, 2003).

Evidence based medicine should be used to help patients make informed decisions (Doll, 1998). Standardized treatments now used for various conditions like myocardial infarction and stroke would not have been possible without randomized clinical trials (Doll, 1998). According to Kunz and Oxman (1998), considerable differences were observed in treatment when results of high quality studies were compared with those of low quality studies in the context of systematic reviews of specific healthcare. The cardiac suppression trial (1989) showed that mortality increased in spite of treating patients with anti-arrhythmic drugs. Similarly, Stampfer,
and Colditz (1991), showed that women fared better on treatment with estrogen drugs than those who were not on estrogen. However, later large-scale trials were not able to confirm these results and showed risks of important side effects (Heckbert, Kaplan and Weiss, 2001).

Medical progress requires well-designed and carefully conducted clinical trials (Heckbert, Kaplan and Weiss, 2001). Such trials hasten the introduction of truly beneficial therapies and prevent the misuse of non-beneficial therapies (Kodish, Lantos and Siegler, 1990). Randomized controlled trials are, in most cases, the type of clinical trial that is most likely to yield reliable and reproducible clinical knowledge quickly and efficiently (Kodish, Lantos and Siegler, 1990).

According to (Kodish, Lantos and Siegler, 1990) randomized clinical trials are difficult to carry out and often, patient or physician preferences for one treatment over another leads to inadequate enrollment or nonrandom selection of patient population. Randomized clinical trials, unfortunately, are difficult to design well and if poorly designed, may generate misleading results (Sidney, Petitti, and Quesenberry, 1997). Randomized clinical trials arose in an era when patient autonomy was not widely respected or encouraged (Sidney, Petitti, and Quesenberry, 1997). Medical paternalism is less acceptable today and medical research is now accepted and supported by both patients and physicians (Kodish, Lantos, and Siegler, 1990).

*Problems in recruiting patients in a trial*

Historically, clinicians have experienced problems in terms of attaining adequate recruitment to clinical trials (Albercht, Blanchard, Ruckdeschel and Strongbow, 1999). Many studies have tried to identify the issues surrounding motivations for clinical trial
participation in healthy volunteers and patients (Richardson, Post-White, Singletary and Justice, 1998). National Cancer Institute (NCI) have publicly stated that cancer clinical trials represent the standard of care for the cancer patient and should be viewed as the treatment of choice for most stages of the various types of cancer (Gelber and Goldhirssch, 1988). According to Wittes and Friedman (1988), of the seven million patients diagnosed with cancer each year, only 25,000 are entered into a NCI approved study.

According to Taylor, Shapiro and Sosklone (1987), a physician’s refusal to enroll patients in a trial is the single most important factor in low protocol participation and it accounted for 52% of all failures to enroll eligible patients (Martin, Henderson & Zacharski, 1984). Physician’s refusals outnumber patient refusals by a margin of two to one (Martin, Henderson & Zacharski, 1984). A survey study of ninety-four principal investigators of the National Surgical Adjuvant Breast and Bowel Project (NSBAP), showed that physicians were not entering eligible patients into trial, because of, doctor-patient relationship in a randomized trial, concerns about informed consent, and physician’s reluctance to discuss openly their uncertainty about the correct treatment (Taylor, Margolese and Sosklone, 1984). Benson, Prokop, Bean, Rademaker, Eshler and Anderson (1991), surveyed 437 physician members of the Illinois Cancer Center (ICC) and found that over 50% of physicians exclude patients from clinical trials based on age. A high percentage of cancer patients are elderly and this reduces their chance of getting the latest treatment for their current condition (Benson, Prokop, Bean, Rademaker, Eshler and Anderson, 1991).
In phase I and II anticancer drug trials, patients enter with intentions of not wanting to give up, to help other cancer patients, or to have some one to talk to about the emotional burden (Rubens, Toulson & Ramirez, 1992). Cox and McGarry (2003) state that nonparticipation in clinical trials can arise due to many reasons such as patients choosing not to participate, clinicians choosing not to enter, physicians not offering their patients trial involvement, lack of knowledge on the part of both patients and clinicians about the trials available or patients not meeting the trials eligibility criteria.

According to Collyar (2000), despite the fundamental role of clinical trials in the development of treatment and care in the cancer field, accrual remains low. In the United States, it is reported that the accrual for adult cancer is approximately 2 to 3 percent (Collyar, 2000). Providing patients with adequate information and the method in which the information is presented, is a key component in the decision making process (Huizanga, Sleijfer, Van de Wiel and Van de Graff, 1999). This is key from a personal perspective and to enable the individual to make an informed decision (Huizanga, Sleijfer, Van de Wiel and Van de Graff, 1999).

The clinician-patient relationship could be quite complex and has been recognized as an important barrier in initial trial consultation and the intervention process (Cox, 2000). In addition, Cox (2000) considers it a crucial step in the recruitment process. Physicians may be concerned that enrollment in a clinical trial may interfere with the doctor-patient relationship and therefore do not raise trial involvement with their clients (Swaka and Pritchard, 2001). Klabunde, Springer, Butler, White and Atkins (1999) in their study for factors influencing enrollment in a cancer clinical trial,
identified that patients were more likely to enroll if they had been evaluated at an academic medical center rather than a Community Clinical Oncology Programme (CCOP).

Clinical trial participation could burden the individual with many factors that relate to practical issues like time, work schedule, transportation, duration of the trial, lack of interest and other commitments. (Hudman, Stolzfus, Chamberlain, Lorimor, Steinbach et al., 1996). Some key influences in relation to non-participation include; discomfort from medical procedure, objection to randomization process, subjective experience of feeling unwell, anger at medical staff, wanting to forget illness, conflict with religious beliefs, adverse effects of treatment, the impact upon patients’ lives and lack of participation in the decision-making process (Cox and McGarry, 2003).

Jordhoy, Kassa, Fayers, Overness, Underland and Ahlner-Elmqvist (1999), reports participant compliance and active withdrawal as an important issue in the clinical trial process. Patient’s withdrawal may be clinician led or patient led and there may be quite distinct differences in terms of both patient experiences, resultant consequences for support, and the adequate recognition of patient needs following withdrawal (Cunny and Miller 1994).

Historically, in general there has been a marked under representation among ethnic minority groups in clinical trials (Roberson, 1994). The Tuskegee study, undertaken in the United States between 1932 and 1972, provides a clear explanation for the enduring culture of mistrust found to exist between researchers and ethnic minority groups (Roberson, 1994). Freimuth, Quinn, Thomas, Cole, Zook, and Duncan (2001) have extensively explored the impact of this study on subsequent recruitment to
research studies among African Americans. Psilidis, Flach and Padberg (1997) have highlighted the value of ‘participant advisors’ as a way of confronting and overcoming some of the barriers to trial participation, including issues relating to mistrust of clinicians and cultural considerations.

Another barrier to recruitment of trial participants is individual’s negative perceptions of the clinical trial process. For example, consequences of media coverage of ‘trial scandals’ and views regarding the underlying motivations of clinicians may discourage potential trial participants (Madsen, Holm, Davidsen, Munkholm, Sclichting and Riis, 2000). In addition, patients also identified being concerned about commercially driven motives for trials. For example, the part of the sponsoring pharmaceutical company and doctors seeking personal benefits (Mead and Williams, 1991). It is necessary to understand the barriers surrounding the decision-making processes of trial participants (Shavers-Hornaday, Lynch, Burmeister and Torner, 1997). This understanding will make recruitment procedures effective and will ensure that the research community provides adequate structures to give information and support to potential trial participants (Shavers-Hornaday, Lynch, Burmeister and Torner, 1997).

Ethical aspects of clinical trial

Research on human subjects is highly privileged and leads to ethical questions. Physicians doing randomized trials must admit that the best treatment for the individual’s disease is not yet known (Kardinal, 1994). Sometimes it is argued that participants may be called to sacrifice their own best interest for the sake of future patients (Edwards, Lilford & Hewison, 1998). According to Grady (1991), clinical trials are considered as the final step in the process of gaining usable knowledge, a meeting
place of medicine and clinical research. As a result, ethical issues need consideration (Grady, 1991). Many researches believe that informed consent makes clinical research ethical (Vanderpool, 1996). It is probably the only tool researchers in United States, bioethicists and Institutional Review Board (IRB) will offer (Vanderpool, 1996).

According to Dal-Re (1992), the concept that informed consent should always be obtained from competent patients was widely, though not universally, accepted.

In a study by Williams and Zwiter (1994); Taylor and Kelner (1987), one in five doctors regularly entered competent patients in trials even without obtaining informed consent. Taylor and Kelner (1987) also reported that, an astonishing 47% of doctors who took part in their study responded that few patients taking part in a multi-national study knew they were taking part in a controlled experiment, even though they had given written consent. To provide informed consent, participants in a clinical trial must be given accurate information about the purpose, methods, risks, benefits, and alternatives to the research (Grisso and Applebaum, 1998). They must understand the above and its bearing on their own clinical situation, and to make voluntary decision whether or not to participate would be appropriate (Grisso and Applebaum, 1998).

Informed consent should include the need to respect persons and their autonomous decisions (Dworkin, 1988). Buchanan (1992) states that children and adults with diminished mental capacity who are unable to make their own decisions participating in research also have interests and values. Showing respect for these non-autonomous persons mean, that research participation is consistent with their interests and values (Buchanan, 1992). This usually requires a proxy decision maker to determine whether to enroll the person in clinical research or not (Buchanan, 1992). Buchanan (1992), also
state that proxies should use great caution in making decisions about a subject’s best interest regarding research.

Edwards, Lilford and Hewison, (1998) state that, a substantial proportion of 58% of doctors from the United Kingdom and Eastern Europe gave all information that was pertinent to the study before the subjects decide to participate. Kardinal (1994) states that, patients with advanced cancer participate in trials mainly with three motivating factors. They hope that the new treatment will offer a better chance for controlling disease (Kardinal, 1994). Altruism, that even if the treatment did not help them as an individual it might ultimately help others (Kardinal, 1994). Thereby, trust that the physician would not recommend that the patient enter investigational therapy unless he thought it might be helpful (Kardinal, 1994). By placing some people at risk of harm for the good of others, clinical research has the potential for exploitation of human subjects (DeCastro, 1995).

Levine (1988) notes that, ethical requirements for clinical research aim to minimize the possibility of exploitation by ensuring that research subjects are not merely used but are treated with respect while they contribute to the social good. For the past 50 years, the main sources of guidance on the ethical conduct of clinical research have been the Nuremberg Code, Declaration of Helsinki, Belmont Report, and International Ethical Guidelines for Biomedical Research Involving Human subjects and similar documents (Levine, 1994). However, many of these documents were written in response to events and to avoid future scandals (Vanderpool, 1996).

According to The Nuremberg Code (1996), to be ethical, clinical research must be valuable. This means that it evaluates a diagnostic or therapeutic intervention that
could lead to improvements in health or well-being (The Nuremberg Code, 1996). For a clinical research, protocol to be ethical the methods must be valid and practically feasible research must have a clear scientific objective (Schain, 1994). Clinical research must be designed using accepted principles, reliable methods. Have sufficient power to definitively test the objective, and offer a data analysis plan. In addition, it must be possible to execute the proposed study (Kodish, Lantos and Siegler, 1989).

Schain (1996), states for selecting subjects, the study should follow specific inclusion and exclusion criteria. Strategies need to be adopted for recruiting subjects such as, which communities will be included and how they will be approached. When clinical research involves drugs, devices, and procedures about which there is limited knowledge, it needs to fulfill three conditions for research to be justified (World Medical Association, 1997). Firstly, it should eliminate if not minimize any potential risks to individual subjects (World Medical Association, 1997). Secondly, it should ensure enhancement to the potential benefits to individuals (World Medical Association, 1997). Finally, the potential benefits to individual subjects and society are proportional to the risks involved (World Medical Association, 1997).

