A Pharmacogenetic Testing Guideline for Utilization in Mental Health

In partial fulfillment of the requirements for the Doctor of Nursing Practice

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Abstract

Depression is one of the most common mental health disorders in the United States. Psychotropic medications are recommended for mental health disorders such as depression. However, their use raises concerns over their efficacy and adverse effects on patients. Pharmacogenetic testing (PGT) has been proposed as a measure for providing prescribers with insights into the medications that would be most suitable for individual patients. However, PGT is underutilized in mental health care. This project involved the development of a standardized PGT guideline for use in a mental health clinic with the aim of enhancing mental health providers' PGT knowledge, reduce repeat appointments for medication management, and reduce adverse medication effects, and improve treatment adherence. The project was guided by Kurt-Lewin's three-step model of change, and it adopted a pre and post-test design. Quantitative data measuring provider knowledge, guideline usage, and the number of return visits was collected. The findings indicated that educating providers on PGT testing increased their application of genetic tests to determine the effective medications for their patients. The findings also showed a mean reduction of -3.7% in the number of return visits in the post-test period. The PGT guideline had a great impact in reducing the number of return visits for medication management for every provider. Mental health providers should embrace the use of PGT testing to increase treatment efficacy, improve patient satisfaction, and provide personalized care to patients.

Keywords: Pharmacogenetic testing, mental health, return visits.

A Pharmacogenetic Testing Guideline for Utilization in Mental Health

Depression is among the most common mental health disorders in the United States. According to Brody, Pratt, and Hughes (2018), 8.1% of the American population aged 20 and above suffered from depression during 2013-2016. The researchers further established that women had a higher likelihood of experiencing depression (10.4%) compared to men (5.5%). One of the ways to treat depression is through medical intervention, however finding the proper treatment can take an extended time. Lake and Turner (2017) found that it can take up to 10 years to obtain treatment after symptoms of depressed mood begin, with more than two-thirds of depressed individuals never receiving adequate care. Use of antidepressants are usually the treatment plan, but limited efficacy, safety issues, and high treatment costs have resulted in a large unmet need for treatment of mental illness. Some depressed patients are unable to work and provide for their families due to the debilitating effects of the mental disorder. According to Lake and Turner (2017), mental illness, including depression, is the leading cause of disability in the U.S. and causes $31 billion loss in productivity annually for those 15 to 44 years old.

The current model of conventional mental health care is mainly founded on psychotropic medications, which form a significant part of treatment for several mental health illnesses. Many patients diagnosed with mental health disorders, such as bipolar disorder, major depressive disorder, and schizophrenia, depend on medications to function as productive members of the society. However, the use of psychotropic medications raises concerns among patients regarding their efficacy and adverse effects such as weight gain, enhanced risk of diabetes and cardiovascular diseases, neurologic disorders, and sudden cardiac death. Research has documented that metabolic syndrome, enhanced risk of diabetes, and coronary artery disease may be due to antipsychotics and psychotropic medications (Lake & Turner, 2017). Patients

may delay taking psychotropic agents due to lack of awareness of the outcomes of treatment. As such, it is crucial for healthcare practitioners to ease the minds of their patients by incorporating appropriate testing and medications to provide the best care.

Genetic testing to determine how the body metabolizes certain mental health medications can give the prescriber insight as to which medications to order as a first line treatment. In the past few decades, increasing optimism has been associated with genetic causal explanations for mental illness. Some health practitioners believe that genetic factors play on the nature of mental illness and that genes provide significant information about a person's propensity to mental illness (Lee et al., 2013, p. 781). These genetic essentialist perspectives suggest that genetic attributions, which imply a high level of uncontrollability, may result in beliefs about the undesirable features when dealing with acute mental illness (Lee et al., 2013).

However, pharmacogenetic testing is underutilized in mental health care as providers generally apply the trial and error technique when prescribing medications. This technique often leads to more trials than necessary, thereby emphasizing the importance of introducing a pharmacogenetic testing guideline in mental health care (Routhieaux, Keels, & Tillery, 2018). Pharmacogenetic testing can prevent the trial and error approach that is commonly adopted by mitigating adverse effects of psychotropic medications. This is achieved by allowing mental health practitioners to prescribe a specific medication regimen that meets the unique needs of each patient and that will lead to the best outcomes early in the treatment process (Routhieaux et al., 2018). The purpose of this Doctor of Nursing Practice (DNP) project is to provide prescribers with a pharmacogenetic testing guideline that can be used in mental health settings.

Background

In mental health care, differences in patients' responses to antipsychotic and mood stabilizers as well as the number of refractory disease processes are some of the key challenges experienced by prescribers (Routhieaux et al., 2018). Pharmacogenetics and pharmacogenomics are emerging issues in the field of pharmacy. Pharmacogenetics involves studying the variability in drug response due to heredity and is influenced by factors such as ethnicity, age, and sex (Routhieaux et al., 2018). Pharmacogenetic testing highlights differences in the effects of medication arising from patients' genetic variations. The practice is adopted since the decision to use a specific medication regimen for treating mental disorders such as schizophrenia or bipolar disorder can be challenging due to the complexity of genetics and variations in drug metabolism with cytochrome P450 enzymes. Medication therapies for the two disorders are patient-specific and require genetic analysis to determine best treatment (Routhieaux et al., 2018).

The history of PGT spans over 40 years to the 1950s when the term was conceptualized. In the 1960s and 1970s, clinicians described two phenotypes: poor metabolizers (PM) and extensive metabolizers (EM). The PMs lack metabolic enzymes required to breakdown drugs while EMs metabolize normally for different drugs including tricyclic antidepressants (TCAs) (de Leon, 2016). The cytochrome P450 (CYP) genes, which cause poor metabolization, the TCA ultra-rapid metabolizers (UMs), which is associated with high (Cyclophilin D) CYPD activity, as well as other pharmacokinetic genes were discovered in the 1980s and 90s (de Leon, 2016). During this period, the first Deoxyribonucleic acid (DNA) microarray, which facilitated testing of diverse DNA sequences was developed, creating a path for further developments in genetic testing and pharmacogenetics. However, the application of pharmacogenetics in mental

health premiered in 1994 where CYP2D6 testing was performed on patients taking TCAs and it was noted that PMs demonstrated high levels of risperidone adverse drug reactions (ADRs). Additionally, it was noted that higher costs were incurred when PMs and UMs were treated with first-generation antipsychotics and antidepressants (de Leon, 2016). The early years are characterized with fear of pharmacogenetic testing as developers of these testing were pessimistic about getting approval from The United States Food and Drug Administration (FDA). Particularly, psychiatry presented a grey area as most mental disorders are syndromes that could not be validated in any way. However, this changed in 2005 when the FDA championed personalized medicine using biomarkers leading to the development of various DNA microarrays for CYP testing (de Leon, 2016; Limandri, 2019).

The popularity of pharmacogenetic testing in mental health has increased since then and the innovation is expected to streamline medication management and prescription practices in psychiatry. According to Pérez et al. (2017), the Clinical Pharmacogenetics Implementation Consortium (CPIC) developed guidelines for drug selection and dosage especially for tricyclic antidepressants as well as selective serotonin reuptake inhibitors founded on CYP2D6 and CYP2C19 genotypes. Additionally, pharmaceutical firms are incorporating details regarding pharmacogenomics into drug labels.

Since completion of the Human Genome Project, researchers have utilized data to isolate individuals predisposed to certain disorders, improve medication options, and prevent adverse treatment effects (Burke et al., 2016). This has been made possible by utilization of pharmacogenetic testing [PGT] (Burke, Love, Jones, & Fife, 2016). Prior to a medication having any effect on the body, it must be absorbed into the body's systems. There is a relationship between pharmacodynamics (how a medication affects the body) and pharmacokinetics (how the

body affects the medication) that is unique within each person (Stahl, 2013). One of these systems is called cytochrome P450 and is a family of liver enzymes analyzed by PGT that plays a significant part in complete drug metabolism, which is a pharmacokinetic process (Burke et al., 2016). The expression of each enzyme is determined by a unique set of mechanisms and factors such as genetic polymorphisms, induction by xenobiotics, regulation by cytokines, hormones and during disease states, as well as sex, age, and others (Zanger & Schwab, 2013, p. 103). Genetic variability can lead to clinical effects when it changes how drugs are processed or activated in the body. For some genes and drugs, there is evidence to support an association between genetic variability and changes in drug levels or effects.

PGT is likely to improve patient adherence to their medication so that patients are less likely to need further mental/medical care thus reducing health care cost. The cost of mental health treatments has increased from $136 per person in 1986 to $626 per person in 2014 (Burke et al., 2016). Burke et al. (2016) further states these high costs are due in part to poor patient adherence to medications. The authors found that during non-adherence to medication treatment, schizophrenia and depressed patients are more likely to have psychiatric admissions than medication adherent patients. Research has shown a saving of $562 per patient versus non-adherent patients over four months while $104 is saved in health care spending for each prescription that is filled (Burke et al., 2016). Salloum et al. (2014) emphasize that the application of PGT is less costly compared to the costs associated with repeated trial and failure, delay in effective treatment, provider compensation, and unexpected adverse effects of medication. The authors established that prescribing medications that are poorly matched with the patients' genotype increases the frequency of their visits to mental health clinics, the amount

of medication required to treat mental disorders, and the costs of care. As such, the cost-benefit ratio strongly favors the use of PGT.

Utilizing PGT in clinical practice has been very slow amongst healthcare providers, including mental health providers (Caudle et al., 2016). Scientific advancements have shown a direct link between genetic variation and variability of a medication's effect and response. However, lack of understanding in how to translate genetic results into clinical action is an issue facing most prescribers (Caudle et al., 2016). Additionally, the use of PGT in mental health is hindered by several barriers including feasibility, unclear clinical validity, lack of guidelines, variability in available tests, and costs (Caudle et al., 2016; Gross & Daniel, 2018).

Problem Statement

Currently, the utilization of PGT in mental health practice is low because of barriers such as lack of guidelines, costs, unclear clinical validity, and variability in the available tests (Gross & Daniel, 2018). These barriers force mental health practitioners to return to the conventional treatment approach founded on medicinal trial and error (Burke et al., 2016). As a result, some patients are being treated with multiple ineffective medications to treat their mental illnesses. Treating the patient ineffectively can lead to several appointments for the same complaint, unnecessary adverse effects from the medications, and ultimately non-adherence for treatable mental conditions. Developing a guideline for application of PGT in mental health practice can improve treatment outcomes by providing a framework of ensuring that practitioners prescribe medications suitable to each individual patient. PGT has been found to enhance health outcomes for individual patients by ensuring that they get specific medication regimen that suits their genetic variations (Routhieaux et al., 2018). Additionally, application of PGT would minimize the adverse effects experienced by patients due to mental health medications due to consideration

of gene-drug interactions during prescription. The intervention would also minimize the medication associated costs or mental health costs by ensuring that patients get the most effective drugs in the early phases of treatment (Chandra, 2017; Gross & Daniel, 2018).

Purpose Statement

The purpose of this DNP project is to design a standardized pharmacogenetic guideline for use by the providers in a mental health clinic. The overarching aims of this project are to improve mental health provider knowledge in the PGT, reduce repeat appointments, and improve patient satisfaction by reducing adverse medication effects and improving treatment adherence.

Project Question

The project will be guided by the following clinical question:

Among providers in an outpatient mental health clinic (P), would the implementation of a pharmacogenetic testing guideline (I), compared with no guideline (C), reduce patient return visits due to medication intolerance (O), within a period of four weeks?

- **(P) – Population:** Outpatient mental health care providers in private practice.
- **(I) – Intervention:** development of pharmacogenetic testing (PGT) guideline with all patients who meet Diagnostic and Statistical Manual of Mental Disorders (DSM–5) criteria for mental illness.
- **(C) – Comparison:** No use of PGT
- **(O) – Outcome:** Fewer returned visits for the same symptoms, increase use of PGT in practice site
- **(T) – Time:** The outcomes would be measured within one month of the pre and post-intervention period.

