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Measuring Knowledge and Attitudes Regarding the Use of Pharmacogenetic Testing among Patients and Prescribers: Diffusion of Innovation Theory

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MEASURING KNOWLEDGE AND ATTITUDES REGARDING THE USE OF PHARMACOGENETIC TESTING AMONG PATIENTS AND PRESCRIBERS: DIFFUSION OF INNOVATION THEORY

By

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A dissertation submitted in partial fulfillment of the requirements for the degree of
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ABSTRACT

An Abstract of a Dissertation Submitted to Nova Southeastern University in Partial Fulfillment of the Requirements for the Degree of Doctor of Philosophy

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Background: Healthcare providers play a key role in patient care. Their knowledge and attitudes may play a critical role in the incorporation of pharmacogenetic (PGx) testing into routine practice. The knowledge and attitudes of patients are also equally important in determining the rate of diffusion and the adoption of PGx testing. This study aims to test Rogers's diffusion of innovation theory to identify and evaluate the influence of knowledge, attitudes, and sociodemographic characteristics of patients and physicians on the adoption of PGx testing in current clinical settings.

Method: A cross-sectional, descriptive survey design was implemented. The sample consisted of patients with chronic diseases and licensed physicians. One-way analysis of variance (ANOVA), linear regression, and path analysis were performed to test the research hypotheses.

Results: Limited knowledge regarding PGx testing was prevalent among patients, despite good attitudes. While the total PGx testing knowledge score was predicted significantly by levels of education, prior experience, and innovativeness, the total attitude score was predicted significantly by gender, relative advantage, compatibility, complexity, and trialability. The acceptance of PGx testing by patients was significantly influenced by their attitudes towards PGx testing and its perceived characteristics. Physicians expressed low levels of knowledge regarding PGx testing; however, the majority had favorable attitudes toward its potential clinical advantages. The total PGx testing knowledge score was predicted significantly by gender, type of practice setting, and prior experience. Physicians' attitude score was predicted significantly by gender, relative advantage, and compatibility of PGx testing. Barriers to the adoption of PGx testing were reported. The acceptance of PGx testing by physicians was significantly influenced by the perceived characteristics of PGx testing and the perceived need for testing.

Conclusion: This dissertation successfully evaluated the relationship among several factors adapted from Rogers's theory and the adoption of PGx testing. The research is expected to provide the scientific community with an increased understanding of the

decision-making process surrounding PGx testing. It will help identify the key factors and barriers that may have a significant influence on the direction of the future implementation of PGx testing, which will ultimately assist patients and physicians with therapeutic decisions.

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Table of Contents

List of Tables

List of Figures

List of Abbreviations

ADRs……....	Adverse Drug Reactions
ANOVA…….	One-Way Analysis of Variance
BCRA1…….....	Breast Cancer Gene 1
BRCA2…….	Breast Cancer Gene 2
CDC……...……	Centers for Disease Control
CFI…….……..	Comparative Fit Index
CME…….	Continuing Medical Education
COPD…….……...	Chronic Obstructive Pulmonary Disease
COX-2……	Cyclo-oxygenase-2
CVD…….…….….	Cardiovascular Disease
CYP2C9……	Cytochrome P450 2C9
CYP2D6…….…..	Cytochrome P450 2D6
DM…….……..	Diabetes Mellitus
DNA…….…….....	Deoxyribonucleic Acid
EPHX1……..	Epoxide Hydrolase 1
FDA…….…….	Food and Drug Administration
GGCX……	Gamma-Glutamyl Carboxylase
GWAS…….…….	Genome-Wide Association Studies
HF…….……	Heart Failure
HIPAA…….....	Health Insurance Portability and Accountability Act
IRB……	Institutional Review Board
IRT……...	Item Response Theory
IT…….…….	Information Technology
MI…….....	Myocardial Infarction
NSU…….…….	Nova Southeastern University
PCPs…….….....	Primary Care Providers
PGx……...	Pharmacogenetics
REDCap…….....	Research Electronic Data Capture

RMSEA……	Root Mean Square Error of Approximation
SNPs…….....	Single-Nucleotide Polymorphisms
SPSS…….….....	Statistical Package for the Social Sciences
Swilk…….……	Shapiro-Wilk
TLI…….….....	Tucker-Lewis Index
X^2…….…….	Chi-Square

Chapter 1

Introduction

Pharmacogenetics (PGx) is a new and dynamic field of medicine. The term PGx was first coined by the German geneticist Friedrich Vogel (1959) and has recently become an integral component of clinical practice. This is due to the completion of the Human Genome Project in 2003 and the availability of cutting-edge DNA technology. The major role of PGx testing is to determine genetic-based variations in drug responses by finding associations between genetic differences and observable clinical traits in individual patients. This allows for careful clinical evaluation of potential drug toxicity and effectiveness prior to the initiation of a specific drug therapy. Yet, despite the prospective benefits of PGx testing in the improvement of both medication safety and efficacy in many therapeutic areas, its acceptance and use in medical practice are still limited.

Since physicians play a key role in patient healthcare, their knowledge and attitudes may play a critical role in the incorporation of PGx testing and genetically recommended therapy into routine practice. Equally important are the knowledge and attitudes of patients, who may also affect the rate of diffusion as stated in Rogers's diffusion of innovation theory and the adoption of PGx testing (Rogers, 2003).

This dissertation investigates different factors associated with patients' and physicians' acceptance of PGx testing. Participants' knowledge and attitudes toward PGx testing are evaluated as a set of variables that constitutes the basis of Rogers's diffusion of innovation

theory. The research method was a cross-sectional descriptive survey. The surveys of patients' and physicians' knowledge and attitudes were derived from the relevant literature and were tested and developed further to accommodate the framed objectives of this study. Then, eligible participants were invited to complete the survey. Results were analyzed using a One-way ANOVA, linear regression, and path analysis models.

This chapter describes the background of the problem and how Rogers's diffusion of innovation model can be used to address the statement of the problem. Additionally, the chapter illustrates the purpose of the study, the research questions and hypotheses, the rationale, and the need for the study.

Background to the Research Problem

Variations in the human deoxyribonucleic acid (DNA) sequence play a significant role in the development of diseases. These DNA variations may also cause a differential response to pathogens, chemicals, drugs, and vaccines (Lazaridis and Petersen, 2005; Zhang et al., 2015). Each individual has a unique set of genetic markers represented by DNA sequences located in specific regions of the chromosomes that may help predict his/her response to medications and the risk of developing a particular disease (Ginsburg and McCarthy, 2001). Research conducted under the genome-wide association study (GWAS) has helped identify genetic variations that result in differential health outcomes (Chasman et al., 2004; Shiffman et al., 2012; Srivastava, 2003; Thompson et al., 2005). Researchers have utilized this information to develop efficient strategies for the detection, treatment, and prevention of various diseases and pathophysiological conditions. GWAS typically searches the human genome obtained from different individuals for single-nucleotide polymorphisms (SNPs) associated with defined traits or major diseases. The role of genetic variability is relevant to medical practice as it eventually enables healthcare

practitioners to customize treatments and prevention strategies to a patient's unique genetic makeup. So far GWAS has successfully identified the association of genetic variations with many chronic diseases such as type 2 diabetes mellitus (DM), Parkinson's disease, heart disorders, obesity, Crohn's disease, and prostate cancer (Eeles et al., 2009; Nalls et al., 2013).

Presently the potential benefits of major therapeutic classes (e.g., analgesics, antipsychotics) have been observed in less than half of patients (Spear et al., 2001). Although many non-genetic factors such as age, body weight, and disease states cause individual variation in drug response, the inherited genetic differences among individuals can significantly alter the pharmacokinetic and pharmacodynamic properties of medications (Roden and George Jr, 2002). Genetic influences on drug response vary widely among patients. The highest beneficial response (80%) was expressed among patients receiving selective cyclooxygenase-2 (COX-2) inhibitors, while the lowest response (25%) was reported among patients receiving chemotherapeutic medication (Spear et al., 2001).

PGx research is aimed at investigating the roles of genetic differences among individuals that impact their response to different medications. The ultimate goal of PGx is to determine the role of genetic variations in drug response by finding associations between genetic differences (e.g., CYP2C19 *2/2 genotype) and physical changes (e.g., poor metabolizer phenotype) in individual patients (Hagymási et al., 2011; Tomalik-Scharte et al., 2008). This relatively new genetic field allows for careful evaluation of potential drug toxicity and effectiveness prior to the initiation of a specific drug therapy (Benhaim et al., 2012; Kitzmilleret al., 2011; Wang et al., 2011). For instance, the human genome encoding cytochrome P450 enzymes (CYPs) is responsible for oxidative metabolism and bio-activation of around 75% of currently prescribed medications (Guengerich, 2007). Inter-individual variations in the genetic sequences involved in

coding CYP450 enzymes may result in a reduced, amplified, or complete loss of functionality in the metabolizing enzymes and, consequently, an alteration in the pharmacokinetics of susceptible medications and inter-individual variability. According to Lee et al. (2002), the inter-individual variability of the DNA sequence for the CYP2C9 gene is responsible for about a 30% to 90% reduction in the enzymatic activity, which typically alters warfarin clearance and the total daily dose.

Drug-related complications are problematic for patients and healthcare systems. Adverse drug reactions (ADRs) can result in serious injuries, hospitalizations, and even death. A combined retrospective patient chart review and patient survey study conducted at eleven general internal medicine sites in the greater Boston area found that among 2,248 patients who self-reported prescription medication use, 18% indicated ADRs associated with their prescription medications (Gandhi et al., 2000). Notably, there was no significant association between gender, age, race, level of education, or insurance status and the reported ADRs. The survey also revealed that 49%, 48%, and 35% of the 397 patients who experienced ADRs reported discomfort, seeking medical attention, and interference with daily activities, respectively (Gandhi et al., 2000).

ADRs are a considerable factor leading to mortality and morbidity. A meta-analysis of 39 prospective studies was conducted to estimate the total incidence of serious ADRs among patients staying in the hospital and those who were admitted to the hospital due to an ADR in the US (Lazarou et al., 1998). The study estimated a total of 2,216,000 (6.7%) hospital patients experienced ADRs and approximately 106,000 (0.32%) death cases were attributed to ADRs in 1994. The study ranked ADRs as the fifth leading cause of death in the U.S. during that year. A more recent national estimate of annual emergency department visits due to ADRs reported

approximately 700,000 adverse drug event cases annually between 2004 and 2005, in which 16.7% required hospitalization (Budnitz et al., 2006).

The treatment of chronic diseases often requires long-term use of medications. Patients with chronic diseases whose physicians do not assess their response to medications are more likely to have inadequate therapy management (Brown and Bussell, 2011; Gordon et al., 2007). Moreover, the lack of time and communication between patients with chronic diseases and their healthcare providers potentially increases patients' risk of experiencing medication-related complications (Gandhi et al., 2000; Østbye et al., 2005). Effective chronic disease management reinforces the need to improve physicians' knowledge about inter-individual variabilities to improve quality of prescribing and minimize medication adverse events among patients responsible for self-administration of their chronic disease medications.

Recent studies have focused on differences in the genetic makeup of individuals that contribute to variation in therapeutic outcomes and increased susceptibility to adverse effects of chronic disease medications. Understanding the effect of genetic differences in drug response among patients enables healthcare providers to select the most appropriate therapeutic choices. It also helps them reduce side effects that may necessitate urgent medical attention. For example, variation in metabolism of simvastatin due to genetic differences is associated with mild to severe myopathy (Owczarek et al., 2005). Likewise, impaired metabolism of clopidogrel is associated with an increased risk of bleeding (Ma et al., 2011). Currently 150 drugs with PGx information on their labels (drug package inserts) have been approved by the Food and Drug Administration (FDA, 2016), indicating that PGx variability should be considered before the drug is prescribed.

Various studies have recognized the importance of PGx in personalized medicine and how the adoption of this tool will primarily help focus on drug selection and dosing (Benhaim et al., 2012; Ginsburg and McCarthy, 2001; Kitzmiller et al., 2011). The integration of PGx testing in routine medical practice may help improve clinical outcomes, minimize ADRs, and boost patients' perception regarding the safety and efficacy of their medications. Consequently, PGx can potentially impact patient adherence to chronic disease medications and may result in more healthcare cost-savings (Haga and LaPointe, 2013; McWilliam et al., 2006).

PGx has become a new field of pediatric research as it has the potential to improve health outcomes for children. Green et al. (2016) reviewed 65 drugs with FDA-approved PGx information in search of a safe and effective use of therapeutic medications in children. Out of the 65 drug package inserts, 28 included prescribing recommendations that were identified based on specific genetic biomarkers (e.g., glucose-6-phosphate dehydrogenase testing is recommended before starting treatment with rasburicase). Four drug package inserts indicated only the availability of genetic tests, three drug package inserts indicated contraindications to use based on a patient's genetic makeup, seven drug package inserts mentioned cautions/avoid use or consider an alternative, and five drug package inserts recommended dosage adjustments. Finally, nine drug package inserts included more than one prescribing recommendation. The authors emphasized the role of PGx in rational use of medications to achieve optimal therapeutic outcomes and decreased ADRs.

Today PGx testing could potentially play a significant role in drug selection and may help minimize ADRs associated with chemotherapeutics and psychiatric drug use (Kitzmiller et al., 2011); however, integrating genetic testing more widely into general diagnostic and prescribing practices has not yet materialized. Studies have shown that lack of awareness and limited

knowledge among patients and physicians have been two of the most significant factors contributing to the slow adoption of PGx testing (Rogausch et al., 2006; Stanek et al., 2012). Unclear ethical guidelines on protection and use of genetic information, unavailability of PGx tests, lack of evidence supporting the clinical utility, and inefficient administrative and regulatory policies are also contributing factors to the limited adoption of PGx testing (Ghaddar et al., 2011; Moaddeb and Haga, 2013).

Theoretical Framework

The Everett Rogers's diffusion of innovation model has been widely used in several disciplines such as political science, public health, communications, technology, and education (Dooley, 1999). It provides an explanatory framework of the domains that have strong influences on the decision to adopt an innovation or new technology (Rogers, 2003). This theory explains the reasoning for the adoption of a new technology as well as the rate of adoption. The present study uses the conceptual framework of Rogers's diffusion of innovation theory to examine the impact of factors, in particular innovation decision-making processes, on the acceptance of PGx testing by patients and physicians.

According to Rogers's theory, people in any defined population go through five stages of the innovation-decision process (knowledge, persuasion, adoption, implementation, and confirmation) as a reaction to an innovation. During the knowledge stage, an individual attempts to learn more about the innovation: what the innovation is and how and why it works. Following the knowledge stage, the individual starts developing favorable or unfavorable ideas. According to Rogers, the formation of a favorable attitude toward an innovation does not always lead directly or indirectly to an adoption. Knowledge and persuasion are the major stages that potentially affect an individual's decision-making regarding adoption or rejection of the

innovation. If the individual decides to accept the innovation, then it will be put into practice. After decision-making process and the innovation is already in practice, the confirmation stage occurs, whereby the individual seeks support for his/her decision to avoid the discontinuance or rejection of the innovation.

Rogers's theory provides a number of factors that influence the knowledge and attitude stages. These factors include prior experience, perceived need for innovation, innovativeness, rurality, sociodemographic variables (e.g., age, level of education), and communication behavior, which are knowledge stage attributes. During the knowledge stage and before making the adoption decision regarding innovations, an individual should become aware of the existence of the innovation. Prior experience about the innovation helps decrease the uncertainty of that innovation and facilitate its rate of adoption. While awareness and knowledge regarding a particular innovation may potentially create a need for it, an individual may also start searching for an innovation that could meet his/her needs. Furthermore, an individual's innovativeness could affect his/her willingness to accept an innovation relatively earlier than other members in the same social system. According to Rogers, implementing innovations occurs greatly in large urban areas due to the availability of resources. Sociodemographic variables may also play a role in the adoption of innovation; Rogers found a positive correlation between education levels and adoption of innovations. Finally, channels of communication may play a significant role in creating knowledge and impact the rate of adoption. Individuals usually start seeking information regarding an innovation only after they become aware of its existence.

The characteristics of innovation (i.e., relative advantage, compatibility, complexity, trialability, and observability) described by Rogers may explain an individual's attitudes toward different innovations and also determine the rate of adoption. Innovations that are perceived as a

better alternative to existing options will be adopted at a higher rate. Similarly, innovations that are greatly perceived as well suited with existing values and norms will be accepted faster. Easy to use and simpler innovations also will be rapidly adopted. Innovations that can be tried and tested before making the decision to adopt will be adopted at a higher rate. Finally, innovations that are more visible and noticeable will be more readily adopted. All these factors were operationalized in this study based on the theoretical lens of Rogers's theory to generate target-specific variables that could be assessed from the participants in the sample. Rogers's diffusion of innovation model will be further discussed in the next chapter.

Statement of the Problem

Although PGx holds great promise to enhance clinical outcomes of patients and may assume a key role in predicting ADRs, its integration in medical practice has been implemented to a limited extent. Aspects beyond medical facts, including knowledge and attitudes of patients and healthcare professionals, need be addressed. Many studies reported that the lack of adoption of PGx testing could be due to the fact that patients and physicians are unaware of the need for testing, do not trust or understand the current evidence of the benefits, or doubt the potential cost-effectiveness of the testing (Haddy et al., 2010; Perlis et al., 2009; Priest et al., 2006). Other factors that may also impact the acceptance of PGx testing are the lack of adequate PGx educational programs and well defined practice guidelines for the use and interpretation of these tests (Haga et al., 2012a; Rogausch et al., 2006).

A few studies have been conducted to measure patients' and physicians' knowledge and attitudes toward PGx testing. While some recognized a major lack of knowledge and experience about genetic tests among physicians, others found that physicians were less likely to have positive attitudes toward the use of PGx testing because of their own concerns about

understanding phenotyping, patient confidentiality, and patient eligibility for health insurance. These studies also revealed that some positive advantages of PGx were perceived by physicians who have more favorable attitudes toward the role of PGx testing in improving general health and minimizing the frequency of drug-related complications. Similarly, based on existing studies, there was a lack of knowledge and awareness about genetic testing among patients with chronic diseases, and this lack of knowledge affected their decision to undergo PGx testing. Yet most patients expressed positive attitudes, were generally supportive of PGx testing, and felt it would be of advantage toward their health.

Since individualized medicine is not fully developed for most drugs, PGx testing has not been recommended by expert committees due to the lack of conclusive and sufficient evidence that testing improves health outcomes. There have been barriers to the implementation of PGx testing in clinical settings reported by several studies, especially lack of awareness and limited knowledge among patients and physicians, lack of clinical practice guidelines that strongly support the clinical utility of PGx testing, physicians' concerns about patient confidentiality, and patients' ability to afford the testing (Fargher et al., 2007; Ghaddar et al., 2011; Haddy et al., 2010; Rogausch et al., 2006). Nevertheless, the number of available PGx tests has increased drastically since 2004, as some ongoing clinical trials are completed (Frueh et al., 2008). Physicians' awareness, understanding, and attitudes regarding PGx testing may play a key role in the rapid diffusion of these genetic tests in clinical practice. Moreover, the knowledge and attitudes of the general public may play a decisive role in the wider acceptance of PGx testing in society. Data from previous studies indicate that the public is open to the adoption of new technology for the betterment of health (Haddy et al., 2010; Rogausch et al., 2006).

The lack of knowledge and variable attitudes toward PGx testing appear to be dominant barriers within healthcare systems. Few studies exist on this topic, and most have been conducted on patients and physicians outside Florida. Only a few publications have focused on knowledge and attitude toward PGx testing among patients with chronic diseases (Calsbeek et al., 2007; Cuffe et al., 2014; Lachance et al., 2015; Morren et al., 2007; Trinidad et al., 2015). Additionally, there have been very few studies that adequately demonstrate the impact of patients and physicians knowledge and attitudes on the adoption of PGx testing based on Rogers's diffusion of innovation theory (Armstrong et al., 2003; Dressler et al., 2014; Nielsen and Moldrup, 2007). Relying only on the findings of existing studies to draw broad conclusions about the knowledge and attitudes towards PGx testing among patients and physicians may not be representative of the heterogeneous population of Florida.

More research is needed to understand if and how patients' and physicians' knowledge and attitudes contribute to the adoption of PGx testing. Knowledge and attitudes toward PGx testing are critical to expanding this evolving field of science. The implementation of PGx in routine medical practice and future personalized medicine will ultimately depend upon patients' and physicians' acceptance of these tests and related recommendations.

There is a significant gap concerning knowledge and attitudes toward PGx testing among patients with chronic diseases and physicians in the State of Florida that may be related to their uncertainty to adopt PGx testing with promising health outcomes. Due to the relationship among knowledge, attitudes, and the adoption of innovation explained by Rogers's diffusion of innovation theory, this study focused on the measurement of knowledge and attitudes as they relate to the acceptance of PGx testing.

Purpose of the Study

This study aimed to identify and evaluate the influence of knowledge, attitudes, and sociodemographic characteristics of patients and physicians on the adoption of PGx testing as a diagnostic tool in the current clinical settings. In order to achieve a better understanding of decision-making processes toward PGx testing and the strategies that help foster efficient adoption, this study was based on Rogers's diffusion of innovation theory, which has been widely accepted as a theoretical model to explore diffusion and adoption of innovations. The knowledge and attitudes toward PGx testing were compared among patients filling their prescriptions for their chronic conditions at the Nova Southeastern University (NSU) Clinic Pharmacy in Fort Lauderdale, Florida, who would be willing to reject or accept PGx testing, if available, for one of their chronic disease medications. The knowledge and attitudes toward PGx testing were also compared among physicians who would be willing to reject or accept PGx testing, if available.

Research Questions and Hypotheses

Previous scholarly work has independently evaluated patients' and physicians' knowledge and attitudes toward PGx testing (Calsbeek et al., 2007; Cuffe et al., 2014; Haga et al., 2012a; Haga et al., 2012c; Henneman et al., 2006; Kobayashi and Satoh, 2009; Lachance et al., 2015; Lanktree et al., 2014; Morren et al., 2007; Nielsen and Moldrup, 2007; Stanek et al., 2012; Stanek et al., 2013; Taber and Dickinson, 2014; Trinidad et al., 2015; Walden et al., 2015). Pursuing this work, the goal of this study was to increase understanding of several factors (sociodemographic characteristics, knowledge, and attitudes) that may play a role in the early adoption of PGx testing among patients and physicians by answering the following research questions:

Research Question 1A:

What is the association between patients' knowledge of PGx testing and their gender, age, ethnicity, level of education, area of living, prior experience, innovativeness, and perceived need for innovation?

H_0 (1A): Gender, age, ethnicity, level of education, area of living, prior experience, innovativeness, and perceived need for innovation are not significantly associated with knowledge of PGx testing among patients.

Research Question 1B:

What is the association between physicians' knowledge of PGx testing and their gender, age, ethnicity, medical specialty, type of practice setting, duration of practice, prior experience, innovativeness, and perceived need for innovation?

H_0 (1B): Gender, age, ethnicity, medical specialty, type of practice setting, duration of practice, prior experience, innovativeness, and perceived need for innovation are not significantly associated with knowledge of PGx testing among physicians.

Research Question 2A:

What is the association between patients' attitudes toward PGx testing and relative advantage, compatibility, complexity, trialability, and observability of PGx testing?

H_0 (2A): The relative advantage, compatibility, complexity, trialability, and observability are not significantly associated with attitudes toward PGx testing among patients.

Research Question 2B:

What is the association between physicians' attitudes toward PGx testing and relative advantage, compatibility, complexity, trialability, and observability of PGx testing?

H_0 (2B): The relative advantage, compatibility, complexity, trialability, and observability are not significantly associated with attitudes toward PGx testing among physicians.

Research Question 3A:

Do knowledge, attitudes, perceived characteristics of innovation, and sociodemographic characteristics significantly influence the acceptance or rejection of PGx testing among patients?

H_0 (3A): There is no relationship between patients' willingness to accept PGx testing and their knowledge of PGx testing, attitudes toward PGx testing, perceived characteristics of PGx testing, and sociodemographic characteristics.

Research Question 3B:

Do knowledge, attitudes, perceived characteristics of innovation, and sociodemographic characteristics significantly influence the acceptance or rejection of PGx testing among physicians?

H_0 (3B): There is no relationship between physicians' willingness to accept PGx testing and their knowledge of PGx testing, attitudes toward PGx testing, perceived characteristics of PGx testing, and sociodemographic characteristics.

Rationale and Need for the Study

Advances in the knowledge regarding human genetic variation and its relation to drug responses have increased significantly since the completion of the Human Genome Project in 2003. Yet, despite the prospective benefits of PGx testing in improving both medication safety and efficacy in many therapeutic areas, the literature shows that the use of PGx testing remains limited in many clinical settings. Further aspects beyond medical facts, including knowledge and attitudes of patients and physicians, need be studied. Although the FDA has reviewed more than 150 labels of prescription medications to include information regarding the impact of

genetic variation on medication safety and efficacy (FDA, 2016), the integration of more widespread genetic testing into general diagnostic and prescribing practices has not yet occurred, possibly due to the limited knowledge and awareness among patients and physicians.

Research is needed to understand if and how patients' and physicians' knowledge and attitudes contribute to the adoption of PGx testing and use of the results to guide prescribing. Haga et al. (2012a) indicated that 76% of physicians were unaware of the drug package inserts including PGx information, and only 13% of physicians indicated they felt comfortable ordering PGx testing. Available studies on sociodemographic characteristics and geographic locations that did not include Florida were conducted a few years ago; since then, much has changed in the field of PGx testing.

This study primarily focused on the initial factors that prompt patients or physicians to either reject or accept the utilization of PGx testing according to Rogers's theory. A more thorough understanding of the underlying barriers that influence the decision-making process can be expected to have important benefits for promoting personalized medicine. Florida has an increasingly diverse general population; thus, a unique opportunity exists to update the knowledge on the use of PGx testing and gather information from a culturally diverse population filling their prescriptions at the NSU Clinic Pharmacy. The contribution of this research is expected to significantly advance patients' and physicians' knowledge, improve their attitudes toward the use of PGx testing, and encourage them to utilize testing not only for drugs available with PGx information, but potentially to inform other treatment decisions currently or in the future. For example, the results of PGx testing for one or more enzymes involved in the metabolism of a particular drug could possibly inform useful treatment decisions for other future prescribed medications that share the same metabolic enzymes (Mills et al., 2013). Additionally,

this study measured the influence of certain sociodemographic factors on the willingness of a patient to use PGx testing. Thus, it may advance physicians' understanding of patients' needs and subsequently the need for change in their current clinical practice.

Patients with chronic conditions are of a growing concern in the U.S. due to their high risk of morbidity and mortality responsible for almost 80% of all causes of death in 2010 (Murphy et al., 2012). Studies have shown that patients with chronic diseases who were less motivated to manage their conditions had a lower rate of medication adherence that impacted their health outcomes (Balkrishnan, 2005; Kripalani et al., 2007). Moreover, patients' concerns regarding the appropriateness of their medications, the possibility of having ADRs, and lack of communication between patients and physicians could negatively influence the optimal outcome of their chronic conditions (Gordon et al., 2007; Stevenson et al., 2004). Stevenson et al. (2004) showed that increasing the role of patients in decision-making and considering patients' preferences toward treatment options have potential benefits on their health outcomes. As such, patients' perceptions of their medication suitability, as well as understanding the rationale behind switching to other medications and/or different doses, have a favorable impact on their health (Balkrishnan, 2005; Gordon et al., 2007). Therefore, more careful assessments of chronic condition medications are needed to provide patients with more information about their therapy of choice and potential side effects, which could enhance their medication utilization. The findings of behavioral research on the acceptance of a new clinical tool such as PGx testing could help support the informed prescribing process.

Definitions of Variables and Concepts

In order to achieve a better understanding of the decision-making process in PGx testing and which strategies would help foster its efficient adoption, this study aimed to identify and

evaluate the impact of knowledge and attitudes of patients and physicians in the adoption of PGx testing as a diagnostic tool in the clinical settings. What follows is a definition of relevant variables within Rogers's diffusion of innovation theory.

Knowledge Stage

Individuals become aware of the existence of an innovation and collect more information to gain a better understanding of its characteristics. The following are antecedents to the knowledge stage:

- Innovativeness: the degree to which an individual is willing to accept the innovation relatively earlier than other members in the same social system.
- Prior experience: the degree to which an individual is aware or familiar with the innovation prior to making an adoption decision.
- Perceived need: the degree to which an individual believes in the utility of the innovation.
- Work environment: the location of an individual workplace (i.e., urban, rural).
- Sociodemographic variables: gender, age, ethnicity, level of education, and area of living.
- Communication channels: the most effective resources of generating knowledge about an innovation.

Persuasion Stage

Individuals acquire positive and negative attitudes toward the innovation. The following are attributes of adopters' attitudes toward the characteristics of innovation:

- Relative advantage: the degree to which an individual believes that the value in the innovation is higher than what it replaces. Greater perception of advantages leads to a higher rate of adoption.

- Compatibility: the degree to which the innovation deviates from the existing values, practice, and prior experiences. Greater perception of compatibility leads to a higher rate of adoption.
- Complexity: the degree to which the innovation is perceived as difficult to understand or use. Simpler innovations are accepted at a relatively higher rate.
- Trialability: the degree to which the innovation can be tested or tried before adoption. The ability to try an innovation reduces the level of perceived uncertainty and ultimately increases the rate of adoption.
- Observability: the degree to which the results and effects of the innovation are noticeable by individuals. Per Rogers's theory, individuals who can more easily see the results of the innovation will be more likely to adopt it.