Weijer, Shapiro, Fuks, Glass and Skrutkowska (1995) state that, ethical requirements for clinical research do not end when subjects sign the consent form for participation. Subjects should be treated with respect from the time they are approached for trial participation, even if they refuse enrollment, throughout their participation and even after trial ends (Ezekiel, Emanel, Wendler and Grady, 2000). Participants need to be updated with new information and any new risks that develop during the course of the trial (Ezekiel, Emanel, Wendler and Grady, 2000). In addition, if they develop any
adverse reaction or any untoward events, they should be treated appropriately (Ezekiel, Emanuel, Wendler and Grady, 2000).

According to Miller, Emanuel, Rosenstein and Straus (2004) ethical requirements must emphasize that clinical investigators be skilled in the appropriate methods, statistical tests, outcome measures, and other scientific aspects of clinical trials. Requirements for ethics in clinical research are constantly changing and they should be revised, reinterpreted and refined (Miller, Emanuel, Rosenstein and Straus, 2004). All requirements must be considered and met to ensure that clinical research is ethical, wherever and whenever practiced (Miller, Emanuel, Rosenstein and Straus, 2004).

Clinical trials to clinical practice

Stroms (2003) states that many treatments are based on trial outcomes and there are several factors that need to be considered before the trial results could be applied to the public. The trial outcome in individual patients may not relate to the trials exclusion and inclusion criteria, adherence to therapy in trials, endpoints used in the trials compared to those used in practice, publication and finally reporting of data (Stroms, 2003).

The primary goal of clinical trials is evaluation of the efficacy of the drug, which should be related to real-life effectiveness (Spahn, 2003). Tonkin (1998) states that, large standardized databases are necessary to assess clinical practices and outcome. Assessment of clinical outcomes depends on interplay between the structure and process of care, patient factor, and chance (Tonkin, 1998).

Bastian (1998) states that, it can be difficult to convert the results of trials into information that is meaningful for individuals, and results are often equivocal or vary
from trial to trial (Bastian, 1998). This is true in regards to the research on mammography. Early detection has been put forward as the best cure (Bastian, 1998). Every woman has been asked to examine their breasts regularly, regardless of their age (Bastian, 1998). One study by Langlands (1996) even claims that having babies before the age of 20 or less lowers the risk of breast cancer. This seems like a promotion of pregnancy among teenagers (Langlands, 1996).

According to Storms (2003), many clinicians base their treatment choices on trial outcomes. Several factors like exclusion and inclusion criteria, adherence to therapy and endpoints used in trials need to be considered before applying the trial results to public (Stroms, 2003). Stroms also adds that, performance and publication of clinical trials can be affected by investigator or publication bias (Stroms, 2003).

Recommendations for clinicians include a careful differentiation of results obtained in different phases of clinical trials and a clear appreciation of the different purposes of those trials (Seeman, 2001). Clinicians should also appreciate that short-term effectiveness is not the same as long-term outcome and that aggregate scores may not apply to individual patients (Seeman, 2001).

Good clinical practice requires researchers to report serious adverse events to clinical trial sponsors, who then have the responsibility to notify all the study investigators or trial sites of these events (Liauw & O Day, 2003). Brady (1998) reported that trials with positive outcome resulted more often in submission of final reports to regulatory authority than those with inconclusive or negative outcomes.

Tonkin (1998) states that, assessment of clinical outcomes depends on interplay between the structure and process of care, patient factors, and chance. Large
standardized databases are necessary to assess clinical practice and outcomes (Tonkin, 1998). Rubins (1994) adds that, practicing clinicians often overestimate the benefits of a therapy and generalize the results of a trial broadly. Ideally, physicians should base treatment decisions on their knowledge of the pathophysiology of disease, the mechanism of action of the proposed treatment, and the clinical characteristics of the individual patient while informing their decision with a critical understanding of the results of relevant trials (Tonkin, 1998).

**Future of clinical trials**

Diagnostic and therapeutic technology is continuing to advance rapidly (Califf, 2003). As we experience unparalleled medical advances, we also face a future in which the balance between our increasing understanding of complex biology and an only rudimentary understanding of clinical evidence and therapeutics impedes our ability to deliver benefits to patients (Califf, 2003).

According to Styring and Jonas (1999), our growing elderly population is more highly educated than past elderly populations and expects a higher level of medical care. At the same time, the dramatic change in the ratio of workers producing resources to pay for medical care to those consuming such resources has not been anticipated (Styring and Jonas, 1999). In the United States alone, this ratio will decline from 4:1 to 2:1 over the next 30 years (Styring and Jonas, 1999).

A relative improvement in the range of 25% are considered outstanding in most areas of therapeutics, and for survival, benefits of 10-15% on a relative scale are considered worthwhile (DeMets and Califf, 2002). Califf and DeMets (2002) also add that, type II error occur when a trial is not large enough to detect the true effect of
treatment, and the study erroneously concludes that there is no difference between the
treatment and control groups. Even though this issue has been addressed for
randomized trials, many negative observational studies continue to have this problem
(DeMets and Califf, 2002).

Califf (2003) also state that to conduct large trials, extensive networks of
investigators are needed and this could be achieved in the future by including vast
numbers of practitioners organized into networks so that trials can be performed rapidly.
In addition, somewhere in the near future, the Internet will offer an efficient mechanism
to allow people with particular diseases to volunteer for participation in clinical trials
(Califf, 2003).

Most clinical trials are based on outcomes on short time frame (Califf, 2003).
Many years of preventive therapy also brings the issue of long-term risks (Califf, 2003).
Future clinical trials need to measure outcomes for relevant and longer period of
treatment (Hamton, 2000). The internet again is likely to offer a great tool for accurate
and less expensive means for long-term follow-up (Califf, 2003).

According to Califf (2003), to meet the demands, future clinical trials must move
into a new era of maturity in which the approach to the prevention, diagnosis, and
treatment of disease is seen as a partnership that is not separate from the practice of
medicine, but represents the ‘state of the art’.
Chapter 3

Methods

Selection of subjects

Subjects who qualified to participate in the study were currently involved in a randomized clinical or surgical trial and were over eighteen years of age. Usually in a randomized double-blinded clinical trial, neither the physician nor the patients are aware of the medication that they will be required to take. They could be on an experimental drug or surgical procedure or even on a placebo. This creates a lot of uncertainty and anxiousness among the subjects participating in a randomized trial. Therefore, the criteria to study the attitudes and perspective of patients who are currently involved in a pharmaceutical or surgical trial was selected. No gender preferences were included. The study mainly focused on patients involved in outpatient clinical trial settings.

Subjects who have previously participated in any type of clinical study and are currently on any trial, also qualified to participate in the study. The independent variable will be the questions intended to study the patient’s attitudes, knowledge, and perspective of a clinical trial. Dependent variable will be the data obtained. The intervening variables include not telling the truth, choosing not to reply to the questions, or letting their friends or family complete the questionnaire. Subjects who fulfilled these criteria were selected on a basis of convenience sampling to complete the survey.

Identification of Principal Investigators

Principal investigators (PI) involved in clinical or surgical trials, at MCO were identified using the institutions official website. The website provided information about various trials that were being conducted and PI’s involved in each study. A letter
approved by Institutional Review Board (IRB) was sent to the PI’s identified (Appendix-A). The letter explained the purpose of the current study and requested their participation. Twelve letters were sent to PI’s involved in various randomized trials. Of which, four PI’s agreed to participate in this study. They were from the department of Oncology, Cardiology and Surgery.

*Study tool*

A questionnaire was designed to elicit information pertinent to the study. The study tool developed by Madsen, Holm, Davidson, Munkholm, Schlichting and Riis (2000), was modified to suit the requirements of this study (Appendix B). Their study tool included nineteen questions, of which, two were eliminated, and five more questions were added to make it pertinent to this study. It included a number of questions printed or typed in a definite order or form. Questions were aimed at collecting information on subjects’ previous trial participation and opinions regarding participation. Questions focusing on subjects attitudes towards medical research, their view of being randomized (drawing lots) and blinding treatments were also included. Different reasons for consenting to participation were also found. Finally, the subject’s evaluation of participating in their current trial and their possible future participation was also elicited. Most of the questions were multiple-choice forms, but some questions provided opportunity to add free text. Before the questionnaire was distributed to the study subjects, it was tested for validity and reliability. A pilot testing was done by the faculty of the department of physician assistant studies at Medical College of Ohio. Their suggestions were also included to make up the final format of the questionnaire.
Consent for participation

All questionnaires had a letter attached to them, which requested the subject’s volunteer participation in the study and assured them that their non-participation will not affect their current treatment or relationship with their physician (Appendix C). Subjects were also informed that all information that was being shared would be kept confidential. The letter also included instruction on filling out the questionnaire. A self-addressed stamped mailing envelope was included with only the author’s address on the envelope.

Approval by the Institutional Review Board

The study proposal along with all the required forms was submitted to the Medical College of Ohio review board for approval (Appendix D). IRB discouraged the student investigator from contacting the study subjects to ensure maintenance of their anonymity and to adhere to HIPPA regulations. IRB recommended that the questionnaires be distributed by the respective PI's or their research coordinators. The study was approved without any modifications.

Data collection

The questionnaires were given to the PI’s for distribution among the subjects who were involved in their respective randomized clinical or surgical trials. Principal Investigators or research coordinators handed out the surveys to their study subject when they came in for an office visit. Volunteer participation was offered to all the selected subjects. Questionnaires were distributed for a period of four weeks in the month of April 2004. After completing the questionnaires, subjects were asked to seal their responses in the given envelope. Subjects had a choice of mailing their
questionnaires to the author directly or returning the sealed envelope to the respective PI's or research coordinator.

Forty questionnaires were distributed to the subjects, who participated in various clinical trials by the principal investigator or their research coordinators. Thirty-one (n=31) completed questionnaires were mailed back to the student investigator via the envelope that was provided to the subjects. None of the subjects, who participated in the study, chose to return the completed surveys back to the PI's office. All returned surveys were kept locked in the office of the study major advisor.

All the data obtained was compiled using MS-Excel 2000. Appropriate statistical analysis was performed using SPSS 11.5. The alphanumeric value was considered statistically significant if it was lesser than or equal to 0.05.
Chapter 4

Results

Descriptive statistics and Chi square tests were performed using SPSS 11.5. Statistical significance was based on a p value less than or equal to an alpha level of 0.05.