Project Objectives

The objectives of this DNP project are:

1. Develop a PGT guideline for use in a mental health clinic.
2. To improve provider knowledge, identify the benefits of PGT, and improve use of the PGT guideline.
3. To decrease the number of patient return visits for the same problem.

The Significance to the Profession

The art of finding the correct medication for the right patient without discouraging side effects or intolerability can be a daunting task. However, this project is critical in various ways, both to the project site and to the profession of nursing. Pharmacogenetic testing may be underutilized in mental health care. Mental health providers generally apply the trial and error method when prescribing medications. This could lead to more trials than necessary. Thus, the issues can be resolved by introducing this study about pharmacogenetic testing guideline in mental health care (Routhieaux, Keels, & Tillery, 2018). This project is also essential because PGT can help in preventing the trial and error approach that is commonly accepted and alleviate the adverse effects of psychotropic medications. This is done by allowing mental health practitioners, including nurses, to prescribe a specific medication regimen that meets the unique needs of each patient and that will lead to the best outcomes early in the treatment process (Routhieaux et al., 2018).

When using the pharmacogenomic recommendations and guidelines, it can help achieve decreased morbidity and lowered cost, mostly from monitoring as well as avoiding adverse reactions of the drugs, executing genetic testing, and considering the ethnicity of the patient. This helps identify the importance of this study to the nursing profession. When considering the

project site, this project is important because it helps those involved in the project site to gain more knowledge regarding how they can assign some of the tasks, such as those that relate to PGT. The guidelines will facilitate adoption of evidence-based practice at the project site; thereby meeting the American Association of Colleges of Nursing essential emphasizing scientific underpinnings for practice. The project further embodies the DNP requirement on demonstration of organizational and systems leadership for quality improvement and systems thinking. This will be attained by improving prescribing procedures at the project site through PGT.

Literature Review

Review Coverage and Justification

A review of available literature on PGT in mental health settings is presented. The reviewed studies were retrieved from peer-reviewed journal articles published within the last five years, between 2014 and 2019. The articles were retrieved from different databases including PubMed, Cumulative Index of Nursing and Allied Health Literature (CINAHL), Medline, EBSCOhost, ProQuest, Google Scholar, PsychInfo, and Emerald. Keywords were used to query the databases and retrieve the articles. The keywords included “pharmacogenetic testing”, “mental illness”, “pharmacogenetic testing guidelines”, and “mental health settings”. The Boolean operator “AND” was used with the keywords to make the search possible. The combination yielded search terms such as pharmacogenetic testing “AND” mental health. Articles were included in the review if they were published within the last five years, were published in English, specifically focused on pharmacogenetic testing in mental health, and were publicly accessible. The search yielded a total of 230 articles. From this, 50 articles were excluded since they were duplicates and 80 articles were not fully accessible. Additionally, 70

articles were excluded since they also focused on other healthcare settings, apart from mental health. The remaining 30 articles were closely examined, and 10 articles were eliminated since they tackled the topic in a generalized manner. The remaining 20 articles were included in the literature review.

Review Synthesis

Application of pharmacogenetic testing in mental health. Genetic information influences the capability of hepatic cytochrome P450 enzymes to metabolize particular medications and determines whether a person clears the medications too fast leading to minimal therapeutic effects. In other instances, the medications can build up to toxic levels leading to side effects. The cytochrome P450 system exists in more than 50 different types of enzymes which facilitate metabolic processes in the body. However, only six variations of the enzymes are used in metabolizing approximately 90% of medications (Burke, Love, Jones, & Fife, 2016). The enzymes used in metabolism of different antidepressants and antipsychotics are CYP2D6 and CYP2CI9, whereby the 85% and 38% of antidepressants are metabolized by CYP2D6 and CYP2C19, respectively. Additionally, CYP2D6 metabolizes 40% of antipsychotics (Burke et al., 2016). Dopamine-D2 receptor gene (DRD2) is one of the pharmacodynamics genes whose influence on treatment outcomes have been studied widely in mental health as it is targeted by every currently available antipsychotic agent (Eum, Schneiderhan, Brown, Lee, & Bishop, 2017; Rahman, Ash, Lauriello, & Rawlani, 2017).

Pharmacogenetics have been applied in treatment of different psychiatric disorders. For instance, it has been used among schizophrenia patients who continue to demonstrate persistent psychotic symptoms even after administration of antipsychotics. The poor response to antipsychotic medications is linked with deletion polymorphism in the DRD2 gene of some

patients (Eum et al., 2017). For example, PGT has been applied on schizophrenic patients who demonstrate a poor response to medications such as aripiprazole. Additionally, pharmacogenetics has been applied on patients with major depressive disorder (MDD) to understand gene-drug interactions and facilitate drug-specific treatment recommendations (Pérez et al., 2017). Pharmacogenetics have also been used in treatment of other mental health disorders including attention deficit/hyperactivity disorder (ADHD) and bipolar disorder (BPD) (Routhieaux et al., 2018). In BPD, PGT has been utilized to understand the metabolism process of lithium in bipolar patients who respond to lithium treatment, as they exemplify a unique clinical population. In most BPD patients, lithium has only a minimal effect on bipolar depression (Alda, 2015). Additionally, PGT is also applied in treatment of alcohol use disorder (AUD) due to differences in the genetic makeup of patients from different ancestral backgrounds, which influences the efficacy of medications used to treat the disorder (Cservenka, Yardley, & Ray, 2017). The innovation has also been used to explain the role of pregabalin (PGB), a gabapentinoid derivative of aminobutyric acid, in positively influencing neurobehavioral behaviors linked with PTSD (Valdivieso et al., 2018).

Even though useful medications for BPD exist, the variability in the outcome results in increased number of medication failures, followed typically by the trial and error procedure, which can take several years (Salloum et al., 2014). However, using PGT and tailoring drug selection to a person can expedite and personalize medication to identify faster treatments more suited to BPD patients. There are several associations created in BPD between treatment reaction phenotypes as well as particular genetic factors. To date, clinical PGT adoption is limited, often posing questions that have never had answers. This emphasizes the need for developing guidelines to facilitate the application of PGT in different healthcare settings.

Efficacy of pharmacogenetic testing in mental health settings. Several researchers have investigated the effectiveness of PGT in treating mental disorders. For example, Lelmini et al. (2018) conducted a quantitative, observational study to investigate the role of PGTs in supporting BPD treatment. The researchers opined that the tests could assist mental health practitioners to identify patients with a high likelihood of experiencing adverse effects as well as expanding their understanding of the influence of genetic variation and drug response. The study was based on a sample of 30 bipolar patients who had been on baseline treatment for a minimum of three months. The follow-up period was also three months. The findings indicated that only 13% of the patients had optimal therapy aligning with PGT recommendations at the baseline. However, this percentage increased to 40% in the three-month follow-up period as changes were made to the patients' medications in line with PGT results. Additionally, Lelmini et al. (2018) noted a statistically significant change in the patients' Clinical Global Impression Item Severity (CGI-S) score among patients whose medications were aligned with PGT suggestions. At the baseline, nine out of 10 patients whose medication therapy was modified experienced adverse effects. However, a significant within group reduction of adverse effects was observed in the follow-up period.

Similarly, Gardner, Brennan, Scott, and Lombard (2014) investigated the effectiveness of PGT in improving patient outcomes in psychiatry using a review of literature on the topic. The researchers noted that PGT enhance the efficiency in identification of effective therapies in mental health practice; thereby, protecting patients from prolonged suffering and high health costs. Gardner et al. (2014) provide examples of successful application of PGT in mental health practice. For instance, they quote a case involving application of the test on an 18-year old with intermittent explosive disorder leading to prescription of lithium. Consequently, the patient's

symptoms abated and improvements were noted in his school, social, and family life. PGT facilitated the identification of variations in the patient's SLC6A4, DRD2, and 5HT2C, which amplified the risk of failure and intolerance to antipsychotics. In another case, Gardner et al. (2014) noted that PGT was applied on a 31-year old female patient presenting with severe depressive symptoms leading to prescription of lamotrigine due to the patient's ANK3 gene variation. The gene is associated with sodium channels and is also engaged in neuronal excitability. As a result, a complete remission of the symptoms was recorded as lamotrigine stabilized the depressive symptoms owing to its sodium activity modulating capabilities. Gardner et al. (2014) noted that PGT facilitates identification of efficacious alternative therapeutic options in cases where conventional treatments do not yield positive results.

In individuals treated for mental illness, a portion of them fail to respond to the treatment provided or the symptoms may reoccur. Health Quality Ontario (2017) assessed the impact caused by GeneSight Psychotropic test in comparison to the standard care provided in support of the choice for psychotropic treatments for patients experiencing mood schizophrenia, disorders, or anxiety within the Ontario Ministry of Health context and long-term care. The results showed that the patients who had been provided with GeneSight test had improved reactions towards depression medication, more significant enhancements in depression measures, and greater clinician and patient satisfaction in comparison to patients who had received the usual treatment. There were no differences observed in the complete remission rates from depression. However, it can be concluded that there exists uncertainty regarding the utilization of GeneSight Psychotropic pharmacogenomic genetic board as a guide to the selection of medication. Health Quality Ontario (2017) associated the uncertainty with lack of clarity in the quality of evidence supporting the classifications in GreenSight report.

Blasco-Fontecilla (2019) conducted a retrospective cohort study to determine the efficacy of PGT among children and adolescents with severe mental disorders. The study used a sample of 20 children and adolescents diagnosed with autistic disorder, MDD, and attention-deficit hyperactivity disorder, and some of the participants were drawn from foster care. The effectiveness of PGT was evaluated based on clinical outcomes, polypharmacy, and adverse events. The results showed that use of PGT enhanced the clinical outcomes in 19 participants as indicated by the Clinical Global Impressions (CGI) Scale. In foster children, the CGI improvement (CGI-I) was 2 (0.79) average (range 1-4) and 2.1 (0.56) (range 1-3) whilst the CGI-I was 1.9 (0.99) (range 1-4) in non-foster care children. Additionally, a 20% decrease was noted in the number of children using polypharmacy. A decrease in the mean number of drugs per children was noted (from 3.3 to 2.4 drugs, p=0.017) as well as a decline in self-reported side effects (p=0.006) (Blasco-Fontecilla, 2018). These results show that PGT potentially assists clinicians to make better informed decisions regarding treatment of mental disorders.

Perez et al. (2017) conducted a 12-week randomized, double-blind clinical trial to investigate the effectiveness of progressive PGT in treating MDD. Patients with a CGI-S of four or more than four were randomly categorized into two groups: the experimental group (n=155) and the control group (n=161). The genotype of patients in the intervention group was determined using a commercial pharmacogenetic test, Neuropharmagen, and the results used to guide the patients' treatment. The control group underwent the usual treatment. The results showed that the experimental group has a higher responder rate to treatment after the 12-week period (47.8% vs. 36.1%, p=0.0476). Additionally, the experimental group demonstrated tolerance to medication and a minimal possibility of developing side effects.

PGT and mental health costs. Brown, Lorenz, Li, and Dechairo (2017) investigated the economic utility of PGTs in medical health settings. The study involves a sub-analysis of a one-year prospective trial comparing the medication costs of patients who had undergone testing. The study used a sample of 2,168 patients and compared the medical costs over a six-month period. The findings showed that use of PGTs offered the most medication cost savings as each individual patient was able to save $3,988 annually. Brown et al. (2017) noted that mental health practitioners could reduce medication costs significantly by applying PGTs in their practice. Similarly, Maciel, Cullors, Lukowiak, and Garces (2018) established that PGT is associated with annual cost savings amounting to $3,962 per patient. The researchers used published healthcare costs along with clinical patient outcome data to create a model of the economic effects of PGT-guided treatment. In another study, Verbelen, Weale, and Lewis (2017) reviewed the economic evaluations for PGTs and established that the tests are cost-effective. Approximately, 57% of the evaluations showed that PGTs are cost-effective (30%) or led to cost-savings (27%) compared with other approaches adopted in mental health practice. As such, mental health practitioners are encouraged to use PGT as a means of improving both clinical and cost outcomes.

