Spring 5-16-2016

Exploring Barriers to the Adoption of Pharmacogenomic Technology in the Clinical Setting by Clinical Healthcare Providers

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Submitted in partial fulfillment of the requirements for the degree of

Doctor of Philosophy

School of Health and Medical Sciences

Seton Hall University May 2016

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By

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_____ Date 3-17-16

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requirements for the degree of Doctor of Philosophy in Health Sciences
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ACKNOWLEDGEMENTS

I would like to gratefully thank all of those who contributed to my doctoral journey. The mentorship, guidance, and support provided by my committee were invaluable assets. I am honored to have had their counsel in designing and directing this study and truly reaped the benefit of their knowledge, experience, and constructive criticism.

I would specifically like to express my gratitude to my committee chair, Dr. Deborah DeLuca, for all of the time and effort that she put into every facet of this study. The breadth and depth of her knowledge and experience was never ending. Her courses were engaging and thought provoking and helped to pave the path for the research that would become the apogee of my journey. Thank you, also, to Dr. Terrence Cahill for encouraging me to join the scholarly conversation in new ways. Much of the depth and new insight from this work came out of a greater respect for investigating the qualitative and its ability to frame information. Dr. Genevieve Pinto-Zipp, thank you for zooming out from the technical, and inspiring me to really critically think about what it all means to the bigger picture. I thank each of you for your unique contributions, not only to this project, but to my scholarly development and personal growth.

I would also like to thank all of the other faculty and the students that provided me with valued feedback and insights, both at Research Forum and in all of the other places that our discourse took place. Your insights were greatly appreciated.

Finally, I'd like to thank my son, Shane, for his patience. From the days he joined me at Seton Hall to the nights that he missed me at home; even at his young age he has been as understanding and supportive as any adult could be. I hope one day that I can be as supportive to him in his endeavors as he has been to me, in mine.

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ABSTRACT

The changing landscape of healthcare in the US has created new questions about how to best provide cost-effective, individualized care. Personalized medicine and more specifically, pharmacogenomic technology have offered new tools for healthcare providers to use to increase the efficacy, safety, and cost-effectiveness of care. However, these tools are not being utilized to their predicted extent in the clinical setting. This study utilized Rogers' Diffusion of Innovations theory to investigate some of the reasons why. A multi-question survey, the PI-created, Pharmacogenomic Adoption Instrument (PAI) ©, was developed to assess the knowledge, attitudes and experience concerning pharmacogenetic technology in a spectrum of different healthcare providers and types, and was administered online. This study found both knowledge and attitude, overall, to be highly correlated to adoption likelihood. Lack of knowledge was the most frequently cited barrier to adoption. This study also found that the perception of clinical benefit, the potential for misuse and genetic discrimination, and the ability of providers to effectively explain, and patients to understand test results, were significant factors in making decisions about utilizing pharmacogenomic technology. Further, the study found that clinical setting and the availability of clinical training may affect the perceptions of compatibility and trialability. These findings suggest that knowledge may be a key requisite, but the most influential factors on the adoption process are likely related to direct observation of a benefit in the clinic, including successful patient communication and a positive perception of protections from misuse of patient data. Therefore, focusing on improvement of the mechanisms for these processes may help to improve the rate of clinical adoption.

Keywords and phrases: pharmacogenomic, precision medicine, healthcare technology adoption, genetic discrimination, clinical setting, patient data protection

Chapter I

INTRODUCTION

Background and Significance of the Problem

Historically, the practice of medicine has operated through trial and error. Patients were prescribed a treatment and if the treatment failed to work or if it caused severe side effects the patient was prescribed a new treatment. This process continued until a patient was allocated to a treatment that is both effective and safe for the patient to use. In his 1962 work, the Structure of Scientific Revolutions, Thomas Kuhn provides a framework for the mechanisms that bring about revolutionary change and scientific advancement. In what he termed a Paradigm Shift, the underlying central precepts of a scientific discipline must be re-written to account for a fundamental shift in the level of scientific understanding. Precision medicine and pharmacogenomics bring the promise of a new and more precise methodology for diagnosing and treating disease. As discussed by President Barack Obama, precision medicine offers a paradigm shift from the historical trial and error model of patient treatment (White House, 2015). Patient care has the potential to be vastly improved through the utilization of precision medicine and pharmacogenomic technology. Simple tests are able to identify predispositions and provide patient treatment with a level of precision and accuracy never before seen in the clinic. Although there are a number of challenges that need to be overcome, personalized medicine potentially offers a new paradigm in medicine, one which makes one-size-fits-all prescribing and trial and error methods obsolete. In the past decade there have been great advances in the development of genetic tests and great amounts of new correlational research that have identified target genes and markers that help to diagnose and treat disease based on specific differences in human genetic variation. Drug, biotechnology, and academic research organizations have been working

to generate more information about specific genes and their relationship to the effectiveness and safety of many drugs. The side effects of drugs can be dangerous and sometimes potentially deadly. Drug related deaths, due to adverse events are the sixth leading cause of mortality in the United States and it is estimated than around 100,000 people in the United States die, annually, from adverse drug reactions (Ng, Murray, Levy, & Venter, 2009) Based on the successful implementation of pharmacogenomic technology in clinical experimentation, it has been theorized that adverse drug reactions could be reduced to a fraction of their current occurrence (Phillips, Veenstra, Oren, Lee & Sadee; Anderson, 2007). Pharmacogenomic technology can provide prescribers and supporting healthcare providers the information that describes an individual's genetic make-up and how they are likely to react to certain drugs. This information and its use can greatly reduce adverse events due to drugs and greatly increase the probability of prescribing a drug in the correct dose that will work effectively for that patient (Crews, 2012).

While the amount of research into genomic biomarkers for disease has been increasing at a rapid rate and the number of pharmacogenomic tests available has increased significantly, the adoption of this technology in the clinic has not come close to keeping pace with the rate of scientific discovery (Hamburg & Collins, 2010). The literature has found that there are many different barriers that impede the path from the laboratory to the clinic, these range from potential philosophical ethical issues to a real lack of training and awareness among practitioners (Leufkens, 2004; Ventola, 2011). In addition to the improvement of the technology itself, several other factors have greatly increased the accessibility. One of the largest barriers of the past was the accessibility of information. Though in the past decade, the landscape of information availability how grown for clinicians, greatly (Marsh and McLeod, 2006). In the current landscape there are numerous databases and sources of information on genotype

associations to drugs, as well as information in the prescribing label of many drugs. The diversity of issues discussed in the literature in different niches, highlights the gap of what is perceived by healthcare providers to be the greatest barrier in translating pharmacogenomic technology from the labs into a standard practice in the clinic.

As the healthcare system in the United States continues to evolve, more and more emphasis has been focused on increasing the efficiency of healthcare delivery. Government health coverage providers, as well as private insurers have changed the way that they evaluate and reimburse for the cost of healthcare (Kaiser Family Foundation, 2014). Legislation, such as the Patient Protection and Affordable care act of 2010 have included measures that hold providers responsible for controlling the costs, as well as the improving the outcomes of their patients (Koh, 2010). To cope with the increasing demands, providers have turned to many new practices and technologies in an effort to reduce the number of return visits, increase the effectiveness of treatments and ultimately reduce the overall cost, while still increasing the effectiveness of treating patients. One promising young technology that has been growing for over a decade, but has yet to be fully utilized to its potential in the clinical setting is pharmacogenetic testing. Pharmocogenomic testing uses a patient's genetic composition to predict how well a drug will work for that patient and whether there are additional safety concerns, by comparing the individual's genotype to set of known genotypes that have been previously been found to have had poor efficacy or adverse events in other patients. A simple, one-time, blood test can provide a lifetime of predictive medical value in prescribing the safest and most effective treatments. Up to this point, medicine has, primarily, been practiced through trial and error. Patients have been prescribed a treatment based on a set of symptoms. Many diagnostic tests have been developed to confirm a patient's diagnosis, but not many tests can

predict how well a patient will respond to a specific treatment. One major problem with this system is that, in some patients, certain drugs will not work as expected. Even worse, other patients may have dangerous, and sometimes deadly, side effects. These side effects are termed "adverse drug reactions" and are a huge issue in medicine, as it is currently practiced, both to patient safety and an issue in the controlling of costs. Patient deaths in the U.S. that occur as a result from adverse drug events are the nation's sixth largest cause of mortality (Vora, Trivedi, Shah, & Tripathi, 2011). Many researchers have hypothesized that it is possible to reduce adverse drug reactions to a fraction of their current occurrence through the use of pharmacogenomic technology (Phillips, 2001; Anderson 2007). The paradigm shift to personalized medicine and pharmacogenomics can offer a novel, and more exact process for diagnosing and treating illness. Patient care can be made greatly more efficient and precise with the adoption of personalized medicine and pharmacogenomic technology. Great improvements have continued to be made in pharmacogenomic testing and in its application in medicine over the past decade. Many stakeholders have funded a great deal of research to improve the catalog of genomic markers and their relation to disease.

Though, while development of pharmacogenomic academic research has been progressing swiftly, the adoption of pharmacogenomic testing and supporting technology has not been utilized in the clinical setting at the same rapid rate (Hamburg, 2010). This poses the pivotal question, "why is this, potentially revolutionary, technology not being implemented more widely in practice?" when it offers the potential to greatly reduce adverse events, save lives and reduce the financial burden of costs associated with adverse drug reactions?

Problem Statement

In the practice of medicine, a trial and error approach has continuously been used to diagnose and treat patients. Physicians prescribe drugs, based on a set of symptoms with very little insight into how these drugs may affect an individual (Crews, 2012). This often leads to dangerous side effects and adverse events. Drug side effects can be very dangerous and, sometimes, potentially deadly. Drug related deaths due to adverse events are the sixth leading cause of mortality in the United States (Vora, Trivedi, Shah, & Tripathi, 2011). It is estimated than around 100,000 people in the United States die, annually, from adverse drug reactions (Ng, Murray, Levy, & Venter, 2009). In addition, the prescribed treatments often are only partially effective or not effective at all. Personalized medicine and pharmacogenomic technology offers the potential for a simple blood sample to predict how an individual will respond to a given treatment based on their unique genetic composition. This technology has the potential to offer healthcare providers a new tool that can help to predict what drugs and doses will work best for them and which drugs may have dangerous side effects. While this, potentially highly beneficial, technology is making great strides in the research laboratory, it is not being adopted at the same rate in the clinic (Hamburg & Collins, of 2010). There are a number of factors that may contribute to the lack of utilization of this paradigm-changing technology. While a number of studies have examined the potential for genetic testing as a tool in the clinic there are several differences between genetic testing and the use of pharmacogenomic technology. While genetic testing is very highly related to pharmacogenomic technology, it typically looks at a limited number of genetic markers and lacks the broader privacy and confidentiality concerns of pharmacogenomics, which examines an individual's entire genomic sequence (Goldman, 2005). Even the number of studies that have examined these issues in genetic testing is relatively small.

However, these studies are the closest insight available in many cases and are highly generalizable on a number of issues. Though, research that investigates pharmacogenomics, specifically, is decidedly warranted.

There are a number of theories that have been utilized to predict the nature of decision making in medical innovations. Three primary frameworks have been used to describe the mechanisms that have been studied in the process of understanding, accepting and utilizing new health advancements. They are the Diffusion of Innovation Theory, The Health Belief Model, and the Theory of Planned Behavior. Yet no one theory provides a comprehensive model that can predict and describe all of the findings that have been researched thus far in the adoption of pharmacogenomic technology. This paper will discuss the primary theories that have been applied to the model of adoption and how various components may relate to one another in an intra-theoretical model that accounts for a number of factors prevalent in the literature.

The Theory of Diffusion of Innovations may help to explain what factors are impeding the translation of this advancement in the clinical setting. Roger's 1967 Diffusion of Innovation Theory describes the way people, as a group, adopt technology (Rogers, 2010). The theory has been applied to many technologies that have emerged in and outside healthcare. This theory has strong applicability and may help to explain how and why the breach exists between the science and the practice. In a recent survey of US physicians, only 10% of those surveyed indicated that they felt sufficiently informed about the accessibility of pharmacogenomic technology and how to appropriately utilize it to aid diagnosis and determine the best course of therapy for patients (Stanek, Sanders, and Taber 2012). In the process of adoption of new technology there are key components that catalyze the process. Of these, are the initial attitudes and knowledge of the potential adopters (Rogers, 2010). When knowledge is insufficient or attitudes toward the

technology are unfavorable adoption of the technology is halted. The next section will propose a review of the literature that examines barriers to the adoption of pharmacogenomic technology as perceived by healthcare providers in the frame of Diffusion of Innovation, as well as in the frame of the Health Belief Model. The Health Belief Model is focused on explaining or predicting health behaviors by examining the attitudes of the individual. The Health Belief Model relies on the three core assumptions in an individual's beliefs that enacting a behavior will have a positive outcome, that it will help to avoid a negative outcome and that the individual has the requisite self-efficacy to enact the behavior with confidence. The idea of self-efficacy helps to explain why knowledge of pharmacogenomic testing is a key factor in the decision-making process (Bloss, 2011). However the theory lacks the breadth to explain the greater decision making process and how this mechanism relates to the diffusion of this new technology at the population level.

Need for this Study

The current literature indicates that there are a number of issues that may affect the adoption of phamacogenmomic technology as a whole; very few studies have investigated these issues in limited sub-groups of the healthcare provider population, and often in a narrow context. This study would be the first to examine a wide breadth of healthcare providers and the cumulative list of factors that emerges from the literature, at this time. As mid-level providers and physician extenders take a larger role in the healthcare setting, their feedback becomes increasingly significant to the question of utilization, overall. The literature also strongly suggests that addressing these issues could have a large impact on the adoption of pharmacogenomic tests and thus, greatly improve the quality and cost-effectiveness of care for many. Determining which specific factors have an effect on the adoption of pharmacogenomic technology and what

knowledge may be lacking could yield strong guidance in planning interventions to improve knowledge in the clinical setting. As discussed earlier, the research into knowledge in this area has been specific to a narrow context and often limited to a single group of healthcare providers. Investigating healthcare providers, as a whole population, would allow differentiation of the groups in a controlled comparison that could contrast the differences in knowledge among practitioner type and specialization.

Purpose of the Study

Though the literature has identified many barriers that may be prohibiting the use of pharmacogenomic testing, only a small number of studies have been done to empirically investigate these factors and what their relationship is to adoption of this technology in clinical practice. Studies, such as Condit's 2003 work, have investigated some factors, but only in one group of providers, in this case physicians. Healthcare providers such as physician assistants, nurse practitioners and others have a direct role in patient prescribing and these groups perceptions of many of the issues discussed have yet to be captured in a an empirical study. This study would allow for an overall assessment of the composite barriers that emerged from the present literature. It will also allow for a direct comparison between groups with the questions standardized to a single instrument, allowing for an "apples to apples" comparison of perception between provider groups.

Research Questions

Previous scholarly work has examined the different types of clinical providers independently. This study will aim to compare differences in adoption likelihood and the related factors that comprise the domains of knowledge and attitude constructs. The theoretical model predicts that overall knowledge and attitude are core constructs in the path to adoption. Thus, these constructs were primary factors in research objectives. Since little is known about the role of provider type or therapeutic specialization of adoption behaviors the four primary questions were addressed:

- RQ1. Which factors are most strongly related to a resistance in the adoption of pharmacogenomic technology by healthcare providers in the clinic and do differences exist among the nominal level variables?
    - RQ1a) Will a relationship exist between likelihood to adopt and demographic factors (age, gender, years of experience)?
    - RQ1b) Will a significant difference exist in likelihood to adopt among different therapeutic areas of practice (e.g. oncology, cardiology, primary care)
    - RQ1c) Will a significant difference exist in likelihood to adopt among different types of practitioners (e.g. MD, NP, PA, etc.)?
- RQ2. Is there a relationship between knowledge of pharmcogenomic testing and the likelihood of adoption of pharmaocegenomic testing by healthcare providers in the clinical setting?
- RQ3. Is there a relationship between attitudes (will be measured on a continuum from strongly positive to strongly negative) toward pharmacogenomic technology and the likelihood of adoption of pharmaocegenomic testing by healthcare providers in the clinical setting?

- RQ4. What factors will best predict the probability of adoption of pharmacogenomic technology in clinical practice?

Research Hypotheses

Based on the research questions that were developed around the emergent gaps in the literature the following hypotheses address the predicted relationships among the factors described, respectively.

- H1a: A significant relationship exist between likelihood to adopt and demographic factors (such as age and years of experience)
    - H1b : A significant difference will exist in likelihood to adopt among different therapeutic areas of practice.
    - H1c : A significant difference will exist in likelihood to adopt among different types of practitioners.
- H2: A significant relationship will exist between knowledge of pharmcogenomic testing and the likelihood of adoption.
- H3: A significant relationship will exist between attitudes toward pharmcogenomic testing and the likelihood of adoption.
- H4: A statistically significant regression model will describe the factors that predict likelihood of adoption.

Chapter II

REVIEW OF RELATED LITERATURE

Introduction

The literature has suggested that there are many different barriers that impede the path from the laboratory to the clinic. These range from potential philosophical ethical issues, to a lack of training and awareness among practitioners (Van Delden, 2004; Ventola, 2011). The literature also shows that there is a great deal of diversity in what different groups of providers consider to be the primary barrier to adoption. What is more, most of the published works on barriers to adoption are expert opinions or position papers. Very few studies have been done to empirically assess what actual healthcare providers perceive to be the largest obstacle in implementing this technology or what other factors may be deterrents to them. Understanding the underlying concerns of healthcare providers in this area is a key step to catalyzing the utilization of this technology to its potential.

Knowledge has been recurrently cited as a factor that may be crucial to the adoption of pharmacogenomic technology (Bonter, 2011; Ghaddar, Cascorbi, & Zgheib, 2011; Higgs, 2008). Therefore, a lack of knowledge can logically be viewed as a barrier. One survey in physicians showed that, indeed, in all of the physicians that were surveyed, the vast majority had a desire to utilize pharmacogenomic technology to improve the effectiveness of their practice, however only 10% felt that that had an adequate enough understanding of pharmacogenomics to utilize and understand pharamocogenomic tests in practice (Stanek, 2010). Knowledge of pharmacogenomic testing is a multi-faceted concept that is made up of many components, some which have been discussed in the current literature, and others, which have not. The effects of

knowledge may be rooted in awareness issues or could range to issues such as self-efficacy in understanding and executing test and their results in the clinic (Bonter, 2011). Empirically determining the role and relationship of pharmacogenomic knowledge in the adoption of pharmacogenomic technology in a diverse group of healthcare providers is an important step in developing a model that will help to predict which educational factors would be most important in training materials. This would be an important first step in catalyzing the adoption and enabling the utilization of this technology.

Attitude is another category of factors that encompasses a wide variety of issues that may inhibit the adoption of pharmacogenomic technology by healthcare providers. Attitudes that are favorable are produced by the benefits or advantages of an innovation, while unfavorable attitudes come from concerns over possible negative consequences from the utilization of the innovation (Rogers, 2010). Issues such as concerns over the loss of privacy have been discussed extensively in the literature as being, potentially, of great concern (Goldman, 2005). A 2003 study of physicians only, found that found that the potential for discrimination was a major barrier in brining genetic testing into practice (Condit, 2003). The potential for misuse of a patient's genetic information could have great consequences for a patient. Negative attitudes toward pharmacogenomic testing may be related to the potential risk of genetic discrimination, or that a patient's genetic data could be used by health insurance providers to discriminate in insurance screening of patients, based on predispositions that may be detectable in their genetic code (Rogausch et al, 2006). Though, these types of risks have been well thought-out in and contemplated in the literature, not much work has been done to quantify the potential for these consequences in many settings. This may have potentially contributed to a host of fears and negative attitudes that could have a prohibitive effect in the adoption of pharmacogenomic

technology in the clinic. Case-based studies have found that found that the potential for discrimination was determined to be a major barrier in implementing the technology in practice in a qualitative manner. However, Quantifying effects from issues such as this, that contribute to the larger picture attitudes toward adoption in the clinic is an important part of understanding what actions could be taken to improve the landscape and rate of adoption in the clinical setting.

The process of adopting of new technology in healthcare has been studied in many applications. When a technology offers significant potential to prevent illness or greatly improve patient outcomes, it is important to understand what steps need to be taken to initiate the use of a new technology in the clinic. When an existing technology has been introduced and offers the potential for a dramatic benefit, but has failed to be utilized to its full potential in the clinic, it is important to understand what factors are contributing to the failure to launch. Rogers Theory of Diffusion of Innovation has been used to study this dynamic in many types of technological advances. Rogers proposes that a core of factors determine the diffusion rate and the subsequent adoption of new technology by its potential users (Rogers, 2010). The primary factors that contribute to adoption are; First, the benefits and disadvantages of the technology. As mentioned the more positive attributes that the target adopting group perceives, the more likely they are to embrace they technology. Inversely, the more potential negative consequences, the more likely that group are to be deterred. Second, the channels of communication through which the innovation will be communicated, affect how the technology is perceived and thus how it will be received by the target adopting audience. Communication channels include a number of pathways that information about the innovation can be transmitted. These often determine the nature of the information that the target audience would receive. These channels of communication are described by Rogers as “any means by which messages get from one

individual to another" (Rogers, 2010). They include scientific publications, peer feedback, institutional policies, and greater media attention, in addition to many other channels. Third, time and finally, the macro-context of the social system are also factors that dictate the tone and breadth of information that is received by potential adopters in a population. The Diffusion of Innovation Theory posits that this process is then further characterized by demographic. Rodgers proposes that there are five primary group types of technology adopters. They are, first the innovators, then the early adopters, then the early majority, followed by the late majority and finally the laggards. These group labels help to portray different segments of the population in factions by their readiness to espouse new technology. It is proposed that adoption of new technology takes happens in a manner described by a typical bell shaped curve. 2.5% of the population will make up the first group of early adopters, these individuals are termed innovators. The 70% of the population will wait to gain feedback from individuals that have already had experience with the innovation before trying it. Finally, laggards make up the small remaining percentage of late adopters that will hold-out in adoption, until after the vast majority of the population has utilized and positively accepted the innovation (Rogers, 2010). The theory describes innovation in a five stage process that depicts contemplation and ultimate reception, by the target members of the population. These stages begin with knowledge of the innovation, then progress to persuasion, followed by decision, then implementation, and finally a confirmation of decision if the resulting implementation yields positive result (Rogers, 2010). In the knowledge stage exposure to new technology has occurred, but the group or the individual lacks the requisite knowledge of the technology and must seek and acquire the amount of knowledge that they perceive as being sufficient to advance to the contemplation and decision-making phase of the innovation adoption process. Rogers' model has been utilized in healthcare

technology numerous times and the model parallels the innovation to the scientific findings around the technology. By enacting the model in this setting, the parallel to the channels of communication and adoption are the transmission and acceptance of novel information in the scientific community (Berwick, 2003). This view of the dynamic has been used to equate the adoption of the new technology from science to practice as the acceptance of the advance in health service in the "community of practice" (Greenhalgh, 2004). While there is a great deal of other theory that supports the significance of this study, Rogers Theory of Diffusion of Innovation is the grounding dynamic that integrates the parts into a cohesive whole.

