“We get patients”: Understanding the culture of patient recruitment organizations

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Abstract

Patient recruitment companies are small, private businesses that specialize in recruiting patients for clinical trials on behalf of pharmaceutical and medical device industries. The emergence of these companies around the 1990's is part of a broader tendency within the pharmaceutical industry to focus on outsourcing clinical trial research. The organizational complexity of clinical trials has led to the emergence of a new sector devoted to the management and administration of clinical trials. The shift of clinical research to the private sector has raised new questions and ethical concerns about relationships that emerge between the industry, regulating bodies, researchers and human participants (Abadie, 2010; Fisher, 2009; Rajan, 2006; Petryna, 2009). This thesis investigates and describes one aspect of the private clinical trial industry—patient recruitment for clinical research studies and ethical issues that emerge from these activities.

The results are based on a year-long ethnographic study including participant observations, document analysis and interviews with stakeholders of recruitment industry. The central argument I develop is that rationales for recruitment tactics are intimately entwined with the market value that these companies see in patient recruitment, and with the market risk that attends this process. This worldview impacts every aspect of the patient recruitment business—starting from the structure of patient recruitment, to the development of marketing campaigns, communication with the public, and all the way through to the relations with clinicians. I argue that the current organization of private industry patient recruitment introduces different ethical questions that are not addressed by the current guidelines.

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Chapter 1: Introduction

Medical research studies and the problem of patient recruitment

On a daily basis, good-looking people on TV and radio with pleasant voices are inviting patients to participate in research studies at any hour of the day. These commercials inform you the listener, for example, that Alzheimer's disease can strike anyone, but that often symptoms are dismissed as just a result of getting old. And, they say, you should join the fight against Alzheimer's by participating in a research study!

Other times ads reveal that an investigational product may help you control your diabetes if you are unhappy with your current treatment regimen. What unites these advertisements is their search for patients who would be interested in donating their time and their bodies to test new medications or medical devices in exchange for medical attention, potential therapeutic benefit and money.

Clinical trials are an important part of every health care system since they inform clinical practices and bring new treatment options for public use. Currently, clinical trials are larger, more expensive and more complex than ever before due to increased subject cohorts required by the FDA, rapid growth of some therapeutic classes, many "me-too" drug trials, an increase in the number of new chemical entities and the development of more complex medications (Petryna, 2009). As a result, more clinical trials participants are necessary to complete clinical studies.

The clinical development process of new medications and medical devices highly depends on patient participation in clinical studies. Finding medically qualified and willing patients for medical research is a challenge, especially since it has been prohibited to massively test new drugs on institutionalized populations such as prisoners and hospital patients (Abadie, 2010). Widely cited data within the clinical trial industry indicates that 80 percent of all clinical trials are delayed at least one month because of unfulfilled enrollment and that each day a drug is delayed from the market sponsors can lose one million dollars in unrealized sales (Fisher, 2009).

There are different opinions as to why recruitment is a major challenge, but what stands clear is that the problem with human selection for medical studies is complex. The most widely cited reasons for low patient recruitment can be grouped into four categories—clinical, financial, educational and logistical. Unsuccessful recruitment is attributed to clinical reasons, for example, for studies with overly restrictive inclusion and exclusion criteria where there are simply not enough patients who could match the criteria (McDonald et al, 2011). Some researchers claim that insufficient budgets for recruitment and understaffed research clinics seriously hinder patient participation (Watson & Torgerson, 2006). It is also thought that low public awareness and the legacy of past tragedies in clinical research is to blame for low participation. Study findings show that 94 percent of people recognize the importance of participating in clinical research to assist in the advancement of medical science (CenterWatch, 2006). Yet, less than five percent of Americans know where to find information about relevant clinical trials (Getz, 2004). The research also shows that only fourteen percent of research

participants have learned about the opportunity from their physicians (CenterWatch, 2006) And, finally, low participation rates are explained by logistical issues—poor planning of the recruitment process, inconvenience for patients (such as traveling to sites or inability to contact the coordinator), and selection of research clinics and principal investigators that are not suited for successful recruitment (Caldwell, Hamilton, Tan & Craig, 2010). Different players in the industry focus on different solutions for low participation rates in research studies.

Patient recruitment companies

Where some see a problem, recruitment firms have seen a business opportunity. In response to this growing need for human participants there emerged small private recruitment companies that promise to find patients for clinical trials. These recruitment companies develop specific knowledge of various social, cultural, psychological, technological, and economic methods for convincing people to participate and to remain in clinical trial studies. And, slowly, patient recruitment undertaken by individual researchers has been replaced by the development of professional, well-managed structured strategies by dedicated staff (Epstein, 2007). Particularly for recruitment firms, patient recruitment is an awareness-building and a logistical issue. It is assumed that by widely advertising studies and by better planning and organizing of the recruitment process, the issues with low participation can be solved.

The emergence of recruitment companies around the 1990's is part of a tendency within the pharmaceutical industry to focus on outsourcing clinical trial research. The organizational complexity of clinical trials led to the emergence of a new sector devoted

to the management and administration of clinical trials. The reason for this trend is to minimize costs and maximize profits. This can be accomplished by increasing the speed of approval and of the research process, including fast and successful human subject recruitment and retention.

It is hard to estimate exactly how many companies there are because they come and go. Some of my informants speculated that there are only about ten "long-term players" in the industry. Of course there are many more companies than that. During my research alone, I came across 40 different firms that offer some type of patient recruitment services to Pharma and to the device industry. Some of these companies are very small and offer only one type of service, such as advertisement. Others are part of large advertising companies or contract research organizations. Even large academic health centers have established their own recruitment centers that assist principal investigators with matching human subjects for their studies.

As mentioned above, patient recruitment companies offer to find, recruit and enroll patients for clinical research studies. Enrolled patients are defined as ones who have met formal inclusion and exclusion criteria, have signed informed consent forms, have been admitted to a study and are scheduled to participate in a trial in accordance with the protocol. Recruitment on the other hand, is the process of enrollment—performing activities such as advertising the research study and screening the patients based on protocol requirements in order to select individuals for enrollment. In other words, recruitment firms promise not only to find willing participants, but also to ensure

that these participants meet inclusion and exclusion criteria and are ready to sign informed consent forms.

In addition, firms claim to assist sponsors and researchers in retaining human participants throughout the duration of a clinical study. In any type of clinical research, but especially in longitudinal studies, participant retention poses a major challenge and issues of dropouts and non-adherence can become frustrating. For example, in weight loss and lifestyle change research, the average dropout rate is 32 percent (Davis & Addis, 1999), but this can be even higher depending on the participant population, the length of the study, and the demands of the protocol. In most clinical research, each participant represents a significant amount of time, effort and other resources, so high dropout rates are costly. High dropout and non-adherence rates also pose a risk to the interpretation and validity of research findings.

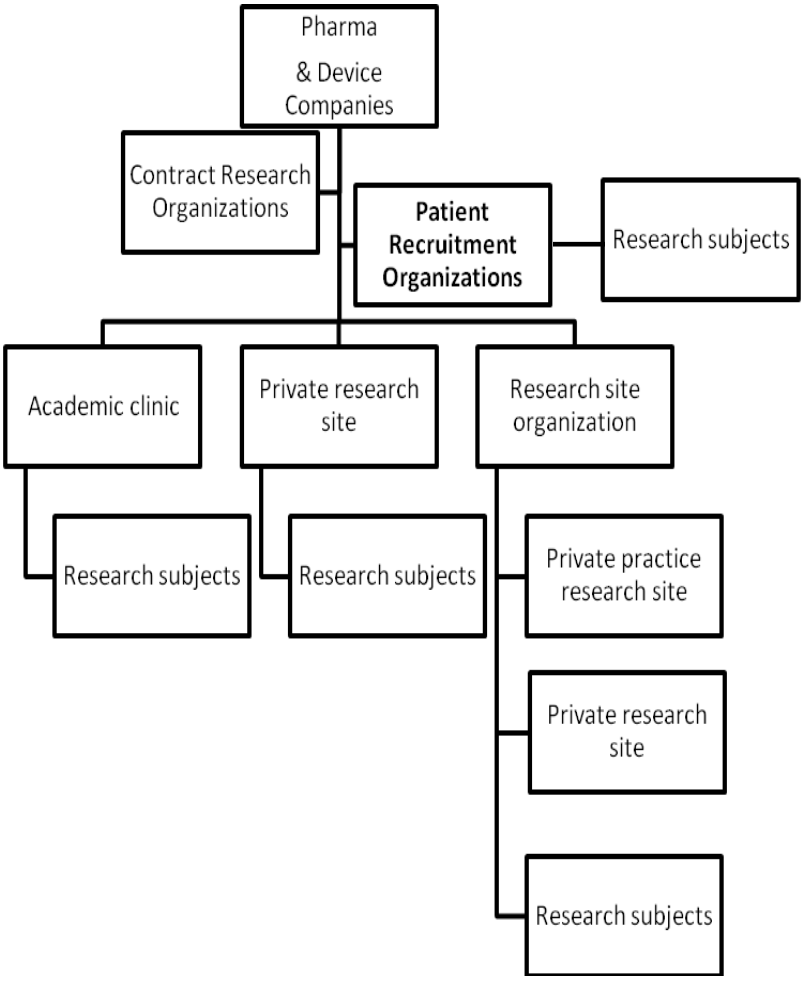


Figure 1. The organization of clinical trials industry.

The structure of clinical trials industry is presented in Figure 1. When developing a new product, pharmaceutical and device companies (sponsor) can conduct clinical research themselves or hire a contract research organization (CRO) to manage the entire research process for them. Then either a sponsor or hired CRO selects investigational research sites and a recruitment company that will assist research clinics in the patient recruitment process. In most cases it is expected that research sites will recruit the majority of research participants, but recruitment firms are contracted to recruit anywhere

from fifteen to thirty percent of required research subjects depending on the complexity of a study protocol.

Recruitment companies operate in a complex clinical research industry. Although these firms are independent entities, they work very closely with other members of the industry—sponsors and research sites—in order to accomplish their goals of enrollment. The formed relationships are such that a firm's activities are dependent on the decisions of a sponsor and of research clinics. For example, recruitment companies are not allowed to actually admit patients to a study and conduct informed consent process with potential participants because this is the duty and responsibility of the principal investigator. As a result, the performance of recruitment firms depends on relations with research clinics and in order to achieve patient recruitment goals, recruitment firms spend a significant amount of time building collaborations with coordinators and educating them on the efficient recruitment process.

In order to accommodate the high demand for human subjects, recruitment and retention strategies are becoming increasingly sophisticated as well as commercialized (Office of Inspector General, 2000). In their own literature, the research industry usually refers to clinical trials participants as consumers, to clinical trials as goods they are selling, and to recruitment methods as marketing strategies (Anderson, 2004). This indicates that recruiters are viewing patients and clinical research from a different point of view than one might traditionally perceive of medical research that is supervised by a physician and a nurse.

Significance and research questions

A long history of controversial cases marks the use of human participants and the protection of their rights and wellbeing in medical research studies. Moreover, the shift of clinical research to the private sector has raised new questions and ethical concerns about relationships that emerge between the industry, regulating bodies, researchers and human participants (Abadie, 2010; Fisher, 2009; Rajan, 2006; Petryna, 2009). This thesis will tackle one significant aspect in the clinical trial industry—that of patient recruitment for clinical research studies. I will examine the daily practices of patient recruitment companies and issues that emerge from these activities.

The clinical research industry is heavily regulated and recruitment firms in particular are carefully following the requirements of Institutional Review Boards (IRBs) and Health Insurance Portability and Accountability Act (HIPAA) since the progress of a particular study and a firm's reputation is at stake. However, the research enterprise has developed and changed faster than regulations have been able to adapt. There are discussions in the academic literature about the ethical issues of various recruitment techniques, but it remains unknown as to what happens when patient recruitment companies see recruitment primarily as a way to make profits and clinical trial participants as consumers. There has not been an assessment of interactions between potential clinical trial participants and commercial recruitment enterprises that go beyond the language of coercion and rational choice. This project will attempt to fill this empirical gap by discussing in detail the general practices of patient recruitment firms and how recruitment firms form and manage relationships with sponsors, clinicians and

patients. Moreover, I will discuss ethical questions that might arise in these new interactions. The goal is not to evaluate the effectiveness of recruitment firms in recruiting patients but instead to understand the processes and values that guide this process.

Analysis of professional patient recruitment activities will add to further understanding of the social organization of private clinical research industry and interactions between different stakeholders within this industry. Qualitative research methods, used in this project, allowed for an intimate understanding of daily practices of recruitment companies. I offer a perspective from inside of patient recruitment companies from the point of view of an observer on social and ethical matters of current patient recruitment and selection process. I also illustrate the complex relations between different stakeholders of a clinical trial industry and how this shapes the recruitment process.

Understanding how corporations go about recruiting patients, how they make sense of the ethics, and what meaning they give this concept, can provide insight into how to improve regulations and oversight. Field research such as this informs policy by grounding it in a firm understanding of how participants construct their social worlds. The purpose of this study is to expand knowledge on corporate recruitment practices and to analyze implications these activities have on other research stakeholders—patients and individual research sites. The results will be of interest to researchers and policy makers that are working with patient recruitment and are aiming to improve the recruitment process and patient protection.

In my thesis I will address the following questions:

1) How do patient recruitment companies work in order to meet the high demand for research participants? I will attempt to answer this question by describing the work process of patient recruitment organizations from an insider's perspective and by discussing methods these companies employ in order to attract research participants.

2) How do patient recruitment companies manage relationships among various stake holders within the clinical trial industry and what are the specific factors that facilitate and hinder patient recruitment? Moreover, I will present the research clinic's perspectives on patient recruitment and collaborations with patient recruitment companies.

3) What ethical aspects are incorporated into the daily practices of these companies and what kind of issues emerge that are not addressed in current regulations?

As I will illustrate in my thesis, rationales for recruitment tactics are completely entwined with the market value that these companies see in patient recruitment, as well as the market risk that attends this process. This worldview impacts every aspect of patient recruitment business—starting from the structure of patient recruitment process, to development of marketing campaigns and communication with the public, and through to the relations with clinicians. In a way, professional patient recruitment has become an information science. Recruiters carefully gather, compile and analyze information about recruitment techniques and outcomes. Subsequently, companies sell this information to the pharmaceutical and medical device industry in the form of expertise. Interactions among recruiters, interested research participants and clinicians are also informed by the larger context of inequalities in the US health care system and the goals of the

pharmaceutical and medical device industries. Finally, as I will show in subsequent chapters, the current organization of private industry patient recruitment also introduces new ethical questions.

In the following chapter I will present a literature review pertinent to my project. I will start by briefly presenting the history of patient recruitment and research. I will proceed with explaining current regulations and weak points in the system.

In Chapter 3 I will focus on the methodology used in this project. I will discuss the philosophical assumptions of qualitative research that serve as the foundation of my project. Furthermore I will provide a theoretical foundation for ethnographic research and I will also discuss the design and methods I used to collect data. I will conclude by discussing how I ensured the quality of this project and by discussing the ethical issues that I considered during the fieldwork.

In the next four chapters I will present the results of the project. In Chapter 4 I will present an overview of the patient recruitment industry—key characteristics of these companies and recruitment approach. Chapter 5 is dedicated to an analysis of the relationships that these companies form with investigational research sites in order to foster patient recruitment. The chapter is divided in two parts—first, I will present the perspectives of patient recruitment companies and second, I will discuss investigational research sites' perspectives on collaborating with patient recruitment companies. In Chapter 6 I will present themes related to recruitment companies' interactions with patients while recruiting and selecting patients for research studies. While selecting candidates for research studies, recruiters have developed specific notions of individuals

who are suitable for participation in clinical research studies. I will discuss this trend and characteristics of individuals that recruiters refer to as “high quality participants” in Chapter 7. I will conclude my thesis with a discussion of the ethical issues present in professional patient recruitment, as well as make concluding remarks and recommendations in Chapter 8.

Chapter 2: Literature review

In this chapter I am presenting a literature review that will provide the background and significance of the project. I will start by presenting the process of developing new medical products. This will be followed by a discussion of a) the history of human subject recruitment, to show how market recruitment began and what forces led to the development of the current system of patient recruitment, b) patient recruitment for publicly funded research, b) the factors that influence patient recruitment, and c) common barriers that researchers at clinics are trying to overcome. I will finish with a discussion of the existing regulatory mechanisms for research participant protection and common ethical concerns in patient recruitment.

The process of clinical drug development in the US

After a new medicinal molecule has been discovered in the laboratory, the further process of developing a new medication or device is divided into preclinical (in microorganisms/animals) and clinical (in humans) research. Researchers seek to identify the optimum dosage range within which efficacy of the medical compound is maximized without compromising safety. The development process is primarily designed to satisfy the regulatory requirements of drug licensing authorities in order to receive permission to market the drug to the public. When a compound has been shown to be successful in animals, then the investigational medicine is further tested in humans. The clinical research is divided into four phases (I will present these in the following section), with the goal of further testing safety and efficacy in human bodies.

Because of the complexity and number of subjects needed, clinical trials are often carried out across multiple centers and are generally sponsored by biotechnology, medical device, or pharmaceutical companies. Academic and publicly-funded research institutions play a major role in the early stages of discovery, such as the identification of potential molecules and conducting pre-clinical tests (Angell, 2004). Although many new medicinal molecules are discovered in publicly-funded institutions, due to the complex regulatory requirements and high costs, promising molecules are licensed to corporations that carry out "in-human"—Phase I, Phase II, and Phase III research studies to further develop the medicinal products.

Clinical trial Phases I through IV

The primary purpose of Phase I clinical trials is to test a drug's safety on a small number of healthy volunteers. The testing normally involves twenty to eighty healthy individuals and can last up to one year (National Institutes of Health, n.d.). Around sixty three percent of all drugs tested in Phase I are further tested in Phase II (Kola & Landis, 2004), which involves one hundred to three hundred participants with the target disease and can last up to two years (the summary of the number of participants and costs per enrolled subject is presented in Table 1: "Phases in clinical research"). At this stage, the aim is to collect preliminary information about efficacy and further information about safety in humans with a particular disease (National Institutes of Health, n.d.). Only about thirty five percent of compounds are deemed to be successful enough to continue with further development (Paul et al., 2010). The next, Phase III, requires several thousand volunteers with the target medical condition and can last up to four years. At this stage,

participants are randomly placed into two or more groups where individuals receive an investigational drug, placebo, or standard of care therapy. These studies are designed to measure the efficacy of the product under investigation in comparison to a placebo or approved therapy (U.S. National Institutes of Health, n.d.). Although fifty-five percent of the compounds that enter Phase III are successful, that corresponds to only sixteen to twenty percent of investigational products that started clinical development (Kola & Landis, 2004). Post marketing research—data collection after the medication has been approved for sale—is classified as Phase IV in the clinical drug development cycle. These studies involve thousands of patients and can last up to ten years. The aim is to obtain information on cost effectiveness, in addition to the short and long term efficacy of the therapy (National Institutes of Health, n.d.).

Cost of patient recruitment

Patient recruitment is a costly endeavor. In the years between 2005 and 2007 the mean cost per patient for Phase I was reported as $17,209, for Phase II—$12,291 and Phase III—$10,428 (the summary of the number of participants per phase and costs per enrolled subject are presented in Table 1: "Phases in clinical research"). The cost per patient varies widely depending on the medical condition. The cost is affected by factors such as rates of prevalence and incidence of a given medical condition, as well as rates of formally diagnosed patients (if a patient just experiences disease symptoms, resources are necessary to carry out medical screening), number of competing studies for the same patient populations, and treatments available on the market, etc. For example, blood

disorder trials cost $19,732 per patient, followed by oncology at $15,968. The cheapest cost per patient trial is dermatology—$4,104 (CenterWatch, 2006; Table 3.62).

Costs per patient in the US may be higher due to the fact that more resources are required to find research participants who are not therapeutically saturated, i.e. not already taking multiple drugs. It is harder to determine the efficacy of the molecule being tested while having to consider drug interactions that could compromise data.

Table 1. Phases in clinical trials.

Phase (National Institute of Health, n.d.)	The purpose (National Institute of Health, n.d.)	Mean participants per trial (CenterWatch, (2006; Table 3.39)	Length (National Institute of Health, n.d.)	Success rate (Mathieu, 2008)	Cost per patient (Cutting Edge Information, 2011)
Phase I	Safety	32.6	Up to 1 year	63%	$21,883
Phase II	Safety& Efficacy	151.5	Up to 2 years	34%	$36,070
Phase III	Efficacy	868.6	Up to 4 years	55%	$47,095
Phase IV	Post-market	1000+	Up to 10 years	n.a.	$17.042

In 2009, $2.3 billion were spent on patient recruitment for clinical studies, and it has been estimated that the size of this market is growing around fifteen percent annually (Mintz, 2010). Patient recruitment has been identified as the most challenging, and the most common, reason for a delay in clinical trials.

Another study by a life science consulting company has estimated that patient recruitment (thirty-two percent of a research budget) and vendor fees (twenty-five percent of a research budget) are the main drivers of growing clinical trial costs (Cutting

Edge Information, 2011). In the following section, I will describe the history of patient recruitment, which will shed light on how patient recruitment has been professionalized and has been shifted to market recruitment.

History of the recruitment of human subjects

Until the 1970s, human subjects for most clinical studies were recruited from institutionalized populations, such as orphanages, mental hospitals and prisons. Prisoners were almost the exclusive subjects in non-federally funded Phase I pharmaceutical trials designed to test the toxicity of new drugs (Advisory Committee on Human Radiation Experiments, 1994). By 1972, FDA officials estimated that more than 90 percent of all investigational drugs were first tested on prisoners (Advisory Committee on Human Radiation Experiments, 1994). General hospital wards often provided poor, unaware subjects for different stages of scientific experimentation. Although there already existed some requirements for human subject protection, like the Hippocratic Oath and the responsibility to obtain consent (Lederer, 1995), medical researchers claimed a right to self-regulation, and no formal ethical guidelines were established until the end of World War II.

However, in the late 60s two whistleblowers, Pappworth (1967) in Britain and Beecher (1966) in the US, published details of unethical experiments routinely conducted, often on marginalized minority groups without their knowledge. In response, the U.S. National Commission issued the Belmont Report in 1979. The Belmont Report is widely regarded as the definitive statement of the ethical framework for human subject research.

One of the contributions of the Belmont Report is the recommendation that institutionalized populations like prisoners or the mentally ill should be excluded from clinical trials. This recommendation was made based on the concept of justice and the lack of autonomy to provide informed consent. In 1980, one year after the Belmont Report was issued, the FDA issued regulations that eliminated prisons as acceptable sites for pharmaceutical testing (Advisory Committee on Human Radiation Experiments, 1994). This regulation signaled the end of easily accessible populations and the shift to a market approach (Abadie, 2010).

There was another major change in the way clinical research is conducted, which led to the market recruitment approach. Until the 1990s, the majority of clinical trials were conducted in medical schools and teaching hospitals. Research studies were sponsored by pharmaceutical companies, but designed and conducted by academic physicians who could offer potential study participants from their practices (Elliott, 2008). However, in the past two decades there has been a drastic increase in the number of drugs being tested; clinical trials have become more complex; and financial pressure to bring medications to the market quickly has increased (Elliott, 2008). Also, due to the complicated bureaucracy and the multiple responsibilities of academic physicians, the research process in academic health centers was too slow and could not satisfy the industry's requirements, so much of the pharmaceutical research has now moved to the private sector (Bodenheimer, 2000). For example, the majority of studies are increasingly conducted at private dedicated research clinics and small research sites that operate within private practices and use existing staff to manage clinical trials. The most widely

known auxiliary companies of the research industry are contract research organizations (CROs). These companies select prospective research sites, negotiate contracts, and monitor the collected data on behalf of pharmaceutical and medical device industries (Fisher, 2009).

Patient recruitment organizations have emerged and expanded around the world in response to the growing need for human research subjects. Until recently, patient recruitment was the responsibility of the principal investigator. Patients were drawn from the physician's practice, and sponsors paid for that access as part of the physician's total compensation. As the numbers of clinical trials increased and competition grew among companies testing similar compounds and procedures, recruiting patients from physician practices was not sufficient. Principal investigators and research clinics started spending money on promotional campaigns with varying degrees of success. However, the return-on-investment was considered too low, and sponsors started to incorporate centrally organized patient recruitment campaigns for all the research sites involved in the trial (Brescia, 2004).

How many patients do we need?

CenterWatch reported that 2.8 million individuals completed initial screenings for industry-sponsored clinical trials in 1999. An estimated twenty-one percent of those who responded to these recruitment promotions showed up for the initial screening, seven percent enrolled in studies, and only five percent completed trials (Krall, 2001).

To get some insight into the current size of the clinical trial industry, on June 6th, 2012, I carried out a simple search at the U.S. National Institute of Health research study registry, www.clinicaltrials.gov, and the results indicated that currently there are 127,018 trials in progress in 178 countries. After excluding Phase I studies and those with unknown recruitment status, approximately 7000 studies were actively recruiting for Phase II-IV intervention studies in the US.

Krall (2010) did a more sophisticated analysis using data from the same website, to assess the current capacity to conduct clinical trials in the US. He concluded that as of August 16, 2009 there were 10,974 interventional trials actively recruiting participants in the US. In total, these trials were seeking to recruit 2.8 million subjects. The author estimated that 1 in every 200 persons in the US would need to participate if the current research portfolio is to be successfully completed, assuming that people participate in one trial at a time. Approximately half of the subjects recruited are for Phase III trials. Two-thirds of the "actively recruiting interventional trials" are designed to study the major diseases: cancer, cardiovascular disease, diabetes, and depression (Krall, 2010). The Center for Information and Study on Clinical Research Participation (CISCRP) estimated that in 2006, 2.4 million people completed clinical trials. The number of people who participated in clinical studies is close to the estimated number by Krall (2010) of the participants necessary to complete existing research studies.

However, Krall (2010) points out that 17% of US investigators fail to enroll any subjects, 56% fail to enroll their target number, and 90% of trials are not completed as planned. The author concludes "this also raises the fundamental question of whether a

controlled clinical trial portfolio that requires the participation of 1 in every 200 US citizens is achievable" (Krall, 2010). His conclusion highlights that recruitment problems might be due to the unproductive performances of investigational sites rather than the lack of interested research participants.

Although other studies within the industry agree that the issue with recruitment is at the site level (CenterWatch, 2006), the experience of a recent Pfizer project shows quite a different picture. The company decided to run the first clinical trial allowing patients to participate from home using computers and smart-phones instead of going to a clinic or doctor's office. The idea was to create a model for saving money that will rely on personal technology to more easily recruit patients and monitor their progress. In this case, where the inconvenience of visiting and contacting research sites was removed, finding patients for the study testing Detrol, a drug for the treatment of overactive bladder, was still a challenge. In an interview published in a blog devoted to the pharmaceutical industry, Pfizer representative Craig Lipset explained:

> We've been able to drive thousands of hits to the website and many (people) created accounts based on the information we put out there. That was everything from Craigslist to Google searching to Facebook to online communities like Inspire and PatientsLikeMe to other online outreach, such as recruitment firms. Each has been able to drive thousands of patients, in terms of impressions, to the site, but the next step is considering whether patients are willing to participate this way; and the conversion rates have been low. That said, we didn't expect each patient who learns about this on their own online to raise their hand and say they

> want to do that. If you put out Google ads, you'll drive traffic but not necessarily the type of patient who's ready to participate, compared with already formed communities where patients are actively engaged. Those are lower in number, but they are an enriched group of patients. (Silverman, 2012)

He attributed failure to attract patients to a low level of understanding by the public of what it means to participate in a clinical study. In addition, as Lipset reflects in the quote above, although there could be interested patients somewhere, it is a challenge to find them and catch their attention in the sea of information available in any media. Although the number of necessary participants for clinical studies is growing, it is unlikely that the pharmaceutical and medical device industry would pursue the development of products without enough patients available to purchase a product. Challenges also lay elsewhere—factors that shape the success of patient recruitment for clinical trials are complex and often appear contradictory to each other, as in the examples I mentioned above.

In the following section I will outline common techniques and challenges with patient recruitment in the published literature. Although the only available literature on the barriers to recruitment is about publicly funded studies, I hope this discussion will provide background on the kind of issues that recruitment companies need to manage. In addition, it will also provide a basis for the discussion of how different research bodies (in this case public and private) go about approaching recruitment issues, as well as the advantages and limitations of these approaches.

Patient recruitment techniques and challenges

Historically clinics have employed a "trial and error" recruitment system, where recruitment methods are assessed throughout the duration of the trial, and only successful methods are kept for further recruitment (Trussel, 2011). As a result, researchers are worried that because of inadequate enrollment, scarce public resources are wasted, and clinically relevant effects can appear to be statistically non-significant and delayed from being incorporated into a clinical practice (Treweek et al 2010; Haidich & Ioannidis, 2001). Moreover, trials failing to meet their quotas in enrollment raise an ethical issue—that participants have been unnecessarily exposed to interventions with uncertain benefits.

In addition to results of a study, successful patient enrollment is also a measure of a new intervention's success. If an enrollment level has been low, it is more likely that research questions have not been adequately addressed, and the results will have low impact in clinical practice (Kye, 2009, McDonald, 2006).

Consequently, because of these concerns and pressures to secure public funding, a body of literature has emerged that exclusively focuses on standardizing and evaluating patient recruitment processes and the barriers that hinder successful enrollment. Another section of literature which is primarily concerned with how to reach and enroll minority patient populations in the US is driven by the National Institute of Health (NIH) guidelines and initiatives (Epstein, 2008). In order to acquire NIH funding, researchers are required to recruit and enroll women and racial and ethnic minorities in their studies (NIH Revitalization Act, 1993).

Despite these attempts to standardize patient recruitment, the reliability and generalization of findings on patient recruitment procedures across different kinds of studies and disease states remain questionable. Findings are often conflicting. Subsequently, I will summarize and present common barriers identified in the academic literature and solutions proposed for enrollment. This section will provide background for discussion of the first research question: how do recruitment companies work in order to meet the high demand for patient recruitment?

Patient recruitment and enrollment is very complex and is influenced by various factors. There are five broad domains that affect patient recruitment. One is the characteristics of the target population, such as age range, prevalence of the disease, and socioeconomic mix (Kye, 2009; Bjornson-Benson, 1993). For example, if a research team is aiming to attract children, recruitment tactics need to be directed towards parents; or if a trial's participants suffer from an orphan disease then it might be more effective to approach specific patient advocacy groups rather than running an ad on the TV; or if researchers are attempting to include patient populations that rarely see a physician, then recruitment could be done at community fairs or churches. Researchers have to collect very detailed information on potential participation and understand what their habits are and where these individuals can be reached.

In addition, some trials aim to enroll from an existing pool of patients, while other trials seek treatment naïve patients where researchers have to wait for new incident-eligible patients. In the presence of a large existing pool of diagnosed patients, enrollment may be rapid, whereas in other cases it is slower because new eligible cases have to be

identified (Haidich, 2001). For example, in the United States, patients with Type 2 diabetes are treated aggressively at an early stage of the disease based on guidelines by American Diabetes Association (American Diabetes Association, 2012). In addition, the prevalence rates of newly diagnosed Type 2 diabetes remain relatively constant, thus further limiting the potential patient population. However, it does not mean that treatment-experienced patients are easy to recruit. If the majority of patients are doing well on their treatments, or reasonably well, both they and their doctor will be reluctant to enter a study. A trial needs to offer a significant improvement for patients to be willing to participate. In this situation recruiters are competing for patients against approved therapies and need to find selected patient groups or offer significant benefits in order to attract participants.

Due to the high cost of health care in the US, a large group of patients have emerged that seek to participate in clinical trials to receive at least some medical attention and treatment. It is widely recognized that the industry is interested in recruiting individuals without adequate health insurance; however, scholars are concerned about their ability to critically evaluate risks when such high incentives are present (Elliott, 2008; Fisher, 2007; Epstein, 2007; Rajan, 2006).

The second domain that impacts patient recruitment is the characteristics of the study (Kye, 2009), such as trial design, correct estimation of the number of patients available for study participation (McDonald, 2011), and randomization (Caldwell, 2010). Clinical trials that compare new therapy with an approved one are more appealing to

patients than those that involve a placebo arm. Moreover, the size of the patient pool depends on how realistic eligibility criteria are (Haidich, 2001). Given the high cost of patient recruitment, a limited budget and resources dedicated to recruitment can also be a hindering factor (CenterWatch, 2006; Table 5.07).

Another critical factor is the attractiveness of the protocol circumstances under which the study is launched. For example, patients might be enthusiastic to participate if the clinical trial presents a promising treatment; or a large number of competing studies targeting the same population of participants can hinder patient recruitment (Peters Lawrence et al, 2012). Additionally, complex trial procedures and the high number of follow up visits can be seen as a burden by the public and result in low participation (McDonald, 2011). Moreover, attitudes toward the clinical study can change as results from another trial or advances in the development of alternative treatments become available (Haidich, 2001).

Third, the characteristics of the disease, such as the likelihood of symptoms or public familiarity with the disease (Bjornson-Benson, 1993) can also affect recruitment. If a disease has a stigma attached to it, as in the case of sexual dysfunction or urinary incontinence, patients are unlikely to talk about it with friends, family, or even care providers.

Fourth, the organizational structure of a research institution can influence patient enrollment in research studies. Factors such as the lack of available staff (Peters Lawrence et al, 2012; McDonald, 2011) or working relationships with nearby care providers and communities can influence enrollment (Peters Lawrence et al, 2012). This

means that researchers and recruiters need to maintain good relationships with nearby practicing physicians that would be open to referring their patients to a study. Community leaders can be helpful by spreading the word about a study and encouraging participation. Organization of a clinic and its locations also plays a role—no matter how useful a clinical trial can appear to patient, if there is no one at a clinic to answer telephone calls or a clinic is far from public transportation, patient recruitment will be a challenge (Peters Lawrence et al, 2012; McDonald, 2011). It also has been suggested that the clinic's location within a well-respected institution in the community can contribute to the overall effectiveness of media promotion (Bjornson-Benson, 1993).

Fifth, physicians can play a huge role in the success of patient recruitment. Physician "buy-in" to the importance of the clinical trial is a common barrier identified in the literature (Trussel, 2011). In these situations, physicians are gate keepers for clinical studies. Their personal beliefs about the treatment options or study design determine if they will present the research study to their patients. In addition, physicians might be reluctant to share information on available studies with their patients because they have too little time dedicated for patient visits (Galvin, Meuser, Boise & Connelle, 2009) and because they might be afraid to lose their patients for follow up (Mansour, 1994). In the US, the widespread use of television, print, and radio advertisement, as well as information available on the internet is an attempt to minimize this barrier.

Barriers identified to patient involvement in clinical research include the lack of interest or a patient's strong preference for one treatment, and their unwillingness to be randomized, or patients who are not willing to commit to the number of visits needed

(Kye, 2009). Refusal rates are seen to be higher in prevention trials than in therapeutic studies. Potential participants are healthy and do not experience any symptoms, and therefore may not perceive any risks associated with a particular condition (Rimer et al, 1996).

It is highly likely that the clinical trials that involve recruitment firms face similar challenges. Given the issues presented above, I will further explore the types of challenges recruitment companies are attempting to solve and how they go about doing that.

Ethical issues with recruitment

Informed consent process

Discussion about ethical issues involved with patient recruitment is mostly based on the concept of informed consent and the principle of autonomy, because patient recruitment materials are defined (I further discuss regulatory requirements in the next section) as the beginning of the informed consent process; meaning that the process of informed choice begins when an individual encounters a clinical trial advertisement meant to attract patients to medical studies.

In the United States, informed consent was introduced in 1981 as a response to public outcry over abuses of human subjects in order to eliminate the deception and coercion of human subjects participating in research (Faden & Beauchamp, 1986). Informed consent is defined as the process of communication between the research participant and investigator during which the research participant agrees to undergo

certain medical intervention. The need to secure a patient's fully-informed consent prior to medical intervention for research purposes is seen as an ethical panacea counteracting the potential danger of paternalistic and autocratic practices (Corrigan, 2003). The assumption underpinning the implementation of informed consent is that doing so will protect the rights and welfare of individuals by offering them the opportunity to make free and informed choices. The foundation of informed consent is the principle of autonomy—recognition that individuals act as autonomous beings who make decisions about participating in research on the basis of the information given to them (Beauchamp, 2010).

Ruth Faden and Tom Beauchamp, in their conceptual work of the informed consent process, identified two senses of informed choice. In the first sense, "actual" informed choice is an autonomous authorization by a patient or a research subject. It consists of acting with intention (i.e., deliberately), with understanding, and without controlling influences that determine the action's outcome (Faden & Beauchamp, 1986, p. 238). According to these authors, informed choice is achieved when an action is substantially autonomous (p. 239). In the second sense, informed choice is analyzed in terms of the degree to which patients and research subjects are treated in accordance with policies or standard practices that require certain standards of disclosure, comprehension, competence, and minimization of controlling influences before informed choice can be said to be obtained. Although not "actual" informed choice, the second sense is an "effective" informed choice used in many health care institutions and ideally based on the first definition.

Many scholars have critiqued autonomy-centered bioethics by pointing out that informed consent is premised largely on the autonomous individual and his or her rights, with little or no conception of the social aspects (Fox & Swazey, 1984; Light & McGee, 1998; Wolpe, 1998). This rational-choice model of action presupposes that autonomous individuals, when presented with adequate information and given time to assess it, will subsequently make a conscious decision whether or not to participate (Corrigan, 2003). Carolyn Ells (2003) explains why the rational-choice model is inadequate:

> We are not the people Faden and Beauchamp conceptualize. There is much more involved in our understanding about persons. For instance, there are relational and fluid aspects to people that Faden and Beauchamp do not consider. Further, persons are found in and through the matrixes of numerous power relations involving economic, sexual, political, racial, class, and other grids, all of which are integral to their identity as well as their interests. (Ells, 2003)

The discussion about the importance of social context in a valid informed consent process is important because social scientists have observed that patients and doctors bring pre-existing norms and values to the clinical trial setting that shape their expectations and direct their behavior (Corrigan, 2003; Fisher, 2007; Abadie, 2010). Scholars have argued that the pharmaceutical industry is profiting from individuals who do not have better alternatives than participation in clinical trials due to the lack of health care or money (Elliott, 2008; Fisher, 2007; Epstein, 2007; Rajan, 2006).

