PHARMACOGENOMICS IN PRIMARY CARE: BARRIERS TO IMPLEMENTATION

A Scholarly Project

Submitted to the

Faculty of Liberty University

In partial fulfillment of

The requirements for the degree

Of Doctor of Nursing Practice

By

Joshua Michael Fleming

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Scholarly Project Chair Approval:

Kenneth D. Thompson, Pharm.D.

ABSTRACT

As technology and research evolve it is essential that practitioners in healthcare remain aware and cognizant of the changes that are going on around them and how these advancements may aid them in providing the best care to the patients that seek care from them. The largest breakthrough in the field of genetics has been the complete sequencing of the human genome. This landmark has paved the way for innumerable insights into every part of how care is delivered and stands to change the landscape of medicine entirely. Pharmacogenomics testing exists as a subset of genetic testing, and pertains to the evaluation of individual genetic variants that may interfere with the normal metabolism of many medications. There are specialty care settings where this modality of testing is more prevalent, but it is not well represented in primary care settings, where it stands to provide a wealth of information to primary care providers as they manage their patients. Literature review was conducted on this subject of interest and it was found that there was precedent for the implementation of pharmacogenomics testing in the primary care setting. Through survey of primary care providers, it was determined that there were deficits in knowledge and perspective barriers that were adequately addressed with an educational intervention. This intervention was shown to promote both the potential implementation of pharmacogenomics testing, generate interest in further education on the subject of pharmacogenomics, and address the identified perspective barriers.

Keywords: Pharmacogenomics, pharmacogenomics cost-effectiveness, pharmacogenomics in primary care, implementation of pharmacogenomics

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Pharmacogenomics (PGx)

Nurse Practitioner (NP)

Medical Doctor (MD)

Physician Assistant (PA)

SECTION ONE: INTRODUCTION

The field of pharmacogenomics is a branch of genetics testing that focuses on the way in which genetic variants affect the different aspects of drug metabolism, which can produce a continuum of negative effects in individuals that possess these variants who are taking these medications currently or may take them in the future. While this testing is widely available to be utilized in clinical practice there is not yet widespread adoption into clinical practice. Pharmacogenomics testing is a young field of research that has great promise for positively changing the way in which medicine is practiced in many ways. It holds the possibility of preventing potentially dangerous or life-threatening medication-related adverse events, promotes cost-effective care for patients, promotes increased patient agency in the care team, creates opportunity for deeper insight into effective management strategies for providers to utilize, promotes preventative versus reactive management of patients, and deepens the overall understanding of how vitally important the field of genetics is to the next steps of healthcare overall.

While there is a large precedent and growing volume of knowledge regarding the benefits of utilizing pharmacogenomics testing in the clinical setting, there are well-studied barriers to the widespread adoption and implementation of this type of testing. There have been many advancements in the field of pharmacogenomics to address these various barriers, but the prevalence of this testing has remained low. There is little evidence on the subject of the effects of a targeted educational intervention that addresses the most common themes that stand as barriers to the implementation and adoption of pharmacogenomics in the primary care setting. The effects of a targeted educational intervention that addresses these barriers needs to be understood for conclusions to be drawn regarding approaches to these barriers in future research

and implementation projects. Therefore, a quasi-experimental study was conducted to determine

the effects of a synthesized educational intervention regarding pharmacogenomics on primary

care providers through comparative analysis of differences between pre and post surveys that

evaluate the perspectives and level of understanding in these providers.

Background

There have been approximately 20 genes that have been evaluated to affect a vast amount

of prescription medications to varying levels of degree. This type of testing focuses on the

identification of genetic variation that affects different aspects of drug metabolism, absorption,

distribution, and elimination. There are also genetic variances known to affect

pharmacodynamics, which disturbs the biological pathways and can represent why patients may

have stronger side effects from certain therapies. Initially, the clinical utilization of

pharmacogenomics testing was through the deployment of monogenic testing on a reactive basis

such as the prescription of pharmacogenetically high-risk drugs. This has, however, proved to be

ineffective and costly, especially in light of advancements in sequencing technology that has

allowed for multiple gene variants to be interrogated simultaneously. There are many potential

cases where multiple genetic variants need to be assessed to understand patients' risk of adverse

outcomes, and because of this the standard has been shifted towards the standardized testing for

many polymorphisms simultaneously to generate the largest amount of actionable data for care

to be correctly guided (Relling & Evans, 2017).

Historically there have been many noted barriers to the translation of research into

clinical practice for pharmacogenomics testing. There is a lack of incentive for clinicians to order

testing for their patients to prevent adverse events, lack of knowledge regarding the use and

interpretation of this testing, lack of clear and definable clinical guidelines that creates actionable

recommendations for the provider to change therapy, lack of formal education implemented in educational curriculum, and lack of laboratories that provide this service, which can be attributed, in part, to the relatively young field of pharmacogenomics testing (Relling & Evans, 2017).

Adherence to prescribed pharmacotherapies is a prevalent problem in any setting, and a recent study at the Mayo Clinic found that 91% of the 1,010 participants reported that they would be more likely to use medications as they are prescribed if the medications were chosen through pharmacogenomics testing (Olson et al., 2017). Clinical validity and utility for pharmacogenomics testing has also been validated through the positive effects that have been evaluated through the ability to predict non-efficacious treatments, as well as providing effective predictions that improve clinical outcomes (Benitez, Jablonski, Allen, & Winner, 2015). These clinical outcomes include previously mentioned possible improvements in medication adherence along with reductions in rates of polypharmacy and avoidance of adverse reactions to medications. The avoidance of adverse drug reactions categorically has the potential for some of greatest impact on clinical validity and utility in pharmacogenomics testing, which has the capacity to comprehensively and accurately assess this type of risk in patients who receive this testing (Phillips, Veenstra, Oren, Lee, & Sadee, 2001).

One of the strongest established barriers regarding the implementation of pharmacogenomics testing in the clinical setting has been the economic implications of this testing and the unclear return on investment with this new means of insight (Wong, Carlson, Thariani, & Veenstra, 2010). Contributing to this issue is the lack of significant insights into the clinical utility and validity of this new testing tool, which is inevitably complicated by the lack of widespread implementation, study, and adherence to recommendations that are based on testing

itself (Berm et al., 2016; Sauver et al., 2016). However, there have been helpful breakthroughs on this discussion of economic utility in the implementation of pharmacogenomics testing that stand to address this issue thoroughly. Berm et al. (2016) found through systematic review of 80 previous studies centered around the cost-effectiveness of pharmacogenomics testing that there was substantial evidence in the majority of evaluated studies that this was not only cost effective but also promoted better clinical outcomes. This review was based on previous evidence that supported the cost effectiveness of pharmacogenomics testing, but did find inconclusive data regarding the clinical utility and validity of testing in some of the evaluated studies (Wong, Carlson, Thariani, & Veenstra, 2010). In another systematic review it was found that there was strong evidence for the utilization of pharmacogenomics testing towards the goal of preventing adverse drug reactions for specific pharmacotherapies (Pumpton, Roberts, Pirmohamed, & Hughes, 2016). It was established in all of these reviews that a limitation of the results that were evaluated was the absolute dependence on comprehensive and accurately reported data from implementation projects on which the outcomes of cost-effectiveness, clinical validity, and improvement in clinical outcomes was based (Berm et al., 2016; Pumpton, Roberts, Pirmohamed, & Hughes, 2016; Wong, Carlson, Thariani, & Veenstra, 2010).

These findings are the basis for an educational intervention being targeted towards addressing the knowledge base as well as the perspectives of providers in the clinical environment. Sauver et al. (2016) highlighted the complications of poor understanding and false perspectives regarding pharmacogenomics, with 52% of clinicians not understanding how to incorporate pharmacogenomics into their future practice along with not expecting this incorporation to take place at all. Additionally, it was found that 53% of the surveyed clinicians had very poor responses to the clinical decision tools set in place to alert them of possible

changes in management, and only 30% of the surveyed clinicians changed their

pharmacotherapy to a different agent based on the recommendations supplied by

pharmacogenomics testing (Sauver et al., 2016). Potential clarification for these findings was

provided through the surveying of healthcare professionals in a different context, which revealed

that while a vast majority of the participants believed that pharmacogenomics was relevant to

their clinical practice, there were very few cases of personal implementation of this testing due to

variables such as interpretation of testing results and knowledge regarding basic principles of

pharmacogenomics (Just et al., 2017).

Due to these factors and variables it has been established that the phenomenon of interest

relating to pharmacogenomics testing include the barriers of poor understanding and negative

perspectives from providers who can provide the testing. There have been initiatives regarding

pharmacogenomics education that have proven to be innovative in their approach and effective at

promoting an enhanced understanding of pharmacogenomics testing (Adams et al., 2016). To

understand the efficacy of pharmacogenomics testing and how to best implement this new

management tool into clinical practice the barriers that exist need to be investigated and

addressed comprehensively.

Problem Statement

There is a vast amount of evidence that exists to support the widespread implementation

of pharmacogenomics testing in regular evaluation and management of patients seeking primary

care, as there are many known and potential benefits through the use of this testing. The barriers

that stand in the way of appropriate translation of research into clinical practice need to be

evaluated thoroughly to appropriately address these variables and implement pharmacogenomics

testing effectively in the primary care setting. There is evidence in the literature regarding the

barriers that exist, but insight needs to be drawn from these findings to create an intervention that should then be validated and refined through further research and implementation.

Purpose of the Project

The purpose of this project is to evaluate the impact of a targeted educational intervention on a population of primary care providers' perspectives and levels of understanding. This will be accomplished through establishing the barriers that are found in the literature that historically stand against the implementation of pharmacogenomics testing, and comparing these findings with the specific barriers that are found within the population of interest by means of surveying. These survey results will be combined with what is known in the literature to provide a targeted educational intervention that is comprehensive while being contextual to the specific needs of the population being studied. The project's primary objective is to evaluate the efficacy of a targeted educational intervention at addressing the barriers to implementation of pharmacogenomics testing in clinical practice.

Clinical Question

How does a targeted educational intervention affect the reported level of understanding and perspectives for providers in a primary care setting?

SECTION TWO: LITERATURE REVIEW
Search Strategy

Systematic search through the literature for original research regarding the subject of pharmacogenomics was conducted. The evaluated databases included ProQuest, ScienceDirect, Public Library of Science, ClinicalKey, SpringerLink, and JAMA Network. The search terms used to procure evidence included "pharmacogenomics", "pharmacogenomics cost-

effectiveness", "pharmacogenomics in primary care", "pharmacogenomics in primary care", and

"implementation of pharmacogenomics". Filters utilized for the review of relevant material

included articles that were published in the English language within the last 10 years. Articles

older than 10 years were not included due to the lack of relevance to the subject of

pharmacogenomics presently. One article that does not meet the aforementioned filters was

included for deeper background and historical context regarding the subject matter. A total of 37

studies were found and of these 15 were kept for final review. The studies that were kept for

inclusion were those that had relevance to the variables that stand as barriers to the

implementation of pharmacogenomics, which are being assessed in this project. The studies

included in this literature review discuss main points of interest in the themes identified as being

important in the evaluation of pharmacogenomics testing.