Characteristics of Innovations

The characteristics of innovations perceived by an adopter include relative advantage, compatibility, complexity, trialability, and observability, which could potentially influence the rate of adoption of innovations.

Pharmacogenetics

The study of inherited genetic differences that influence an individual's responses to drugs (Nebert, 1999). The term is often used interchangeably with the term pharmacogenomics, but there is a difference. The distinction is fully explored in

Chapter 2.

Pharmacogenomics

A comprehensive study of all genetic variants within an individual or across a population to relate their multiple effects on drug response (Evans and Relling, 1999).

Chronic Conditions

A health problem such as cardiovascular disease, asthma, and cancer that lasts for at least three months (Goodman et al., 2013; National Center for Health Statistics [NCHS], 2011). Almost 50% of U.S. adults have at least one chronic condition (CDC, 2017; Ward et al., 2014).

Chronic Medications

Medicines prescribed over a long period of time (at least three months) to control or manage chronic diseases (e.g., antihypertensive and antidiabetic medications).

Summary

PGx testing is a relatively new diagnostic clinical tool. It provides an opportunity to tailor medications based on an individual's genetics. Several studies have recognized the potential benefits of PGx testing to evaluate possible drug toxicity and increase drug effectiveness; however, the slow uptake of PGx testing in clinical practice has resulted in limited information about the acceptance of PGx testing among patients and physicians. The objective of this study was to test Rogers's diffusion of innovation theory on the adoption of PGx testing. It is expected to contribute to the existing literature by identifying a set of potentially modifiable variables that may affect the adoption of PGx testing by patients and physicians, thus increasing understanding of the decision-making process surrounding PGx testing and identifying the key factors and barriers that may highly influence the direction of future implementation of PGx testing in routine clinical practice.

In the next chapter the theoretical framework is discussed. Along with a description of the potential clinical utility of PGx and pharmacogenomics to inform treatment decisions, a review of the relevant studies found in the literature is undertaken.

Chapter 2

Literature Review

Published works related to patients' and physicians' knowledge and attitudes toward PGx testing are presented and discussed in this chapter. Rogers's diffusion of innovation theory, which was adopted as the conceptual framework for this research, is examined in the first part of this review. The concepts of PGx and pharmacogenomics are described in the second part. The relevant literature is reviewed in the last part of this chapter to support the current research questions and hypotheses.

Literature Search Method

Potentially relevant studies were identified by searching MEDLINE EBSCO, EMBASE, and Google Scholar for all articles written in English that reported results based on surveys, interviews, or focus groups. To narrow the scope of search, the following keywords that describe the current dissertation project were used: knowledge, awareness, attitudes, perception, views, perspectives, opinions, adoption, pharmacogenomics, pharmacogenetics, pharmacogenetic testing, genetic factors, diffusion of innovation, barriers, drug response physicians, doctors, clinicians, chronic diseases, patients, and public. These keywords were searched in combination using the Boolean operators "AND, OR, and NOT." Then the corresponding titles and abstracts were carefully reviewed to assess their potential relevance to this dissertation. Included were all the works conducted on patients and physicians to assess their knowledge and/or

attitudes toward PGx testing up to 2017. Studies conducted on genetic diseases or genetic factors linked to diseases were excluded. After applying inclusion and exclusion criteria, 40 studies were identified. After subsequent scrutiny, 27 studies were selected.

Diffusion of Innovation Theory

Rogers's diffusion of innovation theory provides a useful framework for evaluating the factors that might affect acceptance of an innovation such as PGx testing among patients and physicians (Rogers, 2003). According to Rogers, adoption is defined as "full use of an innovation as the best course of action available" and rejection is defined as "not to adopt an innovation." An innovation is described as "an idea, practice, or object that is perceived as new by an individual."

Five distinctive stages are identified: knowledge, persuasion, decision, implementation, and confirmation (see Figure 2.1). The knowledge and persuasion stages were operationalized, defined, and measured in this study using patients' and physicians' perspectives to generate specific items. Knowledge is gained when an individual learns of the innovation's existence and obtains more information to determine how it functions. Having enough information at this stage helps override the problem of uncertainty about the mechanism by which the innovation's capacity solves an individual's problems.

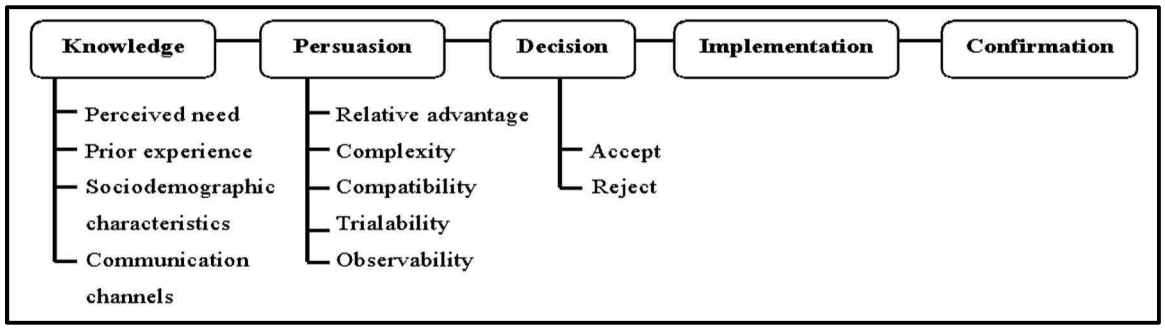


Figure 2.1: Illustration of the various stages in implementing an innovation as adapted from Rogers's diffusion of innovation theory.

The persuasion stage occurs when an individual's attitude toward the innovation changes from positive to negative or vice versa. Availability of new knowledge, along with the individual's attitude, plays a critical role in the adoption decision of the innovation. The decision process takes place when an individual is involved in making his/her own choice to adopt or reject the innovation. Implementation occurs later when an individual makes a decision to adopt and utilize the innovation. Afterwards, an individual starts seeking support for his/her decision. At this point, confirmation occurs and the individual decides to make full use of the innovation or discontinue it.

Rogers's diffusion of innovation theory has been applied in several health studies. Helitzer et al. (2003) applied it to examine the acceptance of telemedicine and its components for an efficient delivery of healthcare services. Chew et al. (2004) used it to assess the acceptance by family physicians of the Internet as an innovative tool for clinical and public health topics. Zhang et al. (2015) applied it to measure patients' acceptability for consumer e-health services, and Dodson (2012) applied it to measure the adoption of PGx testing among oncology nurses. These studies demonstrated that Rogers's theory provides a useful theoretical framework for promoting health behavior or adopting relatively new medical tools.

Rogers's theory identifies five adopter categories based on the number of individuals who adopt the innovation in a given time period. The adopter categories include innovators, early adopters, early majority, late majority, and laggards (see Figure 2.2). These categories are presented as segments of a bell-shaped curve and indicate innovativeness defined as the extent to which an individual is relatively early in adopting new ideas. Innovators are the first to try new ideas regardless of the level of

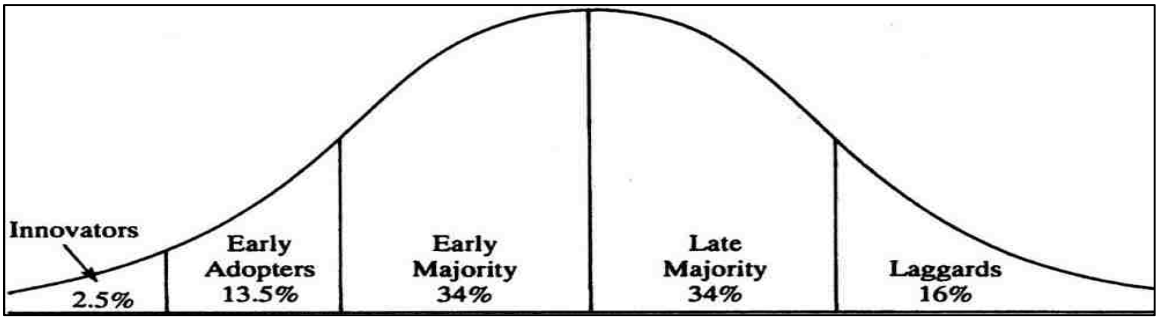


Figure 2.2: Illustration of a normal distribution encompassing adopter categories as described by Rogers's diffusion of innovation theory.

uncertainty. Early adopters come later and serve as role models and opinion leaders for the remaining categories; their well informed decision-making greatly influences the majority of the social system. Early majority and late majority adopters represent the largest section of the social system; they adopt an innovation and start adoption as a result of interpersonal networking and peer adoption and recommendation. The late majority is generally skeptical and reluctant to adopt an innovation due to high levels of perceived uncertainty; however, increasing peer pressure may persuade them to adopt. Laggards are the last to adopt an innovation; their slow decision to adopt is likely because they are more suspicious of innovations and have no opinion leadership.

The successful application of Rogers's theory helps investigate the factors affecting the rate of adoption among potential adopters; it also helps target those who are usually classified as the late majority or laggards to shift into an earlier adoption stage for a more efficient use of the PGx testing tool. A limited number of studies have examined the rate of PGx testing adoption among physicians. Stanek et al. (2012) conducted a cross-sectional survey that showed physicians who were early adopters of PGx testing were more likely to be practicing in an urban setting with a long duration in overall medical practice (15-29 years) and had previous experience ordering genetic testing. The

study also found that early adopters of PGx testing were influenced by medical specialty; the highest adoption rates were reported by oncologists (69%), much higher than those of family medical practitioners (12%) or nonsurgical specialists (10%). In comparison to late adopters of PGx testing, a larger percentage of early adopters had received PGx training in their undergraduate and postgraduate studies. In contrast, late adopters were more likely to be male, older, and with a longer duration of medical practice than early adopters. Physician age and gender had no significant association with early adoption of genetic testing.

This research study focused on the first two stages of the Rogers's diffusion of innovation theory. The first step of the decision-making process focused on initial awareness and knowledge of an innovation. Although knowledge does not guarantee successful adoption of an innovation, it is essential to motivate individuals to seek more information relevant to the innovation. Subsequently individuals begin to shape their own attitudes concerning that innovation. After learning more about the innovation and becoming more involved with it by forming positive or negative attitudes, the individual must then be persuaded to choose to accept or reject the innovation. A meta-analysis of 75 studies, conducted and summarized by Tornatzky and Klein (1982), reported that the more relative advantage, compatible, simple, trialable and visible the innovation is, the more likely it is to be adopted and put in practice.

Pharmacogenetics and Pharmacogenomics

Recent studies have increasingly focused on the evolving role of both PGx and pharmacogenomics in dealing with the impact of genetic variations on drug response. Typical variability in an individual's response to medications creates challenges in

prescribing the correct medication and the optimal dosage regimen. The human genome encodes tens of thousands of proteins. These proteins play a crucial role in several pathways of drug metabolism, disposition, and therapeutic effects. SNPs, DNA sequence variants, are considered the inherited basis of inter-individual variability in drug response (Collins et al., 1998). Across the human genome, the identification of a large number of SNPs could serve as database of genetic markers to predict an individual's susceptibility to diseases or altered drug responses. For instance, SNPs of the genes that encode drug metabolizing enzymes (e.g., CYP2C9, CYP2D6) have been associated with impaired metabolism and variable drug responses for warfarin and codeine, respectively (Evans and Relling, 1999). Therefore, to improve medication safety and efficacy among genetically susceptible individuals, an adjusted dose of warfarin to achieve the therapeutic anticoagulant effect can be predicted on CY2C9 SNPs. Similarly, selecting an individual-specific dose of codeine is important to improve pain relief (Evans and Relling, 1999).

With the completion of the Human Genome Project in 2003, more information about the entire collection of human genes has become available for research. To promote the scientific understanding of human genetics, research has begun to identify not only common disease-causing genetic variants, but also the relationship between genetic variants and drug response (Manolio et al., 2008). The field of PGx examines a single gene-drug interaction, which is determined by the impact of genetic variation (i.e., SNPs) on drug metabolism and disposition in the human body. For example, genetic polymorphism of drug-metabolizing enzymes CYP2C9 could potentially impact the

anticoagulant effect of warfarin; similarly, genetic polymorphism of CYP2C19 could potentially impact the antiplatelet effect of clopidogrel (Roden et al., 2011).

Emerging data about the relationships between phenotypes and genetic variants in multiple genes have advanced the understanding of variable drug response (Manolio et al., 2008). Thus, the term pharmacogenomics has become more recently used to indicate the existence of multiple genetic variants modulating drug response (Roden et al., 2011). Pharmacogenomics examines multiple genetic variants within an individual or across a population to relate their multiple effects to drug pharmacokinetics and drug response. In addition to the genetic variability in drug pharmacokinetics, pharmacogenomics also investigates additional candidate genes encoding drug molecular targets that control the effect of drugs on the body (pharmacodynamics). For example, polymorphisms in CYP4F2, CYP2C18, EPHX1, and GGCX genes may alter the pharmacokinetic and pharmacodynamics of warfarin and contribute to its heterogeneous response (Roden et al., 2011).

The majority of prescribers rely on conventional drug therapy, treating patients as large homogenous groups regardless of whether or not there is a genetic component influencing the outcome of drug therapy (Vogenberg et al., 2010). When considering a shift into more accurate prescribing based on the genetic profiles, however, PGx and pharmacogenomics may help find more appropriate treatment for individual patients (Vogenberg et al., 2010). PGx and pharmacogenomics should be integrated into current medical practice, as they continue to hold substantial promise to improve drug therapeutic outcomes among genetically susceptible patients.

Patients' Knowledge of Pharmacogenetic Testing

Studies have shown that unsuccessful implementation and decreased utilization of genetic testing are linked to the lack of knowledge and negative attitudes toward genetic testing. For example, Calsbeek et al. (2007) assessed and established that less perceived medical knowledge about genetic testing and more perceived social knowledge of genetic testing were responsible for the poor attitudes toward PGx testing in patients with chronic diseases such as asthma, DM, and cardiovascular disease (CVD). They also found that perceived genetic knowledge was inadequate, particularly among older and less educated patients. The authors reported that knowledge and attitudes toward genetic testing did not significantly change over a follow-up period of two years. It should be noted that the strength of their study was its longitudinal nature and that its results corresponded with Rogers's diffusion of innovation theory. However, the study had limitations that could compromise its findings. Its sample size might not have been sufficient to detect small changes in knowledge and attitudes over a period of two years, and it did not clearly define PGx testing.

These findings were supported by another study in which Morren et al. (2007) observed that patients with chronic diseases, including CVD, asthma or chronic obstructive pulmonary disease (COPD), DM, musculoskeletal disease, cancer, neurological disease, and gastrointestinal disease, were not able to make decisions regarding genetic testing. This was not due to their uncertainties about the PGx testing, but the lack of knowledge and awareness about genetic testing that affected their decision to undergo PGx testing. In contrast, Haga et al. (2012b) found that almost 80% of study participants heard of the term genetic testing, and less than 2% of them had been ordered

PGx testing to predict drug response. They also found that White and female participants, as well as those with a college degree, were more aware of genetic testing than the rest of the sample.

Utilizing a national representative sample of patients with chronic diseases, Morren et al. (2007) found that perceived genetic knowledge was limited, particularly among older and less educated patients. Despite the limited knowledge and low awareness, more positive attitudes toward genetic testing were found among younger and more educated patients. One of the strengths of their work was the use of a large sample size; the study also significantly contributed to the knowledge base by suggesting variables that might influence the adoption of PGx testing. A limitation, however, was the use of few response options that might have estimated less accurately participants' knowledge and attitudes. Another limitation was that it used the term genetic testing in general and avoided using the term PGx testing.

A study surveying 3,000 patients in Denmark, conducted by Nielsen and Moldrup (2007), revealed results similar to those of the Morren et al. (2007) study, namely, the public had poor knowledge but good attitudes toward PGx testing. Nielsen and Moldrup (2007) also reported that prior use of medical tests and perceived needs for PGx testing were related to the general knowledge and attitudes toward PGx testing, as well as the future use of these tests. Their work was influential because it was based on Rogers's diffusion of innovation theory and the adapted variables provided consistent results with the theory. Its weakness, however, was the potential selection bias that might have occurred, since only individuals with Internet access could participate.

Understanding factors that could influence the acceptance of well established innovations may support the design and conduct of this dissertation. Or and Karsh (2009) performed a systematic review to identify the variables influencing patients' acceptance of consumer health information technology (IT) applications, which enables them to electronically manage their health information. The review reported an association between patient-related factors and their adoption decision. Among the 52 reviewed studies, more than half found that higher education and prior experience were associated with increased acceptance. Age was examined in 39 studies, and it did not show a consistent effect on the acceptance of health IT application. Gender demonstrated no effect in the majority of the studies, either. Six studies reported that lack of familiarity and perceived benefits were negatively associated with patients' acceptance of health IT applications.

In 2015 a qualitative study was conducted to explore patients' attitudes regarding the role of PGx testing in reducing ADRs and improving medication efficacy (Trinidad et al., 2015). Patients taking chronic disease medications for mental health disorders were recruited. Results showed that the majority of patients were less familiar with the impact of inter-individual genetic differences in medication response and only a few believed that this variability was inheritable. The authors reported that participants perceived the potential benefits of PGx testing on improving their medication response and reducing the challenges of avoiding ADRs. This project was important because it enriched the existing literature about PGx testing from the perspective of patients with mental disease.

A cross-sectional study was conducted on cancer patients, evaluating their willingness to accept and pay for PGx testing (Cuffe et al., 2014). Findings revealed that

the majority of patients (85%), regardless of their lack of knowledge, perceived that PGx testing would help in detecting the therapeutic benefit of medications and avoiding chemotherapy-induced toxicities. The majority of adjuvant and metastatic patients were willing to accept PGx testing if it was offered free with a one-day waiting period for testing results. The majority of the participants were also willing to pay out of pocket for this innovation and devote several weeks of waiting time to receive the testing results. Almost 15% of the participants were reluctant to accept PGx testing, however, because they were worried about the potential of these genetic tests to disclose information about the inheritability of cancer. The strength of this work was the validity of the comparisons between patient groups to detect the perceived benefits of PGx testing. The reliability of the findings also was supported by measuring participants' willingness to pay for PGx testing. Yet recruiting participants from one cancer center limited the generalizability of the findings, plus differences in patients groups' sociodemographic characteristics might have led to biased statistical results.

Patients' Attitudes toward Pharmacogenetic Testing

Lachance et al. (2015) conducted a survey among three groups of individuals: healthy volunteers, heart failure (HF) patients, and heart transplant recipients. The researchers compared the opinions of each group on PGx testing. All three groups expressed high expectations and hope about the usefulness of PGx testing, but were concerned about the confidentiality of the testing results. Healthy volunteers had higher concerns about confidentiality, employability, and insurability compared to HF and heart transplant patients, and the majority of participants expressed concerns about undergoing PGx if there was no suitable alternative drug available. The authors reported that 24%,

13%, and 17%, respectively of healthy volunteers, HF patients, and heart transplant recipients were more likely to consider genetic testing only if the targeted disease of interest was treatable. The study's strength was providing a valid comparison between healthy and unhealthy participants' perspectives toward PGx testing. It also enlightened future studies to address the need for complete confidentiality, enhanced educational programs, and public awareness. Its lack of generalizability to the target population was a limitation. In addition, there might have been a selection bias insofar healthy individuals might have been less interested in PGx testing than participants with chronic diseases.

In 2015 a qualitative study showed that participants taking carbamazepine and antidepressants commonly suffered from multiple drug reactions and reported a lack of therapeutic benefit. These patients required assurance of the optimal therapeutic outcome of PGx testing and whether or not they were on the correct medications (Trinidad et al., 2015). Based on Rogers's diffusion of innovation theory, the association between knowledge and attitudes of patients toward PGx testing is vital to achieving effective use of testing. But the lack of adequate knowledge about PGx testing can lead to apprehension among patients, even though they may agree with the benefits of testing (Trinidad et al., 2015). The authors reported that patients expressed positive attitudes toward the clinical advantages of PGx testing; however, most of them had concerns that might possibly outweigh the perceived benefit of PGx testing. These concerns included vulnerability to unauthorized access to genetic information, risk of discrimination in health insurance, and employability. Similar results were reported by Haddy et al. (2010) when chronically ill patients emphasized the potential advantage of PGx testing but were

worried about the potential discrimination and unauthorized access to genetic information. Both Trinidad et al. (2015) and Haddy et al. (2010) provided a distinctive qualitative insight on the potential barriers of accepting the use of PGx testing. Their findings could not, however, be extended to the whole target population.

Trinidad et al. (2015) also showed that the fear of discrimination and stigmatization was more prevalent among patients with mental health conditions than healthy patients. Participants were concerned about not receiving the therapeutic dose or correct medication if their physicians relied solely on the results of PGx testing and overlooked their patients' feedback on prescribed psychotropic medications. Therefore, some patients perceived PGx testing as an additional source of information about drug response rather than the only source. The study contributed to the understanding of a specific population prior to the transition of PGx innovation into practice, as emphasized by Rogers's diffusion of innovation theory.

A longitudinal study of undergraduate medicine and science students at three Canadian universities aimed to assess the students' attitudes regarding the use of PGx testing for psychotropic medications, assuming that these tests would result in the best therapeutic outcomes (Lanktree et al., 2014). Nine out of ten participants expressed positive attitudes toward PGx testing and its use for the optimal selection of psychotropic medications. About 78% of participants raised concerns about potential discrimination and the potential of using the results for non-clinical reasons. Sociodemographic characteristics such as age, sex, race, and religion group were not significantly associated with the students' attitudes. The strength of this work was that it contributed to the understanding of the use of PGx testing in psychiatric patients who usually experience a

wide range of ADRs; its weakness was the use of a convenient sample with a potential selection bias.

In a random digital phone survey among U.S. adults, Haga et al. (2012b) concluded that people expressed interest in PGx testing to find out about ADRs and seek help with drug and dosage selection. The authors indicated that White participants with a higher educational degree and prior experience of side effects expressed greater positive attitudes toward PGx testing than the rest of the sample. They established that people would be less likely to use PGx testing if their genetic information was shared for non-clinical purposes. The strengths of this study were its large number of participants and its novel insight about the association of sociodemographic characteristics and several benefits of PGx testing as perceived by the public. The limitations included an unclear definition of PGx testing, lack of a theoretical base, and inadequate description of the methods.

In a study conducted in Australia, Haddy et al. (2010) enrolled 35 individuals who personally had, or had an immediate family member with, a chronic medical condition. Patients were generally positive about PGx testing and were supportive of its use as a medical tool to help individualize treatment decisions rather than worrying about the negative effects of medications. Most participants, however, expressed concerns about the ability of PGx testing to determine future sensitive diseases (e.g., mental diseases) because of the potential for discrimination by insurance companies and employers. The study also revealed some potential barriers to the successful implementation of PGx testing, including concerns regarding storage of PGx testing results, the privacy of genetic information, and the cost of the test.

Rogausch et al. (2006) reported that 35% of patients with asthma or COPD expressed concerns about adverse results of PGx testing if a therapeutic alternative was not available while the available drugs were ineffective or caused serious ADRs. Patients' low expectations regarding PGx testing results were evidenced in that 69% and 44% of patients believed that they would be at a disadvantage with employers and health insurance companies, respectively. The majority of patients strongly felt that PGx testing would be advantageous to optimize their medication therapy in terms of avoiding taking wrong medications (75%), selecting a medication that best worked for them (63%), and avoiding ADRs (63%). The possibility of unavailable therapeutic options recommended by the genetic testing worried 72% of patients. Moreover, the study revealed that age and gender were major predictors of a hopeful attitude. The strength was its use of a large sample size to assess patients' and physicians' opinions regarding the use of PGx testing in a common chronic disease; however, providing participants with a leaflet explaining PGx with examples might have created self-report response bias. In addition, the findings might not have been generalized because the study focused on only two chronic disorders.

The authors also reported that younger patients were more likely than older patients to be optimistic about the useful application of PGx testing, while female patients were more likely than male patients to have fears and anxieties. Approximately one-half of physicians had favorable attitudes toward recommending PGx testing for their patients prior to the initiation of the therapy (e.g., anti-asthma medications) only if PGx testing was covered by health insurance. Additionally, physicians were concerned that patients

would be discriminated by health insurance companies if undesirable genetic testing results were disclosed to them.

A qualitative study was conducted in North-West England to explore the views of patients regarding autoimmune conditions and the views of healthcare professionals on PGx testing (Fargher et al., 2007). The study revealed that patients eligible to obtain PGx testing related to their immunosuppressant agents had positive attitudes. Patients also had high expectations of the benefits of PGx services providing healthcare practitioners were confident in interpreting and explaining the testing results. The authors suggested that the gap between patients' anticipated benefits of PGx testing and barriers to delivering PGx testing in clinical practice illustrates the need for awareness, educational, and training programs to facilitate the integration of PGx testing into clinical practice. Similar findings were reported by Moaddeb et al. (2015), who evaluated the experiences and feasibility of applying PGx testing in five community pharmacies. They revealed that offering PGx testing services for patients taking clopidogrel and simvastatin was feasible; however, additional training and effective communication between patients and physicians were required for an enhanced clinical use of these genetic tests. The Fargher et al. (2007) study's strength was that it helped design future research that would shed light on the urgent need for PGx education and training programs, and how these factors may affect the dissemination of PGx testing, although there was a weakness concerning generalizability of the results.

Patients should be given sufficient details to understand the pros and cons of PGx testing to assist in decision making. For example, a single gene in the human genome may influence the therapeutic effects of many prescribed medications; as a result, PGx

tests could potentially help in choosing the most effective available therapies, with the correct dose, and reduce the risk of drug-drug interactions for numerous treatments. The possibility of genetic discrimination, confidentiality of the testing results, the ability of providers to effectively translate and explain the testing results, feelings of being denied access to treatment, the cost of the tests, and the lack of evidence-based clinical information may impact the decision to adopt PGx testing (Fargher et al., 2007; Haddy et al., 2010; Rogausch et al., 2006).

A study conducted on a sample of Dutch individuals found that the perceived compatibility and benefits of genetic testing played a role in patients' decision-making for accepting these tests (Henneman et al., 2006). The authors revealed that having more information on genetics or a higher level of education might not increase participants' attitudes or their acceptance of genetic testing. Supporting the findings by Morren et al. (2007) and Rogausch et al. (2006), they established that variables such as genetic knowledge, education, age, and gender were not significantly associated with positive attitudes regarding PGx testing. This study was informative since it used a representative random sample of participants as well as valid and reliable instruments to accurately measure participants' responses, but it lacked a theoretical framework to evaluate the relationships among variables linked to the acceptance of these tests; it also had a selection bias.

Kobayashi and Satoh (2009) surveyed patients in Japan to assess their attitudes toward PGx and the role of genomic markers associated with ADRs. The majority of patients (88%) had optimistic attitudes toward the role of PGx in medicine and 75% were willing to be tested to investigate the effects of genetic differences on drug response.

Regardless of age and gender, proportionately more patients were likely to have their DNAs tested in PGx research when expecting severe reactions to drugs than when taking medications. The authors concluded that positive attitudes and greater perceived needs for PGx among patients increased their acceptance of PGx research investigating the role of genetic differences in medication response and medication safety, although concerns about protecting private health information, utilizing testing results in research, and finding an association between their genetic structure and the possibility of having ADRs were expressed by patients. Patients expressed higher perceived benefits and positive attitudes (81%) toward PGx as a clinical tool than did the general public (70%); however, they were more reluctant to contribute to the field of PGx by donating their DNAs than were the general public (Kobayashi and Satoh, 2009). The strength of this study was that the authors identified several variables influencing patients' attitudes toward PGx testing, and thus helped future studies to explore the actual roles of patients' medical conditions and severity of experienced side effects in decision-making. Its weakness was that PGx testing was not well defined in the study, and a potential of selection bias existed.

Summary of Patients' Knowledge and Attitudes toward Pharmacogenetic Testing

A comprehensive review of the literature reveals a paucity of studies regarding patients' knowledge and attitudes toward PGx testing. Lack of awareness and limited knowledge regarding PGx testing were prevalent among patients despite good attitudes. Although patients are generally supportive of PGx testing and optimistic about its potential therapeutic benefits, their concerns about confidentiality, employability, insurability, and cost are seen as potential barriers to accepting PGx testing. Many studies have emphasized the need for awareness programs directed at the general patient

population to facilitate the clinical implementation of these genetic tests. A summary of the advantages and disadvantages of PGx testing is presented in Table 2.1.

Table 2.1
Summary of Potential Advantages and Disadvantages of PGx Testing from the Patient Perspective Identified in the Literature Review

Advantages	Disadvantages
- Reducing ADRs - Preventing ineffective or incorrect medication - Predicting the most effective medication - Restoring patients' confidence in the drug-prescribing process - Increasing patients' awareness of their conditions - Improving patients' adherence to prescribed medications	- Negative impact on patients' insurability - Negative impact on patients' employability - Breach of confidentiality - Concerns about physicians' over-reliance on testing results - Denial of certain treatment options - Increased anxiety about negative testing results (i.e., unavailability of a suitable drug) - Disclosing information about the risk of pre-existing conditions

Prescribers' Knowledge of Pharmacogenetic Testing

According to research carried out by Powell et al. (2012) utilizing a sample of family and internal medicine physicians in North Carolina, 39% of participants were aware of genetic testing and only 15% felt competent to answer genetics-related questions. More than half of the physicians who were aware of genetic testing did not perceive its clinical benefits. The majority of those physicians expressed concerns regarding unavailability of clinical guidelines, the clinical utility of these tests, and complexity of testing result interpretation. The likelihood of insurance and employment discrimination based on genetic testing results were less frequently reported. Physicians 50 years or older were more likely to be cognizant of genetic testing than younger physicians. Male physicians were more likely to feel comfortable answering genetics-related questions than female physicians. This study provided preliminary findings for

more specific genetic testing such as PGx testing and was based on a relatively large sample size and appropriate instruments to capture variables of interest. Its weakness was the use of a convenient sample that limited the generalizability of the findings.