General Information about the study subjects

Thirty-one (n=31) subjects participating in various randomized clinical and surgical trials completed the survey. The majority of subjects, 41.9% (n=13) were in the age group of 71 and above. Subjects in the age group of 61 to 70 accounted for 25.8% (n=8), 51 to 60 were 22.6% (n=7) and 9.7% (n=3) were in the age group of 41 to 50. There were no subjects in age group of 18 to 30 or 31 to 40. Female subjects accounted for 67.7% (n=21) of all the participating subjects and the remainder of 32.3% (n=10) were males. Approximately 52% (n=16) were college graduates and 36% (n=11) were high school graduates. Only 13% (n=4) had some college education. There were no subjects with only some schooling. Thirty responses were received when subjects were asked about their annual family income. It was seen that 35.5% (n=11) had an annual family income between 51,000 and 100,000. Subjects having a family income between 31,000 and 50,000 accounted for 22.6% (n=7). Family income between 11,000 and 30,000 accounted for were 22.6% (n=7) and 12.9% had a family income greater than 100,000, with 3.2% (n=1) had an income less than 10,000 per year.
Comparing subject’s thoughts on medical research based on their age, gender, educational qualification, and family income

Subjects were asked their thoughts on medical research. Based on age, 80.6% (n=25) of all the participants stated that they felt positive about medical research and clinical trials. Of this, 87.5% (n=7) were in the age group of 61 to 70 and 85.7% (n=6) were in the age group of 51 to 60. In addition, subjects in the age group of 71 and above who felt very positive about medical research accounted for 76.9% (n=10). About 12.9% (n=4) of all the subjects stated that their opinion changes from time to time and only 6.5% (n=2) had no opinion at all. The results were not statistically significant (p=0.546) even though, 80.6% (n=21) of all the subjects felt very positive about medical research based on age. On comparing the same question based on gender, 90.5% (n=19) of all the females and 60.0% (n=6) of the males, felt very positive about medical research. The remaining 12.9% (n=4), both male and females stated that their opinion changed from time to time. The results were not statistically significant (p=0.110) since the p value is greater than .05. Comparing the subject’s opinion on medical research based on their educational qualification, 81.8% (n=9) of the subjects who were high school graduates, 81.3% (n=13) who were college graduates, and 75.0% (n=3) who had some college education, felt very positive about medical research. Results were not statistically significant based on p value of 0.913. Based on subjects annual income, 90.9% (n=10) of the subjects with income ranging between $51,000 and $100,000 and 85.7% (n=6) with an annual income between $31,000 and $50,000 felt very positive about medical research. No statistically significant difference was noted based on annual family income (p=0.443).
When subjects were asked if it was important to test new drugs and medical procedures before they become available to the public, based on age, 80.6% (n=25) of all the participants felt it was necessary to test new drugs and procedures. All subjects in the age group of 61 to 70 (n=8) and 41 to 50 (n=3) wanted drugs and procedures to be tested before it became available to the public. No statistically significant difference was noted in this comparison (p=0.327). Comparing the subjects response based on gender, a majority of both males and females (80.6%) wanted drugs and procedures to be tested before they became available to the public. Only three (14.3%) female subjects felt that it was not necessary to test drug and procedures, if they were relatively safe. The results were not statistically significant (p= 0.217).
Table 1

Opinion on Medical Research based on Educational Qualification

<table>
<thead>
<tr>
<th>Educational Qualifications</th>
<th>HS Graduate</th>
<th>Some College</th>
<th>College Graduate</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>% within Educational Qualifications</td>
<td>54.5%</td>
<td>75.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>n</td>
<td>6</td>
<td>3</td>
<td>16</td>
<td>25</td>
</tr>
<tr>
<td>Important</td>
<td>6</td>
<td>3</td>
<td>16</td>
<td>25</td>
</tr>
<tr>
<td>If Safe?</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Opinion Changes</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>3</td>
</tr>
</tbody>
</table>

Chi-Square Tests

<table>
<thead>
<tr>
<th>Value</th>
<th>df</th>
<th>Asymp. Sig. (2-sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson Chi-Square</td>
<td>10.484a</td>
<td>4</td>
</tr>
<tr>
<td>Likelihood Ratio</td>
<td>12.393</td>
<td>4</td>
</tr>
<tr>
<td>Linear-by-Linear Association</td>
<td>5.402</td>
<td>1</td>
</tr>
</tbody>
</table>

a. 7 cells (77.8%) have expected count less than 5.

The minimum expected count is .39.

Table 1 depicts the need to test new drugs and procedures based on subject’s educational qualification. All subjects (n=16) who were college graduates wanted testing to be done before the drugs and procedures are made available to humans. Among the eleven subjects with a high school diploma, 54.5% (n=6) thought it was important to test
drugs and procedures. In the same category, three subjects (27.3%) also felt that if the
drug or procedure is considerably safe it need not be tested and 18.2% (n=2) thought
that their opinion changed from time to time. The results are statistically significant
(p=0.033) based on education.

Based on family income, all subjects with an annual income between $51,000
and $100,000 (n=11) and income greater than $100,000 (n=4) thought it was important
to test new drugs and procedures. No statistically significant difference was noted
(p=0.241).

Subject’s previous trial participation

Six (19.4%) subjects had previously taken part in a clinical trial. Of which, five
(23.8%) were females and one (10.0%) was a male. Of which, three (42.9%) were in the
age group of 51 to 60 and three (23.1%) were in the age group of 71 and above.

Subject’s thoughts on how previous trial participation had changed their attitude
towards clinical trials, had to be omitted, due to lack of proper instruction on the
questionnaire. The question was aimed only towards subjects who had previously
participated in clinical trials. This instruction was not given on the questionnaire. As a
result, all subjects answered the question making it invalid for any statistical analysis.

Comparing subject’s thoughts on randomization and blinding of treatment based on
age, gender, educational qualification, and annual family income

When subjects where asked their opinion on being chosen by a computer
(randomization) to receive a particular treatment, based on age a total of 38.7% (n=12)
of all the participants felt positive. Of which, 53.8% (n=7) were in the age group 71 and
above, 50.0% (n=4) were in the age group of 61 to 70 and 14.3% (n=1) were in the age
group of 51 to 60. Five subjects (71.4%) in the age group of 51 to 60 and 38.5% (n=5) in the age group of 71 and above did not know how they felt about being randomized. The results were not statistically significant (p=0.122). Based on gender, 45.2% (n=14) of the participants did not know how they felt being randomized to receive the treatment. Of which, 60.0% (n=6) were males and 38.1% (n=8) were females. Five subjects (16.1%) felt negative about randomization, and four (19.0%) were females and one (10.0%) was a male. Nine females (42.9%) and three males (30.0%) felt positive about being chosen by computer to receive the treatment. No statistically significant difference was noted in this comparison (p=0.508). Among the participating subjects, 45.2% (n=14) did not know how they felt about randomization based on educational qualification. In this group, eight subjects (72.7%) were high school graduates. Twelve subjects (38.7%) felt positive about randomization and among them, 50.0% (n=8) were college graduates. Only 16.1% (n=5) felt negative of which, three (18.8%) were college graduates and two (50.0%) subjects had some college education. The results were not statistically significant (p=0.070) based on educational qualification. Opinions based on family income showed that 46.7% (n=14) of all participants felt negative about being randomized. In this group, six subjects (85.7%) were in the income range of $31,000 to $50,000 and four subjects (57.1%) were earning incomes between $11,000 and $30,000. Five subjects (16.7%) felt negative by the process of randomization, of which, three subjects (27.3%) were in the income range of $51,000 and $100,000. Subjects who felt positive about being randomized accounted for 36.7% (n=11). In this group, seven subjects (63.6%) earned income in the range of $51,000 to $100,000. Comparison shows no statistically significant difference (p=0.070).
Subjects (n=31) thoughts on how they felt not knowing the medicine or treatment (blinding) they received during clinical trials was compared with age, gender, educational qualification and annual family income. Table 2 depicts based on age, subjects thoughts on blinding the treatment during clinical trial.

Table 2
Opinion on Blinding of Treatment

<table>
<thead>
<tr>
<th>Age</th>
<th>Positive</th>
<th>Negative</th>
<th>Don’t know</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>41-50</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>% within Age</td>
<td>.0%</td>
<td>33.3%</td>
<td>66.7%</td>
<td>100.0%</td>
</tr>
<tr>
<td>51-60</td>
<td>0</td>
<td>3</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>% within Age</td>
<td>.0%</td>
<td>42.9%</td>
<td>57.1%</td>
<td>100.0%</td>
</tr>
<tr>
<td>61-70</td>
<td>5</td>
<td>1</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>% within Age</td>
<td>62.5%</td>
<td>12.5%</td>
<td>25.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>71 and Above</td>
<td>3</td>
<td>3</td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td>% within Age</td>
<td>25.0%</td>
<td>25.0%</td>
<td>50.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>Total</td>
<td>8</td>
<td>8</td>
<td>14</td>
<td>30</td>
</tr>
<tr>
<td>% within Age</td>
<td>26.7%</td>
<td>26.7%</td>
<td>46.7%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Chi-Square Tests

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
<th>df</th>
<th>Asymp. Sig. (2-sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson Chi-Square</td>
<td>9.139a</td>
<td>6</td>
<td>.166</td>
</tr>
<tr>
<td>Likelihood Ratio</td>
<td>10.899</td>
<td>6</td>
<td>.092</td>
</tr>
<tr>
<td>Linear-by-Linear Association</td>
<td>1.037</td>
<td>1</td>
<td>.308</td>
</tr>
<tr>
<td>No. of Valid Cases</td>
<td>30</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a. 11 cells (91.7%) have expected count less than 5. The minimum expected count is .80.

An equal number of subjects (26.7%) felt both positive and negative about blinding the treatment. Five subjects (62.5%) who felt positive were in the age group of 61 to 70 and three subjects (25.0%) were in the age group of 71 and above. A majority
of the subjects who felt negative about blinding the treatment were in the age group of 51 to 60 (42.9%). Fourteen (46.7%) subjects did not know how they felt about blinding the treatment they received. Of which, six (50.0%) were in the age group of 71 and above and four (57.1%) were in the age group of 51 to 60. No statistically significant difference was noted (p=0.166). When the question was compared based on gender, five (25.0%) females and three males (50.0%) felt positive about the process of blinding. An equal number of males and females felt negative about not knowing the treatment they received. A majority of 46.7% (n=14) of all the subjects did not know how they felt about the process of blinding. This group included 10 (50.0%) females and 4 (40.0%) males. Comparison shows that the results were not statistically significant (p=0.875). Based on educational qualification an equal number of 26.7% (n=8) of the overall participants, felt positive and negative about the process of blinding. College graduates who felt positive accounted for 36.5% (n=6) and around 31% (n=5) felt negative being randomized. Fourteen subjects (46.7%) did not know how they felt about the whole process. In this majority of subjects, around 70% (n=7) were high school graduates. No statistically significant difference was noted (p=0.401). Comparing the same question on how subjects felt about being blinded based on annual family income, around 44.8% (n=13) of all the participating subjects did not know how they felt about it. In this, six subjects (85.7%) had an annual family income between $31,000 and $50,000. Five (45.5%) with an annual family income of $51,000 to $100,000 felt positive and three (27.3%) participants in the same category felt negative about being blinded to receive the treatment. The results were not statistically significant (p=0.196).
Comparing subject’s reasons for trial participation based on age, gender, educational qualification, and annual family income

When subjects were asked if they took part in the trial because they wanted to be closely monitored by doctors and nurses, based on age, 45.2% of all the participating subjects felt it was a very important reason for their trial participation. In this, seven subjects (53.8%) were in the age group of 71 and above and four subjects (57.1%) were in the age group of 51 to 60. Three subjects (37.5%) in the age group of 61 to 70 and one subject (33.3%) in the age group of 41 to 50 felt it was not an important reason for their participation. No statistically significant difference was noted (p=0.271). Based on gender, 45.2% (n=14) of all the subjects felt it was a very important reason for their trial participation. Of which, ten (47.6%) were female subjects and four (40.0%) male subjects. Seven (33.3%) females and three (30.0%) males felt it was an important reason for trial participation. It was not an important reason for 19.0% (n=4) of the females and 30.0% (n=3) of the male participants. The results were not statistically significant (p=0.790). Making a comparison based on educational qualification, six (37.5%) subjects who were college graduates, three subjects (75.0%) who had done some college and five subjects (45.5%) who were high school graduates thought it was very important to be monitored by medical staff during their participation in the trial. Only six (37.5%), who were college graduates and one (9.1%) who was a high school graduate thought it was not an important reason for their trial participation. Comparison yielded no statistically significant difference (p=0.259). Comparing results based on annual income, six (54.5%) subjects in the income range of $51,000 to $100,000 took part in the trial, as they felt it was very important to be monitored by medical staff. Four
(57.1%) subjects in the income range of $11,000 to $30,000 thought it was an important reason for trial participation. No statistically significant difference (p=0.125) was noted on comparison.

