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Project Report

Pharmacogenetic Testing Education Effect on Psychiatric Prescriber Genetic Testing Practices

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DISCLAIMER: In the early weeks of the 2020 COVID19 Pandemic, graduates of the Daniel K. Inouye Graduate School of Nursing were asked by the University leadership to graduate 6 weeks early to care for the health of the nation in their new APRN roles. All phases of the DNP Project were complete, and met the standards and rigors of a quality DNP Project with an abbreviated dissemination timeframe.

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Abstract

Background: Antidepressant prescribing generally relies on theoretical inference and presenting symptoms with only one-third of patients with major depressive disorder (MDD) reaching full remission in the first trial. Repeated medication trials prolong treatment increasing the risk of suicide, and have a deleterious effect on readiness. Pharmacogenetic testing can provide insights to guide antidepressant prescription decisions in medication selection and dosage to reduce the overall, but pharmacogenetic testing is an underutilized modality.

Clinical Question: Does providing evidence-based pharmacogenetics testing education for the treatment of MDD to psychiatric prescribers at Madigan Army Medical Center (MAMC) and William Beaumont Army Medical Center (WBAMC) affect the pharmacogenetics testing practices between each installation four months post-intervention?

Project Design: The scholarly inquiry project used an educational and awareness toolkit as an intervention to increase psychiatric provider awareness of pharmacogenetic testing. Psychiatric provider beliefs, attitudes, and perceived barriers to pharmacogenetic testing were assessed by a pre-intervention survey. Psychiatric provider pharmacogenetic ordering practices were assessed by analyzing ordering trends two years pre and four months post-intervention.

Analysis of Results: Psychiatric prescribers reported believing that pharmacogenetic testing is a practice that should be utilized and reported a lack of resources and clinical guidance as significant barriers to testing. However, psychiatric prescribers infrequently ordered tests pre and post-intervention. The patients who received pharmacogenetic testing had either extended length

of time on an anti-depressant or multiple anti-depressant trials. Opportunities to strengthen the use of pharmacogenetic testing amongst psychiatric providers exist. Implications for **Practice:** Military behavioral health prescribers using evidence that is complete, easy to use and reflects best practice related to pharmacogenetic testing may result in increased awareness and use of testing to inform pharmacotherapy treatment plans. Prescribers can incorporate pharmacogenetic testing into their decision making for patients with MDD at WBAMC and MAMC. Pharmacogenetic testing is an effective tool to maximize early medication management for MDD, resulting in improved stability for patients and ultimately increased the readiness of the force. When compared with prescribing medication to treat MDD without testing, pharmacogenetic testing is a cost-efficient method that provides greater patient-centered care for soldiers.

Keywords: pharmacogenetic, antidepressant, major depressive disorder

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Introduction

Major Depressive Disorder (MDD) is a globally burdensome psychological disorder and is the leading cause of disability, affecting nearly 300 million people worldwide that has a deleterious impact on job performance, interpersonal relationships and even increases the risk for patient suicide (American Psychiatric Association, 2013; Gaynes et al., 2009; Pompili et al., 2010; World Health Organization, 2018). Within the United States (U.S.), approximately 7% of the population over the age of eighteen suffer from depression annually, and most of the patients whose depression resolves will still exhibit 1 symptom (Anxiety and Depression Association of America, n.d.; Culpepper, Muskin, & Stahl, 2015). The use of clinical practice guidelines advances the selection process of first-line treatments, including evidence-based psychotherapy and pharmacotherapy (Kredo et al., 2016).

Pharmacogenetic testing can be utilized as a predictor of potential response to antidepressants by an individualized patient (FDA, 2020). Numerous authors have reported similar findings over the past decade, but as recently as February 2020, the U. S. Food and Drug Administration (FDA) issued an announcement reiterating the effectiveness of pharmacogentic testing as well as the intent the FDA to continue to provide guidance and oversight on the use of pharmacogenetics (Shuren, & Woodcock, 2020). Pharmacogenetic testing is an effective tool to assist prescribers in the pre prescribing of antidepressants to treat MDD (Bousman et al., 2019; Fabbri, & Serretti, 2020).

Despite the potential positive outcomes of implementing the use of pharmacogenetics in psychiatric clinical practice, it remains an underutilized modality (Castro & Turner, 2017; Frieling & Tadic, 2013; Perlis et al., 2018). This underutilization of pharmacogenetic testing is significant as antidepressants are the third most prescribed class of medications in the ambulatory care setting (U.S. Department of Health and Human Services, 2015). In 2005, the

FDAs cautioned that pharmacogenetic testing should demonstrate clear utility for treating patients (Harper, Philip, Robinowitz, & Gutman). Since that publication, many new studies have been published demonstrating the benefit of pharmacogenetic testing in treating many maladies, including MDD. Increasing psychiatric prescriber awareness of evidence-based pharmacogenetic testing may inform clinical practices by reducing the nonspecific nature of antidepressant prescription practices (Perlis et al., 2018).