Because the social context shapes reasons why certain individuals participate in clinical trials, the process of "informed choice" in clinical trials already begins before

potential participants attend "screening and consent visits", where individuals usually discuss the clinical trial study with research staff and receive an informed consent form to sign. Jill Fisher (2007) points out that most of the prospective research participants have already decided to participate in clinical studies before they receive the informed consent forms (Fisher, 2007). In these cases, the decision was made before individuals had full information about the purposes, risks, and benefits of a particular research study; thus it can hardly be said to have been "informed."

Given the issues described above, in my project I further explore how patient recruitment companies view the process of informed consent and how they incorporate regulatory requirements and their own understanding of the informed consent process in daily practices of patient recruiting.

Advertising clinical trials

The use of language in clinical trial advertisement is a widely discussed topic. It is well recognized that recruitment advertisement often presents investigational medications as definitive treatment and the clinical study as a way to receive free medical care (Office of Inspector General, 2000). The phenomena of blurring the lines between research and treatment is often called "therapeutic misconception" (Appelbaum, Roth, & Lidz, 1982) and it results in human subjects entering research studies with the belief that they are receiving treatment. In this case, an individual's decision to participate in a research study is based on incorrect information, therefore indicating the lack of a valid informed consent process. This matters because there is doubt that participants would have

volunteered if they were clear about the purpose and design of the clinical study (Miller, 2010).

How much does your study pay?

Another widely discussed recruitment strategy is offering financial and non-financial incentives for potential clinical trial participants. Incentives have become an important part of recruitment as researchers struggle to enroll enough human subjects in clinical studies. Sometimes these incentives are seen as welcome offers or reimbursements for the time spent in a study. However, they raise concerns when, a) the risks of clinical trials are increased, b) more attractive inducements are introduced, and c) when subjects are economically disadvantaged or lack other alternatives or resources (Beauchamp, 2010).

Recruiters use money, access to health care and medications to recruit specific populations, such as the poor, uneducated, and uninsured in order to complete research studies (Fisher, 2009; Abadie, 2010). In these cases, participants can gain a short term benefit from participating, but they remain unprotected if they are harmed during the research process (Steinbrook, 2006). They carry the burden of the research process, but subsequent benefits (e.g., medications) remain unavailable to them due to the absence of health insurance and money.

Retaining research participants

In addition to recruitment services, companies offer to develop a retention strategy which focuses on how to persuade participants to remain in the study until the

trial is completed. This is important because if too many participants drop out of the study, the ability to generate scientifically valid conclusions can be questioned. This could lead to a requirement to repeat the study with a new group of volunteers, which would cost pharmaceutical companies more time and money (Anderson, 2004). Retention involves tension between the participant's right to quit the study any time and the pressure for researchers to retain participants in the study.

Although ethical issues with recruitment have been identified and discussed, there is a lack of understanding of what happens when recruitment and retention for clinical trials becomes professionalized and is driven by monetary incentives. Even though professionalization of recruitment and retention can mean improving the research process, and reducing the price and time of the research process, it also can involve potential ethical issues that need to be explored. In addition, recruitment methods and strategies are developing faster than regulations. This situation may impede the process of ensuring alignment between societal values and commercial interests.

Regulations and protection of human subjects

The Food and Drug Administration (FDA) is responsible for protecting the rights and welfare of human subjects participating in clinical research. The FDA delegates most of its direct authority to institutional review boards (IRBs), which are the primary mechanism for protecting research participants. The FDA regulations require that IRBs review all research protocols as well as the methods and materials that are proposed for patient recruitment to ensure that human subjects are adequately protected—not coerced, misled, or offered inappropriate inducements (FDA, 2009a).

The FDA has issued an information sheet that IRBs should use as a guide when reviewing recruitment materials (FDA, 2009b). The information sheet represents the FDA's current thinking on protection of research participants. These requirements apply for protocols that are seeking approval in the US. The direct authority to review human-subject research is delegated to IRBs; thus, it is up to an IRB to interpret it and decide if submitted materials meet the requirements in the information sheet. Different IRBs may differently apply the guidance, and sponsors are not bound to incorporate changes suggested by an IRB (except if a hospital or an academic institution has its own IRB), because there is a good amount of other IRBs, including for-profit IRBs that would be willing to provide approval without requesting any changes.

According to this information sheet, clinical trial advertising to the public is the beginning of the informed consent process. It means that information communicated in the recruitment process is the first a participant will encounter, and the one the patient uses to make a decision. Presumably, patients will use information obtained in the recruitment process to make decisions about participation in the study. Although recruitment materials are considered the beginning of the informed consent process, it is not required to present the same information there as on the informed consent form. For example, risks or disclosure of alternative available treatments that could be beneficial to the patient can be omitted from participant recruitment materials. The main focus of reviewing recruitment materials is to ensure that the information presented is not deceptive and does not promise anything beyond what is outlined in a consent form.

IRBs have to assure that advertising is not unduly coercive and does not promise a certainty of cure. IRBs are encouraged to be especially protective when a study involves subjects that are considered vulnerable, such as; children, prisoners, pregnant women, handicapped, or mentally disabled persons, or economically or educationally disadvantaged persons.

The guidelines also suggest that advertisement is not supposed to make claims about the effectiveness or safety of the investigative medication, or if it is known to be equivalent or superior to any other medication. In addition, recruitment materials should not contain terms like “new treatment” or “new medication” without explaining that the medication is investigational. Advertisements should not promise "free medical treatment" when the intent is only to say subjects will not be charged for taking part in the investigation. Advertisements may state that subjects will be paid, but should not emphasize the payment or the amount to be paid. And finally, the IRB should ensure that all personal and sensitive information about individuals will be handled appropriately.

The FDA guidelines mainly refer to recruitment by mass media advertisement and do not discuss other recruitment or retention methods. New recruitment techniques have been used more frequently, such as reminders sent to patient’s cell-phones, investigator speeches at local health fairs, and brief posts on social networking sites (Anderson, 2004). Due to the lack of up-to-date guidelines, IRBs are confused over whether these methods actually constitute a recruitment method and what they can or should do if they discover violations after they have given approval (Office of Inspector General, 2000). Another problem with oversight is that IRBs review recruitment materials prospectively,

before the clinical study actually starts. There is no monitoring of the actual research site or telephone conversation when recruitment is occurring (Office of Inspector General, 2010). In many cases, even when a particular IRB suggests changes to some recruitment materials or methods, the recruitment company is not bound to incorporate those changes. Recruitment organizations can submit their applications for review to any other IRB, including for-profit IRBs that may be willing to provide approval without requesting any changes (Emanuel, Lemmens, & Elliot, 2006).

When using social media for patient recruitment, basic requirements regarding how to present information are the same as guidelines for media advertisement. However, in social media, which is a place where individuals with similar interests interact, recruiters have no control over the message about clinical trials, and it raises the question of who is responsible for the presented information and what to do about it—and how can online interactions between the participants and researchers be pre-approved? In November, 2009, the FDA organized public hearings to collect information to begin crafting regulatory guidelines for the use of social media by life science companies. The draft guidelines have been issued (FDA 2011, December). However, the FDA does not address any of the questions related to the recruitment for clinical trials, such as how to handle potential unblinding when trial participants share details of their trial involvement online, or what to do about adverse events when trial subjects report them via a blog or social media (Redfearn, 2012).

Patient recruitment for research also means promotion of an investigational product. The aim of the FDA provisions regarding the promotion of investigational

products is similar to recruitment material guidelines—promotion should not claim that an investigational product is safe or effective. However, this provision does not restrict the exchange of scientific information concerning the drug, including dissemination of scientific findings in scientific or lay media (FDA, 2011 April).

Summary

In this chapter I presented an overview of the clinical trials enterprise by focusing on patient recruitment, which has been identified as the most costly and impeding factor of clinical research. I discussed the history of patient recruitment, current costs, and challenges associated with finding patients for research studies, as well as challenges that researchers face when trying to find and admit patients to medical studies. I also discussed in detail current regulations and an approach to patient protection in the field of patient recruitment. The results of my research project will add to the existing literature by describing how private patient recruitment organizations approach existing challenges and go about finding and selecting human participants. Moreover, the results of this project will initiate discussion of the relationships that are in place among recruitment firms, research sites, sponsors, and patients, and how these interactions affects the recruitment process and patient protection in the clinical research.

Chapter 3: Research design and methodology

I spent one year observing and interviewing patient recruitment organizations. Three interrelated issues captured my attention. First, how do patient recruitment companies work in order to meet the high demand for human subjects? Second, how do patient recruitment companies manage relationships among various stake holders within the clinical trial industry and what are specific factors that facilitate and hinder patient recruitment? And third, what ethical issues are involved in these practices? These ethnographic questions required my presence in the world of those whose daily work involves recruiting patients for clinical studies. The descriptive part of ethnography will serve as a context of discussion for the ethical, social and political issues related to patient recruitment which is my main interest in this project.

The most appropriate methodology to answer the research questions described in the first chapter is ethnography. Ethnography is used when there is little information known about the topic and when the research aims to gain a holistic understanding of a group's beliefs and values. Furthermore, ethnographic research is well-suited to the study of ethical issues. Ethical issues and dilemmas are morally charged, laden with meaning, and unfold through social interactions (Gordon & Wolder Levin, 2008). Thus ethnographic research is ideal for opening doors to the world of meanings attributed to health-related events and moral decisions, as well as for understanding the broader socioeconomic and political factors shaping how cultures and cultural members frame, interpret, and respond to such phenomena (Gordon & Wolder Levin, 2008). For these

reasons I identified ethnography as the most appropriate research methodology to answer the questions posed.

In this chapter I will discuss the philosophical assumptions behind qualitative research that serve as the foundation of my project. Further, I will provide a theoretical foundation for ethnographic research as well as for the design and methods employed through the research process. I will finish by discussing how I attempted to ensure the quality of this project and to consider the ethical issues during my fieldwork.

Philosophical foundations of qualitative research

The foundation of my research process was based on the principles of qualitative inquiry. Qualitative inquiry is primarily naturalistic, interpretive, and inductive. By seeking to understand naturally occurring phenomena, qualitative researchers attempt to interpret or make sense of the meaning people attach to their experiences and/or which underlie a particular social phenomenon. Researchers are required to enter into the spaces of the people whom they study and to have face-to-face interactions with them. Moreover, qualitative researchers work inductively from individual cases and not from a preexisting framework or a particular theory (Mayan, 2009).

Qualitative inquiry practitioners share certain theoretical assumptions and methods that guide the research process. Naturalistic paradigm and interpretive inquiry reflect the issues related to the nature of social reality (ontology) and to the nature of knowledge (epistemology) (Guba, 1990). The ontological stance of this study is that social entities are not pre-given, but instead that reality is subjectively constructed by

study participants. The epistemological assumption is that research participants have an active role in the construction of social reality and that qualitative research methods can capture the complex world of lived experiences from the point of view of those who live it and can grasp the meaning of social phenomena (Guba & Lincoln, 1998).

Maria J. Mayan (2009) summarizes the relativist ontology and a subjectivist epistemology that was pertinent to my project. Mayan writes, "Research is dialogic: it is about being in a relationship. It is in the strongest and most powerful sense of the word subjective. We assume that there are multiple realities and multiple truths and that we are presenting just one possibility. The resulting text is historically, culturally, and socially constructed" (Mayan, 2009; Denzin & Lincoln, 2005).

The ethnographic approach

Ethnography is defined as a body of knowledge of cultural descriptions and theory, as well as a research process and product (Germain, 2001). As a qualitative research process, ethnography is a systematic practice that requires ethnographers to do fieldwork with human groups within the context of their daily lives, to see what happens, to listen to what is said, and to ask questions (O'Reilly, 2009; Madden, 2010). As a result, ethnography is also a form of non-fiction writing—richly written accounts based on systematically gathered data from fieldwork and other relevant secondary sources. These written accounts are an attempt to describe the culture of a given group as the individuals in the group see it (Mayan, 2009).

In addition to systematic documentation of the research process—which combines factual writing and reflects field notes, theoretical notes and personal reflection—

ethnographic authority also relies on the personal experience of the ethnographer, that is, the research instrument (Atkinson 1992). By undertaking participant observation, ethnographers are both research guides and also a tool of the research. For this reason it is important for ethnographer to be reflexive in order to understand and manage their influence on the research process (Madden, 2010).

In addition to the concepts mentioned above, all ethnographies have several other hallmark characteristics. Specifically, they: (a) focus on culture; (b) are holistic and contextual in nature; (c) have a reflexive character; (d) incorporate perspectives of study participants (emic data) and researcher (etic data); and (e) result in an end product called ethnography (Boyle, 1994; Fetterman, 2010; Wolcott, 2005).

The distinctive feature of ethnography, among other forms of qualitative research, is its focus on the cultural perspective. Zane Robinson Wolf (2006) writes: "By generating cultural description, ethnographic investigations examine what the world is like for people who have learned to see, hear, speak, think, and act in ways that are different from dominant cultures" (Wolf, 2006). Ethnographic research is based on the assumption that culture is learned and shared among members of a group and, therefore, can be described and understood (Boyle, 1994). During my study of patient recruitment organizations, I also assumed that individuals involved in patient recruitment shared certain intellectual and moral frameworks that shape how group functions within the larger context of the clinical trial industry. By focusing on the culture of patient recruitment companies, I was aiming to understand their routine attitudes, beliefs, and practices towards research participants and towards the recruitment process.

Another critical component of ethnographic research is its emphasis on holism. Although ethnographers are seeking to understand how different people in distinct locales experience daily life, there exists an important claim that people can no longer be understood in their local contexts alone, and so the regional or global context as well as the political, economic, social and cultural relations that influence local contexts must be addressed (O'Reilly, 2009). In order to gain a comprehensive picture of the patient recruitment industry, incorporating a holistic viewpoint meant that I had to evaluate the role of sponsors and research sites in the decisions made by the recruitment company.

Fetterman (2010) argues that it is impossible to capture an entire culture of any group. However, he suggests that a holistic approach forces the researcher to look beyond the immediate scene or event in order to see how "each scene exists within a multilayered and interrelated context" (Fetterman, 2010). Assuming a holistic perspective forces the researcher to be cautious regarding the "holistic fallacy." This fallacy can occur when the ethnographer constructs connections because of her bias to find one instead of checking connections carefully (Agar, 1996). I will outline techniques to avoid this fallacy in the section on ensuring the quality of the research project.

Another important concept of ethnographic research is contextualization. Because meaning changes with context, one needs to be concerned with placing observations into specific contexts (Fetterman, 2010; Leiter, 1980). In my project, a detailed description of the physical context as well as the social context—such as interactions and relationships between informants—helped contextualize the study. Physical as well as social contexts were detailed in the field notes. However, ethnographers caution the researcher to be

aware of the fact that the elements of the context are constantly shifting, as do the meanings of the episodes and events being described (Leiter, 1980; Wolf, 2006).

In addition to placing findings in the participants' physical and social context, ethnographic research, including my project, aims to find a relationship between an emic (insider's) and etic (outsider's) perspective in order to accurately interpret and describe situations and behaviors (Morse, 1986; Madden, 2010). The emic perspective reflects the insider's view on reality while the etic perspective is the outsider's framework, that is, the researcher's abstraction or the scientific explanation of reality (Fetterman, 2010; Morse, 1986). Such accounts of different views of reality help the ethnographer to develop conceptual interpretations (Morse, 1986). Although the main work of ethnography is to capture insider's perspectives, Madden (2010) writes that "the act of cultural translation—be it across perceived cultural gaps or some other communication divide, relies on ethnographers never losing sight on their own etic perspective and the driving questions that brought them to the field in the first place."

In order to ensure holistic view, contextualization and incorporate both emic and etic perspectives in the data collection process, I practiced reflection throughout the entire research process. The reflexive character of ethnography implies that the researcher is part of the world that she studies and is thus affected by it. Moreover, reflexivity means an awareness that ethnographies are constructed by human beings who make choices about what to study, what to read, interpret what they see and hear, decide what to write and how, and they do all of this in the context of their own personal biographies and within scientific and disciplinary environments (Spencer, 2001).

Werner and Schoepfle (1987) explain the significant role reflexivity plays in going beyond ethnographic description. According to them, reflexivity permits the researcher to develop theoretical explanations by incorporating various perspectives on reality:

> As ethnographers, we try to do more than just describe the cultural knowledge of the native. We try to understand and, if possible, explain. We need to be able to explain how the natives could possibly view the world as they do. The paradox of this situation is that all descriptions, understanding, and explanation of the natives' cultural knowledge is based fundamentally on two disparate, incompletely transmittable, presumptive systems of knowledge—the knowledge of the native and the knowledge of the ethnographer.

I have up to this point described the characteristics of ethnographic research—focus on culture, holistic perspective, contextualization, emic and etic perspectives, and reflexivity—that were all incorporated into my research process. In the following section, I will present the specific methods that I used for data collection.

Methods and data collection

The design of this project integrated three data collection methods into an ethnographic framework. I used 1) field observations, 2) interviews, and 3) the examination of documents to gather data. The use of multiple research methods is highly recommended to ensure the data's integrity and thus of sound ethnography (Wolcott, 2008; Fetterman, 2010; Agar, 1996). The combination of these methods permitted me to

incorporate different realities, ways of knowing and perceptions of phenomena while I investigated practices of patient recruitment as well as the relationship between the various stakeholders and the context of practice.

The data collection strategy I chose is also in agreement with the research guidance proposed by Wolcott (2008). He uses three elements to characterize ethnographic data collection: experiencing, inquiring and examining. Observational data are gathered through our experiences—what we see and hear while inquiring or interviewing and requires an active role in asking what is going on, in contrast to experiencing something passively. Examining defines activity where a researcher studies what has already been produced by others (i.e. documents), either by members of a community or by outsiders, but is not available to a larger audience. In this research project I used all three methods—experiencing, inquiring and examining—to gather data. In the following section, I will describe in greater detail the role and application of these methods in my research project.

Participant observation

Participant observation is the method by which the researcher joins the members of a group so that human relationships, events, patterns, and the sociocultural context in which people function can be studied (Jorgensen, 1989). The assumption behind my project is that by physically placing myself in the situation of those I am studying, I gain a deeper understanding of the informants' world than if I had restricted myself only to verbal inquiry (Savage, 2000). Through observation I was seeking to find knowledge that others, i.e. people who work at recruitment agencies, already have. I was attempting to

grasp meanings, norms, patterns, roles of informants, use of language, as well as to learn their function and structure in their culture through focused participant observations.

The participant observation was carried out for approximately eight months, from May 2011 until January 2012. The chosen setting for the majority of my observations was a medium- size recruitment company located in the Midwest. I chose this company for my project for two reasons. First, I selected it because of location—the company was physically accessible for me to conduct prolonged participant observations. Second, this company offered a full service of patient recruitment; that is, they offer services that include preparing marketing materials, working directly with clinicians, and screening patients. This gave me the opportunity to study different aspects of patient recruitment as well as the relations that professional recruiters form with other members of the research industry.

The recruitment company, of medium-size, has approximately thirty full-time employees. The organization of this company is presented in Figure 2. The recruitment company consists of several departments that play a central role in the recruitment process. The coordinators of every recruitment program are program managers. They work closely with sponsors to accommodate their needs and provide weekly updates of the recruitment process. According to the CEO of the company, the program manager needs to be competitive because his role is to constantly sell the recruitment plan and additional services to a client.

Program managers also collaborate closely with the in-house marketing, site service and call center departments. Program managers make the key decisions for recruitment

programs; for example, they decide when to stop or initiate advertising for certain research sites, how to solve recruitment challenges, etc. During the time that I conducted participant observations there were two full-time program managers. One had worked at the company for about one year, but he had many years of experience working in the medical device industry. The second program manager position experienced heavy turnover, being filled by three different managers during my observation period. First it was filled by a former research associate in a contract research organization; second by a former study coordinator who worked at the company only for a very short period; third (this was towards the end of my field work) by a pharmacist who had recently left her job at a large pharmaceutical company.

The role of the marketing department is to design and produce advertisement campaigns, to choose the best media for a campaign, and to negotiate rates for advertising in television, radio stations, newspapers and/or websites. They also conduct detailed analyses of the response rate for each advertisement and adjust the frequency or placement in specific media (newspaper, radio, television, website) when a response rate is low. I had two informants from the marketing department—one was a marketing director and the other, a marketing specialist. Both of them had many years of experience in marketing before they had come to work in the recruitment company.

In the call center, the manager designs and writes scripts for screening. She also coordinates work schedules for employees and monitors calls to ensure that everything goes according to the script. Occasionally, she handles particularly unhappy patients to prevent an escalation of the conflict. Before she had come to work at the recruitment

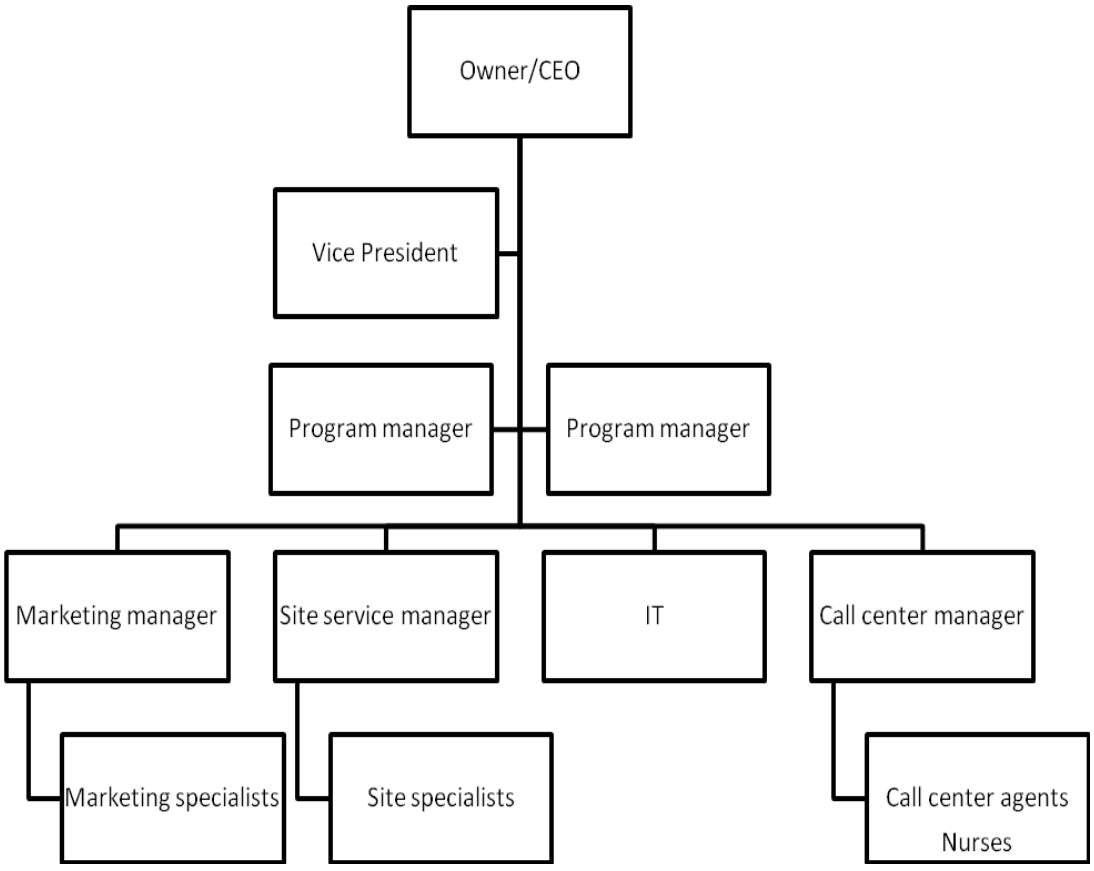
agency, she managed a large call center that served customers on behalf of various retailers.

The call center is the largest department in the company. The company employs two types of screening agents—entry-level call center staff who conduct basic screening as well as nurses who take care of medical screening. The number of employees changes according to the number of projects; during my observations there were up to twenty employees on project-heavy days. There are only two full-time nurses and rest of the call center staff has temporary contracts. During my interviews I learned that it is common practice to employ call center staff on a contract-basis; in this way, recruitment companies reduce the cost of operating recruitment programs.

The role of the site service department is to work closely with research sites to ensure that they follow up on screened and referred research participants. Site service specialists contact coordinators weekly for updates on the recruitment process and to offer help if research sites are overwhelmed with work. The services offered can involve, for example, providing advice on organizing the recruitment process or sending a temporary coordinator to a site who will assist with various recruitment-related tasks. The site service department manager monitors the progress of the recruitment process at the research sites on a weekly basis. If any of the research sites are behind the recruitment schedule, specialists will try to sort out problems and negotiate a solution with a coordinator. If this does not work, information regarding the issue will be forwarded to program managers who will discuss further with a sponsor. Although it was the busiest department in the company I studied, it was also the smallest—having only three

employees. My informants were the manager and a specialist; both of them were former research coordinators.

Figure 2. Organization of the patient recruitment company



Spradly (1979) writes that one of the central tasks of good fieldwork is to think through all the possible places to observe, times to observe, people to watch, and to discover whether or not it is possible and productive to do so. Thus I organized my observations so that I would be able to cover various aspects and components of the recruitment agency's work. I also attempted, as much as possible each week, to spend time in various daily activities with different employees of the recruitment agency. In addition, I attended three different clinical trial informational meetings organized for patients, two online webinars and two industry conferences on patient recruitment. Two

of the three clinical trial informational meetings were organized by the recruitment company for patients who were interested in enrolling in sleep apnea and weight loss studies. In these meetings the principal investigator shared information regarding the investigational product, study design, risks and benefits of participation and answered participants' questions. The third informational meeting was open to the public and was organized by the Center for Information and Study of Clinical Research Participation (CISCRP). CISCRP is a nonprofit organization dedicated to educating and informing the public, patients, medical/research communities, the media, and policy makers about clinical research and the role each party plays in the process. Several times a year CISCRP organizes educational events for the public with an aim to educate people on the importance and benefits of participation in clinical trials. In the meeting I attended in Chicago, a range of academic principal investigators and patients shared their experience with clinical trials.

The first webinar was offered by the Association of Clinical Research Professionals (ACRP). The title of the online presentation was: "Site selection, patient recruitment, and patient stipend management: Industry data and insights." The second webinar, "Patient recruitment: From traditional methods to new age tools," was offered by Compliance Online, a company that offers training for different professionals. Both of these webinars presented information on current trends and issues in patient recruitment and were aimed at research coordinators and other industry members who work with patient recruitment.

The first conference I attended, held in New York in October, 2011 and organized by a company called ALI was, "Patient recruitment, compliance and retention for clinical trials." The conference was small and had approximately 40 participants, including representatives from some of the largest recruitment companies, pharmaceutical organizations, and academic institutions. The second conference, held in Miami in February 2012 and organized by Cambridge Healthtech Institute, was the "3rd Annual Conference for Health Executives." The patient recruitment section in this conference featured speakers from all of the largest recruitment companies as well as from pharmaceutical and contract research organizations.

While conducting field work in the recruitment agency, I mainly observed meetings and interactions between recruitment agency employees and clients, conversations between the call center nurses and patients, as well as between employees themselves. Rarely did I observe individuals working at their computers; only on one occasion did I do so by observing an employee designing recruitment materials.

Entering the field was a gradual process. I learned about the company through an interview I had read in the local newspaper. After meeting with the company's CEO, I was granted access to all the agency's activities. The CEO was enthusiastic about my research idea and was familiar with ethnography. On the first day of my observations he introduced me to managerial-level employees. Gradually I presented myself to other employees when I would encounter them in the office or meetings. Although without the CEO's permission I would not have been able to access the company, I was worried that employees would feel obligated to accommodate my presence due to the CEO's high-

ranking position. Thus I asked each individual's permission to join his or her meetings at all times and I would let him or her know that he or she could ask me to leave at any time. Indeed, there were occasions when I was asked to leave the meeting room or to not make notes.

The quality of an ethnographic study depends on building trust and establishing relationships with gate keepers and informants (Wolf, 2006). Although participant observation provided me the opportunity to acquire the status of a "trusted person" (Glesne, 2006), the first couple of weeks in the field were stressful as I worried about whether people would accept me and I was self-conscious about doing things correctly.

Throughout my field activities I mainly remained an "observer as participant" (Glesne, 2006). For the most part, I was observing, taking notes and interacting with study participants but I did not participate in activities as an employee of the agency.

The company was recovering from the 2008 recession and had lost many of its employees. As new projects kept arriving in the middle of my observation period, everyone was overwhelmed and stressed by the amount of work to be completed. Since I felt I was burdening them with my presence, I offered to help with some small tasks. Only later did I realize that some of the employees perceived this as my attempt to become part of the community with the goal of seeking employment with the recruitment agency at a future point. Occasionally people would joke around saying that I could fill various positions that were needed at the time. I saw this as problematic because I sensed that some younger employees might perceive me as a threat or as a competitor. Thus I

had to take care to establish my researcher role while ensuring that the participants did not view me as a threat to them (Bonner-Tolhurst, 2002).

One of the challenges that a researcher faces during fieldwork is to maintain curiosity and naivety toward the group of people one is studying. Despite the geographical proximity and lack of exotic contingencies, being an international student as well as being unfamiliar with the company's field initially made me susceptible to differences and to the newness of the field. In order to maintain curiosity and openness through the entire process, I followed the advice given by Glesne (2006) and continually questioned my own assumptions and perceptions—regularly asking myself why is it this way and not different?

I always carried with me a notebook to record what I saw. When recording my observations I tried to write as close to verbatim as possible and to include specific and concrete details of observed scenes. I took notes during the events and then as soon as possible expanded on them to include a full description of the event or experience on my personal computer.

The researcher's attempt to find meaning in the behaviors of others requires introspection on the part of the ethnographer, who, by accumulating education and life experiences, brings her own cultural perspectives (etic) to the field (Boyle, 1994). Therefore I kept a field journal for recording my feelings, reactions, biases, and other results of introspection (Koch & Harrington, 1998). This reflexivity was an essential part of the data collected since experience is co-created. I also tried to be mindful of how

features such as age, gender, and personality of the researcher direct the process and the findings.

Interviews

Interviewing was another important data collection strategy for this project. I used two types of interviewing. First, I carried out informal interviews which were part of participant observations. I recorded information obtained through informal interviews in my notebooks in the same way I recorded observations. Second, after completing the fieldwork I conducted thirty-four formal, semi-structured, face-to-face and phone interviews. These interviewees included twenty two employees from seven different recruitment companies (including the primary field site). In addition, I talked to representatives (coordinators and recruiters) from ten research sites regarding their experience with patient recruitment and their work with recruitment firms. Formal, semi-structured interviews ranged from 20 minutes to more than one hour. These interviews, tape-recorded and transcribed verbatim, were conducted after each individual had given his or her oral and written consent.

Informal interviews are used in the field to get immediate input on the meanings of events as they occur, especially of those that are unexpected (Gordon & Wolder Levin, 2008). Fetterman (2010) describes informal interviews as casual conversations with an implicit research agenda. He continues by saying that informal interviews allow the researcher to discover what people think and how one person's perceptions compare with another's. Such comparisons help to unravel shared beliefs and behaviors among the group. At first I felt great discomfort conducting informal interviews—due to the offices'

open space and the employees' tight schedules, which reinforced my feeling of being a burden. Moreover I was afraid to put any of the participants in an uncomfortable position, but as fieldwork progressed and I got acquainted with participants, I became more confident in assessing situations to know when and where it would be appropriate to initiate informal conversations with informants.

I carried out informal interviews while conducting participant observation. When I completed field observations, I conducted formal, semi-structured interviews. Formal interviews served two purposes. First, they served as a check on the validity of my data. Many of my interpretations from field work I rephrased as questions for interviewees. In this way, I could evaluate my assessment against those of the actors in the scene and I could also "fill in" spots where my observational material was "thin." Second, the interviews allowed me to see my observations in a larger context (Bosk, 1979). For example, by exploring questions of how current regulations facilitate or hinder the recruitment process, I was able to place my observations in the larger context of the healthcare system and the clinical trial industry.

Interviewees

To select informants for formal, semi-structured interviews, I used non-probability, purposeful sampling. Since the assumption was that all actors in a setting are not equally informed about the knowledge sought by the researcher (Morse, 1986; Sandelowski, 1995), thus all interviewees were deliberately selected by the researcher according to research needs. For example, after field observations and the initial interviews I had collected a significant amount of information regarding the firm's

interactions with sites, yet I had unanswered questions remaining about how the firm develops its marketing materials. In subsequent interviews I therefore sought out people who were responsible for this aspect of recruiting and designed my research questions according to this research need.

The sample size for formal, semi-structured interviews was determined by data saturation. When I felt confident that the data I had collected was complete, answered the posed research questions, and further interviews did not reveal any new significant information, I concluded the data gathering process.

Initially, I interviewed individuals from the primary field site. Seventeen interviews were conducted with key actors during my participant observations (for interviewee demographics refer to Table 2). I interviewed representatives from all major departments who play significant roles in the patient recruitment process—that is, the CEO, the vice president, representatives from the call center and site service department, marketing specialists and program directors. Excluded individuals were IT specialists and individuals who performed technical tasks and who did not participate in any decision-making process. I invited individuals for interviews by approaching them in-person or by sending them an email. I explained the purpose behind my interest and invited them for coffee. It was my aim to meet outside of the office since I felt that people would be more comfortable talking in places where no one would interrupt or overhear our conversation.

In addition to interviews with individuals from the primary field site, I also interviewed seven individuals from six different recruitment companies. With these interviews my goal was to gain a broader understanding of the recruitment approaches

used by various recruitment firms. When selecting participants I was interested to learn about recruitment processes as well as challenges among the different types of recruitment companies. I attended two industry conferences on patient recruitment where I developed contacts with representatives from different recruitment agencies. Later on I would contact them through email and schedule a phone interview. Overall, the response rate for these interviews was 60%; out of the twelve people I had approached for interviews, seven consented to participate.

Recruitment companies put significant effort to develop working relationships with research sites, but often face resistance from the research sites' employees—in particular, principal investigators and coordinators. I interviewed representatives from ten different research sites which included nine private sector research sites and one academic site. To select interviewees from research sites, I used information available on the website www.CenterWatch.com, a clinical trials information source that is widely used by the public and by members of the clinical research industry. I conducted six interviews in-person and four phone interviews. Inclusion criteria were location (for in-person interviews), broad research study profile and experience working with recruitment companies. For all of the interviews, I contacted a research coordinator by phone, explained my project and asked if he or she would be interested in talking with me. Most of the time, coordinators agreed to talk with me, but on two occasions they directed me instead to a designated recruiter at their clinic.

Table 2. Demographics of Interviewees

Job position	Female	Male	Average estimated age	African American	Hispanic	Caucasian/ White	Unknown race/ethnicity*
Call center director	1		45			1	
Call center nurses	5		29	2		3	
Marketing experts	2		45			2	
Owner		2	55			2	
Program managers	2	1	40			3	
Recruitment company director	3	1	36		1	3	
Research coordinators	7	1	—*			5	3
Research site recruiters	2		—*			1	1
Site service experts	2	1	30			3	
Vice president		2	45			2	
Total	**24**	**8**	**41**	**2**	**1**	**25**	**4**

*Demographics were not collected from four interviewees of investigational research sites

During all interviews, as suggested by Rubin and Rubin (2005), the interviewer and interviewees form a relationship in which there is a mutual influence. The researcher defines the project, introduces the topics of the conversation and steers the course of the interview (Kvale, 1996) while interviewees' answer the suggested topics, and convey concerns and meanings that are important to them and that might be further pursued by the researcher (Rubin & Rubin, 2005).

Because the goal of semi-structured interviews is to *understand* interviewees, it is paramount to establish rapport (Fontana & Frey, 2008; Spradly, 1979). Rapport refers to the researcher's ability to see the situation from the participants' point of view rather than to impose the world of academia and its preconceptions on to the participants. Indeed, on several occasions during the informal interviews, informants reacted towards my

comments by indicating some of my own academic preconceptions; they would say to me, for instance, that my comment was "such an academic way of seeing things." These reactions reminded me that being an international student in addition to having been socialized mainly in academic circles, it was important for me to be very cautious and reflective towards the way that I conducted my interviews in order to attempt to see the world from how they see it versus how I think it should be seen.

In each case I attempted to engage with participants and establish their trust. However, I had to keep in mind that, as Wolcott observes, "Asking does more than merely intrude." He writes, "Our questions as fieldworkers become increasingly intrusive as we seek to understand what is going on. As well, local issues, of purely academic concern may be fraught with political or economic overtones for respondents" (Wolcott, 2005). This was a central issue considering the interest of my project and the group that I was studying. Similar to other researchers (Rajan, 2006; Yeager& Kram, 1995), I experienced an organizational endeavor to protect against both intrusion into potentially sensitive matters and the unproductive use of employees' time (Yeager& Kram, 1995). Early on in the fieldwork I observed recruitment firms struggling to present themselves as legitimate recruitment experts in order to gain trust from clients. Although I was fortunate to have a good response rate to my request for interviews, the interviewing process was a challenge as I often experienced participants' eagerness to present the recruitment agencies in a favorable light. This presented me with the challenge of framing research questions in order to investigate ethical issues in-depth as well as of confronting every researcher's dilemma—is knowledge gained intimately, enough to be genuinely reliable?

In order to avoid formalistic answers and gain in-depth understanding, I used Rubin & Rubin's (2005) advice. They suggest avoiding direct questions that invoke formalistic answers. Instead, researcher should ask for stories on the topic and then analyze them for themes. Another approach is to present a concrete incident and to ask for comment on that incident. I employed both of these strategies during the interviews.

Moreover, I never asserted that my interest was in the ethical dimensions of recruitment and rarely used the words "ethics" or "moral dilemmas," as I discovered early-on that people often associate these terms with legality and IRB approval. Instead I asked participants to think about situations in which they felt ambivalence towards, or cases in which different values conflicted with each other, as relevant to the topic under discussion.