When subjects were asked if they took part in the trial in order to try new treatment for their condition, the following results were obtained on comparison based on age, gender, educational qualification, and annual family income. When asked, 35.5% of all the participants (n=11) thought it was very important for them to try a new treatment. Of which, six (46.2%) subjects were in the age group of 71 and above. Subjects who thought it to be an important reason for their trial participation accounted for 38.7% (n=12). Five subjects (62.5%) were in the age group of 61 to 70. For eight (25.8%) subjects this was not an important reason for their trial participation. Four (30.8%) were in the age group of 71 and above, three (42.9%) were in the age group of 51 to 60 and one (12.5%) was in the age group of 61 to 70. No statistically significant difference was noted (p=0.448). Table 3 depicts subjects who wanted to try new treatment as a reason for trial participation based on gender.
Table 3
Subjects Wanting to Try New Treatment

<table>
<thead>
<tr>
<th>Gender</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>% within Gender</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>40.0%</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>20.0%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>100.0%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>33.3%</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>38.1%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>28.6%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>21</td>
<td>100.0%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>35.5%</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>38.7%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>25.85</td>
<td></td>
</tr>
<tr>
<td></td>
<td>31</td>
<td>100.0%</td>
<td></td>
</tr>
</tbody>
</table>

Chi-Square Tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>df</th>
<th>Asymp. Sig. (2-sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson Chi-Square</td>
<td>.284a</td>
<td>2</td>
<td>.868</td>
</tr>
<tr>
<td>Likelihood Ratio</td>
<td>.291</td>
<td>2</td>
<td>.864</td>
</tr>
<tr>
<td>Linear-by-Linear Association</td>
<td>.252</td>
<td>1</td>
<td>.616</td>
</tr>
<tr>
<td>No. of Valid Cases</td>
<td>31</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a. 3 cells (50.0%) have expected count less than 5. The minimum expected count is 2.58.

Four (40.0%) males and seven (33.3%) females wanted to try a new treatment as a very important reason for their trial participation. It was an important reason for eight (38.1%) females and four (40.0%) males. It was not an important reason for 20.0% (n=2) of the males and 28.6% (n=6) of the females. The results were not statistically significant (p=0.868).

Based on educational qualification, four (36.4%) subjects who were high school graduates and four (25.0%) who were college graduates, felt it to be a very important reason for their trial participation. It was not an important reason for five (31.3%)
participants who were college graduates, two (18.2%) who were high school graduates and one (25.0%) who had some college education. No statistically significant difference was seen (p=0.346).

Comparing subject’s annual income with their reason for trial participation, five (45.5%) subjects who earned an income between $51,000 and $100,000 felt it be a very important reason for trial participation. Three (75.0%) who had incomes greater than $100,000, considered it to be unimportant for their trial participation. The results were not statistically significant (p=0.428).

When subjects were asked whether they took part in the trial to help future patients their responses are documented in table 4.
Table 4
Subjects Wanting to Help Future Patients

<table>
<thead>
<tr>
<th>Age</th>
<th>Participation will help future patients</th>
<th></th>
<th></th>
<th></th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Very important</td>
<td>Important</td>
<td>Not Important</td>
<td></td>
<td></td>
</tr>
<tr>
<td>41-50</td>
<td>n</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>% within Age</td>
<td>33.3%</td>
<td>33.3%</td>
<td>33.3%</td>
<td>100.0%</td>
</tr>
<tr>
<td>51-60</td>
<td>n</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>% within Age</td>
<td>42.9%</td>
<td>42.9%</td>
<td>14.3%</td>
<td>100.0%</td>
</tr>
<tr>
<td>61-70</td>
<td>n</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>% within Age</td>
<td>71.4%</td>
<td>14.3%</td>
<td>14.3%</td>
<td>100.0%</td>
</tr>
<tr>
<td>71 and Above</td>
<td>n</td>
<td>12</td>
<td>1</td>
<td>0</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>% within Age</td>
<td>92.3%</td>
<td>7.7%</td>
<td>.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>Total</td>
<td>n</td>
<td>21</td>
<td>6</td>
<td>3</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>% within Age</td>
<td>70.0%</td>
<td>20.0%</td>
<td>10.0%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Chi-Square Tests

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
<th>df</th>
<th>Asymp. Sig. (2-sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson Chi-Square</td>
<td>8.624</td>
<td>6</td>
<td>.196</td>
</tr>
<tr>
<td>Likelihood Ratio</td>
<td>9.259</td>
<td>6</td>
<td>.160</td>
</tr>
<tr>
<td>Linear-by-Linear Association</td>
<td>6.866</td>
<td>1</td>
<td>.009</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of Valid Cases</td>
<td>30</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a. 11 cells (91.7%) have expected count less than 5. The minimum expected count is .30.

Seventy percent (n=21) of the subjects wanted to help future patients as a very important reason for their trial participation. Of this, 12 (92.3%) were in the age group of 71 and above, five (71.4%) in the age group of 61 to 70, three (42.9%) in the age group of 51 to 60 and one (33.3%) in the age group of 41 to 50. Even with seventy percent wanting to help future patients the results were not statistically significant (p=0.196). Comparing the results based on gender, for 60.0% (n=6) of the males and 75.0% (n=15) of the females it was a very important reason for trial participation. For 20.0%
(n=2) of all males and for 5.0% (n=1) of all females it was not an important reason for trial participation. No statistically significant difference was noted (p=0.424). Based on educational qualification, four (13.0%) subjects who had some college education, nine (60.0%) subjects who were college graduates and eight (72.7%) who were high school graduates it was very important to help future patients with their trial participation. Only three (20.0%) college graduates felt it was not an important reason for their trial participation. It was an important reason for three (27.3%) high school graduates and three (20.0%) college graduates. The results were not statistically significant (p=0.305). When making a comparison based on annual family income, no statistically significant difference was noted (p=0.630). For 72.7% (n=8) who have an income between $51,000 and $100,000 and 71.4% (n=4) each in the income range between $11,000 and $30,000 and $31,000 and $50,000 respectively, felt it to be a very important reason for trial participation. Subjects with income ranges between $51,000 and $100,000 accounted for 18.2% (n=2) and 25.0% (n=1) of subjects with income of greater than $100,000 felt it was unimportant to help future patients with their trial participation.

When subjects were asked if they took part in the trial to get in a good relationship with their doctor, based on age, only 30.8% (n=4) in the age group of 71 and above thought it was a very important reason for their trial participation. Six (75.0%) in the age group of 61 to 70, two (66.7%) in the age group of 41 to 50 and two (28.6%) in the age group of 51 to 60 felt it was an important reason for their trial participation. Six subjects (46.2%) in the age group of 71 and above, five (71.4%) in the age range of 51 to 60, two (25.0%) subjects in the age group of 61 to 70 and one (33.3%) in the age
group of 41 to 50 felt it was not an important reason for their trial participation. The analysis yielded no statistically significant difference \((p=0.078)\).

Table 5 depicts the subjects wanting to get in a good relationship with their doctor as a reason for trial participation based on gender.

Table 5

<table>
<thead>
<tr>
<th>Subjects Wanting to Get in a Good Relationship with Their Doctor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improve relationship with physician</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Gender</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Total</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

Chi-Square Tests

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
<th>df</th>
<th>Asymp. Sig. (2-sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson Chi-Square</td>
<td>2.990</td>
<td>2</td>
<td>.224</td>
</tr>
<tr>
<td>Likelihood Ratio</td>
<td>3.157</td>
<td>2</td>
<td>.206</td>
</tr>
<tr>
<td>Linear-by-Linear Association</td>
<td>.180</td>
<td>1</td>
<td>.672</td>
</tr>
<tr>
<td>No. of Valid Cases</td>
<td>31</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a. 4 cells (66.7%) have expected count less than 5. The minimum expected count is 1.29.

Sixty percent \((n=6)\) of male subjects and 38.8% \((n=8)\) of female subject thought it would improve relationship with their doctor by their trial participation to be an unimportant reason. However, 52.4% \((n=11)\) of the female subjects thought that they
could improve their relationship with their physician by their trial participation. The results were not statistically significant (p=0.224).

Based on educational qualifications, nine (56.3%) who were college graduates and four (36.4%) who were high school graduates thought that their trial participation would improve their relationship with their doctor was an important reason for their participation. Almost, 43.8% (n=7) of the participants who were college graduates thought that their trial participation would improve their relationship with their physician was not an important reason for their trial participation. No statistically significant difference was noted on comparison (p=0.099).

Making a comparison based on annual family income, no subjects in the income range of $51,000 to $100,000 and greater than $100,000 thought that their trial participation would improve their relationship with their physician to be a very important reason for their trial participation. For five (45.5%) subjects with an income range of $51,000 to $100,000, four (57.1%) with an income range of $31,000 to $50,000, two (50.0%) with incomes greater than $100,000 thought that their trial participation would improve their relationship with their physician was an important reason for their participation. The results were not statistically significant (p=0.243).

Subjects were asked if they participated in the trial because of their positive experience from a previous trial. Two (15.4%) subjects in the age group of 71 and above felt it was an important reason for trial participation. It was not applicable for rest of the subjects (n=29). No statistically significant difference was noted (p=0.398). Based on gender, two (9.5%) female subjects participated because of a positive experience from the previous trial. For the rest of the participants (n=29) the reason was not
applicable. The results were not statistically significant (p=0.313). Compared with educational qualification, one (9.1%) subject who was a high school graduate and one (6.3%) who was a college graduate it was an important reason for trial participation. It was not applicable for the rest of the participants. No statistically significant difference was noted on comparison (p=0.817). One (14.3%) subject with an annual family income between $11,000 and $30,000 and one (9.1%) subject with an income ranging between $51,000 and $100,000 thought that positive experience from the previous trial to be an important reason for their trial participation. The results were not statistically significant (p=0.806).

When subjects were asked if they participated in the trial, because they did not have any other immediate medical option, analysis based on age, for one subject in the age group of 61 to 70 this was a very important reason for trial participation. One (33.3%) subject in the age group of 41 to 50 and two (15.4%) in the age group of 71 and above this was an important reason for trial participation. Almost, 74.2% (n=23) of all the participants this reason was not applicable for their trial participation. A majority of the subjects (74%) choose the same answer. However, the results were not statistically significant (p=0.276).

Based on gender comparison, only one (10.0%) male subject felt not having any immediate medical option was a very important reason for his trial participation. For two (9.5%) female subjects and one (10.0%) male, not having any other immediate medical option was an important reason for trial participation. A total of 17 (81.0%) females and six (60.0%) males responded saying, not having any other immediate medical option
was not an applicable reason for their trial participation. The results were not statistically significant (p=0.380).

Comparing the results based on educational qualification, one (6.3%) subject who was a college graduate, not having any other immediate medical option was a very important reason for his trial participation. Twelve (75.0%) subjects who were also college graduates this was not an applicable reason for trial participation. For two (18.2%) high school graduates and two (12.5%) college graduates this was also not an important reason for their participation. The results obtained were not statistically significant (p=0.728).

Now making a comparison based on annual family income, one subject for whom not having any other immediate medical option was a very important reason for trial participation had an annual income between $51,000 and $100,000. For eight (72.7%) more subjects with the same annual income as above this reason was not applicable. No statistically significant difference was noted (p=0.924).

Subjects were asked if getting free trial medication was an important reason for trial participation. For one (7.7%) subject in the age group of 71 and above this was an important reason for trial participation. For the rest of the subjects (n=30) this reason was not applicable. The difference was not statistically significant (p=0.698).