A large, nationally representative survey of U.S. physicians showed that the lack of adequate knowledge was probably the main factor influencing the implementation of PGx testing by healthcare providers (Stanek et al., 2012). The study reported that most physicians across the U.S. had no formal coursework related to PGx during their educational years. For instance, only 15% and 23% reported receiving information on PGx during their undergraduate or graduate training, respectively. The authors also reported that only 10% of physicians believed that they had enough information and training to introduce PGx testing into clinical practice. Few physicians recognized the benefits of PGx testing in improving drug effectiveness (9%), adherence (4%), and lowering ADRs (10%). Almost 10% reported prior experience with ordering PGx testing for their patients. Physicians who were aware of the availability of PGx testing and who believed that genetic difference can cause variability in drug response were more likely to be early adopters of PGx testing. Furthermore, the authors revealed that early adopters were more likely to be oncologists or surgeons and had intermediate to long years of medical practice (i.e., 15-29 years). Male physicians 40 years or older and working in urban areas were more likely to be future adopters. The majority of physicians (67%) refused to order the test and indicated that they did not have enough information about PGx. These findings highlight a need to increase physicians' knowledge and attitudes to appropriately integrate PGx testing into daily clinical practice and communicate testing results to their patients in order to help them with decision making. The study was large

and representative, and indicated reliable results, but it lacked a theoretical framework. Unfortunately, it did not provide additional clarifications on the relationship between attitudes and adoption of PGx testing.

Rogausch et al. (2006) showed that physicians' lack of knowledge and familiarity, in addition to the fearful attitudes toward PGx testing, may impact their decision to implement this technology in the future. Inadequate information about the clinical utility of these tests and the lack of clear clinical guidelines were described as new challenges to the physicians' decision-making process to accept PGx testing. In other words, physicians were portrayed as willing to consider PGx testing as an area of research rather than its clinical application.

According to research carried out by Haga et al. (2012a), physicians' levels of knowledge and experience with PGx testing decreased their preparedness to use genetic testing for their patients. The study reported that only 16% of participants received training about PGx in medical school or post-graduate training, and almost 76% were unaware of PGx information in drug package inserts. Different results were reported by Stanek et al. (2012): a small percentage of physicians (29%) received training about PGx in medical school or post-graduate training, and 39% indicated learning about PGx from drug package inserts. Haga et al. (2012a) also reported that only 13% of physicians felt comfortable ordering PGx testing. Physicians had other concerns related to communicating confounded testing results, reimbursement issues, and the lack of practice guidelines and recommendations regarding PGx testing. This study was enlightening because its major findings have been reported by other studies and it supported the need for incorporating PGx into educational curricula and training programs, but it had a

selection bias and an incomplete and inadequate description of the statistical analyses performed.

Shields et al. (2005) conducted a national survey to assess the adoption of genetic-based smoking cessation treatment among 1,120 U.S. primary physicians. The study aimed to predict physicians' attitudes and decision-making about the future use of PGx testing that may become available in individualized treatment cessation therapy. Most participants were in practice with fewer than five other physicians and in urban areas. Over 75% of respondents received some formal training in clinical genetics from different sources such as medical school (57%), continuing medical education (CME) courses (47%), clinical genetics rotation in medical school (16%), and genetics rotation in residency (4%). Approximately 15% reported that they were early adopters and another 14% were very optimistic about the benefits of PGx testing on the treatment outcomes of nicotine replacement therapy. Although only 4% reported being well prepared for these types of tests, almost 69% of participants were willing to adopt PGx testing for smoking cessation treatment. The study's strength was that it relied on a large sample randomly selected from all U.S. primary care providers (PCPs). The study method, however, was based on a patient scenario rather than on investigating an existing PGx testing, which might have underestimated or overestimated the factors influencing the uptake of genetic testing into practice. The underrepresentation of some medical specialties also might have limited the generalizability of the findings.

In a landmark work conducted by Taber and Dickinson (2014) on physicians from different specialties, only 13% of participants reported being extremely or very familiar with PGx. Similar results were also reported by others (Haga et al., 2012a; Stanek et al.,

2012). Only 11% reported receiving formal training in PGx. Nearly 32% of cardiologists and 12% of psychiatrists had ordered a PGx test. Barriers to ordering PGx testing identified by participants included not knowing what test to order (70%), lack of insurance coverage for the PGx tests (53%), uncertainty about the clinical utility of the test (52%), and cases in which PGx testing was not applicable (18%). The study had a strong description of methods and provided an updated finding on knowledge deficit, which was a major gap in previous studies, but it had a small sample and a possible selection bias.

Genetic differences account for 35-50% of inter-individual variability in warfarin anticoagulant responses (Wen and Lee, 2013). Anticoagulation providers deal with a wide range of warfarin dosing requirements that dictate finding an adequate patient-specific and regular monitoring to avoid serious side effects. Kadafour et al. (2009) assessed the clinical use of PGx testing among anticoagulation providers in North America by comparing their knowledge and attitudes. Most participants (80%) indicated that warfarin PGx testing was not available at their sites. Only about 12% reported using these tests. The study also found that anticoagulation providers' knowledge was not significantly correlated with their attitudes. Participants who had warfarin PGx testing available in their practice sites had a significantly higher knowledge score than those who did not. Similarly, participants who previously used warfarin PGx testing had a significantly higher knowledge score than those who had not.

The authors reported several potential barriers to the acceptance of warfarin PGx testing, including the lack of clear evidence of clinical utility, unavailability of the test, and lack of PGx knowledge among physicians and patients. Similarly, Shishko et al.

(2015) reported that inadequate educational and training programs for healthcare professionals and insufficient education of patients are barriers to the uptake of PGx into clinical practice. The Kadafour et al. (2009) work was one of the largest studies that contributed to the literature by addressing the challenges for integrating PGx testing in warfarin therapy. Its weakness was the improper representation of anticoagulation healthcare providers in North America.

Dressler et al. (2014) studied factors that influence the adoption of PGx testing in cancer treatment. They conducted a survey of 94 North Carolina oncologists and indicated that most of them believed in the beneficial outcomes of using PGx testing; however, only 33% of them were comfortable with their knowledge about PGx testing and 37% felt confident in interpreting testing results. Oncologists in a community setting were more likely than oncologists in an academic setting to be early adopters of new PGx testing (Oncotype Dx™) that potentially determine the benefit of using chemotherapy, as well as more likely to be future adopters of cancer PGx testing. The authors reported that oncologists with more than ten years of medical experience were more likely to be early adopters of PGx testing than the rest, although those with fewer years of experience were more comfortable about their PGx testing knowledge. The authors identified the main factors that enhance acceptance of cancer PGx testing among oncologists, including availability of well-conducted prospective clinical trials, evidence-based studies, and professional guidelines. This study provided additional clarification about the need for optimal communication channels and educational programs to appropriately disseminate PGx information and influence the acceptance of PGx testing in the clinical practice. Its major limitation was a relatively small sample size.

Knowledge should not necessarily be limited to PGx testing only. Knowledge about basic genetic variation underlying some health conditions is also imperative to optimize the benefits of PGx testing and meet the current standard of care. For example, genetic variants of the β-fibrinogen gene may increase the progression of coronary heart disease; more importantly, knowledge about these genetic variations has been useful in predicting patients' responses to statin therapy and improving the overall health outcome (Dornbrook-Lavender and Pieper, 2003).

Genetic testing in the screening and potentially directing the clinical management of patients with mutations in the breast cancer genes 1 and 2 (BRCA1 and BRCA2) has proven to be one of the most successful tests available (Miki et al., 1994; Smith and Isaacs, 2011). Armstrong et al. (2003) studied how the adoption of BRCA1/2 genetic testing initially started and what factors contributed to its subsequent acceptance among women who underwent genetic counseling. The study results reported that only 7% of study participants were recommended by physicians to undergo BRCA1/2 screening. Most participants excluded physicians as a source of information about BRCA1/2 testing, which showed the lack of physicians' awareness about BRCA1/2 screening tests. The study concluded that participants' innovativeness and perceptions about compatibility (i.e., whether the test fits well with patients' personal values), not complexity, and advantage of the test influenced the adoption of BRCA1/2 genetic testing. Although BRCA1/2 mutations are relatively rare, having a family medical history is a strong predictor of the need for BRCA1/2 screening; other factors that might have influenced acceptance of genetic testing could have been previously overlooked.

This study was influential because it utilized a relatively large sample size and was guided by Rogers's diffusion of innovation theory to explain the factors that influence the early acceptance of genetic testing. In addition, the study demonstrated the significance of communication channels in participants' awareness about an innovation. Its major limitation was unavailability of a control group (i.e., women who had not undergone genetic counseling), which was required to determine whether the diffusion of innovation theory adequately explained the acceptance of genetic testing. In addition, there was a high risk of selection bias.

Klitzman et al. (2013) surveyed 220 internal medicine physicians to assess their use of genetic testing, including PGx testing. The majority of participants rated their knowledge of genetics as very or somewhat poor (74%). Most participants indicated a need for more training relevant to ordering genetic testing (79%), patient genetic counseling (82%), interpretation of genetic results (77%), and maintaining patient genetic privacy (81%). The most frequent genetic tests ordered by internists were for Factor V Leiden thrombophilia (15%), breast and ovarian cancers (17%), and cardiomyopathy (8%). Only 6% used PGx testing to prevent drug toxicity. The authors also reported the factors that significantly influenced the use of genetic testing: patients' request to use the tests (62%), working in large practices with more than 1,000 patients (67%), availability of a genetic counselor for patient referral (62%), and having fewer numbers of African-American patients in their practice (56%). Most physicians who adopted genetic testing were White, male, 50-59 years old, and had more White patients in their practice.

This study was important because it included a wide range of genetic tests to assess physicians' acceptance. The study also revealed that African-Americans might

have been deprived of the potential benefits of genetic testing. The major limitation was its use of a non-representative sample. The study also failed to conduct subgroup analysis in order to show the impact of rurality and area of practice on the adoption of genetic testing.

Kudzi et al. (2015) conducted a semi-structured survey study in seven health institutions and four academic institutions in Ghana in which the knowledge of PGx among healthcare professionals and faculty members was evaluated. The authors showed that the majority of participating physicians were aware of PGx testing as a new clinical tool and heard about it from several resources (i.e., colleagues, schools, the Internet). While most healthcare professionals rated their perceived knowledge of PGx as good or very good, most faculty members rated their perceived knowledge as poor or very poor. The study also showed that most healthcare professionals with prior awareness about PGx testing were 25-29 years old with five years or less of practice. Most healthcare professionals agreed on the potential benefits of PGx testing in ensuring drug safety and improving efficacy, but they were uncertain about its role in cost saving and drug discovery.

The strength of this work was that it interviewed healthcare professionals and faculty members to better assess the need for continuous and updated PGx educational programs in medical school curricula. Its main limitation was its reliance on a small and selective sample of participants. A selection bias also might have occurred.

Prescribers' Attitudes toward Pharmacogenetic Testing

Rogausch et al. (2006) showed that while patients were excited to undergo PGx testing because of the possibility of being given a suitable anti-asthma drug with fewer

ADRs, both physicians and patients were concerned about the confidentiality of genetic information. Physicians also were concerned about the cost of these PGx tests and feared that results would be reported to patients' insurance companies and workplaces, raising the possibility of discrimination. In addition, physicians working in rural areas had more fearful attitudes toward PGx testing than physicians working in urban areas. The authors reported that age, gender, and size of practice were not significantly associated with physicians' views regarding PGx testing. In line with other reports of healthcare providers' attitudes toward PGx testing (Fargher et al., 2007; Haga et al., 2012c; Klitzman et al., 2013; Lanktree et al., 2014; Shields et al., 2005; Stanek et al., 2013; Walden et al., 2015), the authors expressed fears toward the potential disadvantages of PGx testing in disclosing pre-existing conditions, exposing patients to potential discrimination at insurance or workplace, and privacy of genetic health information.

Fargher et al. (2007) conducted a focus group study of healthcare professionals to assess their knowledge, attitudes, and experiences of PGx testing. Most participants agreed on the perceived benefits of PGx testing to guide treatment decisions, although they were worried about the possibility of excluding a patient from a specific treatment option based on testing results. Participants also believed that they had a limited role in utilizing PGx testing. Supporting the finding of other studies (Haga et al., 2012c; Rogausch et al., 2006), the authors noted that physicians were concerned about the potential of identifying a genetic biomarker that might be used as an indicator of susceptibility to a particular disease. They explored healthcare professionals' views and opinions about PGx testing at an early stage to help future studies focus on the application of PGx testing in clinical practice. The major limitations of this study were

underrepresentation of some medical specialties in the sample, limited generalizability of the findings, and failure to explore the reasons why participants did not feel that they had a role in utilizing PGx testing.

Haga et al. (2012c) found that many physicians and genetic experts had more favorable attitudes toward currently prescribing practices than PGx testing. Respondents felt that traditional clinical methods were the most effective technique to determine optimal warfarin dosage. Some physicians raised concerns about the cost of PGx testing and insurance coverage. Yet these physicians showed interest in PGx because of the possibility of avoiding severe adverse effects, especially when drugs with a narrow therapeutic index such as warfarin were recommended. Other physicians were concerned about the lack of adequate evidence regarding the clinical utility of PGx testing. Similar to other studies (Fargher et al., 2007; Kadafour et al., 2009; Lanktree et al., 2014; Rogausch et al., 2006; Walden et al., 2015), the researchers indicated that the paucity of test interpretation skills, lack of insurance coverage of PGx testing, delay of treatment, and unclear guidelines for the use and regulation of PGx testing might have a negative impact on its effective clinical implementation. The strength of the study was that it involved three focus groups to gain more detailed information (i.e., ancillary disease risk information) about health professionals' interest regarding the use of PGx testing. Its limitation was that its small and convenient sample might not have been representative of the target population.

The Kadafour et al. (2009) survey study of anticoagulation providers reported that half of the participants agreed or strongly agreed that they were adequately informed about warfarin PGx; about half of them responded that they were comfortable

interpreting warfarin PGx testing results. Nearly 26% of the participants agreed or strongly agreed about potential clinical benefits of warfarin PGx testing in reducing ADRs, and 32% expressed this view regarding achieving a therapeutic outcome quickly. Overall, the lack of confidence regarding interpretation of genetic results was associated with the lack of PGx knowledge. A small fraction indicated willingness to recommend warfarin PGx testing to their colleagues. The strengths of the study were the use of a large sample size and a real case scenario to better capture the factors influencing the uptake of currently existing warfarin PGx testing into practice; the use of tailored scenarios helped resolve conflicts among previous studies findings. However, the study might not have accurately reflected the actual knowledge and attitudes of the target population of anticoagulation providers.

The results of a national survey conducted on 597 internists and family medicine practitioners showed that over 70% were aware of the availability of PGx testing prior to taking the survey, but most felt that they were insufficiently trained to order or use these genetic tests (Haga et al., 2012a). Respondents felt that CME, grand rounds, and training in residency were the best sources to learn about PGx testing. In contrast to the findings of the Fargher et al. (2007) study, these researchers reported that the majority of participants felt responsible for increasing patients' awareness of PGx testing, discussing testing results with their patients, and integrating the testing results in their patients' medical records. Only 10% agreed on pharmacists' roles in determining the optimal therapeutic regimen based on PGx testing results. The study was significant because it used a large randomized sample to provide additional clarification about more efficient

communication channels and addressed barriers to early adoption of PGx testing, but it was susceptible to a form of selection bias.

A survey conducted on 10,303 physicians in the U.S. reported that virtually all respondents believed that genetic testing could influence individual drug response (Stanek et al., 2013). About 42% relied on FDA-approved PGx information in package inserts to predict or improve response to medications, and 10% felt that adequate knowledge about PGx and its application was acquired. Out of 1,319 physicians who had ordered PGx testing for their patients, 73% believed that PGx testing improved drug effectiveness, 80% believed that it reduced toxicity, 61% said that it improved patient understanding of their health conditions, and 31% agreed that it improved patient adherence to medications.

This study also reported that physicians who relied on drug package inserts to learn more about PGx had significantly greater prior education and adequate PGx information than those who did not rely on drug package inserts as a direct source of information. The results also showed that 39% of physicians obtained information on PGx testing from drug package inserts and 42% relied on FDA-approved recommendations. As a result, adoption of PGx testing in clinical practice was higher among physicians who obtained PGx information from drug package inserts and those with prior testing experience. The study also showed that adoption of PGx testing in clinical practice was higher among physicians who perceived the potential benefit of PGx testing to their patients. Other factors associated with obtaining PGx information from drug package inserts included older age, greater years of postgraduate experience, using the Internet or other colleagues as genetic information sources, and greater stability in

their practice careers. The study was able to explore additional factors associated with the dissemination of PGx testing; it provided new findings of the use of FDA-approved PGx information in drug package inserts. The risk of selection bias and inclusion of underrepresented groups of physicians limited generalizability of its results.

Walden et al. (2015) conducted a survey study to assess the opinions of Canadian physicians regarding the use of PGx testing to guide the selection and dosing of antidepressant and antipsychotic medications. The study found that 80% of respondents expressed optimistic attitudes toward the future of PGx testing as the standard of practice for antipsychotic treatment and 76% reported satisfaction for being able to understand and interpret the PGx report provided. There were no gender differences in attitudes toward the clinical application of PGx testing; a similar finding was reported by Klitzman et al. (2013). Supporting the findings of Haga et al. (2012c) and Kadafour et al. (2009), these researchers reported that the cost of PGx testing and the time needed to receive the results were obstacles to accepting the procedure. The study contributed to the literature by proving up-to-date information about physicians' attitudes toward the use of PGx testing after receiving a PGx report for real clinical situations; the small sample size and the possibility of selection bias might have limited statistical inference.

Summary of Prescribers' Knowledge and Attitudes toward Pharmacogenetic Testing

Only a few studies focus on physicians' knowledge and attitudes toward PGx testing. Physicians did not feel well informed about the procedure. Most physicians had favorable attitudes toward PGx testing and its perceived benefits in different therapeutic areas, but expressed concerns about their inadequate knowledge, ability to interpret

genetic testing results, lack of clear clinical guidelines, and patients' confidentiality. The need for educational initiatives focused on training physicians to increase their knowledge base and competency in interpreting and communicating PGx testing results to patients. A summary of the advantages and disadvantages of PGx testing is presented in Table 2.2.

Table 2.2
Summary of Potential Advantages and Disadvantages of PGx Testing from the Prescriber Perspective Identified in the Literature Review

Advantage	Disadvantage
- Determining the appropriate dose or drug selection - Explaining individual variation in drug response - Predicting the most effective medication - Reducing serious ADRs - Improving patient adherence to prescribed medications - Reducing the overall cost of treatment	- Negative impact on patient health insurance eligibility - Negative impact on employment requirements - Risk of treatment delay - Breaches of confidentiality - Risk of unintentional disclosure of information about disease susceptibility - Lack of insurance coverage - Lack of clinical guidelines - Uncertainty about clinical utility

The research methods applied in this dissertation are discussed in Chapter 3. Development of the questionnaire, inclusion criteria, the recruitment process, and data collection are described. A summary of concrete analytical procedures used to address the research questions also is presented.

Chapter 3

Methodology

The methodology used in this study is presented in this chapter to assess and evaluate the effect of knowledge and attitudes on acceptance of PGx testing using a convenient sample of patients and physicians. The setting in which the study took place and the participant pool are described. Also described are the instruments developed and used to collect the data. Justification of the sample size, the data analysis plan, and ethical considerations are discussed.

Research Design

A cross-sectional, descriptive survey design was implemented to assess the knowledge and attitudes of patients and physicians toward PGx testing. Cross-sectional studies are often used to gain information and answer specific research questions based on data collected from a subset of a population at only one point in time (Birch and Malim, 1988). The data collection instrument was a questionnaire containing variables of interest. According to Rogers's diffusion of innovation theory, several independent factors, such as sociodemographic variables (e.g., gender, age, level of education, area of living, current practice setting), prior experience with PGx testing, and perceived need for innovation and innovativeness can influence an individual's knowledge of PGx testing. Other variables, including relative advantage, compatibility, complexity, trialability, and observability, also work as independent variables that may affect an individual's attitude

toward PGx testing. Knowledge and attitudes toward PGx testing are independent variables that can influence the acceptance of PGx testing.

A large, representative sample was planned for the study. The probabilities of type I and type II errors were set in advance to determine an adequate sample size. A type I error (α) occurs when a researcher rejects a true null hypothesis; failing to reject a false null hypothesis is called a type II error (β). Based on the value of β, a power analysis was conducted; power equals to 1 – β.

G*Power 3.1 was utilized to calculate the appropriate sample size required to achieve a sufficient power (Faul et al., 2009). Cohen's f^2 was utilized for calculating the effect size within a multiple regression model in which the independent and the dependent variables are continuous (Cohen, 1977). Cohen's f^2 value, calculated by $R^2 / (1-R^2)$, is an adjusted coefficient of determination indicator of how well a regression equation fits the data values. A medium effect size value of $f^2 = 0.15$ in the analysis of variance context was selected. Using significance level $\alpha = 0.05$, the minimum sample size was determined to consist of 120 observations with up to ten predictors and an actual power of 0.80. Due to the lack of studies that consider the effect size required for this type of research, the necessary sample size required to detect a significant effect with enough statistical power using a 5% to 7% margin of error and a significance level of 0.05 was estimated to range between 126 and 180 participants.

Population and Recruitment of Patients

Patient recruitment took place at the Nova Southeastern University (NSU) Clinic Pharmacy located in Fort Lauderdale, Florida. Potential participants filling a prescription for a chronic disease were personally invited by the author of this dissertation to be part

of the study. A flyer with a brief description of the study was given to patients who showed interest in participating. The eligibility criteria were that potential participants had to fill their prescription for at least one chronic disease, were aged 18 years or older, spoke English fluently, and were willing and able to provide informed consent (see Figure 3.1). If a patient self-reported at least one chronic disease, more about the research project and possible benefits and risks were explained. If the patient was still interested, he/she was given the opportunity to participate in the study and asked to read and sign the consent form. All eligible participants were assured that their decision to participate (or not) would not affect their relationship with the NSU Clinic Pharmacy or other healthcare providers. If the potential participant signed the consent form, the survey was then administered.

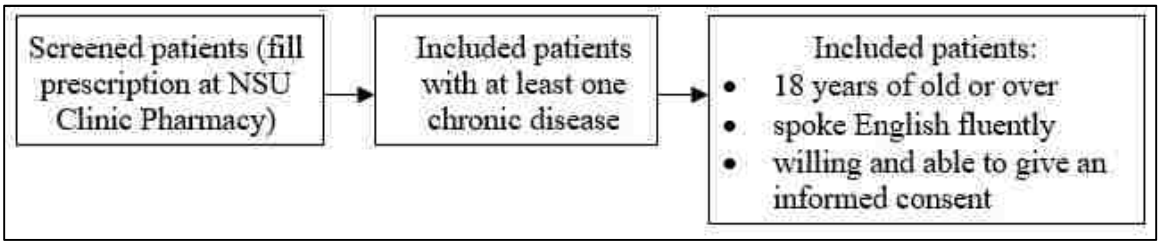


Figure 3.1: Illustration of inclusion criteria for patient recruitment.

Population and Recruitment of Prescribers

NSU physicians, as well as community physicians involved in medication therapy decisions, were asked to participate in an online survey. A letter was emailed with the survey to eligible physicians. Eligible community physicians were also recruited in person from three medical conferences held in Florida. If a potential participant was interested, he/she was offered the opportunity to participate in the study using a tablet computer to sign the online participating letter and subsequently fill out the

questionnaire. Prescribers' inclusion criteria included being a physician licensed to practice in Florida and currently involved in medication therapy decisions, willing to sign the participation letter, and willing to complete the survey online (see Figure 3.2). Respondents who successfully completed the survey were offered an incentive ($5 or $10 gift card) as a token of appreciation. The first 60 respondents were given $10-gift cards and $5-gift cards were assigned to the next 90 expected respondents.

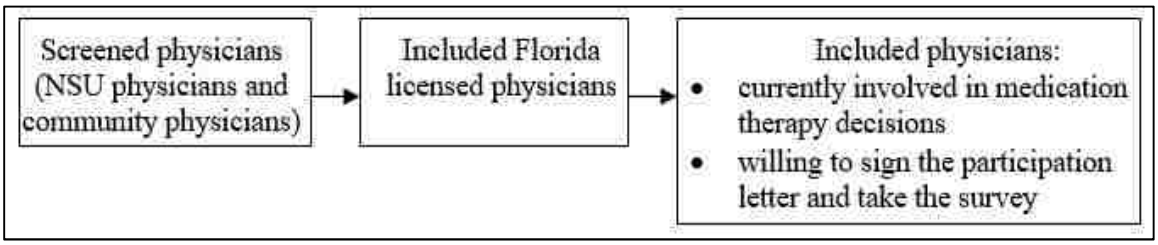


Figure 3.2: Illustration of inclusion criteria for prescriber recruitment.

Development of Patient Survey

The questionnaire survey used in this study was configured following the format of similar studies (Calsbeek et al., 2007; Dodson, 2012; Nielsen and Moldrup, 2007; Lachance et al., 2015; Roederer et al., 2012; Rogausch et al., 2006; Zhang et al., 2014). Several concepts adapted from Rogers's diffusion of innovation theory were incorporated. The patient questionnaire had 46 questions. A copy of the patient questionnaire is presented in Appendix A.

Once the questionnaire was configured, it was tested with nine persons to examine the validity of the items. The results showed an average completion time of nine minutes. Subsequently the format of several questions was changed to make them more understandable. A brief description of PGx testing was provided in the final version. The final patient questionnaire began with seven items assessing participants' knowledge

about PGx testing. This section was followed by 18 items assessing participants' preferences about the use of PGx testing. Questions about patients' prior experience with genetic testing and their willingness to accept the testing were asked. The survey concluded with sociodemographic items. Patient survey questions and corresponding citations are listed in Appendix B. The attitude items showed an internal consistency or reliability (Cronbach's alpha) score of 0.72, while the knowledge items showed a Cronbach's alpha score of 0.65.

Development of Prescriber Survey

The questions posed to prescribers also were configured following the instruments of previous studies (Dodson, 2012; Roederer et al., 2012; Rogausch et al., 2006; Shaw et al., 2011; Taber and Dickinson, 2014). Several concepts adapted from Rogers's diffusion of innovation theory were incorporated as well. The prescriber questionnaire had 42 questions. A copy of the prescriber questionnaire is presented in Appendix C.

Six healthcare professionals agreed to participate in testing the survey. For face and content validity purposes, they were asked to explain their reactions to the wording, order, and clarity of the questions. An average completion time of 6.5 minutes was reported. Changes to the questionnaire were made based on the feedback provided; these reduced average time of completion to four minutes. The final prescriber questionnaire began with six items assessing participants' knowledge about PGx testing. This section was followed by 16 items designed to assess participants' preferences about the use of PGx testing. Questions about prescribers' prior experience with genetic testing and their willingness to accept the testing were asked. The survey concluded with sociodemographic items. Prescriber survey questions and corresponding citations are

listed in Appendix B. The attitude and knowledge items showed Cronbach's alpha scores of 0.78 and 0.60, respectively.

Collection of Patient Data

The original plan for patient data collection was to offer the option of either a paper-based or web-based survey. None of the potential participants showed any interest in using a tablet computer to answer the web-based questionnaire. Thus, after participant number 60 was recruited, the option of answering online was no longer offered. Each participant received the questionnaire on a clipboard. The materials included an adult consent form with a general overview of the study and the two-page, 46-item questionnaire. To protect participants' confidentiality, separate folders were used to collect the consent forms and the questionnaires. After collecting all the survey materials, the data were organized with Research Electronic Data Capture (REDCap) software, leaving only numbers and variable names to be utilized in the analysis. This software was created by a group of clinical researchers in 2004 at Vanderbilt University as a user-friendly data collection tool. REDcap opens a secure survey page and allows researchers to have their participant data auto-populated in the server; it also allows manual data entry. The data collected in this study were entered electronically. Prior to data analysis, a data reconciliation process was conducted to verify the accuracy of the entered data. Data analyses were performed using IBM® Statistical Package for the Social Sciences (SPSS), version 24.0 and Stata version 14.

Collection of Prescriber Data

All prescriber questionnaires were administered and answered online. The questions were programmed into the Snap Survey software (Snap Surveys Ltd.). NSU

physicians and community physicians were invited to complete an online survey about PGx testing from July through October 2016. The survey was terminated after receiving 150 responses. The prescriber survey was anonymous; respondents' identifiable information was removed from the responses before downloading them.

Measurement of Variables

Patient Variables

Patients' knowledge of PGx testing was measured as the number of PGx testing questions answered correctly. Within Rogers's diffusion of innovation theory, knowledge as a dependent variable is influenced by several antecedents, which in this study were treated as independent variables. These included prior experience, perceived need for innovation, innovativeness, area of living, sociodemographic variables (e.g., age, level of education), and communication channels. Attitude toward an innovation was measured by the number of favorable responses toward PGx testing. According to Rogers's diffusion of innovation theory, attitude as a dependent variable was influenced by several independent variables including relative advantage, compatibility, complexity, trialability, and observability of PGx testing (see Table 3.1).