In order to connect with my interviewees, I presented myself in different ways to different interviewees after a quick assessment of a range of visual and verbal clues (Fontana & Frey, 2008). For example, when talking to young nurses at the call center I behaved more casually whereas when interviewing people at higher ranks I presented myself in a more professional and serious manner. Through phone interviews I attempted to be more verbal and descriptive as participants were not able to see my facial expressions or to observe my body language.

I also adapted and changed my interview questions to suit various participants as each of them had different experiences and areas of expertise; this allowed me to tap into their distinctive knowledge. Moreover, questions depended on my relationships with each individual participant, as well as the amount of time granted for an interview. I would

always start with low-profile questions and then gradually move to more sensitive ones (Fontana & Frey, 2008). Finally I would "wrap up" the interview by asking participants to share positive or rewarding experiences of their work.

Although I always prepared my questions in advance I strived to be flexible in my interviews to accommodate new information. I created new questions based on what I had learned in past interviews, thus I analyzed interviews throughout the project rather than just at the end. I incorporated pauses between interviews for reflection time and during such time I compared what I had asked my interviewees with what I should have asked, considered what questions required more depth, and altered questions for future interviews accordingly. I will address other aspects of maintaining the quality of collected data in the section "Ensuring Quality."

Document analysis

As part of the ethnographic research design I also reviewed and analyzed documents pertinent to understanding the culture of patient recruitment organizations. Wolcott (2008) suggests that any document that proves valuable as a source of information may be considered by the researcher. Written accounts can be an important source of data, regardless of whether the materials are formally catalogued or casually provided to a researcher who had had no prior knowledge of their existence. These are usually the various items that research participants have in their personal possession which may be shared with the ethnographer, but are not necessarily available to anyone else.

In my research project I reviewed documents which I was able to access while conducting participant observations. I usually asked my participants to share certain materials with me when I learned about them in a meeting or when someone had mentioned them in a discussion or an informal interview with me. At all times I was granted access to these materials. Documents that I reviewed contained creative briefs, call center scripts and recruitment materials in various stages, recruitment program proposals, as well as internal company policies and procedures.

Before starting my research I signed a confidentiality agreement with this particular firm. This agreement prevented me from collecting data about company's sales and marketing, customers' lists, email databases, pricing information, financial information and other proprietary information. Although it limited the information I was able to collect, but this type of information was not the primary focus of this research project. In addition, I reviewed and analyzed documents which I obtained from different industry sources such as monthly publications of the Association of Clinical Research Professionals, a privately owned publishing and information services provider of clinical trials information for clinical research professionals and patients, as well as of CenterWatch and PharmaVoice, a monthly magazine dedicated to executive and corporate management in the pharmaceutical, device, biotechnology and clinical research industries. I also gathered and analyzed materials from the webinars and industry conferences in which I had participated.

Data analysis

In the data analysis I followed the framework proposed by Emerson, Fretz and Shaw (1995). Their ideas are concurrent with those of other ethnographers, such as Germain (2001), Fetterman (2010), Milles & Huberman (1994) and others. For this project I followed the assumption that data do not stand alone; rather analysis occurs throughout all elements of the research project—as the researcher makes observations, records them in field notes, selects informants, codes notes and finally develops explicit theoretical assumptions (Milles & Huberman, 1994).

As is common in qualitative research, analysis was performed as an ongoing process during the entire research process. The concurrent analysis allowed me to go back and refine questions as well as to pursue emerging themes in further depth (Agar, 1996). I kept notes in my computer on the research process itself from its earliest stages, making notes of suggestions for interview sampling and of how particular materials I was reading might relate to this project. I also kept notes in a separate document that contained initial codes and categories linking notes to particular participants or observations.

The data analysis was seen as an interpretive task. Thus interpretations were not found; rather, they were made, that is, actively constructed through social processes (Ezzy, 2002). The entire ethnographic record was subjected to analysis. As suggested by Emerson, Fretz and Shaw (1995) I conducted analysis of collected data in two phases: 1) open coding; and 2) categorization. I uploaded all field notes and transcribed interviews in the Nvivo software which I used for open coding and then for categorization.

In the first phase of data analysis—open coding—I began with reading my data set, line-by-line (Miles& Huberman, 1984) and looking closely at what had been observed and recorded. The field notes were treated as a data set: I reviewed, re-experienced and re-examined everything that had been written down, while at the same time seeking to identify themes, patterns and variations within this record. In the software I assigned a label or a code to each unique theme. I repeated this process until coding did not seem to generate new ideas or themes.

While carrying out open coding, I sought to generate as many codes as possible without a particular focus. All ideas and concepts that I could link or generate from my data set were treated as containing possible interest. Throughout this process I also wrote "initial memos" where I entertained a wide variety of ideas and insights about what was going on in the data.

When conducting line-by-line reading of a data set and carrying out open coding, I asked myself nine questions suggested by Emerson, Fretz and Shaw (1996) in order to systemize the process:

1) What are people doing?
2) What are they trying to accomplish?
3) How, exactly, do they do this?
4) What specific means and/or strategies do they use?
5) How do members talk about, characterize, and understand what is going on?
6) What assumptions are they making?
7) What do I see going on here?
8) What did I learn from these notes?
9) Why did I include them?

Emerson, Fretz and Shaw (1996) explain that asking these questions while conducting open coding gives priority to process rather than to causes or to internal psychological "motives." In this way, open coding helps to develop interpretations or analytic themes rather than causal explanations. Moreover, these questions force the researcher to notice practical concerns, conditions and constraints that participants confront and deal with in their everyday lives. Thus the ethnographer can unravel patterns that consist of mundane, ordinary and taken for granted events rather than only noticing dramatic or exceptional actions or events.

While conducting line-by-line reading of a data set and assigning labels/codes to each unique theme, I identified many more themes than I was able to pursue in my project. Hence I began to select themes which to explore further. As advised by Emerson, Fretz and Shaw (1996), I gave priority to topics on which substantial amounts of data had been collected and to those directly relevant to my research questions.

Even though I focused on prevalent themes I also considered unusual incidents or negative cases relevant to the research questions. An unusual incident may reveal critical but rarely observed processes within particular settings (Harper, 1992). In the results discussion, I included and discussed negative cases that might contradict prevalent themes (Katz, 1988).

Furthermore, I began to explore how different selected themes can be related to other apparent themes. A theme allowing me to make linkages to other issues noted in the data set was seen as particularly promising, and such themes were identified as subthemes.

When I had completed open coding and had selected coded themes, I proceeded with the second phase of data analysis—categorization. This involved building up and elaborating analytically relevant themes, both by connecting data that initially may not have appeared to go together and by delineating subthemes and subtopics that distinguish differences and variations within the broader topic. I used "initial memos" written while conducting during the open coding phase to further develop my ideas on emerging patterns and connections between the different themes I had identified.

In building categories, I continually made comparisons between incidents, identifying examples that were comparable on one dimension or that differed on some dimension and hence constituted contrasting cases or variations (Germain, 2001). While organizing the coded themes into categories, I wrote "integrative memos" to elaborate on ideas and to begin to link codes and portions of data together. I sought to explore relationships between the coded data set and to provide a more sustained examination of themes or issues by linking together a variety of discrete observations. The central task of my written memos was to develop theoretical connections between field notes and interview excerpts.

Ensuring quality

According to Lincoln and Guba (1987) the main criteria for ensuring quality of qualitative research are credibility, transferability, dependability and confirmability (Lincoln & Guba, 1987). In ethnography, the credibility refers to how accurately the researcher captures the observed reality and portrays this reality in the research report.

Strategies for ensuring credibility include prolonged engagement in the setting and triangulation of data.

Prolonged engagement is necessary to avoid making interpretations based on limited contact. The researcher needs to become familiar with the people and the everyday situations of the recruitment company to be able to distinguish among routines, common occurrences and unusual events (Mayan, 2009). To achieve credibility in my research project, I spent eight months in the primary field site and I concluded participant observations only when I saw data saturation and was no longer gaining any new information relevant to my research questions.

I also used triangulation, which is the application of different data collection methods, purposeful sampling and inclusion of multiple perspectives to test for consistency in collected data (Patton, 1999). In the project, I used participant observation, formal and informal interviews, and purposeful sampling of interviewees in order to achieve triangulation of data.

Prolonged engagement and triangulation also helped me to avoid the holistic fallacy, which is the construction of connection based on the researcher's assumptions where there may be none in fact. Fetterman (2010) suggests that spending sufficient time in the field and collecting data through various methods both help to eliminate the chances of holistic fallacy.

Transferability assesses the applicability of findings to other settings. I used the strategy of providing detailed, comprehensive descriptions of the setting and participants in order to acquire transferability (Mayan, 2009).

Dependability reviews how decisions were made throughout the research and is attained through the use of an audit trail. In other words, it is the documentation of "the researcher's decisions, choices, and insights" (Morse & Field, 1995). I facilitated dependability by documenting why, when, and how decisions were made throughout the research process.

Confirmability is used during the data collection and analysis phase to ensure that the findings are logical. I used an audit trail, and the resulting interpretations, as a technique to ensure confirmability. Confirmability also evolves through the practice of reflexivity, so throughout the entire research process I wrote my reflections on the collected data and the research process. Confirmability was also achieved through "initial" and "integrative" memos where I documented and contrasted emerging themes, categories and connections.

Additional techniques that I used to assure the trustworthiness of this study include purposeful sampling and performing data collection and analysis concurrently. Purposeful sampling is the selection of participants purposefully for the contribution that she or he can make in understanding desired phenomena. It is this process of selection that ensures the final result of ethnography is comprehensive, complete, saturated, and accounts for any negative cases (Morse, 1999). Collecting and analyzing data concurrently forms a mutual interaction between what is being learned and what one needs to learn (Morse, Barrett, Mayan, Olson, & Spiers, 2002). Shifting back and forth between data collection and analysis allowed me to move with the data and to learn about unique and untold aspects about the phenomena.

Trustworthiness in the interviewing process was achieved through long in-depth interviews. Rubin & Rubin (2005) suggest that long conversations give a researcher the opportunity to figure out where and when a person is exaggerating and what areas he or she is ignoring. Moreover, because I used multiple sources of information, the results are more convincing. Interviews with various members of the industry as well as probing techniques and asking some of the same questions to people working in different roles allowed me to check the interviews for consistency and to identify self-serving versions of stories told.

Ethical considerations

Ethnography is an ethical commitment from the very start and this commitment continues through all phases of the research and writing. Because an ethnographic study involves forming close human contacts and contracts, researchers must deal with the responsibilities and obligations that involve these relationships (Madden, 2010). According to many scholars, ethical problems are so inherent in qualitative research that some scholars question if ethnographic research can ever even be ethical (Wolcott, 2008).

The qualitative research process is considered ethical if the researcher follows guidelines advised by an IRB to ensure an ethical research process—such as obtaining informed consent from all participants, guaranteeing right to privacy as well as protecting from harm. Despite all the requirements in place, because of the close human relationships formed in the research process, the ethics of participant observation and interviews are laden with challenges that go beyond rules prescribed by IRB.

The University of Minnesota IRB approval was obtained before initiating the research process (for IRB approved consent forms and a recruitment text refer to Appendix A and B). Moreover, I attained permission from the field site before conducting participant observation as well as oral and written permission from each individual for participant observations and interviews. Obtaining permissions from the field sites and individuals required careful and truthful informing about the research project. In all cases I attempted to be clear about my research project yet I avoided being assertive about my interest in the ethical dimensions as my primary research purpose. Although I felt ambivalent about such a practice, I did so for two reasons. First, I initially wanted to keep my research questions broad as I had little information about patient recruitment organizations in general. Second, I feared that people would be unwilling to talk with me if I used contentious words such as "ethics" since such words are closely associated with legal and regulatory breaches within the industry. Despite this discretion, I was not misleading my participants since the focus of my project was not legal or regulatory breaches but rather routine attitudes and practices towards research participants and in recruitment practices.

Along with obtaining informed consent, researchers must promise anonymity, confidentiality, and privacy for their research participants. Lincoln and Guba (1987) warn that such protection is difficult to provide because qualitative research requires detailed reporting of what is heard and observed in the field. Participants can be recognized, for example, when the community is small and individuals hold unique points of view. As part of my research project I promised to present the results to my primary field site. Call

center nurses were important informants in this project yet I felt uneasy about including their perspectives in the report because their critical viewpoints towards the industry and management practices as well as already-existent tension between them and some managers indicated that I could put them in an even more vulnerable position. Further, I knew that in their case changing names and other details would not protect them from recognition. Robley (1995) suggests that disclosure risks can be avoided by withdrawing revealing materials and, in part, through the process of negotiation outcomes. In this case I decided to share the results with the nurses and to ask for permission to include their viewpoints in the report.

Another area of tension came from my concern of exploitation. I undertook this project to critically examine recruitment practices and so ethnography seemed the most appropriate methodology to investigate "for-profit" patient recruitment. However, after spending some time in the field, my sense of gratitude grew as people showed generosity with their time and effort in interviews. I started to feel uneasy about taking advantage of my role as a researcher. I also became aware that there is no benefit for the research participants. Research relationships in the field are unequal. All of my participants were more powerful than me in terms of their experiences and professional status and thus were more accustomed to negotiating terms and conditions or even to denying access (Smith, 2005). Moreover, they could exercise free will when it came to disclosure during the interviews. Nevertheless, I was the one who defined the setting and interview questions. I also maintained the right to present the data in a way that serves the purposes of my research project. Wolcott (2008) suggests that being ethical means the continual

assessment of weighing risks against outcomes. So my ethical commitment towards the research participants included the obligation to report the observations and interviews accurately and fairly. In addition, I assumed the responsibility to keep promises made to my research participants in order to obtain the interview as well as to ensure no harm to the interviewees (Rubin and Rubin, 2005).

Summary

In this chapter I described the philosophical assumptions of qualitative research which served as the foundation of my project. I based my research on the principles of qualitative inquiry, an inquiry which is primarily naturalistic, interpretive and inductive. Furthermore, I provided a theoretical foundation for ethnographic research as well as for the design and methods employed through the research process.

The key characteristics of ethnography that were incorporated in this research project are (a) focus on culture; (b) holistic and contextual in nature; (c) reflexive character; (d) perspectives of study participants (emic data) and researcher (etic data); and (e) result in an end product called ethnography. Focusing on the culture of patient recruitment companies allowed me to understand routine attitudes, beliefs, and practices towards research participants and in recruitment. By examining these daily practices I was hoping to find insight on ethical issues that may emerge when recruitment companies interact with other members of the research industry—such as patients, clinicians and pharmaceutical companies.

Doing ethnographic research means that I conducted participant observations and semi-structured interviews with employees of patient recruitment companies and

investigational research sites. In order to ensure the quality of collected data I used different tactics to facilitate four main qualitative research quality criteria: credibility, transferability, dependability and confirmability. In the data analysis I used the framework proposed by Emerson, Fretz and Shaw (1995) and I undertook the analysis in two phases: open coding and categorization. For data analysis and documentation of this process I used the Nvivo qualitative research software.

This project was approved by the University of Minnesota IRB and I obtained oral and/or written consent from all my participants where it was necessary. However, given close human relationships, the ethics of participant observation and interviews are laden with challenges that go beyond rules prescribed by IRB.

With this chapter I conclude the theoretical discussion of my project and in the following four chapters I will present the results of this study.

Chapter 4: The art and science of recruiting patients: an overview of the recruitment industry

On a sunny November morning in 2011, I was heading to a meeting with a recruitment company in the US that recruits and retains patients for clinical research studies. The renovated white factory building, located in a business district of a large US city, is the home of the health division of a gigantic public relations agency. People I met in an elevator were young and artsy looking; they cheerfully chatted until we arrived at the 7th floor. By the glass-door entrance to the office, I was greeted by Anna, a young and energetic senior director of the recruitment company. The office was bright, with many windows, the walls and furniture were white, and even the desk computers were white. We settled in a small, glass-walled conference room for a conversation. Anna started by telling me that patient recruitment is like a science and an art. For her, it meant combining scientifically-written research protocols and trying to communicate them to an average person, in the form of an invitation to participate in a clinical trial:

> […] while working at the recruitment company, I have to bridge between people who are scientists and people who are creative. I am trying to pull both of these worlds together into some kind of communication to the average person. Working at a recruitment company really fits me because I'm neither a scientist nor a creative person, but I can try and get all the information down to a point where it is suited to a normal person.

Art and science; this is how many people I interviewed who work in the recruitment industry described what they do. Overall, they explain that recruitment tactics

and methods are backed with data and are scientifically shown to work. Moreover, the scientific approach to recruitment helps them to connect with clinicians in the research industry and to justify pricy endeavor. On the other hand, informants in this research explained that anybody can create an advertisement, but there are special skills and experience necessary to craft an emotionally appealing invitation for patients to participate in clinical studies. And, from what I observed, it is an art indeed, to navigate the expectations of all stakeholders — the patients, research sites, and sponsors. Mainly by focusing on scientifically-justified tactics and creative marketing materials, patient recruitment firms are offering the solution to recruitment and retention challenges that have been haunting the pharmaceutical and device industry for at least three decades.

In this chapter, I discuss the structure and key characteristics of patient recruitment companies. I offer an analysis of recruitment business organization and values that shape and inform recruitment, as well as selection of research participants. This chapter will provide a background for the discussions in subsequent chapters—about interactions with clinicians in investigational research sites and patients who are interested in joining a study.

Regardless of type, all patient recruitment companies practice centralized patient recruitment. Recruitment campaigns are centrally orchestrated, and are therefore supposed to reduce the cost of recruitment. Recruiters also are directly targeting patients with information about available studies, in this way they are attempting to bypass physicians who often are mentioned as major gate keepers for patient enrollment.

One of the things that I show in this chapter is centrality of information in the recruitment industry's existence. Recruitment companies carefully gather data on every recruitment campaign and analyze it, some gather patient contact information and their diseases. This information is used to predict future enrollments, and as a result, recruiters can claim that all recruitment strategies are data driven, and thus are shown to work. Having this type of information is key to delivering the main value to sponsors — a human body willing to join a study — but the data on how to reach a person, what were common caller concerns and reasons for disqualification can be as valuable to a sponsor for next stages of the clinical study, and even an approved product's marketing.

Recruitment companies constantly build their identity as recruitment experts and present their services as both money saving and time saving for pharmaceutical and device companies. In order to achieve these goals, the private sector recruiters operate by principles of business not only in how they organize their work, but also how they approach the recruitment process and view research participants.

Types of recruitment companies

The number of patient recruitment organizations has grown rapidly, and larger companies provide a full service of patient recruitment and retention for pharmaceutical and device companies. The full service entails everything from site selection, recruitment material design and handling IRB submissions, to patient screening and medical chart review at individual research sites. Many smaller firms specialize only in a single service, like renting data from their large patient databases or providing call center services.

Recruitment firms have different origins, but all of them saw a business opportunity in patient recruitment and began to offer services to pharmaceutical, device, biotechnology, and contract research companies. For example, Medici Global was one of the first companies that emerged as a patient recruitment company. Before launching her recruitment firm, Elizabeth Moench spent years working in marketing and public relations departments in various pharmaceutical companies. On the company's website, Moench explains that this experience led her to establish the company called MediciGroup (now MediciGlobal). According to her, she wanted to create a company that addressed the primary cause of clinical trial delays: ineffective patient recruitment.

Some of the smaller health marketing companies also saw a business niche in clinical trial recruitment and slowly transitioned themselves to full service recruitment providers. One of my informants, Adam, a middle aged owner of a recruitment firm, had previously focused on marketing medical devices to wider patient audiences and connecting interested individuals with physicians who are skilled in using medical devices. He explains his transition to patient recruitment, which took place in the 1990s:

> And then along the way, we were asked by a company who had seen this model if we could use the model for patient recruitment for a clinical trial. I hadn't even thought of that. I wish I could say I had been smart enough to think of it, but I hadn't even thought of it. So as we looked at that we said, "Yeah, I guess we could do that." So we used it, and it worked really well, and then we said, "Who else might want to do this? Are there other companies that need help?" And then we uncovered the problem with patient recruitment for clinical trials and what a universal problem it is, and so our business began to grow really rapidly in patient recruitment; and that's what most of it became, patient recruitment.

Some of the recruitment firms are not small businesses. Similar to the company where I interviewed Anna, many are owned by some of the largest advertisement and marketing companies. For example, one of the world's leading public relations agencies, Fleishman-Hillard International Communications, owns Clinical Trial Division, which is a full service clinical trial recruitment and retention agency. Another example is the recruitment firm MMG, along with another agency called Corbett Accel Healthcare Group (owned by Diversified Agency Companies). All of these companies, including Fleishman-Hillard International Communications, are owned by Omnicom Group. Omnicom is the leading corporate media services conglomerate, with sixty three thousand employees and $11 billion in annual revenue. Omnicom became such a big corporation by buying and investing in companies like MMG that serve an expanding sector of the company (O' Meara, 2009).

"Patient recruitment is a gold mine," explained Adam in one of the meetings in which I participated. This attitude can explain the development of countless numbers of recruitment firms that want to profit from recruitment challenges in clinical research. According to a 2003 IBM Institute for Business Value report, 27% of drug development costs are spent on patient recruitment, which equals $5.9 billion annually around the world (IBM Institute for Business Value, 2003). Moreover, results from a recent survey indicate that drug-makers are willing to financially invest in faster patient recruitment. The survey found that nearly 90 percent of drug-makers would prefer reaching patient recruitment goals at least 10 percent faster over cutting Phase II or Phase III trial costs by 20 percent. In fact, only 15 percent of the 72 companies queried chose

reduced expenses over faster patient recruitment (ISR Reports, 2012). All of these companies, regardless of their origins and ownership, offer a service called centralized patient recruitment.

Centralized patient recruitment

As I mentioned in Chapter 2, until recently patient recruitment was the responsibility of the principal investigator. Patients were drawn from a physician's practice, and sponsors paid for that access as part of the physician's total compensation. As the numbers of clinical trials increased, and competition grew among companies testing similar compounds and procedures, recruiting patients from physician practices was no longer sufficient. Principal investigators and research clinics started spending money on promotional campaigns with varying degrees of success.

The centralized recruitment is very similar to promotional campaigns at an investigational site level, but usually it is orchestrated centrally for all sites involved in a study. The idea is that centrally designed marketing campaigns with a unitary target message, central patient screening and referral, significantly reduces the cost compared to what is necessary for marketing budgets for each individual research site. The overall structure of the patient recruitment program is very similar among different recruitment companies.

With recruitment campaigns, firms are utilizing direct-to-patient communication. Although occasionally recruiters may invite neighboring physicians to refer patients to a clinical study, with direct-to-patient advertisement they are trying to avoid doctors who

often are gate keepers (because they can decide based on different subjective reasons whether to share information with a patient or not) for patient enrollment in clinical studies. Moreover, recruiters are aiming to limit dependence on principal investigators to find research participants and to improve effectiveness of research sites. One of my informants even called this approach a new paradigm in patient recruitment:

> The traditional approach by sponsors to speed up enrollment is to add more clinical sites. When adding new research sites, there are charges for that; there is a site qualification expense that could be $15,000, for example. And then there are all the monitoring costs, support costs for that site, and then dollars that the site is going to charge, so it might be 30 – 40 thousand dollars before a new site does anything, when for a small percentage of that we can greatly increase the volume of patients through the existing sites. So it's a much more cost-effective model, and I think that's not really being understood by the industry. The new paradigm relates to the use of direct to patient communication, like getting databases that are similar tools, like social media and television or radio, to find the right patients and communicate directly with them to motivate them to participate in a clinical trial, as opposed to relying upon a clinical site and the investigator and his patient population, and interaction that is third party interaction.

However, despite this attempt to avoid physicians in the recruitment process, as I will show in this and the next chapter, the success of this approach is highly dependent on research clinics'—coordinators and principal investigators—willingness to collaborate with recruitment companies and follow up on firms' referred patients.

The centralized recruitment campaign usually starts by running a TV, internet, radio, or newspaper advertisement. Each medium has its unique toll - free number

assigned to it. The advertisement is designed to produce a "call to action," inviting patients to call a provided phone number and find out if they qualify for a study. It is believed by recruiters that the patients who call in are more proactive and motivated to participate, thus they are more compliant research subjects.

Today, advertisements also invite potential participants to visit a dedicated website to learn more about the study. Study websites contain a basic description of a study and have an toll - free number displayed for people to call in order to get screened. Sometimes websites contain simple questions based on inclusion and exclusion criteria, so individuals can self-screen. The questions are what recruiters call "easy knockouts"—a quick and easy way to eliminate those who do not match broad study criteria, such as age, gender, medical condition, co-morbidities, or past medical history. If an individual does not qualify, usually he or she is invited to provide contact information to receive further notifications about other clinical studies.

Subsequently all patient inquiries are directed to a call center where trained individuals screen patients for eligibility in a study. The recruitment company where I conducted participant observations prefers to talk about the call center as a "patient interaction center." According to them, it takes special skill and care to screen patients over the telephone. However, the main objective of all the telephone conversations, I observed, was to gather the necessary medical information from callers in the shortest possible time period, to decide if they are fitting candidates for a particular study. In addition, callers are clearly informed on the obligations of participation, for example, the

number of follow up visits. It helps to quickly identify and disqualify those who feel that the required number of follow up visits would be too much to bear, since they would be potential drop-outs. However, as further discussed in Chapter 6, callers are not offered information on the risks and benefits of participation, the name of a sponsoring company, or inclusion/exclusion criteria for a given study. Sometimes even the names and locations of research sites are omitted.

All the information obtained from callers is collected, and qualified patients are referred to the research clinic. The coordinators at research sites receive some form of notification—an email or call—that there is a new potential candidate. Sites then are expected to call these patients within 48 hours (recruiters themselves claim that patients' interest deteriorates after 2 days) and further medically screen individuals and randomize them in a study if they qualify.

In some cases, recruitment companies perform "warm transfers" which means that the call from patients who qualify for the study are directly transferred from the patient interaction center to a research site after the screening process. A potential study participant whose participation interest is at the peak is connected with a nurse. In theory, this helps to eliminate endless phone calls back and forth, and it also helps to quickly schedule participants for more screening and consent visits. In reality, patients spend a significant amount of time on the telephone answering a call center staff's health related questions, then waiting to be transferred to a research site, and then answering similar questions from the coordinator.

Sometimes, when it is estimated that there are enough "known patients"—patients available within principal investigators' clinic and/or research sites—recruitment firms offer to review a clinic's medical charts. According to recruiters, such a service is designed to ensure speed and quality. Research clinics are often understaffed and overworked and might not have a full time nurse available for a particular study. In those situations, a recruitment firm sends a contracted nurse who will conduct a review for them. After the qualified patients are identified, they receive a letter from their physician inviting them to participate. Again patients are offered an 800 number to call and get further screening. After a patient is referred to a research clinic, the direct communication between recruitment firms and patients is complete. However, companies usually keep tracking patients until they are randomized into the clinical trial process and sometimes even until the study is completed.

"Consumerism is what drives our business"

As I indicated in the previous section, this recruitment model of reaching out to patient populations and inviting them to participate in clinical trials eliminates the most common gate keeper — a physician. Patients do not need to sit and wait while their physician offers a clinical study. Patients are encouraged to call and find out more about the opportunity to participate in all kinds of studies, even for conditions that require physicians' authority, like cancer or stroke. This recruitment model is possible because of the existent culture and reality of the US. As one of my interviewees explained, the increased consumerism involved in the search for the best outcomes is what drives the business of clinical trials. He expanded:

> There's actually been a lot of research that's been done about why patients get into clinical trials. Consistently, the top reasons are to access a new treatment, something that's not currently available. And usually, these are patients who want a better clinical outcome than what they currently are getting. For example, if I'm a patient and I have MS, multiple sclerosis, and I'm taking a medication for it that is not managing my MS very well, and then a study comes out with a new medication that has the potential to provide a better outcome, I'll probably be motivated to be in that study, because of the potential for a better outcome. That's a big motivator.

Whereas in other health care systems, for example, where patients are assigned to a specific primary care physician, it is harder to run an advertisement where a patient can contact a call center and get referred to another physician. In other places, running patient advertisements can be illegal, but physician referrals are an option for recruitment. Unlike in the US, where physicians are afraid of losing a patient after referral to a clinical study, in countries like UK, Slovakia, and others, the physician's income is not dependent on the number of patients seen in his or her practice.

Most of my informants maintained the point of view that altruism and desire for innovative treatments are the main motivators for people to participate in clinical trials. Only few of my interviewees, nurses in the call center and one management level employee, mentioned that people participate in studies out of desperation for medical attention. However, not all clinical research studies are equally accessible to all patients. As I will discuss in Chapters 6 and 7, often the most beneficial studies—those that offer truly innovative solutions or that aim to compare investigational therapy with a standard of care (rather than placebo)—require health insurance, and as a result these studies are

accessible only to a better-off part of society. Given that recruiters know the patient group a sponsor is interested in enrolling in a clinical study, they often tailor recruitment strategies in order to reach these individuals.

Data driven recruitment

Another important feature offered by these private companies is data. Recruitment firms are well aware that sponsors are not willing to invest large sums of money in something that will not result in patient enrollment. Thus, recruitment solutions offered by these companies are claimed to be "data driven," meaning that the offered services are backed by enrollment data from the past studies. In another words, these companies claim that the tactics they use are shown to work. In addition, by constantly analyzing the gathered data during the recruitment process, the tactics can be quickly adjusted to achieve optimum outcomes. Also, data gathered by these firms in the recruitment process might offer a picture of the patient population that sponsors can further use in the next stages of research or marketing of an FDA approved product. According to an employee of a recruitment firm:

> There are two main focuses that we have, and obviously, enrollment is the number one goal. We are there to enroll patients, but almost as important as enrolling the patients is grabbing data on why the patients are choosing to enroll or not enroll. And that can be just as valuable [as recruiting patients], especially if you look at post marketing and adjusting the protocol amendments. Through our software we actually can track, with data from the sites, why certain patients would disqualify, or why they would enroll, or at what point they would disqualify.

Many companies have developed sophisticated and trademarked patient tracking systems that capture data on how many patients inquired about a clinical trial from specific means, like a television or Facebook advertisement. Furthermore, firms can tell the number of patients screened in their call center, what the most common patient questions and concerns are, why and how many patients are disqualified, and how many are referred to each research site. In some cases, firms also can obtain reports on what happened to each referred patient at the site level. This is explicit in the discourse of a marketing director:

> [in the past, in a similar study] television worked and radio didn't, and so we're going to start off with television […]. That's actually the intellectual capital that drives the business - our company has been involved in a hundred trials, so you take all that data of how, what, when, what ailment, what demographic, what market, what clinical site they worked with. You take all of that and you aggregate it and you have a pretty good picture of how to do it.

Capturing detailed data helps to evaluate effectiveness and return of investment of each recruitment tactic. If a particular tactic proves unsuccessful, based on daily data, it is possible to incorporate a new tactic or change a strategy without losing valuable time. In some cases, a recruitment firm can even advise a sponsor to change a protocol if it turns out that the recruitment process is heavily hindered by unnecessary inclusion/exclusion criteria. Adam explains this process:

> From a standard care continuum for patients, we've seen study protocols that are going to be very, very hard to enroll. And we will tell the sponsor that up front, and we'll build it into our model; the assumption is that it's going to take a lot

> more work than they think it is to get the study enrolled. Sometimes sponsors will go back and will amend the protocol, or after we start recruitment, we'll gather information on patients that are coming through our system, and we'll feed information back to the sponsor, and sometimes they'll change the study protocol based on that.

Although individual research sites capture data on effectiveness and cost of recruitment methods, they are not in a position to offer data on the entire clinical study. Chris, an employee working with research sites, mentions the measurement as a difference in recruitment between firms and research sites:

> The sponsor says they will give the site $5,000 - do what you want with it, recruit patients. Well the sites [think] maybe I will throw out some advertisements, or maybe we will bring patients in, but it's [recruitment tactic] not really tested, it doesn't have metrics. Although other people can do exactly the same [recruitment as us], they do not have metrics. So that data capture is a huge benefit, prior to the way that we approach recruitment, a sponsor maybe had screening data, something that a coordinator would fill out by hand and say, "This is how many patients we have screened", but actually there is no hard data to support that. Sponsors would never really find out why patients didn't qualify for the study, they would only find out why they did. Now we actually opened up that entire area prior to enrollment of all these data, why patients are consulting, why they aren't, what's good about sponsors' protocol, what isn't; which was basically all in the dark prior, as there was no way to capture that, and that's what we do.

According to recruiters, this is the scientific side of patient recruitment. My informants stressed the importance of positioning patient recruitment as a structured, predictable, and measurable process. This quote from a firm's website captures this idea: "Our innovative, data-driven approach helps minimize the guesswork that is often

inherent in clinical trial enrollment." Similar statements can be found in every recruitment firm's website and in industry conferences presentations that I attended.

In order to obtain a recruitment contract, recruitment companies need to submit proposals with timelines, budgets, and solutions for enrollment. Data is a crucial component that helps to justify the chosen approach. A senior executive from a company based on the West Coast describes the beginning of a proposal preparation process:

> […] we got a protocol that came in from the company; it either [could] be a request for the proposal or for information for a Pharma client. Chances are that we will be competing against other companies, so when that project comes in our door we gather the team together […]. We analyze it together with KOL [key opinion leaders], and clinical physicians with experience in that therapeutic area […]. We want to identify right away if this is a recruitment project, if this is a retention project - what that client is asking for. And once we determine what the client asks for, then we will go out and try to pinpoint key barriers and challenges that are [in the way of] successful recruitment. We are trying to find out what are all the challenges that would impede recruitment.

The next step is to prepare a timeline and cost of a recruitment program. The oldest and widely used model for this purpose is called the "recruitment funnel." The idea behind this model is that in order to enroll a necessary number of patients, one needs to advertise a study to a much larger pool of candidates. This larger pool of candidates will be evaluated based on their eligibility and appropriateness for the study and certain number of individuals will drop out at every stage of the recruitment process, thus, creating a "funnel" effect.

The “funnel effect” is always calculated before a study to predict the time frame and cost of patient recruitment. Table 3 is an example of this estimation; it shows how many individuals need to be approached in order to enroll the necessary number of research participants. The assumption is that the predictable percentage of patients will drop out in each milestone of patient recruitment. It is also assumed by recruiters that the percentage of patients that will drop out at each stage can be estimated from past studies of the same patient groups. Given that professional recruiters know the cost of advertisement in geographic locations of research sites, they can predict cost per enrollment and in what time frame they can enroll patients with this money. The numbers can differ greatly based on factors like medical disease, number of competing studies, research sites’ location, etc.

The example in Table 3 I obtained from one of my informants. The example shows recruitment for a study that investigated treatment for lower back pain. Radio and internet were used for the advertisement campaign. The recruitment firm recruited twenty three percent, 170 out of 740 required participants.

Stage of Enrollment	Numbers needed to randomize one individual	Numbers needed to randomize 170 participants
Inquiries from advertisement	59	10,172
Completed screening questionnaire	25	4,301
Qualified for the trial	14	2,363
Consented	2	334
Enrolled/Randomized	1	170

Table 3. Funnel effect.

From Table 3, it is apparent that in order to enroll the necessary number of patients, a recruitment agency needs to reach an impressive number of people. Numbers at every stage of the recruitment process are affected by different factors that recruitment companies can and cannot influence. For example, firms do not have control over who shows up at a visit for screening or how patients screen with a blood-work at a clinic. But firms can ensure that call centers are easily reachable, websites are convenient to navigate and the designed prescreening questions are straightforward for potential patients to answer. Recruitment companies are focusing on specific groups of individuals (I will address this question more specifically in Chapters 6 and 7) and are trying to make

recruitment process as convenient as possible for these individuals. Nevertheless, the decisions on optimizing the process and making it convenient for all participants are guided by financial values. Jake is an employee of a recruitment firm that offers technological solutions for recruitment challenges. When asked about the cases study described in Table 3, he comments on challenges to balancing the cost of a recruitment program and convenience for patients:

> So can we improve and optimize that? Yes. How much time do we have to improve and optimize that? To do that sort of the pre-trial patient type of validation takes time to hone it to where the questionnaire is capturing the highest probability of screening. So recruitment programs generally don't go through that sort of level of testing and verification. Usually we just use the pharma and the patient recruitment providers' best recommendations on how they want to develop something, or how they develop a questionnaire, how they develop navigation of the website, etc.; and then optimize it thereafter based on how well those responses are going, how well the pre-screeners are actually screening out unqualified candidates - and that takes time. That takes so many possible revisions, and you know what? Money. So the question again is, do we have enough time to do that given a certain project under which we have certain resources available to us?

There are many factors that companies take into account when they generate a funnel for sponsors, such as length of recruitment period, competing studies, probable patient outreach response based on budget, average number of sites recruiting, and so on. These factors vary across different conditions, phases, and recruitment companies, and they determine the cost of the recruitment program. If a sponsor decides to conduct a

clinical trial that does not offer significant innovations, or that has a placebo arm or even a very strict inclusion and exclusion criteria, patient recruitment is still possible. It will be more expensive and time consuming, because the number of individuals that need to be reached in order to enroll the necessary number of participants is higher.

Although recruitment firms can account for some factors and offer some predictability, things do not go always smoothly. While conducting participant observations, I encountered a situation where the recruitment company created a recruitment program for a research study based on a similar clinical trial for which they had recently recruited patients. The recruiters had designed the recruitment timelines and budget according to their past experiences. Apparently, the past recruitment went smoothly, but this time they were experiencing slow recruitment. The client was particularly unhappy since the recruitment was behind schedule, and the cost of enrollment was unexpectedly high. The program was haunted by things like a holiday season when response rate was lower; and participants missed appointments due to storms around the site locations. The dissatisfaction of the sponsor was understandable since the promised timelines and costs were not met. However, the issues raised in this specific recruitment plan were beyond the recruitment firms' control at the time of the study.

