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# PSYCHOTROPIC PHARMACOGENOMIC TESTING: EFFECTS ON PROVIDER PRESCRIBING PATTERNS AND PHQ-9 DEPRESSION SCREENING SCORES IN A RURAL MICHIGAN FAMILY PRACTICE

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PSYCHOTROPIC PHARMACOGENOMIC TESTING: EFFECTS ON PROVIDER  
PRESCRIBING PATTERNS AND PHQ-9 DEPRESSION SCREENING SCORES IN A  
RURAL MICHIGAN FAMILY PRACTICE

By

Nicole Marie Madalinski

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## SIGNATURE APPROVAL FORM

### PSYCHOTROPIC PHARMACOGENOMIC TESTING: EFFECTS ON PROVIDER PRESCRIBING PATTERNS AND PHQ-9 DEPRESSION SCREENING SCORES IN A RURAL MICHIGAN FAMILY PRACTICE

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## ABSTRACT

# PSYCHOTROPIC PHARMACOGENOMIC TESTING: EFFECTS ON PROVIDER PRESCRIBING PATTERNS AND PHQ-9 DEPRESSION SCREENING SCORES IN A RURAL MICHIGAN FAMILY PRACTICE

By

Nicole Marie Madalinski

The rate of depression across the United States is on the rise with over 16.2 million people experiencing a depressive episode per year (Siu & and the US Preventive Services Task Force [USPSTF], 2016). Medications to treat depression typically take weeks or months to see clinical improvement (Uphold & Graham, 2013). If the medication is not effective, a dose or medication change may occur, lengthening the time spent in a depressive state. This scholarly project retrospectively analyzed charts at a rural primary care practice that implemented GeneSight® psychotropic pharmacogenomic testing for treatment resistant depression. This project sought to understand if PHQ-9 depression scores were impacted by pharmacogenetic testing. Comparison of PHQ-9 scores across the two measurement periods during the study period was completed by using a paired t-test. The mean PHQ-9 scores decreased from 7 to 3.5 which did not reach a level of statistical significance. A comparison of the total number of visits for depression in the control and test group patients was completed by using independent samples t-test which showed no significant difference in mean number of visits. A major limitation of this study was the small sample size which impacted the statistical analysis. The review of

literature and project findings support the need for further research on the implementation of pharmacogenomic testing to treat refractory depression in a family practice setting.

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Nicole Marie Madalinski, BSN, RN, DNP Candidate

August 3, 2018

## DEDICATION

This scholarly project is dedicated to all of my loving family. Without their never-ending support and encouragement, this project would not have come to fruition. Thank you for never giving up on me.

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## Chapter One

### Introduction to the Problem

Major depressive disorder is the leading cause of disability in adults in high-income countries (Siu & USPSTF, 2016). In 2016, the National Survey on Drug Use and Health (NSDUH) identified 16.2 million adults in the United States that had at least one episode of depression (National Institute of Mental Health, 2017). With such a large number of people experiencing at least one depressive episode, primary care providers are taking on more and more responsibilities with prescribing antidepressants. Of the 16.2 million people identified during the NSDUH survey, only 44% pursued help from a healthcare professional and received a prescription (National Institute of Mental Health, 2017). Furthermore, over the course of one week, nurse practitioners in Tennessee reported that one-third of their patients were seen for mental health concerns (Shell, 2001).

Rural health is a growing topic of concern, notably with the lack of mental health providers available. A survey of 140 rural Midwest women found that 36.4% (51 participants) self-reported themselves as depressed (Groh, 2013). The women of the study also completed a Center for Epidemiologic Studies-Depression Scale (CES-D) which defined depression as a score greater than or equal to 16 (Groh, 2013). Out of the 51 that self-reported as depressed, only 30 scored a 16 or greater on the CES-D confirming their self-report of depression (Groh, 2013). This study identified that there was an incongruence in depression reporting among some of the women (Groh, 2013). Almost 25% of the women were incongruent with their self-report of current depression

and their CES-D scores (Groh, 2013). This study supports the need to screen every patient for depression using a reliable and valid tool.

There are a variety of reliable and validated tools for depression screening in the primary care setting. Depression screening is a Category B recommendation from the U.S. Preventive Services Task Force that recommends pregnant women, postpartum women, and the general adult population should be screened for depression (Siu & USPSTF, 2016). For the purpose of this scholarly project, the nine question Patient Health Questionnaire (PHQ-9) is the main depression screening tool discussed as it is utilized at the clinical site where the project occurred. This tool is self-administered by the patient and involves answering questions regarding depressive symptoms using a scale ranging from 0-3. The PHQ-9 was found to be a reliable and validated tool for depression screening and was preferred over other tools that had similar reliability and validity (Kroenke, Spitzer, & Williams, 2001; Milette, Hudson, Baron, & Thombs, 2010).

### **Prescribing Antidepressants**

The family nurse practitioner role in treating depression has increased as the incidence of depression rises and the number of specialty providers decrease. When considering prescribing antidepressants, there are many items to take into consideration. The provider must consider what symptoms the patient is having, what other medications they are taking, and the potential side effects that may be experienced. A 2001 study discovered that 25 out of 44 nurse practitioners surveyed felt they needed additional education on prescribing antidepressants (Shell, 2001).

There are four common classes of antidepressants prescribed, with a fifth class available for use as a last line treatment. In one study of advanced practice nurse

practitioners, the most common antidepressant classes prescribed were selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitor (SNRIs) (Burman, McCabe, & Pepper, 2015). After the provider selects a medication, there needs to be consistent follow-up to assess the patients' response to the medication including side effects and symptom improvement. It is important to note that it may take up to 12 weeks to notice any significant improvement in symptoms (Uphold & Graham, 2013). With the large number of potential medications that could be prescribed and the variety of side effects a person may have, the field of psychotropic pharmacogenomic testing may be helpful to the prescribing provider.

### **Pharmacogenomic Testing**

Pharmacogenomics are defined as, “the quantitative study of how genetics affects host responses to drugs” (Cascorbi, Bruhn, & Werk, 2013, p. S17). Within the literature, the distinction between pharmacogenetics and pharmacogenomics is not clearly identified (Brennan, 2015). One article distinguished pharmacogenetics as the individual genetic variation and gene expression from pharmacogenomics which was stated to be the broader topic of the entire genome (Brennan, 2015). With the increasing rates of depression, primary care providers need to be aware of the tools that are available to use in their practice to help guide their medication decisions.

GeneSight® Psychotropic is pharmacogenomic test that analyzes genetic material obtained from a buccal mucosa swab. The test analyzes 12 genes and how they affect individual patient responses to over 55 different psychotropic medications (GeneSight, 2018). The provider receives a report that places each medication into one of the following categories: use as directed (green), moderate gene-drug interaction (yellow), or

significant gene-drug interaction (red) (GeneSight, 2018). If a medication is placed in the yellow or red group, additional information regarding the reason why is provided at the bottom of the report. Based on these results, the provider can choose an appropriate medication specific to their genetic analysis.

### **Research Question**

The purpose of this scholarly project was to assess how or if pharmacogenomic testing had any effect on prescribed practices or patient PHQ-9 scores. The specific research questions asked were:

1. As compared to a control group, what effect, if any, does utilizing GeneSight® Psychotropic pharmacogenomic testing have on prescribing patterns of primary care providers?
2. What effect, if any, did medication changes as a result of GeneSight® Psychotropic pharmacogenomic testing have on PHQ-9 depression screening scores?

### **Theoretical Framework**

The theoretical framework applied to this scholarly project was the health belief model. The health belief model is a psychological model that was developed in the 1950s to help explain why people engage in certain health behaviors and to help improve the use of preventative services (Rosenstock, 1974). There are six concepts this model applies to health behaviors. The six concepts include: perceived susceptibility of the health problem, perceived severity, perceived benefits, perceived barriers, cues to action, and self-efficacy (Castonguay, Filer, & Pitts, 2016; Garner, 2014). A patient's opinion regarding their chances of getting a condition, in this case depression, is their perceived

susceptibility (Garner, 2014). The perceived severity is how severe the patient considers their diagnosis of depression to be and how severe the potential consequences may be (Garner, 2014). The perceived benefit is how the patient believes a suggested action will help them, such as taking antidepressants or completing pharmacogenomic testing (Garner, 2014). The patient is also expected to have concerns about the treatment which are known as the perceived barriers (Garner, 2014). Cues to action refers to when the patient decides to act on the treatment plan or on their depressive symptoms (Garner, 2014). The final concept is self-efficacy, which is the patient's belief that he/she can influence their own health by taking a positive action (Garner, 2014). This model assists in explaining how patients and providers can utilize the theory behind the health belief model to help prevent or treat depression with pharmacogenomic testing.