Theoretical Model and Framework:

Diffusion of Innovation Theory in Healthcare Technology

Rogers' theory of diffusion of innovation is based on the premise that new technology is received and adopted at different rates by individuals (Rogers, 2010). The theory proposes to explain the mechanisms for how and why technology spreads through cultures. The theory proposes that the four main factors determine the diffusion and adoption of new technology. These factors are the benefits and disadvantages of the technology, the channels of communication through which the innovation must be communicated, time and the macro-context of the social system. These channels of communication are described by Rogers as "any means by which messages get from one individual to another" (Rogers, 2010). Rogers proposes that the process relies on five groups of technology adopters. These are the innovators, the early adopters, the early majority, the late majority and the laggards. These group labels describe the readiness to accept new technology of individuals. The theory proposes that adoption of technology takes place through the population under a bell shaped curve. The first adoption of new technology is made by roughly 2.5% of the population; this group is termed the innovators.

The majority of adoption lies, roughly, in the middle 70% of the population, in terms of the amount of time in adopting new technology, but relies on cues from the innovators and early adopter group to mitigate risk and perpetuate the technology through communication channels. The theory also posits that individuals considering change move through five stages in the acceptance of a new innovation. These stages, in order, are knowledge, persuasion, decision, implementation, and confirmation. The first stage of an individual's contemplation is knowledge. In this stage an individual is exposed to new technology, but lacks knowledge of the technology and must acquire an amount of knowledge that they perceive as sufficient to contemplate decision-making of adopting the innovation. The second stage of adoption is the persuasion stage. In this stage, the individual has now gathered knowledge of the innovation, and it has piqued the interest of the individual enough that they seek to apply the knowledge. In the next stage, decision-making, the individual must now critically evaluate the advantages and disadvantages of the technology and determine its role in their circumstance. If the individual chooses to accept the innovation, then the technology or idea is implemented. When utilized in healthcare technology, Roger's model parallels the innovation to the scientific findings around the technology, and the channels of communication are equivalent to the transmission and acceptance of the scientific community (Berwick, 2003).

Rogers' characteristic S-shaped diffusion curve is often used to represent the relative rate of diffusion among the population. The curve suggests that the rate of diffusion begins slowly, then sharply rises once the early adopters have vetted the technology and it has diffused into the majority, followed by a tapering to a slower rate in the laggards. In populations the ascending curve corresponds to factors that relate to the adoption process. These are exposure, awareness, understanding, testing, utilization, and institutionalism. These factors correspond to

interpersonal factors at the individual level, as well. Those are attitude, knowledge, persuasion, decision and implementation. All of which would lead up to adoption or a non-adoption decision.

Greenhalgh equates the adoption of the new technology from science to practice as the acceptance of the advance in health service in the "community of practice" (Greenhalgh, 2004). Jenkins et al tested the framework of Roger's theory in genomic technology adoption in a study of 1035 family physicians. The study found that knowledge and education of the technology was a key catalyst in increasing the rate of adoption (Jenkins, 2013).

According to Rodgers, adoption of new technology requires the a vanguard of "innovators" that while time is a factor in adoption, catalysts such as attitudes, knowledge and perception of barriers may increase or decrease the rate of adoption in certain groups. Knowledge of an innovation may be accurate or inaccurate. Often an inaccurate understanding of an innovation may be based on previously factual information that has since changed with time. Other times false assumptions may be based on accurate information that is misapplied or not accurate within the context it is being considered in (Rogers, 2010). Attitudes towards innovation are more complex, and often have some relationship to knowledge. They are, typically, a more visceral reaction to an innovation. Favorable attitudes are typically driven by the benefits or advantages of an innovation and unfavorable attitudes are driven by concerns over the implementation of the innovation (Rogers, 2010). To catalyze adoption, knowledge needs to be sufficient and support a favorable attitude. In pharmacogenomic adoption there are many issues that have existed previously and been discussed, some of which have been addressed in practical terms and some of which may still be valid concerns. Many issues that were previously prohibitive have since changed in the landscape; however, perceptions of the previously held

notions may still persist in the population of healthcare providers. Cost, for example, has long been discussed as a concern in implementing pharmacogenomic protocols in the clinic. In recent studies, cost has been cited as a barrier to adoption of this technology. However cost has been decreasing at a steady rate over the past decade. While this issue represents attitude at face value, it is exemplary of the idea that attitude is frequently tied to knowledge in the adoption paradigm.

Relative Advantage

When a provider is engaging the decision to choose to utilize an innovation for a specified purpose, Roger's theory posits that it should provide some form of benefit for the task considered (Rogers, 2010). More precisely, the technology should endorse a relative advantage over other available options; in this case this would include the technology that is the current standard of care utilized in the clinical setting. The perception that technologies produce this advantage, is related to how likely they are to be adopted. Though, what defines an advantage is specific to the user and not always the same factors in all sub-groups. Lower costs, improved efficacy, increased safety, reduction of time spent on cases can all be relative advantages to different users.

Compatibility

Compatibility is another factor that is considered in Roger's diffusion of innovation theory. Compatibility describes the extent that the components of the innovation integrate with the details of the context and setting in which the technology is being considered for use in. To integrate successfully, the details of the technology must be compatible with the conditions and needs of the proposed setting for use (Rogers, 2010). If the technology is too cumbersome, or if it does not fit with constraints of time, resources, or process it becomes far less likely to become

adopted. In addition to being compatible with the process, and time constraints of the setting, compatibility may also describe the extent that an innovation is compatible with an individual's interpersonal constitution. If an innovation violates the inherent personality characteristic or core values of a user there may be an individual incompatibility with the technology.

Complexity

In making the decision whether or not to adopt an innovation, the complexity of the innovation is identified by Rogers as a key concept in decision making (Rogers, 2010). The complexity of an innovation can be defined as how difficult and how intricate the innovation is to understand and utilize. The more complex an innovation is to explain and understand, the less likely it is to be internalized and utilized. Likewise, if the components to the innovation are complex to execute in practice the innovation is less likely to be adopted. The concept of complexity also ties back to the concept of relative advantage. Users of a technology need to be able to understand the advantages and value of utilizing the technology in practice. If the benefits and advantages are too complex to quantify and explain or understand, then the technology will not likely be adopted.

Observability

One of the key concepts in Roger's theory is that of observability. Observability is the concept that describes how visible use of the innovation is to the potential adopter (Rogers, 2010). Observability describes how accessible the use of the technology is for potential new users to observe to make assertions about the compatibility and relative advantage of the technology in practice. Observing the technology in practice gives potential adopters an opportunity to vicariously gather information used to make determinations and assumptions about the technology, as well as ask questions about the technology to current users.

Observability is a key factor that relates to awareness and the early knowledge. This concept has been identified as one of the key components in communications channels. Communication among peers about a new technology and vicarious learning are highly related to the dispersion of new technology.

Trialability

Another concept in the adoption process is the concept of trialability. Trialability is the extent that a user can utilize the technology on a test basis (Rogers, 2010). Innovations that have many smaller components offer new users the opportunity to participate in their utilization without having to commit to adoption in full. Using smaller components and experiencing the outcome of an innovation on a smaller scale gives new users the opportunity to test the technology and validate assumptions about compatibility and relative advantage before adopting the technology as practice. Technology that has a high buy-in, or rather, that requires a larger scale commitment offers less trialability, and thus has a higher barrier to adoption, thus must be perceived better in terms of relative advantage, compatibility, and complexity.

Health Belief Model

In considering the adoption of new medical technology the Health Belief Model (HBM) is a common theoretical frame that is used to understand the relationship between information and behavior change. The Health Belief Model is one of the most commonly utilized theories in health education and promotion (Glanz, Rimer & Lewis). Dating back to the 1950's the original incarnation of the HBM was developed to help determine why new health screening programs were not being successfully adopted (Hochbaum, 1958). The HBM is driven by the underlying concept that health behavior is determined by a number of factors that create an individual's perception of disease and how they relate these perceptions to the possibility of developing the

disease and strategies for prevention and treatment (Hochbaum, 1958). Many components of the health belief model are used to predict how information may initiate action and what information is needed by the receiver to initiate the utilization of new technology. Though the Health Belief Model is most frequently used to predict the behavior of patients in utilizing information and technology for health intervention, in some cases it has also been used to help to predict the behavior of healthcare providers in utilizing new technology as a channel to make the innovation available to the patient (Bloss, 2011). A key component of the health belief model is called a "cue to action", this is an information providing event that causes the receiver of that information to consider the potential value of the innovation or interventional technology that could cause the receiver of that information to make decisions about the future adoption of behaviors regarding the technology (Hochbaum, 1958). In genomics the illness of a family member is often a cue to seek information about a disease that may have an impact on the individual (Graham, 2001). Maternal breast cancer and BRCA gene variants are a great example of this. In this case, the beliefs of the healthcare provider regarding the value of genomic testing in treating and preventing disease would be related to the amount of information acquired, in conjunction, with the perception of risks associated with the innovation and attitudes related to the individual, cultural context and local or institutional practices that reflect the beliefs about the innovation. In this case, the healthcare provider must first acquire the information needed to fully understand and provide the technology to patients they may benefit. While this type of macro relationship may be described by Roger's Diffusion of Innovation Theory, integrating components from the Health Belief Model also allows for a finer discernment of the concepts that drive decision making at the individual level. While the Diffusion of Innovation Model focuses on communication channels in the larger context, and the available knowledge of the collective

group, the Health Belief Model allow an assessment from a lens focused more toward individual compatibility with adoption of the technology and the execution of the actionable behaviors associated (Carpenter, 2010). One of the key constructs of the Health Belief Model, as it is applied in this instance is the concept of Coping Style, this aspect describes how and individual deals with information that carries potential predictive values of negative outcomes (Ogden, 2012). When individuals encounter this type of information some seek further information to make sense of and contextualize the new information that they have acquired. Other individuals may have personality types that tend to avoid the serious new information, or downplay its significance. It is anticipated that those who are likely to seek new information would be more likely to adopt new technology, such as pharmacogenomic testing. Locus of Control and Self-Efficacy are two highly related constructs considered by the Health Belief model that may have significant predictive value when considered in the context of adopting pharmacogenomic technology (Ogden, 2012). Locus of Control is the extent to which individuals perceive to have control over their own decisions and the extent to which outcomes are related to those decisions. In the Health Belief model an individual needs to perceive that their decisions are likely have an impact on the outcome to become inclined to make the decision to adopt pharmacogenomic technology (Ogden, 2012). Therefore, it is anticipated that those individuals that have had experiences in which they have observed efficacy in genetic testing or other similar related predictive models will be more likely to have a disposition that favors the use of pharmacogenomic technology in future clinical settings. Self-efficacy is the internalized component of Locus of Control. While Locus of Control describes an individual's overall perception of their ability to impact outcomes, Self-Efficacy is their own innate confidence in their own abilities to effectively impact outcomes. Self-efficacy is a highly important construct

that is directly related to one's own perception of knowledge. Typically, high levels of knowledge and experience with content or subject matter correlate to higher levels of self-efficacy. That is, the more an individual has learned and practiced a behavior, the more likely they are to believe that they possess the requisite abilities to understand and execute related skills in a future context. Self-efficacy is a concept that is frequently studied in health technology adoption models that require an individual to process complex and/or a large volume of information. There is a great deal of complexity in the information considered for the adoption of pharmacogenomic testing. Therefore, it is expected that greater levels of prior exposure to genomic technology and greater levels of knowledge will correlate to higher levels of self-efficacy and thus a higher likelihood of adoption of pharmacogenomic technology in clinical practice.

Barriers to adoption of pharmacogenomic technology

The successful adoption of pharmacogenomic technology, in clinical practice, requires overcoming of the barriers to utilization that exist in the clinic. The term barrier is often used to describe a number of issues, concerns or obstacles that impede adoption of this technology. Sometimes these barriers are tangible in nature and may need to be addressed with tangible solutions. In the hypothetical case that cost of testing was a tangible barrier to adoption, funding would need to be allocated to ameliorate the lack of available funds needed. Other times, what are deemed to be barriers are the perceptions of the target adopter, which may be inaccurate or not up to date with current realities of the technology. In the case that a healthcare provider perceives cost to be a barrier, the perception of cost must be compared to the current expectations of cost and available funding to see if the perception is accurate. Only then can a

determination be made on what the solution is. If the perception of cost is inaccurate or outdated, then the potential solution would be to increase awareness of the current cost of technology. To empirically identify what these barriers actually are and determine if they differ by therapeutic specialization, geographic location, or other factors, an assessment of what the primary barriers are perceived to be needs to exist. Though, no U.S. study has done this in all healthcare providers, a 2011 study surveyed oncologists, cardiologists and family physicians in Canada to determine what the greatest perceived barriers were to the adoption of this technology (Bonter, Desjardins, Currier, Pun, & Ashbury, 2011) The study found that the primary perceived barriers to the adoption of pharmacogenomic technology and the practice of personalized medicine were; the lack of clinical guidelines (60% reported to be one of the "main barriers"), limited provider knowledge and awareness (57% reported to be one of the "main barriers"), lack of evidence-based clinical information (53% reported to be one of the "main barriers"), cost of tests prohibitive (48% reported to be one of the "main barriers") These findings are in agreement with what Gurwitz proposes are the primary barriers to pharmacogenomics program development in the European Union (Gurwitz, 2009). Gurwitz cited health professional unfamiliarity, unclear cost-effectiveness, and an unclear regulatory framework as being some of the primary challenges of translating research findings into clinical practice (Gurwitz, 2009). Anderson et al, provide an Australian perspective, which cites that perception of a need for privacy and confidentiality and a lack of formal guidelines are the primary issues, locally (Anderson, 2012). In agreement, with this notion, McKinnon and colleagues propose that one of the biggest challenges to clinical providers is developing consistent clinical protocols that utilize genomic test results to guide clinical practice (McKinnon, Ward, & Sorich, 2007). McKinnon's critical analysis of barriers identified cost-

effectiveness of tests, ethical concerns over the use of DNA, and a gap in technical knowledge of the subject matter. A 2003 study by Condit et al looked at the some of the perceived barriers in the general population and aimed to assess the understanding of individuals, as it related to this barrier. The study found that found that the potential for discrimination was a major barrier in implementing the technology in practice (Condit, Templeton, Bates, Bevan, & Harris, 2003). Indeed, privacy concerns are one of the thematically discussed concerns in the attitudes toward adoption. The sensitive nature of genetic information and the potential impact that it could have on an individual is a major concern in the literature, which has been brought up, philosophically, by many authors. The Clinical Pharmacogenomics Implementation Consortium (CPIC) conducted two survey studies to assess unmet needs in phamacogenomic testing (Relling & Klein, 2011). The focus of this study related primarily to scientific issues in translating scientific findings, specifically, into applications. While the studies primarily dealt with scientific issues that limited testing capabilities, the surveys also had some findings had implications about the suggested challenges to the translation of pharmacogenetics in the clinical setting. One of the findings was that there was an absence of guidelines of the processes to interpret genotype information and a clear path on how to translate that genetic information into clinical practice applications. This finding was coherent with the findings of others, such as Bonter in which a clear framework was perceived as a barrier to the adoption. The study also found that providers may be resistant to considering pharmacogenetic information when making practice decisions. While the specific details of why were not defined as clearly as in other studies, the themes of cost and reimbursement were re-iterated in these findings (Relling & Klein, 2011).

Haga and colleagues also performed a survey study in 597 primary care physicians in 2012. The study found that primary care physicians aim to function as a primary point of

delivery of pharmacogenomic technology, but that they recognize that a deficit of sufficient knowledge and experience is a limiting factor (Haga, 2012). The findings of the study suggest that educational curricula, training and resources have failed to progress, and do not contain an adequate amount of information to satisfy the needs of primary care physicians in prescribing pharmacogenomic testing. This further highlights the need for the development of effective tools for guiding healthcare provider decisions utilizing pharmacogenomics in clinical practice.

There are many factors that can be categorized as "barriers" to the adoption of pharmacogenomic technology in the context of Rogers' Diffusion of Innovation Theory. In most of these factors, there is in interaction between knowledge and attitudes. This paper will attempt to distinguish the nature of the relationship between these factors, as it is described in the literature, to the extent that it is.

Knowledge and attitudes towards cost as a barrier

Cost, at one time, was initially a prohibitive factor in the early development of pharmacogenomic technology. Ginsburg and colleagues addressed the question of cost effectiveness of pharmacogenomic technology in their 2005 position paper (Ginsburg, Konstance, Allsbrook, & Schulman, 2005). At the time, the question of cost had been subject to many conditions. While long run costs showed a favorable ratio, the immediate up front expense had been identified as a large consideration in implications for the development of pharmacogenomic technology into routine clinical practice. Since that time, the costs of use have fallen dramatically. However, cost may still persist as a perceived barrier in attitudes of healthcare providers. It is important that the most up to date understanding of cost effectiveness be understood by the target users of the technology. In actuality, the utilization of patient genotypes has the potential to save healthcare payers the costs of longer term hospitalizations

(Crews, Hicks, Pui, Relling, & Evans, 2012). The term '$1,000 genome' has been a long time target for the genomics industry. This term has been symbolic of the potential for DNA-sequencing capability to become so affordable that any individual could afford the once-in-a-lifetime investment to obtain their own personal genome sequence for future physicians' reference (Church, 2006). In January 2014 the biotechnology company, Illumina introduced the HiSeq X Ten Sequencer which is the first product able to sequence an individual's genome for under $1000 with a sequencing depth of 30x or greater. This huge advancement in the platform scientific technology that drives genome sequencing was a large milestone in cost reduction of pharmacogenomic technology that has long been a goal in the industry. No studies have yet evaluated the topic of cost effectiveness in the post $1000 genome era. Due to this very recent development, cost as a barrier needs further investigation within this cost paradigm.

A 2010 paper suggested that there is complexity in weighing the cost benefit of pharmacogenomic technology by healthcare payers, because of the different efficacy associated with different markers (McKinnon, 2010). Cost-effectiveness is often shown for specific diagnostic test, but no comprehensive framework yet exists for evaluating the technology, overall. Ventola's 2011 paper discusses cost as a concern, further, framed in the structure of reimbursement (Ventola, 2011). Though many payers do cover genomic tests, others have complex policies that may be generic to all diagnostic tests and don't always cover the specific circumstances of the patient. Ventola's study found that some insurers had cited that they had been reluctant to cover pharmacogenomic tests, because the cost-effectiveness of the test was in question. However, even in cases where the cost-effectiveness of a test was clearly demonstrated, that this factor was not the influencing factor for payers to agree to cover the costs (Ventola, 2011). Ventola's research found that, instead, the two most significant factors to

payers in deciding to cover the cost of the test were clear evidence of clinical utility and endorsement by professional guidelines. Deverka,Vernon, and McLeod analyze cost comparative cost-effectiveness from a more holistic model (Deverka,Vernon, & McLeod, 2010). They're analysis suggests that pharmacogenomics has the long-term potential to deliver immense cost savings to the healthcare delivery system. However, there exists somewhat of a catch 22. The net effect of cost savings is cumulative and as more prescribers and physicians participate in genomic profiling and screening the more data is compiled and the more efficiently healthcare providers can prescribe. Therefore, current evidence suggests that not only is there a net cost savings to patients and providers currently, but as the technology continues to be utilized the cost-effect is compounded and will drive greater efficiency into the current healthcare cost model (Deverka,Vernon, & McLeod, 2010). Despite the fact that cost has continued to decrease, historically cost continues to persist as a concern among clinical providers. It is unclear, at the current time, what the effect of the most recent technology cost improvements have had or will have on the perception of cost as a barrier.

Clinician attitudes toward pharmacogenomic technology

Clinician attitudes towards pharmacogenomics encompass a broad array of social, ethical, and emotional considerations that affect how individual practitioners feel toward the use of this innovation. One of the key catalysts to the adoption healthcare technology is the attitudes of the potential adopters. Indeed, many studies, such as the work of Greenhalgh conceives, in agreement with Rodgers, that adopter attitude is key component in the stages of adoption of innovation in healthcare (Greenhalgh, 2004). Though there is a great deal of literature that philosophically examines the potential ethical and social concerns of utilizing pharmacogenomics in the clinic, there have been few empirical studies that examine the attitudes

of healthcare providers in this regard. There has, yet, been no study in the U.S. that has examined the attitudes toward pharmacogenomics of all healthcare providers as a group. In the U.S., a few research studies have looked at the attitudes of pharmacists. (Anderson et al, 2012)

A 2012 study, of over 700 pharmacists utilized an online survey to assess the knowledge, attitudes and education pertaining to pharmacogenetic technology and testing (Roederer, Van Riper, Valgus, Knafl, & McLeod, 2012). The study found that over 90% of participating pharmacists had a desire to acquire more knowledge of pharmacogenetics and genomic testing. The study found that length of time in clinical practice was a factor in the preference of delivery methods for educational and training materials. Pharmacy practictioners with 10 years of experience or less were more likely prefer online web delivered training or education. The study provided further insight into the baseline education and training composition of this group. The majority of pharmacists were found to have limited formal education or continued education training in pharmacogenetics. The survey also found that the ability of this group to self-assess their knowledge of the subject accurately was high. It also empirically supported the theme that pharmacists were more likely to have a positive attitude about clinical pharmacogenetic testing if they had received prior education in pharmacogenetics (Roederer, Van Riper, Valgus, Knafl., & McLeod, 2012).

A 2011 study examined themes in open-ended qualitative responses from over 2000 participants, primarily pharmacists and nurses (Dodson & Van Riper, 2011). This study highlights many of the previous themes of various pieces of literature and had some new concepts emerge. The study was the first to capture information on pharmacogenomic attitudes from a mixed group of healthcare providers. The study captured the perceptions of pharmacists and nurses in North Carolina. The study collected participants' thoughts and concerns on

genomic testing and found five major themes. The themes were negative concerns for the application of genetic testing, lack of successful integration into standard of care, accessibility of genetic testing, potential harm, and optimism. A negative perception towards the application of genomics in the clinic is a common concern in papers philosophically examining ethical considerations of pharmacogenomic technology in clinical practice. This study also employed an open-ended question, which received 184 responses. The publication article only briefly discusses the closed-ended questions, but goes into great depth regarding the open-ended question response and the thematic analysis that was done on this data. One of the themes that emerged from nurses was a concern for patient education. That is how could patients be effectively educated about this technology in the short time that providers have to provide care? Replies included a highlighting of the need for genetic counseling in some situations. This theme in the thematic analysis demonstrated the clinical perception that patient acceptance would be reliant on patient education and this need has been only sparsely addressed (Dodson & VanRiper, 2011).