The studies included in the literature review contained several systematic reviews, which

contributed to important conclusions regarding the variables of cost-effectiveness of

pharmacogenomics testing in clinical use, as well as the clinical validity and utility of this testing

(Berm et al., 2016; Pumpton et al., 2016; Wong et al., 2010). In addition to the literature

providing insight into the cost-effectiveness of pharmacogenomics testing, there was also a

systematic review that demonstrated the worth of pharmacogenomics testing to provide better

clinical outcomes and prevent adverse drug reactions in patients receiving pharmacotherapies

(Phillips, Veenstra, Oren, Lee, & Sadee, 2001). There was also a single correlational design

study that was included to identify specific and practical findings regarding the cost-savings that

are seen with patients undergoing pharmacogenomics testing (Brown, Lorenz, Li, & Dechario,

2017). There were several articles included that had descriptive designs to provide support for

the notion of deficient provider knowledge base of pharmacogenomics testing (Relling & Evans, 2015; Rosenman et al., 2017; Sauver et al., 2016).

Critical Appraisal

The overall body of evidence that was found through the review of literature shows support for the project's interests and the variables that are to be addressed with the intervention included. Systematic reviews that were included in the literature review were evaluated using the CASP (2018) appraisal tool, which revealed that the results were valid and showed strong support for the results and conclusions that were drawn in these reviews. According to the CASP appraisal tool, the only point in which the systematic reviews were deficient was the uncertainty regarding the results being directly applicable to the contextual circumstances of this project's focus.

Important conclusions that were found through the review of literature should be scrutinized for potential bias and inability to generalize results. Examples of this include the findings of Sauver et al. (2016), which showed that there was a large percentage of surveyed clinicians who did not find the direct application of pharmacogenomics in their practice and had only changed practice due to pharmacogenomics results on very few occasions. There may be variables that are not obvious that can account for these findings, such as poor implementation plan of pharmacogenomics testing that did not include adequate education regarding the subject of pharmacogenomics, lack of clinical support in the implementation of this testing, age of the clinicians, previous experience with pharmacogenomics testing, or lack of clinician input into the clinical support tools that were utilized as part of this study by Sauver et al. (2016). Rosenman et al. (2017) found that the implementation of pharmacogenomics testing in their setting required leveraging key stakeholders in both hospital administration as well as clinicians who were

experts in this field to educate and assist other clinicians in the use and interpretation of pharmacogenomics testing. Beyond this, there was also discussion regarding the type of education that clinicians received, the frequency that this training was reinforced, and the support systems that were established to promote this change. If these variables were present in the previously mentioned study, it may have affected dramatic changes on the outcomes that were listed.

Similarly, the findings of Just et al. (2017) can be negatively affected by bias that was not reported or controlled for in the study. The characteristics of the surveyed population were not explained thoroughly, which may have represented several issues of bias or inexperience that cannot be accounted for otherwise. Berm et al. (2016) explained some conflicting results in the systematic review of literature on the subject of economic utility of pharmacogenomics testing. Within the article it was explained that the conflicting results were due to the inadequate reporting of results in evaluated studies or the ineffective implementation of pharmacogenomics testing in the clinical setting, which promotes poor provider adherence to recommendations and subsequent misrepresentation in the data.

Synthesis

Overall, the evidence that was found in the review of literature suggested that there was significant precedent for the cost-effectiveness for pharmacogenomics testing being implemented in clinical practice. However, these studies also concluded that further research was needed to provide conclusive evidence for the recommended scope of implementation with pharmacogenomics, as well as the extent of the clinical validity and utility that this testing provides patients (Berm et al., 2016; Pumpton et al., 2016; Wong et al., 2010). One of the distinct areas of clinical utility and promotion of patient outcomes through pharmacogenomics

testing in primary care settings was mental health care (Brown, Lorenz, Li, & Dechairo, 2017). These findings support this project's goal of addressing this known barrier of pharmacogenomics implementation in clinical practice.

Conceptual Framework/Model

The conceptual framework that is utilized for the formation of this project is the Iowa Model of Evidence-Based Practice. The Iowa Model stands as a valuable tool to clinicians who are seeking to address a clinical problem by providing a framework that can be utilized to answer essential questions regarding the necessary components of any project. This model serves as the underpinning that continually shapes and refines the theoretical intervention for this clinical problem (Iowa Model Collaborative, 2017). In this scholarly project the triggering issue was new evidence regarding the use of pharmacogenomics testing in general, but more specifically how this testing can and should be implemented in the setting of primary care. This general concept was further refined by identifying a subsection of data within the overall scope of pharmacogenomics that pertains to the identified barriers that stand in opposition to the implementation of this testing within the primary care setting. The clinical question of primary care providers' perspectives and level of knowledge regarding pharmacogenomics testing was decided upon as the purpose of this scholarly project.

With the utilization of the Iowa Model it was determined that the next step in this process was to understand if this chosen topic is a priority within the chosen population of primary care providers. It was determined through further literature review that there was significant precedence for the importance of this topic both within the primary care setting and to primary care providers. Once the subject of this scholarly project was determined to have importance, the Iowa Model was followed again in the next step of synthesizing a body of evidence that was in

support of the scholarly project's purpose. This was accomplished with systematic and comprehensive literature review and the use of literature evaluation tools to understand the quality of the evidence that was being gathered.

After it was determined that there was sufficient evidence to support the purpose of the scholarly project, the next step that was taken was to design the intervention that was going to be delivered to the primary care providers who decided to take part in this project's work. The Iowa Model was again followed systematically in the development of the materials that were developed for the intervention and evaluation of potential practice change. Through these materials that were developed for this project it was determined that change in practice was appropriate and that adoption was readily possible. Once these positive results were obtained regarding the purpose of the scholarly project, there were follow-up opportunities identified using the project materials to understand how this potential change in practice could be best supported and nurtured. The results obtained in the course of this scholarly project will be disseminated by potential publication and encouragement for others to validate these results by replication studies.

Summary

The literature review for this project revealed key findings regarding the evidence that exists to support the goals of the project, which is to provide a targeted educational intervention to primary care providers that will address areas of deficient knowledge as well as correcting incorrect perspectives of pharmacogenomics testing. The literature on this subject demonstrates preexisting barriers to successful implementation of pharmacogenomics testing in other settings such as deficiency in knowledge base, financial concerns, lack of clinical guidelines for

therapeutic changes, and efficacy of testing in preventing adverse clinical outcomes, as well as promoting optimal patient care.

SECTION THREE: METHODOLOGY

Design

This project is an evidence-based practice project that is guided by the Iowa Model for Evidence-Based Practice. The design of this project is quasi-experimental, which will guide the outcomes of interest in how they pertain to the clinical phenomenon of interest. This project builds upon the foundation of evidence that has been established in the literature regarding the use of pharmacogenomics testing as a means of regular management and evaluation in primary care settings. Specifically, this project sought to gain an understanding of the levels of knowledge in primary care providers regarding the use of pharmacogenomics testing as well as their perspectives on this type of testing. It has been noted in other settings that deficient knowledge base and perceptions of clinical validity, clinical utility, cost-effectiveness, and lack of clinical guidelines serve as significant barriers to the implementation of pharmacogenomics testing. These variables were evaluated in the population of chosen primary care providers to understand if there was variance or consistency with what is represented in the literature. A chosen group of primary care providers in the state of Virginia were surveyed regarding these variables of interest. The results were compared against what is represented in the literature and a targeted educational intervention was curated and delivered to those that provided responses to the original survey. A post-survey was then administered to determine potential changes in knowledge base or perceptions, as well as likelihood to include pharmacogenomics testing as a result of the intervention.

Measurable Outcomes

Measurable outcomes for this project include positive change in primary care provider behavior regarding the likelihood of ordering pharmacogenomics testing for patients seeking care, positive comparative change in knowledge base or understanding of pharmacogenomics testing and its application in the clinical setting, and positive comparative change in the perceptions of pharmacogenomics testing.

Setting

This project was not carried out in any one specified organization. The project materials were distributed to primary care providers that were identified as having the ability to order PGx testing and act on its results. The project considers nurse practitioners (NP), physician assistants (PA), and medical doctors (MD) to all meet the criteria of being primary care providers. The goals of advancing care outcomes for primary care patients through the implementation of PGx testing was found to be generally recognized as being aligned with the various disciplines of providers included for this project. The primary care providers were all located within the state of Virginia and were verified to be in active practice at various primary care practices throughout the state. Support for the project and its aims were evaluated through voluntary participation in the project.

Population

As stated in the previous section, the participants that were included in this project were those that were verified to be primary care providers that were in active practice in the state of Virginia. Primary care providers were determined to be any provider that had the practice authority and ability to order PGx testing for their patients. Thus, NPs, PAs, and MDs were all

included in the project population. The rationale for this chosen population is to identify those who have the ability to order this testing for their patients within the primary care setting, identify their individual and collective perspectives on PGx testing, and determine if these perspectives change with the application of an educational intervention that adequately describes the basic nature of PGx testing and its applications towards providing better outcomes for patients. Exclusion criteria for this project consisted of either not meeting the determined qualifications for being considered a primary care provider or primary care providers that are not in current practice. The selection process for this project consisted of the primary researcher identifying potential candidates for inclusion in the project and sending information regarding this scholarly project via e-mail to the potential participants' work emails that were obtained via primary care listings and websites. The project sample is one that is purposive in methodology, as there were criteria that were required for participation, but this was not randomized in nature.

There were 21 participants included in this project. There are several descriptive features about this project's population that will be detailed here. The large majority of the project's participants were under the age of 45 with 38.1% reporting to be within the age range of 25-34 years and 38.1% within the age range of 35-44 years. The majority of participants reported to be MDs (47%), which was followed by PAs (33%) and then NPs (20%). The majority of those surveyed reported that their level of experience in their current role was 1-10 years (76%). The participants also reported a slight majority of females (57%) versus males (43%).

Ethical Considerations

This project is intended to be constructed to protect the privacy and responses of all chosen subjects. Research ethics training was completed to ensure the protection of privacy and security of potentially sensitive information obtained from the subjects through the use of survey. The electronic communications to the individuals selected for participation in this project included a formal informed consent document, information regarding consent being given by means of participation, details regarding the use of the data that would be collected, and the measures that would be taken to keep this information secured and private. University IRB approval was obtained and it was determined that further organizational IRB approval for each participant was unnecessary due to the low-risk nature of this project. This was determined through approval from both the scholarly Chair and university IRB representatives.