Impact of PGT on nursing practice. PGT has important implications on nursing practice, especially for advanced nurse practitioners (APNs) who have prescribing privileges as well as the bed side nurses. The innovation will ensure that drugs are no longer prescribed on a trial and error basis but will be selected and dosed through precision medicine which aids the identification of patient genotype and phenotype (Cheek et al., 2015). Consequently, this will reduce adverse drug reactions (ADRs). Nurses have a role of ensuring optimal patient outcomes; therefore, they should have knowledge in pharmacogenomics as a nursing competency (Cheek et al., 2015).

Bedside nurses play a role in monitoring, advocating, educating, and acquiring patients' consent for appropriate PGT tests. Additionally, PGT will enable APNs to base their prescription practices on patients' genetic makeup. Nurses should also educate patients and their families about the results of the genetic tests, the interpretations of the test, as well as discussing the inducers and inhibitors that influence the patients' response to pharmacological therapy (Cheek et al., 2015; Haga & Mills, 2015). Bedside nurses will be required to establish whether PGT tests have been ordered appropriately as well as consider the results before administration of pharmacological agents. The nurses also have a role in assuring patients of the best response to therapy and ensuring they get the correct dosage of medicine. In mental health, nurses have an obligation to educate patients regarding their specific phenotypes of CYP2D6, toxicity risks, as well as poor response to antidepressants and antipsychotics (Cheek et al., 2015).

Review of Study Methods

Most of the reviewed studies adopted quantitative research methods and different types of designs including observational design, retrospective cohort studies, prospective trials, and randomized double-blind control trial (Blasco-Fontecilla, 2018; Perez et al., 2017). However, some of the researchers adopted other approaches such as literature reviews (Gardner et al., 2014). Quantitative methodologies are considered as appropriate for assessing the efficacy of interventions in the healthcare settings. This argument is founded on the fact that quantifiable research is more objective compared with qualitative research as measurable studies are less likely to be affected by researcher bias. Additionally, findings from quantitative studies can be generalized across settings especially where the studies use randomized samples which are representatives of entire populations (Rahman, 2017). As such, quantitative research methods are suitable for the current project as they would facilitate the determination of the effect of

PGTs on medical intolerance and related return visits among patients in the outpatient mental health clinic.

Significance of Evidence to Profession

The available research evidence supports the adoption of PGT in mental health settings. Regardless of extensive professional and scholastic training, the management of medication in psychiatry is relegated towards trial-and-error prescribing (Burke et al., 2016). According to Burke et al. (2016), PGT can speed up the identification of treatments with maximal effectiveness as well as minimal adverse events through recognizing personal genetic inconsistency in drug reactions. The authors also carried out research whose objectives were to outline the basis of PGT, assess the effect of PGT, and improve drug metabolism. Results showed that, regardless of the persistent increase in costs of health care, new biotechnology has resulted in a decreased expense of genetic sequencing as well as the PGT application to practice (Burke et al., 2016). As the PGT becomes more prevalent, nurses must have sufficient knowledge of PGT's possibilities and potential challenges to provide up-to-date and accurate patient information.

Russell et al. (2018) stated that it is unfortunate that several mental illnesses are lifelong states that require therapy and treatment to enhance life quality. However, clinical trial information shows not all patients attain remission. These outcomes show that there is a need for addressing the existing variability amongst the patients in their reaction towards treatment in addition to the developing of medication plans that are tailored to each individual. One approach may assist in explaining the variability of the patient's reaction to treatment is genetic variability (Russell et al., 2018). It was found that the use of PGT helped show gene variants, which could be contributing to poor response to medications prescribed. According to the current evidence,

genetic examination for psychiatric sickness may result in improvement of patient results in addition to lowering health care expenses.

Mental health prescribers have a role to help improve social distancing within mental health patients by providing them with treatment options that meet their specific needs. Genetic contingency theory assumes the genetic attributions will result in an increased social distance from individuals with disorders that are perceived to be dangerous (Lee et al., 2014). Provision of personalized treatment option that align with patients' genetic makeups can assist mental health patients to manage their symptoms effectively and become productive members of the society. However, Caudle et al. (2016) established that the implementation of pharmacogenetics into medical practice is relatively slow regardless of the considerable scientific progress throughout the past decade. The researchers noted that it is upon mental health practitioners to adopt the resources provided by institutions like The Pharmacogenomics Knowledgebase (PharmGKB) and Clinical Pharmacogenetics Implementation Consortium (CIPC) that are necessary for the application of pharmacogenetics into custom clinical practice.

Theoretical Framework

The DNP project will be guided by Kurt Lewin's three-step model of unfreezing, movement, and refreezing. The theory is adopted in organizational settings to solve problems, enhance performance, as well as reframe shared perceptions. Kurt Lewin is widely acknowledged as the founding father of change management as the three-step model has provided a solid foundation for the development of change management literature (Cummings, Bridgman, & Brown, 2016). Lewin was a social scientist who believed that human conditions could be improved through resolving social conflict. Additionally, he believed that this could be achieved through facilitating planned change, learning, and creating opportunities for people to understand, deconstruct, and restructure their views of the world around them (Burnes, 2004).

The three-step model of change is one of the components of the planned change along with field theory, group dynamics, and action research (Lewin, 1951).

Kurt Lewin developed the three-step model in 1951. According to Lewin, human behavior is influenced by dynamic driving and opposing forces. The theorist perceived that driving forces push workers in the desired direction; thereby, facilitating change whereas restraining forces hinder change by pushing individuals in the undesired or opposite direction (Kritsonis, 2005). Lewin developed the model to provide an integrated approach to effective implementation of planned change at the group, organizational, and societal levels (Burnes, 2004).

Lewin's change theory is relevant to the profession of nursing as it is widely used to implement evidence-based practice in clinical settings. Additionally, the theory is applied in quality improvement projects which facilitate the translation of research evidence into nursing practice (Allen, 2016). The model is used to support nurses through planned changes in the healthcare environment by identifying driving forces and restraining forces before implementation of the changes. The theory further facilitates the development of well-thought change plans and active stakeholder participation in the change process (Sutherland, 2013).

Major Tenets

Lewin's three-step change model is founded on the assumption that change entails unlearning and learning new behaviors. As such, exposing stakeholders to disconfirming information enhances the possibility of learning. Under the model, change is perceived as a result of new ideas acquired from experiences, experimentation, and feedback, which are embedded into new norms as well as organizational systems (Sarayreh, Khudair, & Barakat, 2013). The model is also based on the presumption that performance is prone to decline if

measures are not adopted, to cement the improved performance levels, in organizational systems and culture. Additionally, Lewin assumed that people experience tension when presented with a psychological need or intent and the tension only abates when that need is fulfilled. However, the tension can be positive or negative creating facilitating forces and constraining forces. Facilitating forces promote adoption of change while restraining forces create resistance and favor maintenance of the status quo (Kritsonis, 2005). Lastly, the model is founded on the assumption that organizational change occurs as a planned phenomenon.

Unfreezing

Unfreezing involves deconstructing the status quo or the equilibrium state (Batras, Duff, & Smith, 2016). This step entails creating morale for change by preparing stakeholders for change. The key aim is to overcome resistance to change and group conformity (Kritsonis, 2005). Unfreezing is achieved through application of driving forces to direct behavior from the status quo or decreasing restraining forces to minimize resistance to change. The specific activities that can be used to unfreeze an organization from the status quo include emphasizing the need for change, training stakeholders to empower them with knowledge and skills that would enable them to cope with the changes, motivating stakeholders, creating trust, and involving stakeholders in identifying underlying problems and their solutions (Kritsonis, 2005; Siddiqui, 2017). These measures eliminate stakeholders' fears and anxieties in relation to change. Organizations can also use change champions to inspire other stakeholders to support the change process.

Driving forces. Organizational change is caused by different forces arising from either the internal or external operating environment. The external forces include environmental changes such as political, economic influences, technological forces, competitive pressures,

cultural changes, and changes in the legal framework or government regulations. The internal forces include low productivity, employee turnover, strikes or go slows, and sabotage (Rizescu & Tileaga, 2016). A firm's ability to respond quickly to the external and internal changes significantly influences its competitiveness and performance.

Restraining forces. Organizational change initiatives can be hindered by different factors such as insufficient management support, limited understanding of expected changes, and lack of employee training. Additionally, change is hampered by lack of or insufficient communication, resistance by stakeholders, and insufficient funding or resources. Therefore, lack of commitment to the changes by the management ensures that the effects of the changes do not last in the long-term (Mosedeghrad & Ansarian, 2014).

Transitioning/Moving

Transitioning involves moving an organization from the old toward the desired goal. Under this phase, the organization is moved to a new level of equilibrium. The phase is attained through collaboration between leaders and subordinates as well as viewing of organizational challenges from a fresh perspective (Kritsonis, 2005). According to Wojciechowski, Pearsall, Murphy, and French (2016), transition is achieved by embracing new organizational behaviors, systems, processes, and strategies. The transition phase is also supported by training and re-training stakeholders to provide them with new skills set, knowledge, and competencies.

Refreezing

Refreezing involves stabilizing the firm at the new equilibrium by adopting measures to ensure the changes are cemented into the organizational systems. Refreezing protects the organization from regressing to the old norms. The process ensures that the new quasi-experimental equilibrium aligns with the employee behaviors and the work environment (Burnes,

2004). This phase is attained by adopting organizational norms, routines, policies, practices, values, and culture that support the implemented changes. The changes should reflect in the organization's formal structures, systems, and social fabric to ensure that they are entrenched into the organizational culture (Wojciechowski et al., 2016). Appendix A presents a graphical representation of the three-step change model.

Applicability of Theory to Current Practice

Lewin's three-step model is widely used in facilitating change and quality improvement projects in healthcare settings. Allen (2016) notes that the process of implementing change in healthcare organizations is complex and challenging. Lewin's three-step model is adopted to ensure the change process is achieved systematically as well as a means of reducing and avoiding negative outcomes. Allen maintains that the first stage (unfreezing) is for conducting organizational analysis and the preparatory works to create a foundation for the changes. The researcher posits that healthcare organizations can only implement change effectively by adopting a methodical change process.

Thorpe (2015) indicated that the change model could be applied in implementing change in mental health settings. The researcher focused on a change project aimed at improving the quality of physical health care among mental health patients. Specifically, the project involved adoption of a training program for the nurses in the mental health settings to enhance monitoring and recording of respiratory rates among the patients (Thorpe, 2015). The researcher noted that the theory would facilitate planning the service improvements, understanding the driving and resisting forces, and ensuring the project implementation process takes the envisioned direction.

In another study, Sutherland (2013) applied the three-step model in a quality improvement project involving the adoption of bar-coded medication administration in the

clinical environment. The researcher noted that the model offers crucial insights that can be used to overcome the fears and anxieties that predispose such projects leading to resistance. Sutherland further noted that the model offers a better understanding on the impacts of change on an organization, barriers to successful implementation of change, and measures for overcoming resisting forces; thereby, facilitating acceptance of health technologies by nurses.