The purpose of this scholarly inquiry project (SIP) was to provide evidence-based education through a video, algorithm, and information paper to psychiatric prescribers at both Madigan Army Medical Center (MAMC) and William Beaumont Army Medical Center WBAMC. Education on pharmacogenetic testing via the algorithm and information paper was disseminated electronically to psychiatric prescribers at both locations. In addition, the SIP assessed pharmacogenetic testing practices, through each military treatment facilities (MTF) laboratory services for two years prior to the evidence-based educational intervention and four months post-intervention.

Significance of the Problem

Depression. From 2009-2011, the United States U. S. Army had the highest rates of depression within the military (Gallagher, Insel, Badger, & Reed, 2018). The rate of diagnosable depressive disorders, including MDD within the U. S. Army, has grown at a historic pace and is trending higher than the civilian population (Naifeh, Herberman, Stein, Fullerton, Kessler, & Ursanol, 2018; Nock, Stein, & Heeringa, 2014). In the U.S., the rates of MDD are the highest among those aged between 18-25 years (Anxiety and Depression Association of America, n.d.; American Psychiatric Association, 2013). This increased rate of MDD in early adulthood may partially explain the high depression prevalence within the U.S. Army. The U.S. Army has

published stressors singular to military service that can exacerbate depressive symptoms in soldiers with undiagnosed MDD (Army Recovery Care Program, 2019). These stressors include the unique emotional challenge that occurs as the result of a long absence from family-related training and deployments (Army Recovery Care Program, 2019). Some evidence indicates that soldiers who present with suicidal ideation may have had pre-existing conditions to include MDD prior to enlistment (Nock et al., 2015). Having a depressive episode before enlistment, compounded with the emotional challenges of active duty life, may decrease the probability for sustained remission resulting in a negative impact on the service member's ability to deploy (US CENTCOM, 2019). Unit readiness may be impaired if the majority of soldiers with MDD continue to require repeated trials of antidepressants for relief of symptoms (Frieling & Tadic, 2013; Gaynes et al., 2009).

Pharmacogenetic Testing. There is a growing body of evidence that shows promising outcomes from the use of pharmacogenetic testing. Pharmacogenetic testing can provide insights to guide pharmacotherapeutic prescription decisions and possibly higher rates of therapeutic outcomes for service members diagnosed with MDD (Frieling, & Tadic, 2013; Perlis, Mehta, Edwards, Tiwari, & Imbens, 2018). In 2015, President Obama launched the precision care initiative with the goal to promote the precision medicine that includes the use of pharmacogenetics incorporating personal genetics and biomarkers in clinical medication prescription decisions (The White House, 2015; U.S. Department of Health and Human Services, 2018).

Pharmacotherapy is a medical treatment using pharmaceutical drugs and genetic pharmacotherapy is the use of genetic intervention to attain the desired pharmacological effect (Mingote et al., 2015). Genetic pharmacotherapy in the treatment of MDD provides a patient-

centered treatment that is patient-specific in identifying functionality to the liver to metabolism antidepressants such as selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), and norepinephrine-dopamine reuptake inhibitor (NDRIs) (Department of Veterans Affairs Department of Defense, 2016).

Identifying best practice for both medication selection and dosing decisions through the use of pharmacogenetic testing is based upon the predictive enzymatic activity of the individual patient's genetic profile (Fabbri, & Serretti, 2020; Perez et al., 2017). This enzymatic activity is primarily related to the activity of two enzymes that belong to a family of enzymes primarily responsible for metabolizing the majority of all medications within the liver with first-pass metabolism (Fatunde & Brown, 2020) This family of enzymes is the cytochrome pigment (CYP) 450 family and includes the enzymes CYP450 2D6 and CYP450 2C19 and both genes are responsible for the majority of antidepressant medication metabolism by the liver (Fabbri, & Serretti, 2020; Perez et al., 2017). The availability of both CYP450 2D6 and CYP450 2C19 can be identified through pharmacogenetic testing (Fabbri, & Serretti, 2020). The ability to identify the patient's specific genetic profile then indicates whether the patient's liver is likely to adequately metabolize an antidepressant medication based upon the availability of both enzymes (Fabbri, & Serretti, 2020).