Data Collection

The method of data collection for this project was accomplished through electronic communications from the researcher to the intended individuals who met the criteria set forth for inclusion regarding their participation in the project. Project participants were contacted directly by the primary researcher with a request for their participation through completion of project materials. Each participant was provided information regarding the project, its aims, and URL links to complete the project materials. Data were then aggregated utilizing a surveying service.

Tools

There have been tools utilized to understand the barriers to implementation of pharmacogenomics testing, but there are several variables of interest and factors that exist within the intended context of study that require the development of a new tool to adequately determine the variables of interest as well as their relationship with the context and the subject of

pharmacogenomics testing in primary care. The project's pre survey, educational intervention, and post survey were all constructed by the primary researcher. Evidence found within the literature served as the conceptual foundation for the tools that were utilized within the project. However, many of the tools that were found within the literature specifically dealt with providers who already had some modest level of exposure to the concepts of PGx testing, which was not the case within this project. Therefore, all of the identified tools within the literature were not useful for appropriated implementation within this project.

Intervention

This scholarly project began with the identification of this phenomenon of interest. PGx testing was initially evaluated in a generalized manner, but was subsequently considered in light of its potential application within the context of primary care management. This refined phenomenon of interest was investigated further and it was determined that the lack of PGx testing within primary care settings is in itself a subject that had been researched by others previously. With this foundational literature being present, it was determined that this project's aim was to progress the study of this phenomenon by development of materials that both identified primary care providers' perspectives towards PGx testing and attempted to improve these perspectives for the purposes of improved implementation of this testing within the primary care setting.

Once this baseline for the project was established a comprehensive literature review was accomplished. After the aims, goals, and structure of the project were established, the primary researcher obtained university IRB approval for carrying out the project in the chosen population of primary care providers. Potential participants were contacted by the primary researcher via e-mail and were voluntarily enrolled in the project. Once participants had completed all project

materials the primary researcher gathered and aggregated the responses that the participants had provided in both the project pre-survey and post-survey. These data were then analyzed through the use of statistical tools to determine significance and meaningful conclusions were then drawn.

Timeline. The literature review for this project was concluded on June 7, 2019. University IRB approval was obtained on September 18, 2019. Implementation of the project was carried out from November 15, 2019 through March 4, 2020. Data analysis was completed on April 20, 2020.

Feasibility Analysis. The anticipated feasibility of this project is high. The costs associated with carrying out this project include the use of proprietary survey tools to distribute the pre-survey and post-survey, along with included collection methods and data analysis.

Data Analysis

Measurable Outcome 1. The first measurable outcome of interest that was evaluated in this project was the presence and significance of deficits in knowledge regarding PGx testing as a barrier for implementation of this testing.

Measurable Outcome 2. The second measurable outcome of interest that was evaluated in this project was the likelihood of pursuing further education about PGx testing based on participation, as well as the methods by which this would be best accomplished according to the surveyed population.

Measurable Outcome 3. The third measurable outcome of interest that was evaluated in this project was the significance of the educational intervention on changing the perspectives of primary care providers regarding PGx testing.

SECTION FOUR: RESULTS

Measurable Outcome 1

This scholarly project utilized survey tools that were original to this project and were created by the primary researcher. These survey tools were shaped and characterized by evidence that was found within the literature review; however, there was not a survey tool identified within that search that adequately addressed the variables that have been established in the survey tools that were utilized in this scholarly project. There were two surveys developed for this scholarly project. It was the aim of the pre survey to gather baseline information on the level of knowledge and experience that the surveyed providers had with pharmacogenomics testing. Beyond this aim it was also determined that the pre survey should be designed to ascertain if perspectives were present or absent in the surveyed population, which would also help to determine how the educational intervention and post-survey were structured in their content and questioning. The post survey sought to understand changes in the perspectives and level of knowledge in the surveyed providers in comparison to the results that were evaluated on the pre survey tool.

The data gathered from the survey results for this project showed that there was a statistically significant relationship between the current level of knowledge reported by the participants and main barrier for PGx testing being clinical responsibility associated with this testing. This relationship is clarified with knowledge that within the project population, 95% of the participants reported having at most, very little experience with PGx testing. On the pre survey, where this relationship is being evaluated, the qualification for the response of very little experience is that providers had just heard PGx mentioned but have no actual training in the concepts of PGx testing. This is reemphasized with it being noted that 95% of surveyed

providers stated that they never include PGx testing as part of their management for patients currently. The hallmark of the descriptive statistics for the pre-survey in this project was that 90% of surveyed providers stated that the unfamiliarity with testing was the main barrier to the implementation of PGx testing, as well as 90% of surveyed providers also stating that there is no application for PGx testing in their practice currently. This overwhelming presence of responses that indicate a deficit in knowledge and overall unfamiliarity leads quite reasonably to 95% of surveyed providers stating that they are completely uncomfortable interpreting PGx testing results based on their current level of knowledge.

Beyond these descriptive statistics that outline the first measurable outcome are inferential statistics that further develop this theme with statistically significant findings that further reinforce these preliminary findings. A Kruskal-Wallis H test showed that there was a statistically significant difference in participants who found the main barrier for pharmacogenomics testing being clinical responsibility between the current knowledge level of pharmacogenomics, $\chi2(2) = 4.2$, $p = 0.04$ with a mean rank score of 10.0 for participants that responded no and 17.0 for participants that responded yes. The Mann-Whitney U Test statistic is 45.0 with a significance value of 0.08, which shows that there is a significant difference between the two factors. Another Kruskal-Wallis H test showed that there was a statistically significant difference in participants who found the main barrier for pharmacogenomics testing being clinical responsibility between the significance of pharmacogenomics testing, $\chi2(2) = 5.979$, $p = 0.014$ with a mean rank score of 9.75 for participants that responded no and 18.5 for participants that responded yes. The Mann-Whitney U Test statistic is 49.5 with a significance value of 0.017, which shows that there is a significant difference between the two factors.

Measurable Outcome 2

The data gathered from surveying this population of primary care providers also outlined distinctive trends that bore out interesting themes in relation to the second outcome of measurement that has been established. It was noted in the pre-survey portion that given the current level of knowledge regarding PGx concepts, only 14% of providers indicated that they believe it is not very important to include PGx education in medical education curriculum. This is reflected in the responses given regarding what formats are important for increased knowledge regarding PGx concepts. To this question only 19% of providers indicated that graduate school, meaning medical school, PA programs, and NP programs, were important to furthering education on PGx testing. However, in response to this same question, which allowed for multiple answers to be selected, 85% of providers indicated that conferences were important to gain knowledge, while 90% indicated that continuing education courses were important to increasing understanding of PGx testing. Finally, only 5% of surveyed providers indicated in the final question of the pre survey that they were not very interested in receiving education on PGx testing.

Based on the data acquired from the pre-survey there were statistically significant relationships drawn between variables of interest. A Kruskal-Wallis H test showed that there was a statistically significant difference in participants who found graduate schools as the best format for increasing knowledge about pharmacogenomics between the interest regarding pharmacogenomics testing education, $\chi2(2) = 7.508$, $p = 0.006$ with a mean rank score of 9.35 for participants that responded no and 18.0 for participants that responded yes. The Mann-Whitney U Test statistic is 72.0 with a significance value of 0.036, which shows that there is a significant difference between the two factors. Another Kruskal-Wallis H test showed that there was a statistically significant difference in participants who found the Internet as the best format

for increasing knowledge about pharmacogenomics between the importance of

pharmacogenomics education, $\chi2(2) = 5.007$, $p = 0.025$ with a mean rank score of 9.2 for

participants that responded no and 15.5 for participants that responded yes. The Mann-Whitney

U Test statistic is 82.5 with a significance value of 0.019, which shows that there is a significant

difference between the two factors. A Kendall's tau-b correlation was run to determine the

relationships between importance of pharmacogenomics education and the interest regarding

pharmacogenomics testing education, significance of pharmacogenomics testing, and current

knowledge level of pharmacogenomics amongst the 21 providers. There was a strong, positive

correlation between importance of pharmacogenomic education and the three comparative

factors. Interest regarding pharmacogenomics testing education ($\tau b = 0.436$, $p = .0.028$),

significance of pharmacogenomics testing ($\tau b = 0.536$, $p = .0.006$), and current knowledge level

of pharmacogenomics ($\tau b = 0.601$, $p = .0.003$) were all statistically significant. These results are

detailed in Table 1 with the mentioned correlations and statistical significance denoted.

Correlations

		Interest_Regarding_PharmacogenomicsTesting_Education	Current_Knowledge_Level_Pharmacogenomics	Significance_PharmacogenomicsTesting	Cost_Testing_Prohibitive	Comfortability_Interpreting_PharmacogenomicsTesting_Results	Importance_Pharmacogenomics_Education	Likely_To_Pursue_PharmacogenomicsTesting
Kendall's tau_b	Interest_Regarding_PharmacogenomicsTesting_Education — Correlation Coefficient	1.000	.377	.439[*]	−.118	.364	.436[*]	.592[**]
	Sig. (2−tailed)	.	.070	.028	.571	.086	.028	.003
	N	21	21	21	21	21	21	21
	Current_Knowledge_Level_Pharmacogenomics — Correlation Coefficient	.377	1.000	.385	−.050	.410	.601[**]	.368
	Sig. (2−tailed)	.070	.	.062	.814	.061	.003	.069
	N	21	21	21	21	21	21	21
	Significance_PharmacogenomicsTesting — Correlation Coefficient	.439[*]	.385	1.000	−.192	.357	.536[**]	.485[*]
	Sig. (2−tailed)	.028	.062	.	.351	.090	.006	.013
	N	21	21	21	21	21	21	21
	Cost_Testing_Prohibitive — Correlation Coefficient	−.118	−.050	−.192	1.000	−.205	−.075	.125
	Sig. (2−tailed)	.571	.814	.351	.	.350	.713	.537
	N	21	21	21	21	21	21	21
	Comfortability_Interpreting_PharmacogenomicsTesting_Results — Correlation Coefficient	.364	.410	.357	−.205	1.000	.348	.233
	Sig. (2−tailed)	.086	.061	.090	.350	.	.095	.259
	N	21	21	21	21	21	21	21
	Importance_Pharmacogenomics_Education — Correlation Coefficient	.436[*]	.601[**]	.536[**]	−.075	.348	1.000	.375
	Sig. (2−tailed)	.028	.003	.006	.713	.095	.	.052
	N	21	21	21	21	21	21	21
	Likely_To_Pursue_PharmacogenomicsTesting — Correlation Coefficient	.592[**]	.368	.485[*]	.125	.233	.375	1.000
	Sig. (2−tailed)	.003	.069	.013	.537	.259	.052	.
	N	21	21	21	21	21	21	21

*. Correlation is significant at the 0.05 level (2−tailed).