Comparing based on gender, for one (10.0%) male subject this was a very important reason for trial participation. This reason was not applicable to any of the female subjects (n=21) and the remaining nine (90.0%) males subjects. No statistically significant difference was noted (p=0.141). For one (9.1%) participant who was a high school graduate, being provided with free medication was an important reason for trial
participation. It was not applicable for the rest of the participants. No statistically significant difference was noted (p=0.391). Getting free medication by participating in the trial was an important reason for one (14.3%) participating subject who had an annual income between $31,000 and $50,000. The results obtained were not statistically significant (p=0.493).

*Comparing subject’s feelings about current trial participation based on age, gender, educational qualification, and annual family income*

Table 6 depicts the various clinical or surgical trials taken part by the selected subjects.

### Table 6

<table>
<thead>
<tr>
<th>Types of Clinical/Surgical Trial Participated by Selected Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
</tr>
<tr>
<td><strong>n</strong></td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>% within Gender</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>% within Gender</td>
</tr>
<tr>
<td>Total</td>
</tr>
<tr>
<td>% within Gender</td>
</tr>
</tbody>
</table>

There were nine (32.3%) females and one (10.0%) male who were currently on a surgical trial. Three (30.0%) males were participating in a cardiovascular trial. Finally, six (60.0%) males and twelve (57.1%) females were participating in a cancer trial.

Subjects were asked if they had many questions about the trial that they wanted to ask their doctor. When the responses for this question were compared based on age, four (30.8%) subjects in the age group of 71 and above, five (71.4%) subjects in the age group of 51 to 60 and one each in the age group of 41 to 50 and 61 to 70 had many
questions to ask their doctor. Of the participants 54.8% (n=17) had one or two questions to ask their doctor. Two (15.4%) in the age group of 71 and above and one (14.3%) in the age group of 51 to 60 had no questions about the trial. The results obtained were not statistically significant (p=0.162).

Comparing the results based on gender, 50.0% (n=5) of the male participants had many questions to ask their doctor about the trial. and twelve female subjects had one or two questions about the trial. No statistically significant difference was noted (p=0.306).

Looking at the results based on educational qualification, 50.0% (n=8) of college graduates had many questions about the trial and the rest of the 50.0% (n=8) had one or two questions only. Subjects who were high school graduates, 72.7% (n=8) had one or two questions and 18.2% (n=2) had many questions about the trial. Results were statistically significant (p=0.020) on comparison based on education qualification.

Based on annual income, subjects in the income range of $51,000 to $100,000, 63.6% (n=7) had many questions and 36.4% (n=4) had only one or two questions. Six (85.7%) subjects in the income range of $31,000 to $50,000 had one or two questions and one (14.3%) subject in the same income group had no question at all. The results obtained were not statistically significant (p=0.270).

Subjects were asked if doctors gave them enough information about the trial and answered all their questions, the following responses were obtained.

Comparing responses for this question based on age, 96.8% (n=30) of the subjects responded saying they received enough information. One (12.5%) subject in the age group of 61 to 70 felt that some of his/her question remain unanswered. No
statistically significant (p=0.396) difference was noted. Based on gender, one (10.0%) male subject felt that some of his questions remain unanswered. The rest of the participating subjects (n=30) felt that all their questions were addressed adequately. The results were not statistically significant (p=0.141). Comparing based on educational qualification, one (6.3%) subject who was a college graduate, felt some of his questions were unanswered. The rest of the subjects (n=30) agreed that all their questions were answered. No statistically significant difference was noted (p=0.616). Looking at the results based on annual family income, one subject who felt some of his questions were unanswered was in the income range of $51,000 to $100,000. Rest of the subjects (n=29) felt all their questions were answered. One subject did not respond to the question about annual family income. No statistically significant difference was noted (p=0.775).

Subjects were asked how they felt about the time that they had to spend on the study. Response to this question was compared based on age, gender, educational qualification, and annual family income. All the participants (n=31) responded saying that the time they spent on the study was ‘alright’. No statistics was computed because the results were constant.

Subjects were asked about how they felt about their current trial participation. Table 7 depicts participants thoughts about their trial participation based on age.
Table 7

Subjects thought on current trial participation

<table>
<thead>
<tr>
<th>Age</th>
<th>n</th>
<th>Positive</th>
<th>Negative</th>
<th>Feelings change</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>41-50</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>% within Age</td>
<td>100.0%</td>
<td>.0%</td>
<td>.0%</td>
<td>100.0%</td>
<td></td>
</tr>
<tr>
<td>51-60</td>
<td>5</td>
<td>5</td>
<td>0</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>% within Age</td>
<td>71.4%</td>
<td>.0%</td>
<td>28.6%</td>
<td>100.0%</td>
<td></td>
</tr>
<tr>
<td>61-70</td>
<td>5</td>
<td>5</td>
<td>0</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>% within Age</td>
<td>62.5%</td>
<td>.0%</td>
<td>37.5%</td>
<td>100.0%</td>
<td></td>
</tr>
<tr>
<td>71 and Above</td>
<td>8</td>
<td>8</td>
<td>0</td>
<td>5</td>
<td>13</td>
</tr>
<tr>
<td>% within Age</td>
<td>61.5%</td>
<td>.0%</td>
<td>38.5%</td>
<td>100.0%</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>21</td>
<td>21</td>
<td>0</td>
<td>10</td>
<td>31</td>
</tr>
<tr>
<td>% within Age</td>
<td>67.7%</td>
<td>.0%</td>
<td>32.3%</td>
<td>100.0%</td>
<td></td>
</tr>
</tbody>
</table>

Chi-Square Tests

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
<th>df</th>
<th>Asymp. Sig. (2-sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson Chi-Square</td>
<td>1.802a</td>
<td>3</td>
<td>.615</td>
</tr>
<tr>
<td>Likelihood Ratio</td>
<td>2.702</td>
<td>3</td>
<td>.440</td>
</tr>
<tr>
<td>Linear-by-Linear Association</td>
<td>1.246</td>
<td>1</td>
<td>.264</td>
</tr>
<tr>
<td>No. of Valid Cases</td>
<td>31</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a. 6 cells (75.0%) have expected count less than 5. The minimum expected count is .97.

Eight (61.5%) subjects in the age group of 71 and above felt positive about their participation. In addition, five subjects each in the age group of 51 to 60 (71.4%) and 61 to 70 (62.5%) also felt positive participating in the trial. Five (38.5%) subjects in the age group of 71 and above stated that their feelings change from time to time. The results (p=0.615) were not statistically significant. Based on gender, 17 (81.0%) females and 4 (40.0%) males felt positive about their current trial participation. Four (19.0%) females
and six males (60.0%) felt that their feelings change from time to time. None of the participants felt negative about participating in the trial. The results were statistically significant (p=0.023) based on gender. Comparing results based on educational qualification, 81.3% (n=13) of the college graduates felt positive about participating in the trial. Of the subjects who were high school graduates, 45.5% (n=6) felt positive about trial participation and 54.5% (n=6) felt that their feelings change from time to time. No statistically significant difference was noted (p=0.140). Looking at the results based on annual family income, 90.9% (n=10) of the subjects with annual income ranging from $51,000 to $100,000 felt positive about their participation in the current trial. Seventy-five percent (n=3) of the subjects with an annual income greater than $100,000 also felt positive about their current trial participation. Five (71.4%) subjects with income ranging from $31,000 and $50,000 stated that their feelings change from time to time. The results (p=0.078) obtained were not statistically significant.

When subjects were asked if the trial participation changed their attitude towards clinical or surgical trials. Based on age, five (38.5%) subjects in the age group of 71 and above felt that the experience from the current trial has changed their opinion in a positive way. Six (85.7%) participants in the age group of 51 to 60 and six (75.0%) in the age group of 61 to 70 stated no change in their attitude. One (7.7%) subject in the age group of 71 and above felt that, the current trial experience has changed his/her attitude towards clinical trials in a negative way. The results (p=0.616) were not statistically significant. Making a gender comparison of the results, seven (33.3%) females and one (10.0%) male felt a positive change towards clinical trials form the current experience. Thirteen (61.9%) female subjects stated no change in their attitude.
No statistically significant difference was noted (p=0.265). Based on educational qualification, 31.3% (n=8) of the subjects who were college graduates and 27.3% (n=3) of the subjects who were high school graduate felt a positive change in their attitude towards clinical/surgical trials. One (9.1%) subject who was a high school graduate stated a negative change in attitude towards clinical trials. The results were not statistically significant (p=0.461). Subjects in the annual family income ranging between $51,000 and $100,000 about 45.5% (n=5) felt a positive change in attitude and 54.5% (n=6) felt no change in their attitude. One (14.3%) subject with an annual income ranging between $31,000 and $50,000 felt a negative change in attitude towards clinical or surgical trial based on current trial participation. No statistically significant difference was seen (p=0.483).

Comparing subject’s inputs on future trial participation based on age, gender, educational qualification, and annual family income

Subjects were asked if they will participate in any future clinical or surgical trials, based on age, subjects in the age group of 71 and above (n=13), there was distribution of 46.2% (n=6) were willing to take part in future trials and an equal number of them would consider taking part in a clinical trial. One (7.7%) subject in this age group stated that he/she would never take part in a clinical or surgical trial again. In the age group of 61 to 70 about 75.0% (n=6) of the subjects and 71.4% (n=5) in the age group of 51 to 60 responded that they may or may not take part in a clinical or surgical trial in the future. Comparison yielded no statistically significant difference (p=0.808).

Table 8 depicts subject’s willingness to participate in future clinical or surgical trials based on gender.
Table 8

Subjects participation in future trials

<table>
<thead>
<tr>
<th>Gender</th>
<th>Participation in any kind of future trials</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Male</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Female</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>1</td>
</tr>
</tbody>
</table>

Chi-Square Tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>df</th>
<th>Asymp. Sig. (2-sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson Chi-Square</td>
<td>5.163</td>
<td>2</td>
<td>.076</td>
</tr>
<tr>
<td>Likelihood Ratio</td>
<td>5.997</td>
<td>2</td>
<td>.050</td>
</tr>
<tr>
<td>Linear-by-Linear Association</td>
<td>4.656</td>
<td>1</td>
<td>.031</td>
</tr>
<tr>
<td>No. of Valid Cases</td>
<td>31</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a. 3 cells (50.0%) have expected count less than 5. The minimum expected count is .32.

Comparing the results based on gender, 90.0% (n=9) of the males may take part in a clinical or surgical trial in the future. Among the females, 47.6% (n=10) stated that they will participate in a clinical trial in the future and an equal number of 47.6% (n=10) were not sure of their future participation. The results were not statistically significant (p=0.076).

Seven subjects (43.8%) who were college graduates and three subjects (75.0%) who had some college education stated that they will take part in future clinical or surgical trials. Nine (81.8%) subjects with high school diploma and nine (56.3%) subjects with college degree were not sure of their future participation. The results obtained were not statistically significant (p=0.102).
When results for this response was compared with annual family income of the subjects no statistically significant difference was seen (p=0.064). Seven (63.6%) subjects with an annual family income of $51,000 to $100,000 stated that they would participate in a future clinical or surgical trial. Six (85.7%) subjects with an income ranging between $31,000 and $50,000 and four subjects (100.0%) with an income of greater than $100,000 may or may not participate in a future trial.