### **Significance for the Population**

Diagnosing and treating depression is a common occurrence for a primary care provider and is a multifaceted process. The PHQ-9 is a valuable depression screening tool for the primary care provider. The PHQ-9 provides a score that allows the primary care provider to assess the patient's level of depression and can be utilized to monitor treatment effectiveness (Löwe, Unützer, Callahan, Perkins, & Kroenke, 2004). The primary care provider and the patient together create a treatment plan, which may include prescribing an antidepressant medication. Prior to pharmacogenomic testing, the provider had to choose an antidepressant medication based off of recommended treatment guidelines, previous patient experiences with antidepressant medications, and symptoms being experienced. With the addition of pharmacogenomic testing, the provider and



patient can effectively choose an antidepressant medication based from the test results. A literature review supporting this scholarly project is presented in Chapter Two.

## Chapter Two

### Introduction

A review of the literature was completed using a variety of scholarly resources. CINAHL, PubMed, PsycINFO, and Google Scholar were all research search engines utilized for this review. The literature review time frame was generally limited to the last 10 years; however, some historical studies were also utilized from greater than 10 years ago. The topics of depression and depression screening, prescribing practices, and pharmacogenomic testing were searched using the following key words: depression, PHQ-9, family nurse practitioner prescribing practices, pharmacogenomic testing, pharmacogenetic testing, and personalized medicine.

### Depression

Depression in the United States is a one of the most common mental health disorders (National Institute of Mental Health, 2017). The statistics reveal the extent that depression effects individuals, families, and entire communities. The 2016 National Survey on Drug Use and Health (NSDUH) discovered that 6.7% or 16.2 million adults in the United States experienced depression or a depressive episode at least once during the year (National Institute of Mental Health, 2017). Suicide is the second leading cause of death in the world for the 15 to 29 year old age group with nearly 800,000 total deaths each year (World Health Organization, 2018). In 2016, there were nearly 45,000 deaths due to suicidal actions in the United States (Centers for Disease Control and Prevention, 2018).

Despite the increasing numbers that are associated with depression, treatment rates are not at ideal percentages. Only 44% of adults experiencing depression sought

help from a health professional and received medication; 37% did not receive any type of treatment (National Institute of Mental Health, 2017). The National Health and Nutrition Examination Survey (NHNES) between the years of 2013 and 2016 had 20,146 participants complete a public health survey (Centers for Disease Control and Prevention, National Center for Health Statistics, 2014, 2016). The NHNES survey discovered that women were nearly twice as likely to have a depressive episode (Brody, Pratt, & Hughes, 2018). The data from the NHNES interviews also showed that the prevalence of depression did not differ with age and was the lowest in Non-Hispanic Asian adults (Brody et al., 2018).

Depression can present itself in many different ways and there are a wide variety of depression symptoms that patients may experience. The symptoms of depression include feelings of sadness, a decrease in energy levels, weight loss or gain, and recurrent thoughts of death or suicidal ideation (Mayo Clinic Staff, 2018). The *Diagnostic and Statistical Manual of Mental Disorders* (5<sup>th</sup> ed.; DSM-5; American Psychiatric Association, 2013) breaks down depression disorders into seven categories that each have a specific set of diagnostic criteria. The depressive disorders recognized by the DSM-5 include major depressive episode/disorder, dysthymic disorder, bipolar episode/disorder, substance-induced mood disorder, mood disorder due to a general condition, adjustment disorder with depressed mood, and other psychiatric conditions in which depression can be a primary symptom (post-traumatic stress disorder, anxiety disorders, schizoaffective disorder, schizophrenia, and personality disorders) (American Psychiatric Association, 2013).

Major depressive disorder is associated with ICD-10 codes F32.x and F33.x (U.S. Department of Health and Human Services, Substance Abuse and Mental Health Services Administration, Center for Substance Abuse Treatment, 2013). To have a diagnosis of major depressive disorder, five or more symptoms must be present for a two week period that cannot be attributed to another medical condition. One, of the symptoms must be either depressed mood or loss of interest or pleasure, and it must reflect a change from previous functioning (U.S. Department of Health and Human Services, Substance Abuse and Mental Health Services Administration, Center for Substance Abuse Treatment, 2013). Listed below are the nine diagnostic symptoms that must be present for most of the day and nearly every day:

1. Depressed mood
2. Markedly diminished pleasure and interest in all or almost all activities
3. Significant weight loss/gain without dieting or a decrease/increase in appetite
4. Insomnia or hypersomnia
5. Psychomotor agitation or retardation
6. Fatigue or loss of energy nearly every day
7. Feelings of worthlessness or excessive/inappropriate guilt
8. Diminished ability to think/concentrate or indecisiveness
9. Recurrent thoughts of death, recurrent suicidal ideation without a plan, suicide attempt, or a specific plan for committing suicide

(U.S. Department of Health and Human Services, Substance Abuse and Mental Health Services Administration, Center for Substance Abuse Treatment, 2013)

According to the U.S. Department of Health and Human Services, Substance Abuse and Mental Health Services Administration, and the Center for Substance Abuse Treatment (2013), there are several other criteria that need to be met in order to establish a diagnosis of major depressive disorder. The patient must be experiencing clinically significant impairment in social, occupational, or other areas of functioning. The episode cannot be attributed to the effects of a substance or another medical condition. Lastly, the depressive episode is not better explained by any diagnosis on the schizophrenia spectrum and there has never been a manic or hypomanic episode (U.S. Department of Health and Human Services, Substance Abuse and Mental Health Services Administration, Center for Substance Abuse Treatment, 2013).

Research studies have been conducted regarding the effects of depression on the overall health of the patient and the increased risk for disease such as risk for stroke, heart disease, and peptic ulcer disease. A 2011 meta-analysis and systematic review on depression and the risk for stroke was completed by Pan, Sun, Okereke, Rexrode, and Hu (2011). There were 28 prospective cohort studies chosen with a total of 317,540 participants and 8,478 identified strokes (Pan et al., 2011). The reviewers identified depression as being associated with a significant increased risk of stroke morbidity and mortality (Pan et al., 2011). Another prospective cohort study of 63,469 women without baseline coronary heart disease was completed during 1992-2000 via the Nurses' Health Study (Whang et al., 2009). This study identified that women with depressive symptoms

were at an increased risk for fatal coronary heart disease and sudden cardiac death, specifically if they were using antidepressants (Whang et al., 2009). A population-based study completed in Taiwan analyzed data from a depression group (23,536 people) and a control group of similar age and gender (47,069) to assess for the risk of developing peptic ulcer disease (Hsu et al., 2015). The depression group had a twofold higher risk of developing peptic ulcer disease when compared to the control group (Hsu et al., 2015). It was noted that the depression group had an increased number of comorbidities that may affect peptic ulcer disease such as smoking and alcohol use (Hsu et al., 2015). The study suggested that the depressed, aging, female patients with comorbidities should be closely monitored for peptic ulcer disease (Hsu et al., 2015). These studies indicate that there are many different effects depression can have on the overall health of a patient.

The effects of depression stretch far beyond the physical and psychological symptoms that the patient may experience. There are financial effects of depression that are felt within family units, the community, and the workplace. The financial impact in the workplace stems from absenteeism and a reduction in productivity (Greenberg, Fournier, Sisitsky, Pike, & Kessler, 2015). When considering the financial effects of depression, the costs associated with other comorbidity conditions also need to be taken into consideration.

The economic burden of depression and comorbid conditions was estimated to be \$210.5 billion in 2010 (Greenberg et al., 2015). Out of that \$210.5 billion the percentage breakdown is as follows: costs related to suicide (5%), workplace costs (48-50%), and direct costs (45-47%) (Greenberg et al., 2015). The cost solely related to depression was only 38%, while other costs were attributed to comorbid conditions (Greenberg et al.,

2015). When viewing depression as a whole picture, it is important to treat the depression in the most effective way possible in order to alleviate symptoms, decrease the potential for comorbid conditions, and limit the financial impacts that come from depression.

### **Depression Screening and the PHQ-9 Questionnaire**

Before treatment for depression can occur, a clinical diagnosis needs to be made. In family practice, a depression screening tool can be implemented to screen all adults for depressive symptoms. The U.S. Preventive Services Task Force recommends screening for depression in the general adult population, including pregnant and postpartum women (Siu & USPSTF, 2016). It was found that screening for depression with appropriate support systems in place improved clinical outcomes (Siu & USPSTF, 2016). The USPSTF notes that an appropriate support system is one that is able to ensure patients are screened, diagnosed per screening results, and finally either treated for positive results or offered appropriate referrals (Siu & USPSTF, 2016).

There are a number of screening tests or tools available for use. The primary care clinic setting for this scholarly project began using the PHQ-9 in 2017 to screen patients for depression. As a commonly used instrument for depression screening, the Patient Health Questionnaire (PHQ) is considered a valid and reliable tool (Siu & USPSTF, 2016). The PHQ was derived initially from the PRIME-MD (Primary Care Evaluation of Mental Disorders) which is another diagnostic tool. PRIME-MD is a one page questionnaire with 26 yes or no answers (Tamburrino, Lynch, Nagel, & Smith, 2009). PRIME-MD is used as an initial screening for five general mental disorders: depression, anxiety, alcohol, somatoform, and eating disorders (Spitzer, Kroenke, Williams, & the

Patient Health Questionnaire Primary Care Study Group, 1999). Using the PRIME-MD diagnostic instrument as a starting point, the PHQ was formed as a self-administered, three page, depression screening tool (Kroenke et al., 2001). The PHQ was further condensed into the PHQ-9 consisting of nine questions focusing on the nine DSM-IV criteria for depression (Kroenke et al., 2001).