**. Correlation is significant at the 0.01 level (2−tailed).

Table 1: Kendall's Tau-b correlation testing on pre-survey results

It was determined that there was statistically significant evidence in the gathered data regarding interest in PGx education as well as which formats were most desirable in accomplishing this furthered knowledge. It was found that 86% of surveyed providers indicated on the post survey that they were at least somewhat likely to pursue further PGx education as a result of participation in the project. It was also noted that 71% of the surveyed providers completely agreed that PGx should be included in the preparatory curriculum of those entering the medical field or offered as continuing education opportunities for those in the field of primary care. The remaining 29% of surveyed providers indicated on the same question that they somewhat agreed with this notion as well. However, the importance of further efforts to educate primary care providers with more advanced concepts of PGx testing cannot be understated, as 95% of surveyed providers listed insufficient knowledge base as a barrier to implementation of PGx testing.

Measurable Outcome 3

The third and final outcome measurement is defined by the perspectives that were found within the surveyed population in the pre-survey and how these perspectives shifted as a result of the educational intervention that was delivered to them in the course of the project. It was identified on the pre-survey that providers believed that PGx testing did not have much clinical significance, with only 10% indicating PGx testing results were somewhat significant to patient outcomes while 43% indicated that this had very little significance or no significance at all to patient outcomes. It was also identified that 48% of surveyed providers saw the cost of testing as a prohibitive factor in the implementation of PGx testing. In response to asking what the main barrier was to implementation of PGx testing, 24% of providers chose cost of testing, 24% of

providers chose lack of impact on clinical practice, and 52% chose lack of evidence for clinical

use.

A Kruskal-Wallis H test showed that there was a statistically significant difference in the

main barrier for pharmacogenomics testing being the cost of testing when compared with cost

being prohibitive for testing, $\chi2(2) = 5.469$, $p = 0.019$ with a mean rank score of 12.56 for

participants that responded no and 6.0 for participants that responded yes. The Mann-Whitney U

Test statistic is 15.0 with a significance value of 0.04, which shows that there is a significant

difference between the two factors. A Kendall's tau-b correlation was run to determine the

relationship between interest regarding pharmacogenomics testing education and the significance

of pharmacogenomics testing and likeliness to pursue pharmacogenomics testing amongst 21

participants. There was a strong, positive correlation between interest regarding

pharmacogenomics testing education and the two factors. Significance of pharmacogenomics

testing ($\tau b = 0.439$, $p = .0.028$), and likeliness to pursue pharmacogenomics testing ($\tau b = 0.592$, p

$= .0.003$) were both statistically significant.

In the post survey data it was clear that there was a distinct change in the answering of

questions regarding the identified perspectives from the pre survey, with 85% of surveyed

providers who at least somewhat agreed that the educational intervention thoroughly addressed

the barriers to implementation of PGx testing. It was also found that at least 90% of the surveyed

providers at least somewhat agreed that PGx testing has clinical significance in the management

of primary care, 80% at least somewhat agreed that PGx testing is financially viable in the

management of primary care patients, and 95% indicating that they at least somewhat agreed that

PGx testing can greatly reduce adverse drug reactions in patients. When asked who PGx should

be considered for in a multiple response style question, 95% of surveyed providers indicated that

the cases where adverse drug reactions are more likely, and 58% indicated that this should also

be considered for patients where normal therapies are noted to be ineffective.

A Kruskal-Wallis H test showed that there was a statistically significant difference in

participants who planned to pursue pharmacogenomics education due to the project and between

intervention testing considered normal therapy ineffective, $\chi2(2) = 4.365$, $p = 0.037$ with a mean

rank score of 8.0 for participants that responded no and 13.25 for participants that responded yes.

The Mann-Whitney U Test statistic is 85.0 with a significance value of 0.036, which shows that

there is a significant difference between the two factors. Another Kruskal-Wallis H test showed

that there was a statistically significant difference in participants who found pharmacogenomics

testing significant due to the intervention and between testing considered normal therapies

ineffective due to the intervention, $\chi2(2) = 5.47$, $p = 0.019$ with a mean rank score of 7.83 for

participants that responded no and 13.38 for participants that responded yes. The Mann-Whitney

U Test statistic is 82.5 with a significance value of 0.019, which shows that there is a significant

difference between the two factors. A Kendall's tau-b correlation was run to determine the

relationship between participants who found pharmacogenomics testing to have significance

because of the intervention and whether pharmacogenomics concepts should be included in

preparatory curriculum of those entering the medical field amongst 21 participants. There was a

strong, positive correlation between participants found the intervention addressed barriers and

whether intervention testing is viable. Whether intervention testing is viable ($\tau b = 0.663$, $p =$

.0.003) was statistically significant. Kendall's tau-b correlation was run to determine the

relationship between participants who, due to the intervention, found that pharmacogenomics

testing can greatly reduce adverse drug reaction events, whether PGx testing is viable,

participants who stated that they are planning to pursue pharmacogenomics education due to the

project, and if the intervention is appropriate for primary care amongst the 21 providers. There

was a strong, positive correlation between all the three factors. Whether intervention testing is

viable ($\tau b = 0.436$, $p = .0.037$), participants planning to pursue pharmacogenomics education due

to the project ($\tau b = 0.509$, $p = .0.015$), and if the intervention is appropriate for primary care (τb

$= 0.529$, $p = .0.014$) were all statistically significant. These results are detailed in Table 2 with

the mentioned correlations and statistical significance denoted.

Correlations

		Pursue_Pharmacogenomics_Education_DuetoProject	Intervention_Addressed_Barriers	Intervention_PharmacogenomicsTesting_Significance	Intervention_Testing_Viable	Intervention_Preparatory_Curriculum	Intervention_Testing_Appropriate_PrimaryCare	Intervention_Reduce_Adverse_Drug_Reaction
Kendall's tau_b	Pursue_Pharmacogenomics_Education_DuetoProject							
	Correlation Coefficient	1.000	.070	.196	.524**	.486*	.540**	.509*
	Sig. (2–tailed)	.	.730	.358	.010	.022	.009	.015
	N	21	21	21	21	21	21	21
	Intervention_Addressed_Barriers							
	Correlation Coefficient	.070	1.000	-.009	.450*	-.086	.000	.358
	Sig. (2–tailed)	.730	.	.968	.027	.686	1.000	.086
	N	21	21	21	21	21	21	21
	Intervention_PharmacogenomicsTesting_Significance							
	Correlation Coefficient	.196	-.009	1.000	.208	.663**	.175	.280
	Sig. (2–tailed)	.358	.968	.	.331	.003	.425	.202
	N	21	21	21	21	21	21	21
	Intervention_Testing_Viable							
	Correlation Coefficient	.524**	.450*	.208	1.000	.313	.327	.436*
	Sig. (2–tailed)	.010	.027	.331	.	.143	.119	.037
	N	21	21	21	21	21	21	21
	Intervention_Preparatory_Curriculum							
	Correlation Coefficient	.486*	-.086	.663**	.313	1.000	.387	.193
	Sig. (2–tailed)	.022	.686	.003	.143	.	.078	.378
	N	21	21	21	21	21	21	21
	Intervention_Testing_Appropriate_PrimaryCare							
	Correlation Coefficient	.540**	.000	.175	.327	.387	1.000	.529*
	Sig. (2–tailed)	.009	1.000	.425	.119	.078	.	.014
	N	21	21	21	21	21	21	21
	Intervention_Reduce_Adverse_Drug_Reaction							
	Correlation Coefficient	.509*	.358	.280	.436*	.193	.529*	1.000
	Sig. (2–tailed)	.015	.086	.202	.037	.378	.014	.
	N	21	21	21	21	21	21	21

**. Correlation is significant at the 0.01 level (2–tailed).

*. Correlation is significant at the 0.05 level (2–tailed).

Table 2: Kendall's Tau-b correlation testing on post-survey results

SECTION FIVE: DISCUSSION

Implication for Practice

The findings based on the project's measurable outcomes contribute to the growing knowledge surrounding PGx overall, but more specifically the method by which this advent of personalized medicine can and should be implemented in the primary care setting. Previous research has focused primarily on evaluating the efforts to implement PGx testing, the generalized themes that stand as general barriers to the implementation of this testing, and evaluation of the potential benefits of implementing PGx testing in various care settings. In this project it was established that in the surveyed population of primary care providers there was an overwhelming baseline deficit in knowledge regarding the most basic concepts of what PGx testing is, its application, and common misconceptions about the testing itself. Beyond this, it was determined that through exposure to an educational intervention that included the core concepts of PGx testing that providers were willing to pursue the inclusion of this testing in their practice as well as to engage in further education regarding the subject of PGx testing. As a result of the survey responses, this project was also helpful in illuminating the perceived need for education about PGx concepts to be included in preparator curriculum and to be offered as continuing education opportunities for those in the field of primary care.

The importance of these findings for both the surveyed providers as well as the patients that they manage cannot be understated. As previously mentioned, it was identified that a large majority of the surveyed providers indicated that they would be pursuing both continued education as well as implementation of PGx testing in the management of their patients. The surveyed providers identified that the most applicable use case for this testing would be the

avoidance of adverse drug reaction events, which PGx testing results can be leveraged advantageously towards this goal.

The limitations of this project are found within the severely limited number of providers who responded to the invitation and met the requirements of finishing all the project's materials to be included for analysis. The results therefore cannot be generalized to any other context outside of the one that has been studied within the confines of this project. There is also the possibility for bias in those that did both respond to the invitation for inclusion and completed the project's materials, in that these providers may have been more open to both learning and implementing PGx concepts when compared to the general pool of primary care providers. To understand this better these results should be compared against those with similar aims that are carried out in other primary care provider populations to determine if these results can be validated.

Sustainability

The sustainability in accomplishing change of practice when it comes to implementation of PGx testing is high. There is an ever-growing precedent based on many variables for the implementation of PGx testing within the field of primary care. It has been shown in this project that primary care providers will not implement testing that they do not understand, but if this barrier of knowledge deficit can be addressed then it is likely that change in practice is forthcoming. Priorities in the field of medicine are closely aligned with the principles of PGx testing, which contributes heavily to the sustainability of practice change towards implementation of this testing. PGx testing aims to primarily provide better outcomes for every single patient who is evaluated and treated within the primary care context. PGx texting secondarily aims to provide care that is precise, evidence-based, and cost-effective.