In the absence of pharmacogenetic testing, the choice of antidepressant is primarily based on the clinical presentation, patient lifestyle and patient preferences related to potential side effects of the potential medications. Providers usually prescribe antidepressants on an evidence-informed basis in consideration of multiple factors with subsequent changes to medications and doses based on inadequate therapeutic responses. Only one-third of patients reach remission with the first trial of antidepressants (Frieling & Tadic, 2013; Gaynes, Warden, Trivedi, Wisniewski,

Fava, & Rush, 2009). Of the two-thirds of the remaining patients, many fail to meet remission after two or more months of intensive antidepressant pharmacotherapy (Frieling & Tadic, 2013; Gaynes et al., 2009).

More broadly, the implementation of pharmacogenetic testing resulted in a 40% reduction in emergency room visits, 58% fewer hospitalizations, and treatment savings of $2,000 over a six-month period when compared to patients who did not receive pharmacogenetic testing for the selection of pharmacotherapy treatment (Perlis et al., 2018). Recently, studies have demonstrated that pharmacogenetic testing for patients resulted in a reduced cost per individual due to a decreased reliance on unnecessary antidepressant trials as well as reduced costs associated with emergency behavioral health treatment (Frieling & Tadic, 2013; Perlis et al., 2018). These types of fiscal savings may off-set potential concerns regarding the costs of pharmacogenetic testing. Despite the growing evidence for pharmacogenetic testing, its use is still limited (Gillis & Innocenti, 2014).

Literature Review. The project began with an extensive literature review. The construct was aligned with the clinical question, to serve as the basis for all search terminology. Search strategies and concepts included some amalgamation of all or portions of the following terms and phrases: ‘psychiatric precision medicine for depression’, ‘pharmacogenetic testing and major depressive disorder’, ‘pharmacogenetic testing and antidepressant pharmacotherapy,’ and ‘psychiatric prescriber awareness of pharmacogenetic testing.’ To improve accuracy and reduce the potential of extraneous results, databases used included OVID and PubMed. Medical Subject Headings (MeSH) and OVID headings fell within the construct. Only peer-reviewed literature published within the past ten years and in English met inclusion criteria. Literature that addressed precision and pharmacogenetic testing for non-

psychiatric related treatment and studies regarding genetic manipulation met exclusion criteria. The center for evidence-based medicine (CEBM) methodology was utilized to appraise all applicable literature (https://www.cebm.net/2014/06/critical-appraisal/). This methodology was able to streamline the review of the literature to ensure that it met the intent of the clinical question (https://www.cebm.net/2014/06/critical-appraisal/). The search resulted in 28 articles, seven of which met exclusion criteria, and three were duplicates. Eighteen of the articles met the criteria for assessment. All but six of the remaining articles met appraisal criteria, leaving 12 applicable articles to serve as the evidentiary basis for the SIP.

All 12 articles addressed the use of pharmacogenetic testing for reducing the symptoms of MDD, depressive symptoms, or both (*See Addendum 1*). Given the similarities between the theorized causes of both MDD and depressive symptoms, it was determined that articles that addressed depressive symptoms are appropriate for the SIP. These 12 articles indicate that the incorporation of pharmacogenetic testing to treat patients with depression within the MHS may result in a significant and more rapid reduction in symptoms of depression within the ranks.

When considering the articles for the review of literature, the most recent meta-analysis identified examined 5 multicenter prospective double-blinded randomized controlled studies testing for the effectiveness in using pharmacogenetic testing in improved response and remission for patients with either depressive symptoms or Major Depressive Disorder. In all five studies, remission equated to a Hamilton Depression (HAM-D) Rating Scale-17 score of less than seven, within both the experimental group, which had available pharmacogenetic testing results and the control group which did not have access to pharmacogenetic testing results. All five of the studies demonstrated greater improvement of depressive symptoms within the experimental group, ranging from the lowest improvement of a 1% difference in HAM-D to a

44% difference between the results of the experimental and control group. What was consistent with all of the 5 studies evaluated by the article greater improvement in depressive symptoms for patients whose providers had been able to access the patient's genetic profile prior to determining medication (Bousman et al., 2019).

When considering treatment of MDD for service members, individualized patient genetic pharmacodynamic and pharmacokinetic testing is an evidence-based approach to improve patient outcome and increased patient-centered treatment options through more precise and efficacious prescribing (Altar et al., 2015; Bradley et al., 2018; Bousman et al., 2019; Espadaler et al., 2016; Hall-Flavin et al., 2013; Han et al., 2018; Perez et al., 2018; Solomon et al., 2019; Tanner et al., 2018; Torrellas et al., 2017; Walden et al., 2018; Winner et al., 2013).

Clinical Question

Does providing evidence-based pharmacogenetics testing education for the treatment of MDD to psychiatric prescribers at MAMC and WBAMC affect the pharmacogenetics testing practices between each installation four months post-intervention?