Listed below are the nine questions that make up the PHQ-9 depression screening tool with the preceding statement of: “Over the last two weeks, how often have you been bothered by any of the following problems?”

1. Little interest or pleasure in doing things
2. Feeling down, depressed, or hopeless
3. Trouble falling or staying asleep, or sleeping too much
4. Feeling tired or having little energy
5. Poor appetite or overeating
6. Feeling bad about yourself, or that you are a failure or have let yourself or your family down
7. Trouble concentrating on things, such as reading the newspaper or watching television
8. Moving or speaking so slowly that other people could have noticed. Or the opposite, being so fidgety or restless that you have been moving around a lot more than usual
9. Thought that you would be better off dead, or of hurting yourself

Patients are asked to check precoded boxes that indicate on a scale of 0-3 whether or not they are experiencing a particular symptom. Responses include: Not at all (score of



zero), several days (score of one), more than half the days (score of two), or nearly every day (score of three). Patient scores can range from 0-27 with the ranges correlating to five different levels of depression (minimal, mild, moderate, moderately severe, or severe depression). There is a final unscored question added to the end that asks, “How difficult have these problems made it for you to do your work, take care of things at home, or get along with people?” For that question, the patient is able to check one of the following statements: Not difficult at all, somewhat difficult, very difficult, or extremely difficult.

Evaluation of the PHQ-9 indicates that it is a reliable and valid clinical tool. The internal reliability of the PHQ-9 had a Cronbach’s  $\alpha$  of 0.89 in primary care studies with an excellent test-retest reliability (Kroenke et al., 2001). The PHQ-9 was found to discriminate well between persons with and without major depression with a ROC analysis showing the area under the curve to be 0.95 (Kroenke et al., 2001). Based on the statistical and clinical findings, the PHQ-9 can be utilized as a valuable tool for depression screening in the adult primary care setting. A study completed with 566 participants compared the Center for Epidemiologic Studies Depression Scale (CES-D) and the PHQ-9 (Milette et al., 2010). Despite both tools having similar reliability and validity, the PHQ-9 was the overall preferred tool for being shorter in length, easily administered, and simple to score (Milette et al., 2010).

### **The Family Nurse Practitioner Role in Treating Depression**

In many rural areas, mental health providers are a very limited resource. When considering the vast amount of people that may require treatment for a mental health condition, other providers are required to step in and provide treatment. The lack of specialty providers means the role of diagnosing and treating depression falls on the

primary care provider (PCP), and in many cases the PCP may be a family nurse practitioner (FNP). The FNP role in depression management consists of screening for depression, providing medical treatment for depression, and referring out to specialty services if required. A small study of 44 nurse practitioners discovered that they reported one-third of the patients they see in a weeks' time are reporting mental health problems (Shell, 2001). Within the rural county that this project took place in, there are less than ten certified medical providers for mental health. There are numerous licensed counselors and therapists for adjunctive therapies, but they are unable to provide any prescriptions for required medications. Medication management mostly falls on the primary care providers in the area due to the limited resources available. A study completed in 2001 of 44 nurse practitioners indicated that 71% felt they were adequately informed to be prescribing antidepressants, 56% indicated that they needed additional education regarding antidepressant prescribing, and 86% stated they would attend a continuing education class on antidepressants (Shell, 2001).

There are different types of treatment that can be utilized for the treatment of depression. These treatments include cognitive behavioral therapy and prescribed medications. The FNP has to consider many different factors when prescribing an antidepressant medication. The factors considered when treating depression include cost of the medication, possible drug interactions, potential side effects, and other medical conditions that the patient may have been diagnosed with (Shell, 2001). Based on these factors, a medication may be selected from one of the antidepressant medication classes. A study completed in rural community found that advanced practice nurse practitioners

most commonly prescribed SSRIs and SNRIs for the treatment of depressive conditions (Burman et al., 2015).

### **Medication Prescribing Practices**

Primary care providers, such as family nurse practitioners, are able to treat depressive disorders with a variety of medications. The classes of antidepressant medications are selective serotonin reuptake inhibitors (SSRIs), serotonin non-reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), and atypical antidepressants (Uphold & Graham, 2013). Another class of antidepressants that are no longer widely utilized due to side-effect profiles and food/medication interactions are a group called monoamine oxidase inhibitors (MAOIs) (Hirsch & Birnbaum, 2018). This medication class may still be utilized for treatment resistant depression, but they are considered third or fourth line treatment options (Hirsch & Birnbaum, 2018).

The best tolerated medication class are the SSRIs which are considered the first line treatment for depression (Uphold & Graham, 2013). A few examples of SSRIs are citalopram, fluoxetine, and sertraline. Generally, these medications are effective at low dosages and don't require frequent dosage changes (Uphold & Graham, 2013). The evidence does not support that one SSRI is going to be more effective than the other, however, it is important to consider potential drug interactions when deciding on a medication (Uphold & Graham, 2013).

SNRI's are a class of antidepressants that may provide an added benefit to patients that also have a coexisting pain condition such as neuropathic pain (Uphold & Graham, 2013). These medications may not be as tolerated as well as SSRIs in older adults, examples of these medications include duloxetine, venlafaxine, and

desvenlafaxine (Uphold & Graham, 2013). The atypical or “other” antidepressants include bupropion and mirtazapine and have been noted to be relatively safe when it comes to overdose concerns (Uphold & Graham, 2013). TCAs have been found to be the class that causes the most side effects that may result in patient noncompliance and should only be prescribed to patients who have failed treatment from the other classes (Uphold & Graham, 2013).

With all medication classes, there are general standards on initiation, monitoring, and dosage titration. Uphold and Graham (2013) offer the following prescribing guidelines for antidepressants:

1. The initial antidepressant medication should be selected based on patient symptoms, needs of the patient, and the side effect profile.
2. Initiate the chosen medication at half the recommended dose and titrate up slowly over two weeks.
3. Schedule the patient for a follow-up appointment four weeks after medication initiation to assess compliance and symptom improvement.
4. If symptoms have begun to decrease but are not at an optimal level, consider increasing the dosage with another follow-up appointment scheduled for four weeks after the change.
5. If after 12 weeks of treatment, the patient does not have a substantial benefit from the medication; or the side effects are unbearable, the medication should be switched to an alternative medication.

Once an optimal medication regimen has been achieved, the patient should follow up every three to six months with a minimum of six to nine months of close monitoring

(Uphold & Graham, 2013). It is the recommendation that the patient stay on the successful medication for at least six months to prevent symptom relapse (Uphold & Graham, 2013). If the patient has had more than two previous episodes of depression, they are considered high risk of relapse and should stay on the prescribed medication for at least two years (Uphold & Graham, 2013).

Following the guidelines for antidepressant medication selection have been the go-to practice for primary care providers. However, with the increase in pharmacogenomic testing, primary care providers are now able to provide the patient with a personalized list of medications that will work with their genetic makeup and metabolism.

### **Personalized Medicine and Pharmacogenomic Testing**

There are many different factors to consider when deciding what medication to prescribe a patient. The patient's age, gender, renal function, hepatic function, substance use, and genetic factors are a few of the many variables to take into consideration with each and every patient (Hall-Flavin, Schneekloth, & Allen, 2010). The time frame for an optimal therapeutic response in antidepressant medications may take up to 12 weeks' time (Hall-Flavin et al., 2010). Personalized medicine can be defined as, "The use of genotypic information to stratify disease and select a therapy that is particularly suited to an individual patient..." (Hall-Flavin et al., 2010, p. 40). With the use of pharmacogenomic testing, there is the potential for a decrease in medication side effects and a decrease in overall time spent trying different medications that may not be genetically compatible with the patient's metabolism.

Pharmacogenomic testing detects genetic variations that are coded for proteins, specifically, drug-metabolizing enzymes (Hall-Flavin et al., 2010). The specific test utilized at the clinical site used for this project is the GeneSight® Psychotropic pharmacogenomic test which analyzes how multiple genes metabolize medications. The genetic sample is retrieved via a buccal mucosal swab and is sent to an outside lab for processing with results coming within 36 hours of the appointed GeneSight® lab receiving the sample (GeneSight, 2018). The GeneSight® Psychotropic test analyzes 12 different genes to assess how they influence the patient's response to many psychotropic medications (GeneSight, 2018). The pharmacokinetic genes that are tested in the GeneSight® test are the cytochrome P450 (CYP) enzymes, CYP1A2, CYP2B6, CYP2C19, CYP2C9, CYP3A4, and CYP2D6, and also UGT1A4 and UGT2B15 (GeneSight, 2018). The test also identifies SLC6A4 which is a serotonin transporter, and HTR2A which is a serotonin receptor (Altar et al., 2015). There are also two other pharmacodynamic genes, HLA-B\*1502 and HLA-A\*3101, that are associated with a higher risk for dermatologic and hypersensitivity reactions (GeneSight, 2018).