A marketing director of a recruitment firm commented on unsuccessful marketing campaigns:

> So, it's challenging because clients, sponsors, don't understand it, right? They're clinical people. So they're like, "Well, what do you mean by it didn't work?" "People didn't respond to it. I don't know why they didn't respond to it, but they

> didn't respond to it." So we can try to put it on a different channel, or maybe we need to spend more. Maybe we need to look at different timing. You know, there's lots of variables [sic] that we have to evaluate, given that we can't change the creative. So we have to look at all of our different options when it doesn't go right as we want it to, so it's like a constant and steady battle.

Although the scientific side of patient recruitment is important, recruiters also emphasize that the recruitment process requires a creative and innovative approach. On one hand, recruitment companies claim that recruitment process is structured and thus replicable, but on other hand, the recruitment process is subjective and is based on practitioners' special knowledge and skills— "know-how." This knowledge often can be difficult to transfer to another person by means of articulating it. In this way, the recruitment industry is trying to brand itself as unique recruitment professionals within the clinical trials industry.

Patient recruitment as an art

Adam, in our first conversation, compared patient recruitment to cooking. According to him, anyone can follow a recipe, but it takes "a world class chef to cook a great food." He explained that a world class chef could follow the same directions other people would follow, but there are things she is picking up on while food is sautéing in a pot. She smells and hears things. Things trigger her senses in such a way that she can react and perform certain actions. For him, patient recruitment is similar:

> You can have a system, you can have a defined methodology, but once you start applying that system, human interaction begins to come into play, and then it's just a matter of reading people, reading their reaction, tailoring things to fit to people. That's where the art of it comes in.

During my observations it was obvious that working at a patient recruitment company means managing all stakeholders' expectations. It is managing and meeting expectations of a sponsoring company that pays a recruitment firm. It is also working with sites to ensure that they are willing to collaborate and follow up on the company's referrals, and finally, it is keeping patients happy—calling them in a timely manner, being polite and addressing their concerns.

Art is also creating appealing advertisement. Some of my interviewees stressed that the recruitment message is very straightforward and only serves as a tool for informing patients about ongoing clinical studies. According to them, its main purpose is to get patients to contact the call center for a pre-screen. Other informants shared an opinion that a message with an emotional appeal is important, especially in times when there is so much competition for patients between similar clinical trials and already approved treatments. An employee from a marketing department explains:

> So it's about engaging the consumers… and pulling them into the materials so that they just don't read, is low back pain affecting more than your lower back, is it affecting your whole life.' It pulls them in so that they want to read the rest. The whole goal is to get them to that 1-800 [toll free number] at least at some point in the brochure, get them interested enough that they visit the website which again will draw them to the 1-800 number.

The artistic side of patient recruitment is also expressed in companies' attempts to provide innovative and creative recruitment solutions to clinical research industry. In our interview, Anna mentioned the importance of being creative:

> Because the most important thing, like we said before, is charming [sponsors] out with new and creative ways things that are different; for instance like exploring Facebook to see what else social media is out there that we can utilize for advertising. Things like that, if it's a different tool; we can come up with that haven't been done before. We just always want to constantly stay creative and not do the same things.

By claiming that patient recruitment is an art, recruiters are trying to communicate two messages. First, the process requires a special skill and an expert to carry out a patient recruitment. And second, it indicates that recruiters may offer unique solutions to long-standing problems. Despite Anna's confidence in "charming sponsors out with new and creative ways" other informants are more cautious in using this approach to connect with sponsors. One of my informants told me: "What I've learned and I've kind of realized is, you know, just using the play that, 'Oh this is new, and it's innovative and it's exciting,' doesn't get people interested for sure." This quote indicates that initial excitement about quick solutions has faded and recruitment companies need to seek additional solutions to recruitment problems. Moreover, the companies need to re-brand themselves. I will discuss this trend in the following section.

"We are not your regular recruitment firm": recruitment versus enrollment

While collecting data, every single employee of a recruitment firm would say, "We are not your regular recruitment firm, we are different." Even during the Christmas holiday season, I received a corporate greeting card from a recruitment company called BBK that stated: "Uniquely different. Year after year. Happy holidays."

This assertion of being different usually means that a particular company does not just recruit patients, but also enrolls them. This distinction was clarified on my first day of fieldwork. The owner of the company I was observing gave me a short presentation on how patient recruitment companies work. He explained that the preferred terminology to describe what recruitment firms do is "accelerating patient enrollment." According to him, anybody can run a TV campaign and refer all patients that responded to this advertisement to the research sites. Sponsors were not willing to invest in such services because it did not result in any measurable enrollment; and "accelerating patient enrollment" means offering services that go beyond marketing campaigns and helping clinicians to quickly enroll participants. This includes screening patients; so only eligible candidates are sent to sites, and work with sites to ensure that they follow up on these referrals.

> We know what works, we know what types of demographics, we listen to what type of radio station, we do this on a central scale. So, we have experts that will go out and pick the right venues for media or will pick the right things for the site. A lot of other competitors will basically run media, send the referrals to the site and say, okay we are done, we ran advertisement on the TV, we got a thousand

people that were interested in the study and we sent only the most qualified over the site.

The shift from just recruiting to also enrolling is reflected in one of the company's core values, as asserted by Adam, owner of a recruitment firm:

> […] one of our biggest core values is to actually sell value to a customer. We're a service company, but we never want the focus of our company to be on selling services. We want the focus of the company to be on delivering value in the form of what our customers want, which is enrolled patients. So that's a real core value for us, not just selling services, but delivering that value.

However, when focusing on patient enrollment, recruitment companies need to closely collaborate with investigational research sites. Although recruitment firms are aiming to enroll patients, only a principal investigator or dedicated staff can receive an informed consent from a patient and admit him or her in a study. As a result recruitment companies are carefully screening patients and trying to work with research sites to ensure that they follow up on referred candidates. With this approach, recruitment companies are stepping in to the zone of investigational research sites. This situation creates different tensions among industry stakeholders, which I am going to describe in Chapter 5.

Recruitment companies need to assert their uniqueness, also because of high competition with other companies. Asserting the scientific side of recruitment is to show legitimacy of the recruitment company's work and build trust from sponsors and research sites. Although the recruitment industry is stressing its artistic and creative side, it is careful in communicating it's abilities to understand the scientific side of protocols and

issues that clinicians might be facing. The competition is high among patient recruitment companies, but they also have to compete with recruitment departments within contract research organizations (CROs), pharma, and device companies. A senior executive of a recruitment company based in South West explains:

> […] in the last 2 years there has been contraction in the pharma industry—a lot of pharma companies are consolidating—whether it is Roche and Genentech, Pfizer and Wyeth, Merck or Schering-Plough. Because of that, it has ripple effects with other companies who serve pharma, for example, clinical research organizations that generally just perform clinical studies. I am noticing they are starting to get into the area of patient recruitment because they have to make up for lost revenue since they are not getting as much business as they had before, so with that retrenchment I see a lot of competition in our area.

Money in patient recruitment

Usually recruitment firms are contracted to recruit only a certain percentage of patients, from 15 to 40 percent of all the clinical trial participants needed. As one of my interviewees explained, the decision on how many patients will be brought by a recruitment firm is a complex decision:

> […] that's probably one of those intellectual risk based assessments, and a discussion too that should happen early on in the overall development and the study panel. So that you'd have to enter in experience, you'd have to enter in the epidemiologic aspect of the disease, the tactics that are being used. […] There's a bit more gut feeling on what it is and what the expectation is. In addition, one needs to consider how many patients are anticipated from the principal investigator and research sites, in what time frame they are able to recruit, what is the competition in the market place with ongoing clinical studies and approved

> treatments and what is the business' needs of a sponsor? If a sponsor is willing to complete a study faster than sites are estimated to enroll all the patients, then we need to know how many resources a sponsor is open to invest for a message to be able to go out and create awareness and attract patients.

There are two payment models used to reimburse for recruited patients. One is a flat fee for the recruitment program that covers anything from designing recruitment materials, filming TV ads, website design, broadcasting services, call center minutes, program management, or the use of a data tracking system. This payment model is safer for patient recruitment firms, because they will receive payment for their services.

On the other hand, payment for enrollment might seem like the safer investment for a sponsor. Some of the recruitment companies utilize this payment model. It is a convenient model for them in the sense that it limits a sponsor's power in the decision making process. When a sponsor is investing its own money in a program, it usually wants to participate in every decision making process, for example the creative design, and screening the script used in a call center. A sponsor's involvement in designing a recruitment program can significantly slow down the process. In addition, recruitment firms are obligated to submit weekly reports on performance. However, a huge disadvantage for recruitment firms is that they are measured on patient enrollment, which does not entirely depend on them. A Vice President of a recruitment firm explained this situation:

> At our company, we would prefer to utilize performance-based pricing because it gives us control to run the media that we want, to really work with the sites to champion the sites through. But it's a very delicate balance because you have to

> have what we call rules of engagement around it, because if a sponsor wants you to […] put your own money out there and earn it back, and there's not a fair chance for you to earn it back, that's not advantageous to the service provider. So there has to be rules involved that say, "We can't keep generating referrals for a site if the site is not bringing the patients in to see them" because then we could never earn our money back.

Although recruitment companies are willing to assume risks that are associated with their recruitment programs, they are not recruiting for all types of clinical studies. The selection of studies to recruit for is based on the likelihood of the ability to find and attract patients. This is informed by two aspects—first, financial, recruitment companies are businesses and must self-sustain, and second—they want to maintain reputation as successful recruiters. Adam explained to me that if for some reasons (complicated inclusion and exclusion criteria, poor study design, small patient population, etc.) a study might be difficult to recruit for; they would refuse to contract for it. In addition, if in the recruitment process a recruitment firm was losing money, they could stop the program:

> If we're doing a performance based contract where we're getting paid for our performance, then it would depend on a lot of factors. If it turned out that we were losing a lot of money, we wouldn't want to continue the project.

A manager from a different company explains the importance of taking only manageable projects in order to maintain successful self-image:

> Don't take something on if it's not a good fit." It's not as much a lesson learned, but it's more of say no if it's not the right opportunity. Because especially if you offer a newer or more innovative type of approach, one bad project could put a bad taste in people's mouths; so giving your program the credit it's due and being

> selective, just as the sponsor or CROs would be when picking their methods for recruitment. Vendors, I think, also need to be selective around the project they engage in because it's not going to help everybody if everyone has bad experiences when they engage in different tactics.

From the business point of view, such reasoning is welcomed—recruitment companies are practicing sustainable business and are fair to their clients. But this practice also raises questions, such as what kind of clinical studies are more likely to be enrolled? Assuming that recruitment companies' services help to complete struggling research studies, are certain types of studies systematically more likely to be completed than others?

"It is sponsors' faults"

When I started to conduct semi-structured interviews, I noticed that representatives of recruitment companies spend a lot of time criticizing sponsors for the challenges of patient recruitment. Some of the critiques were directed to the failure to timely prepare recruitment plans, poor study designs, and unnecessary stringent inclusion and exclusion criteria or defective site selection processes. However, most often recruitment firms criticized sponsors for their inability to acknowledge the expertise of professional recruiters. Adam explains:

> There also are sometimes conflicts with clients. Sometimes clients don't want to hear the truth. An example might be where a clinical team and a customer develop a study protocol, to do a certain study protocol; they develop an enrollment forecast for the study, and then they come to us and we tell them that it won't work, that we don't think that they can meet that. Well, most people aren't going to go back, because they've already gone through the process of selling their

> senior management on getting approval for the project, and if we tell them it won't work on our end, very few people are going to go back and say well, we were wrong. We went through all the trouble of getting this project approved in the budget and so forth, and it was based on faulty assumptions, and we were wrong. In fact, I've never seen that happen. I can't remember a single time. And so generally, what will happen is that they'll move on to another patient recruitment firm, because they always have the outlet. If they hire somebody and it doesn't work, they always have the outlet of blaming the company.

Saving sponsors' time and money

Recruitment programs offered by the companies are not cheap, and usually are available only to prosperous pharmaceutical, device, and biotech companies. Nevertheless, recruitment firms explain that spending for their services are small when compared to savings that professional recruiters offer to sponsors. One of my informants explains:

> Well the premise of what we do is speeding up enrollment in a clinical trial, because as you know from the statistics, most clinical trials, they don't meet their enrollment timeline goals. And so there is an economic value to doing that, because the time that we save in enrolling a study, translates into an economic return or a monetary return, because if we enroll a study in three months that normally would take six months, well then that's three fewer months that the sponsor has to fund the fixed expenses of the study, but then it's also three months earlier that they are going through the regulatory process. And so, if the product ultimately goes to market, then it's three months sooner for product launch on the back end. And so it's very easy to monetize that into a dollar value in terms of cost savings for shorter time, and then incremental revenue.

Recruitment speed can be explained by financial and labor capacity to do large volumes of advertisement and patient screening in short periods of time. Nevertheless, recruitment companies incorporate additional approaches to speed up enrollment and minimize costs. For example, the company where I conducted participant observations had a "flat" structure. Meaning, the organizational culture was not hierarchical; employees were authorized to make all necessary decisions without constantly obtaining the management approval. In this way, decisions regarding the recruitment process can be made in a short period of time.

Another strategy is used to foster IRBs' approval of recruitment materials and phone screening scripts. It is not a secret that IRB approval can be a lengthy process, so recruitment companies always work with the same private, central IRB, which is much more efficient than academic IRBs. Some research sites do not have IRBs in their organizations, so for them it does not matter which IRB approves materials. But for some sites, like academic research sites, recruitment materials and approaches should be reviewed by the local IRB. The efficiency of centralized patient recruitment is based on the idea that all research sites receive unitary recruitment materials. And it is extremely inconvenient if, for example, one of the local IRBs requires some changes to the recruitment materials. In this case, all recruitment materials need to be revised and resubmitted to all necessary IRBs, and recruiters have to prepare unique materials for the site. In order to avoid such situations, recruitment companies at first submit materials to the central IRB, obtaining approvals for as many research sites as possible. Materials to the local IRBs will be already submitted with a note that materials have been approved

for the most of the research sites involved in a study. Given that academic research institutions and their IRBs are competing with private institutions, this practice creates a pressure to conform and approve materials rather than raise particular issues.

Recruitment companies are trying to minimize labor costs to offer competitive patient recruitment programs. Most of the employees at the call center were hourly based. In this way, a manager can use only employees based on how necessary they are to a project and do not employ them if they make any mistakes. In one of my interviews, a nurse that took part in my study told me that during Christmas her hours were cut completely for three and a half weeks. When I inquired more, she explained that it could be because of the mistake she made. Apparently when she was documenting the call, she misspelled patient's phone number, or it got deleted, and the manager of the call center had to go back and review the record. The nurse told me that the manager was upset and after that her hours were cut. At the time of interview she was back for 12 hours a week.

She did not hold any other job, but was searching for other options. According to her, after this incident she was extremely careful to avoid any mistakes whatsoever and is trying to follow the telephone screening script as close as possible. During our conversation, she shared a similar story about her co-worker. He has been having trouble staying on the script. Finally, the manager called him into the office where they had a tough conversation, and after that he was taken out of the schedule.

My interviewee commented that she understands that amount of job are project-based, and that if media does not run then there is no work at the call center. But there was a case recently where media was run in the wrong locations, and as a result, patients

that were 400 miles from the sites were called to the call center. She concluded our conversation by saying, "I would have more hours if they at least would run media in the right locations." That is not to say that recruitment companies make more mistakes than any other companies, but this example shows the vulnerability of employees of a recruitment firm that is caused by an attempt to minimize costs.

Summary

In this chapter, I presented an overview and key characteristics of patient recruitment companies. Recruitment firms describe what they do as a science and an art. This statement means that firms are using data-driven recruitment strategies, but the artistic side accounts for creative solutions and special skills that are necessary for patient recruitment.

The foundation of the patient recruitment business is information that is gathered from past studies and helps to justify recruitment tactics and sustain the identity of recruitment experts. Private sector recruiters also gather large databases of patient contact information, which helps them easily and conveniently reach different patient populations. This information not only helps them successfully recruit patients, but also position themselves as experts compared to investigational research sites.

For recruitment firms, the challenge of patient recruitment is a logistical one. They are trying to better organize the recruitment process—making it more convenient, and using proper methods and media to reach right type of participants, but recruiters do not focus much on the needs of participants. The recruitment firms mainly work on Phase II – IV research studies, requiring participants with specific medical conditions. Yet they

view research participants as health consumers rather than patients who are sick. As I will discuss in Chapter 5, this distinction has different implications, because by viewing potential participants as consumers, recruiters assume that individuals have all the necessary information to make a choice and do not consider that a lot of participants are calling because they are desperate for health care and treatment.

The competition is fierce in the patient recruitment business, because firms compete not only between themselves but also with contract research organizations and pharmaceutical companies that have their own recruitment departments. Recruitment companies have discovered that in order to fill studies with research participants, it is not sufficient to design and place advertisements in radio. Instead, companies are focusing on patient enrollment. This approach requires close collaboration with investigational research sites. However, as I showed in this chapter, recruitment companies also have complex relations with sponsors that in many ways shape how recruiters work, due to financial ties between recruiters and sponsors.

Despite the recruitment companies' claims of fast and cost-effective recruitment solutions, firms are very careful in selecting studies that they are interested in recruiting for. Such decisions are informed by financial motivation and desire to maintain a successful image. Although in some ways, it is remarkable that recruitment companies optimize and speed up patient recruitment; the means of how they achieve that are questionable—for example, putting a pressure on IRBs, or using cheap and liquidable labor.

As I mentioned before, in order to achieve patient enrollment, recruitment

companies are spending a lot of time on developing partnerships with investigational research sites. I will describe this process and tensions that emerge between the two stakeholders in the next chapter.

Chapter 5: "Sites do not work for us; they work for a sponsor": interaction with research sites

In the preceding chapter I outlined the structure and key characteristics of patient recruitment companies. Collaborating with individual research sites is central to recruitment firms' activities. The current position of patient recruitment companies—removed from clinics, but still operating in the space of medicine—requires partnership between two stakeholders to ensure that research subjects are actually admitted to research studies. In this chapter I will describe relationships that begin during the recruitment period between these companies and research clinics.

As I described in Chapter 4, recruitment firms quickly realized that efficiently targeted clinical trial marketing messages alone do not return the necessary number of enrolled patients in research studies. Even if a patient meets all the criteria required for inclusion and is interested in participating, he or she cannot legally enter a study and receive an investigational treatment until he or she has given informed, voluntary, and capacitated consent to partake in the investigational procedures. If it is a clinician who is testing an investigational treatment, the duty to fully explain all the details of the study and disclose all the involved risks to participants rests with the clinician. As a result, it does not matter how many interested patients recruitment companies find, if a research clinic does not have time or enough staff or motivation to call these candidates and further work with them on admission to a clinical trial, then these patients will not be enrolled. Moreover, technically speaking, research clinics do not work for recruitment

firms; they are selected, contracted, and paid for by a sponsor. This situation creates interesting interactions between firms and clinics which I will further discuss in this chapter.

To ensure that recruiters' efforts to find patients are not wasted, and collaboration between firms and individual research sites is productive, recruitment firms have dedicated employees who are working directly with research clinics. Their responsibility is to ensure that recruited patients receive follow-up, and are additionally screened and scheduled for the informed consent visit with a principal investigator. During my field observations and interviews it was obvious that recruitment companies view interactions with research sites as crucial to fulfilling their goals.

In this chapter I offer analysis of the relationship between recruiters and research clinics and the factors that shape these interactions. I organized my results into two main sections. 1) Interactions from the point of view of recruitment firms, which were identified in the field notes from participant observations and interviews with informants from different recruitment firms. 2) The research clinics' perspectives on working with recruitment firms. In this section I will present categories that I identified in ten semi-structured interviews with representatives from investigational research sites.

The relations between research sites and recruitment firms are full of contradictions. Recruitment companies with dedicated site service departments view themselves as partners for clinicians, aiming to assist with recruitment and relieve some of the workload associated with it. But, as I observed, research sites might be reluctant to receive this assistance. My informants were genuine in their desire to help research sites,

yet the circumstances in which recruiters operate do not necessarily translate into successful collaborations.

Another example of a paradox is that recruitment firms are reimbursed for enrolled patients, but clinicians are the ones who admit participants to a study. Clinicians talk to patients, enroll them or disqualify from a study, and this information is vital for recruiters in order to evaluate techniques used and receive credit for their work. In the existing system, following up on referred patients and providing requested information for some research sites might mean extra work without any benefits. Even more so, it may take away time that sites would use to find their own patients. In this chapter I show that the essence of the conflict between the sites and recruiters is based in the fact that with the privatization of clinical trials for everyone involved, patients represent a certain market value; and thus all efforts are evaluated and justified based on this perceived value. I also illustrate how these situations introduce ethical questions, as patients often remain in the middle of these conflicts.

Only sites can enroll

Unsuccessful collaboration between a recruitment company and a research site will result in zero patients enrolled in a study. In contrast to saving sponsors' money, this can lead to significant increase of clinical research costs because financial resources (i.e. for marketing or contracting a call center) are wasted and do not result in patient enrollment. Recruitment companies' dependence on research sites also sheds light on another paradox— recruitment firms are paid for and measured by something they are not able to perform. An owner of a recruitment company explains:

> Ultimately the sites are the only ones that can enroll patients. So, if you have a problem at the site you can have the best media, pay-per-click advertising, way to throw a 100 patients at the site, but if you can't get them enrolled it's all going to be for nothing. No one thinks of that. Sites enroll patients, we don't. We're compensated based on a performance metric that we don't perform.

Although the FDA does not require a principal investigator to personally conduct the consent interview, the investigator remains ultimately responsible, even when delegating the task of obtaining informed consent to another individual knowledgeable about the research (FDA, 2011). As a result, only a principal investigator or designated study staff who is working for the principal investigator can enroll a patient and sign documents indicating that a patient is now legally part of the study. Patient recruitment companies cannot do that. In order for recruitment agencies to receive a credit for attracted participants, firms need to ensure that research sites are doing their part in the enrollment process.

For each individual clinical trial, research sites are contracted and paid by a sponsor or a contract research organization. The relationships between a research site and a recruitment firm are bound by a business associate agreement. Usually a recruitment firm will not start working until a business associate agreement has been signed by both sides, and the site has been initiated and has obtained IRB approval for marketing materials. It can sometimes be a lengthy process to obtain the approval because sites have their own internal policies (i.e. for marketing materials or requirements for an internal legal review of contracts with outside vendors) that need to be taken into a consideration. It also means that research sites do not have any obligation to the recruitment firms. The

research team often fulfills their requirements, such as updating the status of every referred patient in the software systems, completing the training of each company's software system, and screening referred participants for free. This is not to say that research sites do not gain any benefit from collaborating with recruitment firms, but, as I will show in the second part of the chapter, often costs, associated with this partnership, can outweigh benefits.

Working with research clinics

I am sitting in a small conference room with Ben. He is an ambitious, 29 year old nurse who used to work as a research coordinator. He told me he chose a recruitment firm because he wanted to get involved in the business side of clinical trials. We are seated at a brown, oval wooden table with a phone and microphone on top of it. The room is light with beige walls, and the windows of the room are facing a small parking lot with a lake behind it. Ben is typing on a laptop and preparing for a call with a research nurse at one of the sites they are helping with recruitment.

Ben works in a medium size patient recruitment company located in the Midwest and is hired to work directly with coordinators from research sites. He is responsible for contacting sites weekly, keeping them engaged, gathering necessary information, finding what help they need, determining if they are updating patient tracking software, tracking what happened to referred patients, and identifying which issues they are facing. He is the connection between a recruitment firm and a clinic. His goal is to maintain friendly and casual relationships with coordinators. Recruiters believe that the recruitment business is people driven—people work better with people they like. Every week he calls all

coordinators working with the recruitment firm, and often these calls are brief. Ben is supposed to gather information about the situation at the clinic and assess overall "mood" to ensure that sites are still motivated to keep working and that there are no emergencies at a clinic that would disrupt the recruitment process. These brief conversations are also used to remind coordinators that the recruitment firm is here to help them.

While we sit in the conference room, he calls the first site. The conversation is casual. Ben sounds energetic and determined. A coordinator complains that her research clinic has not yet had any patients identified for a study. Ben listens carefully and sympathetically and says that other sites encounter similar problems. He continues by sharing that he has heard from other sites that it is hard to get in front of patients, and it is challenging to add more treatment for a cancer patient. Ben keeps listening and expressing support. Before he hangs up he reminds her about the business associate agreement, saying that he needs to know when it will be signed by a principal investigator to plan all the logistics for the media. To that the coordinator responds that the principal investigator has been traveling, and there is already a huge pile of papers to sign, but she promises that she will take care of that.

During the conversation, Ben uses the opportunity to remind the coordinator about tasks that she needs to complete. He further delivers collected information to a marketing department, which plans where and how frequently to display advertisement in television, radio or other media. In this way, a recruitment firm can regulate "patient flow" to a research site. For example, if a coordinator can not keep up with a study enrollment or if she or a principal investigator is planning to travel, it can be decided to

stop advertisement in the research clinic's geographical region. Information gathered from a coordinator is also shared with a program manager who can further update sponsors on progress or seek help from a sponsor if necessary.

The role of these types of departments is to continue communications with research clinics until the study enrollement is complete. In essence, recruitment firms are helping sites to find patients who are interested and meet basic inclusion and exclusion criteria (i.e. gender, age, medical condition) for a particular study. According to the research firms' discourse, this is suppose to relieve research clinics from the burden of finding participants. And clinicians need only to follow up on these patients to perform additional medical screenings, if necessary, and guide them through the infomed consent process. However, for a number of different reasons I will outline in this chapter, the system does not always function smoothly. In order to receive a credit for recruited patients, firms need to ensure that recruited patients actually end up in a study, and this is attempted through these dedicated departments. A senior director of a department that is dedicated to work with research sites explains:

> […] the site service [department] is there to work with sites to make sure they are able to process patients, make sure they are getting them in for appointments, make sure they are actually screening them and enrolling them— getting them to sign the consent and get them into the study. And, at any point in the process if they need help we have various tactics to help them […], but that is the whole reason for site services to be able to handle the enrollment process.

"*I know what you are going through"*

Having former coordinators in recruitment firms is a strategy to ensure buy-in of research sites in using centralized recruitment services. In addition, professional recruiters believe that it helps to bond with individual research sites and encourages coordinators to collaborate and share necessary information with them. Later, when Ben and I met for an interview, he told me:

> A lot of times, even just this morning, I was speaking with a clinical research site and they were describing some frustrations with being up at five in the morning, starting surgery, and coming home so late. They were describing that they weren't able to update where patients were at or how they are doing with recruitment because of that. And I was able to say: "I understand it completely, I have been in your shoes, you know. I have also been a coordinator working in clinics and doing surgeries; I know what you are going through and I understand." It helps to meet them halfway as far as getting data on where patients are going through our funnel in the process. So just like anything when you have that common background, it really makes it easier to relate to the people who you are working with. All these site coordinators have very different clinical practices than maybe I have worked in, but at least we have some of that common language, some of those common schedules. So it helps a lot in getting data from them, as well as getting them to buy into the service.

Although the described strategy can help to some extent, I observed that recruitment companies are having a hard time gaining research sites' trust and acceptance.

Sites don't always want to work with recruitment firms

In my observations and interviews I often encountered situations where a recruitment firm struggled to get sites to collaborate with them. This seemed entirely at odds with the discourse of recruitment firms being a great help for research sites. That is not to say that some sites do not find services offered by recruitment firms beneficial, but there are also legitimate reasons why sites are reluctant to collaborate. I will discuss this more in the section on interviews with research sites. Recruitment companies seem to be aware of these reasons, but do not have the power to change them. In fact, they often attribute research sites' attitudes to ignorance, because, for example, some sites believe that it is illegal for a recruitment company to recruit patients. Some of my informants even referred to research sites as lazy.

Often research sites are understaffed and overworked, conducting more than ten clinical trials simultaneously in order to sustain a practice. Even if a recruitment firm runs a television advertisement for them and patients call to a site, it is possible that a coordinator will never have time to answer all telephone calls and talk to every caller. A senior manager of a site service department explains:

> It is still difficult and still not a golden ticket [having a site service department] all the time, because you still have study sites that are still very reluctant to have that additional help; they either want to work at their own pace or own time or think you know it is illegal to allow additional help onsite, or still have bandwidth issues that we cannot help with; say they have only one investigator for the study, and they do not have any sub investigators. He might not only have his day job as a normal physician, but maybe in addition he has 10 additional studies he is doing. There is nothing we can do about that.

Dora, a site specialist working in a recruitment company located on the East coast, shares her experience on collaborating with sites:

> […] other times when they do not appreciate it so much I think we're just adding another job for them to do. So, for instance, we have them update the status of their referrals, and they have a lot of other things going on, so we try to play behind the scenes like we were saying we try not to be a burden to them and add another extra tool, but in every study there's going to be certain things and tasks that they need to follow up on. This sometimes is just another task for them but it's important for them to be involved because […] patient recruitment is ultimately their responsibility.

Due to the fact that patient recruitment companies are removed from medical institutions and are not able to enroll patients in clinical trials themselves, the partnership between the two stakeholders is essential to make sure that studies are filled with a necessary number of participants. A sponsor is picking and hiring research sites and, thus, plays a significant role in motivating research sites to team up with professional recruiters.

"Sites work for the sponsor": a sponsor needs to champion recruitment services

My informants often talked about the importance of a sponsor in engaging sites. Some sponsors leave it optional for sites to participate in recruitment programs. Usually it is then left to a recruitment firm to introduce themselves and engage a site and engage them in collaboration.

> And so there is a huge aspect for study success if the sponsor really buys-in and really champions these services. If the sponsors show sites that this is an option – "You don't have to do this, we will let you do your own things" and they are not

> […] really encouraging the sites to do services with their company. A lot of times the sites don't want to change, and they don't want to bring someone else in; it seems like extra work to them at the front end.

On some occasions, a sponsor is particularly sensitive about letting a recruitment firm communicate with sites. In my observations, I encountered a situation where a large pharmaceutical company was running a Phase II study with 40 research sites. The sponsor was unwilling to let a recruitment firm contact sites. In addition, they were not promoting collaboration between sites and recruiters. The understanding is that sites already have a lot on their plate and do not need someone else to disturb them. In this particular situation, a recruitment program was designed to incorporate medical chart reviews and physician referrals; thus, close collaboration with research clinics was necessary for the program's success. It was a serious disadvantage for the recruitment firm, and halfway through the study the recruitment program was failing. The recruitment firm was complaining that the current organization of the research and the sponsor's attitude were seriously getting in the way of patient recruitment.

After several meetings and lengthy discussions, it was finally agreed that a recruitment firm would be put in touch with the monitors; the staff from the sponsoring company that directly works with research sites. As a result, before recruiters were able to work with research clinics, they needed to "sell" the idea of the service to monitors and ensure they pass the information to the research clinics. This example demonstrates the contentious role of the sponsor—on one hand they hired a recruitment agency to support the enrollment, but on the other hand they are not providing full support that is necessary

for the recruitment program to succeed. In addition, the described example shows that overload of research sites is a serious concern of sponsors.

In an interview, Adam shared another situation where a sponsor was concerned with their research sites being overworked:

> […] we've had sponsors say, well you know, we want to hire you, we want to work with you, but all we ask is that you not make any more work for the sites. Well, how can you speed up the enrollment rate without making more work for the sites? I understand why they say that. They say that because sites are already overworked, they don't have enough resources. So it seems just like an intuitive thing to say, "well we can't add to the site's workload," but how can you get more enrollments without increasing their work? You can't do that.

But there are sponsors who freely let firms talk to sites and encourage sites to engage with a recruitment firm. One of the benefits for sponsors is the availability of up-to-date information on how sites are doing and where they are with enrollment. Most of the recruitment firms have weekly meetings with sponsors where they discuss in detail the situation with each site. Recruitment firms are in a way surveilling sites and reporting to a sponsor. Although exchange of this information is meant to be productive and accomplish recruitment goals, it also limits research sites' abilities to resist, as they may receive pressure from a sponsor. Trust in this triangle is important; otherwise the work is unproductive since no formal relationship binds a recruitment firm and the research sites. I also encountered situations where sites report patient recruitment firms to a sponsor, especially if they think that referrals sent are unqualified, and the staff feels that a recruitment firm is wasting their time.

Sponsors also play an important role in establishing relationships between the sites and a firm in other aspects. Usually it is up to a sponsor to decide how rigorously patients will be screened by a firm's call center, because it is not possible to find out all the medical information through a telephone conversation. Sometimes patients do not remember names of medicines, or medical parameters, or they may not have an official diagnosis. On those occasions, the sponsor might request to refer patients who just experience certain symptoms. The reasons for this kind of decisions are made because the sponsor is concerned that there are not enough patients with an official diagnosis. Or they are willing to reduce costs for recruitment services (i.e. in the cases when few patients have an official diagnosis, recruitment firms will need more resources for marketing to reach these patients) and hoping that research sites will diagnose these people and subsequently enroll them in a study. However, it means more work for sites—they need to schedule, evaluate, and diagnose these patients when they may not even qualify for a study. A call center director shared this with me in an interview:

> They were letting too many people through the first time. Originally I had a question in [a telephone screening script]: "Have you been diagnosed with sleep apnea?" It's a requirement in the study. Well their [the sponsor's] thought was—if someone has it but they haven't been diagnosed, let's get them to the site. We'll have them do the sleep study. We'll have them do all this. Well, then the sites got upset because we were sending all these people that didn't meet the protocol requirements.

As I have shown, sponsors play an important role in setting up relations between a research site and a firm. But in addition to sponsor support, recruitment firms actively use

other techniques to foster trust and engage with research sites, and I will illustrate those in the next section.

Engaging sites

Communication with sites

Communication between recruiters and research site staff always happens through a telephone, rarely do representatives from recruitment firms and coordinators in research sites meet in person. Individuals from companies told me that they are trying to be considerate of how much they reach out to sites for fear of confusing or burdening the sites. Dora, a site service specialist in a recruitment firm, explains:

> […] we try from the very beginning to not annoy them, to not constantly call them, to do what we can to help them, to kind of just say we're here to help. We're not going to call you every week, but you tell us if you need more help, or less help, because we know how sensitive some of them can be, and that often will kind of put them at ease initially and hopefully their experience with us is positive so that when they work with us again it's not bad. But, I do hear them complain about other companies and just say, oh, the worst, and maybe they're saying that about us to somebody else, but we just try to be as patient as we can.

Communication is used for an exchange of information. Recruitment firms are always trying to be updated on a situation at the site—which days are dedicated to a study, when a PI or coordinator is absent, or when someone is sick or leaving for a vacation, or what common recruitment practices are at a research site. When I joined Ben for another meeting, he explained how communication goes with a new site:

> When I am talking to this site, we are still talking generally about recruitment, but when they are in [have signed BA agreement], we slowly start with details—how many hours per week can you see patients, where you have parking, and so on. I try to learn how the site processes patients; who sees patients, and where the disconnect is? Sometimes the problem might be that the scheduling department is disconnected with the coordinator. I try to put my head inside the clinic as much as possible. Then we can give advice […]. We encourage recruitment on the site level and how to find patients outside a patient recruitment organization's program. I try to share what is going on with other sites, what their struggles are, and what are things that work.

Recruitment firms are dependent on research sites— if sites do not collaborate, not only is the sponsor's money wasted, also patients are also frustrated. Patients have responded to an advertisement, spent half an hour or more on the telephone answering different questions related to their health, are hoping to get into a research study, but are never contacted by a site. Because, often in order to control the entire recruitment process and patient flow, recruitment firms will not disclose names and addresses of research sites in the screening process or advertisement[1] and it could be more complicated for a patient to find this information. Even in situations when collaboration between research sites and recruitment firms is successful, for a patient it still means an extra layer to overcome; more time and sharing of their personal health information to several parties in order to participate in a study.

[1] The website clinicaltrials.gov does not list names of research sites. Usually zip code and name of a city is mentioned, but there are cases when only the name of a recruitment firm contracted for a research study is mentioned.

Competitive advantage

Regular communication and engagement of sites also gives a study a competitive advantage over other studies currently happening at a research site. Research sites are small businesses and in order to sustain themselves they often need to conduct more studies than they have labor resources. Anna told me in our interview:

> […] we focus on patients, as well as the sites, because the sites can be doing— I talked to one coordinator, and she said on average her clinic does 15 studies at a time. So, with that many studies going on some of them are competing. We need to make sure that we're engaging the sites as much as we are keeping the patients retained in the study. So we might work with the sponsor to organize meetings […] like rejuvenation meetings or refresher meetings [for research staff]. Preparing newsletters and we have come up with the crossword puzzles anything fun to put in there for the sites. It's very important to keep the sites well, because the more studies they have, the more their site resources are allocated to other studies that may become a priority at other points in time and we may start to fall off the line and may not be important and then the sites sort of just drag off and they're not giving their attention to our study.

Other informants shared similar experiences, telling me that if they got along better with sites and kept them engaged, sites were more likely to give a preference to their study when competition existed for similar patients and labor resources. A former coordinator who briefly worked in a recruitment firm while I was conducting participant observations in a meeting mentioned that when she was a coordinator it was a common practice to put a study on the bottom of a pile if a sponsor annoyed them. So recruitment firms are constantly walking a fine line—trying to not "annoy" research sites meanwhile ensuring they are collaborating and following up on referred patients.

"We care about overall recruitment": educating research sites

Recruitment firms are trying to improve the perception of themselves in the eyes of research sites by giving occasional advice and tips for overall patient recruitment. These attempts are meant to show sites that recruiters are not draining sites' resources just to complete their own share of recruitment, but they care about overall enrollment. Dora shared how her company goes about engaging sites for this reason:

> […] we also do programs where we might call the sites directly and brainstorm with them, and we'll do a search for them and say, "Look, there is this health fair in your community, there is this walk coming up, there is this event that you can talk to these people." We will start relationships with advocacy groups or local groups for them and then maybe find out how much it costs to advertise or get them into the walkathon […]. We will do the mailings for them out to their referring doctors and then turn the relationship over to them and say, "Look, now you have your relationship with your local Alzheimer's association in your community." We guarantee they have other studies; so we keep that relationship going with them, become part of their community, so we try on certain studies where the client will contract us to help the sites be a better part of their community so that when they do need to find patients they know where to go and they have more potential resources as well. So I think from that aspect it is another way that we're different, because we're not just looking at the study; we're looking at every program you might do as a site, and [we show] how can you be a better site.