Knowledge and attitudes related to misuse and privacy concerns

One of the most controversial issues in the utilization of pharmocogenomic technology is the protection of patient's privacy and the potential for future discrimination based on genetic information. Patient genetic information is a very permanent and potentially significant piece of private data, which has implications that heighten the privacy concerns of both patients and providers. Ultimately, the translation of pharmacogenetic technology into routine clinical practice will depend upon the patients' and healthcare providers' acceptance of the use of pharmacogenomic tests in the clinic and a trust that the use of these tests is safe with regards to patient confidentiality and disclosure (Rogausch et al, 2006). Pharmacogemonics offers unique

challenges, as the nature of genomic data is broad in scope and offers a greater risk of loss of confidentiality, when compared to genetic testing (Goldman, 2005). The potential for misuse of this information could have great consequences for a patient. One of the largest concerns is the risk of genetic discrimination, or that a patient's genetic data may be used by a health insurance provider to discriminate in insuring patients, based on predispositions that may show in their genetic code. However, genetic data is for this reason, heavily encrypted and held to rigorous confidentiality standards. Though, the changing nature of informatics and data management technology blurs the actual probabilities of security risks of a breach of these protections. The privacy protection landscape varies by local jurisdiction (Tene, 2011). Within the US, privacy protection and data handling laws regarding genetic information have varied. The perceptions relating to a risk of loss of confidentiality have been a leading concern in the negative attitudes towards pharmacogenomics. However, there have been many measures taken to ameliorate the risk in these potential of these scenarios. Further, the US Congress passed a legal act in 2008, called the Genetic Information Non-discrimination Act of 2008 to legally prohibit health plans and insurers from denying coverage or charging higher premiums to individuals based on genetic predisposition (NHGRI, 2008).

In a 2011 study of 59 third year medical students from the American University of Beirut it was found that privacy was a leading concern in the use of genetic testing for developing treatment plans. The concern for confidentiality of patient data was high there was an overwhelming concern over genetic discrimination and its effect on insurability (Zgheib, 2011). This study highlighted medical students' perceptions of the role of pharmacogenetic testing information and describe the attitudes of medical students considering pharmacogenetic tests in a clinical setting. The study utilized several case scenarios and a questionnaire that measured

several concerns in potential genomic testing scenarios in various therapeutics diseases. The study found that in patients that were found to have negative markers for certain diseases, the sensitive nature of a genomic prognosis induced several ethical issues related to privacy. Many students were found to have concerns initiating a treatment utilizing the pharmacogenomic diagnosis as they were uncertain of the implications of potential genomic discrimination and issues with future insurability of these hypothetical patients. Though the legal, regulatory and cultural landscape of Beirut limits the generalizability of these findings as applied to the application of ethical concerns in the US, the study reflects the theme that is common in the philosophical literature, verified empirically as a major concern in a population of healthcare providers.

Clinician knowledge of pharmacogenomic technology

Knowledge has been repeatedly identified as a key barrier in the adoption of pharmacogenomic technology by clinicians. While Bonter's study identified a lack of knowledge as being one of the primary perceived barriers to clinician adoption (Bonter, Desjardins, Currier, Pun, & Ashbury, 2011), other studies have focused solely on knowledge as a prerequisite to the utilization pharmacogenomic technology in the clinical setting. Qualitative studies found that if healthcare providers lack the pre-requisite knowledge of pharmacogenomics, they will be far less likely to have a favorable attitude toward utilizing pharmacogenomic tests in the clinic (Ghaddar, Cascorbi, & Zgheib, 2011). Higgs and colleagues 2008 study examined the knowledge of pharmacogenomics in 19 British medical students (Higgs, 2008). Though the survey was in medical students and in Britain, some of the content is relevant to the dimension of knowledge in physicians.

In a cross-sectional study by Stanek and colleagues, investigators measured the baseline levels of US physicians' knowledge of pharmacogenomics and their respective utilization of pharmacogenomic technology in clinical practice. (Stanek, Sanders, Taber 2012) 97.6% of participants indicated that they had some knowledge of pharmacogenomics, but only 10.3% felt that they had an understanding of pharmacogenomic technology that was adequate enough to utilize it in the clinic. The incidence of utilization of genetic tests for the purpose of treatment planning was found to be relatively low with only 12.9% of physicians utilizing a pharmacogenomic test in the 6 months prior to the survey. (Stanek, Sanders, Taber 2012) Looking forward 26.4% of physicians indicated that they planned to order a pharmacogenomic test in the next 6 months. Those who scored high in measures of early adopting behaviors of pharmacogenomics were more likely to have received some prior or education training in pharmacogenomics. Only about 29.0% of physicians had ever received any prior professional or academic training in pharmacogenomics (Stanek, Sanders, Taber 2012) These findings further highlight the indication that knowledge and education are important factors in the adoption of pharmacogenomic technology by physicians in the clinic.

Knowledge of the where healthcare providers can find clear, curated, peer-reviewed guidelines that translate pharmacogenomic test results into clinical prescribing protocols for treatment regimens is thematic in the literature that explores knowledge (Relling & Klein, 2011). As mentioned, Bonter and colleagues found this lack of knowledge to be one of the primary barriers to adoption. The CPIC study found that there was an absence of guidelines of the interpretation of genotype information that there was not a clear path on how to translate that genetic information into clinical practice applications. This finding is thematic in studies that examined knowledge as it relates to attitude. The knowledge of clear framework for tests and

treatments was continually perceived as a major barrier to adoption. The study also found that providers may be resistant to considering pharmacogenetic information when making practice decisions (Relling & Klein, 2011). This, again, underscores how the lack of guidelines presents in the barrier of clinical uncertainty.

Therapeutic specialization

There is some evidence that differences exist in knowledge and attitudes by clinical therapeutic area of practice. There is some literature that discusses the differences in adoption by clinical therapeutic field. The specific nature of some disease, as well as the unique nuances of some areas of care, present the possibility that there are differences in the barriers to adoption in various medical specializations. This notion has been presented in the literature philosophically, in a number of forms; however, it has yet to be explored empirically. Ventola's 2011 paper, analyzes industry differences and the potential effects on adoption among practitioners of oncology, cardiology, psychiatry, and infectious disease (Ventola, 2011). The number of genomic diagnostic tests that were available in each field was a product of the environment within that field to pharmacogenomic adoption. Oncology has historically been at the vanguard of pharmacogenomic discovery and translation to practical application (Squassina, 2010). Swen hypothesizes that there may be some specializations that favor the adoption of pharmacogenomic technology more highly than others (Swen, 2012). The paper proposes that generalist providers may lack the technical knowledge and experience to effectively utilize pharmacogenomic tests in the clinic. He proposes that specializations such as oncology that routinely necessitate the utilization of DNA markers may be better equipped and therefore more likely to adopt this technology in full, in clinical utilization. Additionally, the paper proposes that family physicians and oncologists differ greatly in the composition of the routine tests that

they utilize in practice. Most therapeutics are based on complex mechanism of action in which multiple genes effect a number of pathways, which increases the complexity of models around genomic testing. Pharmacogenetic tests available in oncology, however, are more likely to be related to a single drug and a single genetic variation (Swen, 2012). Thus, previous experience and a simpler model may offer a predisposition in the oncology setting. This may help to explain the notion that providers in oncology have greater knowledge and more favorable attitudes toward the adoption of pharmacogenomic technology in the clinic that is thematic in the literature.

Haga looked, specifically, at primary care providers to see if there were barriers in this precise population that limit their ability to utilize this technology in practice (Haga, 2012). This study also found that knowledge was insufficient in primary care providers and that limited training opportunities and limited access to information portals made primary care physicians less confident in utilizing this technology to guide a diagnosis. This study suggests that primary care providers face challenges that are unique to their circumstance. As Swen noted earlier these issues may be related to previous experience, a lack of knowledge and inadequate access to information. Haga notes, though, that primary care providers have a desire to provide pharmacogenomic testing and utilize the results for clinical guidance, but these mentioned "barriers" are preventative.

Based on the factors described in the literature a theoretical model was devised for the study that centered on Rogers Diffusion of Innovations Theory, taking into account the domains of knowledge and attitude and considering the specific factors described in the empirical and philosophical literature. The study framework described the main attitude factors to be measured as Diagnostic/Clinical Value; Cost Effectiveness; Increased Drug Safety; Impact on Quality of

Healthcare; Potential for Misuse of Genetic Data; Genetic Discrimination; Ability of Providers to explain and Patients to Understand Tests. The attitude factors to be measured included Comprehension of Basic Genetics and Pharmacology; Experience in the Clinic; Literature Read; Training; and Education.

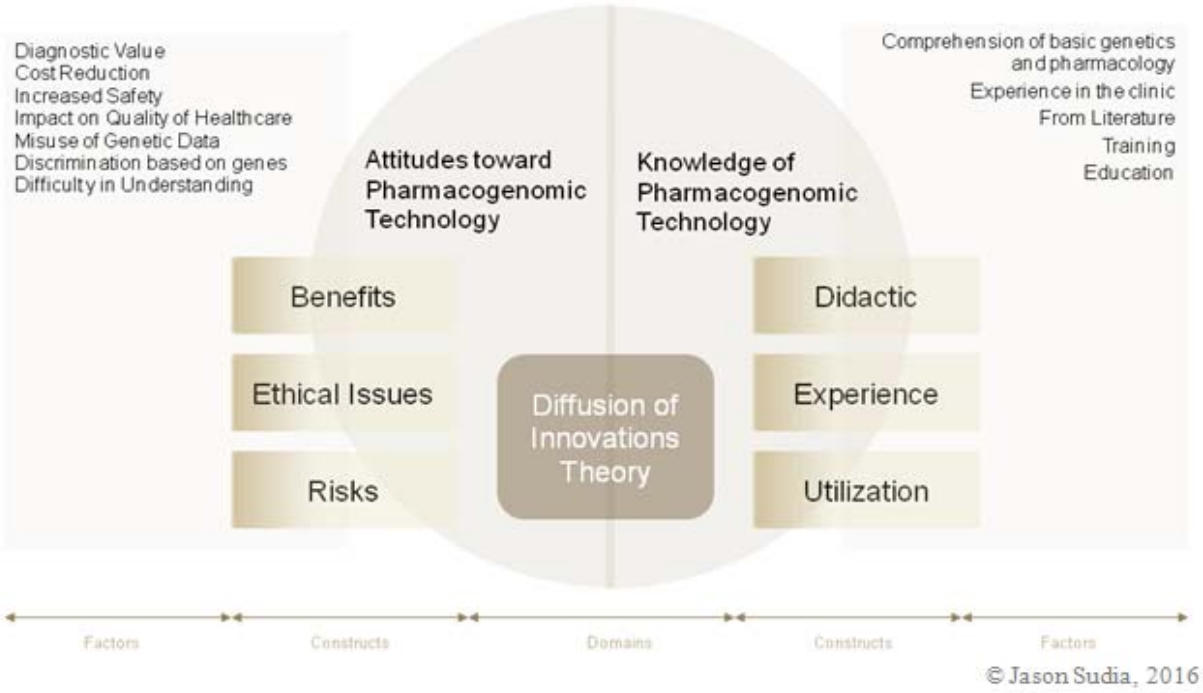

Figure 1: Initial Theoretical Framework for Study. The above figure illustrates the theoretical framework for the study design, incorporating the factors from literature review into Rogers' Diffusion of Innovations Theory.

Chapter III

RESEARCH METHODS

Research Design

The study employed a primary cross-sectional, correlation design with exploratory measures to further characterize the perceived barriers in pharmacogenomic adoption. Some open-ended questions and clarification questions were employed to capture previously undiscovered qualitative concepts. The correlational design allows for relationships to be described between predictor variables and outcome factors (Portney and Watkins, 2008). The exploratory components of the study tool will allow for characterization of perceived barriers through the use of qualitative methods, such as open-ended questions and thematic analysis. Thematic analysis methods can often help a researcher to discover new concepts that have not been previously identified (Maxwell, 2013). Since, some of the provider groups studied had been studied, individually, previously, there was a basis for measuring a number of factors that related to constructs in those groups clinical settings, with the caveat that this overall population was unique and that previous observations may not hold true in a group to group comparison of different providers. This design component is elucidated further in the tools section, in which is discussed how factors were operationalized in an among groups comparison. The study design and plan was submitted to the Seton Hall University and Institutional Review Board approval was obtained (*Appendix A*). Acknowledgement and authorization to conduct the study was provided by PRA Health Sciences (*Appendix D*).

Setting

After receiving IRB approval (*Appendix A*), this study was implemented via an online survey data collection service, Survey Monkey and was open to healthcare providers nationally. Though the initial link was released only to members of the Seton Hall School of Health and Medical Sciences, this group was encouraged to further recruit participants, if desired, through the use on chain-link or "snowball" sample referrals. The study utilized a form of non-probability sampling called chain-referral sampling, also known as snowball sampling. Snowball sampling offers researchers the ability to utilize a target demographic to find other members within the same target parameters through referral by the initial recipients (Goodman, 1961). This sampling technique utilizes the same theoretical structure as social network media, offering the potential to ultimately, possibly access the entire population, given sufficient time (Explorable.com, 2009). The study utilized the base population of Seton Hall University School of Health and Medical Sciences e-mail list to distribute the PI-created PAI© link to the initial subjects. The Letter of Solicitation accompanying the PI-created PAI© incorporated language that encourages recipients to forward the link to any friends, colleagues, or associates that they think may fit the described criteria for inclusion and exclusion (*Appendix E*). Since the recipients may have forwarded the link to any number of secondary recipients and those secondary recipients were then able to forward it to any number of tertiary recipients, this is termed exponential snowball sampling. Since the respondents had to self-qualify according to the inclusion and exclusion criteria provided for at the beginning of the survey, for the inclusion and exclusion criteria, the sampling method was also exponential discriminative snowball sampling (Explorable.com, 2009).

Sample

The sample was obtained through chain link referral sampling as described in the methods section. The initial invitation and link were sent out to the distribution list of the School of Health and Medical Sciences at Seton Hall University after permission was granted (*Appendix C*). Subjects were self-identified as healthcare providers that were involved in patient medication and/or pharmacology decision-making related practice within the United States that responded to the anonymous pharmacogenomics survey link, sent via e-mail. Although the sample was national in scope, the majority of respondents were from the metropolitan NJ, NY and PA area, because non-purposive (snowball) sampling is being used, it becomes impossible to merely limit the respondent pool to a particular region of the United States. Thus the generalizability of these results is representative of this Northeast region. Based on the methods described by Bartlett on survey study sample size determination, about 221 responses were expected to be required to accurately represent the target population (Bartlett, Kotrlik, and Higgins, 2001). This number was based on the PI-created PAI© tool attributes and a 3% margin of error for categorical data and a 5% margin of error for ordinal level data. It was also based on the assumption of a population size estimate of about 1,000,000 healthcare providers and a confidence level of 90%. To achieve this number, assuming a 20% response rate, about 1105 potential subjects were estimated to have needed to receive the PI-created PAI© . Furthermore, a power analysis was conducted to control for the possibility of failing to reject a false null hypothesis, or committing a Type II error. This was preventable by achieving a minimum power of at least 0.8 (Portney and Watkins, 2008). The statistical program, G-power 3.1, (Faul, Erdfelder, Lang & Buchner, 2007) was utilized to calculate the appropriate sample size for sufficient power based on the parameters of the PI-created PAI© instrument *(Appendix B).* This

tool was used to qualify the estimate of n=221 from above to assure that this sample size would meet the statistical requirements for all tests projected to be performed. An f^2 was utilized to determine the appropriate minimum sample size required to test for significance, which is calculated by $R^2/ (1 -R^2)$. In G-power, a multiple regression omnibus (R^2 deviation from zero) test was selected for *a priori* power calculations. A small effect size estimate f^2 of .08 was selected. Using the significance level of 0.05, in order to detect the small effect size of 0.08, the minimum sample size was determined to be 213 with up to 10 predictors with an actual power of .802. Given these results, the original estimate of n=221, based on survey methodology conventions, it was very likely that an effect will be detected, if one exists.

Tools and Instruments – Pharmacogenomic Adoption Instrument

The literature showed that there was not one singular instrument that was equipped to measure all of the factors included in the theoretical framework, in all of the provider groups investigated in this study. There, in fact, were only a few survey tools that have measured perspectives on pharmacogenomics and its use in the clinic. Only one has directly measured barriers to adoption, this was done only in physicians in Canada (Bonter, Desjardins, Currier, Pun, & Ashbury, 2011) Though none of few the survey instruments that captured perspectives on pharmacogenomics, precisely measured healthcare providers perceived barriers to adoption in the clinic, each of those studies offered some insights and helped to, collectively, offer topical themes. Although, no one instrument captured all of the emergent themes in the literature, each survey tool, provided a strong empirical demonstration of its abilities in exploring some of the thematic concepts of interest that emerged.

In Bonter and colleagues 2011 study, the research team aimed to measure barriers to adoption of personalized medicine technology in clinical practice, including pharmacogenomic

technology. The study utilized a survey tool that was provided to Canadian oncologists, cardiologists, and family physicians. The survey instrument questions captured demographic information, training, practice, knowledge and education information about pharmacogenomics and personalized medicine. It measured their perception of its use practice in their area of specialization, and the benefits and barriers to its adoption. The survey had a response rate of about 8.3% and responses were obtained online, by mail or by fax. The survey has not been utilized in U.S. populations or populations other than Canadian physicians. The draft of this survey was reviewed by an expert panel of 11 physicians and modified to include their feedback. The design of the survey was built around adoption of innovation in clinical practice and diffusion of innovations framework was the underlying theoretical model for the structure. Barriers were considered in the context of knowledge and attitudes in the practice of personalized medicine, pharmacogenomic testing to measure perceptions of relative advantages, compatibility, ease of implementation and institutional responses to adoption of pharmacogenomic technology (Bonter, Desjardins, Currier, Pun, & Ashbury, 2011) Bonter's study is one of the few to explore the question of specialization as a factor, which was approached several times philosophically, but only very few times measured empirically. Though Bonter only captured three areas of therapeutic specialization, these three showed some differences in key areas (Bonter, Desjardins, Currier, Pun, & Ashbury, 2011) One item of interest that provided empirical evidence on a question previously philosophically posed in the literature was whether knowledge differed significantly by area of specialization. Bonter's survey measured factors that related to probability of adopting and utilizing genomic tests. It found that those in the specialty of oncology were more likely (27% χ^2 p=.0001) to have

graduate education in pharmacogenomic testing and personalized medicine than the other two areas of specialization.

Stanek and colleagues conducted a cross-sectional study, utilizing a faxed survey instrument from 2008-2012 to measure baseline levels of US physicians' knowledge and utilization of pharmacogenomic technology in clinical practice (Stanek, Sanders, Taber 2012) The survey instrument consisted of an anonymous questionnaire with 26 items. Fifteen were questions about the physicians' knowledge, attitudes, and use of pharmacogenomic technology. An additional eleven questions captured demographics and characteristics of the clinical setting. The instrument captured many of the constructs that were thematic in the literature. The questions were all closed-ended and needed to be completed in entirety, otherwise the survey was excluded. The survey instrument was based in the theoretical framework of diffusion of innovation theory. The primary measures were to assess which factors were associated with the decision to adopt pharmacogenomic technology. A number of variables and factors were measured. These included many that were thematic in the literature. The sample for the survey was drawn from a nationwide physician database obtained from Medco, a pharmacy benefit management company for prescription drug benefits. 397,832 prescribing physicians were sent the survey for potential participation in the study, of all physicians receiving the survey questionnaire, only 10,003 (3%) completed and returned it. It was found that these respondents were statistically representative of the overall physician population in the US. The internal consistency of the survey instrument was then assessed by comparing the direction and frequencies of responses for six pairs of related survey items. Measures were then taken to assess the external validity of the study sample. Variables, including demographic information and practice attributes of participants in the survey study were compared with those of the

physician population of the United States, overall. The factors associated with the adoption of pharmacogenomic technology were evaluated using chi-square tests and multiple regression methods. 97.6% of participants indicated that they had some knowledge of pharmacogenomics, but only 10.3% felt that they had an understanding of pharmacogenomic technology, adequately enough to utilize it in the clinic.

In 2012, Dr. Susanne Haga of the Institute for Genomics Science and Policy at Duke University, conducted the study, "Primary Care Physicians' Knowledge of and Experience with Pharmacogenetic Testing" (Haga, 2012). The study aimed to evaluate the knowledge level and prior experience of pharamcogenomic technology in primary care physicians in community practice. The survey instrument was developed through a multi-disciplinary collaboration among investigators at Duke University and the University of North Carolina, Chapel Hill. The instrument questions were based on a wide-scope literature review and several focus groups. The online survey instrument was subjected to a test and re-test to validate the understandability of the questions. A panel of primary care practitioners participated in the pre-test survey to identify confusing questions, ambiguous terms and to assess the level of confidence in understanding the intent of questions. The final revised survey was composed of six major sections, totaling 101 questions in all. The concepts explored dealt with knowledge of pharmacogenomics, experience in the clinic with pharmacogenomics, and the perceived role of the primary care provider in delivering this technology (Haga, 2012).

Dodson and VanRiper created a survey in 2011 for a study that aimed to measure knowledge and attitude toward pharmacogenomic technology in a large, diverse group of providers (Dodson & VanRiper, 2011). The survey tool was based on a literature review that highlighted many of the major concerns observed in theoretical literature. The survey was

assessed by an interdisciplinary team of nurses, physicians and pharmacists with expertise in pharmacogenomic testing. The tool was pilot tested on a group of five clinicians for clarity and understandability. While the closed ended questions or replies were not published, the open-ended themes were analyzed in Dodson and VanRiper's 2011 article in Personalized Medicine.

A 2012 survey by Roederer, Van Riper and colleagues measured provider knowledge, attitudes and education concerning pharmacogenetic testing. The authors developed an online multi-question survey that assessed healthcare provider knowledge, attitudes and education concerning pharmacogenetic testing. The authors utilized a panel of experts from the University of North Carolina, Center for Genomics and Society and the UNC Institute for Pharmacogenomics and Individualized Therapy (IPIT) to evaluate the survey constructs and provide expert opinion on content. Since the responses to the survey were anonymous, the Institutional Review Board of UNC, Chapel Hill determined that no Institutional Review Board review or approval was required for this study. The survey design was intended to measure not only knowledge of pharmacogenetics, but also assess attitudes regarding pharmacogenetic testing. The survey was evaluated by an interdisciplinary group of healthcare providers, including nurses, physicians and pharmacists that were all considered to hold expertise in pharmacogenetic testing. Pilot-testing of the survey was done with five healthcare providers, the feedback results were reviewed and the survey was revised for clarity. The survey measured various constructs that were thematic in the literature and some that were specific to this population of pharmacy providers. There were six questions related to the general background and demography of participants. There were two questions that measured experiential knowledge and were designed to assess general perceptions of understanding regarding genetics and pharmacogenetics. There were ten basic knowledge questions. Five of which, measured

basic knowledge of genetics and five which measured basic knowledge of pharmacogenetics. There were eight questions that assessed attitudes of pharmacists toward pharmacogenetic testing. Two questions assessed provider interest in future educational offerings regarding pharmacogenetic testing. The survey was sent to 9516 potential participants and over 700 pharmacists responded.