Dissemination Plan

The plan for dissemination of the project's results occurs through several mechanisms. The first mechanism by which dissemination may happen is through the potential and likely change in practice that will occur on the individual level in all the providers that took part in this project. These providers indicated that as a result of participation in this project their perspectives on PGx testing have changed, and that they will likely pursue further PGx testing and implement PGx testing as part of their regular management. This change in practice for these providers will likely cause colleagues or supervising physicians to take note of these changes and evaluate the efficacy of PGx testing just as the surveyed providers have as a result of inclusion in this project. The secondary mechanism for the dissemination of these results is for this project to be published for those who are interested in the field of PGx testing, for those who wish to know how this may affect the management of patients in the primary care setting, and finally for those who are interested in pursuing research regarding PGx testing's impact on clinical practice.

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Appendix A

Evidence Table

Name: Joshua Fleming

Clinical Question: How does a targeted educational intervention affect the reported level of understanding and perspectives for providers in a primary care health system?

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
Example, A. (2015) Title etc. per Current APA	To identify the need for technology to prevent falls	A convenience sample of 44 nurses in an acute care hospital	A non-experimental, descriptive survey	Findings indicate that fall rates decreased by 2% with the introduction of technology into the care setting	Level 6: descriptive design	Conducted in only one setting, small sample size	Does provide some good foundational information even though the level is a 6.

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
Relling, M.V., & Evans, W.E. (2015). Pharmacogenomics in the clinic. *Nature*, *526*(7573), 343	To provide background information regarding the growing field of pharmacogenomic testing and its efficacy in clinical practice.	Literature review of related and relevant literature regarding this subject.	No details regarding processes by which literature was obtained are mentioned in the article.	Authors conclude that there is a growing body of knowledge regarding pharmacogenomics testing, which is greatly impacted by the advent of the human genome project and increased understanding regarding the subject of genetics in general. Discussed here is the potential level of impact that discoveries regarding pharmacogenes can have on the change in treatment methods and patient outcomes.	Level 6: Descriptive design	The study falls short in not providing specific recommendations for further work to be done in order to move the field of study forward.	Yes. This study provides significant general insights into the subject of pharmacogenomics testing as well as the barriers to further implementation of this in clinical practice.

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
Rosenman, M.B., Decker, B., Levy, K.D., Holmes, A.M., Pratt, V.M., & Eadon, M.T. (2017). Lessons learned when introducing pharmacogenomic panel testing into clinical practice. *Value in Health, 20*(1), 54-59.	This study describes the challenges and potential solutions to implementation projects of pharmacogenomics testing being provided.	A diverse population (patients who often have multiple chronic illnesses, in a large urban safety-net hospital and its outpatient clinics).	The study was conducted as a descriptive case study of the implementation of a pharmacogenomics program with wide scope (14 genes, 43 variants, and 27 medications).	The study identified several areas of challenges that were developed through observation and evaluation of the implementation process in this care environment that included both extrinsic factors, patient-mediated factors, and provider-mediated factors.	Level 6: Descriptive design	The problem of cost for testing is addressed by means of correlation with the rise of other interventions that have been promised as revolutionary in theory yet complex and inconclusive in practice. This may be helpful in predicting the complex implementation process of pharmacogenomics testing in primary care, but this relationship is not proven to be concrete or predictive of the future of pharmacogenomics testing.	Yes. The information gleaned through experiencing multi-faceted variables that serve as potentially significant barriers against implementation efforts proves to pave the road forward for further investigation and intervention to address these issues effectively.

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
Just, K.S., Steffens, M., Swen, J.J., Patrinos, G.P., Guchelaar, H.J., & Stingl, J.C. (2017). Medical education in pharmacogenomics—results from a survey on pharmacogenetic knowledge in healthcare professionals within the European pharmacogenomics clinical implementation project Ubiquitous Pharmacogenomics (U-PGx). *European Journal of Clinical Pharmacology, 73*(10), 1247-1252.	To evaluate the attitudes, experience with, and education on pharmacogenomic testing in medical providers who are expected to be the leaders of this new change towards the future where this testing is part of regular evaluation and management of patients.	The sample group was comprised of 70 individuals that was a combination of physicians and pharmacists.	The authors developed a questionnaire including 29 questions. It was spread out to healthcare professionals working at the future implementation sites (in Austria, Greece, Italy, Netherlands, Slovenia, Spain and Great Britain) of the U-PGx project in preparation of an educational programme. Aim of the survey was to analyse the current educational situation at the implementation sites.	The results showed that even though a vast majority of the respondents (more than 84%) showed that pharmacogenomics was relevant to their current practice it was still not prevalent as more than 65% of respondents had not ordered or recommended testing in the last year.	Level 6: Descriptive design	The study showcased a significant barrier to the implementation of pharmacogenomics testing in clinical practice as being a lack of knowledge and specific education regarding the interpretation of testing results, but this study fails to propose any meaningful intervention based on these findings.	Yes. The evidence presented in this study is crucial to understand as part of further research into the education that is necessary for physicians in existing practice as well as the potential for integration of changes to the curriculum of medical students who are going to be the most affected by these potential changes in the future.

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
Plumpton, C. O., Roberts, D., Pirmohamed, M., & Hughes, D. A. (2016). A systematic review of economic evaluations of pharmacogenetic testing for prevention of adverse drug reactions. *PharmacoEconomics, 34*(8), 771-793.	This study is aimed at the cost-effectiveness evaluation of pharmacogenomic testing through systematic review of literature to prevent adverse drug reactions in patients that are about to be placed on medications that can be heavily affected by genetic factors.	47 of a total of 852 articles met inclusion criteria for independent review of both abstract and full text.	The systematic review protocol was registered with PROSPERO, the international database of prospectively registered systematic reviews (identification number CRD42014013673), conducted according to the Centre for Reviews and Dissemination's guidance for undertaking reviews in healthcare.	There was evidence supporting the cost effectiveness of testing for HLA-B*57:01 (prior to abacavir), HLA-B*15:02 and HLA-A*31:01 (prior to carbamazepine), HLA-B*58:01 (prior to allopurinol) and CYP2C19 (prior to clopidogrel treatment). Economic evidence was inconclusive with respect to TPMT (prior to 6-mercaptoputine, azathioprine and cisplatin therapy), CYP2C9 and VKORC1 (to inform genotype-guided dosing of coumarin derivatives), MTHFR (prior to methotrexate treatment) and factor V Leiden testing (prior to oral contraception). Testing for A1555G is not cost effective before prescribing aminoglycosides.	Level 1: Systematic Review	While the study's results were shown to have conclusive findings regarding the cost-effectiveness in providing pharmacogenomic testing in for some medications, there are still those that require further investigation because of inconclusive or mixed results.	Yes. This systematic review evaluates the cost-effectiveness for pharmacogenomics based on reduction in adverse drug side effects. With the financial implications of pharmacogenomics testing it is necessary to understand how this testing will provide economic advantages to both patients, insurance providers, and health systems overall which support the successful implementation of this testing in the future.

Berm, E. J. J., de Looff, M., Wilffert, B., Boersma, C., Annemans, L., Vegter, S., & Postma, M. J. (2016). Economic evaluations of pharmacogenetic and pharmacogenomic screening tests: A systematic review. second update of the literature. *PLoS One, 11*(1)	To evaluate the literature on the economic implications of pharmacogenomics screening tests to help determine if this testing is cost effective.	80 articles were found to meet inclusion criteria of the initial 733 articles that were found regarding the subject matter.	A literature search was performed in PubMed and papers published between August 2010 and September 2014, investigating the cost-effectiveness of PGx screening tests, were included. Papers from 2000 until July 2010 were included via two previous systematic reviews. Studies' overall quality was assessed with the Quality of Health Economic Studies (QHES) instrument.	The literature review found that testing was mostly a cost-effective or cost-saving intervention across the studies that were accumulated and evaluated.	Level 1: Systematic Review	It is difficult to provide conclusive and concrete economic evaluations that are established as a standard because of several different variables such as lack of hard clinical evidence regarding the pharmacogenomics testing's utility in the clinical setting, variability in compliance in physicians who are ordering the testing and not changing management based off of recommendations, and the variability in price of pharmacogenomics testing between different geographical environments.	Yes. This systematic review contains a robust foundation for the validity of pharmacogenomics testing as part of regular screening and management from the perspective of economic implications, which is a large concern surrounding this field in the literature.
Kirchheiner, J., Fuhr, U., & Brockmöller, J. (2005). Pharmacogenetics-based therapeutic recommendations -- ready for clinical practice? *Nature*	The study discusses different variations and factors that affect or inhibit the use and application of pharmacogenomics testing in real-world clinical environments	The study is a literature review that does not have definable search terms or	The article does not contain specific parameters for the methods by which the evidence was	Based on the articles reviewed by the authors, it was found that there are several limitations to the field of pharmacogenomics	Level 6: Descriptive design	The study notes these polymorphisms being detected in patients, but fails to	Yes. This review describes several different case studies where there have been, in some cases, significant adverse

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
Reviews. Drug Discovery, 4(8), 639-647.		inclusion/exclusion criteria listed	compiled or proposed	that limit its implementation and application in clinical practice		substantiate how these findings will be repeated in large-scale studies or the implications to clinical practice based on the results of those hypothetical studies	effects that have been noted in patients with known polymorphisms

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
Wong, W. B., Carlson, J. J., Thariani, R., & Veenstra, D. L. (2010). Cost effectiveness of pharmacogenomics. *PharmacoEconomics, 28*(11), 1001-1013.	To provide a foundational understanding regarding the economics of pharmacogenomics testing through systematic review of literature that discusses these points	34 articles were included in the review of literature from an original 54 articles that were selected based off of other reviews of literature and new evidence	A literature search was performed during October 2009 using the following publically available databases: PubMed, UK National Institute for Health and Clinical Excellence (NICE).Tufts CEA registry and Canadian Agency on Drugs and Technology in Health (CADTH). We employed a literature search strategy similar to a previous CEA of PGx reviews, which involved starting with broad search terms, then narrowing down to specific Medical Subject Heading (MeSH) terms, followed by disease-specific searches and expert recommendations.	The studies that were surveyed and evaluated found that there were many biogenetic markers that had clinical significance, but only two that possessed clinical significance as well as clinical utility based on the economic benefits that these may possess for the patient populations that can be served by them	Level 1: Systematic Review	There are limitations in the current base of evidence on how the results of the studies that were included in this review have on clinical practice based on insufficient evidence and inconclusive results	Yes. There is supporting evidence, though not conclusive, to support the cost-effectiveness of pharmacogenomics testing having a place in regular clinical practice