Comparing subject’s response on how they will advise their family member and friends if they asked them about taking part in clinical or surgical trial. Based on age, all of the subjects (n=8) in the age group of 61 to 70, and 53.8% (n=7) in the age group of 71 and above and 85.7% (n=6) in the age group of 51 to 60 stated that their response would depend on many things. One (7.7%) subject in the age group of 71 and above would advice against taking part in a clinical/surgical trial. Results showed no statistically significant difference (p=0.359). All male subjects (n=10) and thirteen (61.9%) female subjects stated that their advise to family members would depend on many things. Seven (33.3%) female subjects stated that they would advise their family members and friends to take part in clinical trials. One (4.8%) female subject was against advising anyone to take part in any clinical or surgical trail. No statistically significant difference was noted (p=0.077). Comparing based on educational qualification, 75.0% (n=12) of the subjects with college degree stated that their response to their friends and family members would depend on many things. One (9.1%) subject with a high school diploma would advise against taking part in any trial. The results obtained were not statistically significant (p=0.741). All subjects with an annual family income greater than $100,000 (n=4) and 85.7% (n=6) with income
ranging between $31,000 and $50,000 felt that their response will depend on many things. Seven subjects (63.6%) with income ranging between $51,000 and $100,000 responded that they would advise their family members and friends to take part in clinical trials. Comparison showed no statistically significant difference (p=0.064).
Chapter 5

Discussion

The perspective and attitude of subjects participating in randomized trails is unclear. The study mainly focused on subjects currently involved in randomized clinical or surgical trials at the Medical College of Ohio. Of the forty questionnaires that were sent out only thirty-one completed surveys were received. Since IRB discouraged the student investigator not to get in touch with the study subjects. This posed a major challenge in the distribution of the study tool. The student investigator had to depend on the principal investigators (PI’s) and their research coordinator for distribution of the questionnaire. In addition, many principal investigators declined from taking part in the study, as they did not want any additional obligation of distributing the questionnaire during their busy work schedule. The time limit of only four weeks to distribute the questionnaire also posed difficulty in recruiting study subjects. The questionnaires were distributed only when the subjects came in for their regular outpatient check up.

A majority of the study subjects (42%) were in the age group of 71 and above. Many of the subjects were females (68%). The large female participation could be because the surgical and cancer trials were oriented towards breast cancer. Trials like the cardiovascular trial were in their initial recruitment phase and not many participants had been recruited.

Overall, a majority of subjects felt positive towards medical research and clinical trials. Cox (2003) state that subjects could have negative perceptions about the clinical trial process. This could be due to individual views regarding underlying motivations of clinicians or because of media coverage of ‘trial scandals’ (Cox, 2003). None of the
participating subjects felt negative about medical research or clinical trial. Results suggest how subjects have understood the importance of medical research for human well-being.

Approximately, 81% of the overall participants agreed that all drugs and medical procedures should be tested before they become available to public. It was interesting to note that all the subjects who had a college degree wanted drugs and procedures to be tested. Madsen, Holm, Davidsen, Munkhlom, Schlighting and Riis (2000), compared attitudes of participants in two non-cancer trial. Their study showed that the majority of participant’s primary reason for finding research necessary was to avoid any unknown and unwanted effects of something new without testing (Madsen, Holm, Davidsen, Munkhlom, Schlighting and Riis, 2000). Similar results were obtained in this study. In addition, it is predictable that, higher the education, better the understanding of the importance to test drugs and procedures.

Only six subjects had previously taken part in a clinical trial before their participation in the current trial. The question, which was aimed at finding if previous trial participation had changed subject’s attitude towards medical research was important and well worded. However, the questionnaire failed to provide instructions that the question was only for subjects who had previously taken part in a clinical or surgical trial. As a result, all subjects answered the question, there by making it invalid to derive any kind of statistical conclusions.

The results obtained on comparing subjects thoughts on randomization based on age, gender, educational qualification and annual income was not statistically significant. However, the majority of the subjects did not know how they felt about being
chosen by a computer to receive the treatment. This result did not compare with Madsen, Holm, Davidsen, Munkhlom, Schlighting and Riis (2000). In their study, subjects felt very positive about being drawn in lots and thought it was a very fair and just method of distribution (Madsen, Holm, Davidsen, Munkhlom, Schlighting and Riis, 2000). On the contrary, a study by Llewellyn-Thomas, Thiel, and Clark (1989) compared trial entry decisions in a hypothetical cancer trial. The study showed that the primary reason for the participants to refuse hypothetical trial entry was due to aversion towards the process of randomization (Llewellyn-Thomas, Thiel, and Clark, 1989).

Approximately, 47% of the overall participants did not know how they felt about being blinded to receive the treatment. Madsen, Holm and Riis (1999) reported that 80% of their study participants felt positive and a little less than 20% of respondents felt negative about blinding treatments. The high percentages of subjects accepting blinding and randomization are surprising as these issues have the attention of the media with statements that it is unethical to patients (Madsen, Holm and Riis, 1999).

Subjects were asked various reasons for their trial participation. A higher percentage of female participants thought it was either very important or important to be closely monitored by doctors and nurses. In a questionnaire study by Slevin, Mossman, Bowling, Leonard, Steward, Harper, et al (1995) it was reported that patients are attracted by being treated by a specialist doctor and are encouraged by the possibility that their progress will be monitored closely. If patients expect to be treated as a special kind of patients during the trial, they proved to be highly satisfied with the personal benefit experienced (Verheggen, Nieman, Reerink and Kok, 1998).
Wanting to try new a treatment was a very important reason for about 36% of the trial participants. Daugherty, Ratain, Grochowski, Stocking, Kodish, et al. (1995) found in their study that, many cancer patients taking part in phase I trial simply had no choice or are highly motivated by the hope of therapeutic benefits of the new drug.

One of the very important reasons for trial participation by many subjects was that, they wanted to help future patients by their participation. This motive was very high among the elderly subjects over the age of 61. Altruistic motives were also rated high by participants in the study by Madsen, Holm, Davidsen, Munkholm, Schlighting and Riis (2000). Edwards, Lilford, and Hewison (1998) also noted similar results where they studied the perspectives of patients, the public, and the health care professionals in randomized controlled trials. Patients with advanced cancer participate in clinical trials with altruism being one of the very important reasons for participation. Even if the treatment did not help them as an individual, it might ultimately help others (Kardinal, 1994).

It was surprising to see that not many subjects took part in the trial in order to get in a good relationship with their doctor. However, it was interesting to note that for more than half of the female participants it was an important reason for trial participation. The clinician-patient relationship could be quite complex and has been recognized as an important barrier in initial trial consultation and the intervention process (Cox, 2000). In addition, Cox (2000) considers it a crucial step in the recruitment process. Physicians may be concerned that enrollment in a clinical trial may interfere with the doctor-patient relationship and therefore do not raise trial involvement with their clients (Swaka and Pritchard, 2001). It is clear that, subjects want their physicians to do what is best for
them and not to be overly concerned about the effects that it could possibly cause in the doctor-patient relationship.

Positive experience from a previous trial was not an important reason for trial participation for a large majority of the study participants. The question that was intended to find if previous trial participation had changed subjects attitude in a positive or negative way had to be omitted. It is not clear how the subject who had previously taken part in clinical trials felt about randomized trials. However, the results clearly suggest that previous trial participation was not an applicable reason for their current trial participation.

Not having any other immediate medical option was also not an important reason for trial participation by the majority of subjects. Terenius (2000), reports that many patients state that their participation would increase medical knowledge and eventually lead to better treatment for future patients. It is very important that physicians should make the right treatment choice for the patients and not offer trial participation just because they do not have other medical options for treatment. Patient needs to be provided with enough information about the purpose of the trial, its predicted outcome and be allowed to make an informed decision (Terenius, 2000). Physicians doing randomized trials must admit that the best treatment for the individual’s disease is not yet known (Kardinal, 1994).

Free trial medication that was offered to patients was also not an important reason for trial participation for almost all the subjects (n=30). This question was added to the study tool when a Principal Investigator (PI) suggested that many participants take part in their trial mainly because of the free medication that was being offered.
Pharmaceutical companies initiate and run a large part of clinical trials, aiming at registration and marketing of their drugs and there is a likely chance of exploiting patients for personal motives (Iled, 2003).

A large percentage of the subjects who participated in the current study were involved in a cancer or surgical trial. Approximately 32% participated in surgical trials and 58% participated in cancer trials. Cancer trial were mainly aimed at pharmaceutical treatment options for breast cancer. The surgical trial also focused on breast cancer. Hence, it is not surprising that the majority of subjects in this study were females. Not many subjects could be recruited from cardiovascular trial, as it was a new trial and in the process of recruiting more participants.

When subjects were asked if they had questions that they wanted to ask the doctor about the trial. A large percentage of participants (55%) had only one or two questions that they wanted to ask the doctor and the results were statistically significant based on education. Subjects also reported that all their questions about the trial were answered. Clinical trials now not only have doctors, but nurses and research coordinators to answer all questions and concerns that participant might have. This could reflect the fact that trial participants were given enough information before consent for participation was obtained. Edwards and Hewson (1998) report that 80% of the trial participants were satisfied with the information they received and felt they had made an autonomous decision. About 83% of the doctors in the United Kingdom and Eastern Europe reported that patients might be overloaded with information (Edwards and Hewson, 1998). This may reflect a widespread concern that fully informed consent may cause anxiety (Edwards and Hewson, 1998). To provide informed consent,
participants in a clinical trial must be given accurate information about the purpose, methods, risks, benefits, and alternatives to the research (Grisso and Applebaum, 1998). They must understand the above and its bearing on their own clinical situation, and to make voluntary decision whether or not to participate would be appropriate (Grisso and Applebaum, 1998).

All subjects who took part in this study reported that the amount of study that they had to spend for the trial was all right. This is important, as the time involved in trial participation could be an important barrier in recruitment of participants. Cunny and Miller (1994) reported that many participants who consider participating opted out due to factors like, demand on time and the resultant problems with regard to work schedule and other commitments.

A majority of study subjects reported a positive attitude about participating in the trial. Madsen, Holm, Davidsen, Munkhlom, Schlighting and Riis (2000) and Madsen, Holm and Riis (1999) report that study participants reporting a positive attitude could be due to feelings of being involved in the trial, closer relationship to treating physicians or personal satisfaction of getting better treatment and diagnostics. However, a large percentage of the subjects stated they do not know how the current trial participation had changed their attitude towards clinical or surgical trials.

Many subjects claimed that, they may or may not take part in any kind of trial in the future. Whether patients would advise family members and friends to participate in any trial also followed the same pattern of response. Ternius (2000), state that it has been observed, but not well documented, that the willingness to participate in clinical trials has been falling in recent years. Patient satisfaction cannot be calculated before
hand (Ternius, 2000). The importance of having a high satisfaction is many-fold (Ternius, 2000). A satisfied patient is the best advocate for future trials (Ternius, 2000).
Conclusion

The perspective, feelings and attitudes of patients participating in different clinical and surgical trials is unclear. With newer and more sophisticated drugs being invented everyday, clinical trials are the ultimate hope for understanding the nature and uses of these drugs. To conduct research on human beings is a great privilege. Therefore, it is very important to assess patient satisfaction. This will not only improve patient’s trial participation but also promote future trial participation. Physician Assistants not only are part of the health care team but can also play a major role in clinical research. It is very important to understand the patient’s perspective before offering trial participation.

Today clinical research is better than ever. With precise trial designs, improved statistical analyses, presence of an ethical committee, and the need for informed consent have all geared it in the right direction. Properly conducted clinical trials offer the best hope for today and tomorrow.
Reference List


Appendix A: Letter to the Principal Investigator

Patricia A. Francis, MS, PA-C
Director and Assistant Professor,
Department of Physician
Assistant Studies,
Medical College of Ohio,
Toledo, OH 43614.

March, 2004

, MD

RE: Request for participation.

Dear Dr.

I am currently involved in a scholarly project for my Master’s degree entitled “Perspective and attitudes of patients participating in a randomized trial.” The main purpose of this study is to collect information about patient’s attitudes toward medical research, towards randomization, blinding of treatment and their reason for current trial participation and satisfaction. I would really appreciate if you would allow your trial patients to take part in this study.