As a result of the mosaic of constructs and factors that were spread out across multiple studies of multiple provider types, the need for the development of a new measurement tool was apparent to meet the goals and objectives of this specific study. The PI-created PAI© study tool was developed through a multiple stage process colloquially termed as a "modified Delphi." This created tool is based on constructs that are discussed thematically throughout the academic literature regarding pharmacogenomic concerns, which were then ranked (by the creator/principal investigator of this study) by their frequency in publications. Consensus questions were developed and included in the PI-created PAI© tool, based on existing categories and constructs previously developed and evaluated in prior literature. This compiled list of questions was then compared back against the specific categories that were initially measured in the tools that were used in previously conducted studies. Since, no study had yet looked at this entire list of construct categories and the existing studies were limited to single or a small subset of healthcare provider types, no one survey tool was found to be adequate for the purpose of this study and is hence why this new tool, the PI-created PAI©, was developed.

Reliability and validity

This 46 question survey tool, the PI-created PAI©, (*Appendix G*) was developed by modifying questions that showed significant findings in other studies and generating questions to quantify constructs that had not yet been measured empirically. The questions contain either

multiple choice, Likert scale, or bivariate, Yes/No answers. In the yes/no questions, subjects are also given an "unsure" option to choose if they are undecided in their response. Face and content validity was established through an expert panel review. The instrument questions were tested for readability scores (*Appendix F*). A modified Delphi process was used to validate the study instrument (*Appendix H*). Delphi is a technique that utilizes an expert review to establish a consensus on the study instrument and how well its questions measure the constructs. Delphi validation relies on convergent validity to confirm the face validity of the tool amongst blinded experts by comparing their ratings after the fact without allowing them to discuss the content prior to the response (Linstone, 1975). The Delphi process consisted of three rounds of blinded panel of 5 experts that reviewed the intended constructs and provided feedback. The Delphi worksheet requested agreement or rejection of the proposed construct that was measured by each question. Questions that did not achieve 80% agreement were revised to include feedback from the expert committee (*Appendix I*). After administration of the PI-created PAI©, the survey data was then analyzed for reliability. The internal consistency of the PI-created PAI© tool was assessed utilizing Chronbach's alpha coefficient. Chronbach's alpha is a measure of internal consistency and is a commonly used estimate for the reliability of psychometric tests. A psychometric instrument with an alpha score of greater than 0.6 is conventionally considered to have acceptable internal consistency. Each of the scales was analyzed for internal consistency. An overall alpha was calculated for each scale. The scales were also split-half analyzed and split alphas were calculated for the paired halves. Spearman-Brown coefficients were also calculated. The Knowledge Scale questions scored an overall Chronbach's alpha of .770, with a split half alpha of .603 and and .847 on the first and second halves, respectively. The Knowledge Scale scored a Spearman-Brown coefficient of .897. The Attitude Scale questions scored an overall

Chronbach's alpha of .813, with an alpha of .678 and .743 on the first and second halves, respectively. The Attitude Scale scored a Spearman-Brown coefficient of .805. The Adoption Scale questions scored an overall Chronbach's alpha of .853, with an alpha of .908 and .553 on the first and second halves, respectively. The Adoption Scale scored a Spearman-Brown coefficient of .986.

Data Analyses

Quantitative Analyses

The PI-created PAI© was closed and all data was reviewed for completeness. The data was entered into PASW Statistics (Version 20) and stored on a portable USB flash memory drive. That data containing flash drive was kept securely locked in a cabinet with access only by the primary investigator, to assure data integrity. Surveys that were missing responses to greater than 30% of the questions will be considered incomplete and were not be used in the analysis. Otherwise, singular missing data points will be disregarded and the (n) for that calculation of that data will reflect such.

Exploratory and descriptive components were used to further characterize the factors that are relevant to the question of interest. Descriptive statistics were calculated for all demographic variables, standard deviations were conducted for all continuous variables. The descriptive statistics for demography included means, standard deviation, frequencies, and percentages. Descriptive, exploratory data analysis methods were used to analyze the significance of categorical factors in the context of the clinical setting (Abt, 1987).

Correlation coefficients were determined to examine the strength of relationship between variables. The research hypotheses were tested using correlational methods, and regression methods may be used to analyze the factors in a stepwise manner. Ratings from questions

related to pharmacogenomic knowledge were compared with questions relating to likelihood of adoption. Ratings from questions related to attitudes toward pharmacogenomics were compared to ratings representing likelihood of adoption. Demography, type of provider, and the area of specialization were analyzed in a multivariate linear regression model. The use of a multivariate model allowed for determination of the proportion of variance that is contributed from each factor. In a stepwise multiple regression model, each factor was added into a regression equation individually or clustered as one construct. This allowed the model to show what proportion of the variation in a pharmacogenomic adoption decision is contributed by constructs and by each individual factor. In the case of ordinal-scaled variables, Spearman's rho was used. In the case of interval-scaled variables, Pearson's r was determined and regression methods will be used to determine if the independent variable has predictive strength in relation to the dependent variable. A point bi-serial correlation was used to determine the correlation between gender and likelihood of adoption. These tests were dependent on the underlying assumptions associated with each. Importantly, one of the main assumptions of the parametric correlation Pearson's r, is that that the two variables will demonstrate covariation in a joint distribution (Portney and Watkins, 2008). To validate this assumption, each of the data sets were checked for normality, if either is not normally distributed, then the assumption was considered violated and rho was used. Because any single variable may or may not be a strong predictor alone, correlations will be calculated for each factor, however, multivariate methods were explored to determine if a more comprehensive predictive model could be created to describe the relationship of many factors together.

A one-way analysis of variance (ANOVA) was conducted to analyze the differences in the responses on pharmacogenomic adoption by therapeutic area of practice. A one-way ANOVA

was also conducted to analyze the differences in the responses on pharmacogenomic adoption by provider type, as indicated by credentials. These tests helped to determine if there were differences in the likelihood of adoption among different types of health care providers and if there were differences in the likelihood of adoption among the different therapeutic areas of practice. Using an ANOVA reduces the probability of committing a type I error, when compared to using multiple t-tests to discern differences among multiple groups. The ANOVA tests will be contingent to meeting the standard required assumptions of normality, independence of observations, and homogeneity of variance. The appropriate tests were performed to determine if these assumptions were violated in the data. If the data did not meet the assumptions, an equivalent non-parametric test, was used and was dependent on the actual assumption that was violated. All of the data analyzed by ANOVA was analyzed at a minimum alpha of at least 0.05, with a targeted power of .80, which is conventionally recognized as being adequate to protect from the possibility of committing a type II error (Portney and Watkins).

Qualitative Analyses

Additionally, the study PI-created PAI© included a number of open ended and clarification questions that allowed a qualitative clarification on a number of issues and questions. Though only a small amount of qualitative data was collected, relative to the quantitative portions of the PI-created PAI©, open coding was used to analyze the responses and the frequencies of similar responses. This allowed for potential new themes to emerge from the study. Unlike triangulation of qualitative data, a Concurrent Embeded Strategy, embeds one type of data collection into the other predominate form. In this case the qualitative data is considered in context with the quantitative data question to create a fuller picture and create an "overall composite assessment" (Creswell 2009, p. 214)

Concurrent Embedded Design

The Concurrent Embedded Design is a mixed methods design in which one data set provides a supportive, secondary role in a study that employs the other data type as its primary data collection methodology. The basis for this design is that a single data set is not sufficient, alone. Each type of data collection allows for diverse types of questions need to be answered. Each category of question types requires unalike categories of data. This design is employed when there is a necessity to include qualitative or quantitative data to build a composite answer to a given a research question within a principally quantitative or qualitative study or when additional information may be useful to support a concept, develop a finding further or corroborate findings from the other primary method. In this study, this design was used to embed a smaller qualitative component within a larger quantitative design (*Figure 1*). However, the inverse may be true and a larger qualitative study may nest a smaller quantitative component in some cases. In this case the primary endpoints measured for an experimental and correlational design.

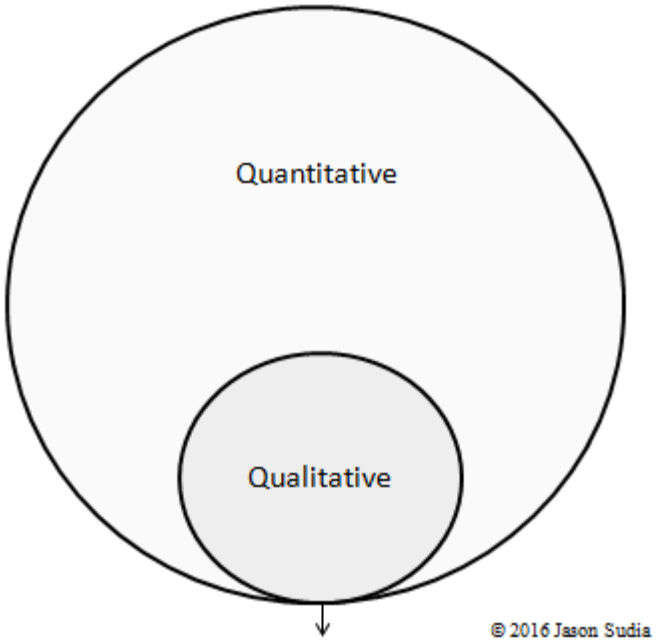

Figure 2. Concurrent Embedded Design. This figure illustrates the elements of Concurrent Embedded Design.

Open Coding

Open coding is one methodology for examining qualitative data. In this method of coding, key word and key phrases are identified in an effort to establish distinct concepts and categories within the data (Creswell, 2009). The themes that emerge then form the basic units of qualitative analysis. The methodology then stratifies the data down into first level concepts, and second-level categories. In this methodology each key phrase received a category. These categories were then transferred to a brief outline, with main concepts being main headings and categories being subheadings.

Chapter IV

RESULTS

Sample characteristics

The majority of participants (36.44%) were in the 40-49 years of age group. The sample was over 58% female. Additionally, the majority of participants (44.22%) had between 20-29 years of experience in their field. 58% of respondents practiced in NJ, 17% of respondents practiced in NY, and 16% of respondents practiced in PA, the remaining responses came from other states in the US. 31.47% of participants worked in a private practice affiliated with an institution. The largest group of participants (26.72%) worked in Primary Care or Internal Medicine. The provider types were Nurses (44.68%), Physicians (33.19%), Physician Assistants (15.32%), Pharmacists (5.96%), PhD (6.18%), and Other (2.55%).

Age

The age group with the highest representation was 40-49 year olds (35.2). Then, in second was followed by 30-39 year olds (27%). Third largest was 50-59 year olds (22.1%). 60-69 year-olds made up 9.8% of the participants and 18-29 year-olds made up 2.5% of participants. Age was found to have a weak (ρ=.260) correlation at the $p<.001$ level, with adoption likelihood.

Table 1

Participant Age Group (N=244)

Age Group	Frequency	Percent
18-29 years of age	6	2.5
30-39 years of age	66	27.0
40-49 years of age	86	35.2
50-59 years of age	54	22.1
60-69 years of age	24	9.8

Provider Type

The largest represented group of healthcare providers was nurses (41.8%). Physicians made up the second largest provider group (31.6%). Physician Assistants were third largest group of providers (15.2%). Pharmacists made up 4.1% and other also made up 4.1% of the sample.

Table 2

Provider Type (N=244)

Type	Frequency	Percent
MD/DO	77	31.6
Other	10	4.1
PA/PA-C	37	15.2
RN/BSN/LPN/NP/DNP	102	41.8
RPh/Pha	10	4.1

Geography

Geographically, 15 states were represented, although 82% of responses came from providers that practiced in one of three states, NJ, NY, and PA. 14.8% of participating providers practiced in PA. 15.6% of participating providers practiced in NY. 52% of participating providers practiced in NJ.

Table 3

State of Practice for Majority of Patient Care Activities (N=244)

State	Frequency	Percent
CA	1	0.4
CO	1	0.4
CT	6	2.5
DE	1	0.4
FL	1	0.4
KY	1	0.4
MA	1	0.4
MD	1	0.4
NJ	127	52.0
NY	38	15.6
OH	1	0.4
OR	1	0.4
PA	36	14.8
RI	2	0.8
TX	2	0.8

Therapeutic area of expertise was varied. The largest percentage of participants specialized in Primary Care or Internal Medicine (25.4%). The second largest group was unexpectedly, Emergency Medicine, representing 14.3% of responses. “Other” was the third largest group and other included Radiology, Gastroenterology, Urgent Care, Hemodialysis, Nephrology, and Rehab Medicine. Other represented 10.2% of responses for primary therapeutic are of practice. A significant difference was found among Mean Adoption Scores by therapeutic specialization. Though, oncology was expected to hold the highest adoption scores,

based on the literature. It was found that Infectious Disease (20.8) was the highest mean adoption score, followed by ENT and Genetics (20), Cardiology (19.29), and then Oncology (18.18).

Table 4

Primary Therapeutic Area of Practice (N=244)

Therapeutic Area	**Frequency**	**Percent**
Bone/ Orthopedics	3	1.2
Cardiology	7	2.9
Dentistry	1	.4
Dermatology	3	1.2
Ear, Nose & Throat	3	1.2
Emergency Medicine	35	14.3
Endocrinology	8	3.3
Genetics	1	.4
Infectious Disease	7	2.9
Oncology	13	5.3
Other (please specify)	25	10.2
Pediatrics	23	9.4
Primary Care/ Internal Medicine	62	25.4
Psychiatry	6	2.5
Surgery	16	6.6
Women's Health/ OB/Gyn	19	7.8

The majority of practitioners were in a private practice setting, affiliated with and institution such as a hospital or university (29.9%). Employees of a hospital were the second most represented (24.2%). Unaffiliated private practices were the third most commonly represented group (20.9%).

Table 5

Primary Clinical Setting (N=244)

Setting	**Frequency**	**Percent**
Employee of Hospital	59	24.2
Employee of University	12	4.9
Free Standing Clinic	8	3.3
Free-Standing Immediate Care Center	8	3.3
Other (please specify)	8	3.3
Outpatient Medical/Surgical Center	9	3.7
Private Medical Practice	51	20.9
Private Practice affiliated with Institutional Setting (e.g. Hospital or University)	73	29.9
Walk-In Care Center affiliated with a Pharmacy	4	1.6

Barriers to adoption

The most commonly cited barrier to adoption was "limited provider knowledge or awareness" (19.5%). This was followed by lack of access to laboratory services (15.6%). "Lack of 3rd party payor reimbursement" was the third most commonly cited barrier (13.9%). These three responses comprised nearly 50% of the reply for this question. 5.6% of respondents did not perceive there to be any barriers to clinical adoption. Only one respondent (0.4%) selected the other response and provided a barrier that was not in the list. The open-end reply was "not familiar", which could possibly be assigned to the "limited provider knowledge or awareness" category.

Table 6

Barriers to Adoption (N=231)

Answer Options	**Response Percent**	**Response Count**
Lack of clinical guidelines	6.1%	14
Limited provider knowledge or awareness	19.5%	45
Lack of evidence-based clinical information	5.6%	13
Cost of tests is prohibitive	4.3%	10
Lack of time or resources to educate patients	11.3%	26
Results take too long for treatment decision	6.1%	14
Lack of 3rd party payor reimbursement	13.9%	32
Lack of access to laboratory services	15.6%	36
Lack of regulatory framework	6.5%	15
Ethical concerns over tests	5.2%	12
Do not perceive there to be any barriers	5.6%	13
Other (please specify)	0.4%	1
answered question		231

81.5% of participants indicated that they had heard the term pharmacogenomics before taking the PI-created PAI© , while 18.5% indicated that they had not. However, only 16.5% of participants had observed the use of a pharmacogenomics test in clinical practice, while 77.2% had not and 6.3% were unsure if they had or not. 80% of participants indicated that they had not acquired any information about pharmacogenomics testing outside of their clinical practice or educational

training, while 20% indicated that they had. In those that indicated that they had and answered the open ended question "please specify where", the sources that they cited for acquiring information were "white papers", "medical journals", "various other places" and "conferences". In the question of "how many times in the past year do you recall the use of pharmacogenomic testing in the clinical setting where you work?" 87% indicated 0, 8.5% indicated 1, 3.4% indicated 2-5, 0.56% indicated 6-9, and 0.56% indicated 10+. When asked about direct participation in the treatment of a patient that utilized a pharmacogenomic test, 84.9% indicated that they had not in the past year, while 7.6% indicated that they had, and 7.6% did not know. 94.3% of participants had not provided information or counseling to a patient about pharmacogenomic tests in the last year. 5.71% of participants had provided information to patients regarding pharmacogenomics testing in the past year, while 94.3% had not.

Instrument Scores

Table 7 shows the mean composite scores for the each category of the PI-created PAI© instrument as well as the range of values. Zero values indicated that no questions from that section of the PI-created PAI© were completed by at least one participant.

Table 7

Mean Instrument Composite Scores

Construct	N	Minimum	Maximum	Mean	Standard Deviation
Adoption Composite Score	198	.00	24.00	14.59	7.095
Attitude Composite Score	196	.00	53.00	31.40	11.91
Knowledge Composite Score	225	.00	85.00	33.47	18.68

Pharmacogenomic Knowledge

Participants indicated that 58.8% had taken no type of pharmacogenomic education or training classes in the last 15 years. 23.0% indicated that they had taken a seminar. 18.6% indicated that they had taken a college course. 14.3% indicated that they had taken a CME course. 8.8% indicated that they had attended an in-service. In the first basic genomic and pharmacology knowledge questions most participants (76.9%) answered correctly, identifying two different alleles for a single trait as heterozygous. In the second basic genomic and pharmacology knowledge questions most participants (79.6%) answered correctly, matching the complementary strand bases to with AAGCCA with TTCGGT. In the third basic genomic and pharmacology knowledge questions most participants (55.2%) answered correctly, identifying the approximate number of genes in human DNA as about 22,000. In the fourth basic genomic and pharmacology knowledge questions only 36.3% of participants answered correctly, and identified differences in response by race as being the option most affected by genetic variations in drug targets. In the fifth basic genomic and pharmacology knowledge questions only 34.8% of participants answered correctly, identifying CYP2D6*10 as being most closely linked with deficient or absent CYP2D6 activity. In the sixth basic genomic and pharmacology knowledge questions most participants (87.3%) answered correctly and indicated that differences in a person's genetic profile could have an impact on how the person responds to drug treatment, while 2.9% indicated it could not and while 9.8% did not know.

Table 8

Knowledge Question Replies

Knowledge Question	**Replies**
8. Have you read any type of literature about pharmacogenomics testing prior to taking this survey?	Yes 85 (39.9%) No 128 (60.09%)
11. Have you acquired information about pharmacogenomic testing outside of your actual clinical practice or educational training, including CME?	Yes 35 (19.9%) No 141 (80.1%)
13. Please indicate if you have you had any of the following types of pharmacogenomic education or training in the last 15 years? (Select all that apply)	None 120 (58.8%) Seminar 47 (23.0%) In-Service 18 (8.8%) College Course 38 (18.6%) Other 2 (1%)
Knowledge Question	**Correctly Answered**
17. An organism that has two different alleles for a single trait is said to be _____ for that trait.	156 (76.9%)
18. A DNA strand has the following bases: A A G C C A: What are the bases on its complimentary strand?	160 (79.6%)
19. Humans have approximately the following number of genes in their DNA:	112 (55.2%)
21. Which property is affected by genetic variations in drug targets?	74 (36.3%)
22. Which allele is most closely associated with deficient or absent CYP2D6 activity?	70 (34.8%)
23. Can differences in a person's genetic profile have an impact on how the person responds to drug treatment?	178 (87.3%)
38. How would you rate your current understanding of pharmacogenomic testing?	Excellent 8 (4.2%) Very Good 35 (18.5%) Good 58 (30.7%) Fair 57 (30.2%) Poor 31 (16.4%)

Self-assessment of knowledge

A comparison was made to gauge how strong the relationship was between participants own perception of their understanding of concepts related to pharmacogenomic testing and the accuracy of their respective replies to the instrument's knowledge questions. A significant correlation was found to exist (ρ=.812, p<.001) between self-rating and actual knowledge composite scores. This suggests that individual's perceptions of their pharmacogenomic knowledge were closely linked to their knowledge composite scores, as measured by the instrument.

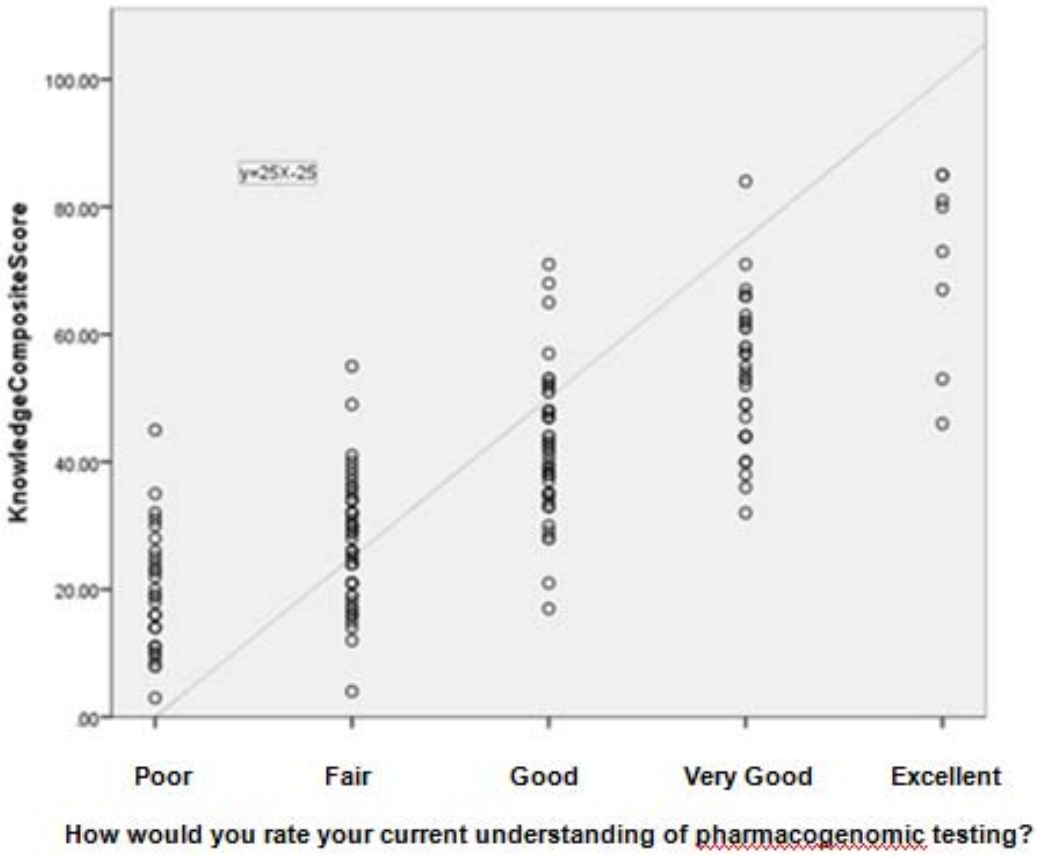

Figure 3. Correlation between self-rating and knowledge question scores. This scatter plot illustrates the relationship between pharmacogenomic knowledge and self-rating of knowledge.