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
Phillips, K.A., Veenstra, D.L., Oren, E., Lee, J.K., Sadee, W. (2001). Potential role of pharmacogenomics in reducing adverse drug reactions: a systematic review. *Journal of the American Medical Association, 286*(14), 2270-2279.	To evaluate the potential role of pharmacogenomics in reducing the incidence of adverse drug reactions	Detailed inclusion criteria were used to select studies. 18 of 333 adverse drug reaction studies and 22 of 61 variant allele review articles were included in the final review	MEDLINE English-language only searches for adverse drug reaction studies published between January 1995 and June 2000 and review articles of variant alleles of drug-metabolizing enzymes published between January 1997 and August 2000.	Results suggest that drug therapy based on individuals' genetic makeups may result in a clinically important reduction in adverse outcomes	Level 1: Systematic Review	The information included here, while being a solid foundation for further study and potential implications to clinical practice, it is old evidence in a subject that is constantly evolving into greater scopes and practices	Yes. Even though the evidence may be old the information here should be referenced in continual work towards further research and greater applications in clinical practice

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
Adams, S. M., Anderson, K. B., Coons, James C, Smith, R. B., Meyer, S. M., Parker, L. S., & Empey, Philip, E. (2016). Advancing pharmacogenomics education in the core PharmD curriculum through student personal genomic testing. *American Journal of Pharmaceutical Education, 80*(1), 1-11.	To evaluate the impact of personal genetic testing on the educational benefits for pharmD students learning these concepts as part of curriculum	Study consisted 110 PharmD students and 10 faculty members	Study involved pre- and post-survey tools to evaluate for changes in perception and level of understanding that was proposed to be affected or changed by the implementation of this new type of curriculum	It was found that students who underwent genetic testing were found to have significant advantages in understanding and manipulation of curriculum materials when compared with students who did not take part in the intervention	Level 3: Quasi-Experimental Design	The study is limited by its poor discussion surrounding the areas of difference in outcomes that were achieved by the students who were participants in the genetic testing as compared to students who did not take part in this	Yes. The study provides insight into novel concepts regarding the education of future clinicians who are expected to have robust understanding regarding genetic testing and implications on clinical practice to achieve higher buy-in from these individuals and, in-turn, provide better outcomes for adherence to testing as well as better understanding.

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
Ferreri, S.P., Greco, A.J., Michaels, N.M., O'Connor, S.K., Chater, R.W., Viera, A.J., Faruki, H., McLeod, H.L., & Roederer, M.W. (2014). Implementation of a pharmacogenomics in a community pharmacy, *Journal of the American Pharmacists Association,* 54(2), 172-180.	To determine the feasibility of implementing a pharmacogenomics service in a community pharmacy	18 patients taking clopidogrel, a drug metabolized by CYP2C19.	A retrospective data abstraction of prescription fills between the dates of May 1, 2011, and October 26, 2011, yielded 53 patients with at least one fill of clopidogrel. Since this was a feasibility project, any patient with a prescription for clopidogrel was included. A final sample of 18 were determined based on other inclusion/exclusion criteria	A pharmacogenomics service can be an extension of medication therapy management services in a community pharmacy. Prescribers are receptive to having community pharmacists conduct pharmacogenomics testing, but reimbursement is a challenge.	Level 4: Correlational Design	The study did not adequately explain why the insurance agencies in these cases were reluctant towards reimbursement or how this difficulty can be overcome in future studies or work towards clinical practice.	Yes. This study demonstrates practical application of pharmacogenomics testing being carried out on a drug with known significant side effects for persons with genetic abnormalities and proposes how the relationship with pharmacists carrying out this testing can work in the care-team environment with suggestions made towards the prescribers based on the results that are examined in these patients

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
Benitwez, J., Jablonski, M.R., Allen, J.D., & Winner, J.G. (2015). The clinical validity and utility of combinatorial pharmacogenomics: Enhancing patient outcomes. *Applied and Translational Genomics, 5*(1), 47-49.	This study evaluates the differences measured in clinical validity, utility, and economic benefit to the patient between single gene evaluations and combinatorial pharmacogenomics panels that are designed to evaluate multiple genes in an individual that is receiving psychiatric pharmacotherapies	The study evaluates three studies done on the clinical validity, three studies on the clinical utility, and an undisclosed amount of clinical research on the economic impact of combinatorial pharmacogenomics testing panels for patients receiving psychiatric pharmacotherapies	The methods by which this evidence is compiled or evaluated is not disclosed in the contents of the article	The authors concluded based on the amassed clinical research that the use of combinatorial pharmacogenomics testing panels showed a significant efficacy in all three defined domains of interest, thus showing preference for this type of testing for better outcomes as well as further implications for the field in evaluating these results on a larger scale	Level 6: Descriptive Design	The study's limitations surround the small amount of evidence in previous studies that support the purported conclusion, and highlights the need for further research and replication of findings that are listed here for increased basis on change in clinical practice	Yes. The study provides preliminary evidence that suggest promising benefits in three variables of pharmacogenomics testing that are often listed as barriers towards greater implementation and effective change in practice

Brown, L.C., Lorenz, R.A., Li, J., & Dechairo, B.M. (2017). Economic utility: Combinatorial pharmacogenomics and medication cost savings for mental health care in a primary care setting. *Clinical Therapeutics, 39*(3).	The primary objective of this study was to determine potential cost savings of combinatorial PGx testing over the course of 1 year in patients with mental illness treated by primary care providers (PCPs) and psychiatrists who had switched or added a new psychiatric medication after patients failed to respond to monotherapy.	Of the 2168 patients, 1662 were taking eligible GeneSight panel medications 365 days after the combinatorial PGx test date and were included in this sub-analysis.	This study was a sub-analysis of a 1-year, prospective trial comparing medication costs of 2168 patients undergoing GeneSight testing. Pharmacy claims were provided by a pharmacy benefits manager, comparing medication costs 6 months before combinatorial PGx testing and followed up for 1 year after the testing. This analysis compared congruence and cost savings per patient based on the type of health care provider administering care.	PCPs congruent with combinatorial PGx testing provided the most medication cost savings for payers and patients at $3988 per member per year	Level 4: Correlational Design	The study failed to explain in detail the potential for lack of congruence in pharmacogenomics testing between PCPs and psychiatrists or explicitly explain points of benefit for PCPs being the primary source of pharmacogenomics testing as it was found that there was greater cost savings for the patients because the PCP was able to not only follow the psychiatric recommendation results from the testing but also the non-psychiatric recommendations that the testing brought as part of the combinatorial panel	Yes. The study supports the economic advantage in providing pharmacogenomics testing with an emphasis that this testing should take place in the PCP setting to provide the best economic impact for the patients seeking care
Romagnoli, K.M., Boyce, R.D., Empey, P.E., Adams, S., & Hochheiser, H. (2016). Bringing clinical	The authors of the article sought to understand the pharmacogenomics information needs and resource requirements of pharmacists as these are	The study included 14 pharmacists located in 6 different clinical environments	The authors conducted qualitative inquiries and used the results	Responses suggest that pharmacists anticipate an imminently growing role for	Level 6: Descriptive Design	The study does not provide explicit statistical data	Yes. This study shows the perspectives of several pharmacists

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
pharmacogenomics information to pharmacists: A qualitative study of information needs and resource requirements, *International Journal of Medical Informatics, 86*, 54-61.	key participants in the decision-making regarding pharmacotherapies in the clinical setting		of those inquiries to develop a model of pharmacists' pharmacogenomics information needs and resource requirements.	pharmacogenomics in their practice. Participants value information from trust-worthy resources like FDA product labels, but found that this information was difficult to accurately and efficiently approach		or evidence that notes the need for increased knowledge and inclusion in pharmacogenomics testing beyond stating that this field is likely to need the clinical knowledge of pharmacists for better patient outcomes	on the subject of pharmacogenomics and the need for increased knowledge and prevalence of succinct and useful clinical resources for the utilization by providers to better provide meaningful clinical decisions

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
St Stauver, J.L., Bielinski, S.J., Olson, J.E., Bell, E.J., McGree, M.E., Jacobson, D.J., McCormick, J.B., Caraballo, P.J., Takahashi, P.Y., Roger, V.L. & Vitek, C.R. (2016). Integrating pharmacogenomics into clinical practice: Promise vs reality, *American Journal of Medicine, 129*(10), 1093-1099.	To evaluate PCPs' response to clinical support systems that are aimed towards providing better patient outcomes by notifying the provider that a change is recommended based on the patient's pharmacogenomics profile	159 primary care physicians in the Mayo Clinic network. Of this original sample there were only 90 respondants	Mayo Clinic primary care practice were sent e-mail surveys to understand their perspectives on the implementation and use of pharmacogenomic testing in their clinical practice. Surveys assessed how the clinicians felt about pharmacogenomics and whether they thought electronic pharmacogenomics clinical decision support alerts were useful.	Our results indicate that clinicians are not comfortable with the integration of pharmacogenomic data into their clinical practice. Because most patients expect that their pharmacogenomic data will help guide their care decisions, further efforts to educate clinicians about the utility of pharmacogenomic data for clinical practice, and efforts to refine PGx-CDS alerts to make them useful and user-friendly, may close the gap between the clinician's approach and patient expectations	Level 4: Correlation al Design	The limited response rate of 57% limits the efficacy of the data that is pulled from this specific population and does not account for individual physicians who are outliers with either negative or positive bias based on personal experience with the clinical decision support tools	Yes. This study features potentially helpful insights into better integration of pharmacogenomics testing clinical decision support systems in future care settings that reflects positive physician interactions and better outcomes with adherence to change in practice based on recommendations

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
Olson, J. E., Rohrer Vitek, C. R., Bell, E. J., Mcgree, M. E., Jacobson, D. J., St Sauver, J. L., Bielinski, S. J. (2017). Participant-perceived understanding and perspectives on pharmacogenomics: The mayo clinic RIGHT protocol (right drug, right dose, right time). *Genetics in Medicine, 19*(7), 819-825.	The purpose of this study was to identify variables included in educational resources that are provided to patients undergoing pharmacogenomics testing that predict understanding as well as how to further refine these materials based on responses from those surveyed	A total of 1010 patients were chosen based off of inclusion and exclusion criteria and of these patients there were 869 respondants	The participants were mailed their individual pharmacogenomics test results along with educational materials and a survey to complete regarding their understanding of the presented materials and potential for this information to improve medication adherence	Even with increased efforts paid towards simplifying patient education regarding the results of pharmacogenomics testing it was found that more than a third of the surveyed patients did not understand the results	Level 4: Correlational Design	The limitations of this study include the potential for these findings to be generalized given specific characteristic of the surveyed population such as patients who have a higher level of education when compared to other samples or a higher likelihood in response rates because of bias factors that may be specific to this population	Yes. This study highlights the necessity of providing patients with the information that they need in a format that is not confusing or using terms that are difficult for lay people to understand. This paves the way for further refinement of educational materials which can have significantly positive impact on the clinical benefits of pharmacogenomics testing in patients

Appendix B

LIBERTY UNIVERSITY.
INSTITUTIONAL REVIEW BOARD

September 18, 2019

Joshua Fleming
IRB Application 3991: Pharmacogenomics in Primary Care: Barriers to Implementation

Dear Joshua Fleming,

The Liberty University Institutional Review Board has reviewed your application in accordance with the Office for Human Research Protections (OHRP) and Food and Drug Administration (FDA) regulations and finds your study does not classify as human subjects research. This means you may begin your research with the data safeguarding methods mentioned in your IRB application.