The pharmacogenomic testing may show that a patient has an altered P450 enzyme which causes certain medications to either be metabolized poorly or ultrarapidly (Altar et al., 2015). The differences in medication metabolism corresponds with the recommendation GeneSight® gives for medication dosing. For example a patient with poor metabolism may require a lower dosage versus a patient identified as being a ultrarapid metabolizer needing a higher medication dosage (Altar et al., 2015). This information is how GeneSight® is able to provide recommendations on whether certain

medications are in the use as directed group (green), moderate gene-drug interaction group (yellow), or significant gene-drug interaction group (red) (Altar et al., 2015).

Along with placing the medications into the appropriate groups, GeneSight® also provides supplemental information on why each medication is in that class. For a medication that was placed in either the yellow or red groups, there are numbers that correspond to footnotes explaining the rationale. For example, an explanation might indicate that for a specific individual, an antidepressant medication, such as citalopram, creates too high of a serum level at a normal dose and therefore, a lower dose is required (Altar et al., 2015). Another example would be the test identifying that an individual is at an increased risk of side effects when taking a certain medication or that the FDA labels this medication as contraindicated for this genotype (Altar et al., 2015).

The information discussed above is computed into an individualized medication list that indicates the best medication choices based on the patients' genetic make-up. The report is available online to the providers office within 36 hours. This personalized report allows the FNP to review all the medications, what group the medication was placed in, and then make an educated decision regarding what antidepressant to prescribe.

### **Application of Testing in Primary Care**

Depression is a common mental disorder with over 300 million people affected worldwide and is the leading cause of disability across the world (World Health Organization, 2018). A large clinical trial of 4,041 outpatients with depression found that after each medication failure there was an increase in intolerance to the treatment plan which subsequently increased again after each failed medication (Warden, Rush, Trivedi, Fava, & Wisniewski, 2007). With the use of pharmacogenomic testing in the primary

care setting, this intolerance and medication failure has the potential to be decreased. Personalized medication in primary care aims to increase medication tolerability, improve treatment outcomes, and increase patient adherence to the prescribed medications (Altar et al., 2015).

A study completed by J. Winner, Allen, Altar, and Spahic-Mihajlovic (2013) found that nine of their 97 study participants were on a medication that was in the red group on the GeneSight® test. Those nine participants had 69% more healthcare visits and more medical absence days than the participants with medications in the green or yellow group. It was also discovered during data analysis that the longer the participant was on a red group medication, the more healthcare visits they had (J. Winner et al., 2013).

A one year study analyzed 2,168 patients that underwent GeneSight® testing along with a control group of 10,880 patients (J. G. Winner et al., 2015). Their study showed that the GeneSight® test group patients saved over \$1,000 in medication costs with an average cost saving of \$2,774.53 when the patient switched to a medication deemed best based on GeneSight® test results (J. G. Winner et al., 2015).

Another notable study was a 10-week long prospective double-blind randomized control trial on the clinical impact of pharmacogenomic testing (J.G. Winner, Carhart, Altar, Allen, & Dechairo, 2013). There were 51 patients that participated in this study and they had a clinical diagnosis of major depressive disorder. It is important to note that this study did exclude patients with a diagnosis of bipolar disorder (any type), schizophrenia, schizoaffective disorders, and an active substance abuse or dependence. There were 25 patients in the randomized treatment as usual (TAU) group and 26 patients



were randomly chosen for the GeneSight® testing group. Assessment data were collected at baseline, four weeks, six weeks, and ten weeks using a variety of tools, including the PHQ-9 Patient Health Questionnaire. During the 10-week study, physicians adjusted medications in the GeneSight® testing group and the TAU group at about the same rate (53% test group and 58% control group). Notably, 100% (seven total) of patients that were in the GeneSight® testing group and were on a red group medication were changed from that medication. Mean PHQ-9 scores in the GeneSight® test group improved by 35.4% versus the TAU group only improved by 21.3% (J. G. Winner et al., 2013).

Hall-Flavin et al. (2013) completed an open-label study with an unguided and guided group that utilized GeneSight® testing to assess the benefit for treatment of major depression. There were 233 study participants with a diagnosis of major depressive disorder or depressive disorder NOS between the ages of 18 and 72 that were included in the study. Exclusions for this study included bipolar type 1, schizophrenia, and schizoaffective disorder; inclusion criteria included a minimum score of 14 on the 17-item Hamilton Rating Scale for Depression (HAM-D-17). After all exclusions were applied, there were 227 participants eligible for the study, 113 were placed in the unguided group and 114 in the guided group. Both groups received GeneSight® testing but the results were withheld from the unguided group until the study completion. Assessment data were collected at baseline, two weeks, four weeks and eight weeks including a HAM-D-17, the Quick Inventory of Depression Symptomatology – Clinician Rated (QIDS-C16), and a PHQ-9. The guided group had more improvement on the HAM-D-17, QIDS-C16, and PHQ-9 at the eight-week mark compared to the unguided

group. The unguided group participants that were prescribed a medication that was not compatible with their genotype experienced the least improvement; while the guided group participants with incompatible medications showed the greatest improvement over the eight-week study. There was a 40.1% decrease in PHQ-9 scores in the guided group versus only a 19.5% decrease in the unguided group. The participants in the guided group had a 26.4% remission rate versus a 12.9% remission rate in the unguided group based on the QIDS-C16 scores (Hall-Flavin et al., 2013).

The information given on the GeneSight® Psychotropic test results are used as a guide to the patients personalized treatment. The test is a tool that the provider should utilize along with direct patient conversations to choose an appropriate medication. The medication the provider and patient chose may be in the green or yellow group. If the chosen medication is in the yellow group, it is important for the provider to read the footnotes and take into consideration what the gene-drug interaction is and make appropriate adjustments to the medication dosage.

### **Patient Views on Personalized Medicine**

The current research on patient perspectives regarding genetic testing for medication selection is limited, but the findings available are pertinent to the prescribing practices of the family nurse practitioner. A study by Haga et al. (2016) completed baseline surveys prior to pharmacogenetic testing and a follow up survey three months after testing. The patients in this study completed pharmacogenetic testing for a variety of medications, not specifically for antidepressants. There were 63 total patients underwent the testing process with only 17 completing the baseline survey and 12 of the 17 completed the follow-up. The top trends identified from the surveys that influenced

the patients decision to undergo genetic testing were that their provider recommended the testing (59%), that patients understood the testing would allow the primary care provider to select the best medication for them (76%), and that there was a perceived value of the testing to optimize their treatment (65%). 83% of patients believed that the testing was helpful to their provider in regard to their treatment plan, but only 58% had increased confidence with the medication that was prescribed in comparison to past prescribed medications. On the follow-up survey, all patients stated they would be very or somewhat likely to undergo pharmacogenetic testing for other medications if it was indicated (Haga et al., 2016).

A participant in a study completed by Trinidad et al. (2015) provided the following quote regarding the use of pharmacogenetic testing in the treatment of her depression:

Even if it takes six months [to get pharmacogenetic test results], I have had --- looking back, it's like, you know, gee, do you think that particular drug was what took like four years out of my life? Yeah. If somebody could go in there and figure it out in four months, yeah, that would be better. (p. 23)

Another pertinent patient quote compared testing to riding on a bus, "You could jump off anywhere downtown and get to a store, but you want to get off closer to the store you're going to" (Trinidad et al., 2015, p. 23). The above statements further support the use of pharmacogenetic testing for appropriate and personalized medication selection. However, some of the study participants felt that the providers may end up relying too much on the test results and could potentially not give appropriate consideration to other factors, such as side effects they may be experiencing (Trinidad et al., 2015).

These findings support that patients find the testing to be useful and pertinent to their overall treatment plan when utilized appropriately by their provider. In the family practice setting, it is important to continue to discuss treatment options with the patient and take their views about pharmacogenetic testing into consideration when ordering said test. The health belief model may help guide the process of relaying the potential perceived benefit of pharmacogenetic testing to patients.

### **Theoretical Framework**

The health belief model was originally established in 1950 by three social psychologists that were working for the U.S. Public Health Services to try and improve the use of preventative services (Rosenstock, 1974). Health behaviors were explained in the health belief model by using the following concepts: perceived susceptibility of the health problem, perceived severity, perceived benefits, perceived barriers, and cues to action (Castonguay et al., 2016). Rosenstock added a sixth concept to his model in 1988 called self-efficacy (Garner, 2014).