Canfield and Galvin (2018) applied the three-step model in implementation of telemedicine in an intensive care unit (ICU). The researchers noted that the model offers a framework for facilitating acceptance of telemedicine in nursing care. The first phase involves creating an understanding on the necessity of the change and supporting the adoption of telemedicine in the ICU. This could be attained through presenting stakeholders with data on system improvements, desired outcomes, and benefits of telemedicine. This should be followed by adaptation of workflow to integrate the tele-ICU component. The nurses are then trained to meet the skills gap among the nurses. This is followed by stabilization of the change process through development of policies to support the application of telemedicine, ongoing education on workflow changes, as well as reinforcing the nurses' behaviors in relation to the technology.

Wojciechowski et al. (2016) applied Lewin's model in a project involving bedside shift reporting. The change process was also supported by the lean systems approach. The researcher maintained, the three-step model is adopted by nurses from different specialties for diverse quality improvement projects. In the study, the model was applied to understand the barriers that would hinder collaboration and bedside shift reporting. A working group was also developed to understand the changes and their implications. The transition phase was achieved through different strategies including training, role modelling, coaching and mentoring, and implementation followed by stakeholder engagement (Wojciechowski et al., 2016). Refreezing

was achieved through evaluation and monitoring and utilizing of key performance indicators (KPIs) as well as development of policies supporting bedside shift reporting. These measures created accountability, stabilized the process, facilitated visual management, and enabled the management to re-evaluate targets and goals using the KPIs.

In a similar study, Vines, Dupler, Van Son, and Guido (2014) applied Lewin's change model in bedside reporting with the aim of enhancing client and nurse satisfaction. Particularly, the model offered a foundation for staff education on the importance of bedside reporting and the significance of the handover process. Under unfreezing, awareness was created among the nurses on the significance of the proposed bedside reporting. The driving and restraining forces were also analyzed and resistance addressed accordingly. The transition phase involved implementation of bedside reporting whereas refreezing entailed evaluation of performance competencies, orienting new staff on bedside reporting, and providing feedback to the nurses.

Application of the Model in the DNP Project

Unfreezing

The project lead has evaluated the practice site and noted the need for adoption of pharmacogenetic testing. The mental health setting has not yet adopted this evidence-based practice, which could benefit patients through improved health outcomes as well as minimized adverse effects and healthcare costs. In this DNP project, unfreezing will be attained by educating the nurses and physicians in the mental health clinic about the need for PGT and its impacts on nursing care and patient outcomes. This will be attained through the use of the evidence available in nursing literature in order to create momentum for the adoption of pharmacogenetic guidelines.

Driving forces. The key driving forces include the need to enhance patient outcomes, reduce adverse effects as well as healthcare costs and improve productivity and effectiveness of mental health services offered by the clinic. Available research evidence shows that PGT testing enables patients to be provided with effective treatment that aligns with their genotype thereby reducing visits to mental health clinics. PGT testing also ensures effectiveness in terms of the amount used to treat patients (Salloum et al., 2014). The project will benefit from the support and goodwill of the management of the mental health center, which encourages quality improvement initiatives. The management will provide funds and resources necessary for project implementation. The management will also rally the other mental health practitioners to support the project.

Restraining forces. The project may be hindered by factors such as lack of or poor communication with involved parties. This barrier will be overcome by ensuring simple, precise written and oral communication to ensure all stakeholders understand the project direction. Initial resistance from practitioners may also act as a barrier to project implementation. However, resistance will be overcome by explaining the need and importance of the project as well as selecting change champions to create buy-in into the project. Available evidence supporting the adoption of PGT testing will also be presented to the stakeholders to create buy-in into the project.

Transitioning/Moving

The practitioners in the clinic will be trained how to conduct PGT tests and taken through the developed guidelines. This will minimize resistance to the proposed changes. The transition phase will involve application of PGT in the clinic whereby the practitioners will be required to test patients who visit the clinic as part of the routine examination. The practitioners will further

ensure that patient prescriptions are based on the PGT results in order to optimize health outcomes and prevent adverse effects. The practitioners will be expected to adopt PGT as the standard practice.

Refreezing

The refreezing phase will involve the development of policies to support PGT testing, evaluation and monitoring of testing practices by regularly reviewing patient records. Monitoring will be performed by the project lead to ensure patients are being screened; practitioners are retrained to empower them with screening skills, and the development of PGT practice policy requiring the practitioners to test patients as part of the routine examinations. These measures will cement the use of PGT test into the organizational culture of the mental health center. For instance, the mental health practitioners at the center are more likely to follow the guidelines when they are aware that PGT testing is part of the practice policy and the management may routinely review patient records to establish whether they adhere to the policy.

Project Design

The project is a quality improvement (QI) project with the purpose of designing a standardized pharmacogenetic guideline and establish whether it will aid to improve mental health provider knowledge in the PGT, reduce repeat appointments, and improve patient satisfaction by reducing adverse medication effects and improving treatment adherence. The project will adopt a quantitative methodology, which is applied to analyze statistical data. A quantitative methodology makes generalization of project findings possible and facilitates the exploration of relationships between variables as well as testing of hypotheses (Eyisi, 2016). A quantitative methodology is suitable for the project as it will allow the determination of the

relationship between adoption of the standardized pharmacogenetic guideline and patient return visits due to medication intolerance.

The project will adopt a pre-survey and post-survey design. The design is adopted in scenarios where it is impossible to perform true experiments, which entail randomization and control groups (Gillan & Abdul, 2017; Lavis, Bärnighausen & El-Jardali, 2017). The pre-survey and post-survey design entails measuring the dependent before and after the intervention with the aim of evaluating the impact of the intervention on the variable. The pre-survey results provide a baseline against which the impacts of the intervention are evaluated (Myers, Well, & Lorch Jr., 2013). In the project, the independent variable is use of the standardized pharmacogenetic testing guideline while the dependent variables are mental health provider knowledge in PGT and reduced repeat appointments. As such, a pre-survey and post-survey design is most appropriate for the project as it will facilitate the effect of implementation of the standardized guideline on mental health provider knowledge and reduced repeat appointments. Data on return visits will be collected before and after the implementation of a standardized pharmacogenetic testing guideline. Additionally, the design will facilitate measurement of the change in the return visits arising from the adoption of the standardized pharmacogenetic guideline.

Descriptive and inferential statistics will be applied to analyze the collected data. Descriptive statistics such as mean and standard deviation will provide a meaningful depiction of the data. Inferential statistics will be used to determine the effect of the guideline on patient return visits due to medication intolerance. Particularly, paired t-test will be used to examine the difference in mean between the pre-survey and post-survey samples. The survey is appropriate for the project as it is applied to compare two groups with means which are co-dependent (Gerald, 2018). The survey will indicate whether there will be statistically significant

differences between provider knowledge and return visits before and after the adoption of the standardized pharmacogenetic guideline.

Population of Interest

Project population is the aggregate of all subjects who are involved in the project. Population can also be termed as the total number of individuals to be studied (Rahi, 2017). Research population can also be referred to as the total quantity of cases or things that are the subject of research investigation (Etikan, Musa, & Alkassim, 2016). The population of interest includes the mental healthcare providers, clinical therapists, and nurse practitioners employed in the clinic where the project will be implemented. The mental health clinic employs five mental health prescribers and three clinical therapists who will form the sample, which will receive education on the use of the standardized pharmacogenetic guideline. The inclusion criteria in the project is that the participants must be prescribing practitioners employed by the practice site. The exclusion criteria consist of prescribers not employed by the practice site and non-prescribing employees of the practice site to include medical assistance, front office clerks, administrators, and billing and coding personnel

Project Stakeholders

The primary stakeholders in the project include the management of the outpatient mental health clinic. The other important stakeholders include the mental health specialists, medical assistants, therapists, nurses, and the office manager. The mental health providers will participate in training sessions on pharmacogenetic testing and use of the standardized pharmacogenetic testing guideline. The project lead will play an important role in the project by retrieving patient data from the clinic's electronic health records (EHR). The mental health patients who visit the clinic are also an important part of the project stakeholders as the overall

purpose of the project implementation is to improve their health outcomes by reducing office visits and improving satisfaction.

Recruitment Methods

The providers in the outpatient mental health clinic will be recruited to participate in the project through the use of flyers, which will be posted on the noticeboards within the project site. The flyers will contain details on the purpose of the project, their role in the project, and the project lead's contact details (see Appendix B). The healthcare providers will be advised on their role in the implementation process by the project lead during a lunch and learn session. This is considered a clinic wide practice change therefore, all prescribing providers are mandated to participate. This is not a condition of employment and no compensation monetary or other will be provided. There are no risks to participate. The benefits only include an increase in knowledge and positive patient outcomes. The providers will be assigned a unique letter that only the project lead will know. The patient's information will be kept confidential during the chart audit and reporting. All patient charts will be kept at the practice site and project lead will perform chart audits alone in a closed room. Additionally, identifiers such as the patients' names or numbers will not be included in the project report. The providers and patients will be assigned a letter and a number as their identifiers, respectively.

Recruitment of Charts to Audit

Data on patients' return visits will be collected to determine the impact of PGT on the return rate among patients. The project lead will conduct chart audits one-month pre/post implementation of the PGT protocol. Five providers evaluate an average of 380 patients a week. The providers will select 25 patient charts that meet the inclusion criteria. The inclusion criteria consist of age, 18 and older, score greater than a five on the PHQ-9, and has a depression

diagnosis based on DSM-5 criteria. Once the charts are selected the provider communicates with the project lead by flagging the patient's chart and placing it in a designated bin. The data will be collected retrospectively from records of 25 random patients treated in the clinic two weeks before and after the implementation of PGT.

Setting

The project will be implemented in a mental health clinic in the United States. The clinic has been in operation since 2007 and is ran by an office manager, mental health prescribers, clinical therapists, and office staff. The clinic provides mental health care for a range of mental disorders including depression, anxiety, and post-traumatic stress disorder, among others. The clinic cares for roughly 500 adult mental health patients every week. The management gave permission for the project to be implemented in the institution as well as the resources required to ensure successful implementation (See Appendix C).

Tools and Instrumentation

The standardized pharmacogenetic guideline that will be developed in the project will be reviewed by experts in this field to ensure content validity. The experts will include health care professionals with expansive knowledge and experience in pharmacogenetic testing. The chart audit tool will capture the number of medication intolerance-related patient return visits both in the pre-survey and post-survey periods. The audit tool will be reviewed by the professor and members of the approving committee to ensure that it aligns with the project purpose. Expert review is one of the means of ensuring validity of data collection instruments whereby experts validate the tools as a means of ensuring they measure what they are supposed to evaluate (Zohrabi, 2013).

To implement this QI project several implementation tools were created or borrowed with permission to ensure organization and understanding for the participants. A standardized PGT protocol was developed, which includes evidence-based guidelines and screening tools. An educational presentation was also developed by the project lead to review screening methods and educate the participants in the benefits of PGT testing as an addition in their personal practice. Other tools used during the implementation phase consist of a pre and post implementation survey for the participants to complete and a chart audit tool to measure if the project objectives were met.

Educational Materials

A PowerPoint presentation will be used to implement the education sessions. The education program will be implemented using three, one-hour sessions. These sessions will be presented as a lunch and learn to enhance participation. The sessions will be provided over a one-week period and will be held in the clinic's boardroom (See Appendix D).

The education materials will be developed using available peer reviewed journal articles that discuss and debate the use of pharmacogenetic testing. The materials will cover a number of questions including what the testing entails, its benefits, and its effect on patient outcomes. The providers will also be educated to use the specific pharmacogenetic testing protocol that will be adopted in the project.