Sometimes education of sites is conducted through newsletters or other forms of electronic or printed materials. One of the examples created by a recruitment firm was called "Tips and techniques for study sites". It was a one page handout in orange and blue

colors with a study logo on the left top corner, designed to provide suggestions on how to keep enrolled patients engaged i.e. retain them throughout a clinical trial. The handout starts by explaining that recruitment is one of the greatest challenges of a clinical trial and that the coordinator plays a critical role in identifying and managing patients through the process. The advice given in this handout appears to be quite basic for individuals who are involved in the research process.

The handout stresses that personal relationships will motivate patients and keep them engaged through the duration of a study. It recommends finding out the obstacles to participation early in the recruitment process, such as transportation options or time availability for the visits. This would help not only to accommodate patients, but also eliminate those candidates who would be non-compliant. Coordinators were advised to involve other people in a candidate's decision making process:

> Sometimes the patient's loved ones are suspicious of investigational therapies and may discourage patients from participating. Invite patients to bring family members to an appointment to address any concerns they might have. Better informed influencers can often become your best advocate.

It is also suggested that the coordinators should get to know patients on a personal level. "Ask about pets, hobbies, children, and jobs, and then find common ground that can open conversation towards building more personal connections." According to this recruitment firm, ongoing participation can be promoted by ensuring that patients are getting satisfaction out of the experience:

> Satisfaction might be from treatment, connection with the study staff, good feelings from their contribution, or discovery. Remind each patient of the ongoing

value they are providing and the important role they play in helping shape the remedies and treatments for this difficult condition.

The decision-making process for sponsors, recruitment firms, and research sites is informed by financial benefits and losses. In turn, patients are encouraged to donate their time and bodies in exchange for hope and satisfaction.

"Sites are too quick to exclude some patients"

Recruitment firms also believe that research sites are too quick to exclude patients and that there are candidates that could be reconsidered or thought about and eventually could become eligible for a research study. Thus, recruitment firms consider their duty to educate sites on a proper approach to patient recruitment:

> And a lot of times they do that just by looking at the answers that they've given, and then disqualify patients without even calling them. Those patients are sitting at home and waiting to hear from the site, and so they end up calling us back again.

Recruitment firms would organize meetings or provide materials to encourage sites to evaluate each patient more carefully:

> We did a workshop just recently where they [clinicians] came up with the ideal patients, like someone who meets all the criteria and are knowledgeable […] and somebody who would fail and then [somebody] that's kind of in the middle of the road—a borderline patient. His or her blood work is a little off or whatever. We tried to have the principal investigators create those different patient types and say these types of patients would meet all of these criteria. That really helps them [to] think through like— so we have a patient who comes in and his blood pressure is a little high and then they [physicians] go and look at the protocol to see what they can do; do they bring him [a patient] back in, do they leave him to sit or do

> they just disqualify him, or do they call the medical monitor? [This exercise] helps them really reevaluate who is eligible for the study and [evaluate] those borderline patients, rather than just cutting them off and disqualifying them. They think through if there's something they can do ethically to actually give him [a patient] a week or two to settle on their medication and then bring him back and reevaluate so that we're not losing too many patients that could be eligible for the study. So that's another way to help them [research sites] is to think through [these] pathways.

Overall, recruitment companies employ different techniques to engage with research clinics. Some strategies are meant to foster collaboration between a research site and a recruitment firm, whereas others serve a larger purpose. For example, regular interaction with a research sites gives a particular study a competitive edge compared to other studies that the site is working on.

In my field notes and interviews it stood out that recruitment companies blame sponsors for the difficulties with patient recruitment. I described one aspect of this attitude earlier, when talking about the importance of a sponsor in motivating sites to work with patient recruitment companies. Another dimension of this attitude is connected to the site selection process. Many of my informants from recruitment companies judged that majority of recruitment difficulties could be solved if sponsors would select right research sites.

Selecting sites and patient recruitment

Recruitment firms often blame pharmaceutical and device companies for poor site selection, resulting in poor patient recruitment. Most of the time, sites are selected by a

sponsor or a contract research organization. When patient recruitment organizations receive an invitation to sumbit recruitment proposals, sponsors or contract research organizations already have selected the research sites. Everyone in the industry has their own criteria for selecting sites. A sponsor is interested in selecting sites based on a site's past performances and principal investigators that are leaders in their field because they could serve as promoters of an approved product. Contract research organizations, on the other hand, want to work with sites that are collaborative, that they have built good relationships with in the past. Recruiters advocate for evaluating sites based on their abilities to recruit for a particular study, instead of relying on personal relationships or past performances. A program manager talks about the site selection process:

> In one of the studies I am working on right now with, a niche study, […], we got in there and once we started assessing their [research sites] process we found out that the site had one coordinator who is overworked, the surgeon did not need more patients, research was kind of on the backburner for them, and that they had a bunch of conferences and fellows coming in, so their schedule is pretty booked. And you just kind of look at the client and say why did you pick this site? The site has told me that they can't enroll any patients for the next 2 months, and once they do start enrolling they can only fit in maybe 1 patient every 2 weeks to be screened. I mean, once you get that information you would say, "Well I will never pick a site like that", but a lot of times that information doesn't come out until you really get to know the site. And unfortunately some of the larger databases and some of the other companies out there don't do it; they don't take that time [to evaluate sites].

It appears that different stakeholders in the research industry have different interests when selecting research sites. Naturally, recruitment companies are advocating

for selecting research sites that would better perform at patient recruitment and would be willing to collaborate with firms. However, as I am going to describe in the second part of the chapter, not all research clinics experience recruitment firms' services beneficial for their practice.

What do research sites say about working with patient recruitment companies?

Up to this point, I have discussed the perspective of patient recruitment companies and how they view the collaboration with research clinics. Here, in the second part of the chapter, I will describe the point of view of research clinics. The results described below are based on ten interviews with coordinators and recruitment specialists at research sites (for more detailed information on participants, please refer to Chapter 3).

After research sites have been selected and approved by the IRB, a recruitment company will make a contact with an investigational site. Research sites typically do not have any say in the selection of the recruitment agency, arrangements of a recruitment program or the number of patients a recruitment firm is contracted to deliver. It is all arranged by the sponsor. Depending on the sponsor, a site can choose to work with a patient recruitment firm or to do recruitment on their own. One of my informants describes the initial work process with a recruitment agency:

> Me, the recruiter receives an email or a call from somebody at the [recruitment] company, a contact. And then typically I have to complete some training, and the training is usually to be able to maneuver on their website to obtain the referrals and then to track the status of the referrals; and so that's the initial contact usually. Once I've completed the training and then the contact will notify, or should be notifying you when the advertisement will take place.

After the initial training is completed and a marketing campaign is on track, contact between the two stakeholders is less frequent. As I described earlier, the communication is used for monitoring the recruitment process at individual research sites to ensure that referred patients are enrolled in a study. In the remaining part, I will present how employees of research sites experienced working with centralized recruitment companies.

Helpful services

Although the overall reaction towards recruitment firms was negative, my informants did identify some aspects that they perceived as beneficial for their practices. First, my informants acknowledged the benefit of new, previously unknown patients coming to a clinic whether for a trial or other clinical services. Second, assistance with preliminary patient screening and exclusion of unqualified patients by call centers was seen as a relief. Third, research clinics appreciated that recruitment firms took care of the logistics of developing advertisement campaigns and organized placement in print media, social media, radio or TV stations.

Unknown patients

For clinical trial recruitment purposes, all potential study candidates are divided into two groups— known and unknown patients. Known patients are those who can be recruited at a site, either from a physician's practice or patient database that a site maintains. Unknown patients are those who are new to an investigational clinic and are

brought in through clinical trials advertisements. All informants, regardless of type of the site they work for, indicated that they benefit from having new patients. New patients that contact a clinic are further directed to a recruiting study. If a person does not qualify for a particular study, his or her name can be included in a patient database for future studies, since sites are continuously trying to expand. Or an individual is offered to become a patient of a principal investigator in his or her clinical practice and receive an approved therapy.

In the example below, one of the coordinators shared her experience on how a patient recruitment company can be helpful for bringing new patients for a particular clinical study:

> I think if it's a really difficult study to recruit for; it's always good to have [patient] referrals. Sometimes you just enroll those studies by going through volumes of people. I mean that's the benefit of working with those firms, they might be giving you people that you wouldn't otherwise have access to.

A surgical clinic that performs device clinical trials used the recruitment program as an opportunity to market approved surgeries performed by the principal investigator. When I attended an informational patient meeting for the clinical trial, I noticed that a coordinator had placed materials on other medical services at this clinic next to clinical trial brochures. If a patient is disqualified from a study or for some reason decides to not participate, he or she might consider other treatment options. In addition, it was explained that when patients enroll for a study they become "patients for life" at this particular clinic. Meaning that the clinic's employees use clinical trials as a way to build the practice and long-term relationships with patients. The coordinator explains: "I mean we

consider them our patients no matter what, but there have been a few that didn't fit the criteria that did want a different procedure."

A coordinator at a small research site explained to me that "[…] we may not get great patients from centralized recruitment, but we always seize an advantage to our database". In this case she saw the opportunity to invite referred, but unqualified patients to opt-in for the site's database for future clinical studies. She expanded:

> I feel like we usually look at centralized recruitment as gravy, something on top. Not the core, but something we hope we get. The sponsor wants us to get patients for their study, but we also look at it as an opportunity that we're getting some free advertising, that we can increase our database. If someone doesn't work for this study, they called us, so we can still get their information and use it.

Eliminating unqualified patients

After creating broad marketing programs, some of the recruitment companies offer prescreening services with an intention to refer to clinics only qualified patients—matching inclusion and exclusion criteria. For a quick filtering of unqualified patients, recruitment companies can develop web screeners where individuals answer several questions and find out if they are a candidate for a particular clinical study. A website with a questionnaire also gives a cheap and convenient opportunity to educate patients on the details of a trial. It is helpful because candidates that then come to a clinic are already familiar and comfortable with the study procedures. This minimizes dropout rates at an informed consent visit and saves research staff time. A coordinator from a private research site explains:

> They [patients] would go to a centralized website, and they would answer some questions, filling their name, the best way to contact them, and so they don't really talk to a live person. And then, also typically on a webpage they would have brochures or literature for them to read that might help them with some of their questions right away, before they come to me.

Although a website can be a cheap and convenient way to screen patients, this format is not suitable for asking complex, health-related questions. Thus, recruitment companies utilize call centers for patient screening, since live conversations help to probe and verify patients' answers and "generate more qualified" candidates. This type of service was found to be helpful by interviewees from small sites or physician practices that conduct clinical trials on the side and do not have enough dedicated research staff:

> […] many times for our patient population, radio advertising is the best. And so they [recruitment firms] do that, and then they have nurses that work with them, trying to pre-screen the patients so that when they come to us, we go more specifically over the inclusion and exclusion. So instead of us seeing 2000 or 3000 patients, we see a 100 or 200 patients.

A different perspective was shared by interviewees from larger research clinics. They thought that recruitment agencies do not have sufficient medical knowledge or experience to appropriately screen participants. They felt that screening services are helpful only when interested individuals are eliminated just by basic criteria, such as age, gender, and presence or absence of a medical condition:

> […] [we prefer when they] eliminate somebody right off the bat that doesn't qualify by asking just one question. Possibly eliminating somebody that may not

> really have the condition or the disease that we're recruiting for, I guess that's where it would be helpful for us.

Communication

For successful recruitment, clear communication between research sites and patient recruitment companies was seen as essential. Coordinators want to know what is happening with the marketing campaign so they can organize their recruitment plan accordingly. Individuals I interviewed indicated that it is also important for them to know information previously collected about a patient in cases when a recruitment firm is carrying out prescreening. These are important aspects because sites are the ones that are responsible for communication with patients, and for doing the enrollment. For example, if a patient is frustrated because she has spent an extensive amount of time for a telephone screen by a recruitment firm, and a coordinator then again asks the same questions, it is the coordinator who needs to keep the patient satisfied so she will still want to participate in the study.

In addition, sites appreciate if the recruitment agency has an efficient system in place that frees them from checking their referral system daily, since coordinators may work on many different clinical studies at the same time, and each of them may use different software systems. A coordinator shared her perspective on the importance of collaborative work between herself and a recruitment agency:

> It's nice to know what the companies are doing because I might not want to do something at the same time. If they're going to run television [advertisement], I don't want to run a television [advertisement]. I want to be in the paper. I want to […] do the opposite. I want to make it a success for both and so that's why it's

helpful to know dates to make sure I can handle the volume of calls, and to be seen kind of everywhere and not focus just on this.

The following quote illustrates a coordinator's concern regarding the importance of having patient information when talking to an individual after he or she has been screened at a call center. Recruitment companies offer "live transfers" to make sure that a qualified patient is scheduled for a first visit promptly after he or she has been screened at a company's call center. Recruitment firms are offering this service because they believe that individuals lose interest in participation within 48 hours if not processed:

> The recruitment companies sometimes offer live transfers after they've gone through their phone script. The problem with that is that they do a live transfer; we don't have any information on the patient in front of us. It's not like we can pull up their information on our computer system that our call center just captured. […] It's a service they offer, and it's a great thing to be able to talk to those patients promptly, but it's difficult when you don't have any information to work off of in front of you, and this patient has already been on the phone with somebody for 15, 20, or 30 minutes sometimes, answering questions. And so sometimes it's frustrating for the patient, because then we're asking them the same kind of questions over.

If research sites are unhappy with some aspects of recruitment firms' work, they are vocal about their concerns, especially regarding patient rights. In the following example, a coordinator shares the situation where a recruitment firm was monitoring calls without the sites' or patients' permission:

> A recruitment firm was recording transferred calls to see how it worked. Well, we thought that they hung up when a call got transferred to us. There was nothing in the IRB approved script saying that they are going to listen to our phone calls. And they did not tell us ahead of time they were going to do that; then they cannot

> do that. We did not agree with them. Because if a patient tells online, when we do the medical history that she has HIV, a recruitment firm does not need to know that. And that is none of their business; they are a central ad campaign, and that is all they are. They do not even need the patient's name. They can maybe monitor calls for their part of conversation, but after they transfer calls to us, they should not be on that phone call anymore. However, if their software required a patient's name or the reason of disqualification; then I would call them [the recruitment firm] and they would tell me that they have to record the call. I would say no. You know, "Sorry, but that is patient information that they [callers] are giving us." They are not consenting to give it to a recruitment firm, or consenting to have it recorded. So, we had to make sure that that was alright, and we looked through every contract to make sure a recruitment firm did not tell us ahead of time they were doing that.

Relieving logistical burden

It was indicated as helpful when recruitment agencies take care of the logistical aspects of the patient recruitment process. These aspects were acknowledged by all interviewees, but more appreciated by the smaller sites with less manpower dedicated to patient recruitment. The services identified as helpful were: creating posters, flyers, placing television and radio advertisements, scheduling patients for visits, marketing expertise, and good technology in place that signals about incoming patients. Here a coordinator shares her experience on how helpful patient scheduling is:

> One thing that was helpful was that they helped set up the initial appointment emails, because when you are doing studies, and you have a smaller group, even just scheduling takes a lot of time. So that's another thing with the recruitment

> agency; what they can do is when they screen them [patients] then they [a recruitment company] can give them their first appointment, which really helps.

In this situation, the coordinator echoes recruitment companies' discourse that clinicians need to focus on clinical aspects of patient recruitment, whereas recruiters can dedicate their time to advertising: "And I think by them specializing in studies they kind of know what works and what doesn't work; whereas like clinical investigators, they really don't have any clue what advertising is."

Despite the fact that my informants felt negatively about working with patient recruitment companies, they were able to identify certain aspects that seemed to be helpful for them. Coordinators appreciated when services were delivered smoothly and without interrupting sites' daily pursuits and when recruitment companies took care of logistical errands. Moreover, coordinators welcomed the opportunity to expand the practice with new patients. Interviewees, however, criticized recruitment firms for invading research sites' business — both medical and financial aspects of it. In the remaining part of this chapter, I will focus on the aspects of recruitment firms' that research clinics did not appreciate.

Limitations of patient recruitment services

Although some aspects were identified as helpful, the majority of my informants remained critical of services offered by recruitment agencies. I organized the critique shared by the investigational sites into three groups: 1) the lack of medical knowledge, 2) the low quality of referred patients, and 3), the burden of additional work that does not

translate into any benefit for them. Moreover, some of the research sites perceived recruitment firms as a threat to their business.

From the recruitment firm's perspective, patient recruitment is treated as a logistical issue to speed up patient enrollment at a site. My informants from research clinics disagree; they think that detailed medical knowledge and understanding of the local patient population is necessary. Although relief from such tasks as poster preparation and placing advertisements is helpful, they still feel that work with recruitment agencies might not be successful in terms of filling research studies. One of the coordinators commented on the fact that recruitment companies put a lot of emphasis on material things that are supposed to help with patient recruitment: "Coffee mugs and posters are nice to have, but they do not enroll patients."

Lack of medical knowledge

Some of the recruitment companies are employing nurses for the telephone screening process, whereas other companies are trying to offer cheaper services and screen patients through regular call centers, automated voice messages, or web-screeners. The coordinator explains the importance of having medical knowledge for patient screening:

> It takes someone who has clinical experience with people, and knows how to do a verbal history. Once you get someone who's more advertising-based, they don't understand the subtleties or the differences; or if you're not used to the clinical disease state that's being examined, you don't really know how to ask the history around that.

Research coordinators also have a very detailed understanding of what a high quality candidate means (I will discuss this aspect in the Chapter 7), and many of them indicated that understanding clinical context is necessary to ensure that only high quality patients enter studies:

> […] to take a verbal history from someone you don't know, over the phone, requires a lot of experience because […] some patients will say what they think you want to hear in order to get into the trial, and so you have to have enough expertise and sophistication to understand the difference between someone who really wants to be in a trial, honestly, versus someone who's tried to get into a trial for […] money […] they just really want it for the financial gain […], and they'll say whatever […] they think you need to hear. So if you're not good at asking the questions or figuring out that someone is changing their answers to fit the box, […] you get someone who's not honest […].

Low quality referrals

Frequently, I heard my informants complaining that referrals they obtain from the recruitment agencies are of a lower quality—meaning that patients do not qualify for basic inclusion/exclusion criteria. This aspect is related to the lack of medical knowledge discussed above, and it leads to the bigger concern of having additional work. Here a coordinator discusses her experience with low quality referrals:

> And what we often find with them is that they might generate a lot of referrals, we might get a lot of names, but once we start talking to those patients, they actually don't qualify, because they [companies] just don't ask enough specific questions in the screening process. So it's not always as effective as we feel it would be if we were doing it ourselves, because we drill down to more details.

Another coordinator shared an experience that illustrates if good communication is in place, and a recruitment firm is open to collaboration, issues associated with low quality referrals can be solved. In the example below, low quality referrals were generated by two things: 1) the limitation of the phone screen, because one can't objectively evaluate someone's weight through a phone conversation, and 2) some screeners were not asking all the questions from a telephone script that were based on inclusion/exclusion criteria. A coordinator explains the situation:

> There are certain criteria that patients need to meet, but they may say that they weigh a certain amount when they truly weigh a different amount. So they don't fit the criteria, and they [screeners] also don't go over the entire inclusion exclusion. […] I think sometimes the patients are kind of desperate to get into […] weight loss [studies]; they are desperate so they come to us even though that they know they may have not have really answered it truthfully.

The coordinator told me that she had a good relationship with the recruitment agency, and was able to complain about the situation, which led to an improved screening process and, thus more qualified patients. However, not all interviewees had such a positive experience. As a result, coordinators need to deal with unhappy patients who think they are qualified for a study, but upon coming to a clinic do not meet the criteria:

> That's probably another drawback to working with those recruitment firms, is that it's sometimes frustrating for patients because they're spending more time on the phone, talking to people about the study because they've gone through the questions with the central recruitment company, and then we repeat some of those

things, because sometimes we find the quality of the answers given to us might not be completely accurate.

One of the notions of low quality referrals was associated with the socioeconomic status of the patient population. A coordinator from a research clinic located in the suburbs of a major Midwestern city told me that one of the problems with receiving referrals is her clinic location. She complained that a lot of patients who are reached through centralized recruitment campaigns do not have sufficient income or a vehicle with which to get to the clinic. This was particularly a problem since there was no available public transport. She told me she prefers focusing on the patient population served by the hospital where the research site is located.

Among my interviewees, there were coordinators who felt that patient screenings offered by patient recruitment organizations were not helpful at all. Marketing campaigns were appreciated, but they felt the screening and documentation process was of a low quality. As a result, coordinators had to repeat the entire screening process and ask the same health-related questions once patients contacted the research site. It was seen as an additional burden to clinics and patients who often feel irritated when they have to go through the same process several times:

> […] generally speaking, the centralized recruitments – if they don't do any screening; it works for us. I'd rather have even the junk calls come in. I'd rather have them not do the screening. So the centralized recruiting or recruitment organizations – if they can really spend the money on a big population base, that works if they don't do their own screening. I'd rather just take the calls.

It is more work for us

As I mentioned earlier, centralized recruitment aims to relieve the logistical burdens of preparing outreach campaigns from research sites to drive new patients to clinics. However, research sites experienced that the additional work that they need to dedicate to collaborating with recruitment firms often outweighed the benefit. This is partially due to the fact that the quality of services offered by different recruitment agencies varied greatly. Because only a research site can enroll patients, the recruitment firm does not have control over what happens to a patient after he or she is referred to a site. Recruitment agencies require coordinators to document the status of referred patients and constantly update information on progress with each individual candidate.

This information is used by a recruitment firm to analyze the performance of a recruitment program and to decide if additional resources should be invested. When a company provides recruitment materials, they want to know the effectiveness of them, and often materials come with a telephone number that directs all callers to a firm's call center. In this way, the number of individuals responding to a particular advertising material can be evaluated, and the success of patients enrolling in a study can be recorded.

This information needs to be collected and updated by the coordinator. Often my informants shared concerns that this was additional work for them to navigate various software programs. It is also duplicate work when sites keep their own documentation systems. Some of them felt that the work they put into documentation for recruitment firms takes away from the time they could dedicate to recruiting patients locally.

One of my informants asserted that in the cases when her clinic is not getting good patient referrals, they nevertheless are required to do all the work for the recruitment firms. Another coordinator explained the nature of additional work she had to do for recruitment agencies:

> Some companies require lots and lots of information back from us on the status of when we contacted these people, and how many contacts we've done. Sometimes we can do it on paper for them, sometimes we have to go into an electronic system that we have to get trained on. So that aspect can be pretty time consuming for us, versus us just identifying a patient, getting them in the study, and moving forward.

Some of the larger sites that are part of a research site network, and have their own dedicated recruitment department, have developed similar processes of patient recruitment as those of recruitment firms. In cases where recruitment services are imposed on them by a sponsor, the site needs to do duplicate work:

> […] lot of times when we work with recruitment companies, it tends to be more work for us, because if a patient calls us, we have a scripted list of questions that are IRB approved, just like that recruitment company would have, and so we've got to update the information in our database, because we generate reports to the pharmaceutical companies on, "This is how many patients we've screened, this is where they've come from; either from our internal database or from this form of advertising or from a mailing or from a physician referral." We generate all of that on our own, and then a recruitment company, if they're doing that, wants that information for their people too. So then it's duplicate efforts for us, where we've

> got to provide it for them, and then we've got to go into our system and do all of that on our end.

However, if a site does not keep updates, it might be penalized. A recruitment firm can complain to a sponsor that a site is not doing a good job or exclude a site from the services or next round of an advertising campaign:

> […] we had every call in our system, and […] we got 200 [patient calls], then they said, "Well, you did not update our system yet." And we were wondering what are they using this system for? Because we did get the patients, and we got them qualified and in as they wanted, obviously the metrics show the sponsor more how well they did […] obviously. And they said, „Well if you cannot keep that updated, you cannot do the next wave." We were like, „what?" […] so we had everybody working on that. And only one patient took around ten minutes, you know, because it was not user friendly at all.

The sites are small businesses. As one coordinator put it, "we're not in this business to just feel good; we're in this business to make money." The coordinator in the private clinic talks about the costs associated with working with patient recruitment organizations. In this case, she talks about the time spent on working for a patient recruitment company. But additional costs may also arise when the site does not have enough time to look for their own patients:

> […] It is additional work for us where we're not getting compensated for anything, especially if a patient doesn't qualify for the study. If they don't come in for a visit, we still have to spend time with those patients. We have to provide information to that recruitment company, and it costs us time, staff time, but there's no remuneration for us for putting in those time and efforts.

Although I could not obtain numbers on how frequently recruitment firms are contracted for clinical trials, coordinators told me that in recent years they have experienced significant decrease of research clinics' budgets for recruitment allocated by sponsors. Informants reasoned that it is because a centralized approach is more appealing to sponsors due to its perceived cost-effectiveness. However, for larger sites who have developed their own recruitment infrastructures (i.e. have their own marketing department, call centers, etc.) this situation means loss of business, because recruitment firms now are doing what research sites are capable of doing themselves.

> […] we have our own database of patients, and all we do is clinical research, so we're not treating patients in a clinical setting outside of the research study. There are recruitment companies out there that are willing to go into a practice and review charts for them and look at their database. It's not something that we can give them access to, because of the nature of our company, because we're strictly doing research, and we do that ourselves, so we don't need somebody else coming in and doing that. We have a recruitment specialist in our office who will mine our database and contact patients. We have a call center as part of our company that can make outbound calls and do screening just like a recruitment company does. And so a lot of times the services that they offer for us as a company, it's not as beneficial as if we were in a private practice trying to do clinical research and didn't have all of the internal resources that we do at our company.

Summary

In this chapter I discuss the nature of collaboration between patient recruitment companies and research clinics by presenting the perspectives of both involved stakeholders. Partnering with research sites is central to recruitment firms' success in

enrolling research subjects, and as a result, recruiters spend a lot of time and effort to advance collaboration with research sites.

In the current system, professional recruiters view research sites as the location of enrollment delays. In order for recruiters to receive a credit for their work and deliver patients to a study, they need to overcome these obstacles. Everyone is trying to accomplish their goals through research sites — pharmaceutical and device companies promote new products, CROs gather clean data, but recruitment firms naturally are advocating for selecting sites that are willing to collaborate with them in the patient recruitment process.

Recruitment companies also spend a significant amount of their time advising clinicians on how to improve recruitment at the site level. One segment of these advices is related to developing personal relations between a clinician and participants, in order to retain them throughout a study. Certainly, close therapeutic relations between a patient and a clinician can be very valuable, yet in the private research context it creates an uneasy feeling. In many cases, participation in research studies is entirely removed from participants' care processes, and clinical trials' primary goal is to gather clean data to obtain FDA approval. Systemically looking, it seems unfair if recruiters and research sites decisions are guided by financial benefits and losses, but they are trying to attract and retain participants who are donating their bodies to test unknown medical products because of emotional attachment.

Although sponsors might be protective of research sites' time, they still can benefit from recruitment vendors. First, a sponsor can have access to detailed, up-to-date

information on the progress of patient recruitment. But second, in situations when research sites conduct up to fifteen studies at a time, having a recruitment vendor gives a study competitive advantage because there is someone regularly and gently reminding participants about this particular study. This situation presents questions as to what kinds of studies are given preference by clinicians and which studies are presented to patients. There is a risk that instead of offering studies to participants that are most promising or most suitable for an individual, patients are presented with studies that a clinician has on the top of his mind, and studies that have most dedicated resources for promotion.

Tension between patient recruitment firms and research sites shed light on the issues that emerge from the fragmented recruitment process. Recruitment companies realized that just by assuming logistical aspects of patient recruitment, such as preparing marketing campaigns (although found helpful by some clinicians), they still couldn't enroll patients in clinical studies. As a result, the companies' entire existence is undermined. But, research sites resist firms' further involvement in the recruitment process. As I showed in the second part of this chapter, coordinators are critical of recruitment firms' abilities to medically screen research candidates. Even more so, some research sites experience recruitment firms as competitors. The negative perception also can be explained by the fact that the recruitment process and enrolled research subjects mean financial income and future contracts for both patient recruitment firms and clinical research sites. Although everyone involved is interested in increasing the accessibility of clinical research studies (in terms of information about available studies, accessible location, available research staff, etc.), often in conflicts between research sites and firms,

patients get lost. For example, a patient might respond to an advertisement, get screened for a particular study, but will not be referred because the site does not provide data for a recruitment firm. Or on the other side, a coordinator might not follow up on a referred participant because he thinks that work with a firm is unproductive.

Up until now, I discussed the relations that form between recruiters and clinicians. In the following chapter, I will talk about other important relations in the patient recruitment business—those that form between recruitment firms and patients. More specifically, I will present how patient recruitment companies communicate and interact with potential research participants.

Chapter 6: "We are not a clinic; they are not patients": communicating with patients

In this chapter, I will turn to another important aspect of a recruitment firm's daily work—interactions with individuals that are interested in participating in clinical studies. Similar to interactions with research sites, recruiters are interested in maintaining good relationships with callers to ensure that they receive a good service throughout the recruitment process. The nature of the interactions, however, is different and as a result, different issues arise. In this chapter, I will outline key characteristics of the interactions between patient recruitment companies and the public that is interested in participating in clinical trials.

The recruitment firms interact with the public in two ways. First, recruiters communicate with the public through the media—internet, television, radio, newspapers—by distributing clinical trial advertisements. Second, communication happens through a call center when patients call in to get screened for a research study. The purpose of a media campaign is to inform the public on existing clinical trials and make them act on this information—to call for a screening. The purpose of a call center is to eliminate individuals that are interested, but who do not match inclusion and exclusion criteria for a particular study. As I will further outline in this chapter, the nature of these interactions is one-sided, as recruitment companies design and carefully control information flow.

Professional recruiters are trying to make the recruitment process as pleasant as possible for potential participants. However, as I argue in this chapter, the way patient

recruitment companies' present information to the public undermines the valid informed consent process. Although having access to information about available studies can be liberating to patients, in the recruitment process the companies exploit pre-existing norms that patients may bring to certain studies in order to attract them to studies. In addition, the unique position of patient recruitment companies—removed from clinical setting—disrupts the meaningful exchange of information, since recruiters neither share full information about the trial which they are recruiting for, nor discuss callers' health conditions.

I also illustrate the built-in conflict between patient interests and business interests. Obviously, recruitment companies are interested in enrolling patients in studies, and when necessary will advocate for their enrollment, which certainly improves access to clinical studies. Yet their decisions are shaped by relationship with a sponsor and business that funds this recruitment process.

Patients are our stakeholders

Field observations made it obvious that recruitment companies' rhetoric was very patient centered. Similarly to research clinics, patient recruitment companies are interested in providing a good service to patients and do not want to displease them in any way. My interviewees shared the perspective that one cannot present outright misleading information to potential participants. Recruitment firms are aware that many participants will complain and voice their concerns if they feel that they have been deceived in any way. In this sense, the internet has been liberating for patients, because recruitment companies fear that patients will be blogging, complaining to IRBs, or

sharing their appalling experiences to journalists. In an interview, Adam was assuring me that his company considers a patient as one of their main stakeholders:

> [...] we really believe that patients are one of our stakeholders. Patients to us are not just faceless people. Patients are really important to us, and because we all could be a patient, we probably all have been a patient, we have family members who are patients, and so the patients we work with at our company want to be treated the same way. We want them to be treated the same way that we would want our family member treated if they were a patient.

Some companies are even going so far as calling themselves "patient advocates" in the field of clinical research. Although there are situations where a recruitment firm can advocate for patients and help them enter a clinical study, there are many situations where recruitment firms have to consider the desires of the sponsor over those of patients. Although recruitment companies can think of themselves as "patient advocates", another example shared by Adam will show that complex relationships between recruitment firms, patients and sponsors raise ethical questions and leave patients as the last ones to be considered:

> We were doing a spine surgery study, and it was for an implant that would help the patient avoid spinal fusion surgery. The randomized control group was spinal fusion surgery. This was an improvement over fusion, as there was nothing else on the market like it, so without this clinical trial most of these patients would have a fusion. It was a randomized study, and as fusion was the control group, the sponsor would not let us tell patients during our screening in the call center that it was a randomized study, and there was a chance patients could end up with fusion. They didn't want us to tell the patient that because they wanted as many patients as possible to be referred to the site, so the site could perhaps talk the

> patients into being in the study. We felt very strongly that this was not an ethical thing to do and just felt very strongly that we shouldn't do that. Initially, the sponsor forbade us from telling patients that, and then as time went on, we got some real negative reactions from patients about the whole thing, so then the sponsor eventually relented […]. And today, you know what patients will do, some, not all of them. Some patients will go home and they'll write on the internet. They'll write on a blog, or they'll write something online, and then it's out there. It's not a good idea to alienate patients in today's world.

One only can wonder how this recruitment approach was approved by an IRB in the first place. Although the recruitment company was advocating for disclosing information, the quote indicates that recruiters are dependent on the desires of sponsors. But this example also shows that patients have very little say or involvement in the decision making process on how the recruitment process is organized for them and what information is provided to them. When recruitment firms talk about patients as their stakeholders, they often mean providing good service to them—a convenient and pleasant recruitment process.

Providing good experience

The recruiters' perspective is that a negative experience during the recruitment process can hinder patient participation in clinical research. My interviewees perceived that providing a good experience and ensuring that the recruitment process is convenient to potential participants is central to their work. Some of my interviewees argued that they are in a service business, meaning that their obligation is to provide good service to sponsors and patients. The vice president of a recruitment firm explains:

> There are fewer and fewer patients who meet the inclusion/exclusion criteria. So every single patient is important because there is not an infinite amount of patients out there who will qualify for a study. Which means, when you do have a patient who raises their hand and says, "I would like to participate," we need to make sure that every single step of the process is maximized so that we don't lose that patient.

When I probed further about providing a good experience to callers, he talked about the importance of good experience in the recruitment process:

> But I think also not having a good experience with a call center, a patient direction center, and/or the site, and/or anyone that they speak to before they get to the site – whether it's viewing the website to get additional information, and/or seeing an advertisement or getting a patient-facing material, a flyer, brochure – can absolutely still have a negative impact on that patient's participation desire, and/or wanting to continue.

Not only managers in recruitment firms, but also nurses working in the call center and directly communicating with patients over the telephone think that they need to provide a good experience for patients. In the quote below a nurse explains how she goes about ensuring that patients feel comfortable about the screening process:

> We are the first person to speak with them [callers] about the study, and so we can do some education and hopefully engage them a little bit, so they want to look into it [participation in a clinical study] more. […] People are real hesitant to give out health information and, you know, their personal date of birth and address, and phone number, and all that stuff; and I get that, and because of that they don't want to go through the screening process and learn the information, so you can at least try to engage them in the beginning by just saying "this is what the study is about; would you be interested?"

According to my informants, they provide a better experience than research sites, because they are trying to organize a call center so patients can always easily access someone with whom to talk. In the firm I conducted participant observations, nurses called each individual at least five times on different days and at different times of the day until they reached a person. Everyone saw it as being helpful and forthcoming to patients. A nurse from a call center explains:

> Sites don't call patients much, but we call five times. If they [patients] call us and leave a message, we start again from the first attempt. You know that clinical coordinators don't have that time, and so they're calling a patient at a specific time. A person might not be there. And coordinators might not have time to call that patient again.

Nurses at the call center often talked about their experiences when dealing with frustrated patients. Callers could be upset because they did not qualify for a study, a coordinator from a research site has not called them, or they felt that they have been given incorrect information about a study. A call center director explains:

> Patients will get very frustrated if we don't process them quick enough, or they're not getting referred to the site fast enough. The only thing we can do at that point is just keep apologizing, keep them warm, and call them and let them know what's going on, and just leave them a message rather than waiting for them to call us when they're going to get frustrated.

A nurse talks about always trying to be nice and understanding towards callers to ensure that they have a good experience with the recruitment process:

> The hardest part is personalities over the phone. Sometimes patients can be kind of rude, you know, but a lot of the times you just have to bring yourself back in and remember. Number one, they're in pain. Number two, they're frustrated; they're facing challenges. So you have to be [understanding]. […]. They can push you too, it's just rude, but you still have to be nice.

As I showed in this section, recruitment firms are trying to provide a good service for patients and make the process as convenient as possible. Recruiters use this position to say that they are more patient-friendly in the field of clinical trials than, for instance, research clinics. Moreover, recruiters are afraid of patients' feedback, and they do not by any means want to jeopardize a study by a negative patient feedback on the process. Also, as I will discuss later in the chapter, a good connection between a recruitment firm and a caller is essential so that patients voluntarily agree to share their health information, which is so important to recruiters.

Up until now I have described the overall recruiters' attitudes toward interactions with patients from the recruiters' perspective. I will continue with the specifics of designing and carrying out a marketing campaign for a clinical trial.

"What should they think or feel?": designing a marketing campaign

A marketing department is responsible for creating advertisement campaigns for clinical research studies in order to attract patients. Every marketing campaign starts with a creative brief — a plan that guides the production of creative materials and addresses questions, such as "What needs to be accomplished with this campaign, how should the target audience react, what should they think or feel, and what type of mood is it

necessary to create?" I had an opportunity to obtain several creative briefs written by marketing employees from the same company where I conducted participant observations. Those were included in my data analysis, and I will discuss some parts in this section.

One of the creative briefs was written for a research study testing a medical device for lower back pain. The brief described the goals of this marketing program:

> It is important to build a strong awareness for alternatives to currently available treatments, and in particular, position investigational devices as a unique and viable potential therapy that has shown great promise in studies already conducted.

The excerpt above indicates that the clinical trial marketing campaign serves a larger purpose than just informing the public about available clinical research studies. It is intended not only to recruit patients for the study, but also to build awareness of the new investigational product eventually coming to the market. Moreover, the campaign is intended to create a trust and communicate to the public that it is worth considering and trying the new investigational product.