The perceived susceptibility of the health problem is the patients opinion on their chances of getting a condition (Garner, 2014). When faced with a diagnosis of depression, the patient may perceive that they never would be depressed or be diagnosed with depression. How serious the patient believes the condition is and what its consequences will be is known as the perceived severity (Garner, 2014). A patient diagnosed with depression for the first time may perceive the severity of the diagnosis to be low; however, a patient that has been diagnosed previously with depression may view this as more severe. The perceived benefits in the health belief model are how the patient believes the suggested action will decrease the seriousness of the problem (Garner, 2014).

This would correlate to a patient being prescribed medications, cognitive behavioral therapy, or pharmacogenomic testing and what he or she believes regarding the benefits from those actions.

On the opposite end of the spectrum, perceived barriers are the patients opinion on the potential barriers to treatment (Garner, 2014). Barriers could range from monetary concerns of the medications, therapy, or potential cost of the pharmacogenomic testing to the patients perceived social stigma of being diagnosed with a depressive condition. Cues to action are the patients readiness to act and begin overt behaviors while self-efficacy is the confidence to perform an action (Garner, 2014). Cues to action would include the positive acts of taking the prescribed medication, completing the pharmacogenomic testing, or going to a therapy appointment. Self-efficacy with a diagnosis of depression could correspond to reading self-help books, exercising, or engaging in other self-care measures that demonstrate a belief that a change in health behavior can positively influence health (Garner, 2014). This is the belief that a change in health behaviors can positively influence health (Garner, 2014).

Pharmacogenomic testing for psychotropic medications is one way to provide a personalized treatment plan for patients with depression. The health belief model demonstrates how the perceived benefit of testing will potentially allow for successful treatment based on genetic make-up and metabolism. By utilizing the health belief model and pharmacogenomic testing, primary care providers could potentially prevent treatment resistant depression and many of comorbidities that are associated with depression.

## Summary

This scholarly project seeks to understand how GeneSight® testing effects the prescribing practices of a nurse practitioner in a rural Michigan clinic and how/if it has any change on the patients PHQ-9 scores at scheduled follow up appointments. The literature supports the use of psychotropic pharmacogenomic testing to help guide the provider in their medication selection process. The studies have shown that the patients in the guided, or the pharmacogenomic testing group, have significant decreases in their PHQ-9 depression screening scores. Based upon the review of literature, the scholarly project methodology was developed and will be discussed in depth in Chapter Three.

## Chapter Three

### Purpose, Sample, and Recruitment

The purpose of this project was to assess if medication changes based on GeneSight® Psychotropic pharmacogenomic testing resulted in improvement of PHQ-9 depression screening scores. The GeneSight® Psychotropic pharmacogenomic testing was implemented at the clinical site under study prior to project implementation in February 2018. The clinical site can be described as a small, family practice clinic located in a rural area. The clinical site currently cares for 1,972 adult patients between their primary care and walk-in clinic. The testing is currently being utilized at the family nurse practitioner's discretion for patients who have had recurrent failed treatment on one or more medications that are FDA approved to treat depression.

The inclusion criteria for the project required control and test group patients to be between the ages of 18-99 years old with a diagnosis of depression that had received treatment from the primary care provider (family nurse practitioner). The control group inclusion criteria also included being seen by the provider within the three months prior to GeneSight® testing implementation. The test group inclusion criteria required that they received GeneSight® testing at the clinical site within three months after testing implementation. The exclusion criteria for both the control and test group included being under the age of 18 and not having a current diagnosis of depression. Patients were excluded from the test group if they did not receive the GeneSight® testing during the specified time frame. The sample size was deemed to be 23 which is the total number of patients seen during the three months prior to testing implementation and the three months after implementation. An online sample size calculator,

<http://www.raosoft.com/samplesize.html>, was used with a confidence level of 95% with a 5% margin of error. The recommended sample size was 22 patients.

There was no recruitment process for the participants of this study. The patients primary care provider, independently of this project, chose the participants for GeneSight® Testing based on their patient assessment and past history of depression treatment. Medical necessity for GeneSight® Testing was determined by the provider and required treatment failure on at least one psychotropic medication that is FDA approved to treat depression.

### **Scholarly Project Approval**

A member from Northern Michigan University Institutional Review Board (IRB) reviewed an IRB proposal and confirmed that IRB approval was not required (see Appendix A). The nature of this project falls under a quality review project as it is a retroactive chart review.

### **Design and Measures**

This DNP scholarly project utilized a quantitative and a nonequivalent control group research design (Terry, 2015). Retroactive chart reviews were completed for ten patients that were treated for depression in the three months prior to the implementation of GeneSight® Testing as a non-randomized control group. All patients who received GeneSight® Testing for treatment resistant depression in the three months after implementation were considered part of the test group and also received a retroactive chart review.

The information retrieved from the charts were deidentified at the point of retrieval. The information retrieved from the charts included gender, race, age, ICD-10



diagnosis code, PHQ-9 scores, medication lists, stated medication side effects, time between visits for depression, other medical diagnoses, what GeneSight® medication grouping type (green, yellow, red) the medications were in for the test group, the number of visits they were seen and treated for depression, and all FDA approved antidepressant medications that had been prescribed.

### **Informed Consent, Risks and Benefits**

This scholarly project was reviewed by a university IRB board member and was deemed exempt from needing informed consent. All information was deidentified and retrieved via retroactive chart review as a quality measure. Overall, this research project posed a minimal risk to all parties involved. The potential risks associated with this project were limited to psychological risk factors of the patients. There are no known physical, economic, or legal risks associated with this study. The psychological risks were very low as all identifying data were removed at the point of data collection.

This study aimed to benefit both the patient and the provider. The benefit for the patient may include a better medication selection based on the GeneSight® Test results and a potential decrease in PHQ-9 scores. The provider may benefit from a patient specific medication list to choose from and a decrease in office visits for depression.

### **Instrument**

The PHQ-9 depression screening tool (see Appendix C) was already being utilized at the clinical site for routine depression screening. It is a reliable and validated depression screening tool that is comprised of nine questions and is completed by the patient prior to office visits. The questions are asked based on the statement of, “Over the last two weeks, how often have you been bothered by any of the following

problems?”. Listed below are the nine questions that are asked on the PHQ-9 patient questionnaire:

1. Little interest or pleasure in doing things
2. Feeling down, depressed, or hopeless
3. Trouble falling or staying asleep, or sleeping too much
4. Feeling tired or having little energy
5. Poor appetite or overeating
6. Feeling bad about yourself, or that you are a failure or have let yourself or your family down
7. Trouble concentrating on things, such as reading the newspaper or watching television
8. Moving or speaking so slowly that other people could have noticed. Or the opposite, being so fidgety or restless that you have been moving around a lot more than usual
9. Thought that you would be better off dead, or of hurting yourself

The patient answers the questions by checking a box for one of the following statements: Not at all (score of zero), several days (score of one), more than half the days (score of two), or nearly every day (score of three). These scores are then added up to a total number that correlates with the following depression severity table (Table 1).

Table 1

*Depression Severity Based on Total PHQ-9 Scores*

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

**Research Questions**

This DNP scholarly project aimed to answer the following questions:

1. As compared to a control group, what effect, if any, does utilizing GeneSight® Psychotropic pharmacogenomic testing have on prescribing patterns of primary care providers?

Hypothesis: Primary care providers will choose medications based off the personalized medication list that are in the green (use as directed) category.

2. What effect, if any, did medication changes as a result of GeneSight® Psychotropic pharmacogenomic testing have on PHQ-9 depression screening scores?

Hypothesis: Personalized psychotropic medication choices based on the GeneSight® test will result in a decrease in PHQ-9 scores within four to eight weeks after medication initiation

## Data Analysis

Data were collected from the electronic medical record, deidentified, and entered into an Excel Spreadsheet. The information collected included gender, race, age, ICD-10 diagnosis code related to depression, PHQ-9 scores, medication lists, stated medication side effects, the total weeks between visits for depression, other medical diagnoses, what GeneSight® medication grouping type (green, yellow, red) the medications were in for the test group, the number of visits patients were seen and treated for depression, and all FDA approved antidepressant medications that had been prescribed. IBM SPSS software application version 20.0 was used to analyze the collected data. The deidentified data will be kept in a locked drawer for the next seven years. Results are discussed in depth in Chapter Four.

## Chapter Four

### Project Summary

This doctoral scholarly project aimed to evaluate if GeneSight® testing had any effect on prescriber patterns/practices and patient reported PHQ-9 depression screening scores. The Chapter Two literature review supports the use of GeneSight® testing in primary care settings for patients that have experienced treatment failure. The rural clinical site for this project implemented the PHQ-9 depression screening tool in 2017. The GeneSight® Psychotropic pharmacogenomic testing was implemented and was utilized on a small number of patients that were considered to have had treatment failure on at least one antidepressant medication. The PHQ-9 is a valid and reliable tool for depression screening that is self-administered by the patient. A retroactive chart review was completed during the time period of three months before GeneSight® Psychotropic pharmacogenomic testing was implemented and three months after implementation.