Attitude towards pharmacogenomics

In the question of attitude toward pharmacogenomics as a valuable diagnostic tool in the treatment of patients 45.6% of participants indicated that pharmacogenomics was a valuable diagnostic tool, 40.9% indicated that it had some value, 2.1% indicated it had no value and 11.4% had no opinion on the value of pharmacogenomics as a diagnostic tool in the treatment of patients. The most common response in the question of pharmacogenomics offering an eventual cost reduction in developing new drugs was that it was perceived to be somewhat likely (29.9%), while 28.6% of respondents thought it was neither likely nor unlikely, 13.9% replied somewhat unlikely, 12.4% replied very likely, 6.7% replied very unlikely and 8.7% had no opinion. When asked if pharmacogenomic testing was likely to help increase drug safety, most respondents (38.1%) replied that it was somewhat likely, while 27.8% replied that it was very likely or it already had, 22.7% replied that it was neither likely or unlikely. Only 3.6% replied that it was somewhat unlikely, and 2.1% that it was very unlikely. When asked how likely it was that genetic data collected for the purpose of patient treatment was to be misused the most common reply was that it was neither likely nor unlikely (36.6%), while 26.3% indicated that it was somewhat unlikely and 19.6% thought that it was somewhat likely that genetic data could be misused. When asked if concerned that a patients quality of healthcare may be adversely affected by the results of their pharmacogenetic testing, the majority of respondents (39.5%), were again neither concerned nor unconcerned, 26.3% were mostly unconcerned, 23.2% were somewhat concerned, 4.2% were completely unconcerned, and 2.6% were very concerned. 4.2% replied that the concern was not relevant to their area of practice. When asked if concerned that the results of pharmacogenomic testing could result in discrimination by insurance companies,

the majority of respondents (37.8%) indicated that they were somewhat concerned. 26.4% were neither concerned nor unconcerned, 20.2% were mostly unconcerned, 9.3% were very concerned, 1.5% were completely unconcerned and 4.6% believed the concern to be not relevant to their area of practice. 32% of respondents were mostly concerned that the results of pharmacogenomic testing could result in discrimination in employment, while 29.9% were neither concerned nor unconcerned, 19.6% were somewhat concerned, 6.7% were completely unconcerned, 4.1% were very concerned and 7.7% believed that the concern was not relevant to their area of practice. When questioned about the cost of genomic testing and whether or not it was likely to be a deterrent to the utilization of pharmacogenomic technology in the clinic, the majority of respondents (42.8%) indicated that it was neither likely nor unlikely to be, while 22.7% indicated that it was perceived to be somewhat likely, 14.4% indicated that they perceived that it was somewhat unlikely, 10.3% indicated that they perceived the cost to be a likely factor in deterring the utilization of pharmacogenomic testing in the clinic, 2.1% said it was very unlikely, 7.7% had no opinion. When asked if they believed that pharmacogenomic testing is difficult for healthcare providers to understand, 23.7% of respondents replied yes, while 61.3% of respondents replied no and 15% of respondents had no opinion. When asked if they believed that pharmacogenomic testing is difficult for patients to understand, 34.7% of respondents replied yes, while 47.9% of respondents replied no and 17.5% of respondents had no opinion.

Table 9

Attitude Question Replies

Attitude Question	**Replies**
26. Do you believe that pharamacogenomics is a valuable diagnostic tool in the treatment of patients?	Has a lot of value 88 (45.6%) Has some value 79 (40.9%) Has no value 4 (2.1%) Have no opinion on value 22 (11.4%)
27. Do you believe that pharmacogenomic testing will help to offer an eventual cost reduction in developing new drugs?	Very unlikely 13 (6.7%) Somewhat unlikely 27 (13.9%) Neither likely or unlikely 55 (28.6%) Somewhat likely 58 (29.9%) Very likely/ It already has 24 (12.4%) No opinion 17 (8.7%)
28. Do you believe that pharmacogenomic testing will help to increase drug safety?	Very unlikely 4 (2.1%) Somewhat unlikely 7 (3.6%) Neither likely or unlikely 44 (22.7%) Somewhat likely 74 (38.1%) Very likely/ It already has 54 (27.8%) No opinion 11 (5.7%)
29. In your opinion, how likely is genetic data, that is collected for the purpose of patient treatment, to be misused?	Very unlikely 11 (5.7%) Somewhat unlikely 51 (26.3%) Neither likely or unlikely 71 (36.6%) Somewhat likely 38 (19.6%) Very likely/ It already has 11 (5.7%) No opinion 12 (6.2%)
30. Are you concerned that a patient's quality of healthcare may be adversely affected by the results of their pharmacogenetic testing?	Completely unconcerned 8 (4.2%) Mostly unconcerned 50 (26.3%) Neither concerned or unconcerned 75 (39.5%) Somewhat concerned 44 (23.2%) Very concerned 5 (2.6%) Not relevant to my area of practice 8 (4.2%)
31. Are you concerned that the results of pharmacogenomic testing could result in discrimination by insurance companies?	Completely unconcerned 3 (1.5%) Mostly unconcerned 39 (20.2%) Neither concerned or unconcerned 51 (26.4%) Somewhat concerned 73 (37.8%) Very concerned 18 (9.3%) Not relevant to my area of practice 9 (4.6%)
32. Are you concerned that the results of pharmacogenomic testing could result in discrimination in employment?	Completely unconcerned 13 (6.7%) Mostly unconcerned 62 (32.0%) Neither concerned or unconcerned 58 (29.9%) Somewhat concerned 38 (19.6%)

	Very concerned 8 (4.1%) Not relevant to my area of practice 15 (7.7%)
33. Do you believe that the cost of genomic testing is likely to be a deterrent to the utilization of pharmacogenomic technology in the clinic?	Very unlikely 4 (2.1%) Somewhat unlikely 28 (14.4%) Neither likely or unlikely 83 (42.8%) Somewhat likely 44 (22.7%) Very likely/ It already has 20 (10.3%) No opinion 15 (7.7%)
34. Do you believe that pharmacogenomic testing is difficult for healthcare providers to understand?	Yes 46 (23.7%) No 119 (61.3%) No opinion (15.0%)
35. Do you believe that pharmacogenomic testing is difficult for patients to understand?	Yes 67 (34.5%) No 93 (47.9%) No opinion (17.5%)

Experience question replies

Experience questions were originally allocated as a sub-set of knowledge, however, in the Delphi validation process of the Pharmacogenomic Adoption Instrument, a consensus of experts agreed that experiential knowledge was distinct from academic knowledge and should be measured independently. When asked if respondents had heard the term pharmacogenomics before taking this survey, 87.1% replied yes, while 18.3% replied no. When asked if respondents had observed the use of pharmacogenomic tests in clinical practice, at any time in the past year, 16.4% replied yes, while 77.4% replied no and 6.2% were unsure.

Table 10

Experience Question Replies

Experience Question	**Replies**
9. Have you heard the term pharmacogenomics before taking this survey?	Yes 187 (81.7%) No 42 (18.3%)
10. At any time in the past year, have you observed the use of pharmacogenomic tests in clinical practice?	Yes 29 (16.4%) No 137 (77.4%) Unsure 11 (6.2%)
13. In the past year, how many times do you recall the use of pharmacogenomic testing information by anyone, in patient treatment, in the clinical setting where you work?	0 155 (87.1%) 1 15 (8.4%) 2-5 6 (3.4%) 6-9 1 (0.6%) 10+ 1 (0.6%)
14. In the past year, have you directly participated in the treatment of a patient that utilized a pharmacogenomic test?	Yes 13 (7.5%) No 147 (85.0%) Do not know 13 (7.5%)
17. In the past year, have you provided information or counseling to a patient about pharmacogenomic tests?	Yes 10 (5.7%) No 166 (94.3%)
16. Have you ever recommended that a patient undergo pharmacogenomic testing?	Yes 16 (9.0%) No 161 (91.0%)

Results of Test Hypotheses

Hypothesis 1a analysis

Research hypothesis 1a posited that a relationship would exist between likelihood to adopt and demographic factors. This first question looked at relationships between likelihood to adopt and demography. The factor age was treated as an ordinal level variable, as age was measured in graduated groups. The factor years of experience was also treated as an ordinal level variable, as years of experience were measured in graduated groups. The factor gender was treated as a nominal variable. Since gender was a dichotomous variable, it was analyzed using point bi-serial correlation. The two ordinal level factors were age and years of experience. The data were assessed for the assumptions of independence, normality, and homogeneity of variances. The factors were analyzed for correlation with likelihood to adopt, as measured by adoption composite score, using a Spearman bivariate test of correlation. Years of Experience yielded very weak (ρ=.148, p<.05), but significant correlation. Age yielded a weak (ρ=.260, p<.001) correlation.

Table 11

Correlation matrix age, years of experience, and adoption composite score

Factor		Years of Experience	Age	Adoption Composite Score
Years of Experience	Correlation Coefficient	1.00	.60	.15
	Sig. (2-tailed)	.	.001	.05
	N	23	224	190
Age	Correlation Coefficient	.60	1.000	.26
	Sig. (2-tailed)	.001	.	.001
	N	224	236	197
Adoption Composite Score	Correlation Coefficient	.15	.26	1.00
	Sig. (2-tailed)	.05	.001	.
	N	190	197	197

An ANOVA of Adoption Composite scores showed that there was a significant difference between males and females at $p<.05$, but the effect size was small. An Eta squared of .028 indicated that, at most, 2.8% of the variation between adoption scores could be attributed to gender (among other possible factors). Since gender was a nominal variable, the only correlative measure that could be used was a point bi-serial correlation. A point bi-serial correlation test, yielded a moderate significant correlation ($\rho = .190$, $p<.01$) between gender (coded) and Adoption Composite Score.

Table 12

Point Bi-serial correlation matrix of gender by adoption score

Test			Adoption Composite Score	Gender Coded
Spearman's rho	Adoption Composite Score	Correlation Coefficient	1.00	.190
		Sig. (2-tailed)		.009
		N	197	197
	Gender Coded	Correlation Coefficient	.190	1.00
		Sig. (2-tailed)	.009	
		N	197	236

Hypothesis 1b analysis

Hypothesis 1b predicted that a significant difference would exist in adoption scores among different therapeutic areas of practice (e.g. oncology, cardiology, primary care). Differences in Mean Adoption Scores were compared by therapeutic area. Though oncology was expected to hold the highest adoption scores, based on the literature, it was found that Infectious Disease (20.8) was the highest mean adoption score, followed by ENT and Genetics (20), Cardiology (19.29), and then Oncology (18.18).

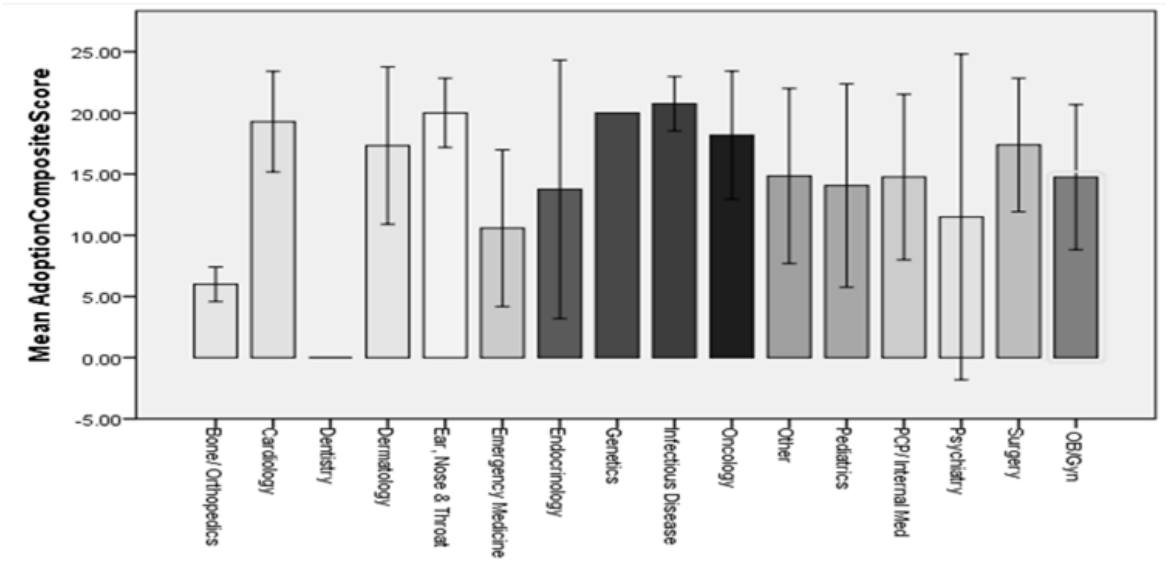

Figure 4. Likelihood of adoption by therapeutic area. The above figure illustrates the mean adoption scores of providers by their primary therapeutic area of practice, as defined by 50% or greater of their caseload.

An ANOVA was performed to test for differences in adoption scores by therapeutic area. An ANOVA of Adoption composite scores ($F(16,186) = 2.20$, $p < .01$) showed that there was a significant difference among specializations at the $p < .01$, but the effect size was small. An Eta squared of .171 indicated that, 17.1% of the variation between adoption scores could be attributed to specialization (among other possible factors).

Hypothesis 1c analysis

Hypothesis 1c predicted that a significant difference would exist in likelihood to adopt among different types of healthcare providers (e.g. MD, NP, PA, etc.). Differences in Mean Adoption Scores were compared by therapeutic area. As expected from the extrapolating from the literature, Pharmacists had the highest likelihood to adopt with a Mean Adoption Composite Score of 19.5. This was followed by physicians, PA's then Nurses. Degrees and/or credentials representing other types of providers included DMD, CRNA, RD and ATC.

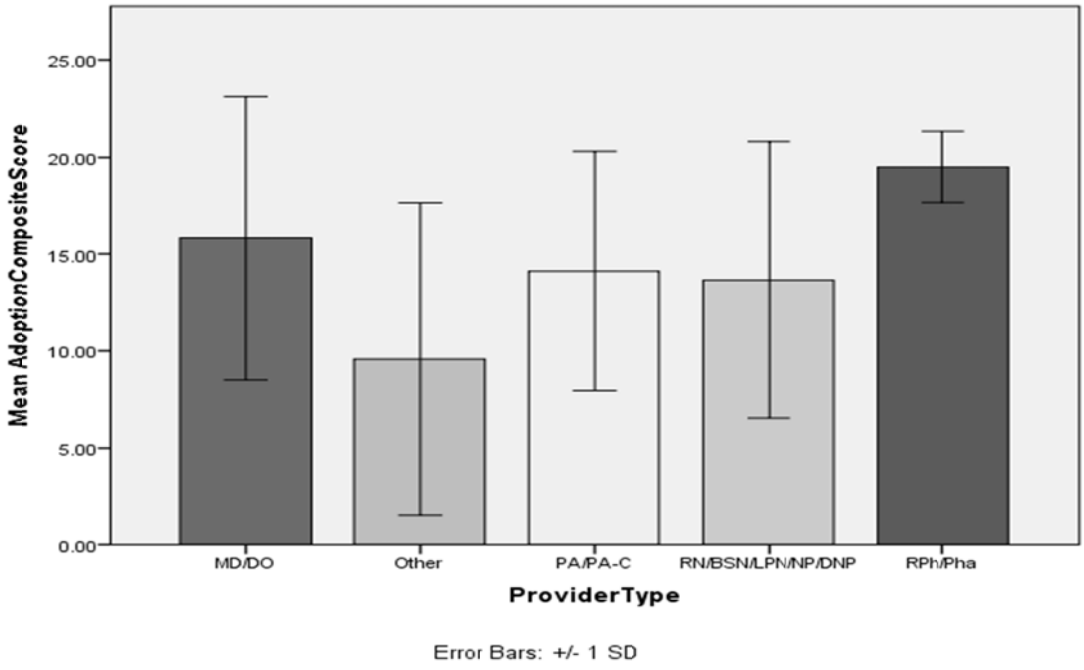

Figure 5. Likelihood of adoption by provider type. The above bar graph illustrates mean adoption composite scores by provider type.

The data were assessed for the assumptions of independence, normality, homogeneity of variances. An ANOVA of Adoption Composite Scores showed that there was a significant difference ($F(5,186)=2.43$, $p<.05$) among provider types at the $p<.05$ level, but the effect size was again small. An Eta squared of .063 indicates that, 6.3% of the variation between adoption scores can be attributed to provider type (among other possible factors).

Hypothesis 2 analysis

Hypothesis 2 predicted that a relationship would exist between knowledge of pharmacogenomic testing and the likelihood of adoption of pharmacogenomic testing by healthcare providers in the clinical setting.

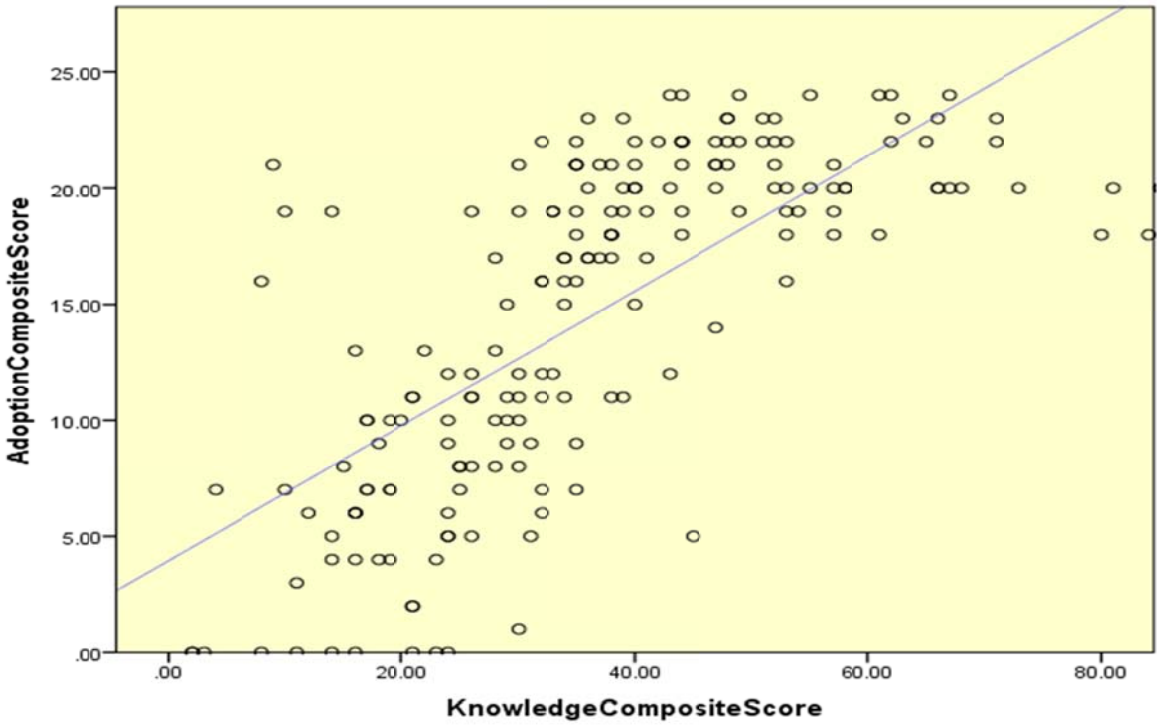

Figure 6. Scatterplot of adoption composite score by knowledge composite score. The above scatterplot illustrates the distribution of knowledge vs. adoption composite scores.

The data were assessed for the assumptions of independence, normality and homoscedasticity. A formal test of correlation shows that, indeed, knowledge overall, as a construct, correlates with adoption ($\rho = .767$, $p < .001$). Since some of the data originated from a Likert type scale, it was treated as ordinal level data. There is some amount of disagreement among publications as to what the level of measurement of this type of data is when it is part of an instrument. Though, there was still a strong significant correlation when the Pearson r was calculated.

Hypothesis 3 analysis

Hypothesis 3 predicted that a relationship would exist between attitude towards pharmacogenomic testing and the likelihood of adoption of pharmacological testing by

healthcare providers in the clinical setting. Figure X shows the scatterplot of the Attitude Composite Scores, as compared to Adoption Composite Scores along with the best fit linear trend line for this data.

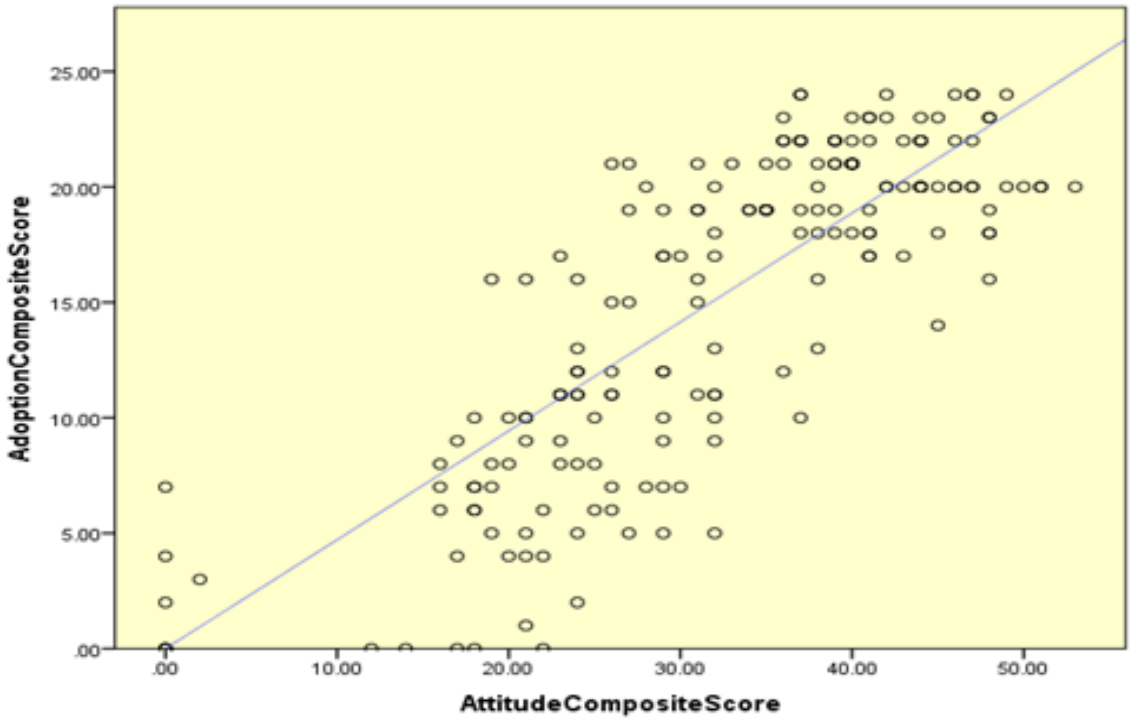

Figure 7. Scatterplot of adoption composite score by attitude composite score. The above scatterplot illustrates the distribution of knowledge vs. adoption composite scores.