Prescriber Variables

Physicians' knowledge of PGx testing was measured as the number of PGx testing questions answered correctly. Within Rogers's innovation of diffusion theory, knowledge as a dependent variable is influenced by independent variables such as prior experience, perceived need for innovation, innovativeness, area of current setting, sociodemographic variables (e.g., age, ethnicity), and communication channels. Attitude toward PGx testing was measured by the number of favorable responses toward PGx

Table 3.1
Measurement of Concepts Utilized in the Patient Survey

Construct/Variable	Measurement	Question(s)
Knowledge of PGx testing	Number of correct answers related to the influence of genetic differences on individual's responsiveness to different medications	1-7
Attitudes toward PGx testing	Number of positive responses toward the use of PGx testing	11-17, 20, 23, 24
Prior experience	Whether the adopter is awareness of the innovation before adoption	8, 9
Innovativeness	Whether the patient is reluctant to adopt PGx testing until he/she sees it providing useful results for other patients	25
Perceived need	Whether an individual feels that there is a useful need for the innovation	18, 19
Sociodemographic variables	Gender, age, ethnicity, and level of education	31-35
Communication behavior	Most effective channels of generating knowledge about the innovation	30
Relative Advantage	Whether the adopter sees a higher value in the innovation than what it replaces	21, 22
Compatibility	Whether the innovation is consistent with the existing values and norms	26
Complexity	Whether the innovation is difficult to understand or use	27
Trialability	Whether the innovation can be tested to reduce the uncertainty	28
Observability	Whether the results and effects of an innovation are visible	29
Willingness to take PGx testing	Whether patients would like to take PGx testing for one of their chronic disease medications	10

testing. According to Rogers's diffusion of innovation theory, attitude as a dependent variable was influenced by several independent variables including relative advantage, compatibility, complexity, trialability, and observability of PGx testing (see Table 3.2).

Table 3.2
Measurement of Concepts Utilized in the Prescriber Survey

Construct/Variable	Measurement	Question(s)
Duration of practice	Duration of overall medical practice	1
Knowledge of PGx testing	Number of correct answers related to the influence of genetic differences on individual's responsiveness to different medications	2-7
Attitudes toward PGx testing	Number of positive responses toward the use of PGx testing	8-12, 15, 17, 19
Prior experience	Whether the physician has ever ordered PGx testing for a patient	25
Innovativeness	Whether the physician is reluctant to adopt PGx testing until he/she sees it working for patients	14
Perceived need	Physician's acknowledgement that there is a useful need for the PGx testing in several instances such as a high risk of genetic variant	21a, 12b
Area of current setting	Rural, Suburban, or Urban	32
Sociodemographic variables	Gender, age, ethnicity, and medical specialty	28-31
Communication behavior	Most effective channels of generating knowledge about PGx	22
Relative advantage	Whether the physician believes that PGx testing is beneficial for his/her patients in the selection of a medication that would better control their health condition in several situations	20a, 20b
Compatibility	Whether the physician believes that PGx testing is compatible with his/her personal values	13
Complexity	Whether the physician believes that the application of PGx testing adds more complexity to the drug prescribing process	18
Trialability	Whether the physician believes that PGx testing is worth trying	16
Observability	Whether the physician has ever talked with a patient about PGx testing	23
The willingness to recommend PGx	Whether the physician is willing to recommend PGx testing to his/her patients	24
Factors affecting PGx adoption	Factors that influence physician's acceptance of PGx testing	26
Pharmacist role in PGx testing	Whether the physician prefers a pharmacist to order and interpret PGx testing	27

Data Analysis

Descriptive Statistics

Univariate analysis was conducted to describe and summarize nominal, ordinal, and continuous data. Measures of central tendency, variation, and normality were used for continuous variables, while counts and percentages were used for categorical variables. Seven testing patient knowledge questions and six testing prescriber knowledge questions utilized yes/no/not sure responses. The correct answer for all knowledge subscale responses was recoded as one, while the incorrect or "not sure" answers were recoded as zero. Ten testing patient attitude questions and eight testing prescriber attitude questions were in the form of a 5-point Likert scale, with 5 being the most favorable answer. Additionally, questions 13-16, 20, and 25-27 (patient data) and 13, 14, and 17-19 (prescriber data) were reverse coded so that larger values for all the questions had the same direction, indicating a more positive attitude. All Likert scale item responses to the attitude statements "Strongly Disagree" or "Disagree" were recoded as zero. The "Neutral" response was recoded as one. All the "Agree" or "Strongly Agree" responses were recoded as two. Since there were very few responses on some of the choices provided for some categorical variables, including age, education, ethnicity, and area of living, some levels were merged based on the results appearing in the frequency tables. Similarly, due to a lack of responses in some of the provided choices, the options in the variable "communication channels" were also collapsed.

The PGx testing knowledge subscale, the PGx testing attitude subscale, and the perceived characteristics of innovation subscale were created using the Rasch model. The Rasch model is a one-parameter logistic model that applies the principles of item

response theory (IRT). This logistic model relates the difficulty of an item to the ability of a respondent to answer that item in order to obtain an interval-level score (An and Yung, 2014). Estimates of item difficulty and respondents' ability are independent of each other, making the scale score relatively distribution-free. After assessing the subscales using the Rasch model, some weak items were removed to better measure the constructs of interest and ensure validity. The total summative scores for the PGx testing knowledge, attitude, and perceived characteristics of innovation questions were calculated for each respondent. Finally, the reliability of the study constructs (subscales) was calculated using Cronbach's Alpha to examine the internal consistency of each subscale. The extent to which each subscale data deviated from normality was also measured (see Tables 3.3 and 3.4).

Table 3.3
Cronbach's Alpha and Shapiro-Wilk (SWilk) Scores for Each Patient

Subscale	No. of Items	*Cronbach's* Alpha	SWilk Test (Signif.)
Knowledge*	7	0.65	0.072
Attitude	10	0.71	0.600
Perceived characteristics of innovation**	6	0.69	0.340

Note. Significance value of the Shapiro-Wilk Test is greater than 0.05; the data are normally distributed. *$\log_{10}$ transformation; ** Square transformation

Table 3.4
Cronbach's Alpha and Shapiro-Wilk (SWilk) Scores for Each Prescriber Subscale

Subscale	No. of items	*Cronbach's* Alpha	SWilk-Test (Signif.)
Knowledge	6	0.60	0.700
Attitude*	8	0.78	0.074
Perceived characteristics of innovation	6	0.60	0.066

*$\log_{10}$ transformation

The gender variable for both patient and physician data was recoded into two categories: male or female. The age variable was recoded into five categories (18-29 years, 30-39 years, 40-49 years, 50-59 years, and 60 years or older) for patient data and four categories (25-39 years, 40-49 years, 50-59 years, and 60 years or older) for physician data. The ethnicity variable was recoded into four categories: White/Caucasian, Hispanic/Latino, Black or African American, and other. The area of living variable and the type of practice setting variable were recoded into three categories: urban, suburban, and rural. The prior experience variable was recoded into two categories: yes or no.

In the patient data set, the level of education variable was recoded into five categories: high school or GED, associate degree, baccalaureate degree, master's degree, and doctorate or professional degree. The communication channel variable for patients was recoded into four categories: one source, two sources, three sources, and four or more sources. The physicians' medical specialty variable was recoded into three categories: internal medicine, family medicine, and others. The communication channel variable for prescribers was recoded into four categories: zero source, one source, two sources, and three or more sources. The duration of practice variable was recoded into three categories: 1-10 years, 11-20 years, and 21 years or more.

Inferential Statistics

Statistical packages IBM® SPSS version 24.0 and Stata version 14 were utilized to check all the assumptions of the One-way analysis of variance (ANOVA) and the linear regression models. One-way ANOVA analysis was performed to address patients' knowledge and identify significant differences within gender, age, ethnicity, level of

education, area of living, innovativeness, prior experience, perceived need for innovation, and sources of communication. A similar analysis was conducted for prescribers' knowledge, plus two predictor variables: duration of practice and medical specialty. A power analysis was conducted to determine the minimum sample size required to achieve a power of 0.8.

The assumptions of the One-way ANOVA model were assessed to determine the validity of the procedure. Statistical tests for a normal distribution of errors (Shapiro-Wilk's test) and homoscedasticity (Levene's test) across two or more groups (Levene, 1960; Shaphiro and Wilk, 1965) were conducted. The presence of asymmetry was addressed and handled using transformations ($\log_{10}$). The presence of influential outliers in a set of independent variables was assessed using Cook's distance (Cook and Weisberg, 1982).

A multiple linear regression model was generated to predict the strength of the relationship between the overall PGx testing knowledge score and the significant predictor variables identified in the ANOVA model. The assumptions of linear regression were assessed, including linearity (using a normal Q-Q scatterplot), autocorrelation (using the Durbin-Watson test), homoscedasticity (using Levene's test), multicollinearity (using the variance inflation factor), and normality (using the Shapiro-Wilk's test).

The multiple regression model was formulated separately for patients and physicians to estimate the overall knowledge and attitudes toward PGx testing as functions of sociodemographic variables and attributes of knowledge and attitude stages as follows:

$$Y_{ijk} = \alpha_{ij} + X_{ijkl}\,\beta_{lji} + A_{ijkl}\,\lambda_{lji} + \varepsilon_{ijk}$$

where

Y_{ijk} was a vector of scores for the *i*th indicator and *j*th type of participant reported by the *k*th respondent;

X_{ijkl} was a matrix of values of sociodemographic variables ($l = 6$ including gender, age, ethnicity, level of education, area of living/type of practice setting, and duration of practice) reported by the *k*th respondent of the *j*th type of participant for the *i*th indicator;

A_{ijkl} was a matrix of attribute values for the *i*th indicator (when $i = 1$, then $l = 4$ including prior experience, innovativeness, perceived need, and communication behavior; when $i = 2$, then $l = 5$ including relative advantage, compatibility, complexity, trialability, and observability) reported by the *k*th respondent of the *j*th type of participant;

α_{ij} was the independent term for the *i*th indicator and *j*th type of participant;

β_{lji} and λ_{lji} were vectors of *l* parameters for the *j*th type of participant for the *i*th indicator estimated within their respective matrix;

ε_{ijk} was a vector of normally and independently distributed stochastic error terms pertaining to the *k*th respondent of the *j*th type of participant for the *i*th indicator;

$i = 1$ for knowledge and $i = 2$ for attitude;

$j = 1$ for patients and $j = 2$ for physicians;

$k = 1, \ldots, n_j$; and

n_j was the number of respondents in the *j*th type of participant category ($n_1 = 192$ and $n_2 = 148$).

One-way ANOVA and multiple regression models were also conducted to probe the association between patients' and physicians' attitudes toward PGx testing and relative advantage, compatibility, complexity, trialability, and observability of PGx testing. Afterwards, sensitivity analysis using an alternative assumption (i.e., count data) was conducted to validate the findings of the linear regression model. The possibility of measuring the outcome variables by counting the number of correct answers (i.e., the overall knowledge equals the number of correct answers, as shown in Table 4.2 and Table 4.14) explains the use of the Poisson model for count data. The key assumption that the mean of the Poisson distribution should equal its variance was assessed in order to determine the goodness of fit of the Poisson model. An ordered Probit model was also utilized since the categories of the dependent variables of this study were ranking with an arbitrary interval between the scores.

Path analysis was performed to explore the influence of knowledge, attitudes, perceived characteristics of innovation, and sociodemographic characteristics on the acceptance or rejection of PGx testing among patients and physicians. The implications of Rogers's theory are based on the prediction of an individual's decisions to either accept or reject an innovation; the decision-making process depends on the magnitude of the relationship between the individual's knowledge and attitudes toward the innovation as well as the antecedent variables that potentially influence knowledge and attitudes. Considering only the direct effect of one variable on another (e.g., the relationship between attitude toward PGx testing and the adoption decision) may not be optimal; the relationship between two variables could influence or be influenced by a third variable. Therefore, to measure the total effect of a variable (e.g., level of education) on another

variable (e.g., attitude), both the direct and indirect effects of level of education must be considered.

A generalized path analysis was created with a Probit link function and robust standard errors to examine the effect of the subscales (knowledge, attitude, and perceived characteristics of innovation), and demographic characteristics on the outcome variable (accept or reject PGx testing). This analysis offered a better methodological tool to establish causality in correlated variables in a model (Wright, 1921). (The following are assumptions of path analysis: linear and additive relations among variables that should be presented in the path diagram, the causal flow between independent and dependent variables should be one-way, the error terms should not be correlated with the independent variables in the model or among themselves, and the errors should be normally distributed.)

Finally, the hypothesized causal relationships were evaluated using the overall goodness of fit. The following tests were conducted: likelihood ratio chi-square (X^2); the root mean square error of approximation (RMSEA), which according to Brown and Cudeck (1993) should be less than 0.08, but according to Steiger (2007) it is preferred when it is less than 0.07; and the Tucker-Lewis Index (TLI) and Comparative Fit Index (CFI), which compare the model of interest to a null model that assumes no correlation among variables. As the values of both the TLI and CFI approach 1.0, the model represents a better fit than the null alternative model; a value of 0.90 is required for the model to be a more acceptable fit (Hu and Bentler, 1999).

Based on Rogers's theory-driven path, demographic characteristics, prior experiences, innovativeness, perceived need for innovation, communication channels,

were perceived characteristics of the innovation are exogenous variables that causally precede all dependent variables in the model. Conversely, knowledge and attitudes were endogenous variables, and they might be either dependent or independent. The adoption or rejection of PGx testing was the main outcome variable.

Ethical Considerations

After reviewing the study design, an exemption was granted from the Institutional Review Board (IRB) at NSU (see Appendix D). The patient and prescriber surveys (see Appendices A and C), informed consent, promotional flyer, invitation e-mail, and participation letter were submitted and approved by NSU (see Appendix E) before the implementation of the study in compliance with the Health Insurance Portability and Accountability Act (HIPAA). The data did not include direct patient or physicians identifiers.

Summary

A cross-sectional design was utilized in this study using data obtained from a convenient sample of patients and physicians. Patients 18 years or older who self-reported at least one chronic disease and physicians licensed to practice in Florida who were involved in medication therapy decisions were included. Paper-based and online survey questionnaires were used to collect data from patients and physicians, respectively. Several concepts (e.g., perceived need, relative advantage, compatibility, complexity, trialability, observability) adapted from Rogers's diffusion of innovation theory were incorporated into the survey questions. Statistical analyses including One-way ANOVA and linear regression were performed to test the hypothesized relationships among the main concepts adapted from Rogers's theory. Then a generalized path

analysis was conducted to predict the factors that influence the acceptance of PGx testing among patients and physicians. The results obtained from these procedures are presented in the next chapter.

Chapter 4

Results

The purpose of this chapter is to report the results of the statistical analysis performed in this study. The characteristics of the sample are provided and the relationship between demographic variables and both knowledge and attitudes toward PGx testing is discussed. The results from the various inferential analyses used to addresses the research questions are also presented. Results are reported separately for patients and prescribers.

Patient Descriptive Statistics

Sample Characteristics

The sample consisted of 192 patients with several chronic diseases. Their distribution of selected demographic characteristics is presented in Table 4.1. Most of them were women and the 40-59 age groups were the most numerous.

Patients' Knowledge of Pharmacogenetic Testing

Seven questions were used to assess patients' knowledge about PGx testing. The mean score was 3.83 out of 7.00, with a standard deviation of 1.62. Younger, White, and male participants with higher education had the highest mean scores. A Cronbach's alpha value of 0.65 was calculated for the PGx testing knowledge subscale, which indicated moderate internal consistency.

Table 4.1
Percentage Distribution of Selected Demographic Variables of Patients in the Sample

Variables	Frequency (%)
Gender	
Male	39.1
Female	61.9
Age (years)	
18-29	14.6
30-39	19.3
40-49	21.4
50-59	25.0
60 or older	19.7
Ethnicity	
White/Caucasian	45.3
Hispanic/Latino	25.0
Black or African American	19.3
Other	10.4
Level of education	
High school or GED	13.5
Associate degree	21.9
Baccalaureate degree	25.5
Master's degree	16.7
Doctorate or professional degree	22.4
Area of living	
Urban	38.0
Suburban	58.8
Rural	3.2

More than 70% of patients were informed about general aspects of genetics and PGx testing, such as knowing that carrying a gene linked to a disease does not necessarily affect health status, and that the genetic makeup can influence drug response among different individuals. Less than 70% correctly answered the question that assessed the association of genetic make-up with the severity of medication side effects, and less than 50% correctly answered knowledge questions regarding availability of PGx testing and its ability to detect medication side effects (see Table 4.2).

Table 4.2
Percentage of Correct Responses by Patients Pertaining to Knowledge of PGx Testing

Questions	Correct Answer (%)
A person who carries a gene associated with a disease may be healthy	74.5
A person's genetic make-up can influence how he or she responds to medicines	72.9
People with genetic differences can respond differently to the same medication (e.g., some patients may benefit; others may not)	78.1
A test that looks at an individual's genes will likely reveal whether a particular medicine would cause side effects for that person	7.3
A test that takes a cotton swab from the mouth of an individual and looks at genes is currently available for some medications (e.g., simvastatin, clopidogrel)	34.9
A test that looks at a person's genes will likely reveal whether a particular medicine would work for that person	46.9
The severity of side effects of some medications may depend on a person's genetic make-up	68.2

Patients' Attitudes toward Pharmacogenetic Testing

Ten questions were used to assess patients' attitudes toward PGx testing. The mean score was 4.80 out of 9.00, with a standard deviation of 2.17. Female and White participants with higher education showed higher mean scores. A Cronbach's alpha value of 0.71 was calculated for the PGx testing attitude subscale, which indicated moderately high internal consistency.

The majority of patients expressed favorable attitudes toward PGx testing and its perceived benefits on health. Patients indicated willingness to take these tests as they believed the results would help their physicians make better treatment options. There were concerns, however, about the financial cost of the testing as well as the potential for discrimination in health insurance and on the job (see Table 4.3).

Table 4.3
Percentage of Favorable Responses by Patients Pertaining to Attitudes toward PGx Testing

Questions	Answers (%)		
	SD or D	N	A or SA
It is important to look at my genes in order to know what is best for my health	7.8	29.2	63.0
I am willing to take a test that measures how a medicine works, based on my genes	17.7	24.0	58.3
It is not useful to take genetic tests because my family physician may not know how to use my tests results	52.6	28.1	19.3
If I had to pay for the genetic test myself, financial cost would be one of my concerns for taking these tests	7.8	9.4	82.8
If I underwent testing, I would be concerned about the effect of the test results on my eligibility for private health insurance	12.5	17.2	70.3
If I underwent testing, I would be concerned about the effect of the test results on my employment opportunities	29.1	21.4	49.5
I believe that physicians should have PGx testing information in their clinical practice	2.2	25.5	72.3
If I took the test, I would be concerned that unauthorized persons may gain access to the results of that test	27.0	14.2	58.8
PGx testing is a promising innovation in medicine	1.0	16.7	82.3
PGx testing can help my physicians to make the right decisions about my health	4.1	21.4	74.5

The attitude scale had five response options: Strongly Disagree (SD), Disagree (D), Neutral (N), Agree (A), and Strongly Agree (SA).

Rogers's Diffusion of Innovation-Based Questions

This study adapted several variables within the content of Rogers's diffusion of innovation theory. These variables were prior experience, innovativeness, perceived need of adopters, and area of living. The variables were included and measured as a subset of the knowledge stage. The knowledge stage begins when an individual becomes interested in gathering more information about an innovation to develop a better understanding of what the innovation is and how and why it works. According to

Rogers's theory, the knowledge stage is influenced by demographic characteristics (e.g., age and education) and communication channels. Other variables, including relative advantage, compatibility, complexity, trialability, and observability, were included as a subset of the persuasion stage.

Almost 78% of participants indicated that they had never heard the term PGx testing, and only 11% had had their genes tested. Many patients perceived the need for PGx testing in two different clinical situations. Most views on relative advantages of PGx testing were positive. Attitudes related specifically to the perceived need, relative advantage, compatibility, and trialability of PGx testing had more favorable responses than attitudes connected to the complexity and observability of PGx testing in general (see Table 4.4).

The majority of participants reported that physicians and physician assistants were the major sources to obtain information about health issues. The Internet was ranked second, followed by pharmacists. Most participants relied on three or more sources of health information.

Patient Inferential Statistics

Research Question 1A Analysis

In this section the findings pertaining to research question 1A, namely, the association between patients' knowledge of PGx testing and their gender, age, ethnicity, level of education, area of living, prior experience, innovativeness, and perceived need for innovation, are reported. Prior to conducting ANOVA tests, the results showed a violation of the normality assumption of ANOVA (i.e., Shapiro-Wilk's $p < 0.05$, Jarque-Bera test for Skewness-Kurtosis $p < 0.05$) due to negatively skewed data. Consequently,

Table 4.4
Percentage of Favorable Responses by Patients Pertaining to Rogers's Theory-Based Questions about PGx Testing

Questions	Answers (%) SD or D	N	A or SA
Innovativeness			
I will be reluctant about accepting PGx testing until I see it providing useful results for people around me	31.3	24.5	44.2
Perceived need			
I think that PGx testing may prevent me from taking the wrong medicine	7.3	28.6	64.1
I believe that PGx testing will help reduce my current medications' side effects	8.3	35.4	56.3
Relative advantage			
I believe that PGx testing can help in the selection of medication that would better improve my medical condition	0.5	25.0	74.5
PGx testing can offer to me a useful alternative to the way that a physician usually prescribes medications	7.8	31.2	61.0
Compatibility			
PGx testing is a type of test that can invade my privacy	35.9	23.5	40.6
Complexity			
The term "Pharmacogenetic Testing" is difficult to understand	53.0	26.2	20.8
Trialability			
I won't lose much by trying PGx testing, even if it doesn't benefit me directly	12.5	28.7	58.8
Observability			
I have discussed (at least once) PGx testing with my healthcare provider	86.0	9.9	4.1

The attitude scale had five response options: Strongly Disagree (SD), Disagree (D), Neutral (N), Agree (A), and Strongly Agree (SA).

the data were transformed using base 10 logarithms in order to bring the skewness score back to zero or close to normality.

The One-way ANOVA results showed a significant effect of age, ethnicity, and level of education on the overall knowledge score. There was also a significant effect of

prior experience, innovativeness, and perceived need. The estimated F values are presented in Table 4.5.

Table 4.5
Estimated F Statistic Values of the One-Way ANOVA Model Pertaining to Patients' Knowledge of PGx Testing

Variables	F Statistic
Gender	0.56
Age	2.76*
Ethnicity	3.30*
Level of education	11.50**
Area of living	1.37
Prior experience	22.00**
Innovativeness	15.80**
Perceived need	9.60*
Communication channels	1.28

* $p < 0.05$, ** $p < 0.01$

Post-hoc Tukey tests were performed after completing the ANOVA tests to determine which groups differed from each other. These showed that the mean score of White participants was significantly higher than the score of Black or African Americans. The mean score of participants who held a doctorate degree was significantly higher than those of the other levels of education. The mean scores of participants who perceived one need or two needs were significantly higher than patients who did not express any need. Mean difference scores and levels of significance are presented in Table 4.6.

A multiple linear regression model was generated using the significant predictors found in the One-way ANOVA tests (age, ethnicity, level of education, prior experience, innovativeness, and perceived need). Assumptions for normality, multicollinearity, autocorrelation, and homoscedasticity were tested prior to estimating the regression equation. The results revealed that level of education, innovativeness, and prior

Table 4.6
Results of Post-Hoc Pairwise Comparison of ANOVA Model Results Pertaining to Patients' Knowledge of PGx Testing

Variables	Mean Difference	Standard Error
Age (years)		
18-29 vs. 40-49	0.114	0.041
Ethnicity		
White/Caucasian vs. Black or African American	0.098*	0.033
Level of education		
High school or GED vs. doctorate degree	-0.159**	0.039
Associate degree vs. master's degree	-0.109*	0.037
Associate degree vs. doctorate degree	-0.220**	0.034
Baccalaureate degree vs. doctorate degree	-0.145**	0.033
Master's degree vs. doctorate degree	-0.112*	0.036
Innovativeness		
Disagree/strongly disagree vs. agree/strongly agree	-0.152**	0.027
Neutral vs. agree/strongly agree	-0.084*	0.034
Perceived need		
No need vs. one need	-0.084*	0.033
No need vs. two needs	-0.039**	0.028

* $p < 0.05$, ** $p < 0.01$

experience best fit the data (see Table 4.7). The adjusted coefficient of multiple determination value was 0.31. Stepwise regression was performed and similar results were found. The results of sensitivity analysis using Poisson and ordered Probit models showed comparable results to the linear models (see Appendix F).

Research Question 2A Analysis

The statistical analysis in this section was designed to address the association between patients' attitudes toward PGx testing and relative advantage, compatibility, complexity, trialability, and observability of PGx testing. One-way ANOVA tests were conducted to determine whether attitudes toward PGx testing differed significantly for each of the variables adapted from Rogers's theory. Gender and level of education

Table 4.7
Predictors of Patients' Knowledge of PGx Testing

Predictors	Regression Coefficient	Standard Error
Age	-0.003	0.008
Ethnicity	-0.018	0.011
Level of education	0.036**	0.008
Prior experience	0.075**	0.027
Innovativeness	0.043**	0.014
Perceived need	0.027	0.014
Independent term	-0.785	0.052

* $p < 0.05$, ** $p < 0.01$

yielded significant differences. Relative advantage, compatibility, complexity, trialability, and observability of PGx testing were also significantly related to the total attitude score (see Table 4.8).

Table 4.8
Estimated F Statistic Values of the One-Way ANOVA Model Pertaining to Patients' Attitudes toward PGx Testing

Variables	F Statistic
Gender	10.10**
Age	0.96
Ethnicity	1.99
Level of education	4.27**
Area of living	1.25
Communication channels	0.04
Relative advantage	44.00**
Compatibility	28.30**
Complexity	25.80**
Trialability	39.30**
Observability	5.75**

* $p < 0.05$, ** $p < 0.01$

Post-hoc Tukey tests were performed for pairwise comparisons of means. These showed that master's degree holders had higher attitude scores than those with associate degree or baccalaureate degree. The mean score of participants who agreed on

two relative advantages of the testing was significantly higher than those who perceived only one advantage or did not perceive any advantages. Additionally, participants who agreed or strongly agreed on the compatibility, easiness of PGx testing, and trialability showed significantly higher attitude mean scores than those who were neutral or disagreed. The results of the post-hoc Tukey tests are presented in Table 4.9.

Table 4.9
Results of Post-Hoc Pairwise Comparison of ANOVA Model Results Pertaining to Patients' Attitudes toward PGx Testing

Variables	Mean Difference	Standard Error
Level of education		
Master's degree vs. associate degree	1.835**	0.494
Master's degree vs. baccalaureate degree	1.437*	0.479
Relative advantage		
Two relative advantages vs. no relative advantage	2.903**	0.346
Two relative advantages vs. one relative advantage	1.996**	0.311
Compatibility		
Agree/strongly agree vs. disagree/strongly disagree	2.326**	0.317
Agree/strongly agree vs. neutral	1.782**	0.368
Complexity		
Agree/strongly agree vs. disagree/strongly disagree	2.185**	0.362
Agree/strongly agree vs. neutral	1.855**	0.335
Trialability		
Agree/strongly agree vs. disagree/strongly disagree	2.770**	0.413
Agree/strongly agree vs. neutral	2.188**	0.302
Observability		
Agree/strongly agree vs. disagree/strongly disagree	2.150*	0.769

* $p < 0.05$, ** $p < 0.01$

A regression equation was estimated for the PGx testing attitude scores after evaluating the underlying assumptions of normality, multicollinearity, autocorrelation, and homoscedasticity. The significant predictors found in the One-way ANOVA models were included as independent variables. The forward selection, backward elimination,

and stepwise models showed similar results. Gender, relative advantage, compatibility, complexity, and trialability were statistically significant (see Table 4.10). The adjusted coefficient of multiple determination value was 0.50. The results of sensitivity analysis using Poisson and ordered Probit models showed comparable results (see Appendix F).

Table 4.10
Predictors of Patients' Attitudes toward PGx Testing

Predictors	Regression Coefficient	Standard Error
Gender	-0.569*	0.234
Level of education	0.100	0.087
Relative advantage	0.948**	0.161
Compatibility	0.548**	0.148
Complexity	-0.354*	0.162
Trialability	0.637**	0.191
Observability	0.409	0.237
Independent term	-0.520	0.530

* $p < 0.05$, ** $p < 0.01$

Research Question 3A Analysis

The analysis in this section was designed to assess whether knowledge, attitudes, perceived characteristics of innovation, and sociodemographic characteristics significantly influence the acceptance or rejection of PGx testing among patients.
A generalized path analysis was conducted to determine the causal effect between knowledge, attitude, perceived characteristics of innovation, demographic characteristics, and the outcome variable, namely, acceptance or rejection of PGx testing. Based on the initial model guided by Rogers's theory, some reproduced correlations were not significant at the 0.05 level. Finding the possible missing paths in the initial model showed that five additional paths significantly contributed to the model. Two non-significant paths to the adoption of PGx testing were removed. The revised model was

statistically significant at the 0.05 level. Computation of the reproduced direct, indirect, and total causal effects of the revised model indicated a good fit model for the collected data. The coefficient of multiple determination values for the predictors were as follows: 0.32 for knowledge, 0.52 for attitudes, and 0.38 for adoption of PGx testing. The goodness of fit scores are presented in Table 4.11.