### Post-Data Collection Practitioner Discussion

An informal discussion was completed post-data collection with the FNP of the rural clinic associated with this doctoral scholarly project. The following topics were discussed with the FNP:

1. Readiness to treat depression
2. PHQ-9 screening tool useful for identifying/treating depression
3. GeneSight® testing usefulness for prescribing practices
4. Patient or provider barriers to ordering the test
5. Financial implications of GeneSight® testing

Themes from the interview with the family nurse practitioner discussion regarding her readiness to treat depression included: 1. Immediately post-graduation, she felt best equipped to prescribe SSRI antidepressants only; 2. Knowledge of antidepressants was only ascertained from formal pharmacology classes in school; 3. SSRIs were initially the main class of antidepressants used in her practice; however she has expanded her knowledge and comfort level with prescribing other antidepressant classes; and 4. Further education has to be sought out post-graduation through medical conferences dealing with the topics of depression and anxiety.

In terms of using the PHQ-9 screening tool, the provider shared that it was implemented at the clinical site in 2017. She has found that it is a useful tool for recognizing, diagnosing, and treating depression. However, she discovered that the PHQ-9 score sometimes does not correlate well with the patient's overall perception of their depression symptoms. It has been noticed that even though patients may score high on the PHQ-9, they may still be happy with their overall progress and not want to make any changes to their medication regimen.

Finally, the usefulness of GeneSight testing, potential barriers for testing, and financial implications were discussed. Currently, the provider has not found that the GeneSight® testing has made a significant impact on her prescribing practices for treating depression. However, it was acknowledged that it has only been used on a small number of patients since implementation. The patients that have utilized the GeneSight® testing have been excited about what it means for their treatment plan. She stated that the test has been utilized when the patient has had treatment failure on multiple antidepressant classes. One of the barriers noticed is the amount of medications that can

still be in the green, use as directed, column. With multiple medications in the green column, the provider has found that some trial and error may still be required to find the best medication for the patient despite the fact that in theory, the GeneSight® testing should reduce the number of medications that the patient must try. This would be true only if the test results show medications in the yellow or red group. Overall, the provider feels that the testing should decrease costs for the patient due to savings on potential multiple medication and visit copays.

### **Data Analysis**

The data for this analysis came from a convenience sample through retroactive chart reviews for both the control and the test group. The control group chart review revealed  $n = \leq 10$  and the test group chart review also was  $n = \leq 10$ . Due to the small sample size, all data will be presented in percentages. The exact  $n$  values for the control and test group will be omitted. This process assists in protecting the study participants from potentially being identified. All data were processed via the IBM SPSS software application version 20.0. Both descriptive and inferential methods were utilized for the statistical analysis. Categorical variables are presented using frequency distribution. Interval scale variables, such as age and PHQ-9 scores, are summarized using means and standard deviations. Matching of distribution of age between control and test groups was completed using independent samples t-test. A comparison of the total number of visits for depression in the control and test group patients was completed by using independent samples t-test. Comparison of PHQ-9 scores across the two measurement periods during the study period was completed by using a paired t-test. All statistical tests were performed at a 0.05 level of significance.

## Results

The majority of the control group participants were female (70%), the remaining participants were male (30%) (See Figure 1). In the test group, 100% of the participants were female. 100% of the patients in the control and test group identified their race as Caucasian. The mean age of patients in the control group was  $M = 38.20$  ( $SD = 16.86$ ). The mean age of patients in the test group was  $M = 56.50$  ( $SD = 23.35$ ). Results of independent samples t-test indicated that there is no significant difference in mean age of patients between the control group and test group ( $t(\leq 10) = 1.341, p = .209$ ).

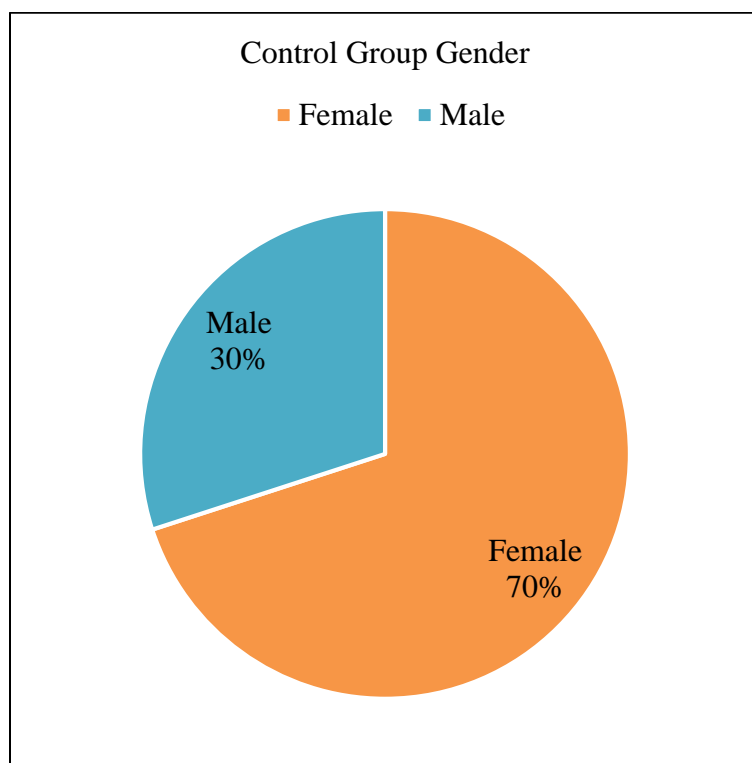


Figure 1. Pie chart of gender of patients in the control group

The patients in the control group had varying ICD-10 diagnosis codes that included F33.0 (Major Depressive Disorder, Recurrent, Mild), F33.1 (Major Depressive Disorder, Recurrent, Moderate), and F32.1 (Major Depressive Disorder, Single Episode,



Moderate) (See Figure 2). 100% of the patients in the test group had an ICD-10 diagnosis code of F33.1 (Major Depressive Disorder, Recurrent, Moderate).

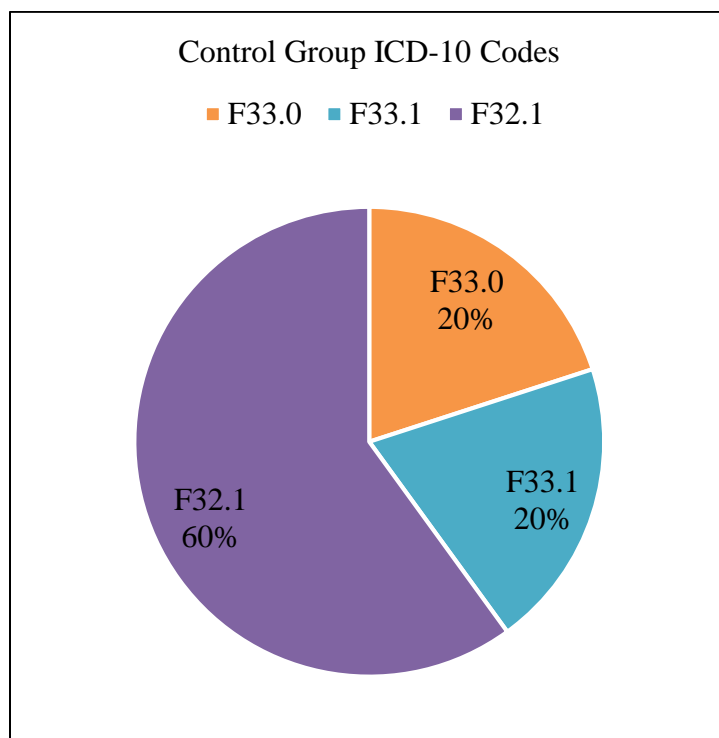


Figure 2. Pie chart of control group ICD-10 Codes

A paired t-test was used to compare the PHQ-9 scores across the two measurement periods during the study period. Table 2 below presents descriptive statistics of PHQ-9 scores for the control group along with summary of results of paired t-test. The mean PHQ-9 score during the first measurement period was  $M = 7.00$  ( $SD = 4.243$ ) which is mild depression. The mean PHQ-9 score during the second measurement period was  $M = 3.50$  ( $SD = .707$ ) which is considered minimal depression.

Table 2

*Comparing control group PHQ-9 scores between two measurement periods*

Measurement	Mean	<i>n</i>	SD	<i>t</i>	<i>p</i>
Period 1	7.00	≤10	4.243	1.40	.395
Period 2	3.50	≤10	.707		

Results of paired t-test indicated that the null hypothesis of no significant difference in the mean PHQ-9 scores cannot be rejected at .05 level of significance ( $t_{(\leq 10)} = 1.40, p = .395$ ). This indicates that in the control group there was no significant difference in PHQ-9 score distribution between the two measurement periods. In the test group, there was only one pair of PHQ-9 scores recorded. Therefore, no statistical test could be performed on the test group PHQ-9 scores. For the recorded pair of PHQ-9 scores, the PHQ-9 score was 24 in the first measurement period and subsequently dropped to 9 during the second measurement period. This is a potential indication that GeneSight® intervention caused a reduction in PHQ-9 scores during the study period. However, there must be a bigger representative sample size to generalize the results with statistical support.