The data were assessed for the assumptions of independence, normality and homoscedasticity. Since some of the data originated from a Likert type scale, it was treated as ordinal level data. A formal Spearman test of correlation showed that attitude correlated with adoption ($\rho = .798$, $p < .001$).

The overall mean for Adoption Composite Score was 31.40. Among provider types, pharmacists were found to have the highest attitude composite scores ($\bar{x} = 42.25$), indicating the most positive attitude toward pharmacogenomic technology. This was followed by the provider type,

physicians ($\bar{x}$ =33.58). Nurses and physician assistants overall, scored close to the same, but fell below the mean with scores of 29.68 and 29.48, respectively.

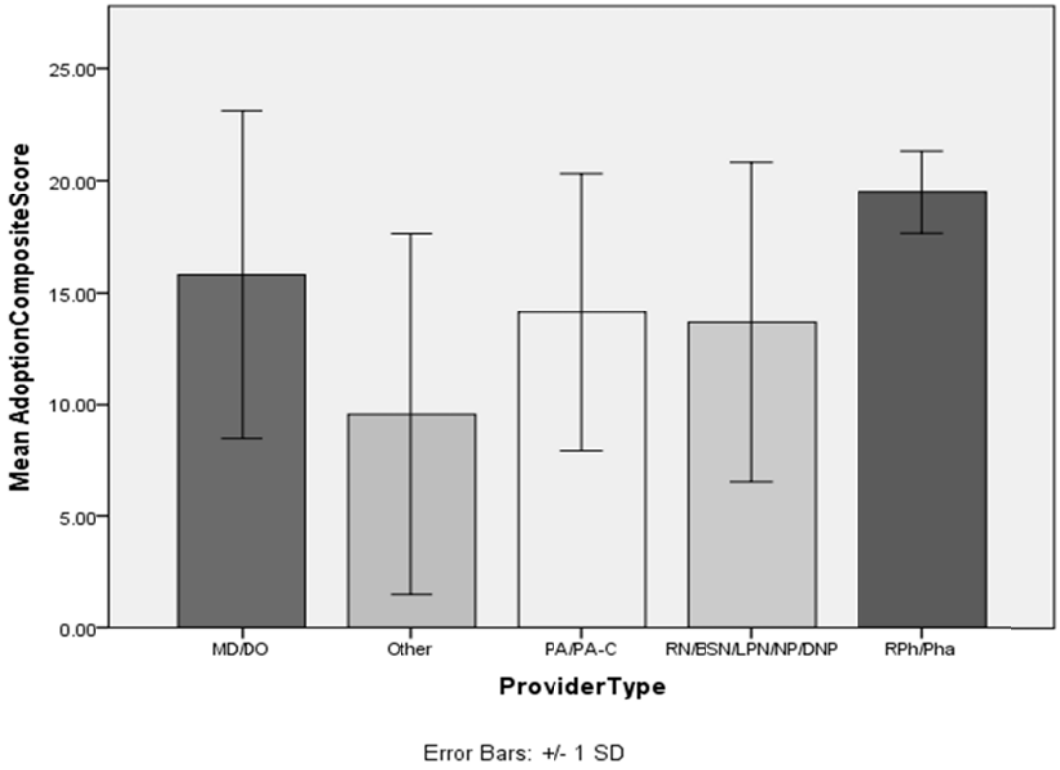

Figure 8. Mean adoption composite score by provider type. The above bar graph illustrates the mean adoption composite score by type of healthcare provider.

Hypothesis 4 analysis

Hypothesis 4 posited that a model would exist that would best predict the probability of adoption of pharmacogenomic technology in clinical practice. The aim of this research question was to describe this model. The table below shows the respective regression coefficients of each factor. The factors considered were age, years of experience, pharmacogenomic experience, academic knowledge, clinical benefit, and cost effectiveness, potential for misuse and/or discrimination, and patient/provider ability to understand. Variables that were found to be multicollinear were excluded from the regression analysis.

Table 13:

Regression Model of Factors Predicting Adoption Composite Scores

						Correlations		
Model	**B**	**Std. Error**	**Beta**	**t**	**Sig.**	**Zero-order**	**Partial**	**Part**
(Constant)	-1.870	2.860		-.654	.514			
Age	.238	.405	.038	.587	.558	.186	.048	.031
Years of Experience	-.252	.828	-.020	-.304	.761	.188	-.025	-.016
PGx Experience	-.040	.066	-.052	-.616	.539	.458	-.050	-.032
Academic Knowledge	.084	.060	.156	1.412	.160	.651	.115	.074
Clinical Benefit	.676	.196	.302	3.453	.001	.698	.272	.181
Cost Effectiveness	.371	.213	.124	1.742	.084	.564	.141	.091
Misuse/Discrimination	.496	.233	.142	2.126	.035	.536	.172	.111
Patient/Provider Understand	.410	.126	.242	3.266	.001	.636	.258	.171

A regression model was generated for adoption composite scores. Factors that were found to have significant effect in the previous ANOVAs were utilized as predictor variables. A forward regression model was first completed. The forward regression revealed a significant model ($F(8,157)=27.02$, $p<.001$). A backward elimination was then performed. Among the predictor variables in the forward model, Clinical Benefit, Attitude toward Misuse or Discrimination, and Ability for Patient/Provider to Understand, were found to be statistically significant in predicting likelihood of adoption of PGx technology. The forward model was determined to be the best fit, because it yielded the lowest Akaike information criterion (AIC). Akaike weights can be used in model averaging. They represent the relative likelihood of a given model. To calculate the AIC for each model the relative likelihood of the model was first determined, using the equation, exp (-0.5 * ΔAIC score for that model). The Akaike weight for the model was this value divided by the sum of these values across all models. Based on this, the following regression equation was be generated: Likelihood of Adoption = .68(Clinical Benefit) + .50(Attitude toward Misuse/Discrimination) + .41(Ability to Understand) – 1.87.

Summary

A weak relationship existed between likelihood to adopt and the demographic factors of age, years of experience. There was a significant difference between genders, but effect size was very small. Infectious Disease practitioners had the highest likelihood of adoption. A significant difference existed among specializations, 17.1% of the variation between adoption scores can be attributed to specialization. A significant difference was found to exist among provider type groups. Pharmacists had the highest likelihood of adoption, 6.3% of the variation between adoption scores can be attributed to provider type. A strong correlation ($\rho = .767$, $p < .001$) was found between knowledge of pharmacogenomic testing and the likelihood of adoption of by healthcare providers in the clinical setting. A strong correlation ($\rho = .798$, $p < .001$). was found between attitude towards pharmacogenomic testing and the likelihood of adoption of pharmacogenomic testing by healthcare providers in the clinical setting. Among the predictor variables examined, Clinical Benefit, Attitude toward Misuse or Discrimination, and Ability for Patient/Provider to Understand, were found to be statistically significant in a model predicting likelihood of adoption of PGx technology.

Chapter V

DISCUSSION

General discussion of key study findings

This study investigated factors that contributed to the likelihood of adoption. The study measures were centered around constructs emergent from the health belief model and Rogers Diffusion of Innovation theory. Though previous literature has identified a number of barriers that could inhibit the use of pharmacogenomic testing, this study specifically, empirically investigated a number of these factors and what their relationship to adoption of this technology was in clinical practice. Studies, such as Condit's 2003 work, have investigated some factors, but only in one group of providers, in this case physicians. This study looked at factors that were common among many healthcare provider types, such as physician assistants, nurse practitioners and others have a direct role in patient prescribing and these groups perceptions of many of the issues discussed had yet to be captured, side by side in a an empirical study. This study also compared the effect of therapeutic specialization and found that there was a difference between specializations in likelihood to adopt. This study allowed for an overall assessment of the composite barriers that emerged from the present literature. It also allowed for a direct comparison between groups with the questions standardized to a single instrument, allowing for a side by side comparison of perception between provider type groups, different therapeutic areas and a number of other factors.

Barriers to adoption

This dissertation study found the most commonly cited barrier to adoption to be limited provider knowledge or awareness, which was consistent with Bonter's 2011 study (Bonter,

Desjardins, Currier, Pun, & Ashbury, 2011) that found limited knowledge to be the second most cited factor among Canadian physicians. This was followed by lack of access to laboratory services (15.6%). "Lack of 3rd party payor reimbursement" was the third most commonly cited barrier (13.9%). These three responses comprised nearly 50% of the reply for this question. Though many barriers that had ranked highly in previous studies, they were not found to be statistically significant in this study. For instance, in Bonter's study a "lack of evidence-based clinical information" was cited as the third most highly cited barrier to adoption (Bonter, Desjardins, Currier, Pun, & Ashbury, 2011). Though, in this dissertation study, "lack of evidence based clinical information" was in the lower half of responses for greatest perceived barriers by frequency. There is some discord in the consensus on the level of evidence required to recommend clinical pharmacogenomics tests. Though this dissertation study and Bonter's study had different finding in terms of validation required by clinical evidence, other studies have had mixed results on this topic (Guzauskas, Serbin, & Veenstra, 2015). The objective of Guzauskas' study was to quantitatively compare the evidence levels of two contested drug-attenuating interactions and assess the value of obtaining additional evidence to inform clinical practice guidelines. Guzauskas' findings suggested that there was not a clear consensus in weighting the value of the evidence in each case. Overall, it is likely that a more in depth assessment of the validation of pharmacogenomic evidence levels in relation to other clinical interventions is needed as a helpful tool to guide policy makers in evaluating the clinical importance of evidence in test recommendations.

Other factors, such as cost-effectiveness have become less significant as the landscape and technology has changed since earlier studies were conducted. Studies such as Wong had previously looked at cost-effectiveness and the cost effectiveness of pharmacogenomic

technology was reported to be a significant factor in utilization decision making (Wong, Carlson, Thariani, & Veenstra, 2010). This study, however, did not find cost-effectiveness to be a statistically significant factor in determining the likelihood of adoption of pharmacogenomic technology. Dynamic factors like the cost of tests have dramatically fallen in the past decade, making previous assessments of cost to benefit less relevant to today's landscape. A 2015 assessment of cost-effectiveness of one-time genetic testing to minimize lifetime adverse drug reactions found cost-effectiveness to be highest ever reported (Alagoz, Durham, & Kasirajan, 2015). Additionally, the predictive value of tests has improved and expanded in more recent years. Thus, cost has become perceived by many to be less of a barrier, than it had been previously. It has now become more widely accepted that the relatively reduced cost of genotyping is far outweighed by the clinical utility of the genotyping information. This may explain why cost has previously been found to be a prohibitive factor in the adoption of pharmacogenomic testing in previous studies, but was not found to be a significant factor in this study. The changing healthcare landscape and the changing of the technology that comprises innovation in pharmacogenomics create a fluid model, in which factors may rise and fall in their relationship with adoption outcomes and with respect to their place in a model of the process.

Demography

The first research question looked at the relationship between likelihood to adopt and demographic factors. The weak correlation between age and adoption likelihood and the weak correlation between years of job experience suggest there is a relationship between these variables; however the amount of variation that could be attributable was very small, when considered in the regression model. The demographic factors, while statistically significant, didn't appear to yield a large effect size in terms of variation in adoption likelihood outcomes.

However, an ANOVA of Therapeutic Specialization did yield an eta squared of about 17%. This was corroborative with the qualitative finding that the Emergency Medicine and Urgent Care settings may have a lower likelihood of adoption than other settings. Though other studies have found differences to exist among physicians by therapeutic specialization, this was the first to identify Emergency Medicine and Urgent Care as different from other specializations in potential for adoption (Swen and Guchelaar, 2012; Stanek, Sanders, & Taber, 2012).

Pharmacogenomic knowledge

Findings from the study were consistent with other studies in the literature. The study findings on knowledge were in line with the predictions of adoption in other study populations. In Stanek's 2012 study of physician adoption, 97.6% of physicians that responded believed that a patient's genetics could affect their response to a drug, whereas in this study of healthcare providers as a whole, only 87.3% answered yes to a similar question (Stanek, Sanders, Taber, 2012). This further supports the thought that physicians may have better knowledge of pharmacogenomics than healthcare providers, overall. A theme that emerged in the open-ended portion of this study was that insufficient knowledge or training was available. This is consistent with Haga's study of primary care providers of the primary barriers in this group. In Haga's study it was cited that there was limited opportunity to utilize this technology in practice (Haga, 2012). This study also found that knowledge was insufficient in primary care providers and that limited training opportunities and limited access to information portals made primary care physicians less confident in utilizing this technology to guide a diagnosis. This suggests that not only primary care physicians, but perhaps all non-specialized clinical healthcare providers, as a whole face challenges that are unique to that circumstance. The results of this study would be in accord with Swen's posit that these issues may be related to previous opportunity to gain

experience, a lack of knowledge and inadequate access to information. This study and Haga's indicate that primary care providers have a desire to provide pharmacogenomic testing and utilize the results for clinical guidance, but knowledge and training opportunities are limited and this are preventative.

Academic Knowledge

Knowledge, overall, was strongly correlated with increased adoption composite scores. However, academic knowledge alone was not found to be a significant predictor in regression analysis. This suggests that acquiring of knowledge of pharmacogenomics may be a necessary step in the adoption process, but it is not necessarily sufficient as a factor to predict adoption behaviors. While those that had a low likelihood of adoption typically scored low in knowledge, many that scored high in knowledge had a somewhat low likelihood of adoption. This suggests that knowledge of basic genomics and theoretical knowledge of the underlying scientific mechanisms for the pharmacogenomic test, may be less important to a diverse group of healthcare providers than the experiential knowledge gained from hands-on experiences in clinical practice. It may be that many of the physician extenders did not necessarily believe that understanding basic genomics was directly related to their role or the scope of their role within the clinical setting. Among the many measured factors that made up the domain of knowledge in the instrument, the only one that was found to be predictive of adoption outcomes was experiential knowledge or observation of pharmacogenomics in the clinical setting. Experience with pharmacogenomics was found to be thematic in the qualitative responses, as well. This finding suggests that academic knowledge alone may not sufficiently support the factor of observability, as described by Roger's theory, while experiential knowledge may produce its effect on observability. Observability influences the domain of persuasion, thus it is a key factor

in the decision making portion of the adoption process. This concept is one of the five elements that describe direct influence to the persuasion domain. Persuasion factors are latter stage of the adoption process, as compared to knowledge and attitude factors. Thus, these factors are more likely to be predictive of adoption than others. Not knowing all of the specific factors that comprise the concept of experiential knowledge and "in the clinic training". It is difficult to determine how the variation is spread amongst this construct. What can be inferred is that, though academic knowledge was not found to be a predictive factor, experiential knowledge, which was, may be a factor that accounts for some of the unexplained variation, in the best fit regression model. Stanek's study, a majority of physicians reported that they believed that a person's genetics influenced their drug response (Stanek, 2012). This dissertation study had similar findings, though in this study the role of knowledge was slightly more nuanced. The increasingly rapid development of discovery in pharmacogenomics will drive an urgency to expand medical school curricula to include components that address the role of pharmacogenomic testing and integration of this technology into clinical practice. Inferences from this study suggest that when developing educational materials, it is as, if not more important to include the humanities of pharmacogenomics in the curricula, as it is to include the molecular and biological basis of the technology. Information about privacy protections; legal and social protections against misuse and discrimination; informed consent in pharmacogenomics, are all equally important to inform future healthcare providers on and knowledge of these topics may have a greater impact on the adoption of this technology in students, that the molecular basis for the tests. A recent study compared knowledge, attitudes and practices of student physicians and student pharmacists in Malaysia (Yau & Haque, 2016). The findings of Yau's study were in alignment with the implication discussed here.

Accordingly, healthcare organizations and government authorities will have to drive forward the task of medical schools with training future healthcare providers to be competent in their knowledge of genomic implementation and to understand the social context and mechanisms of this technology in their respective settings.

Attitude

Attitude factors were the strongest predictors in the regression model for likelihood of adoption of phamacogemonic technology in the clinic. The attitude composite score was highly correlated with the adoption composite score. Findings from the literature showed that early and future adopters of pharmacogenomic testing were more likely to have received training in pharmacogenomics, and that only a third of physicians, overall had received any education in the field (Stanek, 2012). However, this dissertation revealed that while knowledge was correlated to adoption, it was not necessarily a strong predictor for high likelihood of adoption as a factor. This suggests that the variation in adoption likelihood from knowledge, overall, is likely shared with other factors and that knowledge may be a necessary factor, but not one sufficient to change adoption outcomes. Thus, in other provider type groups, many of the high adoption scorers were not associated with the expected training or education in pharmacogenomics. These findings highlight the need for more effective education on topics related to attitude in diversified provider groups on the clinical benefit, misuse and discrimination, and understanding of and interpretation of pharmacogenomic tests between providers and patients. It was expected from previous findings in the literature that age and attitude could have a relationship, however, no significant relationship was found to exist. Among providers, pharmacists had the highest attitude scores, followed by physicians, these two groups scored higher than the overall mean, suggesting that these two groups had a more positive attitude toward pharmacogenomics. Nurses

and physician assistants fell below the overall mean, suggesting that they have a less favorable attitude toward pharmacogenomics than the aforementioned groups. These findings were consistent with Roederer's 2012 study of pharmacists and Stanek's 2012 study of physicians.

Clinical Benefit

Clinical benefit was found to be one of the three significant predictor variables in the best fit regression model. This suggests that the perception of a benefit to using pharmacogenomics is a significant factor that has a strong predictive value in the adoption process. This finding speaks to the concept of Relative Advantage in Roger's theory (Rogers, 2010). While Clinical Benefit was categorized as an attitude factor, the perception of relative advantage exerts its effects on persuasion. That is, that the user must perceive the innovation to provide an advantage in its use, when compared to the alternatives. This concept is one of the five elements that describe direct influence on the persuasion domain of Rogers stages of adoption. Persuasion factors are in the latter stage of the adoption process, as compared to knowledge and attitude factors, indicating that requisites for knowledge and attitude have been satisfied and the potential adopter has progressed to the persuasion stage. Thus, these factors are more likely to be predictive of adoption than the others prior stage factors.

Recently, a study by Guzauskas assessed the value of obtaining additional evidence to inform clinical practice guidelines (Guzauskas, Serbin, & Veenstra, 2015). In weighting evidence, it was found that consensus was unclear as to what constituted clinical value. So, though clinical benefit is a highly predictive factor in relation to adoption, the precise factors that create value are subjective and are different among providers. These findings are in agreement with what McKinnon found in a 2010 study. McKinnon's 2010 paper suggested that there is complexity in weighing the cost benefit of pharmacogenomic technology by healthcare

payers, because of the different efficacy associated with different markers (McKinnon, 2010). This dissertation study found that increased drug safety and improved probability of efficacy were both contributing factors to the perception of clinical benefit. Though, clinical value and benefit is clearly a significant factor, the significant components that comprise value and benefit may be differentially focused among different provider groups. This corroborates the notion in Roger's theory that Relative Advantage is a subjective consideration and that when determining value or benefit, the endpoints for making the determination, may be highly individualized.

Cost Effectiveness

Cost-effectiveness was not found to be a significant factor in this study. This is in disparity with prior studies, but may be found to be in alignment with future studies. In the contemporary background, cost may be becoming increasingly less significant as a factor. Further, pharamcogenomic technology has improved in efficacy and predictive value since many of the earlier studies were conducted. As mentioned, Studies such as Wong's had previously looked at cost-effectiveness of pharmacogenomic technology. Though it had previously been reported to be a significant factor in adoption decision making, this dissertation study found evidence to the contrary (Wong, Carlson, Thariani, & Veenstra, 2010). This dissertation study did not find cost-effectiveness to be a statistically significant factor in determining the likelihood of adoption of pharmacogenomic technology. This may be due the inherent changes in cost mentioned earlier. A 2015 assessment of cost-effectiveness of one-time genetic testing to minimize lifetime adverse drug reactions found cost-effectiveness to be highest ever reported (Alagoz, Durham, & Kasirajan, 2015). Additionally, the predictive value of tests has improved and expanded in more recent years. Thus, cost has become perceived by many to be less of a barrier, than it had been previously. It has now become more widely accepted that the relatively

reduced cost of genotyping is far outweighed by the clinical utility of the genotyping information. This may explain why cost has previously been found to be a prohibitive factor in the adoption of pharmacogenomic testing in previous studies, but was not found to be a significant factor in this study. The changing healthcare landscape and the changing of the technology that comprises innovation in pharmacogenomics create a fluid model, in which factors may rise and fall in their relationship with adoption outcomes and with respect to their place in a model of the process.

Misuse and discrimination

One of the most thematic factors in this dissertation study was the perception for potential for misuse and discrimination as a barrier to adoption. This factor was another that was highly predictive of adoption outcomes. As in previous studies, one of the most concerning issues is the utilization of pharmocogenomic technology and the protection of a patient's privacy and the potential for future discrimination based on genetic information. This study asked about the potential for genetic discrimination by health insurance companies, genetic discrimination, by employers, privacy concerns and general misuse of data collected for the purpose of patient treatment. A recent study found similar results in physicians, and found that these physicians had lower knowledge of protections against discrimination (Laedtke, O'Neill, Rubinstein, & Vogel, 2012). This study found that knowledge was limited regarding the existence of protections against misuse, and the pertinent facts about these protections. Though in Laedtke's study, physicians who were aware of legal protections persisted to have major apprehensions concerning the potential risk of genetic discrimination. Thus, even when educated further on the topic, adoption would not likely improve. This may suggest that knowledge alone is not sufficient and vicarious observation may be required to internalize the value of legal and social

protections. Both studies suggest that there is a need to further educate physicians about the existence of protections, and that this education may need to be supplemented with hands-on activity to aid in internalizing the value of these protections.