Table 4.11
Goodness of Fit Scores for Statistics Pertaining to Path Analysis of Patients' Adoption of PGx Testing

Goodness of Fit Test		Value
Likelihood Ratio	chi^2_ms	7.550
	$p > chi^2$	0.374
Population Error	RMSEA	0.020
Baseline Comparison	CFI	0.998
	TLI	0.996

The results of the path analysis showed that the overall attitude score and the total perceived innovation characteristic score were significant predictors of patients' adoption of PGx testing (see Table 4.12). Participants who scored higher on the attitude subscale and on the perceived characteristics of innovation subscale were more likely to accept PGx testing.

Prescriber Descriptive Statistics

Sample Characteristics

Of the initial 1,000 physicians contacted via email, there were 850 deliverable messages and 60 participants successfully completed and submitted the online survey. In addition, 70 physicians were contacted at regional conferences and 20 were contacted at NSU's Health Professions Division. In two surveys, the majority of the questions were

Table 4.12
Predictors of Patients' Adoption of PGx Testing

Predictors	Regression Coefficient	Standard Error
Knowledge		
Level of education	0.249**	0.062
Prior experience	0.148*	0.064
Innovativeness	0.122	0.073
Perceived characteristics of innovation	0.281**	0.076
Independent term	-5.606	0.360
Attitude		
Perceived need	0.201**	0.059
Perceived characteristics of innovation	0.706**	0.036
Independent term	-1.404	0.223
Adoption of PGx testing		
Knowledge	0.112	0.064
Attitude	0.348**	0.078
Perceived characteristics of innovation	0.258**	0.084
Independent term	-0.661	0.480

* $p < 0.05$, ** $p < 0.01$

blank, either due to a software error or due to lost Internet connection that led to data loss. These surveys were deleted. A total of 148 physicians completed the online survey for a response rate of 15.7%. Most of them were men and White, and they were evenly distributed in terms of age groups. The most numerous group had been in practice for over 20 years (see Table 4.13).

Prescribers' Knowledge of Pharmacogenetic Testing

Six questions were used to assess physicians' knowledge about PGx testing. The mean score was 3.40 out of 6.00, with a standard deviation of 1.53. Younger, non-White and female respondents practicing in suburban areas had higher mean scores than their counterparts. A Cronbach's alpha value of 0.60 was calculated for the PGx testing knowledge subscale, which indicated moderate internal consistency. The majority of physicians answered correctly that PGx testing can determine whether people with

Table 4.13
Percentage Distribution of Selected Demographic Variables of Prescribers in the Sample

Variables	Frequency (%)
Gender	
Male	66.4
Female	33.6
Age (years)	
25-39	18.4
40-49	24.7
50-59	29.5
60 or older	27.4
Ethnicity	
White/Caucasian	71.7
Hispanic/Latino	10.3
Black or African American	10.0
Other	8.0
Medical specialty	
Internal Medicine	18.4
Family Medicine	31.3
Others	50.3
Type of practice setting	
Urban	45.3
Suburban	48.7
Rural	6.0
Duration of practice (years)	
1-10	25.0
11-20	31.1
21or more	43.9

genetic differences can respond differently to the same medication. Almost one-half felt challenged to find the correct answer about the availability of PGx testing (see Table 4.14).

Prescribers' Attitudes toward Pharmacogenetic Testing

Eight questions were used to assess prescribers' attitudes toward PGx testing. The mean score was 4.97 out of 8.00, with a standard deviation of 2.04. Older, White, and female participants practicing in urban areas had relatively higher mean attitude

Table 4.14
Percentage of Correct Responses by Prescribers Pertaining to Knowledge of PGx Testing

Questions	Correct Answers (%)
Genetic variations account for as much as 95% of the variability of an individual's response to a medication	43.2
PGx testing can determine whether people with genetic differences can respond differently to the same medication	89.2
PGx testing of an individual's genes guarantees whether a particular medicine would cause adverse events for that person	52.0
PGx testing is currently available for all medications	59.5
Some medications have FDA-approved PGx information in their package inserts	50.7
The package insert for clopidogrel (Plavix®) includes a warning about possible worse outcomes in individuals who have specific genetic variants	44.6

scores. A Cronbach's alpha value of 0.78 was calculated for the PGx testing attitude subscale, which indicated high internal consistency for this subscale.

The majority of physicians expressed favorable attitudes toward the perceived benefits of PGx testing in prescribing effective medication, reducing medications side effects, and educating patients regarding PGx testing. However, physicians expressed concerns about potential discrimination for their patients by health insurance companies and unauthorized access to testing results (see Table 4.15).

Inhibitors of Recommending Pharmacogenetic Testing

Physicians who had never ordered PGx testing for their patients or were not willing to accept it in routine medical practice identified several reasons for their response. The most common reasons were lack of insurance support for these tests, unavailability of PGx testing at the workplace, and uncertainty about the clinical utility of these tests (see Table 4.16).

Table 4.15
Percentage of Favorable Responses by Prescribers Pertaining to Attitudes toward PGx Testing

Questions	Answers (%)		
	SD or D	N	A or SA
Prescribers should use PGx testing information in clinical practice	8.1	33.8	58.1
Patients should be educated about the purpose, benefits, limitations, and risks of PGx testing	5.4	16.9	77.7
PGx testing will potentially help decrease the number of adverse drug events	4.7	21.0	74.3
PGx testing may prevent me from prescribing an ineffective medicine	8.1	17.5	74.4
PGx testing is a promising innovation in medicine	5.4	14.9	79.7
PGx testing can offer a useful tool to the way I usually prescribe/recommend medications	8.1	25.0	66.9
I am concerned about the effect of the test results on my patients' eligibility for private health insurance	26.4	27.7	45.9
I am concerned that unauthorized personnel may gain access to the results of that test	39.9	27.7	32.4

The attitude scale had five response options: Strongly Disagree (SD), Disagree (D), Neutral (N), Agree (A), and Strongly Agree (SA).

Table 4.16
Barriers to Implementing PGx Testing in Clinical Practice Identified by Prescribers

Barriers	Frequency (%)
PGx testing is not available at workplace	60.6
Concerns about patient confidentiality	19.7
Concerns about patients' employment opportunities	9.8
Not enough time to order	16.4
Waiting for PGx testing results would delay treatment	32.7
Uncertain about the clinical utility of the test	55.7
Insurance does not cover test	62.3
Not applicable for my patients	14.8
Patient refused test	14.8
Other	6.6

Respondents were allowed to answer one or more than one reason.

Rogers's Diffusion of Innovation-Based Questions

This study adapted several variables within the context of Rogers's diffusion of innovation theory. These variables were prior experience, innovativeness, perceived need of adopters, demographic characteristics (e.g., gender, age, ethnicity, and site of practice), and communication channels. In addition, relative advantage, compatibility, complexity, trialability, and observability were included as a subset of the persuasion attitude stage.

Only a fraction of respondents said that they had ever ordered PGx testing for a patient, and only about a third replied that they had ever talked with a patient about PGx testing. Most participants expressed the need for PGx testing when information about the test is included in the package inserts and when the practice guidelines for the use and interpretation of these tests become available. Likewise, the majority of prescriber agreed on the relative advantages of using PGx testing to avoid the risk of non-response to an essential drug and to select a medication that better controls a patient's health condition. In general, attitudes toward the perceived need, relative advantage, and compatibility of PGx testing had more favorable responses than attitudes toward its trialability and complexity (see Table 4.17).

Almost 16% of respondents reported that they had not received education in genetics, and about one-half identified the use of only one source of information about PGx testing. Sources included genetics training in medical/pharmacy school, CME courses, graduate or undergraduate genetics courses, genetics-related seminars or workshops, grand rounds, genetics training in residency, and other sources such as direct experience, the Internet, and scientific articles (see Table 4.18).

Table 4.17
Percentage of Favorable Responses by Prescribers Pertaining to Rogers's Theory-Based Questions about PGx Testing

Questions	Answers (%) SD or D	N	A or SA
Innovativeness			
I will be reluctant to adopt PGx testing until I see it working for patients	39.0	26.0	35.0
Perceived need			
When information about the test is included in the package inserts	14.2	25.7	60.1
When practice guidelines for the use and interpretation of these tests are available	4.7	16.2	79.1
Relative advantage			
In case of non-response to an essential drug (e.g., analgesic) / Refractory patients	4.1	10.8	85.1
In the selection of medication that better controls a patient's health condition	11.5	16.9	71.6
Compatibility			
PGx testing is not compatible with my personal values	78.0	12.0	10.0
Complexity			
The application of PGx testing adds more complexity to the drug prescribing process	13.0	15.0	72.0
Trialability			
I would like to try PGx testing on some patients before I decide whether I will adopt it or not	23.0	26.0	51.0
Observability			
Have you ever talked with a patient about PGx testing?	67.0	0.0	33.0

The attitude scale had five response options: Strongly Disagree (SD), Disagree (D), Neutral (N), Agree (A), and Strongly Agree (SA).

Prescriber Inferential Statistics

Research Question 1B Analysis

In this section, the findings pertaining to research question 1B, namely, the association between physicians' knowledge of PGx testing and their gender, age, ethnicity, medical specialty, practice setting, duration of practice, prior experience,

Table 4.18
Percentage Distribution of Sources of Genetic Information Reported by Prescribers

Source	Frequency (%)
Genetics training in medical school	33.1
Genetics training in residency	8.1
Undergraduate genetics course	19.6
Genetics course in graduate school	8.1
Grand Rounds	15.6
CME course	31.8
Genetics-related seminar or workshop	17.6
Other	18.2

Respondents were allowed to answer one or more than one source.

innovativeness, and perceived need for innovation, are reported. As in the data analysis section, the assumptions of One-way ANOVA were tested to determine the applicability of the model. The empirical evidence indicated that gender, type of practice setting, prior experience, perceived need, and sources of communication showed significant differences in scores of knowledge about PGx testing by physicians (see Table 4.19).

Table 4.19
Estimated F Statistic Values of the One-Way ANOVA Model Pertaining to Prescribers' Knowledge of PGx Testing

Variables	F Statistic
Gender	5.39*
Age	0.21
Ethnicity	0.39
Medical specialty	1.94
Type of practice setting	4.81*
Duration of practice	1.66
Prior experience	8.38**
Innovativeness	1.79
Perceived need	3.40*
Communication channels	4.50**

* $p < 0.05$, ** $p < 0.01$

Post-hoc Tukey tests were performed to determine which groups differed from each other. The results showed that the mean PGx testing knowledge score of participants who perceived two needs was significantly higher than the score of those who expressed no need, and the mean scores of participants who used one or two resources were significantly greater than those who did not report any source of heath information (see Table 4.20).

Table 4.20
Results of Post-Hoc Pairwise Comparison of ANOVA Model Results Pertaining to Prescribers' Knowledge of PGx Testing

Variables	Mean Difference	Standard Error
Perceived need		
Two needs vs. no need	0.900*	0.135
Communication channels		
One source of information vs. no source	1.178**	0.359
Two sources of information vs. no source	1.383**	0.407

* $p < 0.05$, ** $p < 0.01$

A multiple linear regression model was generated using the significant predictors found in the One-way ANOVA tests (gender, type of practice setting, prior experience, perceived need, and sources of communication). The forward, backward, and stepwise regression versions revealed that gender, type of practice setting, and prior experience were significant variables that best fit the data (see Table 4.21). The adjusted coefficient of multiple determination value was 0.22. The results of sensitivity analysis using Poisson and ordered Probit models showed comparable results to the linear models (see Appendix F).

Table 4.21
Predictors of Prescribers' Knowledge of PGx Testing

Predictors	Regression Coefficient	Standard Error
Gender	0.798**	0.267
Type of practice setting	-0.742**	0.255
Prior experience	0.771*	0.314
Perceived need	0.255	0.179
Communication channels	0.159	0.134
Independent term	3.500	0.374

* $p < 0.05$, ** $p < 0.01$

Research Question 2B Analysis

The statistical analysis in this section was designed to address the association between physicians' attitudes toward PGx testing and relative advantage, compatibility, complexity, trialability, and observability of PGx testing. One-way ANOVA tests were conducted to determine whether attitudes toward PGx testing differed significantly for each of the variables adapted from Rogers's diffusion of innovation theory. Gender, relative advantage, compatibility, and observability were significantly related to the total attitude score (see Table 4.22).

Post-hoc Tukey tests were performed to determine which groups differed from each other. They showed that the mean score of participants who agreed on two relative advantages of PGx testing was significantly higher than the mean of those who did not report advantages. The mean score of participants who agreed or strongly agreed with the statement about compatibility of PGx testing was significantly higher than the mean of those who disagreed or strongly disagreed. The results of the post-hoc Tukey tests are presented in Table 4.23.

Table 4.22
Estimated F Statistic Values of the One-Way ANOVA Model Pertaining to Prescribers' Attitudes toward PGx Testing

Variables	F Statistic
Gender	5.98*
Age	0.53
Ethnicity	0.83
Medical specialty	0.32
Type of practice setting	0.78
Duration of practice	1.93
Prior experience	2.42
Relative advantage	6.52**
Compatibility	11.50**
Complexity	1.02
Trialability	1.62
Observability	6.52*
Communication channels	0.76

* $p < 0.05$, ** $p < 0.01$

Table 4.23
Results of Post-Hoc Pairwise Comparison of ANOVA Model Pertaining to Prescribers' Attitudes toward PGx Testing

Variables	Mean Difference	Standard Error
Relative advantage		
Two relative advantages vs. no relative advantage	0.180**	0.057
Compatibility		
Agree/strongly agree vs. disagree/strongly disagree	0.140**	0.056

* $p < 0.05$, ** $p < 0.01$

The predictors found to be significant in the One-way ANOVA tests were utilized as independent variables in the estimation of a regression equation. Forward selection, backward elimination, and stepwise regressions were conducted. All three models revealed that coefficients for gender, relative advantage, and compatibility were significant (see Table 4.24). The adjusted coefficient of multiple determination value was 0.21. The results of sensitivity analysis using Poisson and ordered Probit models showed comparable results (see Appendix F).

Table 4.24
Predictors of Prescribers' Attitudes toward PGx Testing

Predictors	Regression Coefficient	Standard Error
Gender	0.078*	0.037
Relative advantage	0.061*	0.026
Compatibility	0.155**	0.044
Observability	0.061	0.038
Independent term	-0.730	0.060

* $p < 0.05$, ** $p < 0.01$

Research Question 3B Analysis

The analysis in this section was designed to assess whether knowledge, attitudes, perceived characteristics of innovation, and sociodemographic characteristics significantly influence the acceptance or rejection of PGx testing among physicians. A generalized path analysis was conducted to determine the causal effect among knowledge, attitude, perceived characteristics of innovation, demographic characteristics, and the outcome variable, namely, acceptance or rejection of PGx testing. Based on the initial model guided by Rogers's theory, some reproduced correlations were not significant at the 0.05 level. Finding the possible missing paths in the initial model indicated that seven additional paths significantly contributed to the model. Two non-significant paths to the adoption of PGx testing were removed from the model. Computation of the reproduced direct, indirect, and total causal effects of the revised model indicated a good fit model for the collected data. The coefficient of multiple determination values for the predictors were as follows: 0.19 for knowledge, 0.23 for attitudes, and 0.18 for adoption of PGx testing. The goodness of fit scores are presented in Table 4.25.

Table 4.25
Goodness of Fit Scores for Statistics Pertaining to Path Analysis of Prescribers' Adoption of PGx Testing

Goodness of Fit Test		Value
Likelihood ratio	chi^2_ms	12.75
	$p > chi^2$	0.388
Population error	RMSEA	0.021
Baseline comparison	CFI	0.998
	TLI	0.997

The results of the path analysis showed that the total perceived innovation characteristic score and the total perceived need score were significant predictors of prescribers' adoption of PGx testing (see Table 4.26). Participants who scored higher on the perceived characteristics of innovation subscale and on the perceived need items were more likely to accept PGx testing.

Table 4.26
Predictors of Prescribers' Adoption of PGx Testing

Predictors	Regression Coefficient	Standard Error
Knowledge		
Age (years)	-0.359**	0.129
Type of practice setting	-0.196**	0.074
Duration of practice	0.401**	0.128
Perceived need	0.151*	0.080
Perceived characteristics of innovation	0.146	0.079
Independent term	2.617	0.439
Attitude		
Innovativeness	0.320**	0.075
Perceived characteristics of innovation	0.261**	0.076
Independent term	-1.732	0.339
Adoption of PGx testing		
Knowledge	-0.028	0.079
Attitude	0.128	0.081
Perceived need	0.261**	0.079
Perceived characteristics of innovation	0.197*	0.086
Independent term	1.756	0.445

* $p < 0.05$, ** $p < 0.01$

In the next chapter, a discussion of the empirical findings of this dissertation is undertaken. Also discussed is the applicability of the adapted theoretical framework and how the evidence relates to previous scholarly works. Limitations and recommendations for future research are addressed.

Chapter 5

Discussion and Conclusions

This study was guided by Rogers's diffusion of innovation theory to test the relationship between patients' and physicians' willingness to use PGx testing and their knowledge of PGx testing, attitudes toward PGx testing, and sociodemographic characteristics. Understanding these relationships may help promote the diffusion of these genetic tests, which may potentially predict medication response and improve medication safety in clinical practice. In this chapter key findings and conclusions are addressed for both patients and physicians, along with the results of path analysis describing the relative importance of model-based relationships to the decision to adopt PGx testing. Study limitations and recommendations for future research are also discussed.

Patients' Knowledge of PGx Testing

In contrast with findings from previous studies that included patients with chronic diseases (Calsbeek et al., 2007; Cuffe et al., 2014; Morren et al., 2007; Nielsen and Moldrup, 2007; Rogausch et al., 2006), most patients here were knowledgeable about general aspects of genetics and PGx testing, although less than half were familiar with the availability of PGx testing and its potential to detect medication side effects. Education and prior experience were significantly correlated with knowledge of PGx testing; educated patients with prior experience of PGx testing had greater overall knowledge of

it. The relatively higher overall knowledge of patients who participated in this study might have reflected their higher level of education compared to participants in other studies. In addition, patients' knowledge about PGx testing might have been influenced by their previous awareness regarding PGx testing as a new clinical tool.

Another explanation for the relatively higher knowledge scores observed in this study might have been the use of more than one resource of health information by patients to find out more about PGx testing. The results indicated that healthcare professionals, including physicians, physicians' assistants, and pharmacists, as well as the Internet, were the most popular sources of health information for patients.

Variables Associated with Patients' Knowledge

Patients' knowledge of PGx testing showed strong association with several factors of the Rogers's diffusion of innovation theory such as prior experience, age, ethnicity, level of education, perceived need, and innovativeness. Prior experience was associated with more knowledge about PGx testing; this finding was consistent with previous works that showed prior experience was related to patients' acceptance of consumer health information technology applications (Or and Karsh, 2009), genetic knowledge (Henneman et al., 2004), patients' support to PGx testing (Haga et al., 2012b), and better understanding of personalized medicine (Haddy et al., 2010). The findings also revealed that young, White, and more educated patients were more knowledgeable about PGx testing than older, Blacks or African Americans, and those with lower levels of education. Gender and area of living were not associated with overall knowledge of PGx testing.

The fact that gender was not associated with overall knowledge might be a sign that neither males nor females were aware of PGx testing. Although the majority of studies reviewed by Or and Karsh (2009) showed that gender had no effect on the acceptance of health IT application, other studies reported that women had a higher level of genetic knowledge than men (Haga et al., 2012b; Henneman et al., 2004; Morren et al., 2007).

This study found no association between channels of communication of health information and patients' knowledge of PGx testing. The importance of effective communication in understanding the barriers to actual implementation of PGx testing, however, has been recognized in other studies, especially between patients and their healthcare providers (Haddy et al., 2010; Haga et al., 2012b; Henneman et al., 2006). Since PGx testing has been slowly integrated into clinical practice, it was not expected to be widely known among non-adopter medical groups and appear as a central issue in social media. Additionally, evidence-based guidelines for PGx testing have not yet been developed for the majority of chronic medications. Therefore, healthcare providers may not consider it to be a relevant point of discussion with patients. Communication channels might have provided a better measurement if patients had been asked to mention the sources from which they received information about personalized medicine.

No association between patients' overall knowledge of PGx testing and area of living was found either. This might have been due to the fact that most patients lived in either urban or suburban areas, so access to health information resources might have been equal across different areas; this would accord with Rogers's diffusion of innovation

expectation about innovations occurring in large urban centers/hospitals due to greater availability of resources.

This study also found a significant association between patients' perceived need for PGx testing and their knowledge of it. Most patients agreed on the need for PGx testing in order to avoid being prescribed the wrong medication and reduce ADRs that might be associated with their chronic medications. Although this association has not been specifically addressed in the literature, several studies have reported that the perceived need among patients regarding genetic testing or other health-related innovations influenced the adoption of the studied innovations. Several studies stressed the importance of perceived need in decision-making. For example, Shah (2004) expressed the medical need to improve patient's quality of life as one of the criteria for the medical use of PGx testing. Henneman et al. (2006) showed that less than half of participants in their study perceived a need for genetic testing; the perceived usefulness of these tests were linked with patients' acceptance of genetic testing. Cuffe et al. (2014) showed that the majority of cancer patients wanted PGx testing due to their high need to detect the risk of severe toxicity associated with chemotherapy. Furthermore, Or and Karsh (2009) concluded that meeting patients' needs was of great importance to implement and accept telemedicine among patients. These studies support the view that increased perceived need for PGx testing as an antecedent of knowledge may play a pivotal role in decision making as described by Rogers's theory.

Another independent variable investigated here was innovativeness. The empirical evidence revealed that patients who were more willing to adopt PGx testing

also were more knowledgeable, a clear illustration of adopters' behavior as described by Rogers's theory.

Patients' Attitudes toward PGx Testing

The overall attitudes of patients with chronic diseases toward PGx testing were positive. In line with previous studies (Fargher et al., 2007; Haga et al., 2013; Kobayashi and Satoh, 2009; Lachance et al., 2015), patients expressed high expectations and hopes regarding the benefits of PGx testing and its potential role in preventing medications prescribed erroneously and enhancing medication safety. Most participants felt optimistic and preferred to have their genes tested to find the medications that best worked for them, and nearly all patients agreed or strongly agreed that PGx testing was a promising innovation in medicine that could eventually help physicians make educated decisions about their health.

Yet most participants expressed concerns regarding the cost of testing, the handling of confidential testing results (e.g., unauthorized access to the results), employment opportunities, and their eligibility to purchase a health insurance plan. Previous studies also reported that patients were worried about confidentiality issues, the impact of testing results on their eligibility to private health insurance, and employment opportunities (Fargher et al., 2007; Haga et al., 2013; Kobayashi and Satoh, 2009; Lachance et al., 2015; Rogausch et al., 2006). Patients from other studies were also concerned about the possibility of disclosing a future risk of chronic diseases after undergoing genetic tests (Cuffe et al., 2014; Rogausch et al., 2006).

The optimistic attitudes revealed here indicated that patients' high expectations of advancements in the field of genetics were not necessarily dependent on their knowledge.

According to Rogers's diffusion of innovation theory, knowledge and comprehension among patients about PGx testing should precede the attitude stage; in this study, however, although patients' knowledge of PGx testing was positively correlated with their attitudes, their high expectations of the role that PGx testing could play in effective therapeutic options seemed to be overrated because other factors (e.g., age, type of disease, health status) that also influence drug response were not studied. This finding was consistent with the conclusions of Rogausch et al. (2006), who reported that patients were optimistic about the benefit of PGx testing but more than half of them would not change their ineffective current therapy if the PGx-recommended optimal therapy was not available. Since this dissertation did not specifically measure patients' overall knowledge of non-genetic factors that might also impact therapeutic outcomes, which is a fundamental concept of Rogers's diffusion of innovation theory, the potential effect of this type of knowledge on patient attitudes cannot be overlooked.

Variables Associated with Patients' Attitudes

The empirical evidence showed that patients' overall attitudes toward PGx testing were correlated with the factors originated in Rogers's diffusion of innovation theory. Women were more likely to have positive attitudes toward PGx testing than men. Women also were less likely to be concerned with the perceived disadvantages of PGx testing (i.e., cost of testing, confidentiality, insurability, employability). This is the opposite of findings in other studies (Haga et al., 2013; Henneman et al., 2006; Rogausch et al., 2006). The discrepancy might be explained by a higher percentage of women in this dissertation having attained higher levels of education. The findings here were also consistent with previous studies (Haga et al., 2013; Haga et al., 2012b) insofar as more

educated patients expressed more positive attitudes toward PGx testing than those with a lower level of education.

No significant association was found between patients' attitudes toward PGx testing and either age or ethnicity. Similar findings were reported in other studies (Henneman et al., 2006; Lanktree et al., 2014; Or and Karsh, 2009). In line with the findings of Rogausch et al. (2006), area of living had no influence on patients' attitudes toward PGx testing; the absence of a link might be attributed to 97% participants living in urban and suburban areas, with approximately the same access to resources and innovation.

The results of this study revealed a significant relationship between patients' attitudes toward PGx testing and relative advantage, complexity of understanding the term of PGx testing, compatibility, trialability, and observability of PGx testing. This study showed that patients who agreed on at least one relative advantage (i.e., PGx testing may help in prescribing the best available treatment for chronic conditions) had more positive attitudes than those who did not perceive PGx testing as advantageous. Rogausch et al. (2006) also revealed that patients who perceived the potential advantages of PGx testing (e.g., reducing side effects, avoiding ineffective medications) were more optimistic about the advantages of PGx testing.

Patients who were able to understand the term PGx testing expressed more positive attitudes toward PGx testing than those patients who perceived it as a complex concept. Comparable results on adopting different innovation were reported by Or and Karsh (2009). A strong correlation also was found between patients' favorable attitudes towards PGx testing and standards of care that maintain health information privacy.

Similarly, Henneman et al. (2006) reported that compatibility of PGx testing with moral values played a role in patients' acceptance of PGx testing. Moreover, this dissertation illustrated the degree to which PGx testing could be tried by patients. Patients willing to try PGx testing expressed more positive attitudes. When measuring the level of observability, almost 86% of patients never had a discussion with their healthcare providers about PGx testing. The observability of PGx testing was significantly associated with patients' hopeful attitudes toward PGx testing. Yet after conducting regression analysis, observability was not a significant predictor of patients' attitudes toward PGx testing.

Adoption of PGx Testing among Patients

A distinguishing feature if this study is that different PGx testing predictors were measured to determine the factors that influence patients' acceptance of PGx testing. A generalized path analysis was conducted to assess the factors that predict acceptance of PGx testing. Path analysis is a subset of structural equation modeling that uniquely provides information about the strength of causal relationships between factors of a hypothesized model. The results showed that more than 50% of patients with chronic conditions were willing to undergo PGx testing. When path analysis was originally applied based on the initial model guided by Rogers's diffusion of innovation theory, some reproduced correlations did not appear to be significantly associated with the acceptance of PGx testing; however, finding the possible missing correlations (i.e., direct and indirect pathways) using a path analysis model between the defined factors and the outcome variable (i.e., willingness to accept PGx testing) resulted in a well fit model for the collected data.

Patients' attitudes, as well as the perceived characteristics of PGx testing (e.g., relative advantage, compatibility, complexity, trialability, and observability), had a direct and indirect influence on the acceptance of PGx testing, while knowledge was not significantly related to the outcome variable. Rogers's diffusion of innovation theory provides a plausible explanation for these findings about the relationship between attitudes toward PGx testing and the decision to adopt; the lack of association between the two reported in this study might be attributed to patients' non-involvement in decision making about their healthcare needs that might affect their actual knowledge. The association between knowledge and adoption may appear after patients acquire more detailed knowledge about PGx testing.

Prescribers' Knowledge of PGx Testing

Most physicians knew that PGx testing can determine whether people with genetic differences respond differently to the same medication; they also were aware that PGx testing is not available for all medications. Relatively few, however, knew about the impact of genetic variability on an individual's response to a medication or were familiar with the availability of PGx testing for Plavix® (clopidogrel). Younger, non-White, and female participants practicing in suburban areas had the highest mean knowledge scores.

Physicians' overall knowledge of PGx testing in the sample was greater than the knowledge of physicians who participated in other studies (Dressler et al., 2014; Haga et al., 2012a; Powell et al., 2012; Rogausch et al., 2006; Stanek et al., 2013; Taber and Dickinson, 2014). Perhaps this differential reflects an ongoing trend in the growth of the PGx field and the surge in interest to know more about PGx testing.

Variables Associated with Prescribers' Knowledge

Physicians' overall knowledge of PGx testing was significantly associated with gender, perceived need, prior experience, type of practice setting, and sources of communication. The absence of association with age, ethnicity, and duration of practice might be explained by the fact that participants received similar education and training programs in genetics. The lack of correlation between overall knowledge of PGx testing and type of specialty may reflect uniform genetics education and training across specialties.

Physicians made conscious efforts to gain more information about genetics from a variety of sources. Compared to other studies (Dressler et al., 2014; Haga et al., 2012a; Shields et al., 2005; Stanek et al., 2012), the percentage of physicians who reported receiving formal education in genetics was higher. The majority reported using two or more sources of genetic information and testing. These sources included genetics training in medical school, CME courses, undergraduate genetics courses, genetics-related seminars or workshops, and grand rounds.

Physicians who relied on at least one source of genetic information had a higher level of overall PGx knowledge than physicians who did not report any source. This was consistent with other studies (Dressler et al., 2014; Haga et al., 2012a, Stanek et al., 2012, 2013; Taber and Dickinson, 2014). Physicians who perceived the need for PGx testing in reducing ADRs and preventing ineffective therapies were more knowledgeable about PGx testing than those who did not perceive the need. Stanek et al. (2012), Stanek et al. (2013), and Haga et al. (2012a) reported similar findings.