The antidepressants prescribed in the control group were changed for 50% of the patients between the two appointments. In the control group, 30% had dosage increases, 10% had a dosage decrease, and 10% discontinued the medication. 20% of the control group patients had no medication changes and the last 30% did not have any follow-up appointments on record. The majority of the patients were taking an SSRI (80%) and the rest of the control group patients were taking an SNRI (20%). See Table 3 for a breakdown of the medications utilized and their respective drug class. 10% of patients in

the control group were prescribed alprazolam for anxiety and 20% were prescribed trazodone for insomnia.

Table 3

*Control group medication class breakdown*

Medication	Drug Class	Percentage
Escitalopram	SSRI	30%
Citalopram	SSRI	30%
Paroxetine	SSRI	10%
Fluoxetine	SSRI	10%
Venlafaxine	SNRI	20%

After GeneSight® test results were received, 50% of the patients in the test group had subsequent medication changes. Any medication that was listed in the red category on the GeneSight® test was discontinued in 100% of the test group patients. Table 4 lists the medications and the drug classes that the patients were on before and/or after the GeneSight® testing was completed. Unlike the control group, the medications utilized for the patients in the test group were from a wider variety of classes. This could be attributed to previous treatment failure on the first line medications that were being utilized in the control group patients. It is important to note that the test group patients may have been on more than one antidepressant medication at the time of this study.

Table 4

*Test group medication class breakdown*

Medication	Drug Class	Percentage
Bupropion HCL	NDRI	50%
Trazodone	SARI	100%
Citalopram	SSRI	50%
Desvenlafaxine	SNRI	50%
Quetiapine	Atypical	50%

In the control group, the time between a medication/dosage change and their follow-up appointment ranged between 2.5 weeks to 18 weeks with a mean of 6.86 weeks (SD = 5.178). In the test group, the time between a medication/dosage change and their follow-up appointment ranged between 4 weeks to 8 weeks with an average of 6 weeks (SD = 2.828). Results of independent samples t-test indicated that there was no significant difference (see Table 5) in the mean weeks' time between medication/dosage changes and their follow-up appointments between the control and the test groups ( $t_{(≤10)} = .218, p = .834$ ).

Table 5

*Time gap between medication change or appointments between control and test groups*

Group	Mean	<i>n</i>	SD	<i>t</i>	<i>p</i>
Control	6.86	≤10	5.178	.218	.834
Test	6.00	≤10	2.828		

Table 6 presents descriptive statistics for total number of visits made by patients for the treatment of depression. Patients in the control group visited on an average 2.80

times (SD = 2.044). In the test group, patients visited on an average 4.50 times (SD = 2.121) for treatment of depression. Independent samples t-test is used to test the significance of the difference in mean number of visits made by patients in control and test group. Results of independent samples t-test indicates that null hypothesis of no significant difference in mean number of visits between control and treatment groups cannot be rejected at .05 level of significance ( $t (\leq 10) = 1.070, p = .310$ ). It is concluded that there is no significant difference in average number of visits for depression between patients in control and treatment groups.

Table 6

*Number of visits for treatment of depression*

Group	<i>n</i>	Mean	SD	<i>t</i>	<i>p</i>
Control	$\leq 10$	2.80	2.044	1.070	.310
Treatment	$\leq 10$	4.50	2.121		

There were a variety of other health conditions found in the control group (See Figure 3). It is an interesting finding that a large percentage of control group patients had a concurrent diagnosis of anxiety which may have impacted the providers decision making process for medication selection. The test group participants also had concurrent medical diagnoses of anxiety, insomnia, and vertigo (Figure 4). In the control group, brain foginess and sweating were reported as side effects to the prescribed antidepressants. There were no side effects recorded in the providers note for patients in the test group.