Your study does not classify as human subjects research because evidence-based practice projects are considered quality improvement activities, which are not considered "research" according to 45 CFR 46.102(d).

Please note that this decision only applies to your current research application, and any changes to your protocol must be reported to the Liberty IRB for verification of continued non-human subjects research status. You may report these changes by submitting a new application to the IRB and referencing the above IRB Application number.

If you have any questions about this determination or need assistance in identifying whether possible changes to your protocol would change your application's status, please email us at irb@liberty.edu.

Sincerely,

G. Michele Baker, MA, CIP
Administrative Chair of Institutional Research
Research Ethics Office

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Appendix C

COLLABORATIVE INSTITUTIONAL TRAINING INITIATIVE (CITI PROGRAM)

COMPLETION REPORT - PART 1 OF 2
COURSEWORK REQUIREMENTS*

* NOTE: Scores on this Requirements Report reflect quiz completions at the time all requirements for the course were met. See list below for details.
See separate Transcript Report for more recent quiz scores, including those on optional (supplemental) course elements.

- Name: Joshua Fleming (ID: 5903591)
- Institution Affiliation: Liberty University (ID: 2446)
- Institution Email: jmfleming2@liberty.edu
- Institution Unit: Nursing
- Phone: 919-810-5427

- Curriculum Group: Biomedical Research - Basic/Refresher
- Course Learner Group: Biomedical & Health Science Researchers
- Stage: Stage 1 - Basic Course
- Description: Choose this group to satisfy CITI training requirements for Investigators and staff involved primarily in biomedical research with human subjects.

- Record ID: 21139807
- Completion Date: 28-Sep-2018
- Expiration Date: 27-Sep-2021
- Minimum Passing: 80
- Reported Score*: 88

REQUIRED AND ELECTIVE MODULES ONLY	DATE COMPLETED	SCORE
Conflicts of Interest in Human Subjects Research (ID: 17464)	24-Sep-2018	5/5 (100%)
Belmont Report and Its Principles (ID: 1127)	12-Oct-2016	3/3 (100%)
History and Ethics of Human Subjects Research (ID: 498)	16-Oct-2016	7/7 (100%)
Basic Institutional Review Board (IRB) Regulations and Review Process (ID: 2)	24-Sep-2018	5/5 (100%)
Informed Consent (ID: 3)	24-Sep-2018	5/5 (100%)
Social and Behavioral Research (SBR) for Biomedical Researchers (ID: 4)	28-Sep-2018	4/4 (100%)
Records-Based Research (ID: 5)	28-Sep-2018	3/3 (100%)
Genetic Research in Human Populations (ID: 6)	28-Sep-2018	5/5 (100%)
Populations in Research Requiring Additional Considerations and/or Protections (ID: 16680)	07-Jul-2017	1/5 (20%)
Research and HIPAA Privacy Protections (ID: 14)	28-Sep-2018	4/5 (80%)
Recognizing and Reporting Unanticipated Problems Involving Risks to Subjects or Others in Biomedical Research (ID: 14777)	28-Sep-2018	4/5 (80%)
Liberty University (ID: 15111)	28-Sep-2018	No Quiz

For this Report to be valid, the learner identified above must have had a valid affiliation with the CITI Program subscribing institution identified above or have been a paid Independent Learner.

Verify at: www.citiprogram.org/verify/?k1b559d0a-ecb0-456c-b130-1c2d541c10c3-21139807

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COLLABORATIVE INSTITUTIONAL TRAINING INITIATIVE (CITI PROGRAM)

COMPLETION REPORT - PART 2 OF 2
COURSEWORK TRANSCRIPT**

** NOTE: Scores on this Transcript Report reflect the most current quiz completions, including quizzes on optional (supplemental) elements of the course. See list below for details. See separate Requirements Report for the reported scores at the time all requirements for the course were met.

- Name: Joshua Fleming (ID: 5903591)
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- Course Learner Group: Biomedical & Health Science Researchers
- Stage: Stage 1 - Basic Course
- Description: Choose this group to satisfy CITI training requirements for Investigators and staff involved primarily in biomedical research with human subjects.

- Record ID: 21139807
- Report Date: 28-Sep-2018
- Current Score**: 96

REQUIRED, ELECTIVE, AND SUPPLEMENTAL MODULES	MOST RECENT	SCORE
History and Ethics of Human Subjects Research (ID: 498)	16-Oct-2016	7/7 (100%)
Students in Research (ID: 1321)	12-Oct-2016	5/5 (100%)
Liberty University (ID: 15111)	28-Sep-2018	No Quiz
Informed Consent (ID: 3)	24-Sep-2018	5/5 (100%)
Social and Behavioral Research (SBR) for Biomedical Researchers (ID: 4)	28-Sep-2018	4/4 (100%)
Belmont Report and Its Principles (ID: 1127)	12-Oct-2016	3/3 (100%)
Records-Based Research (ID: 5)	28-Sep-2018	3/3 (100%)
Genetic Research in Human Populations (ID: 6)	28-Sep-2018	5/5 (100%)
Research and HIPAA Privacy Protections (ID: 14)	28-Sep-2018	4/5 (80%)
Basic Institutional Review Board (IRB) Regulations and Review Process (ID: 2)	24-Sep-2018	5/5 (100%)
Recognizing and Reporting Unanticipated Problems Involving Risks to Subjects or Others in Biomedical Research (ID: 14777)	28-Sep-2018	4/5 (80%)
Populations in Research Requiring Additional Considerations and/or Protections (ID: 16680)	28-Sep-2018	5/5 (100%)
Conflicts of Interest in Human Subjects Research (ID: 17464)	24-Sep-2018	5/5 (100%)

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Verify at: www.citiprogram.org/verify/?k1b559d0a-ecb0-456c-b130-1c2d541c10c3-21139807

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COLLABORATIVE INSTITUTIONAL TRAINING INITIATIVE (CITI PROGRAM)
COMPLETION REPORT - PART 1 OF 2
COURSEWORK REQUIREMENTS*

* NOTE: Scores on this Requirements Report reflect quiz completions at the time all requirements for the course were met. See list below for details.
See separate Transcript Report for more recent quiz scores, including those on optional (supplemental) course elements.

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- Institution Affiliation: Liberty University (ID: 2446)
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- Institution Unit: Nursing
- Phone: 919-810-5427

- Curriculum Group: Social & Behavioral Research - Basic/Refresher
- Course Learner Group: Social & Behavioral Researchers
- Stage: Stage 1 - Basic Course
- Description: Choose this group to satisfy CITI training requirements for Investigators and staff involved primarily in
                           Social/Behavioral Research with human subjects.

- Record ID: 21183261
- Completion Date: 28-Sep-2018
- Expiration Date: 27-Sep-2021
- Minimum Passing: 80
- Reported Score*:   90

REQUIRED AND ELECTIVE MODULES ONLY	DATE COMPLETED	SCORE
Belmont Report and Its Principles (ID: 1127)	12-Oct-2016	3/3 (100%)
History and Ethical Principles - SBE (ID: 490)	16-Oct-2016	5/5 (100%)
Defining Research with Human Subjects - SBE (ID: 491)	16-Oct-2016	5/5 (100%)
The Federal Regulations - SBE (ID: 502)	07-Jul-2017	5/5 (100%)
Assessing Risk - SBE (ID: 503)	07-Jul-2017	5/5 (100%)
Informed Consent - SBE (ID: 504)	07-Jul-2017	5/5 (100%)
Privacy and Confidentiality - SBE (ID: 505)	07-Jul-2017	5/5 (100%)
Populations in Research Requiring Additional Considerations and/or Protections (ID: 16680)	07-Jul-2017	1/5 (20%)
Unanticipated Problems and Reporting Requirements in Social and Behavioral Research (ID: 14928)	07-Jul-2017	5/5 (100%)
Liberty University (ID: 15111)	28-Sep-2018	No Quiz
Research and HIPAA Privacy Protections (ID: 14)	28-Sep-2018	4/5 (80%)

For this Report to be valid, the learner identified above must have had a valid affiliation with the CITI Program subscribing institution
identified above or have been a paid Independent Learner.

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COLLABORATIVE INSTITUTIONAL TRAINING INITIATIVE (CITI PROGRAM)
COMPLETION REPORT - PART 2 OF 2
COURSEWORK TRANSCRIPT**

** NOTE: Scores on this Transcript Report reflect the most current quiz completions, including quizzes on optional (supplemental) elements of the
course. See list below for details. See separate Requirements Report for the reported scores at the time all requirements for the course were met.

- Name: Joshua Fleming (ID: 5903591)
- Institution Affiliation: Liberty University (ID: 2446)
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- Curriculum Group: Social & Behavioral Research - Basic/Refresher
- Course Learner Group: Social & Behavioral Researchers
- Stage: Stage 1 - Basic Course
- Description: Choose this group to satisfy CITI training requirements for Investigators and staff involved primarily in
                           Social/Behavioral Research with human subjects.

- Record ID: 21183261
- Report Date: 28-Sep-2018
- Current Score**:   98

REQUIRED, ELECTIVE, AND SUPPLEMENTAL MODULES	MOST RECENT	SCORE
Students in Research (ID: 1321)	12-Oct-2016	5/5 (100%)
Liberty University (ID: 15111)	28-Sep-2018	No Quiz
History and Ethical Principles - SBE (ID: 490)	16-Oct-2016	5/5 (100%)
Defining Research with Human Subjects - SBE (ID: 491)	16-Oct-2016	5/5 (100%)
Belmont Report and Its Principles (ID: 1127)	12-Oct-2016	3/3 (100%)
The Federal Regulations - SBE (ID: 502)	07-Jul-2017	5/5 (100%)
Assessing Risk - SBE (ID: 503)	07-Jul-2017	5/5 (100%)
Informed Consent - SBE (ID: 504)	07-Jul-2017	5/5 (100%)
Privacy and Confidentiality - SBE (ID: 505)	07-Jul-2017	5/5 (100%)
Research and HIPAA Privacy Protections (ID: 14)	28-Sep-2018	4/5 (80%)
Unanticipated Problems and Reporting Requirements in Social and Behavioral Research (ID: 14928)	07-Jul-2017	5/5 (100%)
Populations in Research Requiring Additional Considerations and/or Protections (ID: 16680)	28-Sep-2018	5/5 (100%)
Conflicts of Interest in Human Subjects Research (ID: 17464)	24-Sep-2018	5/5 (100%)

For this Report to be valid, the learner identified above must have had a valid affiliation with the CITI Program subscribing institution
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Appendix D

This project took place outside of any formal organizational structure, which excludes this requirement of documented organizational approval. This decision was corroborated with the researcher's chair and Liberty University IRB personnel. Both of these entities agreed that given the low risk status of this project's aims that forgoing organizational approval for surveyed providers was unnecessary.