Finally, the strength of the relationship between overall knowledge of PGx testing and the significant factors identified in the One-way ANOVA model was probed using a multiple linear regression model. Forward selection and backward elimination regression models yielded similar results, with three significant predictors: gender, prior experience, and type of practice setting. Female physicians practicing in suburban areas with prior experience had a higher overall PGx testing knowledge score. Participants practicing in suburban areas might have had better access/exposure to educational resources regarding PGx testing. More research is needed to confirm this finding and further investigate whether suburban-practice physicians are more likely to have longer interaction with patients over a longer period of time, which might lead to increased awareness of inter-individual variation in drug response.

Other studies showed findings different from those reported here. Walden et al. (2015) found that more male than female physicians believed that they had a better understanding of the PGx report. Klitzman et al. (2013) found that White and male physicians were associated with increased ordering of genetic testing. Stanek et al. (2012) reported that physicians who were willing to accept PGx testing were more likely to be male, older, having practiced 30 years or more since graduation, practicing in urban settings, and working in general/family practice settings.

Similar to the findings of this work, several studies revealed an association between lack of prior experience with PGx testing and the knowledge gap that influenced decision making toward the adoption of PGx testing (Haga et al., 2012a; Stanek et al., 2012; Stanek et al., 2013). According to these studies, physicians' levels of knowledge

of PGx testing and experience with patients who undergo genetic tests might significantly impact their preparedness for accepting genetic tests.

Prescribers' Attitudes toward PGx Testing

Physicians' overall attitudes toward PGx testing were positive, which was consistent with the findings of other studies (Dressler et al., 2014; Haga et al., 2012a; Moaddeb et al., 2015; Shields et al., 2005; Walden et al., 2015). Rogausch et al. (2006) revealed more reserved attitudes toward PGx testing among healthcare professionals when considering the potential discrimination by health insurance companies as well as employers; in this dissertation, however, the levels of concern shared by physicians were much lower.

The findings here suggest that physicians' attitudes toward PGx testing are becoming increasingly receptive, and this may be due to more perceived benefits of genetic tests in improving medication safety and efficacy. Supporting the findings of other studies (Fargher et al., 2007; Haga et al., 2012a; Haga et al., 2012c; Rogausch et al., 2006; Stanek et al., 2012) regarding physicians' concerns about PGx testing, the results showed that some concern existed about the cost of PGx testing, patients' confidentiality, and the uncertainty about the clinical utility of these tests.

Variables Associated with Prescribers' Attitudes

The regression model indicated that physicians' total attitude score toward PGx testing was predicted significantly by gender, relative advantage, and compatibility. Duration of practice, medical specialty, and urban-rural practice setting were not significantly associated with attitudes toward PGx testing. The lack of statistical significance of duration of practice might be due to a low comfort level of physicians'

knowledge about these tests, regardless of years of practice, because of lack of exposure to, and experience with, PGx testing. The lack of statistical significance of medical specialty might be due to a possible selection bias or because participants did not perceive the benefits of PGx to be directly related to their specialties. The lack of statistical significance of practice setting might be attributed to the absence of substantial differences among rural, suburban, and urban areas in terms of accessibility to genetic information and/or type of patients encountered.

The findings of this study did not accord with the results of Klitzman et al. (2013) and Walden et al. (2015), who showed that male physicians had more favorable attitudes than female physicians toward the clinical application of PGx testing. This discrepancy might be due to the fact that female physicians in this study had higher level of knowledge about PGx testing than their male counterparts.

A significant relationship was found between attitudes toward PGx testing and relative advantage, compatibility, and observability. The significant effect of the observability variable, however, disappeared after conducting regression analysis. Haga et al. (2012a) also reported an impact of the relative advantage of PGx testing toward predicting potential ADRs and improving therapeutic outcomes on physicians' attitudes and their decision to accept PGx testing. In this dissertation trialability and complexity were not significantly associated with attitudes toward PGx testing. In contrast, Taber and Dickinson (2014) and Fargher et al. (2007) indicated that the complexity perceived by physicians in terms of describing the role of PGx testing in healthcare, ordering the tests and interpreting the results, and unperceived clinical benefits negatively impacted attitudes and the ordering of these tests. Stanek et al. (2012) also indicated that the

complexity of multiple genetic predictors involved in the variability of drug response might present a barrier to adoption.

Adoption of PGx Testing among Physicians

The adoption of PGx testing by physicians was significantly influenced by the perceived characteristics of PGx testing as well as the perceived need for innovation. Along with the initial path-analysis model guided by Rogers's diffusion of innovation theory, some reproduced correlations between variables were not significant. After finding the possible missing correlations in the initial model and computing the direct, indirect, and total causal effects of the revised model, however, the model provided a good fit for the data.

Over 50% of physicians were willing to accept PGx testing. Supporting the results of other studies (Dressler et al., 2014; Haga et al., 2012a; Stanek et al., 2012; Taber and Dickinson, 2014), this dissertation showed that lack of knowledge and poor attitudes toward PGx testing negatively impacts the PGx-based prescribing decisions among physicians. Other factors contributing to the low use of PGx tests included availability of PGx testing, the cost of testing, privacy issues, and absence of clinical guidelines. Almost half of physicians agreed that pharmacists' role was crucial in the process of ordering PGx testing and interpreting results.

Limitations

Although the response rate of patient participants was high, the convenient nature of the sample might limit the generalizability of the findings. Underrepresentation of Hispanics/Latinos also might have affected the results. Using flyers to recruit patients might have resulted in patients' self-selection; thus the likelihood of selection bias should

be taken into consideration. Finally, the knowledge instrument had a slightly lower than adequate internal reliability (Cronbach's alpha) score. Avoiding an excessively long questionnaire that might have limited participants' response and caused survey fatigue was important; therefore, several redundant items, which might have increased the Cronbach's alpha score but not necessarily provided additional information, were removed from the scale.

The relatively low response rate of physicians might have limited the generalizability of the findings. Since physicians had to answer and submit the questionnaires on line, some might not have participated due to the inconvenience of responding via e-mail. Underrepresentation in some medical specialties was a limitation. Finally, using a relatively low reliability knowledge instrument also might have affected the findings.

Recommendations for Future Research

As the number of drug package inserts with FDA-approved PGx information increases, the need to measure physicians' knowledge and attitudes becomes imperative. More accurate findings may be obtained from replicating this study, applying Rogers's diffusion of innovation theory or other models to a larger sample of physicians from a wider variety of specialties. It is also important to recruit a representative sample of patients with a wide array of chronic diseases to assess their knowledge of PGx testing. Different measurement instruments may be used to capture accurately separate factors such as trialability, observability, innovativeness, area of practice/living, and communication channels.

Future research should be geared toward recruiting physicians working in medical settings in which PGx testing is available and proportionately include minority ethnic/racial groups. Younger and older physicians practicing in both rural and urban areas should be included. Using a larger sample size would allow conducting additional subgroup analysis that may provide a better insight into the adoption behavior of patients and physicians as well as the predictors of knowledge and attitudes. A mixed-methods approach using qualitative and quantitative data collected simultaneously may be best suited to provide a deeper understanding of the acceptance of PGx testing in medical practice.

Significance of the Findings in the Field of Pharmacy

Pharmacists play a key role in patient care through a wide array of services that focus on monitoring the prescription process and optimizing drug utilization to ensure the safety and effectiveness of prescribed medications (Bush and Daniels, 2017). The unique position of pharmacists as access points to care has several advantages leading to the integration of patients' health information with rational drug use. As the focus of health care shifts into personalized medicine, pharmacists' knowledge and awareness about genetic-based treatment have become a necessity. The FDA has already approved more than 150 drug package inserts with pharmacogenetic information, and the Clinical Pharmacogenetics Implementation Consortium (CPIC) has published therapeutic guidelines based on individual genetic differences (Relling and Klein, 2011) that mandate healthcare providers, including pharmacists, to take the lead, seek education, and gain experience in the field of genetics.

Integrating genetic information with other health information may maximize the benefits of medications that patients should receive as well as diminish the occurrence of ADRs (Ma et al., 2011; Owczarek et al., 2005). To fulfill the Accreditation Council for Pharmacy Education (ACPE) Standards, several pharmacy schools have included genetic courses in their curricula to fortify the level of knowledge pertaining to medication response (ACPE, 2015; Adams et al., 2016). These pharmacogenetic courses are designed to familiarize future pharmacists with the genetic basis of diseases as well as the role of metabolizing enzymes, which are susceptible to inter-individual genetic variation in medication response.

The American Society of Health-System Pharmacists (ASHP) has emphasized the role of pharmacists in promoting personalized medicine and taking the lead in understanding genetic variability among individuals responsible for aggravating the burden of preventable side effects (ASHP, 2015). To maintain the ongoing responsibility of pharmacists toward optimizing therapeutic benefits and minimizing adverse drug reactions, the barriers to adopting PGx testing as a diagnostic tool should be studied further. In addition, the interpretation of testing results and the most effective ways of communicating these results to patients and other healthcare providers should be investigated and evaluated. The work described in this dissertation has revealed several factors that significantly influence acceptance of genetic tests by both physicians and patients. In the presence of clinical guidelines (Relling and Klein, 2011; Swen et al., 2011), the ability of a pharmacist to understand both physicians' and patients' motives and concerns regarding acceptance of PGx testing may help advocate its application in

practice and promote the optimal use of PGx testing in order to achieve positive health outcomes.

Conclusion

Advances in the field of PGx in modern medicine are increasingly becoming a transforming point in the way chronic conditions are treated, medications are prescribed, and in developing trusting relationships among patients, pharmacists, and physicians. In a preliminary step toward searching for a more extensive acceptance of PGx testing in clinical practice, this study carefully assessed the decision-making process and subsequently provided a significant insight into factors pertaining to enhancing the rate of adoption of PGx testing among patients and prescribers.

Incorporating patients' genetic information as part of their medical history will optimize the use, safety, and effectiveness of many medications. However, transforming this technology into practice can only be accompanied with increased knowledge and more positive attitudes among patients and physicians alike, as they play a key role in its diffusion. This dissertation considered the fact that participating patients suffered from several chronic conditions that have a genetic predisposition. Therefore, the research focused on measuring actual knowledge of genetics and PGx testing rather than perceived knowledge, and it was found predictive for less reluctance toward accepting the tests. This conclusion highlights the need for establishing educational programs and revising existing medical curricula geared toward gaining knowledge as a precedent factor to the formation of favorable attitudes toward PGx testing.

This study measured the influence of sociodemographic characteristics on patients' willingness to accept PGx testing and on prescribers' understanding of patients'

medical needs and the need for change in their current clinical practices. It strongly suggested that obtaining higher levels of education, being innovative, and gaining prior experience with genetic testing should ultimately improve patients' acceptance of this diagnostic tool. The empirical evidence showed an increase in patients' awareness and attitudes regarding genetic testing. In addition, several factors connected to the characteristics of PGx testing were significantly linked to its future acceptance. Thus, this study provided a thorough understanding of society's need and opinions toward PGx testing. Patients believed that PGx testing helps select the effective medication, avoid wrong medications, and reduce potential adverse events. Several barriers reported here could contribute to reforming institutional policies regarding patients' confidentiality and potential for discrimination that might impact patient's attitudes and subsequently the decision to adopt.

The findings also showed that general knowledge of, and attitudes toward, the use of PGx testing increased physicians' tendency to select the technique and implement it on their patients to improve health outcomes. Physicians' acceptance of these tests was exclusively linked to their prior experience with, and perceived need for, genetic testing as well as perceived characteristics of PGx testing. Also identified were several barriers for the adoption decision that need be considered by the medical community and healthcare systems to meet society's need for PGx testing and reduce healthcare costs, unnecessary medications, and ADRs that will ultimately improve patient adherence. Moreover, the findings may help develop clinical trials and conduct epidemiological studies to promote the uptake of genetic tests and overcome the key barriers.

This dissertation added an additional value by delineating factors that need be addressed to foster PGx implementation in a clinical setting. It may have a large impact on developing education and training programs, mitigating future concerns, and on PGx companies that could improve the characteristics of PGx testing and alleviate currently foreseen barriers. It provided an insight into the perception of patients with chronic diseases that might represent and reflect comparable results drawn from a larger population. The extent of the findings may be expanded to include pharmacoeconomic and health outcome measures. The findings also may be used to assess the inhibitors of accepting individual PGx tests in different clinical settings and may be applied to other healthcare professionals and their response to health-related innovations.

The theoretical framework, Rogers's diffusion of innovation theory, was a useful and highly reproducible model. A generalized path analysis method posed new correlates among different sets of adapted variables. The modified data collecting instruments validated and used in this research significantly contributed to capturing patients' and physicians' factors that have not been investigated in prior studies.

Appendix A

Research Questionnaire (Patient Version)

Knowledge

For each of the following items check (X) if you think it is true or false:

1. A person who carries a gene associated with a disease may be healthy
   ☐ True ☐ False ☐ Not Sure
2. A person's genetic make-up can influence how he or she responds to medicines
   ☐ True ☐ False ☐ Not Sure
3. People with genetic differences can respond differently to the same medication (e.g., some patients may benefit; others may not)
   ☐ True ☐ False ☐ Not Sure
4. A test that looks at an individual's genes will likely reveal whether a particular medicine would cause side effects for that person
   ☐ True ☐ False ☐ Not Sure
5. A test that takes a cotton swab from the mouth of an individual and looks at genes is currently available for some medications (e.g. simvastatin, clopidogrel)
   ☐ True ☐ False ☐ Not Sure
6. A test that looks at a person's genes will likely reveal whether a particular medicine would work for that person
   ☐ True ☐ False ☐ Not Sure
7. The severity of side effects of some medications may depend on a person's genetic make-up
   ☐ True ☐ False ☐ Not Sure
8. Before this survey, have you ever heard about the term "Pharmacogenetic Testing"?
   ☐ True ☐ False ☐ Not Sure
9. Have you ever had your gene(s) tested?
   ☐ True ☐ False ☐ Not Sure
10. Would you agree to take a pharmacogenetic test (via cotton swab from the mouth) for one of your chronic medications?
    ☐ Yes ☐ I already have one ☐ No ☐ Not Sure

Attitude

This survey asks about your preference with regard to the following statements:

11. It is important to look at my genes in order to know what is best for my health

□ Strongly Disagree/Disagree □ Neutral □ Agree/Strongly Agree

12. I am willing to take a test that measures how a medicine works, based on my genes
    □ Strongly Disagree/Disagree □ Neutral □ Agree/Strongly Agree
13. It is not useful to take genetic tests because my family physician may not know how to use my tests results
    □ Strongly Disagree/Disagree □ Neutral □ Agree/Strongly Agree
14. If I had to pay for the genetic test myself, financial cost would be one of my concerns for taking these tests
    □ Strongly Disagree/Disagree □ Neutral □ Agree/Strongly Agree
15. If I underwent testing, I would be concerned about the effect of the test results on my eligibility for private health insurance
    □ Strongly Disagree/Disagree □ Neutral □ Agree/Strongly Agree
16. If I underwent testing, I would be concerned about the effect of the test results on my employment opportunities
    □ Strongly Disagree/Disagree □ Neutral □ Agree/Strongly Agree
17. I believe that physicians should have pharmacogenetic testing information in their clinical practice
    □ Strongly Disagree/Disagree □ Neutral □ Agree/Strongly Agree
18. I think that pharmacogenetic testing may prevent me from taking the wrong medicine
    □ Strongly Disagree/Disagree □ Neutral □ Agree/Strongly Agree
19. I believe that pharmacogenetic testing will help reduce my current medications' side effects
    □ Strongly Disagree/Disagree □ Neutral □ Agree/Strongly Agree
20. If I took the test, I would be concerned that unauthorized persons may gain access to the results of that test
    □ Strongly Disagree/Disagree □ Neutral □ Agree/Strongly Agree
21. I believe that pharmacogenetic testing can help in the selection of a medication that would better improve my medical condition
    □ Strongly Disagree/Disagree □ Neutral □ Agree/Strongly Agree
22. Pharmacogenetic testing can offer me a useful alternative to the way that a physician usually prescribes medications
    □ Strongly Disagree/Disagree □ Neutral □ Agree/Strongly Agree
23. Pharmacogenetic testing is a promising innovation in medicine
    □ Strongly Disagree/Disagree □ Neutral □ Agree/Strongly Agree
24. Pharmacogenetic testing can help my physicians to make the right decisions about my health
    □ Strongly Disagree/Disagree □ Neutral □ Agree/Strongly Agree
25. I will be reluctant about accepting pharmacogenetic testing until I see it providing useful results for people around me
    □ Strongly Disagree/Disagree □ Neutral □ Agree/Strongly Agree
26. Pharmacogenetic testing is a type of test that can invade my privacy
    □ Strongly Disagree/Disagree □ Neutral □ Agree/Strongly Agree
27. The term pharmacogenetic testing is difficult to understand

□ Strongly Disagree/Disagree □ Neutral □ Agree/Strongly Agree

28. I won't lose much by trying pharmacogenetic testing, even if it doesn't benefit me directly

□ Strongly Disagree/Disagree □ Neutral □ Agree/Strongly Agree

29. I have discussed (at least once) pharmacogenetic testing with my healthcare provider

□ Strongly Disagree/Disagree □ Neutral □ Agree/Strongly Agree

30. Which of the following sources, if any, do you usually use to get information about health issues (for example, medications, treatment, and side Internet effects)? (Check all that apply)

□ TV □ Radio □ Internet □ Newspapers □ Magazines

□ Physicians/Physician Assistants □ Nurses □ Pharmacists

31. Gender

□ Male □ Female

32. Ethnic Group

□ White/Caucasian □ Hispanic/Latino □ Black or African American

□ Others

33. Age Group (years)

□ 18-29 □ 30-39 □ 40-49 □ 50-59 □ 60+

34. Education

□ High School or GED □ Associate Degree □ Bachelor's Degree

□ Master's Degree □ Doctorate or Professional Degree

35. Area where you live

□ Urban □ Suburban □ Rural

Appendix B

Study Constructs and Corresponding Sources

Table B.1
Patient Survey Constructs

Construct/Variable	Survey Items	Reference
Knowledge of PGx testing	1	(Calsbeek et al., 2007)
	2,3, 5	(Roederer et al., 2012)
	4, 6, 7	(Lachance et al., 2014)
Attitudes toward PGx testing	11, 17, 23, 24	Self-developed
	12, 20	(Rogausch et al., 2006)
	13 - 16	(Zhang et al., 2014)
Prior experience	8, 9	Self-developed
Perceived need	18, 19	(Rogausch et al., 2006)
Innovativeness	25	Self-developed
Area of living	35	(Dodson et al., 2012)
Sociodemographic variables	31 - 34	Self-developed
Communication channels	30	(Nielsen et al., 2007)
Relative advantage	21, 22	Self-developed
Compatibility	26	Self-developed
Complexity	27	(Dodson et al., 2012)
Trialability	28	Self-developed
Observability	29	Self-developed
Willingness to take the test	10	Self-developed

Note. The patient survey used in this study was developed and modified from previously published studies to collect information about patients' knowledge and attitudes toward PGx testing. Several survey questions were adapted from the above authors.
*PGx = Pharmacogenetic

Table B.2
Prescriber Survey Constructs

Construct/Variable	Survey Items	Reference
Duration of practice	1	Self-developed
Knowledge of PGx testing	2, 3, 5 - 7	(Roederer et al., 2012)
	4	(Shaw et al., 2011)
Attitudes toward PGx testing	11	(Rogausch et al., 2006)
	10,17,19	(Roederer et al., 2012)
	9	(Dodson et al., 2012)
	8, 12, 15	Self-developed
Prior experience	25	(Taber et al., 2014)
Perceived need	21a, 21b	(Rogausch et al., 2006)
Area of Current Setting	32	(Dodson et al., 2012)
Sociodemographic variables	28-31	Self-developed
Communication channels	22	(Taber et al., 2014)
Relative advantage	20a, 20b	Self-developed
Innovativeness	14	Self-developed
Compatibility	13	Self-developed
Complexity	18	Self-developed
Trialability	16	Self-developed
Observability	23	Self-developed
Willingness to recommend PGx	24	Self-developed
Factors affecting PGx adoption	26	(Taber et al., 2014)
Pharmacist role in PGx testing	27	Self-developed

Note. The prescriber survey used in this study was developed and modified from the relevant literature to collect information about physicians' knowledge and attitudes toward PGx testing. Several survey questions were adapted from the above authors.
*PGx = Pharmacogenetic

Appendix C

Research Questionnaire (Prescriber Version)

1. How long have you been in practice (years)?
   ☐ 1-10 ☐ 11-20 ☐ 21 years or more

Knowledge

For each of the following items, check if you think it is true or false.

2. Genetic variations account for as much as 95% of the variability of an individual's response to a medication.
   ☐ True ☐ False ☐ Not Sure
3. Pharmacogenetic testing can determine whether people with genetic differences can respond differently to the same medication.
   ☐ True ☐ False ☐ Not Sure
4. Pharmacogenetic testing of an individual's genes guarantees whether a particular medicine would cause adverse events for that person.
   ☐ True ☐ False ☐ Not Sure
5. Pharmacogenetic testing is currently available for all medications.
   ☐ True ☐ False ☐ Not Sure
6. Some medications have FDA-approved pharmacogenetic information in their package inserts.
   ☐ True ☐ False ☐ Not Sure
7. The package insert for clopidogrel (Plavix®) includes a warning about possible worse outcomes in individuals who have specific genetic variants.
   ☐ True ☐ False ☐ Not Sure

Attitudes

On a scale from 1 to 5, indicate your agreement with the following items:

8. Prescribers should use pharmacogenetic testing information in clinical practice
   ☐ Strongly Disagree/Disagree ☐ Neutral ☐ Agree/Strongly Agree
9. Patients should be educated about the purpose, benefits, limitations and risks of pharmacogenetic testing.
   ☐ Strongly Disagree/Disagree ☐ Neutral ☐ Agree/Strongly Agree
10. Pharmacogenetic testing will potentially help to decrease the number of adverse drug events.
    ☐ Strongly Disagree/Disagree ☐ Neutral ☐ Agree/Strongly Agree
11. Pharmacogenetic testing may prevent me from prescribing an ineffective medicine.
    ☐ Strongly Disagree/Disagree ☐ Neutral ☐ Agree/Strongly Agree
12. Pharmacogenetic testing is a promising innovation in medicine.

□ Strongly Disagree/Disagree □ Neutral □ Agree/Strongly Agree

13. Pharmacogenetic testing is not compatible with my personal values.
    □ Strongly Disagree/Disagree □ Neutral □ Agree/Strongly Agree
14. I will be reluctant to adopt pharmacogenetic testing until I see it working for patients.
    □ Strongly Disagree/Disagree □ Neutral □ Agree/Strongly Agree
15. Pharmacogenetic testing can offer a useful tool to the way I usually prescribe/recommended medications.
    □ Strongly Disagree/Disagree □ Neutral □ Agree/Strongly Agree
16. I would like to try pharmacogenetic testing on some patients before I decide whether I will adopt it or not.
    □ Strongly Disagree/Disagree □ Neutral □ Agree/Strongly Agree
17. I am concerned about the effect of the test results on my patients' eligibility for private health insurance.
    □ Strongly Disagree/Disagree □ Neutral □ Agree/Strongly Agree
18. The application of pharmacogenetic testing adds more complexity to the drug prescribing process.
    □ Strongly Disagree/Disagree □ Neutral □ Agree/Strongly Agree
19. I am concerned that unauthorized personnel may gain access to the results of that test.
    □ Strongly Disagree/Disagree □ Neutral □ Agree/Strongly Agree
20. There is a relative advantage for pharmacogenetic testing in the following cases:
    a. Non-response to an essential drug (e.g., analgesic) / Refractory patients
       □ Yes □ No □ Not Sure
    b. Selection of medication that better controls a patient's health condition
       □ Yes □ No □ Not Sure
21. There is a need for pharmacogenetic testing in the following situations:
    a. When information about the test is included in the package inserts
       □ Yes □ No □ Not Sure
    b. When practice guidelines for the use and interpretation of these tests are available.
       □ Yes □ No □ Not Sure
22. How/where have you learned about genetics and genetic testing? *[Please select all that apply.]*
    □ No, I have not received education in genetics
    □ Genetics training in medical/pharmacy school
    □ Genetics training in residency
    □ Undergraduate genetics course
    □ Genetics course in graduate school
    □ Grand Rounds
    □ CME course
    □ Genetics-related seminar or workshop
    □ Other
23. Have you ever talked with a patient about pharmacogenetic testing?
    □ Yes □ No □ Not Sure

24. Would you recommend pharmacogenetic testing for medications that recommend such tests in their package inserts?
    □ Yes □ No □ Not Sure
25. Have you ever ordered pharmacogenetic testing for a patient?
    □ Yes □ No
26. Which of the following factors would inhibit you from ordering/recommending pharmacogenetic testing for a patient? *[Please select all that apply.]*
    □ Pharmacogenetic-testing is not available at my work place
    □ Concerns about patients' confidentiality
    □ Concerts about patients' employment opportunity
    □ Not enough time to order
    □ Waiting for pharmacogenetic testing results would delay treatment
    □ Uncertain about the clinical utility of the test
    □ Insurance doesn't cover test
    □ Not applicable for my patients
    □ Patient refused test
27. Would you prefer a pharmacist order, interpret, and send you a report about your patients' pharmacogenetic testing results?
    □ Yes □ No □ Not Sure
28. Gender
    □ Male □ Female
29. Ethnic Group:
    □ White/Caucasian
    □ Hispanic/Latino
    □ Black or African American
    □ Other
30. Age Group (year)
    □ 25-39
    □ 40-49
    □ 50-59
    □ 60+
31. What is your medical specialty?
    □ Internal Medicine
    □ Family Medicine
    □ Other
32. Type of current setting: [Please select all that apply]
    □ Urban
    □ Suburban
    □ Rural

Appendix D

NSU-Institutional Review Board Approval Memorandum and Amendment Approval Letter

D.1. MEMORANDUM

To: Suhaib Muflih Muflih
College of Pharmacy
From: William "Bill" R Wolowich, Pharm.D.,
Center Representative, Institutional Review Board
Date: March 22, 2016
Re: IRB #: 2016-77; Title, "Measuring Knowledge and Attitudes Regarding The Use of Pharmacogenetic Testing Among Patients and Prescribers: Diffusion of Innovation Theory"

I have reviewed the above-referenced research protocol at the center level. Based on the information provided, I have determined that this study is exempt from further IRB review under **45 CFR 46.101(b) (Exempt Category 2)**. You may proceed with your study as described to the IRB. As principal investigator, you must adhere to the following requirements:

1) CONSENT: If recruitment procedures include consent forms, they must be obtained in such a manner that they are clearly understood by the subjects and the process affords subjects the opportunity to ask questions, obtain detailed answers from those directly involved in the research, and have sufficient time to consider their participation after they have been provided this information. The subjects must be given a copy of the signed consent document, and a copy must be placed in a secure file separate from de-identified participant information. Record of informed consent must be retained for a minimum of three years from the conclusion of the study.

2) ADVERSE EVENTS/UNANTICIPATED PROBLEMS: The principal investigator is required to notify the IRB chair and me (954-262-5369 and William "Bill" R Wolowich, Pharm.D., respectively) of any adverse reactions or unanticipated events that may develop as a result of this study. Reactions or events may include, but are not limited to, injury, depression as a result of participation in the study, life-threatening situation, death, or loss of confidentiality/anonymity of subject. Approval may be withdrawn if the problem is serious.

3) AMENDMENTS: Any changes in the study (e.g., procedures, number or types of subjects, consent forms, investigators, etc.) must be approved by the IRB prior to implementation. Please be advised that changes in a study may require further review depending on the nature of the change. Please contact me with any questions regarding amendments or changes to your study.

The NSU IRB is in compliance with the requirements for the protection of human subjects prescribed in Part 46 of Title 45 of the Code of Federal Regulations (45 CFR 46) revised June 18, 1991.

cc: Barry A. Bleidt, PhD, PharmD

D.2. Amendment Approval Letter

To: Suhaib Muflih, College of Pharmacy
From: William Smith, JD Director, Institutional Review Board
Date: August 3, 2016
Re: 2016-77-Measuring Knowledge and Attitudes Regarding The Use of Pharmacogenetic Testing Among Patients and Prescribers: Diffusion of Innovation Theory

I have reviewed the amendment to the above-referenced research protocol. On behalf of the Institutional Review Board of Nova Southeastern University, the amendment to Measuring Knowledge and Attitudes Regarding The Use of Pharmacogenetic Testing Among Patients and Prescribers: Diffusion of Innovation Theory is approved and the study is still EXEMPT.

cc: Barry A Bleidt, PhD, PharmD; Matthew Seamon, JD, PharmD

Institutional Review Board
3301 College Avenue Ft. Lauderdale, Florida 33314-7796
Phone: (954) 262-5369 Fax: (954) 262-3977 Email: irb@nova.edu Web Site:

www.nova.edu/irb

Appendix E

Adult Informed Consent, Promotional Flyer for Recruiting Patients, Prescriber Invitation E-Mail, Prescriber Participation Letter

E.1. Adult Informed Consent

Consent Form for Participation in the Research Study Entitled "Measuring Knowledge and Attitudes Regarding the Use of Pharmacogenetic Testing Among Patients and Prescribers: Diffusion of Innovation Theory"

Funding Source: HPD Grant
IRB protocol #: 2016-77

	Principal Investigator
Name	Suhaib Muflih
Complete mailing address	3301 College Avenue, Fort Lauderdale, Florida 33314-7796
Contact phone number	954-980-3890
E-mail	sm231@nova.edu
Degree	PharmD

	Co-Investigator 1 (Faculty Advisor)
Name	Barry Bleidt
Mailing Address	3301 College Avenue, Fort Lauderdale, Florida 33314-7796
Contact Phone Number	954-262-1855
Email Address	bbleidt@nova.edu
Degree/Academic Information	PhD, PharmD, FAPhA

For questions/concerns about your research rights, contact:
Human Research Oversight Board (Institutional Review Board or IRB)
Nova Southeastern University
954-262-5369/Toll Free: 866-499-0790
IRB@nsu.nova.edu

Site Information:
NSU Clinic Pharmacy
3200 S. University Drive
Ft. Lauderdale, FL 33328
Tel.: 954-262-4550
Fax: 954-262-3865

Why are you asking me?