If you decide to participate, the study questionnaires along with self-addressed, stamped envelopes will be sent to you. The questionnaires can then be distributed to the subjects during their office visits. It would only take a brief 8-10 minutes for completing the questionnaire. After completion, the survey can be mailed to me or returned to your office by the participants. Sealed envelopes returned to your office will be collected on a weekly basis. This method was chosen to ensure protection of patient’s rights to privacy.

If you have any further questions or need, more information please let me know. Thank you very much for sparing me your most valuable time.

Thank you,

Sincerely,

Vidya Krishnamurthy, PA-SII
Physician Assistant student
Department of Physician Assistant studies,
Medical College of Ohio,
Toledo, OH 43614.
E-mail: vkrishnamurthy@mco.edu
PH: 419-536-3863

Patricia F. Hogue, MS PA-C
Chair & Assistant Professor
Principal Investigator

IRB # 104637
Appendix B: Study Tool

Please use √ mark in the box to select your best answer. For the multiple choice questions, just circle your best answer. After you finish answering the questions, please place your response in the given envelope and SEAL it. You can mail the envelopes to me directly or return it to the nurse or doctor who gave it to you.

General Information:
1. Age: 18-30 □ 31-40 □ 41-50 □ 51-60 □ 61-70 □ 71 & above □

2. Gender: M □ F □

3. Educational qualification:
   a. Some schooling
   b. High school graduate.
   c. Some college
   d. College graduate.

4. Family income per year:
   a. less than 10,000 per year  d. 51,000-100,000 per year.
   b. 11,000 -30,000 per year  e. greater than 100,000 per year.
   c. 31,000-50,000 per year

Your thoughts on Medical research:

5. How do you generally feel about medical research and clinical trials?
   a. I feel very positive
   b. I don’t have any opinion
   c. I feel very negative
   d. My opinion changes from time to time.

6. Do you think it is necessary to test ‘new’ drugs and surgical procedures on humans before they become available to general public?
   a. Yes, it is very important that the drug or surgical procedure be tested.
   b. If it is a safe medicine or surgical procedure it need not be tested.
   c. No, it does not need to be tested at all.
   d. My opinion changes from time to time.
Information on previous trial participation:

7. Have you ever participated in a clinical trial before?
   Yes ☐ No ☐

8. Has the participation changed your feelings about clinical trials?
   a) Yes, participation has changed my feelings in a positive way.
   b) Yes, participation has changed my feelings in a negative way.
   c) No, I don’t feel any different.

9. How do you feel about being selected by a computer (“randomization”) to receive a particular treatment option?
   a. I feel positive about being picked by chance to receive the treatment.
   b. I feel negative about being picked by chance to receive the treatment.
   c. I don’t know how I feel about it.

10. How do you feel about not knowing anything about the medicine or treatment you will receive (blinding) during the trial?
    a. I feel positive.
    b. I feel negative.
    c. I don’t know how I feel about it.

Reasons for trial participation:

11. How important were the following in your decision to participate in the clinical/surgical trial?

   A. “I participated in the trial because, I wanted to be closely monitored by doctors and nurses.”
     a. Very important.
     b. Important
     c. Unimportant.

   B. “I wanted to try the new treatment for my condition.”
     a. Very important
     b. Important
     c. Unimportant.
C. “I thought my participation will help future patients.”
   a. Very important.
   b. Important.
   c. Unimportant.

D. “By participating, I will get in a good relationship with my doctor.”
   a. Very important.
   b. Important.
   c. Unimportant.

E. “I participated because of my positive experience from a previous trial.”
   a. Very important.
   b. Important.
   c. Unimportant.
   d. Not applicable.

F. “I did not have any other immediate medical options.”
   a. Very important.
   b. Important.
   c. Unimportant
   d. Not applicable.

G. “I participated in the trial because, trial participants were given free medication and I could not afford to buy those medicines.”
   a. Very important.
   b. Important.
   c. Unimportant.
   d. Not applicable.

**Information about how you feel about current trial participation:**

12. You are currently participating in a____________________
   a. Surgical trial.
   b. Cardiovascular trial.
   c. Cancer trial.
   d. _______________________________(Please write your answer in the space provided.)
13. Were there questions that you wanted to ask the doctor about the trial?
   a. I had many questions that I wanted to ask the doctor.
   b. I had one or two questions that I wanted to ask the doctor.
   c. I had no questions.

14. Did you feel that your doctors gave you enough information about the trial and answered all your questions?
   a. I was given enough information that answered all my questions.
   b. I still feel that some of my questions were unanswered.
   c. I feel that the information given was inadequate.

15. What do you think about the amount of time that you spent on the study?
   a. Study was very time consuming.
   b. It was all right.
   c. I could have used more time.

16. How do you generally feel about participating in the trial?
   a. I feel positive about participating in the trial.
   b. I feel negative about participating in the trial.
   c. My feelings change from time to time.
   d. __________________________ (Use the space to fill in your opinion.)

17. Did your experience in this trial change your attitude towards clinical/surgical trials?
   a. Yes, my experience changed my attitude in a positive way.
   b. Yes, my experience changed my attitude in a negative way.
   c. No, I don’t feel any change.

Inputs on future trial participation:

18. In the future, will you participate in any kind of clinical trial again?
   a. Yes, I will participate in a clinical trial again.
   b. No, I will never participate in a clinical trial again.
   c. Maybe, I will participate in a clinical trial again.
19. What will you advise your family members or friends if they asked you about taking part in a clinical/surgical trial?

   a. I will advise them to take part in a clinical/surgical trial.
   b. Not to take part in a clinical/surgical trial under any circumstances.
   c. My answer will depend on many things.
Appendix C: Consent Form for Participation

Dear sir/madam,

My name is Vidya Krishnamurthy. I am a second year Physician Assistant student doing a research project called “Perspective and attitudes of patients participating in randomized trials”. You will be given a questionnaire along with a self addressed, stamped envelope. PLEASE RETURN THE SURVEY BY APRIL 30, 2004.

The main purpose of this study is to understand how patients feel about participating in a clinical drug or surgical trial. You have been asked to complete this questionnaire because you are participating in a clinical drug/surgical trial.

Your participation in this survey is greatly appreciated and is voluntary. Please understand that your decision to participate, or not to participate, will not in any way affect your current treatment with your doctor. If you wish to participate, it is important to know that all the information that is being shared will be kept confidential. In addition, all returned surveys will have only the investigator’s address on them, and will be kept in a secure location within the investigator’s office. Once all information has been analyzed, the surveys will be kept for three years in a locked and secured location, unable to be accessed by anyone, other than the investigators.

The only foreseeable risk in the participation of this survey is the possibility of loss of confidentiality if you attempt to contact the investigators.

Completion of this questionnaire will be considered as your permission to participate in this survey.

If you have any questions or comments regarding this survey please contact the investigators via email at vkrishnamurthy@mco.edu, or pfrancis@mco.edu. You can also reach us via telephone at 419-383-5408. Please understand that an attempt to contact us will lead to the loss of confidentiality.

Patricia Francis, PA-C, MS
Principal Investigator,
Dept Chair/Assistant Professor
Dept of Physician Assistant Studies
Medical College of Ohio

Vidya Krishnamurthy, PA-S, MS
Student investigator,
Physician Assistant student,
Medical College of Ohio

Patricia Francis, PA-C, MS
MCO IRB # 104637

Vidya Krishnamurthy, PA-S, MS
Appendix D: IRB Research Proposal

Introduction

Good health is the greatest gift that any human being can enjoy. Medicine has made tremendous progress over the years. This progress would not have been possible without the development of new treatment, diagnostic protocols and more effective drugs. The mystery of human genome project has opened the doors for infinite number of newer drugs to be developed. This of course would increase the need for more animal experimentation and clinical trials.

Increased longevity does not come without a price. While the ideal vision for everyone may be to lead a physically and mentally healthy life well into old age, every year millions die prematurely or are disabled by diseases and conditions that are to a large extent preventable. Longevity in itself could become a punishment as well as a boon. A large part of the price to be paid is in the currency of chronic diseases like heart disease, stroke, and cancer seen prevalent in adult and elderly population (WHO, 1997). With an increasing need to prevent and cure diseases, there is an increased need to test and compare the newer treatment regimens being developed. For some patients clinical trials offer the only hope. Yet, all too often the very best treatment comes too late and offers too little.

The first large clinical trial was conducted in 1946 which evaluated the efficacy of streptomycin for pulmonary tuberculosis (Gehan, 1979). The 1950’s saw the emergence of chemotherapeutic revolution for the treatment of cancer (Gehan, 1979). Pharmaceutical companies tried to establish their credibility by packing their advertising literature with citations of studies performed (Gehan, 1979). The first randomized
controlled clinical trial for cancer patients was done in the mid-1950’s (Gehan, 1979). Since then tremendous progress has been made in the field of cancer research. With clinical studies for breast cancer, like the Tamoxifen trial, the prevention of breast cancer is finally becoming a reality (Meldrum, 2000).

We now practice evidence-based medicine. This helps to deliver quality health care and also reduces the need for the use of unwanted resources thereby achieving cost control (Meldrum, 2000). The need for scientific evidence has tremendously increased the need to conduct flawless clinical trials. Clinical trials offer the tool to assist in making precise clinical decisions, but not to replace clinical judgment (Meldrum, 2000).

The ethical dilemma in conducting clinical trials is based on the risk-benefit ratio of the new therapy. Everyday new and more sophisticated drugs are being invented. New drugs have to go through the three classic phases of clinical study beginning with clinical pharmacology (Phase I). Researchers test a new drug or treatment in a small group of people (20-80) for the first time to evaluate its safety, determine a safe dosage range, and identify side effects. Phase II is efficacy screening and role delineation. Study drug or treatment is given to a larger group of people (100-300) to see if it is effective, and to further evaluate its safety. Of these, Phase III is primarily designed to answer questions of clinical efficacy. Here the study drug or treatment is given to large groups of people (1,000-3,000) to confirm its effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow the drug or treatment to be used safely (Klein, 1979). By identifying treatments with less morbidity, clinical trials have contributed to improving the quality of life of patients.
Many patients participate in clinical trials thinking they might get better medical care (Cassileth, Lusk, Miller & Hurwitz, 1982). It becomes very important to assess the satisfaction of patient’s participation in a clinical trial especially when a newer therapy, which may cause pain and discomfort, is being tested.

According to Grimes and Schulz (2002), randomized clinical trials have become the gold standard, to avoid bias in the study. Patients generally are not aware of the treatment regimen they are on. It sometimes could be very frustrating, not knowing if you are on actual medication or just a placebo. Many times the researcher does not know the drug that is being offered to his or her patient, as all drugs tested or compared might be designed to look the same in a double blinded, placebo controlled clinical trial.

Randomized clinical trial is relatively a new tool and results reflect the average patient in the trial group (Yusuf & Devereaux, 2003). Patient satisfaction in a clinical trial is important, as they become advocates for future clinical trials. Before participating in the trial a realistic view should be given, about what the trial could mean to them and to their health.

Objective
There is a lack of knowledge about patient’s attitudes, perspective and how they experience clinical trial participation.

The following study aims at understanding the attitudes and perspective of patients who are currently on a clinical trial. The study is crafted with the following objectives:

a. Identify and select Principal Investigators involved in pharmaceutical clinical trial.
b. Distribution of study tool to the subjects by the identified Principal investigators.

c. Study the patient’s attitudes towards medical research, participation in a previous clinical trial, towards randomization and blinding of treatment, reasons for participation, their overall satisfaction of participation and possible future participation.

d. Compile the data and perform appropriate statistical analysis.

**Hypothesis**

There is no change in attitudes and perspective of subjects participating in randomized trials based on age, gender, and previous trial participation and education level.