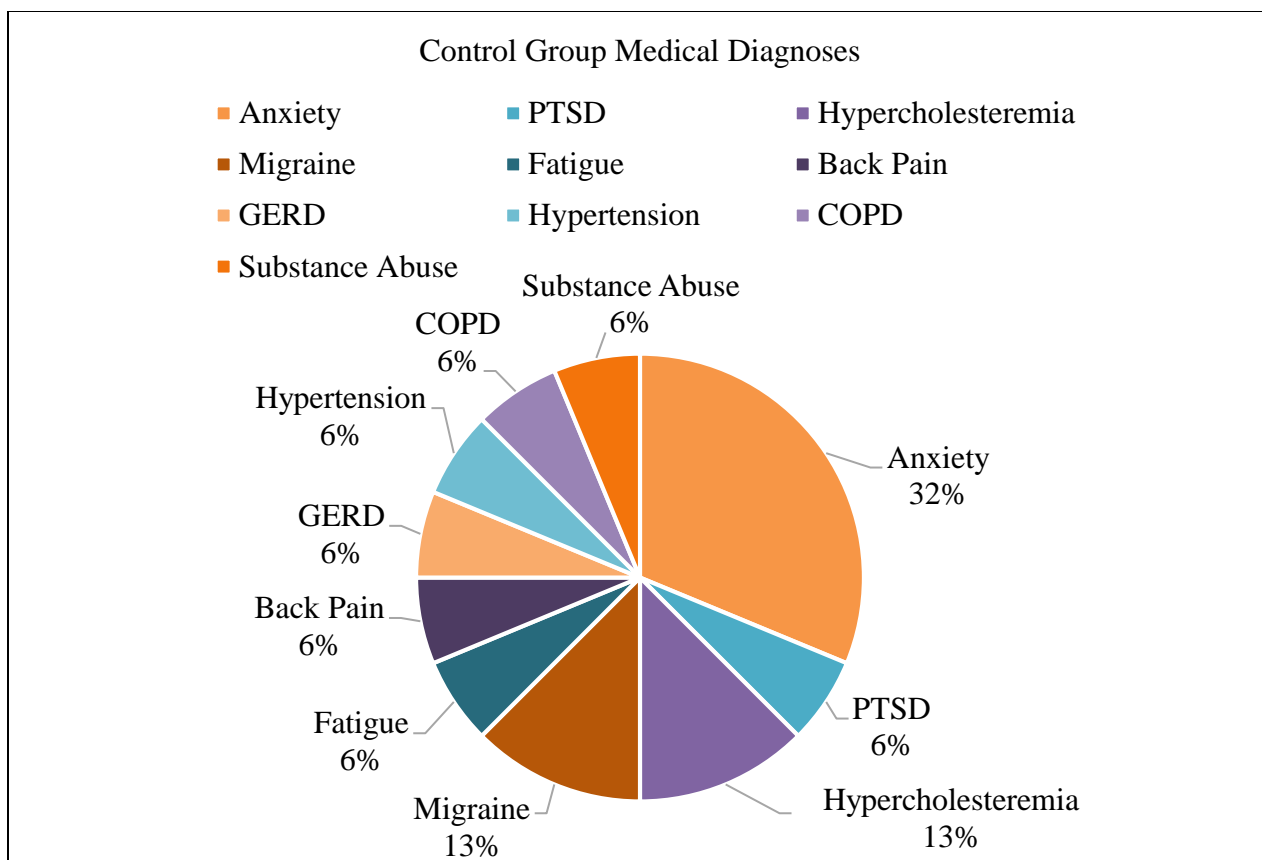


Figure 3. Control Group Medical Diagnoses

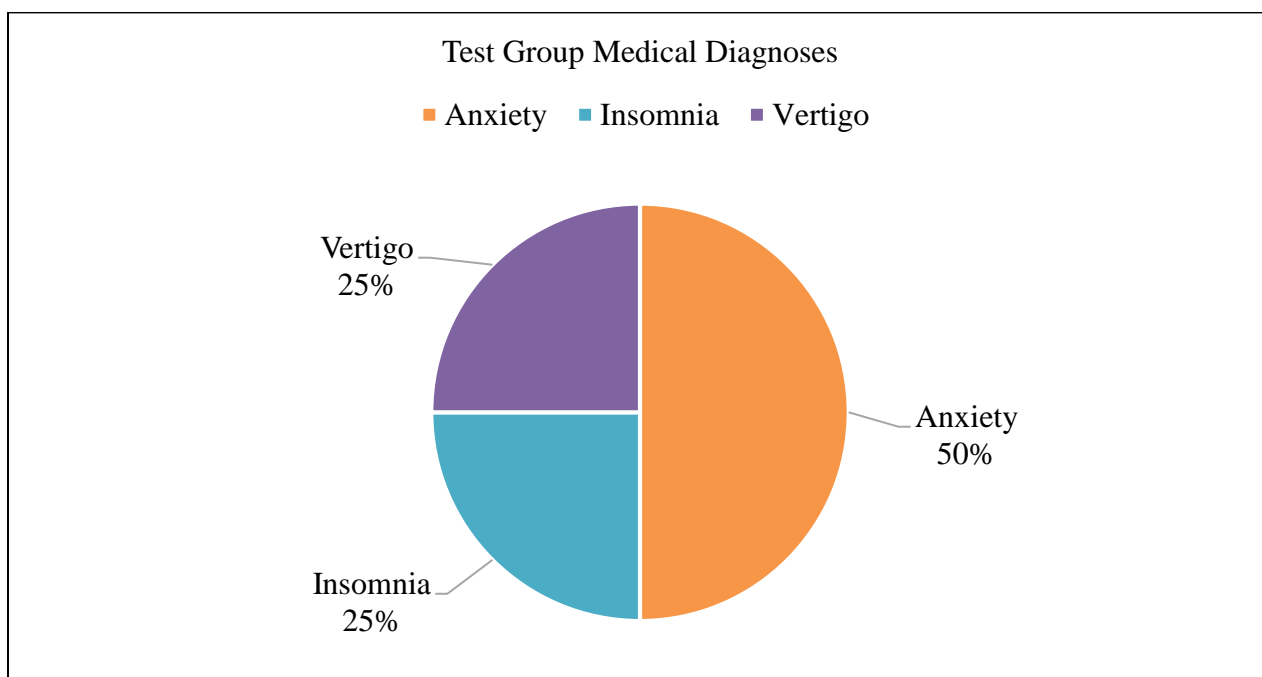


Figure 4. Test Group Medical Diagnoses

## **Strengths and Limitations**

The most significant limitation of this project was the lack of test group participants and the lack of documented PHQ-9 scores for both the test and the control group. As this project was a retroactive chart review, there was no opportunity for participant recruitment or for the researcher to intervene and make sure screening was completed or charted in the electronic medical record. The time frame of the study is also a notable limitation. Three months prior to testing implementation and three months post testing implementation was the timeline for this project. A longer time frame would have allowed for a larger control group and a potentially larger test group. The project design is also a limitation for that reason. A different project design that included participant recruitment, monitored PHQ-9 screening at each visit, over a longer period of time would have been an ideal situation.

A strength of this project was that the intervention of the GeneSight® test had been studied in the past and was already been proven to have a significant impact on the treatment of depression. Another strength is that the clinical site already had the PHQ-9 in place as a validated and reliable tool for depression screening. Finally, the clinical site and practitioner were both willing and helpful with their time and access to the electronic medical records.

## **Future Studies**

Future studies could benefit from utilizing a qualitative questionnaire for both the patient and the provider. The qualitative data from patient experiences could include background on why they did or did not utilize the GeneSight® test, how they felt about the idea of genetic testing for medications, and how they felt the provider responded to

the test results. This information could help primary care providers understand what patients are thinking about the test, the testing process, and the test results. Qualitative data from the providers perspective could potentially include their thoughts on when and why to order the GeneSight® test for patients. Exploring the training and comfort level of practitioners in rural settings acting as the primary prescribers for symptomatic depression might also add insight to whether or not the practitioner feels that the GeneSight® testing is necessary for proper and effective patient care. Future studies could also investigate what other nonpharmacological therapies the patients had tried prior to the GeneSight® testing and what role they may have played in their overall treatment plan.

Future studies could also benefit from a cost analysis in a control group and test group to assess what financial effects GeneSight® testing may have on the overall costs associated with depression. At the time of this study, patients have a maximum out of pocket cost of \$330 for GeneSight® testing (GeneSight, 2018). Many insurance companies are covering a portion or all of the cost of the test (GeneSight, 2018). The cost analysis study could include individual patient costs for transportation to each office visit, insurance deductibles, office visit costs/copays, prescription co-pays, and even the cost of lost productivity hours. In the case that the out of pocket GeneSight® testing cost is the maximum of \$330, there is the potential for the patient to still have a large overall cost saving.

### **Recommendations and Conclusions**

While this scholarly project failed to have significant findings for the research questions asked, the amount of literature supporting the use of GeneSight® testing and



PHQ-9 depression screening in primary care is sufficient to support the implementation at the clinical site (Altar et al., 2015; Hall-Flavin et al., 2013; J. Winner et al., 2013; J. G. Winner et al., 2013; J. G. Winner et al., 2015; Kroenke et al., 2001; Siu & USPSTF, 2016). Findings in this study support current prescribing guidelines, appointment follow-up times, and GeneSight® testing.

The results from this study show that the FNP at the clinic is following prescribing guidelines for the control group with SSRIs or SNRIs as first line treatment (Uphold & Graham, 2013). The test group were prescribed a variety of medications that are appropriate for patients that are having difficulty finding an effective medication. There was a lack of follow-up appointments in both the control and test group, but the average time for follow-up after medications changes was within the standard time frame.

There were several patients that did not keep their follow-up appointments as scheduled after their initial visit for depression. The health belief model can be utilized to help the provider stress the importance of keeping follow-up appointments for depressive disorders. For the patients that have had missed follow-up appointments, it would be important to discuss their perceived severity, benefits, and barriers to coming to their scheduled appointments. By discussing those concepts, the provider may learn that the patient doesn't feel that their depression is severe or that a follow-up appointment is needed since they already have a prescription medication. This would allow the provider to educate the patient on why keeping their follow-up appointment is important to their plan of care. Furthermore, the provider could discuss self-efficacy. This final concept could be explained to the patient that there are positive actions they can take on their own, such as exercising or bibliotherapy, that can positively influence their health.

Accurate documentation is important for all clinical sites and providers, especially when implementing and analyzing a new evidence-based practice such as pharmacogenomic testing. This research study discovered that the clinical site had missing PHQ-9 score documentation that is important to the treatment and evaluation of depressive disorders. This finding was shared and will improve the future documentation practices of the clinical site.

The GeneSight® test provided rational for the prescriber to discontinue a medication that one patient was currently trialing due to it being the red category. This suggests that the testing could be a valuable tool for Family Nurse Practitioners to use for explaining and justifying medication decisions to patients. Unfortunately, due to the very small sample size in this study, no generalizations can be made for any of the study variables. Larger studies of rural family practice clinics have the potential to show a statistical significance with GeneSight® testing and PHQ-9 depression screening scores.

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## Appendix A

## Northern Michigan University Institutional Review Board Member Email

From: **Derek Anderson** <[dereande@nmu.edu](mailto:dereande@nmu.edu)>  
Date: Mon, May 21, 2018 at 9:37 AM  
Subject: Re: IRB question  
To: Kristi Robinia <[krobinia@nmu.edu](mailto:krobinia@nmu.edu)>

Hi Kristi,


Your instincts were correct - no need for IRB review.

I hope all is well with you as summer begins :)

- Derek

## Appendix B

## PHQ-9 Pfizer Statement


Welcome to the  
Patient Health Questionnaire (PHQ) Screeners

## Screeners Overview

Recognizing signs of mental health disorders is not always easy. The Patient Health Questionnaire (PHQ) is a diagnostic tool for mental health disorders used by health care professionals that is quick and easy for patients to complete. In the mid-1990s, Robert L. Spitzer, MD, Janet B.W. Williams, DSW, and Kurt Kroenke, MD, and colleagues at Columbia University developed the **Primary Care Evaluation of Mental Disorders (PRIME-MD)**, a diagnostic tool containing modules on 12 different mental health disorders. They worked in collaboration with researchers at the Regenstrief Institute at Indiana University and with the support of an educational grant from Pfizer Inc. **During the development of PRIME-MD, Drs. Spitzer, Williams and Kroenke, created the PHQ and GAD-7 screeners.**

The PHQ, a self-administered version of the PRIME-MD, contains the mood (PHQ-9), anxiety, alcohol, eating, and somatoform modules as covered in the original PRIME-MD. The GAD-7 was subsequently developed as a brief scale for anxiety. The PHQ-9, a tool specific to depression, simply scores each of the 9 DSM-IV criteria based on the mood module from the original PRIME-MD. The GAD-7 scores 7 common anxiety symptoms. Various versions of the PHQ scales are discussed in the Instruction Manual.


**All PHQ, GAD-7 screeners and translations are downloadable from this website and no permission is required to reproduce, translate, display or distribute them.**

**Select a Screener**

**PHQ and GAD-7 Screeners**

[Click here to access the Instruction Manual](#)

[Bibliography by author](#)



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## Appendix C

## PHQ-9 Patient Questionnaire

<b>PATIENT HEALTH QUESTIONNAIRE-9 (PHQ-9)</b>				
Over the <u>last 2 weeks</u> , 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 fidgety 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 in some way	0	1	2	3
FOR OFFICE CODING <u>  0  </u> + <u>    </u> + <u>    </u> + <u>    </u> =Total Score: <u>    </u>				
If you checked off <u>any</u> problems, how <u>difficult</u> 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 <input type="checkbox"/>	Somewhat difficult <input type="checkbox"/>	Very difficult <input type="checkbox"/>	Extremely difficult <input type="checkbox"/>	

Developed by Drs. Robert L. Spitzer, Janet B.W. Williams, Kurt Kroenke and colleagues, with an educational grant from Pfizer Inc. No permission required to reproduce, translate, display or distribute.