You are invited to participate in a research study. Your participation is voluntary which means you can decide whether to participate. If you choose not to participate, there will be no loss of benefit to which you might otherwise be entitled. Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of participating in this study, and what you will have to do in this study. If you decide to participate, you will be asked to sign this form.

The purpose of this consent form is to provide you information so that you can decide whether you want to provide information about yourself, your knowledge and attitude toward the use of pharmacogenetic testing. The Principle Investigator (the researcher) will collect the information about you through a survey questionnaire. There are a particular number of participants expected to participate in this research, but we are aiming to recruit over 120 participants.

What will I be doing if I agree to be in the study?

If you agree to participate in the study and sign this informed consent, you will fill out a survey questionnaire (using clipboard survey or tablet computer) that will collect data that will assess your level of knowledge and attitude toward pharmacogenetic testing. After you complete the survey (the clipboard survey), please put it in the envelope and give it back to the Principle Investigator.

Is there any audio or video recording?

No

What are the dangers to me?

We do not anticipate any risks to your participating in this study by filling out a survey questionnaire. However, if you feel uncomfortable with any question in the survey, you don't have to answer it.

Are there any benefits for taking part in this research study?

Although it is not anticipated that there will be any direct benefit to you as a result of your participation in this study, your participation may contribute to an increase in the knowledge and understanding of how different individuals pharmacogenetic testing.

Will I get paid for being in the study? Will it cost me anything?

You will not be compensated for you participation in this study. There are no costs associated with participating in the survey.

How will you keep my information private?

The Principle Investigator is the only person who will know who you are and any personally identifiable information about you. We will not share any information that you give us. The Principle Investigator will replace your personal information with a coded identification number. All of your information will be stored in a database which is password-protected and secure. Only the Principle Investigator will have the access to the database. The researcher will not use any information to identify or contact you.

What if I do not want to participate or I want to leave the study?

You have the right to leave this study at any time or refuse to participate. If you do decide to leave or you decide not to participate, you will not experience any penalty or loss of services you have a right to receive.

Other Considerations:

"If significant new information relating to the study becomes available, which may relate to your willingness to continue to participate, this information will be provided to you by the investigators."

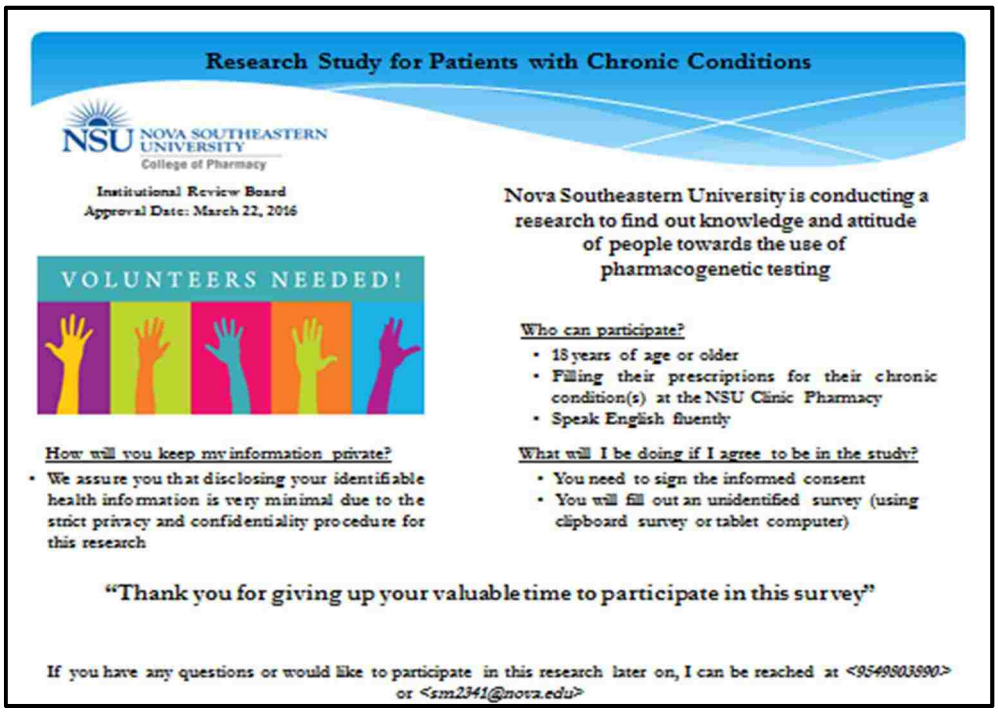
Voluntary Consent by Participant:

By signing below, you indicate that

- this study has been explained to you
- you have read this document or it has been read to you
- your questions about this research study have been answered
- you have been told that you may ask the researchers any study related questions in the future or contact them in the event of a research-related injury
- you have been told that you may ask Institutional Review Board (IRB) personnel questions about your study rights
- you are entitled to a copy of this form after you have read and signed it
- you voluntarily agree to participate in the study entitled "Measuring Knowledge and Attitudes Regarding the Use of Pharmacogenetic Testing Among Patients and Prescribers: Diffusion of Innovation Theory"

Participant's Signature: _____ Date: _____
Participant's Name: _____ Date: _____
Signature of Person Obtaining Consent: _____
Date: _____

E.2. Promotional Flyer for Recruiting Patients



E.3. Prescriber Invitation E-Mail

Dear Physician,

The link below will direct you to a survey on pharmacogenetic testing. The information this survey will collect is vital for an important research project regarding pharmacogenetic testing/patient personalized medicine. Your answers are important to publish and totally confidential. Please see the participation letter at the beginning of the survey for further information on IRB.

Thank you for taking the time to answer this 4-minute survey.

Please note that the survey should be completed in one sitting, and a $10 Starbucks code will be sent directly via email to the first 120 participants.

Here is the URL:

http://www.nova.edu/~snap/pharmacogenicprescriber.htm

E. 4. Prescriber Participation Letter

Research Explanation and Letter of Consent
Title of Study: Measuring Knowledge and Attitudes Regarding the Use of Pharmacogenetic Testing Among Patients and Prescribers: Diffusion of Innovation Theory.

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Description of Study:

Dr. Suhaib Muflih is a doctoral student at Nova Southeastern University engaged in research for the purpose of satisfying the requirements for a Doctor of Philosophy degree. The goal of this dissertation is to increase our understanding of several factors (e.g., sociodemographic knowledge, and attitudes) that may play a key role in the acceptance or rejection of pharmacogenetic testing among patients and prescribers. The process by which pharmacogenetics will be implemented in the future of both personalized medicine and routine medical practice will ultimately depend upon patients' and physicians' acceptance of these tests and related recommendations. If you agree to participate, you will be asked to complete the survey questionnaire below. The questionnaire will help the researcher assess prescribers' knowledge and attitudes toward

pharmacogenetics testing, and the barriers that interfere with its uptake in the routine clinical practice as a new diagnostic tool. The questionnaire will take approximately four minutes to complete.

Risks/Benefits to the Participant:

We do not anticipate any risks to your participation in this study. There are no direct benefits to you for agreeing to be in this study. Please understand that while you may not benefit directly from participation in this study, you have the opportunity to enhance the serious gap in our knowledge about the barriers that may prevent the adoption of pharmacogenetic testing. There is a growing body of evidence that pharmacogenetics will allow you as a prescriber to make improved prescribing choices that will increase drug efficacy and minimize adverse effects. If you have any concerns about the risks/benefits of participating in this study, you may contact the Principle Investigator and/or the university's human research oversight board Institutional Review Board at the numbers listed above.

Cost and Payments to the Participant:

There is no cost for participation in this study. Participation is completely voluntary, however, an incentive will be provided as a token of appreciation for giving your valuable time to complete the survey.

Confidentiality:

Information obtained in this study is strictly confidential unless disclosure is required by law. All data will be secured in password-protected computer. Your name will not be used in the reporting of information in publications or conference presentations.

Participant's Right to Withdraw from the Study: You have the right to refuse to participate in this study and the right to withdraw from the study at any time without penalty.

I have read this letter and I fully understand the contents of this document and voluntarily consent to participate. All of my questions concerning this research have been answered. If I have any questions in the future about this study, they will be answered by the investigator listed above or his/her staff.

I understand that the completion of this questionnaire implies my consent to participate in this study.

Please initial in the space provided below

_____

Please provide the consent date in the space provided below

_____

Appendix F

Sensitivity Analyses Using Count Models

Table F.1
Patient Data. Poisson Regression Model

	Knowledge				
				95% Conf. Interval	
Variable	*IRR*	*SE*	*p-value*	*LL*	*UL*
Gender (Male)	1.020	0.079	0.797	0.877	1.186
Age	0.986	0.028	0.623	0.933	1.043
Ethnicity	0.955	0.037	0.236	0.886	1.030
Level of education	1.089	0.032	0.004	1.028	1.153
Area of living	1.048	0.074	0.506	0.913	1.202
Perceived need	1.080	0.055	0.131	0.977	1.193
Innovativeness	1.119	0.056	0.024	1.015	1.233
Prior experience	1.146	0.102	0.127	0.962	1.364
Cons	2.154	0.502	0.001	1.364	3.402

Note. Knowledge of PGx testing is the response variable in the Poisson regression. IRR: incidence rate ratios for the Poisson model; SE: standard errors of the individual regression coefficients; LL: Lower limit; UL: Upper limit. As a patient's level of education increased by one unit, his/her knowledge of PGx testing would be expected to increase by a factor 1.089, while holding all other variables in the model constant. Similarly, as a patient's innovativeness score increased by one unit, his/her knowledge of PGx testing would be expected to increase by a factor 1.12, while holding all other variables in the model constant.

Table F.2.
Patient Data. Ordinal Dependent Variable Regression Model

	Knowledge				
				95% Conf. Interval	
Variables	*B*	*SEB*	*p-value*	*LL*	*UL*
Gender (Male)	0.090	0.157	0.565	-0.217	0.398
Age	-0.024	0.059	0.679	0.139	0.091
Ethnicity	-0.135	0.078	0.082	0.287	0.017
Level of education	0.263	0.061	0.000	0.144	0.383
Area of living	0.090	0.142	0.524	0.188	0.368
Perceived need	0.208	0.100	0.038	0.012	0.405
Innovativeness	0.322	0.103	0.002	0.120	0.524
Prior experience	0.520	0.199	0.009	0.131	0.910

Note. B: Standard interpretation of the ordered logit coefficient; SEB: Standard error of regression coefficients. Ordinal Probit Model is used when the dependent variable (knowledge) is neither interval nor ratio; the distances between different levels of knowledge are not equal. For a one unit increase in the level of education, the log-odds of having a higher level of knowledge would increase by 0.26, given that all of the other variables in the model are held constant. A one unit increase in the perceived need score would result in a 0.21 increase in the log-odds of having a higher level of knowledge. A one unit increase in the innovativeness score would result in a 0.32 increase in the log-odds of having a higher level of knowledge, given that all of the other variables in the model are held constant. The log odds of having a higher level of knowledge is 0.52 greater among patient with a prior experience of PGx testing than those have no prior experience, given that all of the other variables in the model are held constant.

Table F.3
Patient Data. Poisson Regression Model

	Attitudes				
				95% Conf. Interval	
Variables	*IRR*	*SE*	*p-value*	*LL*	*UL*
Gender (Male)	0.883	0.063	0.082	0.767	1.016
Level of education	1.023	0.026	0.365	0.973	1.076
Relative Advantage	1.249	0.066	0.000	1.126	1.386
Compatibility	1.112	0.048	0.014	1.021	1.210
Complexity	0.915	0.054	0.075	0.991	1.205
Trialability	1.187	0.076	0.007	1.047	1.344
Observability	1.059	0.065	0.349	0.939	1.195
Cons	1.323	0.239	0.121	0.929	1.885

Note. Attitude toward PGx testing is the response variable in the Poisson regression. IRR: incidence rate ratios for the Poisson model; SE: standard errors of the individual regression coefficients; LL: Lower limit; UL: Upper limit. As the relative advantage score increased by one unit, the patient's attitude toward PGx testing would be expected to increase by a factor 1.25, while holding all other variables in the model constant. As compatibility score increased by one unit, the patient's attitude would be expected to increase by a factor 1.11, while holding all other variables in the model constant. As trialability score increased by one unit, the patient's attitude would be expected to increase by a factor 1.19, while holding all other variables in the model constant.

Table F.4
Patient Data. Ordinal Dependent Variable Regression Model

	Attitudes				
				95% Conf. Interval	
Variables	*B*	*SEB*	*p-value*	*LL*	*UL*
Gender (Male)	-0.408	0.158	0.010	-0.718	-0.099
Level of education	0.070	0.059	0.233	-0.045	0.185
Relative Advantage	0.629	0.113	0.000	0.408	0.849
Compatibility	0.375	0.101	0.000	0.177	0.573
Complexity	-0.210	0.109	0.054	-0.424	0.004
Trialability	0.434	0.130	0.001	0.179	0.689
Observability	0.268	0.160	0.094	-0.046	0.582

Note. B: Standard interpretation of the ordered logit coefficient; SEB: Standard error of regression coefficients. Ordinal Probit Model is used when the dependent variable (knowledge) is neither interval nor ratio; the distances between different levels of attitude are not equal. The log-odds estimate for males being in a higher level of attitude is -0.41 less than females when the other variables in the model are held constant. A one unit increase in the relative advantage score, the log-odds of having a higher level of attitude would increase by 0.63, given that all of the other variables in the model are held constant. A one unit increase in the compatibility score would result in a 0.38 increase in the log-odds of having a higher level of attitude. A one unit increase in the complexity score would result in a 0.21 decrease in the log-odds of being having a higher level of knowledge, given that all of the other variables in the model are held constant. A one unit increase in the trialability score would result in a 0.43 increase in the log-odds of being having a higher level of knowledge, given that all of the other variables in the model are held constant.

Table F.5
Prescriber Data. Poisson Regression Model

	Knowledge				
				95% Conf. Interval	
Variables	*IRR*	*SE*	*p-value*	*LL*	*UL*
Gender (Male)	0.777	0.078	0.013	0.638	0.948
Type of practice setting	1.248	0.102	0.007	1.063	1.465
Prior-experience	1.257	0.143	0.044	1.006	1.571
Perceived need	1.087	0.077	0.238	0.947	1.247
Communication Channels	1.039	0.054	0.462	0.938	1.150
Cons	2.179	0.407	0.000	1.512	3.142

Note. Knowledge of PGx testing is the response variable in the Poisson regression. IRR: incidence rate ratios for the Poisson model; SE: standard errors of the individual regression coefficients; LL: Lower limit; UL: Upper limit. The knowledge scores among male physicians would be expected to decrease by a factor 0.78 compared to female physicians, while holding the other variable constant in the model. Knowledge among physicians who practiced in non-urban areas would be expected to increase by a factor 1.25 compared to physicians who practiced in urban areas, while holding the other variable constant in the model. Knowledge among physicians who had prior experience with PGx testing would be expected to increase by a factor 1.26 compared to physicians with no experience, while holding the other variable constant in the model.

Table F.6
Prescriber Data. Poisson Regression Model

	Attitude				
				95% Conf. Interval	
Variables	*IRR*	*SE*	*p-value*	*LL*	*UL*
Gender (Male)	0.876	0.068	0.087	0.753	1.020
Relative Advantage	1.160	0.071	0.016	1.029	1.308
Compatibility	1.195	0.079	0.007	1.049	1.361
Observability	1.049	0.042	0.229	0.970	1.135
Cons	3.063	0.495	0.000	2.231	4.205

Note. Attitude toward PGx testing is the response variable in the Poisson regression. IRR: incidence rate ratios for the Poisson model; SE: standard errors of the individual regression coefficients; LL: Lower limit; UL: Upper limit. The attitude scores among male physicians would be expected to decrease by a factor 0.88 compared to female physicians, while holding the other variable constant in the model. As the relative advantage score increased by one unit, the physician's attitude toward PGx testing would be expected to increase by a factor 1.16, while holding all other variables in the model constant. As compatibility score increased by one unit, the physician's attitude would be expected to increase by a factor 1.20, while holding all other variables in the model constant.

Appendix G

FDA-Approved Drugs with Package Inserts Containing PGx Information in Warnings and Precaution Labeling Sections

Table G

Examples of Medications with FDA-Approved PGx information

Drug	Therapeutic Area	Biomarker
Abacavir	Infectious Diseases	HLA-B*57:01
Amitriptyline	Psychiatry	CYP2D6
Atomoxetine	Psychiatry	CYP2D6
Azathioprine	Rheumatology	TPMT
Capecitabine	Oncology	DPYD
Carbamazepine	Neurology	HLA-B*15:02
Carbamazepine	Neurology	HLA-A*31:01
Cetuximab	Oncology	EGFR
Cetuximab	Oncology	EGFR
Cevimeline	Dental	CYP2D6
Chloroquine	Infectious Diseases	G6PD
Chlorpropamide	Endocrinology	G6PD
Citalopram	Psychiatry	CYP2C19
Clomipramine	Psychiatry	CYP2D6
Clopidogrel	Cardiology	CYP2C19
Codeine	Anesthesiology	CYP2D6
Dabrafenib	Oncology	BRAF
Dabrafenib	Oncology	G6PD
Dapsone	Dermatology	G6PD
Dapsone	Infectious Diseases	G6PD
Denileukin Diftitox	Oncology	IL2RA (CD25 antigen)
Desipramine	Psychiatry	CYP2D6
Dextromethorphan and Quinidine	Neurology	CYP2D6
Eltrombopag	Hematology	F5 (Factor V Leiden)
Erythromycin and Sulfisoxazole	Infectious Diseases	G6PD
Everolimus	Oncology	ERBB2 (HER2)
Everolimus	Oncology	ESR1
Fluorouracil	Dermatology	DPYD
Fluorouracil	Oncology	DPYD
Fluoxetine	Psychiatry	CYP2D6
Glimepiride	Endocrinology	G6PD

Glipizide	Endocrinology	G6PD
Glyburide	Endocrinology	G6PD
Iloperidone	Psychiatry	CYP2D6
Imipramine	Psychiatry	CYP2D6
Irinotecan	Oncology	UGT1A1
Lenalidomide	Hematology	del (5q)
Lidocaine and Prilocaine	Anesthesiology	Not specified
Lidocaine and Prilocaine	Anesthesiology	G6PD
Lomitapide	Endocrinology	Not specified
Mafenide	Infectious Diseases	G6PD
Mercaptopurine	Oncology	TPMT
Methylene Blue	Hematology	G6PD
Metoclopramide	Gastroenterology	G6PD
Mipomersen	Endocrinology	Not specified
Mycophenolic Acid	Transplantation	HPRT1
Nalidixic Acid	Infectious Diseases	G6PD
Nefazodone	Psychiatry	CYP2D6
Nitrofurantoin	Infectious Diseases	G6PD
Nortriptyline	Psychiatry	CYP2D6
Olaparib	Oncology	BRCA1, BRCA2
Oxcarbazepine	Neurology	HLA-B*15:02
Pegloticase	Rheumatology	G6PD
Perphenazine	Psychiatry	CYP2D6
Pertuzumab	Oncology	ERBB2 (HER2)
Phenytoin	Neurology	HLA-B*15:02
Pimozide	Psychiatry	CYP2D6
Primaquine	Infectious Diseases	G6PD
Propafenone	Cardiology	CYP2D6
Protriptyline	Psychiatry	CYP2D6
Quinidine	Cardiology	CYP2D6
Rasburicase	Oncology	G6PD
Sevoflurane	Anesthesiology	RYR1
Sodium Nitrite	Toxicology	G6PD
Sulfasalazine	Gastroenterology	G6PD
Tamoxifen	Oncology	F5 (Factor V Leiden)
Tamoxifen	Oncology	F2 (Prothrombin)
Tetrabenazine	Neurology	CYP2D6
Thioguanine	Oncology	TPMT
Thioridazine	Psychiatry	CYP2D6
Tolterodine	Urology	CYP2D6
Trastuzumab	Oncology	ERBB2 (HER2)
Tretinoin	Oncology	PML-RARA
Trimipramine	Psychiatry	CYP2D6
Valproic Acid	Neurology	POLG
Vemurafenib	Oncology	BRAF

Vemurafenib	Oncology	NRAS
Venlafaxine	Psychiatry	CYP2D6
Warfarin	Hematology	PROS1
Warfarin	Hematology	PROC

References

Accreditation Council for Pharmacy Education (2015). Accreditation standards and key elements for the professional program in pharmacy leading to the doctor of pharmacy degree. Retrieved from https://www.acpe-accredit.org/pdf/ Standards 2016FINAL.pdf

Adams, S. M., Anderson, K. B., Coons, J. C., Smith, R. B., Meyer, S. M., Parker, L. S., et al. (2016). Advancing pharmacogenomics education in the core PharmD curriculum through student personal genomic testing. *American Journal of Pharmaceutical Education, 80*(1), 3.

American Society of Health-System Pharmacists (2015). ASHP statement on the pharmacist's role in clinical pharmacogenomics. *American Journal of Health-System Pharmacy, 72*(7), 579-581.

An, X. & Yung, Y. (2014). Item response theory: What it is and how you can use the IRT procedure to apply it. *SAS Institute Inc. SAS364-2014*.

Armstrong, K., Weiner, J., Weber, B., & Asch, D. A. (2003). Early adoption of BRCA1/2 testing: Who and why. *Genetics in Medicine, 5*(2), 92-98.

Aron, A. & Aron, E. N. (2003). *Statistics for Psychology* (3rd ed.). Upper Saddle River, NJ: Prentice Hall/Pearson Education.

Balkrishnan, R. (2005). The importance of medication adherence in improving chronic-disease related outcomes: What we know and what we need to further know. *Medical Care, 43*(6), 517-520.

Benhaim, L., LaBonte, M. J., & Lenz, H.-J. (2012). Pharmacogenomics and metastatic colorectal cancer: Current knowledge and perspectives. *Scandinavian Journal of Gastroenterology, 47*(3), 325-339.

Birch, A. & Malim, T. (1988). Research methods in developmental psychology. In *Developmental Psychology: From Infancy to Adulthood*. London, UK: Palgrave Macmillan, pp. 1-6.

Blankfield, R. P., Goodwin, M., Jaén, C. R., & Stange, K. C. (2002). Addressing the unique challenges of inner-city practice: A direct observation study of inner-city, rural, and suburban family practices. *Journal of Urban Health, 79*(2), 173-185.

Brown, M. T. & Bussell, J. K. (2011). Medication adherence: WHO cares? *Mayo Clinic Proceedings, 86*(4), 304-314.

Brown, M. W. & Cudeck, R. (1993). Alternative ways of assessing model fit. *Sociological Methods & Research, 154*, 136-162.

Budnitz, D. S., Pollock, D. A., Weidenbach, K. N., Mendelsohn, A. B., Schroeder, T. J., & Annest, J. L. (2006). National surveillance of emergency department visits for outpatient adverse drug events. *Journal of the American Medical Association, 296*(15), 1858-1866.

Bush, P. W. & Daniels, R. (2017). Health care systems and transitions of care implication on interdisciplinary pharmacy services. *North Carolina Medical Journal, 78*(3), 177-180.

Calsbeek, H., Morren, M., Bensing, J., & Rijken, M. (2007). Knowledge and attitudes towards genetic testing: A two year follow-up study in patients with asthma, diabetes mellitus and cardiovascular disease. *Journal of Genetic Counseling, 16*(4), 493-504.

Centers for Disease Control and Prevention (2017). Chronic diseases: The leading causes of death and disability in the United States. Retrieved from https://www.cdc.gov/chronicdisease/overview/index.htm

Chasman, D. I., Posada, D., Subrahmanyan, L., Cook, N. R., Stanton Jr, V. P., & Ridker, P. M. (2004). Pharmacogenetic study of statin therapy and cholesterol reduction. *Journal of the American Medical Association, 291*(23), 2821-2827.

Chew, F., Grant, W., & Tote, R. (2004). Doctors on-line: Using diffusion of innovations theory to understand internet use. *Family Medicine, 36*(9), 645-650.

Cohen, J. (1977). *Statistical Power Analysis for the Behavioral Sciences (revised ed.)*. New York, NY: Academic Press.

Collins, F. S., Brooks, L. D., & Chakravarti, A. (1998). A DNA polymorphism discovery resource for research on human genetic variation. *Genome Research, 8*(12), 1229-1231.

Cook, R. D. & Weisberg, S. (1982). *Residuals and Influence in Regression*. New York, NY: Chapman and Hall.

Cuffe, S., Hon, H., Qiu, X., Tobros, K., Wong, C., De Souza, B., et al. (2014). Cancer patients' acceptance, understanding, and willingness-to-pay for pharmacogenomic testing. *Pharmacogenetics and Genomics, 24*(7), 348-355.

Desta, Z., Zhao, X., Shin, J., & Flockhart, D. A. (2002). Clinical significance of the cytochrome P450 2C19 genetic polymorphism. *Clinical Pharmacokinetics, 41*(12), 913-958.

Dodson, C. (2012). *Diffusion of innovation: Knowledge and attitudes of oncology nurses regarding pharmacogenomic testing.* (Doctoral dissertation), The University of North Carolina at Chapel Hill, Carolina Digital Repository. Retrieved from

https://cdr.lib.unc.edu/indexablecontent/uuid:a9f34e42-d78f-4f52-9474-1e766ae48bf2

Dooley, K. E. (1999). Towards a holistic model for the diffusion of educational technologies: An integrative review of educational innovation studies. *Educational Technology & Society, 2*(4), 35-45.

Dornbrook-Lavender, K. A. & Pieper, J. A. (2003). Genetic polymorphisms in emerging cardiovascular risk factors and response to statin therapy. *Cardiovascular Drugs and Therapy, 17*(1), 75-82.

Dressler, L. G., Deal, A. M., Patel, J., Markey, J., Riper, M. V., & McLeod, H. L. (2014). Cancer pharmacogenomics, adoption by oncologists and patient benefit. *Personalized Medicine, 11*(2), 143-153.

Duhachek, A., Coughlan, A. T., & Iacobucci, D. (2005). Results on the standard error of the coefficient alpha index of reliability. *Marketing Science, 24*(2), 294-301.

Durbin, J. & Watson, G. S. (1951). Testing for serial correlation in least squares regression. II. *Biometrika Trust, 38*(1/2), 159-177.

Eeles, R. A., Kote-Jarai, Z., Al Olama, A. A., Giles, G. G., Guy, M., Severi, G., et al. (2009). Identification of seven new prostate cancer susceptibility loci through a genome-wide association study. *Nature Genetics, 41*(10), 1116-1121.

Evans, W. E. & Relling, M. V. (1999). Pharmacogenomics: Translating functional genomics into rational therapeutics. *Science, 286*(5439), 487-491.

Fargher, E. A., Eddy, C., Newman, W., Qasim, F., Tricker, K., Elliott, R. A., et al. (2007). Patients' and healthcare professionals' views on pharmacogenetic testing and its future delivery in the NHS. *Pharmacogenomics, 8*(11), 1511-1519.

Faul, F., Erdfelder, E., Buchner, A., & Lang, A. (2009). Statistical power analyses using G*Power 3.1: Tests for correlation and regression analyses. *Behavior Research Methods, 41*(4), 1149-1160.

Frankfort-Nachmias, C. & Leon-Guerrero, A. (2010). *Social Statistics for a Diverse Society* (6th ed.). Thousand Oaks, CA: SAGE Publications, Inc.

Frueh, F. W., Amur, S., Mummaneni, P., Epstein, R. S., Aubert, R. E., DeLuca, T. M., et al. (2008). Pharmacogenomic biomarker information in drug labels approved by the United States food and drug administration: Prevalence of related drug use. *Pharmacotherapy, 28*(8), 992-998.

Gandhi, T. K., Burstin, H. R., Cook, E. F., Puopolo, A. L., Haas, J. S., Brennan, T. A., et al. (2000). Drug complications in outpatients. *Journal of General Internal Medicine, 15*(3), 149-154.

Ghaddar, F., Cascorbi, I., & Zgheib, N. K. (2011). Clinical implementation of pharmacogenetics: A nonrepresentative explorative survey to participants of WorldPharma 2010. *Pharmacogenomics, 12*(7), 1051-1059.

Ginsburg, G. S. & McCarthy, J. J. (2001). Personalized medicine: Revolutionizing drug discovery and patient care. *Trends in Biotechnology, 19*(12), 491-496.

Goodman, R. A., Posner, S. F., Huang, E. S., Parekh, A. K., & Koh, H. K. (2013). Defining and measuring chronic conditions: Imperatives for research, policy, program, and practice. *Preventing Chronic Disease, 10*.

Gordon, K., Smith, F., & Dhillon, S. (2007). Effective chronic disease management: Patients' perspectives on medication-related problems. *Patient Education and Counseling, 65*(3), 407-415.

Green, D., Mummaneni, P., Kim, I., Oh, J., Pacanowski, M., & Burckart, G. (2016). Pharmacogenomic information in FDA-approved drug labels: Application to pediatric patients. *Clinical Pharmacology and Therapeutics, 99*(6), 622-632.