Pharmacogenetic Testing Protocol

The pharmacogenetic testing protocol developed for use at the clinic will be based on the guidelines by the Clinical Pharmacogenetics Implementation Consortium (CPIC). The institution has published nine guidelines on well-known pharmacogenetic associations. The CPIC guidelines adopt a standard format and contain a standard system for grading levels of

evidence associating genotypes to phenotypes as well as assigning a level of strength to each prescribing recommendation (Caudle et al., 2014). Patients screened with the Patient Health Questionnaire (PHQ-9) and diagnosed with depression will meet the criteria for the PGT protocol. There will be no additional assessments required. Patients' that are referred for PGT will follow up with the medical assistant for saliva sampling. The protocol also contains a PHQ-9 Self-Screener and PHQ-9 Patient Depression Questionnaire. Additionally, it captures dosing recommendations for CYP2C19 and SSRIs (see Appendix E).

Pre/Post Survey

A competency evaluation survey will be used to collect data on provider's knowledge and attitudes towards protocol usage in the pre-implementation and post- implementation periods. The survey will be distributed on the first week of the project implementation just before conducting the PGT education sessions. The participants will also complete a post-survey based on the same survey on Week 4 to determine whether the education sessions will have an impact on the prescribers PGT knowledge and attitudes. The survey will be evaluated to ensure both construct and content validity. The survey will contain 10 questions evaluating the provider's knowledge of pharmacogenetic testing, its benefits, and its application in mental health pre and post administration (See Appendix F).

Content Validity Index

A content validity index (CVI) will be completed to determine the relevance of the items in the questionnaire ((Appendix G). The CVI captures an expert rating form which was filled by experts who reviewed the survey's content validity. The final section provides a formula for calculating the content validity index of the questionnaire based on the scores assigned by the reviewers. The mean total CVI was 3.93 indicating that the questions were moderately or highly

relevant. The item-level content validity index (I-CVI), which represents the proportion of content experts who gave individual survey items a relevance rating of 3 or 4, was 1.5. This indicates that the questions are highly relevant. According to Halek, Holle, and Bartholomeyczik (2017) an I-CVI score of 0.78 and above is usually acceptable.

Chart Audit Tool

The chart audit tool (Appendix H) will cover the details such as the patient's initial exam, key complaint, medical history, family history, depression PHQ-9 screening, medications, dosage, and dates and progress notes. The form will also contain details of medications based on PGT results, side effects, and changes in medications. The tool contains a column where additional notes on these items can be recorded.

Data Collection Procedures

The project will involve collection of data regarding provider knowledge, attitudes, protocol usage, and number of return visits in the pre and post implementation period. The project lead will collect the data from the providers and the clinic's records during the four weeks of project implementation. Measures will be adopted to protect the privacy and confidentiality of the data collected. Measures such as carefully collecting only needed documentation (such as patient's assigned number, response to medication, return visits) while obtaining only unidentifiable information concerning providers and their patients. Protection of participants' privacy and confidentiality is one of the ethical principles in research (Friesen, Kearns, Redman, & Caplan, 2017). As such, identifiers such as provider's names, patient names, date of birth and employee numbers will be omitted from the provider checklist. Additionally, the chart audit and review form will be stored in a password protected folder in the project lead's personal computer. Hard copies will be kept in a locked drawer only accessible to the project lead.

Intervention/Project Timeline

The project involves development of a standardized pharmacogenetic guideline for directing medication prescription activities in a mental health clinic. The whole project is expected to take an eight-month period to complete from April 2019 to December 2019. Background reading took a month, while another month was dedicated to topic selection and approval. The literature review was completed during the month of July. Development of the project methodology and intervention was prepared during August. Approval for implementation of the PGT, participant recruitment, implementation, and data collection will take two months to accomplish, between September and October. In November, data analysis, documentation of the project findings, and submission of working draft will be finished. The final version of the project report will be completed in December 2019. Table 1 details the breakdown of the timeline for the entire project.

Table 1: Project timeline

Activity/Time	**May**	**June**	**July**	**Aug**	**Sept**	**Oct**	**Nov**	**Dec**
Background Reading								
Topic Selection								
Approval of the Topic								
Literature Review								
Methodology development								
Intervention development								
Approval for PGT implementation								
Recruit Participants								
Implement PGT								
Support & Data Collection								

Preliminary Analysis & Data Interpretation								
Documentation of Findings								
Submission of Draft Work & Editing								
Final Submission								

The project intervention will be implemented in November 2019 after receiving Approval in October 2019. Table 2 presents a breakdown of these activities.

Table 2. Intervention timeline

• Project Timeline	
• Weeks	• Activities
• Week 1	• Emailed a reminder to participants of time, date, and location of educational sessions lunch and learn • Organize the resources to be used during the education sessions such as writing materials. • Collect pre- educational data on PGT knowledge. • Hold four education sessions on PGT

• Week 2	• Clinicians start using the PGT
	  • Begin monitoring for compliance
	  • Rounding with providers to provide support
	  • Collect data on patient return visits and reported side effects

• Week 3-Week 4	• Clinicians continue application of PGT • Continued monitoring for compliance • Continue rounding with providers to offer support • Collect post-educational session survey data • Collect data on patient return visits and reported side effects.
• Week 5	• Analyze the pre- educational survey and post- implementation survey data • Finish, compile, edit, and proofread the project report

Ethics and Human Subjects Protection

Ethics entails a system of principles that offer guidance to the choices and actions in a project based on what is considered to be right and wrong. The professional codes of ethics dedicate that one cannot reveal confidential information or collect information without receiving permission (Fouka & Mantzorou, 2011). However, the project should be exempted from review by the Touro University's Institutional Review Board (IRB) since it is a quality improvement

project. The project site does not have an IRB and the management has already approved the project to be implemented at the clinic.

The project is a mandated practice change for the providers in the mental health clinic and it has the support of the clinic's management. As such, all providers will be required to participate in the project. The project lead will not gather private and personal identifiable data, or such data will not be included in the final report. Steps will be taken to code, encrypt or secure private data to make sure that such information remains anonymous. Also, the data will be stored in a password protected folder in the project lead's personal computer (Faden et al., 2013). Hard copies will be kept in a locked drawer only accessible to the project lead. The hard copies of the data will be shredded while soft copies will be deleted three years after completion of the project.

Furthermore, according to the principle of beneficence, it is vital that the project benefits, better serves and promote the well-being of the constituents as well as does not harm the subjects. Hence, while no monetary incentives will be offered for participating in the project, the mental health practitioners who will be part of the project will gain significant knowledge on pharmacogenetic testing guideline in mental health care. The participating mental health practitioners will access the findings of the project on request. Nonmalificence calls for high sensitivity to subjects to avoid harmful practices (Fouka & Mantzorou, 2011). Consequently, due diligence will be taken to ensure the project does not cause any emotional, economic, physiological and social harm to the participants.

Plan for Analysis/Evaluation

The project will adapt a systematic quantitative data analysis approach to find evidence to support or negate the hypothesis. A statistician was consulted to ensure appropriate statistical

testing will be used to measure the desired outcomes. Chart review will be conducted to assess trends in patient follow up visits. Data analysis will be achieved using R software, which is commonly used in social sciences. The software offers exceptional control in organizing and managing data as well as quick and accurate analyses. Data obtained from the audit tool will be imported into R software for further analysis. The results will be presented in textual, tabular and figures.

Descriptive and inferential statistics will be applied to analyze the collected data. Descriptive statistics such as mean and standard deviation will provide a meaningful depiction and summaries of the data. Inferential statistics will be used to determine the effect of the guideline on patient return visits due to medication intolerance. Particularly, paired t-test will be used to examine the difference in mean between the pre-survey and post- survey samples. The survey is appropriate for the project as it is applied to compare two groups with means, which are co-dependent (Gerald, 2018). The survey will indicate whether there will be statistically significant differences between provider knowledge before and after the implementation of education sessions on PGT.

Data regarding patient return visits will be analyzed using unpaired t- survey as it will be collected from two different samples. Unpaired t-test will facilitate determination of the impact of PGT on patient return visits in the clinic through comparison of the number of visits two weeks before and after adoption of the standardized pharmacogenetic guideline. The results will be evaluated at a 0.05 level of significance.

Significance/Implications for Nursing

The proposed project has broad-reaching implications significant to patient outcomes, cost of care, mental health systems and nursing practitioners as well as prescription resources in the

ever-changing and multifaceted system of pharmaceuticals. Depression is a prevalent and significant co-morbid health condition to other associated problems such as: obesity, cardiovascular disease, and diabetes. Therefore, the debate is no longer about its impacts but how to minimize its prevalence and suffering (Keyes, Dhingra & Simoes, 2010). The combination of chronic illnesses associated with mental conditions cost the United States more than $300 billion and another $210 billion due to the work absenteeism costs attributed to employees' impairment (Kittelsrud, 2016). For instance, Reeves et al. (2011) established that in South Dakota, about three days each month were used for treating mental illness including depression, which results in loss of work hours. Remmers et al. (2009) revealed that medication adherence in chronic mental condition is poor and it escalates re-hospitalization as well as worsens patient outcomes. According to Stieffenhofer and Hiemke (2010), the occurrence of side effects due to personal enzymatic pathways associated with individual genetic make-up play a significant role in discontinuation of medications. Hall-Flavin et al. (2013) assert that pharmacogenetic guidelines in selecting medication can minimize symptoms and side effects while improving clinical outcomes of patients.

Patients who undergo pharmacogenetic testing are likely to show improvement in activation and ultimately better mental health outcomes such as; decreased depression, decline is side effects and symptoms as well as improved quality of life. Notwithstanding the expansive knowledge and training, psychiatry medications are often relegated to trial-and-error prescription approaches (Burke et al., 2016). The use of PGT is likely to hasten the identification of medications with utmost effectiveness and reduce side effects by identifying individual genetic inconsistencies in relation to drug reactions. Therefore, PGT will equip nurses with adequate

knowledge and offer up-to-date or accurate information about patients to enhance effective prescription.

Furthermore, PGT can ensure the provision of personalized mental health care that aligns to a patient's genetic makeups to help patients manage their systems more effectively (Lee et al., 2014). Thus, this will reduce mental illness burden and associated costs. Patients will be activated on the right medication since the mental health practitioners comprehend the clinical and genetic picture of patient's drug metabolism, which will significantly enhance outcomes. Patients could experience fewer side effects minus the costs associated with regular changes in medications or extra regiments to control side effects. Open communication with the patients due to pharmacogenetic testing might enhance patient activation and adherence to the medication. It will increase active participation of patients in the treatment process, minimize suicides, reduce missed clinical visits and ensure efficient use of limited resources (Kittelsrud, 2016).

The use of inter-professional care can impressively benefit patients as well as alleviate some of the challenges faced by nursing practitioners especially information provision regarding the effect of PGT testing on medication. Effective inter-professional care involves well-defined responsibilities for every care provider (Haga & Mills, 2015). The ordering practitioner has the primary role of interpreting PGT results and making necessary alterations to patients' medications, while the nurses can help physicians in executing the medicine changes, educating patients about the importance of the tests and findings as well as addressing any emerging questions from the patients. Additionally, the pharmacists can offer support to physicians in interpreting results and help nurses in comprehending the interpretations of the results plus the implications of the test results on medication decision. Haga and Mills (2015) note that when a

multidisciplinary panel of health practitioners and patients work together to undertake PGT and review medication regimen for patients, it significantly reduces medication errors. Therefore, the project is not only beneficial to nurses and patients, but also to pharmacists, physicians and other practitioners involved in ensuring the well-being of mental health patients.

Analysis of Results

The primary aim of the project was to implement a standardized pharmacogenetic guideline to be used by the care providers in the mental health clinic. In particular, the guideline would help improve the mental health providers' knowledge in the PGT, minimize repeat appointments, and enhance patient experience through the reduction of adverse medication effects while boosting treatment adherence (Cho & Han, 2018). Based on the data collected, summary statistics was performed on the data to give a general overview for the sets of variables. The results provide information on the efficiency of the proposed standardized pharmacogenetic guideline that could provide better management of patients in the mental health clinic.