Since patient genetic information is highly permanent and can potentially contain significant information about an individual's health predispositions, the implications related to concerns of misuse of this data is likely a great consternation factor in the perception of providers (Rogausch et al, 2006). The data collected in pharmacogemonic tests is highly sensitive and identifies information that may be highly predictive of an patients health outcomes. Evidently, the permanent and highly confidential nature of genomic offers the potential for a great risk of loss of confidentiality (Goldman, 2005). The suggestion of this study in conjunction with the literature is that providers perceptions of the protections for the potential misuse of this information could have grand the resultant consequences to patients are highly influential in the adoption process.

Knowledge of data encryption and the rigorous confidentiality standards that protect patients from genetic discrimination is likely a proximal factor that effects perception of the potential for these events. In the US, privacy protection and data handling laws regarding genetic information have become steadily more and more stringent with the aim of protecting patients. In the US, the Genetic Information Non-discrimination Act of 2008 protects patients from misuse and discrimination by legally prohibiting health plans, insurers and employers from denying coverage or charging higher premiums to individuals based on genetic predisposition (NHGRI, 2008). The legal statute's mission language proposes "to fully protect the public from discrimination" and "allay their concerns about the potential for discrimination, thereby allowing individuals to take advantage of genetic testing, technologies, research and new therapies."

Though, this legal protection and others are currently in place, this dissertation study still found that perceived potential for genetic misuse and discrimination was a strong predictive factor in the adoption process and that a large portion of responders with low adoption had negative attitudes toward the potential for misuse and discrimination, meaning that the perceived these events to be likely to happen.

Provider ability to explain/Patient ability to understand

The final factor that was quantitatively significant in the regression model was related to the ability of providers to effectively explain the implications and results of pharmacogenomics tests to patients and the patients' ability to understand the information provided. This factor relates to the complexity concept in Roger's Diffusion of Innovation Theory (Rogers, 2010). Some studies have shown that when clinicians provide explanation for genomic tests, the patient may sometimes overestimate the clinical benefit, thus it is important that the provider be able to adequately describe the nature of a specific test and markers and clearly be able to detail the exploratory nature of any components (Brewer et al., 2014). Providers need to have an adequate base of knowledge to be able to communicate the implications of tests to patients and make the meaning of the results clear and definitive to the patient. Some of the variation from this factor may be shared with knowledge. Providers must first have the knowledge of the specific genotype or have confidence in their ability to utilize tools such as databases and drug labeling to make determinations about genetic factors and how they relate to their patients drug response. The notion that their ability to explain these factors to patients is tied to knowledge was supported by the qualitative responses that were provided in this dissertation study. The qualitative responses in this dissertation study included language such as "Complex information would need to be communicated in a short amount of time" and "The population I work with has

many health literacy challenges even with more basic concepts". These support the notion that some providers have concerns about the complexity of the information, the comprehension levels of different patients and the amount of time available for providers to discuss complex information with patients in the clinical setting. When questioned about their perception of providers ability to explain information about pharmacogenomics testing to patients, responses in this dissertation study included "lack of education about the testing" and "Teaching or education is required", which suggest that additional training and support on the communication of pharmacogenomics test implications are desired by provides in the clinic, but not readily available. Additionally, comments such as "understanding pharmacology is difficult for mid levels", indicate that there is a differential among provider types in the level of knowledge and self-efficacy to effectively explain pharmacogenomics tests to patients.

Need for in-clinic training

This study showed a need for additional training and support within the clinical setting. Responses to study questions indicated a need for on the job experience and observation. Additionally, qualitative feedback suggested that while many providers were interested in learning more about pharmacogenomics, training opportunities were not available in their settings. This may relate to the concept of trialability in Rogers theory (Roger, 2010). Possibly, individuals desire on-the-job opportunities to work with pharmacogenomics in their setting on a test basis to experience and observe the practices and make further determinations about the technology as well as validate assumptions that they may have about it. These findings were in agreement with similar, recently conducted studies. A 2015 study by Unertl found that, based on analysis of interview data, three high-level theme categories existed. The themes were preparation and knowledge, pharmacogenomics usage in practice, and future implementation

challenges (Unertl, Field, Price, & Peterson, 2015). The findings from this study support the notion that additional training and support on-the-job are necessary to improve adoption.

Compatibility in the emergent setting

One of the themes in the qualitative data also suggested that Urgent Care and Emergency providers perceived that pharmacogenomic testing was not compatible with the Emergent setting. Comments such as, "doubtful this would be useful in urgent care as we don't usually do send out tests that require follow up" and "Impractical in ER setting given time line of treatment", suggest that providers in the emergent care setting perceive a lack of compatibility of pharmacogenomic technology with the emergent care setting. Compatibility is a major factor in the persuasion construct of Diffusion of Innovations theory. This suggests that in some cases, even if attitude is otherwise positive and knowledge is sufficient this factor may be prohibitive to adoption and could be a new factor that was not measured in this study quantitatively. To test support for this, the likelihood of adoption was compared by therapeutic setting to see if there was a lower probability of adoption measure by adoption composite PI-created PAI© scores in Emergency Medicine providers when compared to all other types. Indeed, this comparison showed an odds ratio of 1.26, meaning other providers were 1.26 times more likely to adopt than Emergency Medicine providers. This may not include Urgent Care providers, as some Urgent Care providers selected the other category when selecting therapeutic specialization. This result should be interpreted with caution, as whether these two areas may be distinctly different quantitatively was not considered in the initial design of this study tool. The post-data collection literature search initially suggested that this may be a novel finding, as no previous literature had discussed this topic. However, a study was then published in February 2016, which discussed the potential role of pharmacogenomics in the Trauma setting (Samai, K., 2016). Samai's study

had mixed positions on the use of pharmacogenomics in the trauma setting. The paper posits that while the potential exists for clinical benefit in the trauma setting, the setting-specific challenges that prevent its initiation may outweigh those benefits. The study cites a potential lack of time to properly provide informed consent to patients, as well as a high potential for reduced capacity in patients to provide consent in this setting. Both Samai's paper and this dissertation study are in agreement with regard to these findings and the need to further explore the specific barriers that exist in the Urgent/Emergency/Trauma setting, as they may differ from those in other settings.

Refinement of the theoretical model

Based on the findings from this study, the data did not support the theoretical frame as it was proposed. This study's findings suggest revisions to the theoretical frame. Figure X shows the conceptual model of study variables in context of Rogers Diffusion of Innovation Theory. The conceptual model denotes the receiver variable characteristics, those which are inherent to the potential adopter, in this case they included provider type, therapeutic specialization, years of experience in their practice, adopter category, and other basic demography including age and gender. The conceptual model highlights the fact that experience in the clinic was found to be a qualitative concern in adoption and the only knowledge variable that significantly predicted adoption outcomes. The conceptual model also shows that attitude variables were the most significant predictors of outcome. Diagnostic value, increased safety, impact on quality of healthcare, misuse of genetic data, genetic discrimination, and patient/provider ability to understand were all found to be significant predictors of adoption outcome. Compatibility in the Emergent setting was proposed to be a potential factor that may contribute to the adoption process. In the persuasion domain the elements of relative advantage, compatibility, complexity,

trialability and observability were all discussed in terms of the relation of the factors measured and their effects within the persuasion construct.

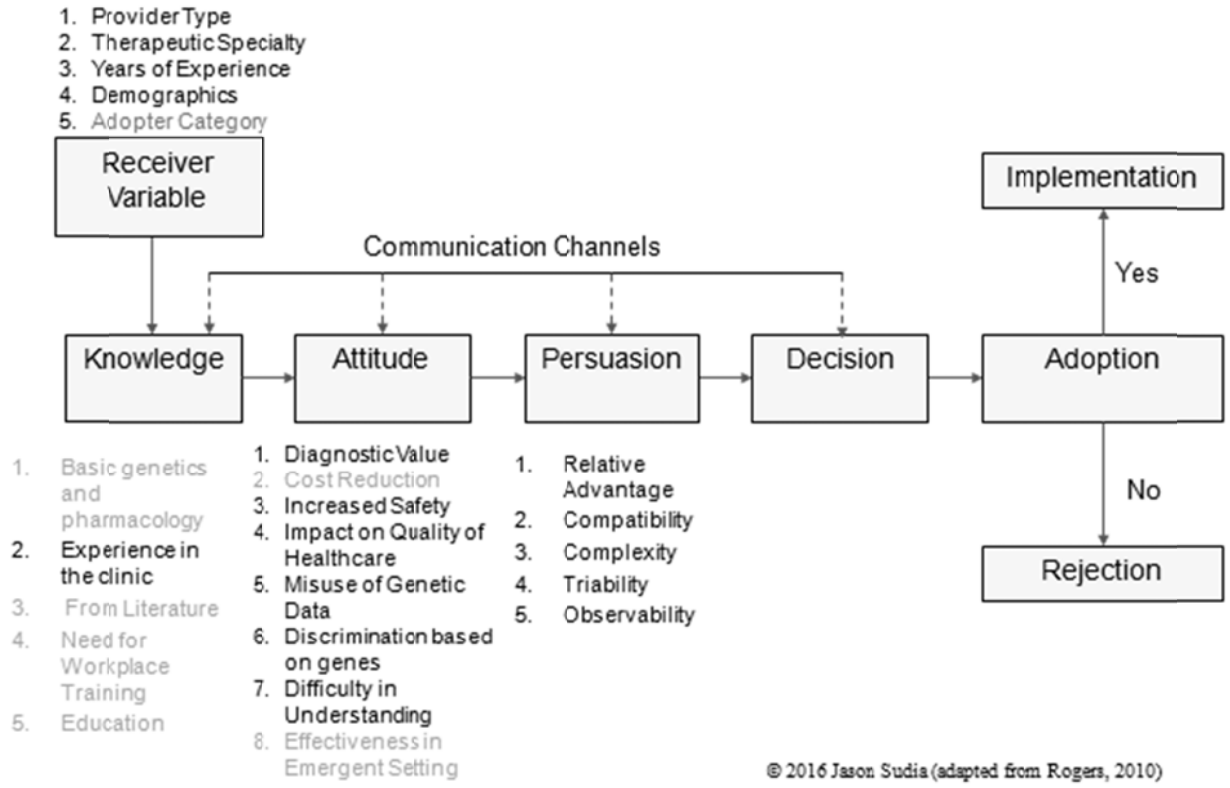

Figure 9. Conceptual model of study variables. The above conceptual diagram illustrates the components of Rogers' Diffusion of Innovations Theory, as related to the variables in this study.

Limitations

There were a number of limitations to this study. The first was related to the chain-referral sampling methodology. There were benefits to using this method of sampling; however there were also drawbacks that were a result of this sampling. Namely, since this sampling method allows invitations to be forwarded outside of the original recipients, it becomes impossible to control the geographic dispersion or the number of participants in any given group. This resulted in a geographic representation that was highly skewed towards 3 northeast states. The states of NJ, NY and PA made up about 50% of all PI-created PAI© responses. Though other geographic regions were represented to a smaller extent, the representativeness of this study may be limited to healthcare providers in the majority states represented. Another issue with the chain referral methodology is that there was no contact information collected for respondents, making a follow-up or longitudinal subsequent study not possible. The Survey Monkey link was also only provided to participants electronically via e-mail, therefore, the study may have excluded those without access to e-mail or those.

Further, the nature of non-purposive sampling, as a whole, limits the generalizability of the findings to the members of the sample as the population. This sample of convenience may be inferentially informing, but places limitations on what can be deduced. Thus, while we can make inferences about how these findings may relate to the greater population, the lack of randomization and selective sampling limits the extent to which data from this sample can be extrapolated to make inferences about a larger population.

Another limitation of the study is the correlational design measuring knowledge with adoption and attitudes with adoption. Though, both of these constructs can be compared with adoption likelihood, the use of correlational methods makes it impossible to establish causality

between either of these factors. So, while the study can say that there is a relationship between pharmacogenomic knowledge and adoption likelihood, and a relationship between attitude and adoption likelihood, it cannot say that higher knowledge or positive attitude, overall, can be causally linked to the likelihood of adoption. The findings do, however, support the greater model predicted in regression, in the framework of Rogers Diffusion of Innovations theory.

The study tool offered limitations in measuring adoption. Since the study used the PI-created PAI© to measure the construct of adoption likelihood, what was actually being measured was self-reporting of likelihood to adopt. All prior studies that have investigated adoption of pharmacogenomics have used this measure as a surrogate marker for adoption behavior, however no study has yet looked at actual implementation rates of pharmacogenomic testing in clinical practices among these groups and validated how closely a reported likelihood of adoption correlates with actual follow-through.

Directions for future research

This study yielded many questions that create the basis for future scholarly inquiry. For one, the geographical limitations of the study sample limited the generalizability of the results, as mentioned in the study limitations. A subsequent study that geographically expands the sample to have a more nationally representative sample, would offer much more generalizability to the US provider population and allow much broader inferences and implications. This may be achieved with purposive sampling. Though in a purposive sample, the recipients must be pre-selected and arranged to provide a representative sample from the selected centers. A purposive sample would need to take caution in selecting the centers and invitees to ensure representative response.

There has been little investigation of pharmacogenomics in the Emergency Care Setting. Further investigating the findings from the Emergency/Urgent Care setting, qualitatively in more depth, may reveal the factors that make this different from other clinical settings. While time was cited anecdotally in this dissertation study, it would be of benefit to investigate this factor empirically. Literature has suggested, philosophically that the potential exists for clinical benefit in some types of emergent settings, however it has been suggested that the specific challenges that prevent its initiation may outweigh those benefits. The literature supports the notion of potential time constraints to employ pharamacogenomics in the clinic, but it has not been investigated empirically.

Finally, this study utilized a survey tool and measured likelihood of adoption through questions that estimated a providers potential for adoption. That is, it used a cross-sectional design, employing the PI-created PAI© tool to measure likelihood of adoption. To increase precision and accuracy, it could be beneficial to conduct a study that looked at actual use of pharmacogenomic technology in providers in the clinic and then retrospectively investigate factors as compared to a control group, which is not utilizing pharmacogenomic techonolgy in practice. Employing a case-control design may eliminate some of the confounding effects that are encountered when measuring outcome through an endpoint that requires estimation. A study of actual users of pharmacogenomics could eliminate additional variation that could attenuate the effect of a predictive model.

Chapter VI

CONCLUSION

This study investigated a number of thematic factors from the literature in a diverse group of providers studied sided-by-side. Though, the literature identified a number of barriers that may be prohibiting the use of pharmacogenomic technology. Only some of these factors were shown to have an effect on adoption likelihood, in this study. This study looked at provider types that have been studied very little, if not all. These healthcare providers, such as physician assistants, nurse practitioners and others have a growing role in patient prescribing and decision making. This study collected perceptions of these provider types and measured the issues that had yet to be examined in an empirical study. Qualitatively, new themes emerged from the data collection that implicated the basis for future research. These themes suggested that setting may have a larger role than previous literature anticipated and the emergent setting may be qualitatively different from other clinical settings. The themes also suggested that on-the-job training opportunities may help to reduce barriers related to these factors, although nuances in the quantitative data caveat that the training needs to be designed to address the appropriate factors and address not only knowledge, but issues related to attitude and informing on attitudinal concerns. The information gained from the conduct of this study will, hopefully, help to inform on the issues discussed, and have an impact on the adoption of pharmacogenomic tests in the post-genomic era and thus, greatly improve the quality and cost-effectiveness of care for patients in this new paradigm.

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APPENDIX A

Seton Hall IRB Approval Letter

SETON HALL UNIVERSITY
1 8 5 6

May 27, 2015

Jason Sudia
[redacted]

Dear Mr. Sudia,

The Seton Hall University Institutional Review Board has reviewed your research proposal entitled "Exploring Barriers in the Clinical Adoption of Pharmacogenomics Technology among Healthcare Providers" and has categorized it as exempt.

Enclosed for your records is the signed Request for Approval form.

Please note that, where applicable, subjects must sign and must be given a copy of the Seton Hall University current stamped Letter of Solicitation or Consent Form before the subjects' participation. All data, as well as the investigator's copies of the signed Consent Forms, must be retained by the principal investigator for a period of at least three years following the termination of the project.

Should you wish to make changes to the IRB approved procedures, the following materials must be submitted for IRB review and be approved by the IRB prior to being instituted:

- Description of proposed revisions;
- *If applicable*, any new or revised materials, such as recruitment fliers, letters to subjects, or consent documents; and
- *If applicable*, updated letters of approval from cooperating institutions and IRBs.

At the present time, there is no need for further action on your part with the IRB.

In harmony with federal regulations, none of the investigators or research staff involved in the study took part in the final decision.

Sincerely,

Mary F. Ruzicka, Ph.D.

Mary F. Ruzicka, Ph.D.
Professor
Director, Institutional Review Board

Office of Institutional Review Board
Presidents Hall · 400 South Orange Avenue · South Orange, New Jersey 07079 · Tel: 973.313.6314 · Fax: 973.275.2361 · www.shu.edu

REQUEST FOR APPROVAL OF RESEARCH, DEMONSTRATION OR RELATED ACTIVITIES INVOLVING HUMAN SUBJECTS

All material must be typed.

PROJECT TITLE: ***Exploring barriers in the clinical adoption of pharmacogenomics technology among healthcare providers.***

CERTIFICATION STATEMENT:

In making **this application,** I(we) certify that I(we) have read and understand the University's policies and procedures governing research, development, and related activities involving human subjects. I (we) shall comply with the letter and spirit of those policies. I(we) further acknowledge my(our) obligation to (1) obtain written approval of significant deviations from the originally-approved protocol BEFORE making those deviations, and (2) report immediately all adverse effects of the study on the subjects to the Director of the Institutional Review Board, Seton Hall University, South Orange, NJ 07079.

RESEARCHER(S) — May 8, 2015 DATE
Jason E. Sudia

Please print or type out names of **all researchers below signature.
Use separate sheet of paper, if necessary.**

My signature indicates that I have reviewed the attached materials of my student advisee and consider them to meet IRB standards.

RESEARCHER'S FACULTY ADVISOR [for student researchers only] — May 8, 2015 DATE
Deborah A. DeLuca, MS, JD

Please print or type out name below signature

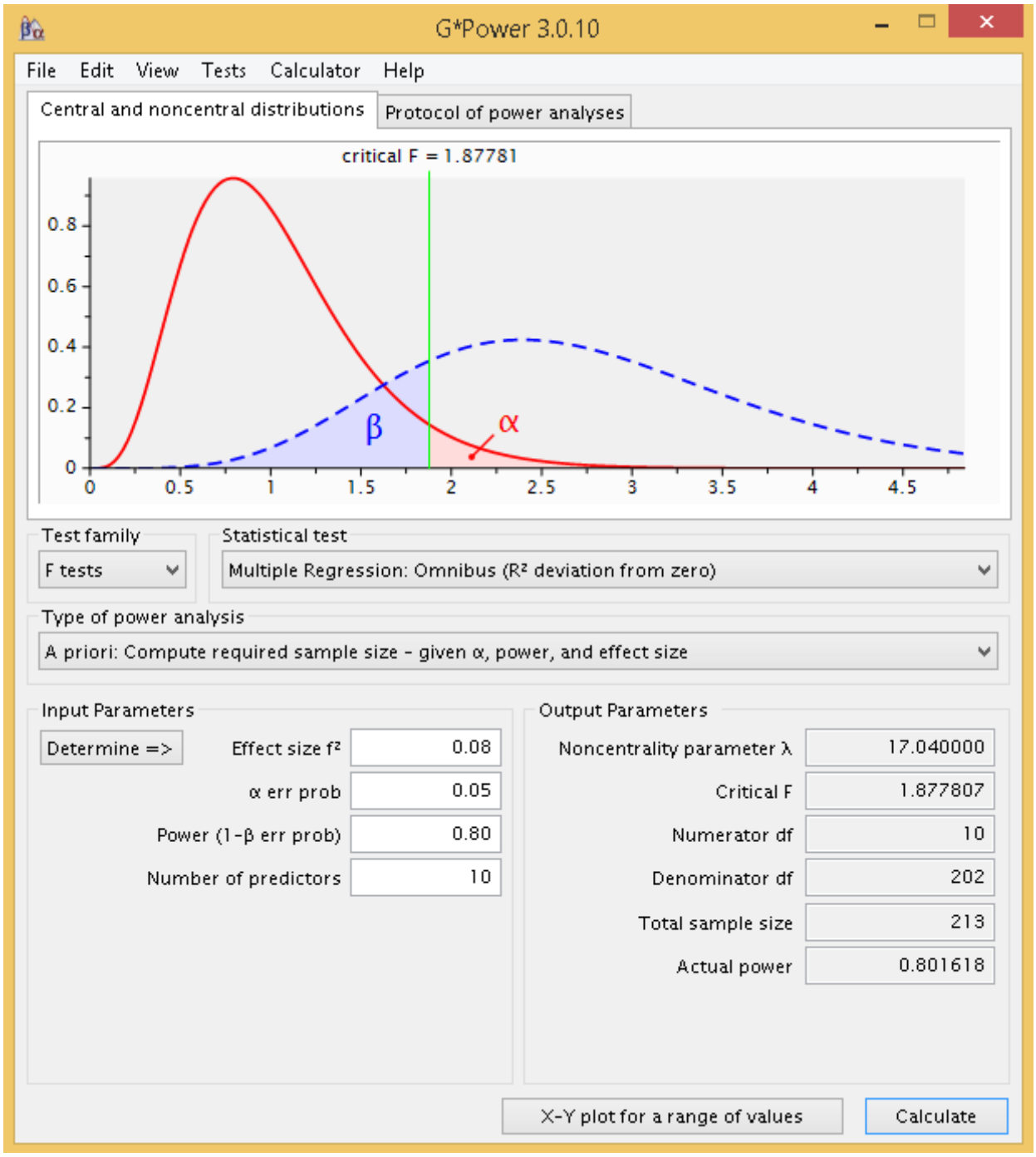
The request for approval submitted by the above researcher(s) was considered by the IRB for Research Involving Human Subjects Research at the May 2015 meeting.

The application was approved ✓ not approved ___ by the Committee. Special conditions were _____ were not ✓ set by the IRB. (Any special conditions are described on the reverse side.)