Guengerich, F. P. (2007). Cytochrome P450 and chemical toxicology. *Chemical Research in Toxicology, 21*(1), 70-83.

Haddy, C. A., Ward, H. M., Angley, M. T., & McKinnon, R. A. (2010). Consumers' views of pharmacogenetics—a qualitative study. *Research in Social and Administrative Pharmacy, 6*(3), 221-231.

Haga, S. B. & LaPointe, N. M. A. (2013). The potential impact of pharmacogenetic testing on medication adherence. *The Pharmacogenomics Journal, 13*(6), 481-483.

Haga, S. B., Barry, W. T., Mills, R., Ginsburg, G. S., Svetkey, L., Sullivan, J., et al. (2013). Public knowledge of and attitudes toward genetics and genetic testing. *Genetic Testing and Molecular Biomarkers, 17*(4), 327-335.

Haga, S. B., Burke, W., Ginsburg, G. S., Mills, R., & Agans, R. (2012a). Primary care physicians' knowledge of and experience with pharmacogenetic testing. *Clinical Genetics, 82*(4), 388-394.

Haga, S. B., O'Daniel, J. M., Tindall, G. M., Lipkus, I. R., & Agans, R. (2012b). Survey of US public attitudes towards pharmacogenetic testing. *The Pharmacogenomics Journal, 12*(3), 197-204.

Haga, S. B., Tindall, G., & O'Daniel, J. M. (2012c). Professional perspectives about pharmacogenetic testing and managing ancillary findings. *Genetic Testing and Molecular Biomarkers, 16*(1), 21-24.

Hagymási, K., Müllner, K., Herszényi, L., & Tulassay, Z. (2011). Update on the pharmacogenomics of proton pump inhibitors. *Pharmacogenomics, 12*(6), 873-888.

Helitzer, D., Heath, D., Maltrud, K., Sullivan, E., & Alverson, D. (2003). Assessing or predicting adoption of telehealth using the diffusion of innovations theory: A practical example from a rural program in New Mexico. *Telemedicine Journal and e-Health, 9*(2), 179-187.

Henneman, L., Timmermans, D. R., & Van der Wal, G. (2004). Public experiences, knowledge and expectations about medical genetics and the use of genetic information. *Public Health Genomics, 7*(1), 33-43.

Henneman, L., Timmermans, D. R., & Wal, G. V. D. (2006). Public attitudes toward genetic testing: Perceived benefits and objections. *Genetic Testing, 10*(2), 139-145.

Hu, L. t. & Bentler, P. M. (1999). Cutoff criteria for fit indexes in covariance structure analysis: Conventional criteria versus new alternatives. *Structural Equation Modeling: A Multidisciplinary Journal, 6*(1), 1-55.

Jarque, C. M. & Bera, A. K. (1987). A test for normality of observations and regression residuals. *International Statistical Review/Revue Internationale de Statistique, 55*(2), 163-172.

Kadafour, M., Haugh, R., Posin, M., Kayser, S. R., & Shin, J. (2009). Survey on warfarin pharmacogenetic testing among anticoagulation providers. *Pharmacogenomics, 10*(11), 1853-1860.

Kitzmiller, J. P., Groen, D. K., Phelps, M. A., & Sadee, W. (2011). Pharmacogenomic testing: Relevance in medical practice: Why drugs work in some patients but not in others. *Cleveland Clinic Journal of Medicine, 78*(4), 243.

Klitzman, R., Chung, W., Marder, K., Shanmugham, A., Chin, L. J., Stark, M., et al. (2013). Attitudes and practices among internists concerning genetic testing. *Journal of Genetic Counseling, 22*(1), 90-100.

Kobayashi, E. & Satoh, N. (2009). Public involvement in pharmacogenomics research: A national survey on public attitudes towards pharmacogenomics research and the willingness to donate DNA samples to a DNA bank in Japan. *Cell and Tissue Banking, 10*(4), 281-291.

Kripalani, S., Yao, X., & Haynes, R. B. (2007). Interventions to enhance medication adherence in chronic medical conditions: A systematic review. *Archives of Internal Medicine, 167*(6), 540-549.

Kudzi, W., Addy, B., & Dzudzor, B. (2015). Knowledge of pharmacogenetics among healthcare professionals and faculty members of health training institutions in Ghana. *Ghana Medical Journal, 49*(1), 50-56.

Lachance, K., Korol, S., O'meara, E., Ducharme, A., Racine, N., Liszkowski, M., et al. (2015). Opinions, hopes and concerns regarding pharmacogenomics: A comparison of healthy individuals, heart failure patients and heart transplant recipients. *The Pharmacogenomics Journal, 15*(1), 13-19.

Lanktree, M. B., Zai, G., VanderBeek, L. E., Giuffra, D. E., Smithson, D. S., Kipp, L. B., et al. (2014). Positive perception of pharmacogenetic testing for psychotropic medications. *Human Psychopharmacology, 29*(3), 287-291.

Lazaridis, K. N. & Petersen, G. M. (2005). Genomics, genetic epidemiology, and genomic medicine. *Clinical Gastroenterology and Hepatology, 3*(4), 320-328.

Lazarou, J., Pomeranz, B. H., & Corey, P. N. (1998). Incidence of adverse drug reactions in hospitalized patients: A meta-analysis of prospective studies. *Journal of the American Medical Association, 279*(15), 1200-1205.

Lee, C. R., Goldstein, J. A., & Pieper, J. A. (2002). Cytochrome P450 2C9 polymorphisms: A comprehensive review of the in-vitro and human data. *Pharmacogenetics and Genomics, 12*(3), 251-263.

Levene, H. (1960). Robust tests for equality of variances. In *Contributions to Probability and Statistics* (Vol. 1). Palo Alto, CA: Stanford University Press.

Levin, K. A. (2006). Study design III: Cross-sectional studies. *Evidence-Based Dentistry, 7*(1), 24-25.

Ma, T. K., Lam, Y. Y., Tan, V. P., & Yan, B. P. (2011). Variability in response to clopidogrel: How important are pharmacogenetics and drug interactions? *British Journal of Clinical Pharmacology, 72*(4), 697-706.

Manolio, T. A., Brooks, L. D., & Collins, F. S. (2008). A HapMap harvest of insights into the genetics of common disease. *The Journal of Clinical Investigation, 118*(5), 1590-1605.

McWilliam, A., Lutter, R., & Nardinelli, C. (2006). *Health Care Savings from Personalizing Medicine Using Genetic Testing: The Case of Warfarin*. Washington, D.C.: AEI-Brookings Joint Center for Regulatory Studies.

Miki, Y., Swensen, J., Shattuck-Eidens, D., Futreal, P., Harshman, K., Tavtigian, S., et al. (1994). A strong candidate for the breast and ovarian cancer susceptibility gene BRCA1. *Science, 266*(5182), 66-71.

Mills, R., Voora, D., Peyser, B., & Haga, S. B. (2013). Delivering pharmacogenetic testing in a primary care setting. *Pharmacogenomics and Personalized Medicine, 6*, 105-112.

Moaddeb, J. & Haga, S. B. (2013). Pharmacogenetic testing: Current evidence of clinical utility. *Therapeutic Advances in Drug Safety, 4*(4), 155-169.

Moaddeb, J., Mills, R., & Haga, S. B. (2015). Community pharmacists' experience with pharmacogenetic testing. *Journal of the American Pharmacists Association, 55*(6), 587-594.

Morren, M., Rijken, M., Baanders, A. N., & Bensing, J. (2007). Perceived genetic knowledge, attitudes towards genetic testing, and the relationship between these among patients with a chronic disease. *Patient Education and Counseling, 65*(2), 197-204.

Murphy, S. L., Xu, J., & Kochanek, K. D. (2012). Deaths: Preliminary data for 2010. Retrieved from https://pdfs.semanticscholar.org/3e72/c0cafc21400569b34331d2d4fed8ae96d78b.pdf

Nalls, M. A., Saad, M., Noyce, A. J., Keller, M. F., Schrag, A., Bestwick, J. P., et al. (2013). Genetic comorbidities in Parkinson's disease. *Human Molecular Genetics, 23*(3), 831-841.

National Center for Health Statistics (2011). Health, United States, 2010: With special feature on death and dying. Retrieved from https://www.cdc.gov/nchs/data/hus/hus10.pdf

Nebert, D. W. (1999). Pharmacogenetics and pharmacogenomics: Why is this relevant to the clinical geneticist? *Clinical Genetics, 56*(4), 247-258.

Nielsen, L. F. & Moldrup, C. (2007). The diffusion of innovation: Factors influencing the uptake of pharmacogenetics. *Public Health Genomics, 10*(4), 231-241.

Nunnally, J. & Bernstein, I. (1994). *Psychometric Theory* (3rd ed.). New York, NY: McGraw-Hill, Inc.

Or, C. K. & Karsh, B.-T. (2009). A systematic review of patient acceptance of consumer health information technology. *Journal of the American Medical Informatics Association, 16*(4), 550-560.

Østbye, T., Yarnall, K. S., Krause, K. M., Pollak, K. I., Gradison, M., & Michener, J. L. (2005). Is there time for management of patients with chronic diseases in primary care? *The Annals of Family Medicine, 3*(3), 209-214.

Owczarek, J., Jasiñska, M., & Orszulak-Michalak, D. (2005). Drug-induced myopathies. An overview of the possible mechanisms. *Pharmacological Reports, 57*(1), 23-34.

Perlis, R. H., Patrick, A., Smoller, J. W., & Wang, P. S. (2009). When is pharmacogenetic testing for antidepressant response ready for the clinic? A cost-effectiveness analysis based on data from the STAR* D study. *Neuropsychopharmacology, 34*(10), 2227-2236.

Powell, K. P., Cogswell, W. A., Christianson, C. A., Dave, G., Verma, A., Eubanks, S., et al. (2012). Primary care physicians' awareness, experience and opinions of direct-to-consumer genetic testing. *Journal of Genetic Counseling, 21*(1), 113-126.

Priest, V. L., Begg, E. J., Gardiner, S. J., Frampton, C. M., Gearry, R. B., Barclay, M. L., et al. (2006). Pharmacoeconomic analyses of azathioprine, methotrexate and prospective pharmacogenetic testing for the management of inflammatory bowel disease. *Pharmacoeconomics, 24*(8), 767-781.

Relling, M. & Klein, T. (2011). CPIC: Clinical pharmacogenetics implementation consortium of the pharmacogenomics research network. *Clinical Pharmacology and Therapeutics, 89*(3), 464-467.

Roden, D. M. & George Jr, A. L. (2002). The genetic basis of variability in drug responses. *Nature Reviews Drug Discovery, 1*(1), 37-44.

Roden, D. M., Wilke, R. A., Kroemer, H. K., & Stein, C. M. (2011). Pharmacogenomics: The genetics of variable drug responses. *Circulation, 123*(15), 1661-1670.

Roederer, M. W., Van Riper, M., Valgus, J., Knafl, G., & McLeod, H. (2012). Knowledge, attitudes and education of pharmacists regarding pharmacogenetic testing. *Personalized Medicine, 9*(1), 19-27.

Rogausch, A., Prause, D., Schallenberg, A., Brockmöller, J., & Himmel, W. (2006). Patients' and physicians' perspectives on pharmacogenetic testing. *Pharmacogenomics, 7*(1), 49-59.

Rogers, E. M. (2003). *Diffusion of Innovations* (5th ed.). New York, NY: Free Press.

Shah, J. (2004). Recent developments: Criteria influencing the clinical uptake of pharmacogenomic strategies. *British Medical Journal, 328*(7454), 1482-1486.

Shaphiro, S. & Wilk, M. (1965). An analysis of variance test for normality. *Biometrika Trust, 52*(3), 591-611.

Shaw, K., Amstutz, U., & Carleton, B. C. (2011). Using pharmacogenetics to understand adverse drug reactions in children. *Paediatrics and Child Health, 16*(9), 537-538.

Shields, A. E., Blumenthal, D., Weiss, K. B., Comstock, C. B., Currivan, D., & Lerman, C. (2005). Barriers to translating emerging genetic research on smoking into clinical practice. *Journal of General Internal Medicine, 20*(2), 131-138.

Shiffman, D., Trompet, S., Louie, J. Z., Rowland, C. M., Catanese, J. J., Iakoubova, O. A., et al. (2012). Genome-wide study of gene variants associated with differential cardiovascular event reduction by pravastatin therapy. *PLoS One, 7*(5), e38240.

Shishko, I., Almeida, K., Silvia, R. J., & Tataronis, G. R. (2015). Psychiatric pharmacists' perception on the use of pharmacogenomic testing in the mental health population. *Pharmacogenomics, 16*(9), 949-958.

Smith, K. L. & Isaacs, C. (2011). BRCA mutation testing in determining breast cancer therapy. *The Cancer Journal, 17*(6), 492.

Spear, B. B., Heath-Chiozzi, M., & Huff, J. (2001). Clinical application of pharmacogenetics. *Trends in Molecular Medicine, 7*(5), 201-204.

Srivastava, P. (2003). Drug metabolism and individualized medicine. *Current Drug Metabolism, 4*(1), 33-44.

Stanek, E. J., Sanders, C. L., & Frueh, F. W. (2013). Physician awareness and utilization of food and drug administration (FDA)-approved labeling for pharmacogenomic testing information. *Journal of Personalized Medicine, 3*(2), 111-123.

Stanek, E., Sanders, C., Taber, K., Khalid, M., Patel, A., Verbrugge, R., et al. (2012). Adoption of pharmacogenomic testing by US physicians: Results of a nationwide survey. *Clinical Pharmacology and Therapeutics, 91*(3), 450-458.

Steiger, J. H. (2007). Understanding the limitations of global fit assessment in structural equation modeling. *Personality and Individual Differences, 42*(5), 893-898.

Stevenson, F. A., Cox, K., Britten, N., & Dundar, Y. (2004). A systematic review of the research on communication between patients and health care professionals about medicines: The consequences for concordance. *Health Expectations, 7*(3), 235-245.

Swen, J., Nijenhuis, M., Boer, A. d., Grandia, L., Maitland-van der Zee, A.-H., Mulder, H., et al. (2011). Pharmacogenetics: From bench to byte—an update of guidelines. *Clinical Pharmacology and Therapeutics, 89*(5), 662-673.

Taber, K. A. J. & Dickinson, B. D. (2014). Pharmacogenomic knowledge gaps and educational resource needs among physicians in selected specialties. *Pharmacogenomics and Personalized Medicine, 7*, 145-162.

Table of pharmacogenomic biomarkers in drug labeling (2017). Retrieved from https://www.fda.gov/drugs/scienceresearch/researchareas/pharmacogenetics/ucm083378.htm

Thompson, J., Man, M., Johnson, K., Wood, L., Lira, M., Lloyd, D., et al. (2005). An association study of 43 SNPs in 16 candidate genes with atorvastatin response. *The Pharmacogenomics Journal, 5*(6), 352.

Tomalik-Scharte, D., Lazar, A., Fuhr, U., & Kirchheiner, J. (2008). The clinical role of genetic polymorphisms in drug-metabolizing enzymes. *The Pharmacogenomics Journal, 8*(1), 4-15.

Tornatzky, L. G. & Klein, K. J. (1982). Innovation characteristics and innovation adoption-implementation: A meta-analysis of findings. *IEEE Transactions on Engineering Management, 29*(1), 28-45.

Trinidad, S. B., Coffin, T. B., Fullerton, S. M., Ralston, J., Jarvik, G. P., & Larson, E. B. (2015). "Getting off the bus closer to your destination": Patients' views about pharmacogenetic testing. *The Permanente Journal, 19*(3), 21-27.

Vacha-Haase, T., Kogan, L. R., & Thompson, B. (2000). Sample compositions and variabilities in published studies versus those in test manuals: Validity of score reliability inductions. *Educational and Psychological Measurement, 60*(4), 509-522.

Vogel, F. (1959). Moderne probleme der humangenetik. In *Ergebnisse der Iinneren Medizin und Kinderheilkunde*. Berlin, Heidelberg: Springer Berlin Heidelberg, pp. 52-125.

Vogenberg, F. R., Barash, C. I., & Pursel, M. (2010). Personalized medicine, Part 1: Evolution and development into theranostics. *Pharmacy and Therapeutics, 35*(10), 560-562.

Walden, L. M., Brandl, E. J., Changasi, A., Sturgess, J. E., Soibel, A., Notario, J. F. D., et al. (2015). Physicians' opinions following pharmacogenetic testing for psychotropic medication. *Psychiatry Research, 229*(3), 913-918.

Wang, L., McLeod, H. L., & Weinshilboum, R. M. (2011). Genomics and drug response. *New England Journal of Medicine, 364*(12), 1144-1153.

Ward, B. W., Schiller, J. S., & Goodman, R. A. (2014). Multiple chronic conditions among US adults: A 2012 update. *Preventing Chronic Disease, 11*.

Wen, M.-S. & Lee, M. T. M. (2013). Warfarin pharmacogenetics: New life for an old drug. *Acta Cardiologica Sinica, 29*(3), 235-242.

World Health Organization (1994). The role of the pharmacist in the health care system. Retrieved from http://apps.who.int/medicinedocs/en/d/Jh2995e/1.6. html #Jh2995e.1.6

Wright, S. (1921). Correlation and causation. *Journal of Agricultural Research, 20*(7), 557-585.

Zhang, S. C., Bruce, C., Hayden, M., & Rieder, M. J. (2014). Public perceptions of pharmacogenetics. *Pediatrics, 133*(5), e1258-e1267.

Zhang, X., Yu, P., Yan, J., & Spil, I. T. A. (2015). Using diffusion of innovation theory to understand the factors impacting patient acceptance and use of consumer e-health innovations: A case study in a primary care clinic. *BMC Health Services Research, 15*(1), 71.

CURRICULUM VITAE 2017

SUHAIB M. MUFLIH

PERSONAL INFORMATION

Address:	10237 SW 59 St, Cooper City, Florida
	Tel: 954-395-6500
	Email: sm2341@mynsu.nova.edu
Date of Birth:	January 22nd, 1985
Nationality:	Jordanian
Marital Status:	Married

EDUCATION

Year	**Institution**
2012 - 2017	Doctor of Philosophy Nova Southeastern University Fort Lauderdale, Florida
2010 - 2012	Pharmacy Intern Iowa University Hospital Iowa City, Iowa
2003 - 2009	Doctor of Pharmacy Jordan University of Science and Technology Irbid - Jordan
2002 - 2003	General Secondary Certificate Khalid Ibn AL-Waleed High School Irbid - Jordan

SKILLS AND LANGUAGES

Computer Skills	Internet
	Microsoft Word, Excel, Power point
Languages	English: Excellent
	Arabic: Excellent
Statistical Software	IBM SPSS®
	Stata

EXPERIENCES

2015 - 2016	Class Facilitator/ Microbiology and Pharmacotherapy/ NSU, Florida
2014 - 2017	Primary Data Collection Survey Construction and Validation Statistical Analyses Grant Review Experience
2011- 2012	Pharmacy internship, University of Iowa Hospitals and Clinics: - Training for providing clinical consultative services to patients and therapeutic recommendations to nurses and physicians - Training for the sterile compounding and aseptic techniques
2009 - 2010	Teaching Assistant, Department of Clinical Pharmacy, Jordan University of Science and Technology
2009 - 2010	Supervising PharmD and Msc Clinical Pharmacy Students: Cardiology and Endocrinology Rotations at King Abdullah University Hospital (KAUH) and other local hospitals, Jordan
2008 - 2009	Community Pharmacy Training, Platinum Pharmacy, Irbid - Jordan
2007 - 2008	Hospital Pharmacy Training, Princess Basma Hospital, Irbid - Jordan

PROFESSIONAL MEMBERSHIPS

- The Jordanian Association of Pharmacy (JPA)
- Pharmacy Graduate PhD Association-SGA
- The Rho Chi Pharmacy Honor Society
- American Society of Health-System Pharmacists (ASHP)
- International Society For Pharmacoeconomics and Outcomes Research (ISPOR)
- American Association of Colleges of Pharmacy (AACP)
- Florida Society of Health-System Pharmacists (FSHP)
- The American Pharmacists Association (APhA)
- American College of Clinical Pharmacy (ACCP)

WORKSHOPS

January 2016	Faculty Development Workshops. NSU-Fort Lauderdale, Florida
March 2014	Institutional Review Board Workshop. NSU-Fort Lauderdale, Florida
February 2014	Grant Workshop. NSU-Fort Lauderdale, Florida
April 2010	Updates in Therapeutics. American college of clinical pharmacy (ACCP). Charlotte, North Carolina
December 2009	Drug Information Resources, Jordan Pharmaceutical Association. Amman - Jordan

ACTIVITIES AND COMMUNITY SERVICES

April 2016	Heart Walk/ NSU-Fort Lauderdale, Florida
February 2016	Conference Moderator at NSU Research Day. Fort Lauderdale, Florida
February 2016	Community Festival. NSU-Fort Lauderdale, Florida
August 2009 - January 2010	Primary Data Collector as a part of the Medicine Transparency Alliance (MeTA) Project held by the World Health Organization (WHO) and High Health Council (HHC). Collecting data regarding medicine availability, affordability, accessibility and rational use among randomized sample of the population. Amman - Jordan

SERVICES TO STUDENTS

2015 - 2016	President/International Society for Pharmacoeconomics and Outcomes Research (ISPOR)
2009 - 2016	Student Tutoring

RESEARCH OF INTEREST

- Pharmacogenetics
- Clinical Pharmacy
- Outcome Research
- Sociobehavioral aspects of Pharmacy

PUBLICATIONS

- Alameddine, S., **Muflih, S.**, Hale, G., & Khanfar, N. M. (2016). Development and Implementation of Customized Intravenous to Oral Conversion Protocol: Cost-Saving Analysis. *Value in Health*, 19(3), A272. DOI: 10.1016/j.jval.2016.03.879.
- Halum, A. S., Bhinder, M. T. M., Shawaqfeh, M. S., & **Muflih, S. M**. (2016). An In-Depth Look at the Clinical Relevance of Pharmacogenetic Testing Ascertained. *Journal of Molecular and Genetic Medicine*, 2016. DOI: 10.4172/1747-0862.1000210.
- Shawaqfeh, M. S., Bhinder, M. T., Halum, A. S., Harrington, C., & **Muflih, S**. (2015). Adverse Drug Events Related to Canagliflozin: A Meta-Analysis of Randomized, Placebo-Controlled Trials. *Advances Pharmacoepidemiology and Drug Safety*, 4(196), 2167-1052. DOI:10.4172/2167-1052.1000196.
- Bhinder, M. T. M., Halum, A. S., **Muflih, S. M**., & Shawaqfeh, M. (2015). Pharmacogenetic Testing for Methotrexate Treatment in Leukemia Patients. *Journal of Biomolecular Research & Therapeutics*, 4(134), 2. DOI:10.4172/2167-7956.1000134.
- Al-Azzam, S. I., AlOmari, M., Khader, Y. S., AlMahasneh, F. A., **Muflih, S. M**., & Altawalbeh, S. (2012). Effects of pioglitazone add-on to gliclazide and metformin on glycemic control in patients with type 2 diabetes. *Endocrine research*, 37(1), 7-11. DOI: 10.3109/07435800.2011.566238.

POSTERS PRESENTED IN SCIENTIFIC MEETING

- **Muflih, S.**, Bleidt, B., Popovici, I., & Khanfar, NM. (2017, November). *Community physicians' knowledge and attitudes towards pharmacogenetic testing*. Poster session will be presented at the American Public Health Association 145th Annual Meeting, Atlanta, GA.
- **Muflih, S.**, Bleidt, B., Khanfar, NM., & Popovici, I. (2017, March). *Measuring knowledge and attitudes regarding the use of pharmacogenetic testing among patients*. Poster session presented at the American Pharmacists Association 164th Annual Meeting, San Francisco, CA.
- **Muflih, S.**, Bleidt, B., Khanfar, NM., & Popovici, I. (2016, December). *Measuring knowledge and attitudes regarding the use of pharmacogenetic testing among physicians*. Poster session presented at the American Society of Health-System Pharmacists 51st Annual Midyear Clinical Meeting, Las Vegas, NV.

- Sherbeny, F., **Muflih, S.**, & Barry, B. (2016, December). *Pharmacist's Role in HF Patient's Transition of Care: RCT*. Poster session presented at the American Society of Health-System Pharmacists 51st Annual Midyear Clinical Meeting, Las Vegas, NV.
- **Muflih, S.**, Bleidt, B., Khanfar, NM., & Popovici, I. (2016, October). *Measuring Knowledge and Attitudes Regarding the Use of Pharmacogenetic Testing among Patients and Prescribers: Diffusion of Innovation Theory*. Poster session presented at the American College of Clinical Pharmacy 45th Annual Meeting, Hollywood, FL.
- Hale, G., **Muflih, S**., Alameddine, S., & Khanfar, NM. (2016, October). *Prescribing Patterns of Thiazide Diuretics*. Poster session presented at the American College of Clinical Pharmacy 45th Annual Meeting, Hollywood, Florida.
- **Muflih, S.**, Bleidt, B., Khanfar, NM., Popovici I., & Sanchez, J. (2016, August). *Knowledge and attitudes regarding the use of pharmacogenetic testing among patients and physicians: a systematic review*. Poster session presented at the Florida Society of Health-System Pharmacists 50th Annual Meeting, Orlando, FL.
- Alameddine, S., **Muflih, S**., Hale, G., & Khanfar, N. M. (2016, May). *Development and Implementation of Customized Intravenous to Oral Conversion Protocol: Cost-Saving Analysis*. Poster session presented at the International Society for Pharmacoeconomics and Outcomes Research 21st Annual Meeting, Washington, DC.
- **Muflih, S.**, Khanfar, NM., Shawaqfeh, M., Bleidt, B., & Popovici I. (2016, February). *Knowledge and attitudes towards pharmacogenetic testing among a cohort of patients and prescribers: diffusion of innovation theory*. Poster session presented at the NSU Research Day, Fort Lauderdale, FL.
- **Muflih, S.**, Fore, J., Shawaqfeh, M., & Khanfar, NM. (2016, February). *Literature Based Evidence of the Clinical Relevance of Pharmacogenetic Testing for Simvastatin*. Poster session presented at the NSU Research Day, Fort Lauderdale, FL.
- **Muflih, S.**, Khanfar, NM., Shawaqfeh, M., Bleidt, B., & Popovici, I. (2015, December). *Knowledge and attitudes towards pharmacogenetic testing among a cohort of patients and prescribers: diffusion of innovation theory.* Poster session presented at: American Society of Health-System Pharmacists 50th Annual Midyear Clinical Meeting, New Orleans, LA.

RESEARCH IN PROGRESS

- Measuring Patients' Knowledge and Attitudes towards Pharmacogenetic Testing: Diffusion of Innovation Theory
- Measuring Physicians' Knowledge and Attitudes towards Pharmacogenetic Testing: Diffusion of Innovation Theory
- Knowledge and Attitudes regarding the Use of Pharmacogenetic Testing Among Patients: A Systematic Review
- Knowledge and Attitudes regarding the Use of Pharmacogenetic Testing among Physicians: A Systematic Review
- Literature Based Evidence of the Clinical Relevance of Pharmacogenetic Testing for Simvastatin"
- Prescribing Patterns of Thiazide Diuretics
- Impact Of IV to PO Antibiotic Conversion on Cost Saving

LOCAL CONFERENCES

- The 12th International Association for chronic fatigue syndrome/myalgic encephalomyelitis Research and Clinical Conference: Emerging Science and Clinical Care conference; October, 2016. Nova Southeastern University, Florida
- Future of Medicine Summit/ the 10th Anniversary; September, 2016; Palm Beach County Convention Center, Florida
- Emerging Challenges in Primary Care/ the 15th Annual Conference; September, 2016. Fort Lauderdale Marriott Coral Springs
- The Medical Marijuana Program; August, 2016. Nova Southeastern University, Florida

GRANTS

- October 2016: Awarded received from PanSGA Professional Development Grant to present at the 2016 ACCP Annual Meeting, 10/23/2016 to 10/26/2016. Measuring Knowledge and Attitudes Regarding the Use of Pharmacogenetic Testing Among Patients and Prescribers: Diffusion of Innovation Theory
- June 2016: Awarded $4,990 by HPD Research Committee. Measuring knowledge and attitudes regarding the use of pharmacogenetic testing among patients and prescribers: diffusion of innovation theory
- February 2016: Awarded $450 from Pan SGA Professional Development Grant to present at the 2015 ASHP Midyear Clinical Meeting, 12/06/2015-12/10/2015. Knowledge and attitudes towards pharmacogenetic testing among a cohort of patients and prescribers: diffusion of innovation theory (New Orleans, LA)

POINTS OF INTERESTS

- I am interested the outcomes of therapeutics using Pharmacogenetic testing.
- I am interested in continuing to learn more about pharmacoepidemiological research and the outcomes of therapeutics
- I am interested in doing research about good pharmacy practice especially the collaboration between physicians and pharmacists to choose the best healthcare plan that decrease the economic burden on healthcare system
- I am interested in conducting more research on knowledge and attitudes towards pharmacogenetic testing among patients, pharmacists, and prescribers using diffusion of innovation theory

AWARDS AND HONORS

- February 2016: Award received for poster presentation, HPD Research Day. The award is given for the outstanding poster presentation of my research titled Knowledge and attitudes towards pharmacogenetic testing among a cohort of patients and prescribers: diffusion of innovation theory, during NSU Research Day, held on February 12, 2016
- September 2014: Member of Rho Chi national pharmacy honor society

HOBBIES

- Swimming, Kayaking, Biking, Ping Pong, Chess