The response variables for each provider was the number of visits with a genetic test/return visit and the number of visits without a genetic test/return visit. The independent variables were time (before and after the education) and the provider. Effects of time and provider were estimated in a mixed effects logistic regression (separate models for the number of genetic tests and the number of return visits), where time was a fixed effect and provider was a random effect. The statistical analysis was completed in R software. The software was chosen on the basis that the sample sizes for the different providers was not the same. Hence, the software would take into account the difference in the sample size and provide more accurate results during the analysis. Across all providers, there was a mean of 3.1% (standard error 0.2%) within-provider increase in visits that included a genetic test after the education compared to

before education (Table 1). Every provider showed an increase, although starting values for each provider varied between 1-3% (Figure 1). The results showed that visits after education increased significantly.

Table 1:

Change in Genetic Test rating by Provider

	Genetic Tests	Return Visits		
	Pre-Education	Post-Education	Diff	
A	2.0%	4.8%	2.8%	
B	1.3%	3.9%	2.6%	
C	1.6%	5.3%	3.8%	
D	1.3%	4.2%	2.9%	
E	3.2%	6.7%	3.5%	
				SE
		All	3.1%	0.2%

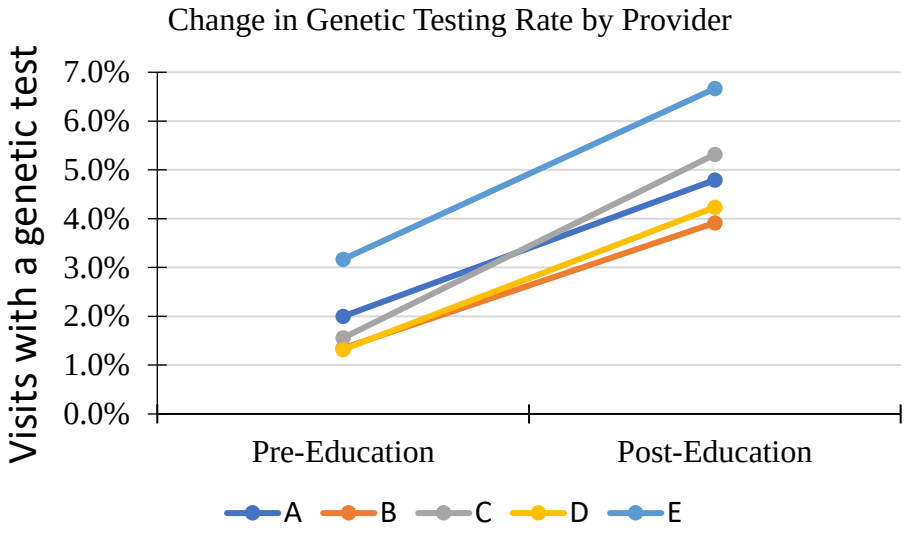

Figure 1: Change in Genetic Testing Rate by Provider

In the evaluation of the change in return visits by provider, it emerged that there was a reduction in the number of return visits after the education with a mean reduction of -3.7% and a standard error of 0.6. The analysis was performed using linear mixed effects model in r. This shows that the proposed standardized pharmacogenetic guideline had a great impact in reducing the number of return visits for every provider within the mental health clinic.

Table 2:

Change in Return Visits by Provider

	Genetic Tests	Return Visits		
	Pre-Education	Post-Education	Diff	
A	7.7%	3.2%	-4.5%	
B	5.1%	2.5%	-2.6%	
C	5.9%	4.0%	-1.9%	
D	6.9%	2.9%	-4.0%	
E	9.5%	4.0%	-5.5%	
				SE
		All	-3.7%	0.6%

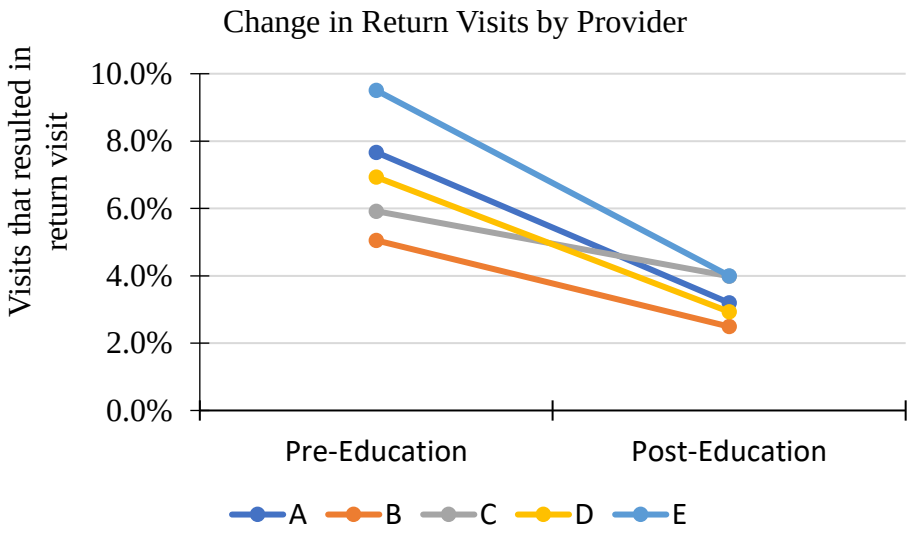

Figure 2: Change in Return Visits by Provider

Based on (Figure 2) above, it is clear that there was a decrease in the percentage of the return visits after the PGT education and guideline. This shows the intervention had a significant impact in reducing the number of return visits. The analysis showed that indeed there was a need to develop a standardized pharmacogenetic guideline for the caregivers in the mental health clinic to improve their service delivery levels by increasing knowledge (Relling et al., 2019). Also, the guideline would be critical in reducing repeat visits by ensuring there is proper scheduling of appointments.

Discussion of Results

The data from the project revealed an increase in visits that included genetic test following the implementation of education intervention. Specifically, among all the providers, there was a mean of 3.1% (standard error 0.2%) within-provider increase in visits that included a genetic test after the post-implementation period compared to the pre-education period. Therefore, the education program administered to the providers was effective in increasing the providers' application of genetic tests to determine the effective medicines for patients. The findings are consistent with the existing literature on the application of pharmacogenetic testing in mental health. For instance, Eum et al. (2017) found that when the genetic tests are conducted for schizophrenia patients, effective treatment is attained. Similarly, Perez et al. (2017) found that pharmacogenetics has been effective in identifying the drug specific treatment recommendation for patients experiencing major depressive disorder. Hence, training providers on conducting genetic tests for patients have the potential of ensuring the appropriate medication is prescribed. This reduced the costs of treatment incurred by patients as correct medication is used during the first visit. Similarly, genetic tests before medication prescription ensures reduction in return visits by patients. As explained prior by Lelmini et al. (2018) in a

quantitative study, genetic tests have the potential of assisting mental health practitioners to identify patients with a high likelihood of experiencing adverse effects as well as expanding their understanding of the influence of genetic variation and drug response.

Another major result from the project was reduction of return visits by patients for every provider following the training program. Specifically, there was a mean reduction of -3.7% with a standard error of 0.6. The result can be attributed to an increase in pharmacogenetic testing which ensured the right treatment medication was administered and hence reducing side effects which would make patients return to the providers. The findings therefore concurred with the existing literature on the effectiveness of PGT in reducing patients return visit due to complications with the administered medication. For instance, the results support the findings of Blasco-Fontecilla (2019) that PGT enhances the clinical outcomes of patients with autistic disorder. Similarly, the results were in line with findings of Perez et al. (2017) that progressive PGT was effective in treatment of major depressive disorder. Another study with similar findings was that of Health Quality Ontario (2017) which established that patients who had been provided with GeneSight test had improved reactions towards depression medication, more significant enhancements in depression measures, and greater clinician and patient satisfaction in comparison to patients who had received the usual treatment.

Further, from the results, it can be inferred that the cost of treatment reduced due to the reduction of return visits. In addition, few returns visits make it possible for providers to seek more patients which foster their productivity. These results are well supported by the existing literature. According to Brown, Lorenz, Li, and Dechairo (2017), use of PGTs offered the most medication cost savings as each individual patient was able to save $3,988 annually. In another study, Verbelen, Weale, and Lewis (2017) reviewed the economic evaluations for PGTs and

established that the tests are cost-effective. Approximately, 57% of the evaluations showed that PGTs are cost-effective (30%) or led to cost-savings (27%) compared with other approaches adopted in mental health practice.

Significance to Nursing

The results obtained from the project has major implications and significance to nursing practice. Nursing is interested in wellbeing of patient and should be concerned with providing effective treatment. Consequently, PGT provides and avenue for nurses to ensure increased patient satisfaction through providing effective medication as opposed to relying on trials and errors in medicine administration (Fulton et al., 2018). Further, the implementation of PGT ensures nurses make a contribution in ensuring improved health outcomes of patients. Healthcare costs is another issue of concern not only in the United States, but in the entire world. The implementation of the protocol in the use of PGT presents an opportunity for nurses to reduce the cost of healthcare and reduce financial burden among patients. Additionally, the results are significant to nursing practice through ensuring provision of personalized level of care. Medication works differently among different mental patients and not all patient attain remission (Russell, 2018). However, implementation of PGT ensures personalized medication is administered to different patients as per their reactions to different medications. This ensures equality of care among different patients.

The APNs with prescriptive privileges, as well as the nursing field in general, can benefit from the findings showing decrease in return visits after PGT education and guidelines. This innovation further advances the argument that pharmacogenetics has the potential to optimize medication response and identify medication toxicity (Kudzi, Addy & Dzudzor, 2015). Nurses play a vital role in ensuring patient safety outcomes and should be knowledgeable in the effects

pharmacogenetics has on the population they serve. APNs can enhance positive patient outcomes by adopting precision medicine through implementation of PGT (Fulton et al., 2018).

Limitations

One design-related limitation of the project was the use of quantitative research method. Data collected with the use of a quantitative approach is narrower and sometimes superficial when compared to the qualitative data. A quantitative methodology overlooks the underlying meanings and explanations of social phenomena (Rahman, 2017). Additionally, quantitative design presents limitation because results are only constrained to numerical descriptions as opposed to the detailed narrative provided by the qualitative approach. As such, the design cannot explain how social reality is molded and maintained (Rahman, 2017). Moreover, preset questions utilized in the quantitative approach may fail to reflect the feeling of people at the given time. To limit the impact of quantitative design limitations, the quantitative project results were discussed in light of existing literature.

The major limitations regarding participants' recruitment was related to the small sample size utilized. The project relied on data from five providers in the private practice. As explained by Miočević, MacKinnon, and Levy (2017), having too small of a sample size minimizes the power of the research while increasing the margin of error. Very small sample sizes can therefore, reduce the reliability of project findings. Having small sample sizes also leads to variability in limitation where it could be difficult to generalize the findings to the entire population (Miočević et al., 2017). Uncovering bias is also a limitation associated with having a small sample size where some subjects in the population do not have an opportunity to participate (Miočević et al., 2017). To address this limitation, the findings were compared with the available literature on pharmacogenetic testing.

The other limitation relates to the recruitment of the project participants. For instance, not all charts for patients diagnosed with depression were recruited to participate. The use of purposive sampling also limited representativeness of the reviewed patient charts. Purposive sampling created a limitation due to possibility of bias based on the selection of specific charts by the providers (Etikan et al., 2016). According to Chow, Shao, Wang, and Lokhnygina (2017), for a sample to be representative and devoid of bias, random sampling techniques need to be used. Therefore, non-adherence to the random selection procedure led to the risk of adversely impacting the validity of results and findings.

Data was analyzed quantitatively; which presented limitations. For instance, the method entails development of standard questions leading to structural bias as well as false representation. The analyzed data may reflect the view of the project lead as opposed to the participating subjects. To reduce the limitation, the DNP scholar approached the project with objectivity and openness to any findings.