Mary J. Ruzycka, Ph.D — 5/27/15 DATE
DIRECTOR,
SETON HALL UNIVERSITY INSTITUTIONAL
REVIEW BOARD FOR HUMAN SUBJECTS RESEARCH

APPENDIX B

G*Power – sample size power calculations


G*Power 3.0.10
File Edit View Tests Calculator Help
Central and noncentral distributions
Protocol of power analyses
critical F = 1.87781
0.8
0.6
0.4
0.2
0
0 0.5 1 1.5 2 2.5 3 3.5 4 4.5
β
α
Test family
F tests
Statistical test
Multiple Regression: Omnibus (R² deviation from zero)
Type of power analysis
A priori: Compute required sample size – given α, power, and effect size
Input Parameters
Determine =>
Effect size f²
0.08
α err prob
0.05
Power (1-β err prob)
0.80
Number of predictors
10
Output Parameters
Noncentrality parameter λ
17.040000
Critical F
1.877807
Numerator df
10
Denominator df
202
Total sample size
213
Actual power
0.801618
X-Y plot for a range of values
Calculate

APPENDIX C

Permission to use SHU e-mail

SETON HALL UNIVERSITY
1 8 5 6

Date: April 14, 2015

Re.: Permission to Invite Our IHSA PhD Students to Participate in your Dissertation Study

To: Jason Sudia

From: Terrence F. Cahill, Chair, IHSA

This is to confirm that you will have access to invite our IHSA PhD in Health Science students to participate in your study concerning the use of pharmacogenomic testing in clinical practice. As only a portion of our students will have the experience that you are studying and/or know someone else who may have the experience that they can snowball the invitation to, you will need to clearly address this matter in your solicitation, Jason.

School of Health and Medical Sciences

Department of Interprofessional Health Sciences and Health Administration

Tel 973 275 2076 Fax 973 275 2370 TDD 973 275 2169

400 South Orange Avenue South Orange, New Jersey 07079

APPENDIX D

Work Authorization to Conduct Research

PRAHEALTHSCIENCES

721 Arbor Way • Suite 150 • Blue Bell • Pennsylvania • 19422 • USA
P +1 215.591.1029 • F +1 215.591.5025

prahs.com

April 15, 2015

Mr. Jason Sudia

Via E-Mail: [redacted]

Re: Authorization to Conduct Research for Ph.D. Dissertation

Dear Jason,

I am writing to acknowledge that PRA Health Sciences ("PRAHS") is aware of your study entitled "Exploring Barriers in the Adoption of Pharmacogenomic Technology among Healthcare Providers", which you will be completing in partial fulfillment of your Ph.D. dissertation at Seton Hall University School of Health and Medical Sciences under the oversight of your dissertation chair, Dr. Deborah A. DeLuca.

PRAHS policies do not require you to submit your IRB application to us for review as your study is not within the scope of your employment at PRAHS. Furthermore, the study will not be conducted using any facilities or resources or on company time of PRAHS.

No further action relating to your study, consistent with the above, is needed as this pertains to PRAHS. If required by the university's IRB, PRAHS will maintain a copy of your application's IRB approval letter from the university on file. Please advise us if this is necessary.

If either you or the university has additional questions on this matter, please feel welcome to contact me by telephone at the number above or by e-mail at RonemusDave@PRAHS.com.

Sincerely,

Dave Ronemus

Senior Legal Counsel

APPENDIX E

e-mail Solicitation Message Text

Dear Healthcare Provider,

My name is Jason Sudia. I am a student at the School of Health and Medical Sciences at Seton Hall University. I am conducting this research study as part of my doctoral dissertation.

What is the purpose of the study?

You have been invited to participate in this survey study. You have been invited because you may be a healthcare provider that works in the clinical setting. Previous research has suggested that some factors may prevent the use of pharmacogenomic tests in the clinic. The purpose of this study is to determine how much clinical healthcare providers understand about pharmacogenomic testing. Another purpose is also to find whether they are using it in the clinic. Another is to find if the main reason why they may not be using it.

What is the study procedure?

You are being asked to complete the survey if you fit the requirements. The requirements are, being a healthcare provider that has interaction in the pharmacological treatment of patients. You may complete the survey by clicking on the link below. This study will also be utilizing a recruitment technique known as chain-referral or snowball sampling. This means you are encouraged to forward this e-mail to anyone that you think meets the requirement of being a clinical healthcare provider. They may then determine if they have interaction in the pharmacological treatment of patients. Anyone who fits that requirement may participate in the study. They may then complete the study, even if you do not. This allows the survey to reach a greater audience. Thus, it may gather more information than it would, otherwise. The attached link is not unique to you. It may be forwarded to anyone. No record will be kept regarding whether or not you completed the survey. Nor will a record of be kept of who you forwarded it to. Completing the multiple choice question portion of the survey will take about 10-15 minutes. There is an open-ended question. You can take as much time as you would like to complete this.

Is participation voluntary?

Your participation in this research study is completely voluntary. You may decide not to participate at any time. If you choose not to participate, you will not be penalized nor lose any benefits to which you are otherwise entitled to. By clicking the link below, you acknowledge that you are providing your consent to participate in this study.

Is the survey anonymous?

Your identity will not be collected as part of this study. Your name, address, and other specific personal identifying information will not be collected. The information that will be collected is general demographic information. There will be no records identifying you, specifically. All of your answers will be recorded anonymously. There will be no way to contact you or link your answers to you. If you forward the survey to others, no specific identifying information will be collected from them. The research data may be published. If it is, it will not identify any individual.

What will happen to the study data?

The study data will be kept confidential to protect its integrity. The data will be stored on a USB drive. The USB drive will be locked in a cabinet in the office of the principal investigator. The principal investigator, Jason Sudia, will have access to all of the data for a period of up to three years after the end of the study. After that time, the research data will be destroyed.

Can I request further information?

If you decide that you have an interest in learning more about pharmacogenomics and its application in the clinic please feel free to contact me at the e-mail address below for more information. You may send questions about the survey. You may also request the correct answers to the knowledge questions.

Thank you for taking the time to read this and consider participating in this study.

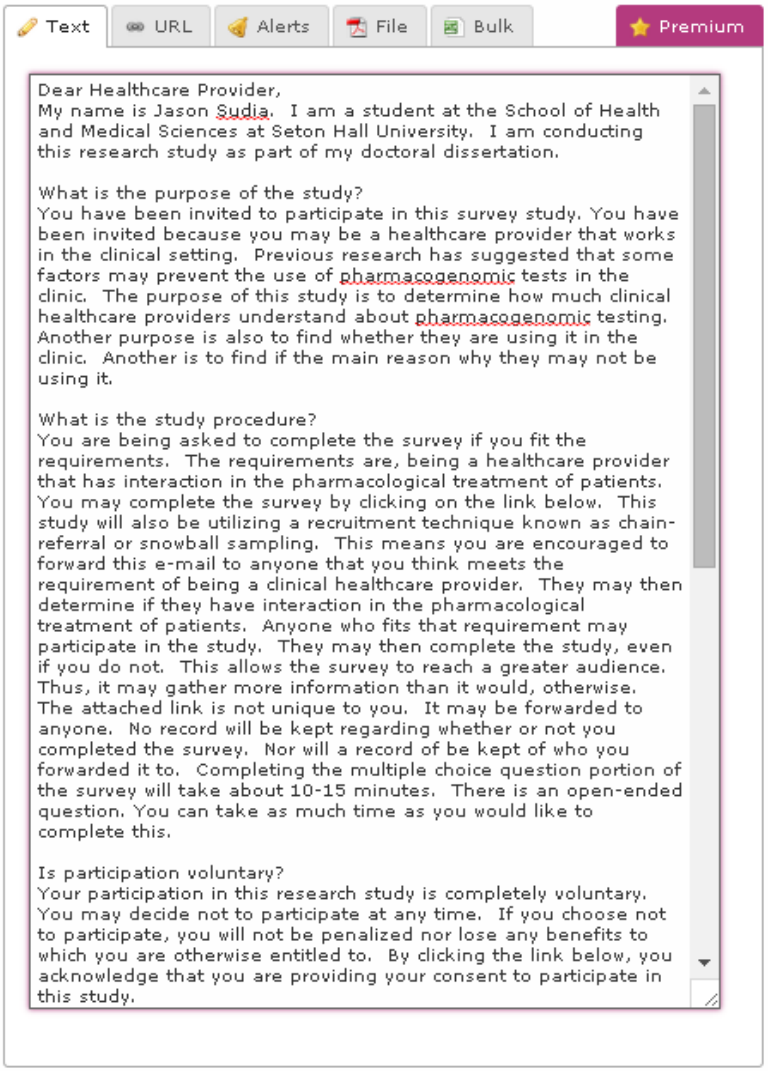
Best Regards,

Jason Sudia

Jason.sudia@student.shu.edu

APPENDIX F

Flesch-Kincaid Readability Score for E-mail solicitation message text



Reading Ease

A higher score indicates easier readability; scores usually range between 0 and 100.

Readability Formula	Score
Flesch-Kincaid Reading Ease	58

Grade Levels

A grade level (based on the USA education system) is equivalent to the number of years of education a person has had. Scores over 22 should generally be taken to mean graduate level text.

Readability Formula	Grade
Flesch-Kincaid Grade Level	8
Gunning-Fog Score	10.3
Coleman-Liau Index	12.2
SMOG Index	7.7
Automated Readability Index	6.6
Average Grade Level	**9.0**

Text Statistics

Character Count	3,160
Syllable Count	1,080
Word Count	665
Sentence Count	59
Characters per Word	4.8
Syllables per Word	1.6
Words per Sentence	11.3

Flesch Reading Ease score: 57.9 (text scale)
Flesch Reading Ease scored your text: fairly difficult to read.
[r] | [a] | [r]

Gunning Fog: 10.3 (text scale)
Gunning Fog scored your text: fairly easy to read.
[r] [a] [r]

Flesch-Kincaid Grade Level: 8
Grade level: Eighth Grade.
[r] [a] [r]

The Coleman-Liau Index: 10
Grade level: Tenth Grade
[r] [a] [r]

The SMOG Index: 7.8
Grade level: Eighth grade
[r] [a] [r]

Automated Readability Index: 6.7
Grade level: 11-13 yrs. old (Sixth and Seventh graders)
[r] [a] [r]

Linsear Write Formula : 6.5
Grade level: Seventh Grade.
[r] [a] [r]

Readability Consensus

Based on 8 readability formulas, we have scored your text:
Grade Level: 8
Reading Level: fairly difficult to read.
Reader's Age: 12-14 yrs. old (Seventh and Eighth graders)

APPENDIX G

Pharmacogenomic Adoption Instrument Survey Sample Page

(First page example as appears in Survey Monkey, for the full PAI© survey, please contact the author at jason.sudia@student.shu.edu)

Description of Healthcare Provider Type and Setting

The following questions will ask you about the details of the type of healthcare setting you work in and your role.

1. Which credentials best describe your education? (Check all that apply.)

- [ ] MD/DO
- [ ] PA/PA-C
- [ ] RN/BSN/LPN/NP/DNP
- [ ] RPh/PharmD
- [ ] PhD
- [ ] Other (please specify)

2. In what state do you practice the majority of your patient care activities?

3. What is your primary (defined as greater than 50% of your caseload) therapeutic area of practice? (select one)

- ○ Bone/ Orthopedics
- ○ Cardiology
- ○ Dentistry
- ○ Dermatology
- ○ Ear, Nose & Throat
- ○ Emergency Medicine
- ○ Endocrinology
- ○ Genetics
- ○ Infectious Disease
- ○ Oncology
- ○ Pediatrics
- ○ Primary Care/ Internal Medicine
- ○ Psychiatry
- ○ Surgery
- ○ Women's Health/ OB/Gyn
- ○ Other (please specify)

APPENDIX H

Delphi Review Expert Panel Methodology and Procedures

Delphi Review Expert Panel Methodology and Procedures

A structured, modified Delphi procedure was performed to achieve face validity of the survey questions. The procedure included the key elements of Delphi according to Fowles (Fowles, 1978). These include anonymity of the panelists from one another, controlled feedback and integrated moderation and summarization of comments and revisions, and a statistical characterization of the panelists responses to achieve a predetermined threshold, in this case greater than eighty percent consensus in approval of construct.

1. **Selection of the five member pharmacogenomics adoption expert panel reviewers.**
   A five member panel was selected based on a few factors. The first was publication of a paper that examined the utilization of pharmacogenomic technology in the clinical setting. This was a first criteria. The second was publication of a paper that examined this issue via survey methodology. The third selection factor was the number of papers that met the first two criteria and the frequency of citation of these papers as reported by EBSCO Academic databases. The 10 leading candidates were contacted and were then asked if they were willing and available to provide review. Seven of ten were willing and 5 were selected as panelists.

2. **Development of the first round modified Delphi questionnaire.**
   The author and project academic advisor, in conjunction with the doctoral committee, created a worksheet to measure agreement with the proposed constructs in the survey questions that were drawn from topics in the literature and other studies that had investigated some of these issues independently or in other populations. The constructs were mapped and identified with the question in the worksheet and the sheet asked for comments and for expert agreement or objection with the proposed construct.

3. **Testing the questionnaire for precision and clarity with dissertation committee.**
   The doctoral committee then met to review the proposed worksheet and provided revisions for clarity and precision. The revised worksheet and questions were then sent out to an expert reviewer that was not a member if the panel to determine if any content specific issues arose from the language revisions. The worksheet was revised and reviewed by the academic chair and doctoral committee.

4. **Transmission of the first round questionnaires to the panelists.**
   The worksheet and questions were then sent out to the panelists. The panelists were instructed to review each question and the related construct or factor associated with the question. They were then asked to determine if the question measured the construct or factor described. They then checked yes or no to indicate their position. Expert reviewers were instructed to provide comments or further explanation if they indicated no. Reviewers were also instructed that they may make suggestions or any additional comments, even if the construct was in agreement with the question. They were instructed to return the comments for the first round of the Delphi within seven days of receipt.

5. **Analysis of the first round responses.**

The first round responses to the Delphi worksheet were calculated and summarized. A consensus was calculated (Appendix I). A minimum consensus of 80% agreement of the panel was sought. Questions that did not achieve 80% consensus were modified per the Delphi members' feedback. The proposed revisions were reviewed and refined by the doctoral dissertation committee.

6. **Preparation of the second round questionnaires.**

Once the final revisions were reviewed and refined by the doctoral committee, the revised questions were reformatted into a final version worksheet. The worksheet included a check box asking if the revised question measured the intended construct indicated for the questions that achieved below 80% consensus in the first round. The worksheet also included a comments box for all questions and the questions that achieved greater than 80% consensus were included for a final quality check.

7. **Transmission of the second round questionnaires to the panelists**

The second round questions and worksheets were then sent to the panelists for review Expert reviewers were instructed to provide comments or further explanation if they indicated no to the question of construct and question agreement. Reviewers were also instructed that they may suggest any additional comments even if the construct was in agreement with the question. They were instructed to return the comments for the first round of the Delphi within seven days of receipt.

8. **Analysis of the second round responses**

The second round responses to the Delphi worksheet were calculated and summarized. A consensus was calculated (Appendix I). A minimum consensus of 80% agreement of the panel was sought. All questions achieved 80% consensus or greater in the second round, however some feedback was given by the expert panelists on improving the clarity of the question. The suggested clarifications were made per the Delphi members' feedback. The proposed revisions were reviewed and refined by the doctoral dissertation committee.

9. **Final quality control review by expert reviewers**

The final revisions of the survey questions were entered into Survey Monkey for quality control testing by an expert independent to the expert panelists. The link to the survey was sent to the expert reviewer. The expert reviewer indicated that the survey questions were satisfactory in structure and clarity. The link to the survey was then sent to the members of the expert panel. The panelists indicated that the questions accurately reflected the intentions of the feedback and revisions and were acceptable in structure and clarity.

APPENDIX I

Delphi Expert Reviewer Instructions

Dear Expert Panelist,

Thank you for agreeing to provide your expert opinion on the **Pharmacogenomic Adoption Instrument (PAI)** tool. You have been asked to provide your feedback, based on your specific expertise, which has been identified as a subject matter that is highly relevant to the tool. Your feedback will be used to refine and improve the questionnaire, so any insight you have **will** be greatly appreciated ***and used for this purpose***. Your input will be integrated **along with the other Expert Panelists' responses through** a **Modified Delphi** process **to** achieve face and content validity for this instrument.

The purpose of the instrument **once it is reviewed and revised by the expert panelists and distributed to survey participants is** to examine *healthcare providers' knowledge of and attitudes toward pharmacogenomics technology* to help address a gap in the **current** literature. The survey questions are rooted in themes that recur in the current literature that **discuss** pharmacogenomic technology and its adoption by healthcare providers. The survey tool utilizes Roger's Diffusion of Innovation Theory (Rogers, 2010). The questions in the survey have been written to reflect themes in the literature in the context of this theory.

Please review each question and the related construct or factor associated with the question. You will then be asked to determine if the question measures the construct or factor described. Please check yes or no to indicate your decision. If you have comments or questions in any of the above categories, you may then use the comments box to elaborate your suggestion for refinement or improvement in that specific category. Your comments **for this first round of the Delphi** are requested within (7) days of receipt. The survey tool will then be modified based on the responses that were received from the expert panel. A consensus (80% agreement) of the panel will be sought. If consensus is not met you will be asked to participate in a second review round but only specific to those questions not reaching consensus. For the second round you will again be asked to provide your comments within (7) days of receipt. If consensus is not met following the second round, then a third and final round will be conducted to reconcile these disagreements. Further instructions will be provided to you at that time. Majority panel recommendations will be followed for each round. A majority is represented by agreement between 80% or more of the panel.

Also, if there is/are any question(s) that you think would improve the survey that you think might relate to or provide more insight into the adoption of pharmacogenomic technology by healthcare providers in their practice now or in the future, but was/were not captured ***appropriately as written here or not included at all but you feel should be***, ***your suggestion(s) on what and how to include this***

information please feel free to write the question and corresponding answer in the appropriate section comment box.

Your anticipated support in this project is greatly appreciated!

Very Respectfully,

Jason Sudia

Doctoral student, Seton Hall School of Health and Medical Sciences

Jason.sudia@student.shu.edu

Background and Rationale

The literature has found that there are many different barriers that impede the path of pharmacogenomic technology and its adoption by healthcare providers in the clinic. Pharmacogenomics is the field of study that deals with understanding the differences in human genetic variation and the effects of these differences on the safety and efficacy of pharmacological treatments. This information and its use can greatly reduce adverse events due to drugs and greatly increase the probability of prescribing a drug in the correct dose that will work effectively for that patient (Crews, 2012). These barriers range from potential philosophical ethical issues to a real lack of training and awareness among practitioners (Bonter, Desjardins, Currier, Pun, & Ashbury, 2011; Leufkens, 2004; Ventola, 2011).

Theory of Diffusion of Innovations

The Theory of Diffusion of Innovations may help to explain what factors are impeding the translation of this advancement in the clinical setting. Roger's 1967 Diffusion of Innovation Theory describes the way people, as a group, adopt technology (Rogers, 2010). The theory has been applied to many technologies that have emerged in and outside healthcare. This theory has strong applicability and may help to explain how and why the breach exists between the science and the practice. In a recent survey of US physicians, only 10% of those surveyed indicated that they felt sufficiently informed about the accessibility of pharmacogenomic technology and how to appropriately utilize it to aid diagnosis and determine the best course of therapy for patients (Stanek, Sanders, Taber 2012). In the

process of adoption of new technology there are key components that catalyze the process. Of these, are the initial attitudes and knowledge of the potential adopters (Rogers, 2010). When knowledge is insufficient or attitudes toward the technology are unfavorable adoption of the technology is halted.

Purpose

The purpose of the research that this tool will be used to conduct is multiple. First, the research will aim to determine, which factors are most strongly related to resistance in the adoption of pharmacogenomic technology by healthcare providers in the clinic? The literature and current theory on technology adoption in healthcare provides a background that suggests that a relationship may exist between knowledge of pharmacogenomic testing and the likelihood of adoption. Therefore pharmacogenomic knowledge will be assessed as a primary measure of this tool. The literature and current theory on technology adoption in healthcare also provides a strong case that suggests that a relationship may also exist between attitudes toward pharmacogenomic testing and the likelihood of adoption. Thus, attitudes toward pharmacogenomics will also be a primary measure of this tool. The survey instrument below is based on the constructs and evidence found in a number of previous studies. This survey tool has no previous, demonstrated, history of reliability or validity. Thus requiring some level of validation before it can be implemented and tested in a healthcare provider population.

Questions

The following survey consists of 40 questions. The construct questions will utilize a two digit score. A score value of 100 on a single question indicates uncertainty about that topic or question. The hundreds value will be considered for this purpose. Questions that appeared in multiple studies in the literature were selected to represent some constructs of interest. Other questions were developed using concepts from the literature to address gaps that have not been previously investigated. The overall scoring of the questions will be analyzed according to the following guidelines:

Demography

Questions 1, 4, 5, 7, 36, 38, and 39 aim to characterize the demography and attributes of the sample. This data will be descriptive in nature and will provide a depiction of the distribution of factors that this sample represents. These questions also aim to capture the frequency of factors that were described in the literature regarding pharmacogenomic adoption.

Qualitative Barriers

Questions 2 and 3 aim to identify the primary barriers to the adoption of pharmacogenomic technology in the clinical setting.

Scores will be a composite of hundreds value and a two digit number (e.g. 999) the two digit number are interpreted as follows:

Attitudes

Questions 6, 24, 25, 26, 27, 28, 29, 30, 31 aim to measure attitudes of subjects toward pharmacogenomic technology. The range of scores in this category is 9-45. A lower score indicates a more unfavorable attitude towards pharmacogenomic technology, while a higher score represents a more favorable attitude towards pharmacogenomics technology.

Experience

Questions 8, 10, 12, 14, 15 and 16 aim to measure experience with pharmacogenomic techonology in the clinic. The range of scores in this category is 6-30. A lower score indicates a less experience with pharmacogenomic technology, while a higher score represents more experience with pharmacogenomics technology.

Knowledge

Questions 9, 11, 13, 17, 18, 19, 20, 21, 22, 23 and 32 aim to measure knowledge of pharmacogenomic technology. The range of scores in this category is 11-55. A lower score indicates a less knowledge of pharmacogenomic technology, while a higher score represents greater knowledge of pharmacogenomic technology.

Likelihood of Adoption

Questions 33, 34, 35 and 37 aim to measure likelihood of adoption of pharmacogenomic technology in the clinic. The range of scores in this category is 3-20. A lower score indicates a lower likelihood of adopting pharmacogenomic technology in clinical practice, while a higher score represents greater likelihood of adopting pharmacogenomic technology in clinical practice.

Uncertainty

In the event a participant selects a “do not know” answer a score of 100 will be assigned. Scores of 100 on a response, indicate uncertainty in making a decision. Thus the hundreds value of the total score is considered separately from the two-digit value, which indicates a definitive response. A high hundreds value score indicates high uncertainty and likely unfamiliarity with pharmacogenomics technology.

Scores indicated in survey below in (red).

The scoring of the responses will not be disclosed to the survey participants, but are indicated in red (x) to demonstrate the scoring scheme of the survey for this review.