Appendix E

Pharmacogenomics Pre-survey Questions

1. What is your current level of knowledge on pharmacogenomics testing?
    a. Never heard of it
    b. Very little experience (Heard of it mentioned)
    c. Limited understanding (Received any amount of formal training)
    d. Solidified understanding (Feeling confident in simple concepts surrounding testing)
    e. Advanced understanding (Received extensive education on concepts of testing)

2. How often is pharmacogenomics testing part of your management currently?
   a. Never
   b. Sometimes (Less than 10 cases in a year)
   c. Often (Less than 50 cases in a year)
   d. Frequently (More than 50 cases in a year)
   e. Every day
3. In your current practice, what is drug dosing primarily based on? (Select all that apply)
   a. Renal function
   b. Hepatic function
   c. Age
   d. Weight
   e. Sex
   f. Comorbid conditions
   g. Clinical guidelines
   h. Personal preference and familiarity
   i. Biomarkers from pharmacogenomics testing
4. How clinically significant do you believe pharmacogenomics testing results are to patient outcomes?
   a. No significance at all
   b. Very little significance
   c. Neutral
   d. Somewhat significant
   e. Very significant
5. Do you see the cost of testing as a prohibitive factor in implementing pharmacogenomics testing?
   a. In all cases
   b. In most cases
   c. Neutral
   d. In some cases
   e. In no cases

6. What is the main barrier for the implementation of pharmacogenomics testing in your current management of patients? (Select all that apply)
   a. Unfamiliarity with testing
   b. Cost of testing
   c. Lack of evidence for clinical use
   d. Lack of impact on clinical practice
   e. Clinical responsibility for testing results
7. What do you believe is the best application of pharmacogenomics testing in your current practice?
   a. Preventative management
   b. Polypharmacy concerns
   c. Ineffectiveness of conventional therapies
   d. Complex patient presentation and needs
   e. No application at all
   f. As part of regular management
8. How comfortable are you with interpreting pharmacogenomics testing results based on your current level of knowledge?
   a. Completely uncomfortable
   b. Somewhat uncomfortable
   c. Neutral
   d. Comfortable
   e. Very comfortable
9. How important do you believe it is to include pharmacogenomics education in medical education curriculum?
   a. Not important at all
   b. Not very important
   c. Neutral
   d. Somewhat important
   e. Very important
10. What formats do you believe are important for increased knowledge surrounding pharmacogenomics testing?
    a. Conferences
    b. Continuing education courses

    c. College

    d. Graduate school (Medical school, PharmD school, PA school, NP school)

    e. Internet-based education modules

11. What is your age?

    a. < 25 years old

    b. 25-34 years old

    c. 35-45 years old

    d. 45-55 years old

    e. > 55 years old

12. What is your discipline?

    a. Medical Doctor

    b. Physician Assistant

    c. Nurse Practitioner

    d. Doctor of Osteopathic Medicine

    e. Pharmacist

13. How many years of experience do you have in your current role?

    a. 1-3 years of experience

    b. 4-6 years of experience

    c. 7-10 years of experience

    d. 11-15 years of experience

    e. 16-21 years of experience

    f. 22-30 years of experience

    g. > 30 years of experience

14. What is your gender?

    a. Male

    b. Female

15. How interested are you to receive education regarding pharmacogenomics testing?

    a. Not interested at all

    b. Not very interested

    c. Neutral
    d. Interested
    e. Very interested

Pharmacogenomics Post-survey Questions

1. How likely are you to pursue including pharmacogenomics testing in your clinical management of patients as a result of the information provided in the educational intervention?
   a. No likelihood
   b. Not likely
   c. Neutral
   d. Somewhat likely
   e. Very likely
2. What factors are still present that stand as barriers to implementation of testing? (Select all that apply)
   a. Lack of foreseeable clinical impact
   b. Cost of testing
   c. Insufficient knowledge base
   d. Clinical responsibility for testing
   e. Not knowing when and who to test
3. How likely are you to pursue further pharmacogenomics education as a result of your participation in this project?
   a. No likelihood
   b. Not likely
   c. Neutral
   d. Somewhat likely
   e. Very likely
4. The educational intervention in this project thoroughly addressed the barriers to implementation of pharmacogenomics testing.
   a. Completely disagree
   b. Somewhat disagree
   c. Neutral
   d. Somewhat agree

e. Completely agree

5. Based on the project's educational intervention, pharmacogenomics testing has clinical significance in the management of primary care patients.
    a. Completely disagree
    b. Somewhat disagree
    c. Neutral
    d. Somewhat agree
    e. Completely agree

6. Based on the project's educational intervention, pharmacogenomics testing is financially viable in the management of primary care patients.
    a. Completely disagree
    b. Somewhat disagree
    c. Neutral
    d. Somewhat agree
    e. Completely agree

7. Based on the project's educational intervention, pharmacogenomics concepts should be included in the preparatory curriculum of those entering the medical field or offered as continuing education opportunities for the field of primary care.
    a. Completely disagree
    b. Somewhat disagree
    c. Neutral
    d. Somewhat agree
    e. Completely agree

8. Based on the project's educational intervention, pharmacogenomics testing is most appropriately accomplished for patients within the primary care setting.
    a. Completely disagree
    b. Somewhat disagree
    c. Neutral
    d. Somewhat agree
    e. Completely agree

9. Based on the project's educational intervention, pharmacogenomics testing implementation can greatly reduce adverse drug reaction events.
    a. Completely disagree
    b. Somewhat disagree
    c. Neutral
    d. Somewhat agree
    e. Completely agree

10. Based on the project's educational intervention, pharmacogenomics testing should be considered for (Select all that apply):
    a. No primary care patients
    b. In cases where adverse drug reactions are more likely
    c. In cases where polypharmacy is a concern
    d. In patients where normal therapies are noted to be ineffective
    e. In all primary care patients

Appendix F

CONSENT FORM

Pharmacogenomics Testing in Primary Care: Barriers to Implementation

Joshua Fleming

Liberty University

School of Nursing

You are invited to be in a research study on how the current perspectives and level of understanding pertaining to the use of pharmacogenomics testing in primary care settings are affected by targeted educational intervention. You were selected as a possible participant because of the setting in which you work, the capability that you possess in potentially ordering pharmacogenomics testing, specific perspectives and level of understanding that you may possess as it relates to the subject of pharmacogenomics in the primary care setting, and availability for participation in educational intervention and post-surveying. You were also selected based on your role in the primary care setting as either a physician, nurse practitioner, or physician assistant. Please read this form and ask any questions you may have before agreeing to be in the study.

Joshua Fleming, a doctoral candidate in the School of Nursing at Liberty University, is conducting this study.

Background Information: The purpose of this study is aimed towards understanding the level of understanding and perspectives of primary care providers, which include physicians, nurse practitioners, and physician assistants, on the subject of pharmacogenomics testing. Specifically, the outcome being measured through this study is the level of impact that a targeted educational intervention has on the level of understanding and perspectives of primary care providers. This will be evaluated through establishing baseline results through pre-surveying and comparing this to the results that are evaluated through post-surveying after the targeted educational intervention regarding pharmacogenomics is delivered.

Procedures: If you agree to be in this study, I would ask you to do the following things:

1. Provide an accurate and unbiased baseline regarding current level of understanding and perspectives of pharmacogenomics in the primary care setting. This will be established through the answering of questions in the pre-survey that will be delivered electronically to your organizational email. It is asked that you answer all survey questions completely within two weeks of initial dispersal.

2. Be willing to receive targeted educational intervention on the subject of pharmacogenomics testing that will be developed to address barriers that have been noted in the literature as well as those that are identified to be prevalent among respondents, based on pre-surveying results.

3. Provide an accurate and unbiased report regarding post-education level of understanding and perspectives of pharmacogenomics testing in the primary care setting. This will be established through the answering of questions in the post-survey that will be delivered electronically to your organizational email. It is asked that you answer all survey questions completely within four weeks of initial dispersal of post-survey, which will coincide with dispersal of targeted educational intervention.

Risks: The risks involved in this study are minimal, which means they are equal to the risks you would encounter in everyday life.

Benefits: The direct benefits participants should expect to receive from taking part in this study are gains in knowledge base regarding the potential application of pharmacogenomics testing in the primary care setting, which contains many potential benefits for both patients receiving care as well as providers who are managing these patients' care. Benefits to society include the possible increasing acceptance of pharmacogenomics testing in the primary care setting, and subsequent possible prevalence of this testing in regular care and management, which stand to benefit patients seeking care in the primary care setting through affecting many different patient outcomes positively.

Compensation: Participants will not be compensated for participating in this study.

Confidentiality: The records of this study will be kept private. In any sort of report I might publish, I will not include any information that will make it possible to identify a subject. Research records will be stored securely, and only the researcher will have access to the records. Data will be stored on a password locked computer and may be used in future presentations. After three years, all electronic records will be deleted.

Voluntary Nature of the Study: Participation in this study is voluntary. Your decision whether or not to participate will not affect your current or future relations with Liberty University. If you decide to participate, you are free to not answer any question or withdraw at any time.

How to Withdraw from the Study: If you choose to withdraw from the study, please inform the researcher that you wish to discontinue your participation prior to submitting your study materials. Your responses will not be recorded or included in the study.

Contacts and Questions: The researcher conducting this study is Joshua Fleming. You may ask any questions you have now. If you have questions later, **you are encouraged** to contact him at (919)-810-5427 / jmfleming2@liberty.edu. You may also contact the researcher's faculty chair, Ken Thompson, at kthompson55@liberty.edu.

If you have any questions or concerns regarding this study and would like to talk to someone other than the researcher[s], **you are encouraged** to contact the Institutional Review Board, 1971 University Blvd., Green Hall Ste. 2845, Lynchburg, VA 24515 or email at irb@liberty.edu.

Please notify the researcher if you would like a copy of this information for your records.

Statement of Consent: I have read and understood the above information. I have asked questions and have received answers. I consent to participate in the study.

_____

Signature of Participant   Date

_____

Signature of Investigator   Date

(Liberty University, 2019)