Dissemination

The project findings will be shared with mental health specialists and the administrators at the clinic through the use of a PowerPoint presentation and a poster. The administrators will also be provided with an executive summary, which will capture the findings and their implications. The findings will also be presented in mental health seminars and workshops at the local or state level. Lastly, the project findings may be disseminated to other scholars and practitioners through publication in a nursing journal such as the Journal of Psychiatric and Mental Health Nursing. The project report will also be submitted to the DNP repository where it will be shared with the university's instructors and students.

Areas for Further Quality Improvement

The project involved the development of a pharmacogenetic testing guideline with the aim of improving mental health providers' knowledge in PGT, minimizing repeat appointments, and enhancing patient experiences. PGT can be evaluated in other settings to establish whether similar results would be obtained. For instance, PGT can be tested for other mental disorders such as schizophrenia and bipolar disorder (Routhieaux et al., 2018). Further QI projects need to be conducted using a larger sample size to determine whether the present results were affected by the small sample used.

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Appendix A: Lewin's Three-Step Model

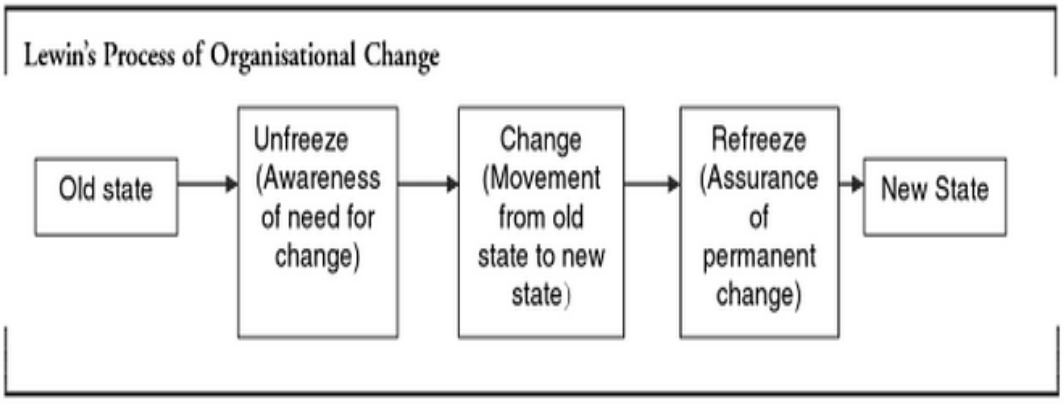


Figure 3. Lewin's change management model. Source: Singh, K. (2010). *Organizational change and development (2nd Ed)*. New Delhi, India: Excel Books.

Appendix B- Recruitment Flyer

Pharmacogenetic Testing Education

Calling all medication prescribers to participate in quality improvement education on pharmacogenetic testing (PGT).

Location: Board Room
Time: 12-1pm (lunch provided)
Date: Nov 11, 12, 13

Purpose: proposed guideline to improve mental health provider knowledge in PGT, reduce repeat appointments, and improve patient satisfaction by reducing adverse medication effects and improving treatment adherence.

Prescribers Role: request PGT testing on 5 patients diagnosed with depression and monitor their experience on medications considered best fit. Report findings to project lead

Project Lead: Ibha Sedenu
ibhased@gmail.com
Office: #4A
Hours 9am-4pm M-F

Appendix C: Project Site Agreement Letter

Millenia Psychiatry & Research
6052 Turkey Lake Rd. Suite 118
Orlando FL 32819

April 2, 2019

To whom it may concern,

Mrs. Ibha Sedenu and I have discussed her proposed DNP Project focusing on implementation of pharmacogenetics testing guideline into clinical practice. Note I am providing full authorization for Mrs. Sedenu to implement her project within Millenia Psychiatry & Research. No affiliation agreement is required. Additionally, Mrs. Sedenu is authorized to access electronic / physical medical records in order to collect primary and secondary data relevant to her DNP Project.

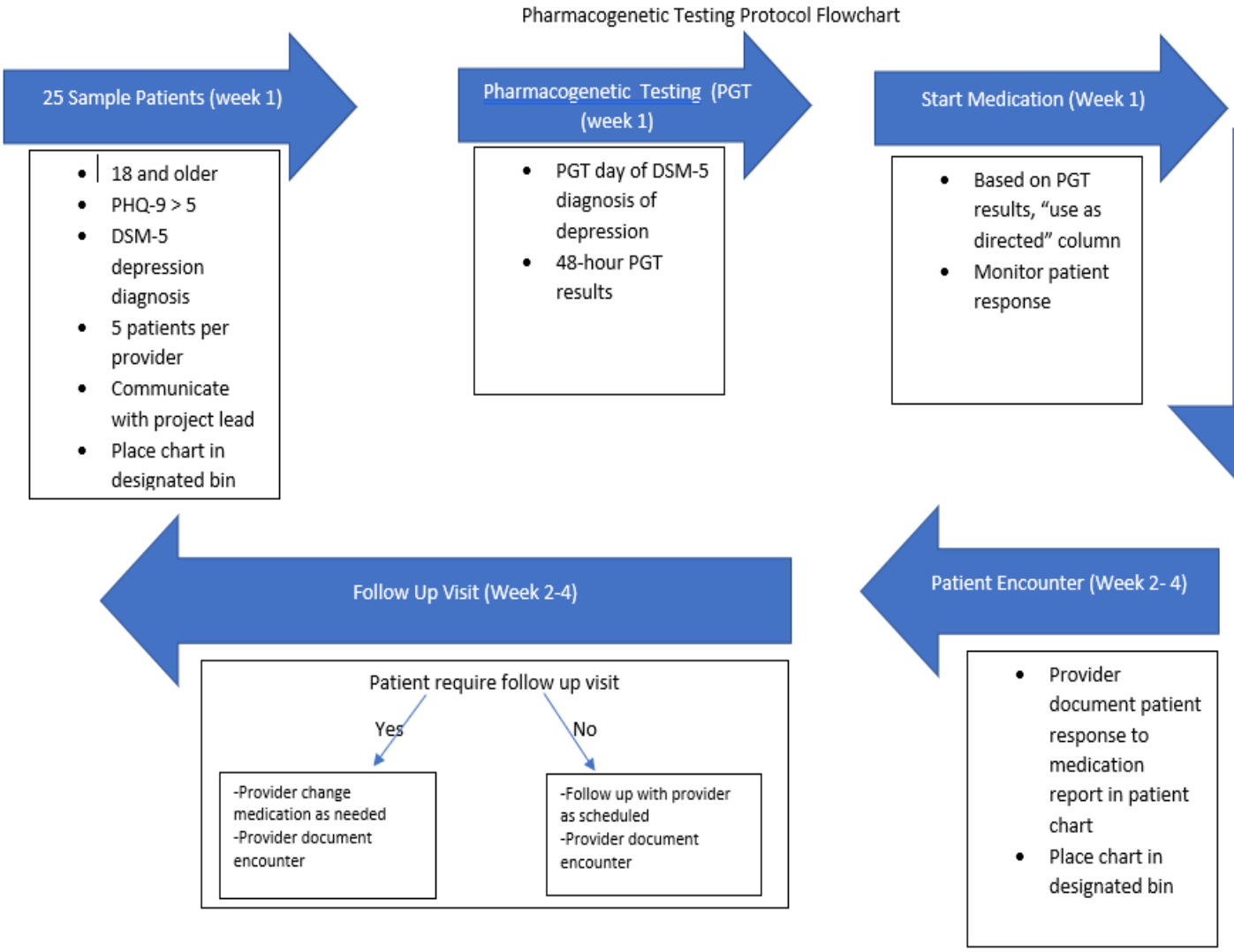
Please do not hesitate to contact me at 407-830-0773 if I can be of further assistance.

Sincerely,

Aloma Alcober, MD
Millenia Psychiatry & Research

Appendix D: Power Point Presentation

Appendix E: Pharmacogenetic Protocol Flowchart and Supporting Documents



PHQ-9 Self-screener

PATIENT HEALTH QUESTIONNAIRE (PHQ-9)

NAME:_____ **DATE:**_____

Over the last 2 weeks, how often have you been bothered by any of the following problems?
(use "✓" to indicate your answer)

	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself—or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed. Or the opposite — being so figety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead, or of hurting yourself	0	1	2	3
add columns		+	+	

(Healthcare professional: For interpretation of TOTAL, please refer to accompanying scoring card). TOTAL:

10. If you checked off *any problems*, how *difficult* have these problems made it for you to do your work, take care of things at home, or get along with other people?

- Not difficult at all _____
- Somewhat difficult _____
- Very difficult _____
- Extremely difficult _____

Figure 4. Patient Health Questionnaire. Source: Select a Screener. (n.d.). Retrieved from https://www.phqscreeners.com/select-screener/36

PHQ-9 Patient Depression Questionnaire

For initial diagnosis:

1. Patient completes PHQ-9 Quick Depression Assessment.
2. If there are at least 4 ✓s in the shaded section (including Questions #1 and #2), consider a depressive disorder. Add score to determine severity.

Consider Major Depressive Disorder

- if there are at least 5 ✓s in the shaded section (one of which corresponds to Question #1 or #2)

Consider Other Depressive Disorder

- if there are 2-4 ✓s in the shaded section (one of which corresponds to Question #1 or #2)

Note: Since the questionnaire relies on patient self-report, all responses should be verified by the clinician, and a definitive diagnosis is made on clinical grounds taking into account how well the patient understood the questionnaire, as well as other relevant information from the patient.
Diagnoses of Major Depressive Disorder or Other Depressive Disorder also require impairment of social, occupational, or other important areas of functioning (Question #10) and ruling out normal bereavement, a history of a Manic Episode (Bipolar Disorder), and a physical disorder, medication, or other drug as the biological cause of the depressive symptoms.

To monitor severity over time for newly diagnosed patients or patients in current treatment for depression:

1. Patients may complete questionnaires at baseline and at regular intervals (eg, every 2 weeks) at home and bring them in at their next appointment for scoring or they may complete the questionnaire during each scheduled appointment.
2. Add up ✓s by column. For every ✓: Several days = 1 More than half the days = 2 Nearly every day = 3
3. Add together column scores to get a TOTAL score.
4. Refer to the accompanying **PHQ-9 Scoring Box** to interpret the TOTAL score.
5. Results may be included in patient files to assist you in setting up a treatment goal, determining degree of response, as well as guiding treatment intervention.