A creative brief also defines and establishes an intended tone that an advertisement campaign is going to produce. For example, in the brief mentioned above, the intended tone of the campaign was described as authoritative not authoritarian, compassionate and humane, solution oriented and fact-based. Later, when I interviewed the marketing department employee, Larisa, she explained:

> Authoritative means they are getting directed to the point, and it's that credibility thing again, that this particular company putting this out knows what they are

> doing, they have done their research, they have done their homework; so that's kind of the authoritative voice.

Rarely would the message in a clinical trial marketing campaign come across as cautionary. “Tone needs to be convincing and confident,” Larisa explained. Credibility is an overall concern of recruiters, and I will keep showing in this chapter how recruiters employ different techniques to enhance trustworthiness among all involved stakeholders, including the public. Moreover, with this strategy recruiters are trying to remove negative connotations associated with clinical research, and present investigational products as a legitimate and safe treatment option for those in need.

Clinical trial marketing campaigns are designed with consideration toward existing therapies and competing clinical trials. Consider the excerpt from the creative brief on competition:

> This is an extremely competitive environment. As such, the strategy will be to set the new device apart from currently available treatment, but also apart from the growing number of devices that are either in trial or coming onto the market. Age is the main factor in the development of this condition. As the majority of baby boomers move into the 50+ range, more diagnoses will be made. We need to position the new device as an innovative and promising motion-preserving therapy for this condition.

As can be seen from the quote above, advertisement of a clinical research study is already the beginning of an approved product’s marketing. Moreover, the visual appearance of materials is very important in order to ensure that patients recognize the study and the product. Another marketing department employee who I interviewed

commented: “We want patients to recognize the brand — associate this color and style with the device and study.” When designing marketing campaigns, recruitment companies have a very particular group in mind toward which the advertisement will be targeted.

The target audience

Another important aspect of designing a clinical trial marketing campaign is to define a target audience — a narrow group of people who a sponsor is interested in recruiting to a study. A creative brief defines the target audience for the campaign, and an advertisement will be directed to and designed to appeal to this narrow group of people. As it is noticeable from the example below, target patients are defined based on demographic characteristics, medical condition, and also by lifestyle and attitudes:

> The stated age range for potential patients is 40-80, but the most promising patient range will probably be closer to 55-75. All will have tried and failed with conservative treatment (non-surgical). These are people who feel a desperate need to find a solution — they are tired of the pain and more specifically, the lowered quality of life caused by this condition. While many may lead a sedentary to slightly active lifestyle, they likely regard themselves as people who still have something to contribute to society and who are far from ready to be spectators in their own lives. Most still work and or have families with whom they would like to participate in a variety of activities. A majority of these prospective subjects will be fairly savvy about their condition and looking for alternatives to current treatment.

Although an approved research study protocol may identify a target group based on age, gender and a medical condition, recruitment firms define their own core groups

according to the need of the marketing campaign. A marketing director explains the importance of a defined target group in her work:

> The trick is to reach the target population by ailment and to kind of try to figure out how to narrow that down to a core group. So some clinical studies will say that anyone 18 and older is eligible, okay? Well, from a marketing standpoint, that's a family reunion and then some. So what an 18-year-old is going to respond to is going to be completely different than what a 55-year-old is going to respond to. So what I do is help to narrow that down so we understand kind of our core group that we could most likely reach, and that's where we put the emphasis of our campaigns. And it's not to say that we won't reach people outside of that, but we can't afford to buy everybody and their brother, 18 and older, and we can only afford to buy a 25- to 44-year-old age group. And then you get a little outside of that.

I showed in this section that recruitment firms are defining the target group for marketing purposes, as they are interested in recruiting specific types of patients. However, recruiters are interested not only in patients who meet the defined criteria, in addition to inclusion and exclusion criteria defined in a research protocol, they are also looking for individuals who are interested in participating at all times. I will attend to this issue in the following section.

"Patients who are willing at all times"

In addition to the criteria described above, recruitment companies are interested in individuals who are willing to donate their time and body for a clinical study at any time. Recruitment companies intentionally direct their marketing efforts to people who desperately want to participate in the particular moment of their lives. Although

marketing campaigns are meant to build some awareness of existing studies, they are not designed to educate the public on research, and thus increase participation rates. Instead, the industry thinks about itself as an organization offering solutions to people who are seeking new options, because they cannot fix their health problems on their own. A director of a recruitment firm explains:

> And the recruitment messaging, I would say, is very geared to call to action from a particular patient population. That's where the money, if you will, from a sponsoring pharma and sponsoring entity really goes. When you start to talk about creating awareness; to increase the overall awareness in specific patient populations, you know, it's tough to get a measurement on the return of [investment] […]. There's not a whole lot of evidence out there. There are some individuals suggesting that investment in awareness building for patient populations can increase the level of calls to action in response to true messaging from recruitment campaigns. But there's no hard evidence that is in the public domain, that I know of, that really does support that. So I would say it mostly is directed to the patients who are willing and want to respond.

Mass media advertisement, such as television and radio ads, is a convenient way to reach patients who are willing to participate. A nurse working in a call center talks about the motivation of patients who respond to advertisements versus those who are selected from physicians' practices:

> Most of them have decided. Which, you know, that's the beauty of media. It's that they hear about the clinical study a lot more like, "Yes, I want to enroll in it," versus we've had studies where […] they do chart review at the clinic. And then you have to call them. And they're more likely to say, "I don't like it. I'm not interested." But the ones that call in [in response to mass media advertisement] are definitely into it.

Other informants also shared a similar perspective by saying that they are not trying to change patients' perceptions of clinical research or convince them to participate in clinical studies. Precisely because recruitment firms are seeking participants who are readily available to participate, they can claim that their goal through a marketing campaign is to present information, and at the end it is up to a patient to decide on participation. Adam explains:

> There's not much you can do, because you can't influence patients. You can't be dishonest with them. We have to give them honest information. We can't try to sell them or influence them to be in the study. All we can do is put the information out there, and then have them make a decision. And then it may mean that we have to find more candidates in order to end up with the number that will agree to be in the study. So yeah, there's not much we can do about that.

A nurse that recently started working in the call center at the time of our conversation shared her perspective on the role of "patients' willingness to participate in research" in the patient screening process. At the time of our interview, she experienced a shift in the way she saw patients who are considered for a study:

> In the beginning, you really are trying to overly help the patients. And you're almost — not pushing them into the study, but — encouraging them to be a part of the study until they feel a study is not a good match for them. And after some time, you really just start to look for the patients that are willing at all times to be a part of the study. I don't want to throw other nurses under the bus at all, but I think people that have worked at the call center longer are just like, "Okay, if you're not willing, then sorry, this will be the end of the screening process for you".

To maintain patients' initial willingness to participate in a particular study, recruitment companies are forced to work quickly with patients. Among industry employees, it is accepted that patients need to be contacted by a research clinic within 48 hours of the moment a person has been screened and told that she or he qualifies for a site visit. In the words of my interviewees: "patients need to be processed quickly." Otherwise patients lose interest or find other treatment options or different clinical studies to participate in. Anna talks about the issues associated with maintaining patient interest:

> I think people are changing generationally, their behavior is changing, and people now are seeking instant gratification on everything, like instant information. Part of the things that we talk about is that people don't like not knowing what they're on, and so clinical trials in general may have to change in order to deal with the changes of human behavior and expectations.

Although mass media advertisement is a widely used and a convenient way to recruit willing patients for clinical studies, the approach is expensive. A lot of companies are building large patient databases which are mined for particular studies to select individuals who match some inclusion and exclusion criteria. This approach entirely changes the dynamics of interactions between patients and recruiters, but it is a cheap solution compared to mass media advertisement.

"Expanding the pool by non-proactive patients": patient databases

Some of the companies prefer using patient databases to recruiting participants, because it is a significantly cheaper option. The organization of the recruitment process is similar to what was described earlier, except that an individual agrees to receive information about clinical studies, and when there is a matching study conducted in her geographical area, a patient receives a letter of invitation to participate as well as study advertisement materials that state a phone number that she can call to receive more information and to get screened for a study. For some of the companies building patient databases, maintaining them and selling data is actually a profitable business. Companies like Target and Wal-Mart are selling patient data from pharmacy claims data. Some other companies have collected patient information themselves. For example, a recruitment company called Acurian is focused on recruiting patients through direct mailings.

In order to build its patient database, in 2009 Acurian launched a Facebook and MySpace application called "Click it forward"[2]. The application was designed to promote clinical trial awareness by appealing to users' altruism. The idea was quite simple: first individuals had to register and install the free "Click it forward" application on their Facebook or MySpace page from the Acurian webpage. When registering, individuals needed to pick one of the twenty medical causes they would like to support. After that, they just needed to invite their online friends to join and install this application on their profile. If their friends and acquaintances accepted the invitation, the company made a

[2] https://ols14.acuriantrials.com/jsp/facebook/getinvolved.html

contribution to the cause one originally selected. The more friends an individual engaged, the more money Acurian donated to the medical cause.

The company's generosity had limits — Acurian stated on its website that it will contribute no more than $50,000 per year. Acurian already owns a database with more than 50 million individuals (Pharma Live blog, 2009). This application became part of peoples' social media profiles, and therefore Acurian could send all of them the latest clinical research opportunities in a specific area, or one could register and become part of their databases. This is just one example of how recruitment companies are building their own databases.

The dynamics of recruitment through direct mailing are different compared to mass media advertisement. First, all participants whose names are in the database might not be motivated to participate. Sometimes they might not even be aware of how their name got into the database. On the other hand, the target group is much more likely to qualify for a study because individuals are targeted based on their condition and known medications.

A managing director from a company that recruits patients through pharmacy claims data explains the different dynamics:

> Even if a patient is very interested and proactive, they still may not be a good fit. I think there's a bunch of statistics out there; around only 5 percent of patients participate in studies. There are all these surveys that everybody wants to know about, and clinical research they want to participate in, and they would if they knew about it. And so we are kind of providing that option that says, "Here, now we're telling you about the opportunity, and you appear to be the right person to

tell, and all you have to do is answer some questions. We don't ask you to go fill about of surveys or questionnaires or go online, but we will come to you."

Databases are queried according to inclusion and exclusion criteria for a clinical study, and then a letter is sent to all identified patients inviting them to call a call center to find out more about a particular research study. My informants explained that usually the response rate to mailed letters is quite low, so it means that a large number of letters need to be mailed out. In order to optimize a mailing process, Acurian even has come up with a doctor brand — Dr. Haines brand. In this case, all letters sent to potential participants regardless of who is principal investigator are signed by the same doctor — Dr. Haines. Dr. Haines is a physician in Philadelphia and apparently has rented his name to the recruitment firm. It seems that this helps to ease up the logistics of sending out large number of letters, but also it means that patients do not know the research site, so they are forced to call a centralized call center to get screened, and where they need to share their health information. In this way, the recruitment firm can keep track of patients screened and can get paid per patient enrolled.

Promoting the benefits of participation

When targeting individuals of interest, recruitment campaigns also inform everyone on the benefits of participating. Perceived benefits can include free health care, or free treatment. In addition to showing a benefit, the goal when communicating through advertisement is to catch someone's attention in the sea of information targeted toward different individuals. Larisa explains:

> They [a sponsor] did a photo shoot of the device actually strapped around the legs so that people could see, and then a photo that showed the movement of the foot so that you could see that it is helping lift the leg up; and when we created the advertisement, we just added a headline: "Have you had a stroke, do you have difficulty walking?" Because we had those photos, we could have such a bold straightforward headline. When the ad is in a newspaper, you are catching someone's attention for just a short period of time […] because think about a newspaper, there is so much text in it.

According to my informants, studies that do not offer any benefits to participants (i.e. research studies with a placebo arm) are very hard and expensive (as a larger number of individuals need to be screened in order to find interested and qualified participants) to recruit. Anna talks about studies that involve a placebo arm:

> They [participants] may go through this [research procedures] and have all tests done to them; come in a clinic for visits weekly or whatever the schedule is. It is a burden to travel to that place and to have to undergo all those things, and then nothing happens for them. There's nothing in it for them at all, and when we have a placebo arm, that's an automatic challenge there [for recruitment].

Recruitment companies are well aware that people participate in research because of a lack of better options. One of my informants even said that the economic downturn has played out in favor of her recruitment firm. However, she feels that this situation is a great opportunity to improve the image of clinical research by providing a good experience for middle class people who might not have health insurance. A vice president of a recruitment firm explains the reasons why people choose to participate in clinical trials:

> […] for example, if they have diabetes, they know that they have diabetes because they've been diagnosed. They're seeing a primary care physician or an endocrinologist. They don't have the need to be under consideration for free study examinations and/or medication. This is often the reason why people who are of a lower socioeconomic consideration would have the desire to participate — because they don't have health insurance.

Another form of benefit that recruitment firms are promoting is offering compassionate treatment to suffering patients. Not only call center employees need to express compassion in their conversations with patients, but this notion also needs to be incorporated into an advertisement in order to attract participants. Larisa is explaining the importance of compassion in the advertisement:

> […] the compassionate [voice in an advertisement] is — whoever is conducting this trial - the audience wants to know that they understand what they are going through, whether it was Alzheimer's or stress urinary incontinence or COPD, the audience wants to know that whoever is doing that trial has done their homework again, and that they understand what patients are feeling. For example, through the language, you need to hit on disease symptoms like we tried to do in our urinary incontinence studies […]. Or sometimes we have included things as "not being able to pick up your grandchild." That's the compassionate part. Because then the audience is saying: "They get me, they understand me."

A third aspect that recruiters are trying to promote in advertisement is hope for an improvement in a patient's medical condition. Larisa explained that they used a focus on hope for quality of life in a clinical trial advertisement:

> A client wanted to focus on hope for an active life for [patients], to try to show that when you have back pain most people are sitting around, they are lying in bed; it hurts, it hurts to move, and it hurts to stand. The client wanted to focus on quality of life. You know that after [using the investigational device], they can still do their everyday activities. It could help them; if they are gardener, they bend over and it doesn't hurt; they are bike rider, they can still do that.

When I continued to probe her answer on the role of hope in the recruitment process, she explained:

> We are trying to create hope; we are trying to create the image that this could change their life. You know, it may not change their life, so we are trying to, through the imagery, show that because we can't say that. We can only say 'may,' or 'its possible'.

When I discussed a similar issue with Anna, she shared her doubts of promoting the benefits of clinical trials through an advertisement:

> Like we talked about before, not every study succeeds. We worked on a couple of cardiovascular studies, and I saw on the news a few years ago that the drug was killed; it didn't work. I also worked on a study where the thought was that the drug would slow the disease progression of Alzheimer's. Nobody knew. The research showed otherwise, and I think back to the materials that I wrote and what I said and if I convinced someone in those materials to get into the study, and now it's negatively impacted their life; and that made me feel horrible. I still feel awful about it, but when I look at the materials there's nothing unethical in them, and that's why we have regulations that say you can't promise anything; and those materials were written to say you may not get better, you may get worse, you may have no benefit, the thought is that this drug might help, but it's not been proven.

In this quote, she touches on an interesting point — on one hand she feels uneasy about advertising studies that eventually showed that particular investigational products failed, on the other hand she points out that her written material was acceptable according to ethical guidelines. However, as I showed in this section, recruiters use different, often inexplicit techniques to promote clinical trials. Despite the uncertainty of an investigational product's effects, it would be naïve to expect that it is ever possible to promote clinical trials in a neutral way without highlighting the benefits of participation.

"Education leads to better compliance": communicating requirements for compliance

Sharing information on a study

A lot of information that is shared by recruitment companies is framed to enhance compliance. From the early contact, patients receive information on the importance of staying in a study until the end. Usually the advertisement, in any medium, is very short and contains only very basic information. Websites are used as relatively cheap venues to share more in-depth information about a recruiting study. A call center director explains:

> People seem to have a preconceived idea of what they have or what they think that study is. And you can only give so much information over the phone. We can't deviate. We can't go into too many specifics or details. So when you're talking about educating a patient, the important piece is to do as much of that on the website as you can.

Another informant, a program manager, explains the role of information presented on websites:

> The website may have the information on the product; it may have information on previous studies if a sponsor has information on the study and enough of information on the time burden and the risks and relevant possible benefits to participants. We're trying to get patients enough information so they feel comfortable to be willing to start answering questions.

After further probing on the importance of education, the same informant explained the connection between patient education and compliance:

> Again, better education leads to better compliance and better retention; and understanding of the patient who's willing enough to go through the informed consent process and have an understanding of what their responsibility is, and what their accountabilities are for the amount of time, and driving distance and etcetera. So, the better the education, the better the outcomes for patients in general and the ability to go ahead and retain them all the way through.

Cultivating commitment

Informing patients on their commitment to a research study can happen at two points in the recruitment process — either at the call center or patient information meeting. In my research, I had an opportunity to participate in one of the informational meetings organized by a recruitment company. An informational meeting is a seminar where a principal investigator provides information stated in the clinical study's informed consent form to potential research participants, usually those who have met the initial inclusion and exclusion criteria stated in a research protocol. Organizers explained that these informational meetings serve several purposes — 1) they save time because principal investigators can present all the information at once to all the candidates, 2) they provide an opportunity for participants to ask questions and hear what other

individuals think about participation, 3) a meeting is an opportunity for potential candidates to meet with a principal investigator and a coordinator, 4) they help to test patients' compliance based on their attendance, 5) organizers believe that participants who attend these meetings and see that there are many other interested individuals, become competitive and thus, are more prone to enroll in a study.

Although the information presented in these meetings is based on an informed consent form, they are not meant to replace the informed consent visit, where participants sign the form and confirm that they are agreeing to participate in a study. But these meetings help to reduce the time spent at these visits providing basic information on a study. The meeting is mandatory — in addition to other qualification criteria, patients must attend a meeting like this if it is part of a recruitment program. Only patients who attend it will be referred to a research clinic for further screening.

This particular meeting that I attended was for a weight loss device study. The presentation was given by a principal investigator of the research site. During the presentation, he was very explicit that he is presenting a research study and that there is a lot that is unknown about the investigational device. In addition, he made it very clear that he was looking only for those patients that were able to commit for the entire study. The quote below is an excerpt from my field notes that I captured from what he said at one of these meetings:

> The study was very carefully designed, and although we cannot guarantee improvement for everyone, we can provide an important clinical trial. Every participant is very valuable to the company [the sponsor] and society — results of the trial will help society at large. And if you quit in the middle of the study, you

> will undermine the hard work of other participants. If you can commit, come to the study; if you cannot come to visits and participate in the program, please do not join. If you are not doing a good job of participating, you are going to undermine everyone's effort. The data won't be of high quality, we will not be able to publish in respectable journals, and the impact will be less.

The organizer of these meetings explained that it is very important that patients trust and like the principal investigator; in her experience patients are more likely to sign up for a study if they have a good experience at such meetings.

Similarly to these meetings, during the phone screening, the only information nurses share with callers about a study, besides a simple description of an investigational product, are the duties expected from a participant. The script is IRB approved information that nurses must use in the call center when talking to callers. This quote is an excerpt from a phone screen script; this is what nurses are supposed to say to a caller after he or she has answered all the questions and pre-qualified for a study:

> There are 3 steps in this clinical research study. Step 1 is where you will meet with the site personnel, ask questions, and continue the screening process. All patients who meet the eligibility criteria will have the opportunity to review and sign the consent form, and enroll in this clinical research study. Upon enrollment into the research study, you will begin Step 2, where you will be scheduled for the surgical procedure to have [the device] implanted. Once the device has been implanted, the physician will perform conversion testing and device evaluation, and complete post-implant x-rays and post-surgical monitoring. You will continue to be monitored until discharge. Prior to discharge, testing and evaluations will be completed, along with x-rays to evaluate the device placement. Step 3 consists of the follow-up schedule. You will have follow-up visits scheduled at 30 (1 mo), 90 (3 mo), and 180 (6 mo) days from the date of your implant procedure and then

> visits twice a year, until the device is removed or the study closes. Once the research study has closed, you will continue to be followed, at the research site, according to the standard of care for [this type of device].

After the nurse has read all of this to a caller, she asks: "Are you willing and able to comply with the requirements for this clinical research study?" If the patient says they are, her or his information is transferred to a research site. If the answer is no, the person is disqualified.

As I tried to show in this section, recruiters are promoting compliance at different stages of a recruitment process to ensure that only the most committed individuals participate in studies. Up until now, I have focused on information that is directed to patients so they are aware of clinical studies and the commitment it requires from them. In the following section, I will focus on the interactions that take place in the call center where a nurse is aiming to collect patient health information.

Screening patients over the phone

Caring in exchange for information

It is common to hire nurses in a call center because it is perceived that one needs to have some medical training and understanding in order to screen patients over the phone. Nurses' image as carers creates some misunderstanding about their role in the call center, among nurses themselves and among patients who call to be screened. Recruiters actually use this confused role to connect with patients and gather their health information, which is crucial for their work. A nurse explains:

> And being a nurse and knowing, being taught all those things in school about compassion and caring, it just kind of all accumulates together to help make the recruitment process the most enjoyable thing for the patient, as well as keep them interested and joining in the study. Because if you just ignore their issues and just move onto the next question and not say, "Oh, I'm so sorry that happened to you"; if you don't make some kind of compassionate comment, then they're not going to want to tell you anything.

Although nurses have to follow specific IRB approved scripts, and their main role is to collect health information from patients, they still view themselves as helping patients:

> I think a lot of times, you look at it [callers information] once, you say their name at the beginning, but then you don't - you just look at them as a number, you tend to look at them as a number instead of who they are. They're a person; they need help. My role is providing the best care I can for the patient. I mean I know that sounds kind of corny because you're working in a call center, and you're just talking to people over the phone, but a lot of people haven't, they don't talk to other people [medical personnel]. […] And so it is important to just be able to be considerate about that and be compassionate about their problems while still trying to stay on script.

On some occasions, nurses in the call center can practically help patients, especially if this is related to the particular study. A nurse that has been working in the center for several years explains that she sees her role as patient advocate for their participation in a clinical trial:

> I'm an advocate for them. Like patients are calling and [complaining that] this doctor is not the nicest person; and I'll go and report that to the program manager,

> or site services, let them know. Or if like I said, patients are calling in and haven't heard from the site, I take a look in our system and then I see they've been disqualified. And I'll go to the site services and a program manager and work around, like this site has not been calling patients. So I feel like I advocate for them. We talked earlier about being there to listen to people, or giving people some kind of hope […], like the people that get implanted with these devices. Knowing that they would never get it at the hospital because it's not an approved, procedure, device, treatment plan or treatment option; knowing that you can influence somebody's life that way is really great.

Here a nurse touches on the confusing role of a nurse and a phone screener — she might be willing to listen and provide help, but her main duty is to gather health information in order to decide if the patient is qualified or not:

> At the same time, you're working on a time schedule. I mean, everyone's supposed to be done in a certain amount of time; screened in a certain amount of time. It should take about 15 minutes, but I let the patients talk through their problems without trying to interrupt them as much as possible, but still trying to direct them back to the questions. I think that's a big key to being a successful call nurse or personal representative of the company, as you have to be caring and listening, as well as try to redirect them back on track.

The role of nurses in the call center may cause a misunderstanding from patients' perspective when they are seeking medical advice. Another nurse:

> A lot of times I'll just redirect them if they need to speak with their physician. A lot of people are looking for somebody just to talk to, but to keep my nursing license you really can't give medical advice. And a lot of people can't afford to go to the doctor, so if they can ask a question they will. But if somebody asks me what osteoarthritis is or what something is, yes I can tell them, but not if they're looking for medical advice — and what I hear a lot is — "am I the candidate for

this study?" And I just have to tell them that I am not able to determine – "I can't determine that over the phone. A doctor has to assess you."

Nurses can help navigate a particular clinical trial that their company is recruiting for, but they are in no position to provide assistance to those who are seeking advice for their health. A call center director talks about the fine line between collecting information for the purposes of a study and giving medical advice to someone:

> So say somebody calls in and they're like, "Can you explain what osteoarthritis is? Because I know I've got arthritis, but I don't… I mean there's osteo, there's rheumatoid, there's a lot of different joint ailments." So if the nurses just start going through and say, "It sounds like from what you're telling me, you have osteoarthritis." It's a diagnosis over the phone. You can't do that. And it's just because they want to be helpful. But you can't do that. You can say osteoarthritis is this. Rheumatoid arthritis is this. And you can say have you been diagnosed with, but you if someone says, "Well I'm not sure which category do you think I fall into…", you can't say, "Well it sounds like you might have this…"

A nurse speaks about the difficulty of maintaining both roles in the call center; caring for patients and gathering the necessary health information for evaluation:

> And yes, you need someone [listening] to what's going on [in patients' lives], but sometimes you just feel like an automated voice. Which, I mean, I probably knew before coming in that yes it's going to be scripted, but it's just one of those things that you don't even realize until you really start working with it; how difficult it is to remain on script, and try to keep these patients plodding along when they could have major disasters going on in their lives.

Although nurses may see themselves as caring and helping patients, a call center director has a different perspective:

> You have to follow the good clinical practice, and you have to follow HIPAA regulations. But the other thing we have to remind ourselves is that we're not a clinic. They're technically not patients when they come through the call center. They're candidates. When they're referred and they're signed on, then they're a patient. But if we treat them like a patient then we're more of a clinical medical type organization, but we're just an extension of that, and that's what I try to get the call center staff to understand. It's protected data, its protected information, but the information they're giving us is not creating a medical history like a medical chart would. Nurses are […] used to a clinical environment. They've been trained that patients are patients. So when I first started here they had a registered nurse that did what I do. And the whole thing [the call center] was treated more like a clinical type of an organization. And when you do that it locks you into more stringent than necessary guidelines. Where for me, I'm more about let's follow the protocol. It's an IRB approved script, but it's not a medical record.

An individual from another company also explains the difference between a recruitment firm and a medical organization. He very clearly positions his company as a vendor that provides services and tools for medical organizations to enhance the recruitment process; thus they are not assuming any responsibility for participants' health issues:

> So we're really not there at the site, and we're not a monitoring organization or a medical organization. We can provide the tools, we can provide the technology to help facilitate getting patients through that screening process, but we're not really handholding the sites to do that. We have the technology to track, to provide the

> training, to provide the tools, and hopefully the sites will do what they need to do to input data and to utilize the tools. It's really on their shoulders to do that.

As I explained in this section, recruitment companies are in an ambivalent position. Managers of recruitment companies very clearly position themselves as vendors that provide tools to clinicians. When they do not view patient recruitment as a medical endeavor, they have less responsibility toward patients and their health related issues. However, on the other hand, recruitment firms employ nurses — medical professionals who tend to view the recruitment process and interactions with callers from a health care provider's perspective. Both perspectives on patient recruitment are in conflict with each other and raise some issues. Moreover, recruiters use the concept of caring to attract patients, and connect with them in order to gather their health information. In the following section, I will explain how nurses go about evaluating information that is provided by a caller.

Nursing judgment

On the surface it appears that it should be pretty straightforward to screen patients based on inclusion and exclusion criteria that are stated in a research protocol. However, criteria cannot always be interpreted unambiguously. In addition, patients might not know their diagnosis in medical terms. My interviewees' nurses that work in the call center used a term "nursing judgment" to describe their decision-making process when evaluating patients. As I will describe in this section, it involved deviating from an approved script and critically evaluating patients' answers in order to evaluate if he or she qualified for a study. Due to the complexity of medical information and patient subjective

understandings of their conditions, it often might be complicated to collect the necessary information. The call center manager speaks about the difficulty of collecting medical information from callers: “A lot of patients understand their diagnosis, or they understand their ailments but they medically do not understand where they’re going to fall within that category or that criterion that they have to meet.”

Moreover, not all information can be collected over a telephone conversation. For example, one cannot objectively evaluate body weight or blood pressure. In other instances, patients might not know their specific diagnosis, and in cases where it is judged that callers might not be able to answer a question, it might not be included in a script. On occasions when this information is crucial to determine if a caller qualifies for a study, it is a serious disadvantage for the recruitment process. An interviewee explains:

> If you have a question that is for a cancer patient, for instance, ”Are you currently receiving chemotherapy?” There are different types of chemotherapy. And sometimes patients may only understand that they are on chemo. They don’t know the type of chemo that they might be on. So we don’t want a patient to guess and disqualify someone. So we’ll use that question more as a data gather, or we’ll leave it out of the screening completely.

In the company where I conducted participant observations, telephone scripts were developed by a manager who did not have any medical training. Nurses who were actually using it in day-to-day patient screening did not always find it easy to use. They often went beyond scripted questions in order to select the necessary information. A nurse explains how she goes about soliciting necessary information from a caller:

> Sometimes you'll just have to ask a more complex question. Just like, for an example, if you ask the question for our knee study, "Do you have osteoarthritis?" well, a lot of people don't really know what that means so it's just giving them in layman's terms what that is, or asking how their doctor explained it, knowing what kind of condition this is; another way of asking the question. Instead of just following the script and checking the boxes, you have to be able to understand what the question's about.

Another nurse from the call center shares how her nursing knowledge of a disease helps to understand what patients are saying and to decide if a caller is a fitting candidate for a study:

> For example, for the knee study that we're doing right now, I ask a caller, "Do you have this kind of [medical condition]? Have you had this kind of surgical procedure or have you been diagnosed with osteoarthritis?" And they say, "I had a procedure, but I'm not sure, it's worthy, you know, they went and scraped off some cartilage." And as a nurse, I know right away that a caller is talking about an arthroscopic surgery. So it helps, because a lot of patients use layman's terms.

Another nurse similarly explains that she is using her nursing background to critically evaluate each patient's answers, but in the quote below, she also points out the apparent subjectivity of screening questions:

> In the script and the protocol, it says you have to have one knee that is injured and the other one has to be fully stable and healthy, and some patients say that their other knee is not fully functional because your body compensates; if you have an injured knee, your right knee is injured for 10 years, your left knee is going to be affected because it's been used more. And so I guess if you were to just ask, like today for example, I spoke with the patient on the phone and I asked him, "Now, is your other knee healthy, fully functional?" and he said, "No" but it was, you

know, a subjective question because he - his knee was fine. He'd never had any damage to it.

Medical professionals like nurses can have a more holistic understanding of a disease process, and in some situations their decisions when screening patients can be in conflict with those above them in the company who might not have a medical background. Another nurse that left her job in the call center shortly after I completed my fieldwork experienced conflicts with her manager regarding some patients — whether they should be considered as qualified or not. She told me that in those situations she usually sought someone else's advice within the company:

> My boss isn't medically trained so she doesn't understand the whole nursing process and the disease process, and she knows the protocol standards, which you can read on paper, but if you don't understand it — the process — then it's a whole other story so I guess it's kind of a fine balance, when it comes to who you accept or who you push through.

Although it appears to be the right thing to do, to use one's medical background and deviate from an approved screening script to evaluate patients' answers more closely, I observed that nurses have very subjective understandings on when it is appropriate to change the script and when it is not.

Following the script when convenient

As some of the quotes indicated above, nurses feel that it is alright to go off the IRB approved script when it is necessary to gather information from patients in order to make a decision if they would qualify for a study or not. But there were particular

situations where nurses judged it as unacceptable to deviate from the approved text. In this quote, a nurse expresses her concern over rigorously following the script:

> You saw that we have the scripts that we follow […], but it's much more important than just the script. So, you know, you can't go by the script all the time. So there are situations that don't apply and, you just have to use your nursing judgment and sometimes do a little research, you know, because we do studies from drug studies to device studies, and so there's a lot of things that we don't know of, so we need to figure it out, do some research on it.

It was considered acceptable to deviate from an approved script when they needed to collect or gather patient provided information, but in the cases when it was necessary to disclose information to callers that recruiters felt might jeopardize the recruitment process, it was considered wrong to deviate from the text:

> But the financial part is the hardest, for me, only because I know, […] a lot of patients are coming because they don't have any insurance. And so, even when they ask, "Am I going to be reimbursed for the study?" and knowing very well that probably they won't be reimbursed, you're like, "Oh, that's a good question for the site." Because it's not in the script, and I'd like to tell them, that I wish we could be more open to stuff like that.

In this section, I presented the issues associated with following the IRB approved script in the call center. As I showed, nurses have a specific decision making process based on the needs of recruiters whether it is appropriate or not to deviate from the approved script when talking to patients. These findings are closely related to the next category — controlling information. There are several types of information that nurses

are more reluctant to disclose to callers, because it might put the quality of referred patients at risk.

Controlling information

Recruitment companies are trying to be very forthcoming when explaining the patient commitment towards a clinical trial. However, there are certain things that they are not sharing with patients or are trying to avoid talking about. In this category I will discuss a recruitment firm's tendency to control the information it is disclosing to patients. The category includes the following three subcategories: "we know more than we tell", "sharing information online", "we do not want them thinking about other treatment methods."

"We know more than we tell."

As I mentioned above, telephone scripts are approved by the IRB and are designed in a way that helps to eliminate unqualified callers as quickly as possible. As a result, the information that nurses share with patients is limited. Although my informants from the call center said that they can spend as much time with a caller as they need, they are encouraged to complete calls quickly. In addition, employees at the call center are trying to "protect the integrity of the study." Some patients are so desperate to enroll in a study that when they do not qualify in the first attempt, they try to call back and change their answers in order to qualify for a study. Employees of a recruitment company believe that they can minimize this risk, if they do not disclose the reasons for disqualification directly to a caller. A nurse explains:

> One challenge that can present itself is patients wanting to be in a study and trying to falsify their medical condition so that they can pass the inclusion and exclusion criteria. We've seen a fair amount of that. One of the ways that we see that is a patient will call in, and as our nurse is screening them over the telephone, if the patient screen fails, we don't tell them why they failed. They'll call back, maybe from a different phone number, they'll use a different name, and they'll try to answer the questions differently so that they can be pre-qualified and referred to the site for the study.

This situation of not disclosing reasons for disqualification is somewhat ridiculous because information on inclusion and exclusion criteria for all clinical trials is publicly available in the website www.clinicaltrials.gov, maintained by the National Institute of Health and National Library of Medicine. One of the nurses that had been working in the call center for a short period of time at the time of the interview shared her frustration:

> For me those basic questions are hard, because they can be found on the [study] website. They [callers] can see on the website, but you can't tell them that, but you can send them to the website so they can find out for themselves. On www.clinicaltrials.gov, all the disqualifier information is available. And it's like do I tell the patients, "Hey if you want to know more about this study, go to clinicaltrials.gov, and you can learn more about this study." I mean, I'm not going to tell them — if you want to know the reason you're disqualified, this information's public. But it's true; I mean all this information is out there for them to discover. I'm just not allowed to say, "Go to this website. You'll find out why you're disqualified." I just have to say, "To protect the integrity of this study I can't provide that information."

A different nurse speaks about her feeling of being torn in situations where she is not allowed to disclose certain information to a caller:

> Like just basic questions about the study, […], "How do they implant it?" And you really can't say that […]; you'll direct them to the website, and they say, "Well it's not on the website." All I can respond is "Well, you're going to have to wait until you go to the study site before you get that information." And often they're upset because you can't provide them that information. So it becomes a challenge as far as what you can say and what you can't say. When you have all this wealth of knowledge and you're not allowed to say it, it becomes hard because you have to keep your mouth shut.

In the same manner, recruiters did not share risks associated with participation and side effects of an investigational product. In order for a patient to learn this information, they should attend a site visit and talk to a research staff. A call center director explained this trend by saying that the company does not operate like a clinic and thus call center employees are not well equipped to share details or risks of a given study. According to her, it seems that one needs to be specifically trained to share this information:

> If somebody asks a question [about risks or side effects], we refer them to the website or we'll say, "That's a really good question. If you get referred you'll need to talk to the study site because we're not equipped to handle [this information]." Again, you don't want to say one thing because sometimes people will hear something else and get the wrong impression. So we don't go down that road.

This is another contradictory point in the communication process with patients. On one hand, nurses are well equipped to screen patients and collect medical information, but on the other hand they are not well suited to share the risks associated with participation. The nurse explains her perspective on not disclosing study risks for callers:

> Well, because I kind of think of it as its out of my nursing scope, so that's really the doctor's job to describe and educate about the risks. And I'll be honest, we're not really trained on these programs like we are used to, so a lot of times I don't even know the risks and I don't know the results, so in my tiny little scope that we're allowed to work in, most recently, it is just education and gathering information.

When I participated in the informational meeting about the weight loss research study described earlier, the principal investigator indeed disclosed all information from the informed consent form, including side effects. However, in his discourse he was dismissive regarding the seriousness of side effects. Consider an excerpt from my field notes: "A woman in the room asks how much she needs to be concerned about side effects. To which the doctor replies: "Can they happen — yes. Have I seen any — no." And in this fashion he names all side effects on the list and dismisses the likelihood of those. However, when the same woman further asks how many of these surgeries he has performed, he replies: "About 20.""

The principal investigator is a well-accomplished surgeon, he is confident about himself and he really believes in this new treatment, so why would not you believe him? In fact, he is competing for patients with other 199 weight loss studies that were listed in the clinicaltrials.gov registry around the same time in October of 2011. And in fact the principal investigator might be right about the side effects, but as he asserted so many times in this meeting — this is a research study — no one can be sure about anything. And it is important to note that based on heard and perceived information in the meeting, patients make the decision whether to participate or not in this study.

Studies that involve one arm of the standard of care treatment usually require health insurance or out of pocket payments from a patient, because the sponsor is willing to pay only for experimental treatments. To increase the flow of patients to research clinics, sponsors can choose to not explicitly disclose to patients that there might be costs associated with participation in a clinical trial. A person working in a marketing department explains a reason for not disclosing some information:

> We try to not shout out about the Medicare, Medicaid, or insurance or things like that, because the potential of getting a patient to do a study is low, if they were to focus on the insurance aspect of it. It may deter patients from wanting to do it or deter them from calling. However, if you don't focus on that [do not disclose that patients need health insurance], patients still may call, and they may find another way to do it. You know, even some insurance covers, some doesn't.