**Review of Literature**

Exhaustive review of literature will be performed using Medline, pub med, cancer lit, psychinfo and md consult. Pertinent articles in newspaper and magazines will also be included.

With the increasing need for more precise diagnostic, prognostic and therapeutic methods, the scope design and conduct of clinical trial has vastly improved. This of course has coincided with the need for so called evidence based medicine. Clinical research, until about 50 years ago, was mainly based on observational and epidemiological methods (Iiled, Wedel, & Wiliielmsen, 2003).

According to Doll (1998) tremendous progress has been made in areas of conducting clinical trial since 1948. Before clinical trials, there were no set standard of care and treatment for a specific disease varied from one text book to the other.
Fifty years ago, the trial of streptomycin in patients with pulmonary tuberculosis, published by the British Medical Research Council heralded the arrival of the randomized clinical trial into medical research (Medical Research Council, 1948). The last two decades have seen exponential growth in the use of randomized clinical trial in medical research. By 1998 more than 5000 reports of clinical trials were being published each year, and that figure increased to more than 12,000 a decade later. Now, more than 200 clinical trials are being published every week (Sackett & Hoey, 2000).

The first randomized clinical trials were conducted in the area of infectious diseases and then were expanded to preventive interventions, which needed large trials. The polio vaccine trial randomized more than 400,000 children to active vaccine or placebo (Meldrum, 2000). The shift from small inconclusive trials to large trials evaluated major clinical outcomes (Yusuf, Collins & Peto, 1984).

The cardiac suppression trial (1989) showed that mortality increased in spite of treating patients with anti-arrhythmia. Similarly, Stampfer, and Colditz (1991) and Sidney, Petitti, and Quesenberry (1997) showed that women fared better on treatment with estrogen drugs than those who were not on it. But, later large-scale trials were not able to confirm these result and showed risks of important side effects (Hulley, Grady, & Bush 1998; Heckbert, Kaplan & Weiss 2001).

With a need for larger clinical trials and with demands for effective and high quality performance, the challenge for scientists and hospitals, pharmaceutical companies and authorities and finally the society is becoming increasingly difficult (Iiled, Wedel, & Willielmsen, 2003).
Historically, clinicians have experienced problems in terms of attaining adequate recruitment to clinical trials (Albercht, Blanchard, Ruckdeschel & Strongbow, 1999). Many studies have tried to identify the issues surrounding motivations for clinical trial participation in healthy volunteers and patients (Richardson, Post-White, Singletary & Justice, 1998).

In phase I and II anticancer drug trials, patients enter with intentions of not wanting to give up or to help other cancer patients or for their family and to have someone to talk to (Rubens, Toulson & Ramirez, 1992). Cox and McGarry (2003) state that nonparticipation in clinical trials can arise due to many reasons like patients choosing not to participate, clinicians choosing not to enter or offer their patients trial involvement, lack of knowledge on the part of both patients and clinicians about the trials available or patients not meeting the trials eligibility criteria.

The clinician-patient relationship could be quite complex and has been recognized as an important barrier in initial trial consultation and intervention process (Cox, 2000). Also, Cox (2000) considers it to be a crucial step in the recruitment process.

Trial participation could burden the individual with many factors which relate to practical issues like time, work schedule, transport, duration of the trial, lack of interest and other commitments. (Cunny & Miller, 1994; Hudman, Stolzfus, Chamberlain, Lorimor, Steinbach et al. 1996)

Doing research on human subjects is considered to be highly privileged and leads to lot of ethical questions. Physicians doing randomized trials must admit that the best treatment for the individual's disease is not yet known (Kardinal, 1994). Sometimes
it is argued that participants may be called to sacrifice their own best interest for the sake of future patients (Edwards, Lilford & Hewison, 1998).

According to Grady (1991), clinical trials are considered as the final step in the process of procuring usable knowledge, a meeting place of medicine and clinical research. As a result there are many ethical issues that need to be considered.

Stroms (2003) state that many treatments are based on trial outcomes and there are several factors that need to be considered before the trial results could be applied to the general public. The trial outcome in individual patients may not relate to the trials exclusion and inclusion criteria, adherence to therapy in trials, endpoints used in the trials compared to those used in practice, publication and finally reporting of data.

The primary goal of clinical trials is evaluation of the efficacy of drug which should be a related to real-life effectiveness (Spahn, 2003). Tonkin (1998) states that large standardized databases are necessary to assess clinical practice and outcome. Assessment of clinical outcomes depends on interplay between the structure and process of care, patient factor and chance.

Methodology

To qualify for participation in the study subjects will have to be currently involved in a clinical drug trial and should be over eighteen years of age. Usually in a randomized double-blinded clinical trial, neither the physician nor the patients are aware of the medication that they will be required to take. They could be on an experimental drug or a placebo. Hence, the criteria to study the attitudes and perspective of patients who are currently involved in a pharmaceutical clinical trial are selected.
No gender preferences will be included. Subjects interested in participating should be involved in a trial for at least a month or greater. The study will mainly focus on patients involved in outpatient clinical trial settings. Subjects who have previously participated in any type of clinical study will also qualify to participate in the study. The independent variable will be the questions intended to study the patient’s attitudes, knowledge and perspective of a clinical trial. Dependent variable is the data obtained. The intervening variables include lying, choosing not to reply the questions, or letting their friends or family to fill the questionnaire.

Subjects who fulfill these criteria will be selected on a basis of convenience sampling to fill out the survey. In convenience sampling the cases that are judged to be typical of the population is hand picked and thus develops samples that are satisfactory in relation to one’s research (Kothari, 1993).

A questionnaire was designed to elicit information pertinent to the study. The study tool was modified from Madsen, Holm, Davidson, Munkholm, Schlichting and Riis (2000). Their study tool included nineteen questions, of which, two were eliminated and seven more questions were added to make it pertinent to this study. It includes a number of questions printed or typed in a definite order or form. It deals with their previous participation in a clinical trial and opinions regarding participation. Questions focusing on the subject’s attitudes towards medical research, their view of being randomized (drawing lots) and blinding treatments will be included. Different reasons for consenting to participation will be found. Finally, the subject’s evaluation of participating in trial and their possible future participation will also be elicited. Most of the questions
will be multiple-choice forms, but some questions will provide opportunity to add free text.

Principal investigators (PI) especially involved in clinical or surgical trials, at MCO will be identified. A letter approved by IRB will be sent to the PI’s identified. The letter will explain the purpose of the current study and will request their participation. If the Principal investigator decides to participate in the study, the survey questionnaires approved by IRB will be sent to them.

Principal Investigators or research coordinators will hand out the survey questionnaires to the subjects involved in their study. Volunteer participation will be offered to the selected subjects.

To the questionnaire will be attached a letter, requesting the subjects volunteer participation and promising them that their non-participation will in no way affect their current treatment or relationship with their physician and the information shared will be kept confidential. Letter will also include instructions on filling out the questionnaire. Self-addressed mailing envelopes with paid postage will also be attached to the questionnaire.

After completing the questionnaires subjects will be requested to seal their responses in the given envelope. They have the choice of returning the sealed envelopes to the research coordinators or nurse or the PI’s in the office. They can also mail in the responses, if they choose to do so.

Every week the student researcher will visit the offices of the principal investigators involved in the study to collect the sealed envelopes. The questionnaires
collected personally and the surveys received via mail will be kept locked in the office of the study advisor for data compilation and processing.

All the data obtained will be compiled. Parametric and non-parametric statistical analysis will be performed using SPSS 10.0.
Medical College of Ohio
INSTITUTIONAL REVIEW BOARD
MEMORANDUM

TO: Patricia F Hogue, M.S.
Department of Physician Assistant Studies
MCO

FROM: Eric Schaub, M.D.
Chair, Institutional Review Board
Research and Grants Administration

DATE: March 4, 2004

SUBJECT: IRB #104637- Perspective and Attitudes of Patients Participating In a Randomized Trial

The above project was reviewed and approved by the Chairman of the Institutional Review Board as an expedited review (category #7). This review and approval includes the survey tool submitted with the MCO IRB application. The requirement to obtain a signed consent/authorization for use and disclosure of protected health information form has been waived as this research is determined to be minimal risk and a signed consent/authorization document would be the only record linking the subject to the data. It was determined that this waiver for signed consent/authorization for use and disclosure of protected health information form will not adversely affect the rights and welfare of the participants. The Principal Investigator must provide a copy of the introductory letter (version date March 2004) and the questionnaire cover letter (no version date) to all participants prior to participation. The full board will review it at its meeting on 03/18/2004.

NOTE: THE ATTACHED INTRODUCTORY LETTER (VERSION DATE MARCH 2004) AND THE QUESTIONNAIRE COVER LETTER (VERSION DATE 04/01/2003) WITH THE MCO IRB APPROVAL STAMP ARE THE ONLY VALID VERSIONS. THESE FORMS MUST BE COPIED AND USED FOR ALL STUDY PARTICIPANTS BEING RECRUITED FOR THIS RESEARCH. STUDY PARTICIPANTS MUST BE GIVEN A COPY OF THESE FORMS PRIOR TO CHOOSING TO PARTICIPATE IN THIS RESEARCH. THE FIRST PAGE MUST DISPLAY APPROPRIATE MEDICAL COLLEGE OF OHIO LETTERHEAD, ORIGINAL OR COPIED.

APPROVAL DATE: 03/04/2004
EXPIRATION DATE: 03/03/2005

It is the Principal Investigator's (P.I.'s) responsibility to:

1. Abide by all federal, state, and local laws and regulations; the MCO federal assurance and institutional policies for human subject research and protection of individually identifiable health information including those related to record keeping and be sure that all members of your research team have completed the required education in these areas.

2. Ensure that all subjects, or their legally authorized representatives, are provided a copy of the Cover Letter prior to choosing to participate in this research.

3. Comply with the Health Insurance Portability and Accountability Act of 1996 (HIPAA) Privacy Rule Privacy Rule (45 CFR 164) and institutional policy regarding the accounting and tracking of uses and disclosures of protected health information.

4. Promptly notify the MCO IRB at (419) 383-4251 of any untoward incidents or unanticipated adverse reactions that develop in the course of your research on human subjects. Please complete and submit RGA Form 317 for ALL SUCH REPORTS for this protocol. The Principal Investigator is also responsible for submitting to the MCO IRB reports of adverse events that occur at other sites conducting this study and for maintaining an up-to-date cumulative table of adverse events (RGA Form 316) and submitting it to the MCO IRB for each research project. The Principal Investigator is responsible for reporting adverse events to the appropriate federal agencies and the sponsor (when one exists).

5. Report promptly to the MCO IRB any deviations, violations or participant non-compliance from the MCO IRB approved protocol in accordance with the procedures outlined in RGA Form 309. In your report include the protocol number and title, the subject's initials and study I.D. number, date of the event, a brief description of the occurrence and a description of any corrective actions taken. The Principal Investigator is responsible for reporting deviations,
Abstract

**Objective:** The purpose of this study was to understand the attitudes, feelings, and perspective of patients currently involved in randomized trials. **Method:** Principal Investigators (PI's) involved in various clinical trials at MCO were identified. A survey tool was distributed to forty subjects participating in cancer, cardiovascular and surgical trials by the respective PI's or their research coordinators. **Results:** No statistically significant difference was noted in subject’s attitudes and perspective based on age, gender, annual income, and education level. Wanting to help future patients was a very important reason for trial participation, for 70.0% of the subjects. Positive experience about their current trial participation was reported by 67.7% of the participating subjects. **Conclusion:** It is critical to learn about the various experiences and concerns of subjects participating in randomized trials. Such studies would not only improve the level of satisfaction but also promote current and future trial participation.