Scoring: add up all checked boxes on PHQ-9

For every ✓ Not at all = 0; Several days = 1;
More than half the days = 2; Nearly every day = 3

Interpretation of Total Score

Total Score	Depression Severity
1-4	Minimal depression
5-9	Mild depression
10-14	Moderate depression
15-19	Moderately severe depression
20-27	Severe depression

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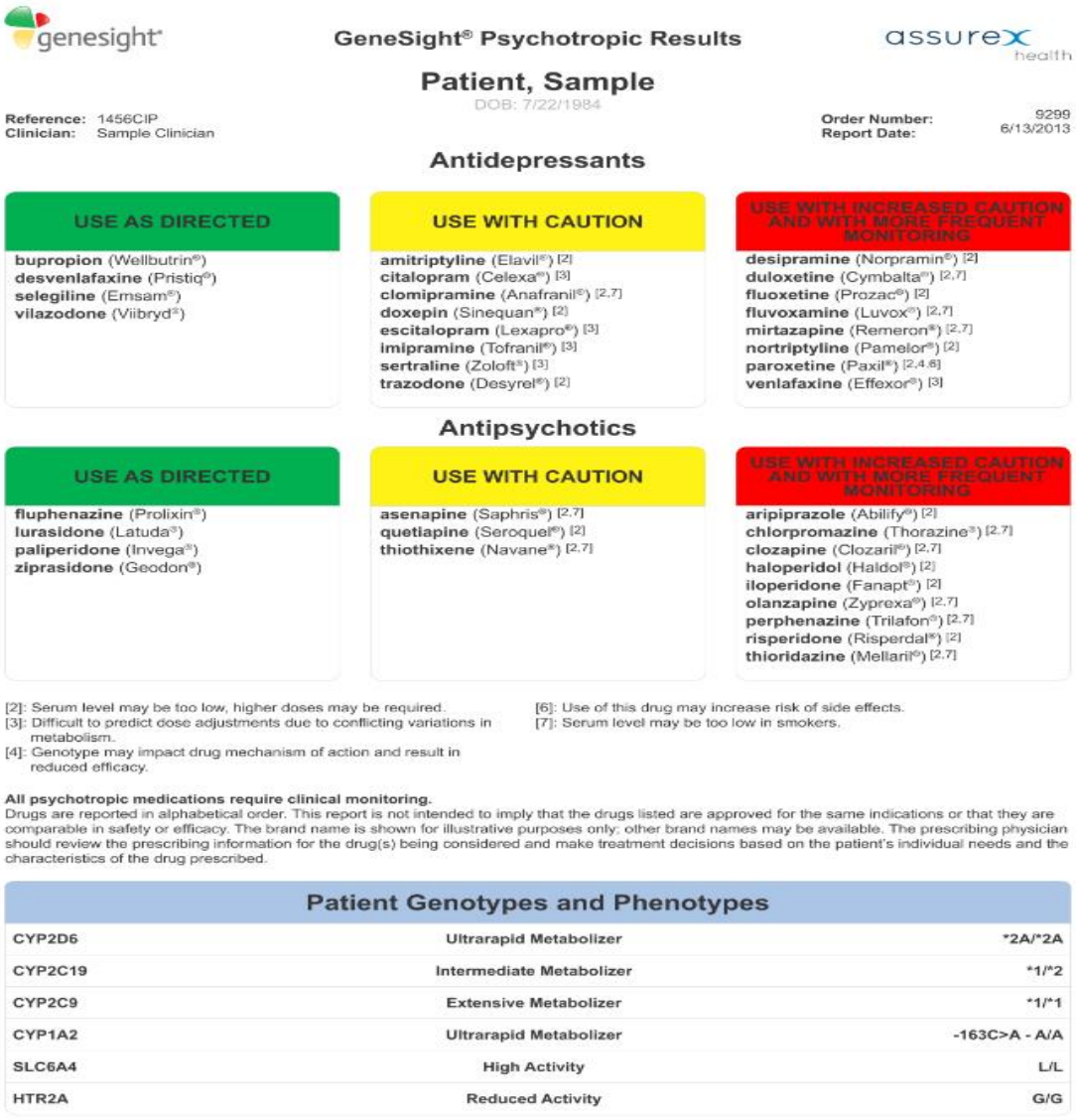
Figure 2. Patient Health Questionnaire Scoring. Source: Select a Screener. (n.d.). Retrieved from https://www.phqscreeners.com/select-screener/36

Dosing recommendations for CYP2C19 and SSRIs

Phenotype	Implication	Therapeutic recommendation	Classification of recommendation[a]
CYP2C19 Ultrarapid metabolizer	Increased metabolism when compared to extensive metabolizers. Lower plasma concentrations will increase probability of pharmacotherapy failure.	Consider an alternative drug not predominantly metabolized by CYP2C19.[b]	Moderate
CYP2C19 Extensive metabolizer	Normal metabolism	Initiate therapy with recommended starting dose.	Strong
CYP2C19 Intermediate metabolizer	Reduced metabolism when compared to extensive metabolizers.	Initiate therapy with recommended starting dose.	Strong
CYP2C19 Poor metabolizer	Greatly reduced metabolism when compared to extensive metabolizers. Higher plasma concentrations may increase the probability of side effects.	Consider a 50% reduction[c,d] of recommended starting dose and titrate to response or select alternative drug not predominantly metabolized by CYP2C19.[b]	Moderate

Figure 2. *Dosing recommendations for CYP2C19 and SSRIs*. Source: Hicks, et al. (2015). Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline forCYP2D6andCYP2C19Genotypes and Dosing of Selective Serotonin Reuptake Inhibitors. *Clinical Pharmacology & Therapeutics*, *98*(2), 127-134.

GeneSight Sample Test Results



genesight

GeneSight® Psychotropic Results

assurex health

Patient, Sample

DOB: 7/22/1984

Reference: 1456CIP
Clinician: Sample Clinician

Order Number: 9299
Report Date: 6/13/2013

Antidepressants

USE AS DIRECTED	USE WITH CAUTION	USE WITH INCREASED CAUTION AND WITH MORE FREQUENT MONITORING
bupropion (Wellbutrin®)	**amitriptyline** (Elavil®) [2]	**desipramine** (Norpramin®) [2]
desvenlafaxine (Pristiq®)	**citalopram** (Celexa®) [3]	**duloxetine** (Cymbalta®) [2,7]
selegiline (Emsam®)	**clomipramine** (Anafranil®) [2,7]	**fluoxetine** (Prozac®) [2]
vilazodone (Viibryd®)	**doxepin** (Sinequan®) [2]	**fluvoxamine** (Luvox®) [2,7]
	escitalopram (Lexapro®) [3]	**mirtazapine** (Remeron®) [2,7]
	imipramine (Tofranil®) [3]	**nortriptyline** (Pamelor®) [2]
	sertraline (Zoloft®) [3]	**paroxetine** (Paxil®) [2,4,6]
	trazodone (Desyrel®) [2]	**venlafaxine** (Effexor®) [3]

Antipsychotics

USE AS DIRECTED	USE WITH CAUTION	USE WITH INCREASED CAUTION AND WITH MORE FREQUENT MONITORING
fluphenazine (Prolixin®)	**asenapine** (Saphris®) [2,7]	**aripiprazole** (Abilify®) [2]
lurasidone (Latuda®)	**quetiapine** (Seroquel®) [2]	**chlorpromazine** (Thorazine®) [2,7]
paliperidone (Invega®)	**thiothixene** (Navane®) [2,7]	**clozapine** (Clozaril®) [2,7]
ziprasidone (Geodon®)		**haloperidol** (Haldol®) [2]
		iloperidone (Fanapt®) [2]
		olanzapine (Zyprexa®) [2,7]
		perphenazine (Trilafon®) [2,7]
		risperidone (Risperdal®) [2]
		thioridazine (Mellaril®) [2,7]

[2]: Serum level may be too low, higher doses may be required.
[3]: Difficult to predict dose adjustments due to conflicting variations in metabolism.
[4]: Genotype may impact drug mechanism of action and result in reduced efficacy.
[6]: Use of this drug may increase risk of side effects.
[7]: Serum level may be too low in smokers.

All psychotropic medications require clinical monitoring.
Drugs are reported in alphabetical order. This report is not intended to imply that the drugs listed are approved for the same indications or that they are comparable in safety or efficacy. The brand name is shown for illustrative purposes only; other brand names may be available. The prescribing physician should review the prescribing information for the drug(s) being considered and make treatment decisions based on the patient's individual needs and the characteristics of the drug prescribed.

Patient Genotypes and Phenotypes

CYP2D6	Ultrarapid Metabolizer	*2A/*2A
CYP2C19	Intermediate Metabolizer	*1/*2
CYP2C9	Extensive Metabolizer	*1/*1
CYP1A2	Ultrarapid Metabolizer	-163C>A - A/A
SLC6A4	High Activity	L/L
HTR2A	Reduced Activity	G/G

Figure 3. *GeneSight sample test result*. Retrieved from http://www.discoverymedicine.com/Joel-G2013/11/discovery_medicine_no_89_joel_g_winner_figure_-Winner/files/2.jpg.jhtml?id=2%7Cattachment_14/

Appendix F: Mental Health Provider Pharmacogenetic Use Survey

Mental Health Provider Pharmacogenetic Use Survey

Please respond to all the following items. DO NOT write your name anywhere on this paper or make any mark on the paper which might reveal your identity. This research is only interested in trends and, thus, there is no need to identify any individual. Thank you for your cooperation.

Age

☐ 18-25

☐ 26-35

☐ 36-45

☐ 46-55

☐ 56-65

☐ 65+

Gender

☐ Female

☐ Male

Level of Education

☐ Bachelor's Degree

☐ Master's degree

☐ Doctoral Degree

Years of Employment

☐ 1-5

☐ 6-10

☐ 11-15

☐ 16-20

☐ 21-25

☐ 26+

1. I have a great understanding of what pharmacogenetic testing is

☐ Not at all true

☐ Hardly true

☐ Moderately true

☐ Exactly true

2. If required I would choose to first conduct pharmacogenetic testing before prescribing psychotropic medications

☐ Not at all true

☐ Hardly true

☐ Moderately true

☐ Exactly true

3. It is easy for me to identify patients that will benefit from pharmacogenetic testing.

☐ Not at all true

☐ Hardly true

☐ Moderately true

☐ Exactly true

4. I am confident that I could identify patients that will benefit from pharmacogenetic testing

☐ Not at all true

☐ Hardly true

☐ Moderately true

☐ Exactly true

5. Thanks to my resourcefulness, I know how to handle unforeseen medication side effects

☐ Not at all true

☐ Hardly true

☐ Moderately true

☐ Exactly true

6. I can identify the most appropriate psychotropic medication necessary for my patients symptoms

☐ Not at all true

☐ Hardly true

☐ Moderately true

☐ Exactly true

7. I can remain calm when faced with a treatment resistant client because I can rely on my coping abilities

☐ Not at all true

☐ Hardly true

☐ Moderately true

☐ Exactly true

8. When I am conflicted on appropriate medications options, I can usually find several solutions

☐ Not at all true

☐ Hardly true

☐ Moderately true

☐ Exactly true

9. If I am not getting the results needed for patient. I can usually think of a solution.

☐ Not at all true

☐ Hardly true

☐ Moderately true

☐ Exactly true

10. I can manage patients who have tried and failed 3 or more psychotropic medications

☐ Not at all true

☐ Hardly true

☐ Moderately true

☐ Exactly true

Appendix G- Content Validity Index

Calculate your Content Validity Index

Content Validity Index Table

Item	Expert 1	Expert 2	Expert 3	Mean
1	4	4	4	4
2	4	4	4	4
3	4	4	4	4
4	4	4	4	4
5	4	4	4	4
6	4	4	4	4
7	4	4	4	4
8	4	3	4	3.67
9	4	3	4	3.67
10	4	4	4	4

The CVI is calculated based on the ratings of experts on every question based on a four-point scale of relevance. The item (CVI) (I-CVI) is computed as the number of experts giving a rating of 3 or 4, divided by the number of experts-the proportion in agreement about relevance.

The content validity index is calculated using the following formula:

CVR = [(E-(N/2)) / (N/2)] with E representing the number of judges who rated the item as Moderately Relevant or Highly Relevant and N being the total number of judges.

The mean total of all of the means was 3.93 indicating that all of the questions were moderately/highly relevant.

The calculation is as follows:

CVR = [(3-(3/2)) / (3/2)]

CVR = [(3-1.5) /1.5]

CVR = 1.5/1.5

Appendix H: Chart Audit

Pharmacogenetic Chart Audit and Review Form

Chart Number: Date:

Comments:

Overall Appearance of Chart Good / Fair / Poor Chart

Organization Good / Fair / Poor

Chart Contents	Y/ N	If no, give Reason
Dated Entry documented		
Patient's Initial Exam		
Chief complaint/initial assessment		
Medical History (current & past)		
Family History (current & past)		
Depression PHQ-9 Screening		
Medications (SSRI,SNRI, etc.) and dosage (dates)		
Progress Notes		
Physician/Provider signature		
Date/vital signs		
Medications (based on GeneSight results)		
Problem Management (Side Effects/Intolerable)		
Medication Changed		