A nurse talks about a similar situation that she experienced as dishonest, where a sponsor, for the first half of a recruitment process, did not allow disclosing to callers that there is a payment associated with participation. The decision was made out of fear that a lot of patients would not be interested in a study:

> Now some of the scripting has on it: "You may be billed; you or your insurance may be billed for portions of the procedure costs," which is really nice. But some of the sites still haven't had the IRB approval for that part of the scripting, so you're not allowed to say it unless a patient asks. I feel weird because I think a patient should know that even if they don't ask, and I don't think it should be – "I'm going to the study site and finding that information out" because that's a big deal breaker for a lot of people is if they have to pay any money out-of-pocket for this study, for a lot of them it's no go. A lot - most people - think that clinical studies are all paid for, which obviously is a misconception. They don't think that

> they should have any charge to themselves, so I think they come in believing that the study's all paid for and […] they don't ask that question […]. But I think I'd be upset as a patient having to go to the site and finding out "oh I have to pay $1,000 out-of-pocket to have an MRI done because I don't have insurance."

However, there are situations when the patient recruitment firm is not willing to disclose information about health insurance as well, because they are not willing to answer patients' questions that might come up about health insurance and billing. The program manager's quote below is an excerpt from field notes in one of the meetings at the company:

> A client wants us to include information about insurance in the screening script. I do not think it's a good idea. It will only generate questions from patients. We will leave it as it is, that nurses and call center representatives will keep saying what they are saying right now, and if patients ask about cost or insurance they will be referred to the sites. The information about insurance would add only minutes.

As a result, nurses have developed a system of how they decide what kind of information is appropriate to disclose. It is similar to how they choose to follow the script or not. As a quote shows below, these decisions are guided by understanding of what is best for the company. Another nurse who has worked in a call center for at least two years explains:

> It is unethical for me to, like if I know […]. I'll just say what I'm told because once I start reading too much into it, it will be lying […]. I just go ahead and say that I do not know, because it is really not my place to tell them. And patients really don't need to know that. Unless, they're disqualified. Patients will call, for example, then ask, "I'm disqualified; why?" And its right then I'll tell them the

> truth, […] — I do not know. And if it's at the site level — I'll tell them. […] "This is what the site said — you are disqualified." And a lot of times they [coordinators] do that just by looking at the answers that they've [callers] given, and then disqualify patients without even calling them. Those patients are at home sitting and waiting to hear from the site, and so they end up calling us back again. So in situations like that, I will tell the patient because that is my job. But when it comes to the little stuff as to why they haven't heard from the site; sometimes it's because they are not even IRB approved. So, I just make that nursing judgment — what's right for me as a nurse to be telling the patient. Other stuff, I just don't get into.

As she indicates in this quote, it can be unfair to callers, when all the information is not shared. The limited information shared when patients are screened is a result of optimization and cost reduction at the call center. A nurse explains how the situation has changed over the years:

> We used to have in-depth training on the study before we screened callers. Companies would come in and train us. Then we would do more detailed screening, but then they realized that it is more effective to do study informational meetings and then a principal investigator sells the study than to do it through the phone, going over all the information with each individual patient.

Another type of information that is carefully guarded by recruitment firms is a name and location of the research sites involved in a study — so recruitment firms can take credit for recruited patients and also protect sites from being overwhelmed by callers. Even if patients ask at the beginning of a call where is the closest clinic, they receive a response that they will be given this information when they qualify. Centrally sent letters with a Dr. Haines brand have the same issue. Patients receiving a letter informing them on where a study is, do not have any information about the clinic or the

doctor.

To summarize, in this section I presented issues associated with transparency and disclosing information to patients. Nurses often experienced discomfort when they knew more information than they were allowed to disclose to callers. I described three occasions when information is guarded — to protect the integrity of a study, location of a site, and disclosing information that would prevent patients from being initially interested in a study — the risks and financial costs associated with participation. All these activities are performed to ensure that only the most qualified and committed individuals are referred to research sites. In the following section I will talk about a similar issue, but will focus on the willingness to control information online — using social media in patient recruitment.

Sharing information online

Among industry members, there is a lot of excitement and discussion about using social media in patient recruitment. This method significantly reduces outreach costs compared to advertising on television and radio. In addition, it gives researchers an opportunity to reach a younger generation of patients who might not use traditional media such as TV or radio.

The opinions expressed in industry articles, blogs, conferences, and from my informants range from enthusiastic that social media will solve all recruitment problems to more cautious view points that social media is just another venue to advertise.

Many of my informants expressed reluctance to use it, because they are concerned that patients are going to share negative experiences about participation. During my

observations, a recruitment firm was developing a new marketing campaign, and creating an online campaign was decided against based on the concern that patients might share negative experiences or complain about something, and that it could possibly ruin the whole campaign.

Another concern is about patients disclosing medical information and potentially unblinding a study. Anecdotal evidence indicates that sometimes the situation can go as far as asking participants to sign a form that prohibits sharing information in social media on a particular study.

Recruitment companies are trying to control the information online to ensure that negative information about them does not appear on the web. Some of them maintain online blogs where they write about news and trends in patient recruitment. Although a comment section is available, my posted comments or questions have never appeared as visible to the public on their websites.

Social media such as Twitter, Facebook, blogs, and others is interactive media, but due to regulations and the sensitive nature of clinical trials, it is challenging. A marketing director explains:

> It's more like, well for example, social media is kind of a tough one because we're restricted by the IRB with what we can say. Social media is an interactive medium; it's completely opposite of a traditional advertising medium. It's not just us telling people something. It's people participating in a conversation, and that conversation is two-way. And if they [patients] throw something out there and you don't respond, then there is a perception that goes with that, or can, right? That you're not listening to them or not participating or whatever. Well, with IRB and our restrictions on what we can and cannot say, we can't just ad hoc respond.

Another issue is associated with what to do with information discovered on the web. Although technologies allow obtaining such information and using it in marketing campaigns to learn habits of participant population, the research industry pretends to not know. Anna, director of a recruitment firm explains:

> I mean, we can do search engine optimization, but do they [a sponsor] want to pay for it? Not really. We do online advertising, Facebook advertising. We can scour. We have capabilities to scour blogs and see what people are saying and keep track, and look at what's happening on the web and communications. Do clients want to see that? Maybe not, because if we come across something that, if a patient says, "Oh I took [a pill], and my hair fell out." If we see this kind of information online it has to get reported as an adverse event. All this information would obviously be reported back to sponsors and; they have to put that as an adverse event and they have to do something with that information. So there's a lot we can do it's just what make sense for sponsors because we might do that and we do that for marketed drugs. But do we want to do it for clinical trials and what happens if we see someone say "yeah I'm in a study for drug R2-75 and blah, blah, blah happened but I didn't tell my doctor"? Do we report it? Do we tell the sponsor? […] And so when it comes to technologies, again you just have to be very careful about what roads you go down and what you might see. Have we thought about doing patient discussion boards or closed Facebook groups? Yes, but again who monitors it, what happens if someone chooses to report an adverse event on Facebook, and they don't call 911 or their doctor? We just want to back out of it until there are sound rules and regulations about what can and can't be done.

"We do not want them to think about other treatment options"

Recruitment firms argue that they are attempting to be neutral in their sharing of information, and it is up to patients to decide what would be the best option for him or her, however it is not always the case. During my observations, a team was creating educational material for patients who were enrolled in an overactive bladder study. The disease itself has been controversial, with some scholars arguing that once again Pharma has turned normal biological activity into a disease. According to recruiters, the disease was widespread among females, but not widely diagnosed. In addition, my informants acknowledged that most of the "sufferers" have other means of coping with the situation, such as using replaceable female pads or avoiding high volumes of liquid consumption when leaving the house. While conducting participant observations, I obtained educational material for people enrolled in the study that was designed for the purpose of a retention program — to ensure that patients remained in the study until the end. In addition to guidelines on what a participant should expect in the upcoming visit, and a reminder of how data is important for science and society, the material also reminded participants of how unpractical living with this condition is:

> Until you think about it, the many ways that overactive bladder affects your life may be conveniently forgotten. But in looking back, you probably can relate to some of the significant lifestyle changes that patients have made because of overactive bladder. Here are few common ones: choosing a seat nearest the restroom at social events or always looking for an aisle seat on the plane, not for comfort — but for-you-know-what, or in long car rides planning ahead for rest stops […].

In the process of developing this material it was decided to include tips and techniques on how to cope with the condition. The tips included: "avoid foods and beverages that can irritate your bladder, such as caffeine, alcohol, acidic foods […], double void before bedtime." The material was supposed to also include a tip for exercising — "Do Kegel exercises regularly to strengthen the pelvic floor muscles." However in the meeting it was decided to take out this suggestion for the simple reason that was articulated by a marketing specialist: "We do not want to introduce this idea for patients."

Although it might appear as a minor problem, and in fact introducing a new therapeutic option could possibly bias results, the situation also shows that recruitment firms are in no position to advocate for the overall well being of patients. They might facilitate some participants' entrance into a study, but firms' main duty is to enroll qualified patients for the purposes of a clinical trial.

Summary

In this chapter I discussed patient recruitment companies' interactions with patients who are interested in participating in clinical studies. There are two ways how companies interact with the public — one is through advertisement, and the second is in a call center, when interested patients call to be screened for a study.

The patient recruitment business is very sensitive towards critical or negative information in the media. As a result, recruiters are very concerned about patient experiences throughout the recruitment process. Moreover, recruiters position themselves as superior to research sites because they are trying to provide good recruitment

experiences, and thus they are fostering people's participation in clinical trials.

Through the entire process, recruitment firms are carefully considering and controlling information shared with the public. When designing a marketing campaign, my informants are concerned about other available treatments and competing clinical trials to ensure that a new study appears to be a unique solution. Moreover, the created tone and feel of an advertisement is confident, authoritative, but empathetic and understanding - exactly what a desperate patient might be looking for.

The way recruiters present information to patients has implications for the validity of the informed consent process. This problem is reflected in the way recruitment companies advertise and present information to a wider public. By trying to promote benefits of participation recruiters contribute to blurring the line between investigational and approved treatments. Moreover, recruitment companies are well aware that often individuals who respond to clinical trial advertisements already have decided to participate in studies. Recruiters also are reluctant to disclose all information related to a particular clinical research study. The absence of information shapes the perception of potential research participants as much as the way the information is presented.

The conflicting feelings experienced by nurses shed light on the nature of private patient recruitment, which is removed from the patient care process. When these companies assume recruitment responsibilities, patients are not communicating directly with their own physicians, but rather with employees of a private company working on the behalf of pharmaceutical and device companies. On one hand, the call center nurses are healthcare professionals, but on the other their role is very limited. Given that

recruiters target individuals who are motivated to participate to receive a treatment, it is very hard to draw a line between care and participation in a study. But also the nature of the recruitment process — patient screening through a phone as quickly as possible — limits the interactions between recruiters and patients.

Chapter 7: Recruiting "high quality" patients

In the previous chapter I described how patient recruitment companies interact with the public, and more specifically how they interact with patients who are interested in participating in clinical trials. The recruitment process, including clinical trials', advertising, and the patient screening process, is shaped by the industry's notion of "high quality" candidates. In this chapter, I will describe what kind of patients that clinicians and recruiters view as "high quality" and how the recruitment process is organized in order to select these types of individuals. I will also highlight similarities and differences in recruiters' and clinicians' understandings of "high quality" candidates. The results presented in this chapter are based on field observations and interviews with recruitment companies' and research sites' employees.

Early in my fieldwork and interviews I observed that coordinators and recruiters refer to certain individuals as "high quality" patients. Prospective candidates are evaluated subjectively and are considered "high quality" patients when they meet all inclusion and exclusion criteria, and when they are compliant with all the activities throughout the recruitment process. In addition, during the recruitment process, recruiters and clinicians are trying to evaluate if a candidate will also comply with complex research protocols.

This patient assessment goes beyond medical requirements, such as having the right type of cancer, or having diabetes, or being off a certain kind of treatment. Social, psychological, and economic factors are incorporated into this complex evaluation

process. According to my informants, these factors determine if patients are able to comply throughout the entire study and provide "good" data.

As I mentioned in the previous chapter, by widely advertising studies and convenient screening process, recruiters are making clinical trials more accessible to the public. However, as I will illustrate in this chapter, recruiters are selective as to what kind of candidates they perceive as suitable for research, thus in a way restricting access to participation.

This situation brings up questions not only about the validity and generalizability of clinical trial results but also about who has access to different type of research studies. Studies that offer truly innovative solutions and does not involve placebo arm for wide spread medical conditions, naturally, attract more interested candidates; hence, recruiters can apply subjective criteria in selecting participants. It can be said that participation is shaped by socioeconomic class, because recruiters consider educational and economic factors when selecting research participants.

"High quality candidates"

Both recruiters and clinicians from research sites used the expression "high quality" patients when talking about the recruitment process. The main characteristic of these types of patients, mentioned by all interviewees, is their ability to comply with research procedures. Perspectives on other characteristics, which I will describe in this chapter, varied between individuals from recruitment firms and research clinics. For example, coordinators are interested in selecting patients who are less likely to experience serious side effects and who will carefully report necessary data for study

purposes. Research coordinator perspectives are associated with their accountability for each patient's health outcome during the study. In contrast, recruitment firms were less concerned about patients' medical issues that went beyond inclusion and exclusion criteria, but were more concerned that referred candidates show up for a visit in the clinic. Although a lot of perspectives of "high quality" candidates were similar, the differences can be attributed to the business goals of recruitment firms and research sites. For the most part, recruitment firms are concerned only if patients enroll in a study, whereas research sites, in addition to enrollment, also are interested in ensuring that participants complete a study and report reliable data.

An interviewee from a private research site located in the Midwest explains what she means by "high quality" candidates and the importance of them in her practice:

> You want somebody that when they come in and do the consent that [they understand that] these visits are in the morning, you have to be fasting, you have to take your drug, or you have a BP monitor, you have to take it home with you, you have to do this, and come back in the next day, and there is an MRI involved, or whatever, you know? So, you want to know that when you are telling them this, they are committed to being in the study, because we know the sponsors do not want dropped patients; obviously that is not good for a site. So, I think the better stability you have in your patients, the better you are obviously going to be as a site. The sponsors are going to want you, and then obviously the results of the research are going to be a lot better.

In contrast, individuals from recruitment companies are defining "high quality" candidates more in terms of their ability to show up for visits at research clinics:

> To me, that means you're looking for somebody that's going to be a really good candidate for the study; somebody that is going to not only meet all the inclusions

> for the study, but understand what the follow-up is about. You know, in one of our studies there's a five-year follow-up, and a lot of people after the first year kind of just drop out, forget about it. It's follow-up, it's hard for a lot of people. And sometimes, you know, five years for a study; it might be hard.

Economic factors

In the industry it is perceived that patients who are economically better off are more suitable candidates because they have their fundamental needs covered — they have a car or other means of travel to a site, have some health insurance and have received an official diagnosis, as well as medical examinations related to the condition. It is preferred that individuals come to the clinic having already been diagnosed, because then examinations do not need to be repeated, thus saving time and money for everyone involved.

The quote below is an excerpt from my field notes on an observation in the call center. This quote illustrates how a patient who has received some previous health treatment is described as a good candidate:

> A female patient calls in. The caller is very kind. She says that she is having a lot of pain and recently had cortisone shot. A nurse says, "Oh, that is fine, it won't disqualify you." After the nurse has asked all the health questions, she announces, "Good news, it looks like you pre qualify for this study. You met initial screening criteria." She continues by asking if the caller is willing to participate and attend all the visits. After receiving an affirmative answer, the nurse explains that information will be forwarded to the site, and that they should be contacting the patient soon. At the end, she asks for permission to leave a voicemail regarding the study info if necessary. After the call is finished, the nurse comments that this patient will be a good candidate. "She already did her MRI, and it will be easy to

see if she further qualifies at the site. Patients need to get an MRI on their own if they do not have one. It is very expensive, and the study does not pay for that."

The "high quality" patients were also defined as those who have a general interest in, and concern, for their health. While the nurse at the call center was pleased to hear that a caller has received a medical examination particular to the study, a coordinator in an interview shared that for her, patients who take regular care of their health are "better" candidates. In her experience, this meant that patients who see a doctor on a regular basis have a higher chance of understanding the purpose of a research study.

But more importantly, individuals who have been previously diagnosed and know their health situation will ensure a low screen failure rate at the research site. Low screen failure rate is an indicator that is commonly used to evaluate research sites' performance and show how well site personnel can identify subjects that would be expected to qualify. For research clinics, it is important to recruit subjects that are the most likely to pass screening tests and qualify for the study. Although screen failures are an accepted part of clinical research (the cost of doing business), a high ratio of screen failures to randomized subjects is not desirable. A coordinator explains what a "high quality" candidate means in her practice:

> […] if they are seen by a doctor, and they have regular care, I think that helps a lot, too. And [patients] knowing their health when they come in. […] And then, research, too, they do not mind doing […]. That way, I think knowing they are otherwise healthy for their labs helps a lot to break down with the screening failures anyways.

With the two examples above, I tried to show the role of economic factors associated with patients' health in the industry's opinion of "high quality" candidates. Another dimension of economic factors was connected to the participants' income because it determined candidates' reliability and their ability to travel to a research site. For example, my informant from a private research site located in a large Midwest city suburb complained that recruitment firms refer candidates that cannot afford to come to her clinic. Because of the site's location, for this particular research clinic, high quality candidates are those who can financially afford to visit a research site:

> I would prefer [that recruitment firms run TV advertisement in] a specific time. They usually run advertisements during the day, which means that, yes, you have people that may see it, but usually these people can't get to our site. If they're not working, they might not have a vehicle. Or they might advertise outside our service areas, and so it's a little hard for transportation and things like that.

Another coordinator explained to me that she is interested to know the patient's income, if they are homeowners, and what their level of education is. In cases when she does her own patient recruitment (rather than working with patient recruitment company), she places an advertisement at the radio stations where the majority of listeners (according to listenership's reports issued by each radio station) are elderly, middle income, and homeowners. People who have higher income levels and mostly own their houses, in her opinion, are more reliable and thus labeled as "high quality" participants:

> In our clinic, we prefer retired patients — people who can come in during the day and do studies, more than college kids or working adults. You want somebody that is going to come in and not blow off a visit. So, you do kind of look for a little more stability, you know, in the people that come in.

Although coordinators might not want to intentionally discriminate against people with low socio-economic status, the structure of clinical studies and locations of research sites requires considering individuals' income. A coordinator who runs a private site located in the downtown area of a large Midwest city explains her experience with recruiting lower income participants in clinical studies:

> For example, we have asthma studies that are recruiting children, and it makes sense that you would try to recruit children from an inner city, poor urban area because you could provide some benefit to those children. The problem is that you can't get those children – just like in the clinic, you can't get them here, or if you can get them here once, you may not be able to get them here the next time and the next time and the next time. So all the factors in their lives, social or economic, that make it difficult for them to get to a regular doctor's visit in a clinic make it just as difficult for them to get here. Even though I can offer them the benefit of medication, attention, money, I can't get them here. It is the situation– and we have tried. We've gotten money for transportation. We just literally – when people's lives are in chaos, they can't do that next – they can't do that next piece.

Right type of motivation

In addition to economic factors, a high quality patient is also the one who has the right motivation to participate in the clinical study. It is perceived that motivation is sufficient for those who have untreatable conditions, because they see benefit from participation in the research for themselves and future generations. Those who are motivated to participate in research because of a lack of health insurance and health care

are also considered to have the "right" type of motivation.

According to my informants, preferable participants' motivations are altruistic ones, because those are the ones who will stay in the study until the end. In the quote below, a coordinator critiques individuals who are "study shopping" — interested only in payments that are offered for participation. Her main concern is that these individuals are not reliable for the purposes of research studies. I observed similar attitudes among recruitment companies' employees. They often spoke negatively of those who are interested in money when seeking participation in clinical trials. The notion of having the right type of motivation is again connected of being compliant to a research study requirements and producing good data:

> You'll get people who are now study-shopping. You know, we get sometimes calls where people say: "Well, don't you have a study that's paying more?" And that puts us into a tough spot because we'll say: "No, we're really only recruiting for the study that I'm telling you about," because we don't want people picking a study based on how much they're going to get paid. Mainly, because they're not going to give you right answers when you're collecting the data. So if my job is to collect data, the patient's job is to give me good data; and if they're only giving me data that they think I want to hear, they've skewed the study, and I'm not getting good data.

Educated patients

The level of education about clinical research is another important characteristic of "high quality" patients. It is understandable that individuals who have a good understanding of the research process are preferred by the industry, because it takes a lot of time and effort to educate someone on the purpose of clinical research. Everyone in the

industry labeled as “high quality” patients are those who have participated in research in the past or well understand the purpose of a clinical trial. According to my informants, individuals who were educated about clinical trials were more likely to be compliant and less likely to be scared during the informed consent process. These types of patients are also easy to screen because they can decide right away if they are going to participate. When they are eliminated early in the process, obviously it saves money for everyone in the industry. A nurse from the call center explains:

> They [high quality patients] have done other research studies. They're educated, so they are interested in learning more about [a study] at least. Then there are patients that I know they don't want anything to do about it, they say: “I’ll talk to my doctor about it.

I also had an impression that by educated patients, my informants often meant “obedient individuals”. For example, my informant, a nurse in the call center, shared the perspective that individuals who ask too many questions and have a lot of concerns, are usually less likely to participate in clinical trials:

> Patients who are probably going to be the ones that do not want to do the study are the ones that are questioning everything — what about the insurance, what about this, what about that? And they have a lot of concerns about the clinical study.

In addition to a good understanding of the research process, interviewees felt that exceptional candidates are able to assess their own health situation and evaluate risks in their own body. Individuals who are generally educated about health issues and understand their body, according to interviewees, make better study candidates — for two reasons. First, they are perceived as more committed, and second, they are aware of their

health, already have a diagnosis, medical records that are helpful for the site, and they are comfortable assessing their own symptoms. A coordinator explains:

> We don't want to have serious adverse events, either here. We don't want the person to get hurt, but there is a lot of fallout if you know that you're going to put someone in a situation where you're going to have to deal with all of the stuff that falls out from that.

In the following quote, the same coordinator talks about the importance of a patient being able to assess their own symptoms in her decision whether to admit them to a study or not:

> Some of our asthma patients – we know that they'd be able to tell us right away if they were having a problem. But if we know that there are people that aren't very good at assessing their own symptoms, and we don't want anyone having a problem, and we don't want the problems to result from problems.

A program director who works for a company that is using medical records in community pharmacies to recruit patients describes the connection between patients' level of education about health care and research with the ability to comply and thus be a high quality candidate:

> If someone for example is not compliant with their medications at all - they don't pick up their prescriptions on time, or they don't taken them properly, I don't even know if that would be the right patient you would want put into a clinical trial unless it was an observational study or something about medication adherence. Because it would be hard if you know that the patient to be taking medication every day and has to keep track of it in a diary is not taking it in the first place, but also who is highly unlikely to be taking an investigational product as well. So that is probably one example; versus the patient who is quite the

> opposite, who's always on time for their prescriptions, or asks a lot of questions, or is very invested in their healthcare. That would be the other end of the spectrum. That sort of a no brainier, a very motivated, compliant patient versus someone who is sort of aloof and is a little bit disconnected from their own health and their healthcare outcomes and isn't compliant.

A nurse in the call center also agrees that better candidates are those who have a vested interest in a study and have educated themselves on the process. According to her, those are patients who have significant motivation to participate:

> They already know something about the study. They have researched, and been on the website. Some you can sense as desperate, and how bad they want to participate. Its circumstantial, they do not have insurance. They need it real bad. It's their last chance for health.

Local vs. central patient recruitment: the importance of the relationship between a patient and a site

My informants, particularly individuals from research sites, discussed the "quality" of research participants in a dichotomy of centralized and local recruitment. By "local", they refer to the recruitment activities that are done at the research site and the central ones that are organized and carried out by patient recruitment organizations. Essentially the methods used in both central and local recruitment are similar. The main difference is that a research site is trying to recruit patients just for itself, but recruitment companies are organizing advertisement and screening for many sites at the same time.

This distinction is important, because although coordinators welcome new patients to research clinics, many believe that the best research candidates and most

committed patients are those individuals who previously have been in contact with clinic staff and have had a good experience. A coordinator explains: "Since we are a part of a hospital and clinic organization, usually the patients when they come from our service area they're just loyal […]."

Interviewees also mentioned that initially they view new patients with mistrust in terms of their ability to comply with research requirements. In contrast, patients who are seeing a doctor at the clinic or have participated in research studies in the past are seen as more reliable candidates. As a result, coordinators feel that individuals recruited locally are "higher quality." A coordinator explains how she sees the difference between patients recruited locally and centrally:

> […] we tend to see a less reliable patient sometimes coming from the recruitment agencies. Its' probably not because they're targeting a different population, but I just think the no-show rate, the conversation rate is not as high as us mining our own database. We certainly have no-show rates even from our own database or from our own local advertising, but I think just in part because there's not as much one-on-one communication and you don't establish as strong of a relationship with that referral, the conversion rate is not always as good. Or if they change their mind, they don't necessarily know who to call, or they've lost that information.

My informants disclosed a perspective that a relationship between a patient and a doctor, as well as familiarity with a medical institution, is very important in recruiting "high quality" research participants. One of the reasons for this attitude is, as my informants reported, that patients who are familiar with the research staff themselves might feel more comfortable with the research process. The coordinator explained to me:

"[…] most of our really successful recruitment happens because we have patients in a database, patients that trust us." Moreover, my informants felt that these types of patients were more likely to come to appointments and follow required research procedures:

> But if we do outside referrals, you know, you do want new patients all the time to come in, and I would say one out of three probably is. Where if we have our own database of patients, and they come in for a pre-screen, I would say almost 80 percent continue on after reading the consent [form] and what it involves. Where if it is somebody just off the street coming in and reading that consent [form], they are like "whoa!" Because they do not really know too much about research, and they are scared, or they have heard things.

While there are cases when recruitment firms will put the doctor's name (usually if it's he or she is very well known in the field) in advertisement materials, firms are often reluctant to display research sites' telephone numbers or logos on advertisement materials, because then callers will bypass the firms' call centers. As a result, firms' will be unable to track the outcome — enrollment or disqualification of a patient to receive a credit. Instead, as described earlier, there are listed 1-800 numbers, so patients do not have much of a choice whether to call this call center. This might be a particularly pressing issue in the cases where recruitment firms' use performance driven payment models. Every recruitment company is interested in tracking every referred and enrolled patient, because if a recruitment firm does not enroll participants, it does not get paid. However, individuals from research sites feel that in this way they are missing out on good participants — those who are familiar with a research clinic:

> They [patients] just might not respond to the advertisement because they might not recognize that it is their doctor's facility. Sometimes the central ad campaigns will let you put participating doctors; they'll let you list a name, which is helpful especially when the advertisement doesn't look like our organization.

Up until now I have introduced recruiters' and clinicians' perspectives of what they perceive as "high quality" participants. As described, those are patients who are seen as loyal and committed to the research procedures. According to my observations and interviews, individuals who are financially secure, sufficiently motivated, educated about health and the research process are preferred for participation in research studies. I also observed different mechanisms that recruitment companies incorporate into their work in order to select what they call "high quality" individuals. I will describe these tactics in the following section.

Screening for "high quality" patients

Through the recruitment process, medical screening recruitment companies and research sites find out if a candidate meets inclusion and exclusion criteria stated in a research protocol, and this allows them to evaluate the patient's ability to adhere to research procedures. Research sites, and particularly recruitment companies, have incorporated mechanisms into the recruitment process to evaluate if screened patients are going to be good candidates.

Call center

When screening patients over the telephone, nurses are not only collecting medical information, but also trying to assess if a caller has a "sufficient level" of interest

and if there is something that might be going on in the patients' lives that would hinder their participation in the study. A telephone screening script is designed to quickly eliminate unqualified patients, but it also serves as a tool to reiterate the number and frequency of follow up visits. Moreover, nurses specifically ask every patient if they are willing to attend the visits, and if they are willing to travel to the research site.

While observing nurses in the call center, I noticed that after the call they often commented regarding the "quality" of patients based on different factors, such as voice tone, type of questions a caller asked, or type of answers a caller provided. For example, if a nurse hears doubt in a caller's voice or a caller asks a lot of questions, the nurse can judge this patient to be an unfit candidate. Although this does not mean that a patient will be necessarily excluded based on these characteristics, but a nurse can leave a written note for a coordinator regarding her concern, or she can advise a patient that "this study is not a good match for you." A nurse working in the call center shared her experience of assessing callers:

> I think experience teaches you a lot too, and then you kind of know some obvious things. You know if somebody's is not answering their calls when you call at all times of the day, and the evening nurses can't get them, or they're calling back to us after hours, after we've closed; you know that they are not going to be able to make the visits.

Another nurse speaks about the factors she considers when evaluating a caller's suitability for a study. She shares that at times she will discourage patients from participation because she has doubts about their ability to comply with follow up visits or procedures:

> Sometimes you can see the person is not interested. Sometimes they can be the ideal candidate, but they have something going on. Other things like they're ninety miles away from the site. And the follow up is to start every three weeks for example. Common, you know what I mean? Sometimes is it better for me to discourage them. Or you can hear the hesitancy in their voice like, "Oh well how many visits it will take?" or, "well I work from 8am until 6pm every day." And sites see [patients only at] specific hours, you know, clinic hours.

The situations I mentioned above appear to be logical. However, sometimes the decision making is unclear to outsiders. One day I joined one of the nurses in the call center, and she screened two callers in a row and behaved totally different with each of them. Consider an excerpt from my field notes:

> A female patient calls in and qualifies for attendance at an informational meeting. She asks if she should call someone if she is not able to attend the meeting. She explains that her child has a lot of medical issues, and that they might need to see the doctor at that time. A nurse kindly advises that she should do her best to attend the meeting, because, the nurse explains, if they fill the quotas during the October talks, the study won't be recruiting anymore. "So if you are interested, I would encourage you to attend."

Right after the nurse completed the telephone conversation with the woman mentioned in the excerpt above, the nurse talked to another patient who called about the same study:

> A nurse is talking to a male patient; he is also qualified to attend one of the meetings. He says I am very interested, but I am working from 2pm to midnight every day. "How about the informational meeting tomorrow at noon?" the nurse asks. He replies, "I already have a doc appointment at 11." She says that she will just make a note saying that only mornings work for him. Before the end of the

call, the nurse just said that if any more meetings will come up they will contact him.

Afterwards, when I asked her about this situation, she just replied that the male caller did not seem that interested, saying, "He could have canceled his doctor's appointment." This example indicates that nurses are making subjective evaluations about callers and who would be an appropriate participant or interested enough in order to take an extra step for them. To an outsider, like me, both of these people sounded like fine candidates for a clinical study.

Only one nurse out of all the interviewees who mentioned "high quality candidates" questioned her ability to predict which patients will turn out to be the best candidates:

> I've seen that people are so excited they'll do anything, just help them, like in our weight loss study; people are really excited. There are some people that have tried the same product in an earlier research phase, and it worked great. But then you find out later that they refused to do the follow-up or something, so it's really hard to tell. I mean, you think that somebody is going to be a good candidate by the enthusiasm that they show over the phone, and then they're not.

Despite the nurse's doubts about predicting which participants will be compliant research study participants, professional recruiters in their practice often consider these details as predictors for compliance. Recruitment companies are striving to accumulate experience and knowledge to precisely predict good study participants. One of my informants, an owner of a firm, told me he hopes that someday there will be programs that analyze phone conversations and have the unique capacity to evaluate each caller based on what she or he says.

Clinical research informational meetings

These types of meetings were organized by the recruitment company that was my primary site for field observations. Meetings are organized for patients and their friends or family members to educate them on a particular clinical study — to present information that is available in the informed consent form. Individuals are invited to attend these meetings after they have met basic inclusion and exclusion criteria. For patients to enroll in a study, they must attend one of these meetings. Some of the purposes of these meetings I have discussed in the previous chapter. Nevertheless, another purpose of the meetings is to evaluate patients' interest and ability to attend the meetings. A nurse at the call center explains:

> We are doing a lot of informational meetings now, so […], where we use to spend a little bit more time educating patients on the type of surgery, medication, and what it does for your body and what side effects you're going to have. [Now] they're doing more of the informational meetings. So we're giving them the basic information, going through the basic health screening, and then sending them to the informational meetings where they'll learn more. I actually think it's a good thing because if patients are taking the time, two hours to schedule this in their own personal time and travel to and to go sit in the lecture room and listen. They're going to be interested more in the study, and they're going to want to at least learn more — sign up and follow up, and do all the follow-up visits.

If individuals are too busy to attend one of the meetings, they cannot enroll in a clinical study. Employees at the company feel differently about these individuals. For example, the president of the company thought that "these people did us a favor by not showing up," meaning that they would have been non-compliant anyway. In contrast,

according to the vice president, people are not necessarily unreliable or have lost interest, but rather they have other things happening that might prevent them from attending a meeting:

> And then they just don't show up for their appointment, but it's not because they don't want to, or they have lack of desire, or they have lack of interest, but lack of one or more of fundamental needs like — I can't get myself to the site.

The two quotes above show that recruiters acknowledge the role of economic factors in people's abilities to participate in clinical studies. But despite understanding and compassion, recruitment firms are interested only in patients who meet the necessary criteria — medical as well as social and economical. If a sponsor refuses to offer transportation assistance, then the recruitment firm is in no position to help these individuals.

Individuals with particular medical conditions, like obesity for example, are considered by recruiters as a particularly non-compliant group of individuals. According to my informants, these studies have very high no-show rates for visits, and dropout rates, especially when patients do not experience a quick solution for their conditions. For these types of patient groups, informational meetings serve as a test of commitment for these individuals. It is assumed that only the most serious candidates attend the meetings, and as a result, cost and dropout rates will be reduced later in the research process. Below, this situation is illustrated in a quote from my field notes:

> Tiffany said that the weight loss population is notorious for non-compliance. "They cannot even put down a donut. That's part of the problem for low attendance in the last meeting." To which Nash replied, "But we had a good

response rate from the ads." Tiffany said, "Yes, but for that they did not have to leave their couch. And for the meeting they needed to do so." Both of them agree that attendance to meetings for this patient population usually is only 50%.

My findings indicate that recruiters have developed a specific type of attitude toward some patient groups; in this case, specifically overweight people. But they also demonstrate how these informational meetings, designed by a recruitment agency, serves recruiters' purposes — helping recruiters select only, according to my informants, the most compliant research participants.

Summary

In their brief encounters with potential study participants, recruiters evaluate callers in specific and nuanced ways in order to select research participants who are going to commit to a study until its end. Among my informants it was assumed that factors such as income, education level, and attitude determines callers' ability to commit to visits and investigational procedures. In addition, centralized patient recruitment is set up to evaluate the level of commitment potential participants have at different stages of the recruitment process.

Clinical trials are structured in such a way that studies are not accessible to everyone in society, and as a result, for some individuals of a lower socioeconomic status it might be difficult to commit to a research study, due to things like travel expenses, taking time off work, day care, etc. One of the problems with this subjective evaluation is that it does not apply equally to all studies and is very much shaped by the nature of a study design. For example, if a study is recruiting for patients with conditions that already

have many treatment options available on the market, it makes it harder to recruit participants, subjective evaluation will be less applied, and there might even be financial support for individuals to join a study. In cases when medical products are developed for unmanaged conditions, or study design incorporates standard of care research sites that might require participants to have health insurance, and may not provide any support for expenses associated with participation, these studies immediately become less accessible to certain groups of society. This is also reflected in the way patients are screened at the call center.

Chapter 8: Conclusion

This thesis critically examined one aspect of the clinical trial industry—patient recruitment for clinical research studies. I investigated the daily practices of patient recruitment companies, interactions with other research industry stakeholders and the ethical issues that emerged from these activities.

The central argument I developed in my project is that rationales for recruitment tactics are completely entwined with the market value that these companies see in patient recruitment, and the market risk that attends this process. This worldview impacts every aspect of the patient recruitment business—starting from the structure of patient recruitment, to the development of marketing campaigns, and communication with the public and all the way through to the relations with clinicians. I argue that the current organization of private industry patient recruitment introduces different ethical questions that are not addressed by the current guidelines. In this concluding chapter I will summarize three main areas of ethical tensions that emerge from the practices of recruitment firms.

From this research it is apparent that recruitment companies are knowledgeable about ethical and legal guidelines and make every effort to carefully obtain and follow IRB approvals. Misconducts and violations would be too damaging to the industry. However, my findings indicate that there are areas of ethical tension that go *beyond* ethical requirements for the industry. Much of the tension documented in this thesis can be seen not as a clash of different moral values that represent different worldviews but rather as the tension between moral and market values in patient recruitment. Yet, the

situation with private sector patient recruitment is not exceptional; rather, it is indicative of larger trends in the clinical research and health care industry in general.

The three main areas of tension involving the ethics of patient recruitment that emerged from the descriptive questions of the thesis are: 1) the way professional recruiters organize the recruitment process brings about several ethical questions; 2) the way patient recruitment companies distribute and present information on clinical trials as well as gather health-related information from patients; and 3) finally, issues that emerge from recruiters' and clinicians' subjective evaluation and selection of research participants.

Organization of patient recruitment

The organization of professional recruitment reveals the centrality of market values in patient recruitment. It is not to say that recruitment firms are not thinking about ethical practices, but rather that the marketplace, by its very nature, is more likely to emphasize return on investment than enhancement of social good as the primary responsibility to its shareholders. The tension between market values and ethical commitments is reflected in the way that recruiters select research studies to work for, organize the workforce and work with investigational research sites.

Clinical trials, including the patient recruitment portion of it, have become so complex that groups of specialized professionals have emerged to manage different aspects of the process. Recruitment companies assume that by informing the public of available research studies and organizing the recruitment process, then patients can be found for most of the studies. My informants admitted that through extensive

advertisement they *can* recruit patients for almost any study, but it just might take more resources and time. This is troublesome because rather than focusing on the improvement of common barriers of patient participation such as: 1) improving health care provider involvement in patient selection process, or 2) increasing patient involvement in the design of medical research studies, or 3) working towards research protocols that are more beneficial to participants and society, instead professional recruiters are developing methods to recruit patients *regardless* of barriers, including for studies that may offer little or no benefit to patients and to society. As I showed in my thesis, recruitment companies do not engage in evaluating the usefulness of research studies. Instead, the decisions are based on the likelihood of recruitment success and financial cost-benefit calculations.

Since recruitment companies compete with other firms at a price, everyone is trying to offer the relatively cheapest recruitment services to sponsors. Recruitment firms use different strategies to reduce costs, and one of them is hiring part-time, low-skilled employees. As other researchers have pointed out, the issue of patient exploitation in clinical research is customary (Abadie, 2010; Fisher, 2009). In addition, as I presented in Chapter 4, the recruitment companies exploitation of employees to achieve fast patient enrollment also raises ethical questions.

When I started my fieldwork I was surprised by how little patient recruitment companies actually talked about patients. Instead, recruitment firms work "behind the scenes," meaning that they spend a lot of time working with investigational research sites. Although recruitment companies are constantly looking for new ways to reach and

motivate patients to participate in research studies, they also need to be attuned to the recruitment situation at individual research sites. Recruitment companies removed from clinics but still operating in the space of medicine are required to partner with research sites to ensure that participants are admitted to clinical trials. As I described in chapter 5, these circumstances create complex relations between the two stakeholders.

Recruitment companies position themselves as research site saviors. Recruiters explained to me that research sites are constantly overwhelmed by work and that recruitment services are supposed to relieve their workload by taking care of patient recruitment. Although recruitment services can be helpful for investigational research sites, in the current organization of the recruitment process, recruitment companies are entering the area of expertise of research sites; thus, they encounter resistance from clinicians. On one hand, recruitment firms are assuming the logistical aspects of patient recruitment, claiming that "clinicians need to focus on the clinical aspects of patient recruitment so recruiters take care of advertising." However, as I showed in my thesis, recruitment companies are interested in medically screening patients, reviewing charts and advising clinicians on how to interpret protocols and on which patients to enroll in a study.

In one aspect, the recruitment companies' role is to monitor the research sites' performance with patient enrollment. Monitoring is done to ensure a smooth enrollment process, but if a site refuses to collaborate it might be reported to a sponsor. I observed that it is very common among industry members to check on each other and to report to a sponsor. For example, in my observations, research sites occasionally would make test

calls to the call center and if something did not go smoothly a complaint was immediately submitted to a sponsor. Although I never heard that someone would report unethical conducts to IRBs, research sites and recruiters definitely complain to a sponsor who then has the power to influence one party or another.

In many cases patients suffer because of the conflicts and competition between research sites and recruitment. If a recruitment firm has run an advertisement for a research site that has not provided all the data, it can stop patient referral. This means that interested patients are screened for a study but are not referred to a principal investigator for further medical screenings. Or sometimes research sites do not follow up on referred patients, and in those cases, again, patients are endlessly expecting a call from a clinician which they will never receive.

To avoid the situations described above, recruitment companies need to maintain frequent communication with research sites, meanwhile trying not to bother or overwhelm clinicians. Yet, recruitment vendors can also provide a competitive advantage to a research study. According to my informants, by constantly contacting investigational research sites they keep a certain study on top of the clinician's mind. These situations raise several concerns, such as, what types of research studies are preferred by the investigators. From my observations it appears that the most innovative and beneficial studies to participants may not always be given preference; as a result, patients do not have equal opportunity to participate in all relevant studies. Again, in this case it can be said that market forces, rather than the considerations of best health outcomes, shape the clinical research process.

Sharing and collecting information

Information is a foundation of the patient recruitment business. There are several types of information with which recruiters operate. One is information regarding the kind of tactics that are successful in different situations. Recruitment companies acquire this type of knowledge by carefully gathering data of various recruitment tactics. In this way they can predict if a certain recruitment tactic in a certain geographical region with certain patient populations will be effective. Increasingly, these companies are developing a body of empirical data scientifically indicating the efficacy of various means of attracting and convincing people to participate in clinical research.

On one side this is remarkable because patient recruitment is a challenge, and replacing the trial and error method with verified recruitment tactics can potentially save money and time in the clinical research process. However, unlike academic researchers who are eager to share their discoveries, recruitment companies are carefully guarding their knowledge and expertise. This means that only clinical trials which have a lot of funding can benefit from this expertise. In addition, recruitment companies are watchfully selecting studies that will be profitable for them—as mentioned above, decisions are made based on cost and benefit calculations. As a result, recruitment companies, similar to other players in the clinical research industry, are profiting from patients' voluntary participation in clinical trials that are made available for financial reasons.

Another area of controversy regarding information is the gathering of patients' health information. In order for recruitment firms to efficiently screen patients and refer them to a clinic, they need to gather the caller's address, phone number and health-related information. However, one of the problems associated with this is that patients often cannot opt-out from sharing their health information with a vendor where the patient may have decided to disclose it only to the principal investigator. The name and location of research sites is often not disclosed to patients in order for recruitment companies to receive a credit for recruited patients and to "protect" research sites from the burden of receiving too many patient calls. If a patient decides not to share his health information with a recruitment vendor, he cannot participate in a study.

By gathering health information, nurses in the call center evaluate if patients are qualified for a certain study; however, their role can be perplexing to both patients and to the nurses themselves. Nurses at the call center are trying to provide the best service to callers yet in some respect they exploit their role as health care providers to gather information from patients. Although nurses might care about patients' overall health, their main duty is to gather callers' health information. While nurses are very helpful to patients in the recruitment process, the fact that patient recruitment firms are removed from the clinical setting creates an unusual situation. Patients are calling to find out more about an investigational treatment for their medical condition but they are unable to receive any advice or consultation about the disease at hand.

By carrying out centralized patient recruitment, firms are trying to eliminate one of the key barriers to patient recruitment—the physician. For the most part, recruiters are

communicating directly with patients. On one hand, this is very good for patients since physicians have been reported as one of the main barriers to patient involvement in clinical trials. In this way patients who do not have their own physician, or whose physician is not involved in clinical research and does not inform her patients out of fear of losing clients, or a physician who is too busy to learn about available studies, can still learn and participate in clinical studies if they desire.

My informants from recruitment companies claimed that they are in fact solving an ethical problem because in their view it is unethical not to inform patients about available opportunities to participate in clinical research. However, this situation also brings about other ethical issues. All responsibility for evaluating available information about a study is placed on the patient. Although many patients are savvy and well-informed about their condition and available treatments, most of the information about a study is prepared by a recruitment firm or a sponsor. This is not to say that they always are trying to be misleading, but as I showed in Chapter 6, recruitment companies are very careful when it comes to what kind of information they present to patients. The information that is placed on websites, shared in the telephone call or informational meetings, is carefully designed. Although patients are encouraged to discuss participation with their physicians, there are no reasons to believe that these physicians might have the time to dwell on this information and discuss it with a patient.

Unequal relationships among the industry and patients in terms of access to information were particularly apparent during the phone call screenings and informational meetings. Individuals try to gather information to evaluate their

participation in a study, but instead, nurses refer them to a study website and principal investigators claim that they are testing only the most promising treatments in their clinic, which may or may not be the case. As I showed in Chapter 6, recruiters in initial encounters with patients are reluctant to disclose risks associated with participation out of fear of scaring patients. However, also at informational meetings, principal investigators try to minimize the seriousness of risks. Although it can be the case that risks are minimal, but since researchers are uncertain about the benefits of investigational treatment they should be uncertain also about the risks. My research shows that there is a tendency to put stress the certainty of benefits and uncertainty of risks associated with a particular research study. Obviously there are financial incentives for professional recruiters to not disclose full information to potential research participants since recruiters are often paid based on the number of referrals to a clinic.

Subjective evaluation and selection of research participants

Through advertisements, recruitment companies are seeking patients who are willing to participate in research studies. The direct-to-patient and "call to action" advertisements conveniently bypass physicians and recruits patients who have sufficient motivation to participate. Although widespread clinical trial advertisement sensitizes the public towards participation in research, recruitment companies are not aiming to educate everyone on clinical trials. Rather they are targeting individuals who are ready to participate in clinical trials. In fact, recruitment companies are benefiting from the complicated economic conditions of patients.

The types of patients that the research industry is interested in enrolling in clinical trials, are called "ready to consent" populations by Jill Fisher, meaning populations who have no better alternatives than participating in clinical trials (Fisher, 2007). Like other scholars, she argues that research participants decide to participate before they receive the full information on risks, benefits and requirements of a particular study. As I showed in Chapter 6, recruiters already design clinical trial advertisement campaigns with an intention to position investigational products as a legitimate treatment option. In this way recruitment companies are producing therapeutic misconception—or a failure to distinguish that there may be major disadvantages with the treatment and participation in the clinical research (Appelbaum, Roth, & Lidz, 1982). Moreover, recruiters are designing messages trying to sound credible and trustworthy. The way recruitment companies present information is problematic. The recruitment process is the beginning of the informed consent process so technically patients do not need to find out all the information about the participation in a clinical study through advertisements and telephone screenings. However, if patients indeed make decisions about their participation in research based on their perceptions of seen and heard information in advertisements and telephone screenings, the recruitment process is very misleading. As I discussed, recruiters are reluctant to disclose any information regarding the participation in clinical research.

Although recruiters often rely on disenfranchised groups for whom clinical trials are the only source of healthcare, my research findings indicate that some clinical trials are available only to those who have access to health insurance. More specifically,

clinical trials that involve standards of care or particularly innovative treatments, and hence can be the most beneficial to participants, require health insurance or out-of-pocket payments. Sponsors are not willing to pay for standards of care procedures or expensive medical examinations that are needed to establish diagnosis. In the search for more participants, recruiters or sponsors often are reluctant to disclose costs associated with participation. Situations like these demonstrate that the goals of sponsors and recruitment firms can take precedence over the interests of individual patients. In some cases hiding this type of information from patients may cause significant harm because the information presented is misleading and influences patient decisions to or not to participate. Moreover, it is disrespectful to individuals who disclose their health information, spend time answering screening questions and travel to research sites potentially for no point or benefit.

Recruitment companies are defining their own patient target groups based on the appeal to the marketing materials. The recruitment process, including clinical trials' advertising and the patient screening process, is shaped by the industry's notion of "high quality" candidates. Individuals at recruitment firms and research sites have developed subjective understandings of patients who are suitable for clinical research. These notions not only shape who gets recruited for clinical studies, but also how referrals from patient recruitment firms are evaluated at research clinics. As described, recruiters select patients who are seen as loyal and committed to the research procedures. According to my observations and interviews, individuals who are financially secure, sufficiently motivated, educated about health and the research process are preferred for participation

in research studies. I also presented different mechanisms that recruitment companies incorporate in their work in order to select what they call "high quality" individuals.

Such subjective evaluation is problematic for several reasons. This type of understanding introduces bias in the results of clinical research—a bias that is associated with characteristics of social class, such as the financial and educational ability to comply with the prescribed treatment. However, more worrisome is the fact that the research industry exploits certain groups of individuals and denies access to others based on a subjective evaluation of suitable candidates for clinical trials.

Similar observations have been made by Jill Fisher (2009) and Joseph & Dohan (2009). In her book, Fisher (2009) also shows that clinicians have developed a subjective understanding of research participants; specifically, women and individuals of Hispanic descent are seen as more compliant in research studies. Joseph & Dohan (2009) observed similar phenomena in cancer studies that were held in a large academic medical center. They observed that the subjective selection of cancer patients is aimed to increase compliance throughout the duration of a clinical study so that "good data" can be gathered.

However, subjective patient evaluation and selection do not exist only in academic cancer research, but also exist in different types of research studies both in private and academic research settings. Moreover, economic aspects play an important part in patient selection for research studies and evaluation methods used by recruitment companies to assess and select patients.

The findings of this project shed light on the prevalence of financial aspects in private patient recruitment. Scholars in areas such as politics, ethics and economics have pointed out the deterioration of moral values through market interactions (Sandel, 2012; Falk & Szech, 2013). Similar tendencies can be observed in various aspects of health care and clinical research. Traditionally clinical research ethics focus on physician and patient interaction; as a result, private organizations that take part in clinical research do not view these as applicable in their practices. In the private patient recruitment industry, ethical dilemmas emerge as a result of the firm's necessity to survive in a competitive environment and the primacy of market values over social values. I suggest that some of the quandaries can be resolved through the development of national ethical guidelines and regulations for private organizations that engage in clinical trials. Although some suggestions might appear contradictory to the current organization of the recruitment business (for example, if a caller refuses to disclose his health information to a third party, he can be directly referred to a clinic;in this case, it would complicate a firm's ability to track this person and receive a payment) they could encourage the development of more responsible business models and interactions between research sites and these companies. In light of this I suggest the following policy recommendations:

1) Require recruiters to fully disclose information about a research study to individuals who are interested to join a study, including the risks and the location of research sites.

2) Develop for patients an independent information source that accessibly describes in detail the available clinical research studies in the context of

currently approved treatment options (pharmacological and non-pharmacological). (This also could be achieved by expanding the currently available clinicaltrials.gov website.)

3) Offer financial assistance to individuals who are eligible and interested to join a study but normally are excluded because of lack of health insurance.

4) Encourage ethics committee members to randomly select and attend clinical trials' informational meetings as well as to monitor screening calls.

Bibliography

Abadie, R. (2010). *The professional guinea pig: Big pharma and the risky world of human subjects.* Duke University Press.

Advisory Committee on Human Radiation Experiments. (1994). *Chapter 9: History of prison research regulations.* Retrieved October 7, 2010, from http://205.254.131.69/healthsafety/ohre/roadmap/achre/chap9_4.html

Agar, M.H. (1996). *The professional stranger: an informal introduction to ethnography*. Oxford: Blackwell Publishing

Anderson, D. L. (Ed.). (2004). *A guide to patient recruitment and retention.* Thomson Healthcare, CenterWatch.

Angell, M. (2004). *The truth about the drug companies: how they deceive us and what to do about it.* New York: Random House.

Appelbaum, P. S., Roth, L. H., & Lidz, C. (1982). The therapeutic misconception: Informed consent in psychiatric research. *International Journal of Law and Psychiatry, 5*, 319-329.

Atkinson, P. (1992). *Understanding Ethnographic texts.* Newbury Park, CA: Sage

Beauchamp, T. L. (2010). Autonomy and consent. In F. G. Miller, & A. Wertheimer (Eds.), *The ethics of consent: Theory and consent.* Oxford University Press.

Beecher, H.K. (1966). Ethics and Clinical Research. *New England Journal of Medicine, Vol.274, No. 24*, 1354-1360

Bjornson-Benson, W.M., Stibolt, T.B., Manske, K.A., Zavela, K.J., Youtsey, D.J., Buist, A.S. (1993). Monitoring Recruitment Effectiveness and Cost in a Clinical Trial. *Controlled Clinical Trials 14:52S-67S*

Bodenheimer, T. (2000). Uneasy alliance--clinical investigators and the pharmaceutical industry. *New England Journal of Medicine, 342*(20), 1539-1544.

Bonner, A., Tolhurst, G. (2002). Insider-outsider perspectives of participant observation. Nurse researcher, 9 (4), 7-19

Bosk, C. L, (1979). *Forgive and remember: Managing medical failure.* The University of Chicago Press.

Boyle, J. S. (1994). Styles of ethnography. In J. M. Morse (Ed.), *Critical issues in qualitative research methods*. Sage Publications.

Brescia, B.A. (2004). Budgeting and contracting in patient recruitment. In D. L. Anderson, (Ed.), *A guide to patient recruitment and retention* (143-165). CenterWatch

Caldwell, P.H.Y., Hamilton, S., Tan, A., Craig, J.C. (2010). Strategies for increasing recruitment to randomized controlled trials: systematic review. *Plos Medicine, November*

Campbell, R., Quilty, B., Dieppe, P. (2003). Discrepancies between patients' assessments of outcome: qualitative study nested within a randomized controlled trial. *British Medical Journal, 326,* 252-253

CenterWatch (2006). State of the Clinical Trials Industry. Boston: Thomson Center-Watch.

The Center for Information and Study on Clinical Research Participation (CISCRP). Retrieved November 3, 2012 from http://www.ciscrp.org/professional/facts_pat.html

Corrigan, O. (2003). Empty ethics: the problem with informed consent. *Sociology of Health & Illness, Vol. 25, No. 3,* 768-792

Cutting Edge Information. (2011). Clinical Operations: Benchmarking Per-Patient Trial Costs, Staffing and Adaptive Design. Retrieved October 20, 2012, from http://www.cuttingedgeinfo.com/2011/patient-recruitment-clinical-vendor-fees-top-trial-cost-drivers/

Davis, M. J., & Addis, M. E. (1999). Predictors of attrition from behavioral medicine treatments. *Annals of Behavioral Medicine, 21, 1-12*

Delamon, S. (2004). Ethnography and participant observations. In C. Seale, G. Gobo, J. F. Gubrium and D. Silverman (eds.), *Qualitative Research Practice* (pp. 205-218). London: Sage

Denzin, N.K., & Lincoln, Y.S. (2005). Preface. In N.K. Denzin & Y.S. Lincoln (Eds.), *The Sage handbook of qualitative research 3rd ed.* (pp.ix-xix). Thousand Oaks, CA: Sage

Elliott, C. (2008, January 7). Guinea-pigging. *New Yorker,*

Emanuel, E. J., Lemmens, T., & Elliot, C. (2006). Should society allow research ethics boards to be run as for-profit enterprises? *PLoS Medicine / Public Library of Science, 3(7)*(e309)

Ells, C. (2003). Foucault, feminism, and informed choice. *Journal of Medical Humanities, Vol. 24, No.3/4*

Emerson, R.M., Fretz, R.I., Shaw, L.L. (1995). *Writing Ethnographic Fieldnotes.* Chicago: The University of Chicago Press

Epstein, S. (2007). *Inclusion: The politics of difference in medical research.* The University of Chicago Press

Ezzy, D. (2002). *Qualitative analysis*. London: Routledge

Faden, R. R., & Beauchamp, T. L. (1986). *A history and theory of informed consent.* Oxford University Press

Falk, A., Szech, N. (2013). Morals and Markets. *Science*. 340: 707 - 711

FDA. (2009a). *Institutional review boards and protection of human subjects in clinical trials.* Retrieved October 20, 2010, from http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm164171.htm

FDA. (2009b). *Recruiting study subjects- information sheet.* Retrieved October 10, 2010, from http://www.fda.gov/RegulatoryInformation/Guidances/ucm126428.htm

FDA, (2011). A Guide to Informed Consent - Information Sheet. Guidance for Institutional Review Boards and Clinical Investigators. Retrieved on November 12, 2012 from http://www.fda.gov/RegulatoryInformation/Guidances/ucm126431.htm

Fetterman, D.M. (2010). *Ethnography Step by Step*, 3rd ed. Thousand Oaks, CA: Sage

Fisher, J. A. (2007). "Ready-to recruit" or "ready-to-consent" populations? informed consent and the limits of subject autonomy. *Qualitative Inquiry, 13*(6)

Fisher, J. A. (2009). *Medical research for hire.* Rutgers University Press.

Fontana, A., Frey H.J. (2008). The interview: from neutral stance to political involvement. In N.K. Denzin, Y.S. Lincoln (eds.), *Collecting and interpreting qualitative materials 3rd ed.* Sage Publications.

Fox, R. and Swazey, J. (1984). Medical morality is not bioethics – medical ethics in China and the United States. *Perspectives in Biology and Medicine*, 27, 337–61.

Galvin, J.E., Meuser, T.M., Boise, L., Connell, C.M. (2009). Predictors of physician referral for patient recruitment to Alzheimer disease clinical trials. *Alzheimer disease & associated disorders vol 23, 352 – 356*

Germain, C. P. (2001). Ethnography the method. *Nursing research: A qualitative perspective* ()

Getz, K. (2004). Survey of 1,170 adults at the Clinical Trial Congress in Philadelphia, Institute for International Research, February

Glesne, C. (2006). *Becoming qualitative researchers: An introduction.* Boston: Allyn& Bacon

Guba, E.G. (1990). The alternative paradigm dialog. In E.G. Guba (Ed.), *The paradigm dialog* (pp. 17-30). Newbury Park, CA: Sage

Guba, E.G. and Lincoln, Y.S. (1998). Competing paradigms in qualitative research. In N.K. Denzin & Y.S. Lincoln (Eds.), *The landscape of qualitative research* (pp, 195-220). Thousand Oaks, CA: Sage

Gordon, E. J., & Wolder Levin, B. (2008). Contextualizing ethical dilemmas: Ethnography for bioethics. In L. Jacoby, & L. A. Siminoff (Eds.), *Advances in bioethics volume 11, empirical methods for bioethics: A primer* () Elsevier.

Haidich, A.-B., Ioannidis, J.P.A. (2001). Patterns of patient enrollment in randomized controlled clinical trials. *Journal of Clinical Epidemiology 54, 877-883*

Harper, D. (1992). Small N's and Community Case Studies. In C. C. Ragain, H. S. Becker (eds.), *What is a case? Exploring the Foundations of Social Inquiry* (pp. 139-158). Cambridge: Cambridge University Press

IBM Institute for Business Value. (2003). Delay no more: Improve patient recruitment and reduce time to market in the pharmaceutical industry. Retrieved October 23, 2012 from http://www-935.ibm.com/services/us/imc/pdf/ge510-3320-02.pdf

ISR Reports.(2012).Optimizing patient recruitment in clinical trials. Retrieved October 23, 2012 from http://www.isrreports.com/industry-reports/the-state-of-patient-recruitment

Jorgensen, D.L. (1989). *Participant observations: A methodology for human studies.* Newbury Park, CA: Sage

Joseph G, Dohan D. (2009). Diversity of participants in clinical trials in an academic medical center: the role of the 'Good Study Patient?'. *Cancer.* 115(3):608-15

Katz, J. (1988). A theory of Qualitative Methodology: The System of Analytic Fieldwork. In R. M. Emerson (ed.), *Contemporary field research: A collection of readings* (pp.127-148). Prospect Heights, Ill.: Waveland

Koch, T., & Harrington, A. (1998). Reconceptualizng rigour: The case for reflexivity. *Journal of Advanced Nursing, 28*(2), 882-890.

Kola, I. & Landis, J. (2004). Can the pharmaceutical industry reduce attrition rates? *Nature Reviews Drug Discovery 3,* 711-716

Krall, R.L. (2011). State of the controlled clinical trial enterprise in the United States. *Clinical Pharmacology& Therapeutics 89-2,* 255-228

Kvale, S. (1996). *InterViews: An introduction to Qualitative Research Interviewing*. London: Sage Publications.

Kye, S.H., Tashkin, D.P., Roth, M.D., Adamsb, B., Nie, W-X., Maoa, J.T. (2009). Recruitment strategies for a lung cancer chemoprevention trial involving ex-smokers. *Contemporary Clinical Trials 30,* 464–472

Lederer, S. E. (1995). *Subjected to science: Human experimentation in America before the Second World War*. The Johns Hopkins University Press

Leiter, K. (1980). *A primer on ethnomethodology*. New York: Oxford University Press

Light, D. and McGee, G. (1998). On the social embeddedness of bioethics. In DeVries,R. and Subedi, J. (Eds.) *Bioethics and Society*. New Jersey: Prentice Hall.

Lincoln, Y.S., Guba, E. (1987). Ethics: the failure of positivist science. *Review of Higher Education, 12,* 221-240

Madden, R. (2010). *Being Ethnographic: A guide to the theory and practice of ethnography*. London: Sage Publications

Mansour, E. G. (1994). Barriers to clinical trials: Part III: Knowledge and attitudes of health care providers. *Cancer. 74: 2672–2675*

Mayan, M.J. (2009). *Essentials of Qualitative Inquiry.* San Francisco, CA: Left Coast Press

Mcdonald, A.M., Treweek, S., Shakur, H., Free, C., Knight, R., Speed, C., Campbell, M.K. (2011). Using a business model approach and marketing techniques for recruitment to clinical trials. *Trials 12:74*

Miles, M.B., Huberman, A.M. (1994). *Qualitative Data Analysis.* 2nd ed. Sage Publication

Miller, F. G. (2010). Consent to clinical research. In F. G. Miller, & A. Wertheimer (Eds.), *The ethics of consent: Theory and consent* Oxford University Press.

Mintz, C. (2010). Social media's impact on clinical trial enrollment. *Life Science Leader* November

Morse, J. M. (1986). Qualitative and quantitative methods: Issues in sampling. In P. Chinn (Ed.), Nursing Research Methodology: Issues and Implementation (pp. 181-193). Rockville, MD: Aspen.

Morse, J. M., & Field, P. A. (1995). *Qualitative research methods for health professionals* (2nd ed.) Thousand Oaks, CA: Sage.

Morse, J. M. (1999). Qualitative generalizability. *Qulitative Health Research, 9*(5)

Morse, J. M., Barrett, M., Mayan, M., Olson, K. & Spiers, J. (2002). *Verification strategies for establishing reliability and validity in qualitative research.* Retrieved October 20, 2010, from http://www.ualberta.ca/~iiqm/backissues/1_2Final/html/morse.html

National Institute of Health. (n.d.). Understanding Clinical Trials, retrieved June 6th, 2012 from http://www.clinicaltrials.gov/ct2/info/understand

NIH Revitalization Act (1993). Retrieved September 20, 2012 from http://grants.nih.gov/grants/funding/women_min/women_min.htm

Office of Inspector General. (2000). *Recruiting human subjects: Pressures in industry sponsored clinical research.* Retrieved October 10, 2010, from http://oig.hhs.gov/oei/reports/oei-01-97-00195.pdf

O' Meara, A. (2009). *Chasing medical miracles: the promise and perils of clinical trials.* New York: Walker& Company

O' Reilly, L. (2009). *Key concepts in Ethnography.* London: Sage Publications

Papworth, M. (1967). Human guinea pigs. Boston: Beacon Press

Patton, M. Q. (1999). Enhancing the quality and credibility of qualitative analysis. *Health Service Research, 34*(5)

Paul, S.M., Mytelka, D.S., Dunwiddie, C.T., Persinger, C.C., Munos, B.H., Lindborg S.R., Schacht, A.L. (2010). How to improve R&D productivity: the pharmaceutical industry's grand challenge. *Nature Reviews Drug Discovery, 9, 203-214*

Peters-Lawrance, M.H., Bell, M.C., Hsu, L.L., Osunkwo, I., Seaman, P., Blackwood, M., (…), Minniti, C.P. (2012). Clinical trial implementation and recruitment: Lessons learned from the early closure of a randomized clinical trial. *Contemporary Clinical Trials 33(2):*291-7

Petryna, A. (2009). *When experiments travel.* Princeton University Press.

Pharma Live blog. (January 21, 2009). *Social networking meets patient recruitment.*, April 25, 2012, from http://blog.rddirections.com/index.php/2009/01/21/social-networking-meets-patient-recruitment/

Rajan, K.S. (2006). *Biocapital: The constitution of postgenomic life.* Duke University Press

Redfearn, S. (2012). First FDA draft guidance on social media leaves clinical trials industry waiting for more. *Center Watch Weekly,* January 9.

Rimer, B.K., Schildkraut, J.M., Lerman, C., Lin, T.H., Audrain, J. (1996). Participation in a women's breast cancer risk counseling trial: who participates? Who declines? *Cancer Vol. 77, No. 11,* 2348-2355

Robley, L.R. (1995). The ethics of qualitative research. *Journal of Professional Nursing, 11 (1),* 45-48

Rubin, H.J., Rubin, I.S. (2005). *Qualitative Interviewing: the art of hearing data* 2nd ed. Sage Publications

Sandel, M. (2012). *What money can't buy: the moral limits of markets.* Allen Lane

Sandelowski, M. (1995). Sample Size in Qualitative Research. *Research in Nursing and Health, 18 (2),* 179-183.

Savage, J. (2000). Ethnography and health care. *BMJ, 321 (7273),* 1400-1402.

Silverman, Ed. (2012). Pfizer, Social Media & Clinical Trials: Lipset Explains. An interview retrieved November 4, 2012 from http://www.pharmalot.com/2012/03/pfizer-social-media-its-clinical-trial-lipset-explains/

Smith, K.E. (2005). Problematising power relations in 'elite' interviews. *Geoforum 37 (2006),* 643–653

Spencer, J. (2001). Ethnography after postmodernism. In P. Atkinson, A. Coffey, S. Delamont, J. Lofland and L. Lofland (eds.), *Handbook of Ethnography.* London: Sage

Spradley, J.P. (1978). *The Ethnographic Interview.* Wadsworth, Cengage learning

Steinbrook, R. (2006). Compensation for injured research participants. *New England Journal of Medicine, 354*(18)

The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. (1979). *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*. Washington, DC: Department of Health, Education, and Welfare.

Treweek, S., Mitchell, E., Pitkethly, M., Cook, J., Kjeldstrøm, M., Taskila, T., (…), Jones, R. (2010). Strategies to improve recruitment to randomised controlled trials (Review). *The Cochrane Library, Issue 1.*

Trussell, J.C., Christman, G.M., Ohl, D.A., Legro, R.S., Krawetz, S.A., Snyder, P.J. (), Zhang, H. (2011). Recruitment challenges of a multicenter randomized controlled varicocelectomy trial. *Fertility and Sterility. Vol. 96, No. 6.* 1299-1306

Yeager, P.C., Kram, K.E. (1990). Fielding Hot topics in cool settings: The study of corporate ethics. *Qualitative Sociology 13 (2)*, 127-148.

Watson, J.M., Torgerson, D.J. (2006). Increasing recruitment to randomized trials: a review of randomized controlled trials. *BMC Medical Research Methodology*, 6:34

Werner, O., Schoepfle, G.M. (1987). *Systematic fieldwork: Foundation of ethnography and interviewing* (Vol. 1). Newbury Park, CA: Sage.

Wolcott, H.F. (2005). *The Art of Fieldwork*, 2nd ed. AltaMira Press

Wolcott, H. F. (2008). *Ethnography: A way of seeing* (2nd ed.) AltaMira Press.

Wolf, Z. R. (2006). Ethnography: The method. In P. Munhall (Ed.), *Nursing research: A qualitative perspective* 4th ed. (pp. 293-330). Boston: Jones & Bartlett.

Wolpe, P. (1998). The triumph of autonomy in American bioethics: a sociological view. In DeVries, R. and Subedi, J. (Eds.) *Bioethics and Society*. New Jersey: Prentice Hall.

Appendix A: UMN IRB approved informed consent forms

CONSENT FORM- INTERVIEW

Study title: "We get patients": Understanding the culture of patient recruitment organizations

You are invited to be in a research study on patient recruitment for clinical trials. You were selected as a possible participant because you work with patient recruitment. We ask that you read this form and ask any questions you may have before agreeing to be in the study.

This study is being conducted by Elita Poplavska. She is a graduate student in the Social and Administrative Pharmacy program at the University of Minnesota. The results of this study will be included in her PhD dissertation.

Background Information

Human participant recruitment for clinical trials is crucial for new pharmaceutical development and has been an ongoing challenge for clinical researchers. The purpose of this study is to learn about patient recruitment process, how individuals deal with the various regulations, and what challenges you face on a daily bases.

Procedures:

If you agree to be in this study, I will interview you for 30 to 60 minutes in a place convenient to you. I will ask you questions about your experiences working with research participant recruitment. With your permission, the interview will be audio taped. The tapes will be erased after the interview is written down (transcribed) and your name will never be associated with the information obtained. During this interview you have a right to refuse to answer any question for any reason.

Risks and Benefits of being in the Study

The risk of being in the study is that you can feel embarrassed when talking to the researcher about your work activities and experiences. If you feel any discomfort, you are free to deny any answer during the interview.

There are no direct benefits to you as a participant in this study.

Compensation:

There are no costs involved in participating in this study. You will not be paid for your participation in this study.

Confidentiality:

The records of this study will be kept private. They will be kept in a locked file. Only I will have access to the records. The interviews will be recorded on voice recorder with your permission and written down (transcribed). The recorded files will be kept in a password protected computer. Also, the written interviews will be stored in a password protected computer to make sure that I am the only one to access it. The recorded files and the transcribed interviews will be kept until the end of this study and then they will be destroyed by me. The information obtained will be used only for educational purposes. I may publish the findings of the study. Names will not be mentioned. I will remove any information that would make it possible to identify you as a participant in this study.

Voluntary Nature of the Study:

Participation in this study is voluntary. Your decision whether or not to participate will not affect your current or future relations with the University of Minnesota or with your employer. If you decide to participate, you are free to not answer any question or withdraw at any time without affecting those relationships.

Contacts and Questions:

The researcher conducting this study is Elita Poplavska. You may ask any questions you have now. If you have questions later, **you are encouraged** to contact Elita Poplavska at popl0017@umn.edu, (612) 237-0315, or her advisor Prof. Linda M. Strand at lstrand1@medsmanagement.com, (952) 746-8185.

If you have any questions or concerns regarding this study and would like to talk to someone other than the researcher(s), **you are encouraged** to contact the Research Subjects' Advocate Line, D528 Mayo, 420 Delaware St. Southeast, Minneapolis, Minnesota 55455; (612) 625-1650.

You will be given a copy of this information to keep for your records.

Statement of Consent:

I have read the above information. I have asked questions and have received answers. I consent to participate in the study.

Signature: _____Date: _____

Signature of Investigator: _____Date: _____

CONSENT FORM- OBSERVATIONS

"We get patients": Understanding the culture of patient recruitment organizations

You are invited to be in a research study on patient recruitment for clinical trials. You were selected as a possible participant because you work with patient recruitment. We ask that you read this form and ask any questions you may have before agreeing to be in the study.

This study is being conducted by Elita Poplavska. She is a graduate student in Social and Administrative Pharmacy program at the University of Minnesota. The results of this study will be included in her PhD dissertation.

Background Information

Human participant recruitment for clinical trials is crucial for new pharmaceutical development and has been an ongoing challenge for clinical researchers. The purpose of this study is to learn about patient recruitment process, how individuals deal with the various regulations, and what challenges you face on a daily bases.

Procedures

If you agree to be in this study, I will observe you while you are working. I will not interrupt you. I might make notes while observing you.

Risks and Benefits of being in the Study

The risk of being in the study is that you may feel embarrassed or self-conscious while being observed. You are free to refuse to be observed at any time.

There are no direct benefits to you as a participant in this study.

Compensation

There are no costs involved in participating in this study. You will not be paid for your participation in this study.

Confidentiality

The records of this study will be kept private. Research records will be kept in a locked file. Only I will have access to the records. The notes I take during my observations will be stored in a password protected computer so that I am the only one who can access it. The information obtained will be used only for educational purposes. I may publish the findings of the study. Names will not be mentioned. I will remove any information that would make it possible to identify you as a participant in this study.

Voluntary Nature of the Study

Participation in this study is voluntary. Your decision whether or not to participate will not affect your current or future relations with the University of Minnesota or with your employer. If you decide to participate, you are free to not answer any question or withdraw at any time without affecting those relationships.

Contacts and Questions

The researcher conducting this study is: Elita Poplavska. You may ask any questions you have now. If you have questions later, **you are encouraged** to contact Elita Poplavska at popl0017@umn.edu, (612) 237-0315, or her advisor Prof. Linda M. Strand at lstrand1@medsmanagement.com, (952) 746-8185.

If you have any questions or concerns regarding this study and would like to talk to someone other than the researcher(s), **you are encouraged** to contact the Research Subjects' Advocate Line, D528 Mayo, 420 Delaware St. Southeast, Minneapolis, Minnesota 55455; (612) 625-1650.

You will be given a copy of this information to keep for your records.

Statement of Consent

I have read the above information. I have asked questions and have received answers. I consent to participate in the study.

Signature: _____Date: _____

Signature of Investigator: _____Date: _____

Appendix B: UMN IRB approved study participant recruitment text

My name is Elita Poplavska, I am a PhD student at the University of Minnesota Social and Administrative Pharmacy Program. For my doctorate thesis I am working on a project on patient recruitment for clinical trials. As part of my project I am interested to understand the process of clinical trial participant recruitment as well as what facilitates and hinders this process in your institution. I am calling to find out if you would be willing to participate in my research study and answer some interview questions.

Appendix C: Analytical categories with respective sub-categories and themes

1. **The art and science of recruiting patients**

    1.1. Types of patient recruitment companies
    1.2. Centralized patient recruitment
    1.3. "Consumerism is what drives our business"
    1.4. Data driven recruitment
    1.5. Patient recruitment as an art
    1.6. "We are not your regular recruitment firm": recruitment versus enrollment
    1.7. Money in patient recruitment
    1.8. "It is sponsors' fault"
    1.9. Saving sponsors' time and money

2. **"Sites do not work for us; they work for a sponsor"**

    2.1. Only sites can enroll
    2.2. Working with research clinics
    2.3. Sites don't always want to work with recruitment firms
    2.4. "Sites work for the sponsor": a sponsor needs to champion recruitment services
    2.5. Engaging sites
        2.5.1. Communication with sites
        2.5.2. Competitive advantage
        2.5.3. "We care about overall recruitment": educating research sites
        2.5.4. "Sites are too quick to exclude some patients"
    2.6. Selecting sites and patient recruitment
    2.7. Helpful services (for research sites)
        2.7.1. Unknown patients
        2.7.2. Eliminating unqualified patients
        2.7.3. Communication
        2.7.4. Relieving logistical burden
    2.8. Limitations of patient recruitment services (for research sites)
        2.8.1. Low quality referrals
        2.8.2. It is more work for us

3. **"We are not a clinic; they are not patients": communicating with patients**

    3.1. Patients are our stakeholders
    3.2. Providing good experience
    3.3. "What should they think or feel?": designing a marketing campaign

3.4. The target audience
3.5. "Patients who are willing at all times"
3.6. "Expanding the pool by non-proactive patients": patient databases
3.7. Promoting the benefits of participation
3.8. "Education leads to better compliance": communicating requirements for compliance
  3.8.1. Sharing information on a study
  3.8.2. Cultivating commitment
3.9. Screening patients over the phone
  3.9.1. Caring in exchange for information
  3.9.2. Nursing judgment
  3.9.3. Following the script when convenient
3.10. Controlling information
  3.10.1. "We know more than we tell"
  3.10.2. Sharing information online
  3.10.3. "We do not want them to think about other treatment options"

4. Recruiting "high quality" patients

4.1. "High quality candidates"
4.2. Economic factors
4.3. Right type of motivation
4.4. Educated patients
4.5. Local vs. central patient recruitment: the importance of the relationship between a patient and a site
4.6. Screening for "high quality" patients
  4.6.1. Call center
  4.6.2. Clinical research informational meetings