Focus Areas

Focus Area 1. The purpose of this focus area was to increase the use of pharmacogenetic testing by behavioral health prescribers within the local MTF. This focus area included the educational intervention, which consisted of a pre-recorded instructional video, an information paper synthesizing the current literature and an evidence-based pharmacogenetic testing algorithm. An algorithm was created as a tool for successful implementation of the SIP because the use of algorithms in medicine results in a sustainable tool that provides precise clinical decision-making recommendations that are patient-centered according to patient-specific variables and the best evidence (Komaroff, 1982).

Focus Area 2. This focus area examines practices and ordering patterns of prescribers in ordering pharmacogenetic testing appropriately for the treatment of service members with depression. To increase the efficacy of pharmacogenetic testing, prescribers are encouraged to order testing tailored medication selection to the specific needs of the individual patient. The purpose of the evidence-based pharmacogenetic testing algorithm is as a clinical tool for informing a standardized decision-making process of both when to order labs as well as which labs may be indicated.

Relevance to Military Nursing

The use of pharmacogenetic testing to manage patients with MDD has the potential to result in better patient outcomes such as early improvement in depressive symptoms and a potential reduction in the risk for attempted suicide (Frieling et al., 2018; Han et al., 2018; Pompili et al., 2010). Utilizing pharmacogenetic testing may reduce the risk of adverse reactions and improve the health and overall wellbeing of treated service members by requiring fewer medication trials to identify an effective and tolerable antidepressant medication (Haga, & LaPointe, 2013, Xue, Zhang & Cai, 2018). Military nurses, as change agents, can positively influence the systemic shift from solely relying on theoretical inference to incorporating pharmacogenetic testing into their practice. The anticipated impact is earlier remission of depressive symptoms for patients being prescribed antidepressants in a behavioral health environment initially at MAMC and WBAMC. These results from testing can then be replicated by behavioral health prescribers at other MTFs.

Obtaining pharmacogenetics results from testing typically requires a 3 to 14-day turnaround (Freund, & Gregory, 2004; Kapoor, Tan-Koi & Teo, 2016; Lui, & Shuch, 2019) and this inability to process and obtain immediate test results prevents pharmacogenetics from being used within emergency medicine or austere environments. Hence, pharmacogenetic testing cannot

be completed at less than a Role IV military hospital, which is a hospital that provides an echelon of long-term definitive care which includes surgical specialties, rehabilitation, convalescence and other medical specialties and is typically a classification assigned to fixed MHS facilities within the continental United States (Bagg et al., 2006; Lynn, Lesemann & Detro, 2014).

Organizing Framework

The Academic Center for Evidence-Based Practice (ACE Star) model of knowledge transformation was selected to guide the implementation of the project (*See Figure 1*). The goal of the ACE Star model is to affect health outcomes through the evolution of translated evidence (White, Dudley-Brown, & Terhaar, 2016). The implementation of the SIP required translating and analyzing pharmacogenetic testing evidence for psychiatric prescriber use and subsequent efficacy assessment. The actualization of the SIP required a review of the literature and providing a complete summary of the best evidence in the form of an evidence table (*See Appendix F*). This table outlined the best-evidence for the use of pharmacogenetic testing in the treatment of MDD. Prescribers were provided an algorithm and information paper identifying best practice recommendations related to the SIP. The goal of the intervention was to increase psychiatric prescriber awareness and knowledge of evidence-based use of pharmacogenetic testing for the treatment of MDD.

Each point of the model directly coincided with the intended aims and goals of the project. Point one was knowledge discovery (White et al., 2016). This point directly applied to the evidence inquiry phase of the SIP, which was to identify indications for the use of pharmacogenetic tests from the review of the literature. The development of an information paper summarizing these findings was a simple transition into the second point. Point two of the model is the evidence summary (White et al., 2016). Point three of the model is the translation

of practice (White et al., 2016). The translation of practice was the development and deployment of an algorithm. The algorithm provided a concise easy to follow guide detailing out clinical recommendations for psychiatric prescribers of the indications for the use of pharmacogenetic testing. Point four, integration into practice (White et al., 2016) includes informing, educating, and providing synthesized evidence and clinical recommendations. Point four was achieved via the information paper and an algorithm distribution to psychiatric prescribers, at both MAMC and WBAMC. The information paper provided a concise explanation of the latest evidence supporting the use of the algorithm for patient care. Electronic dissemination of both the algorithm and information paper was fundamental to integrating the evidence-based intervention into practice. To assess the efficacy of both psychiatric prescriber education as well as the implementation of evidence into practice, analysis of pharmacogenetic testing practices was completed by reviewing the surveys and also an inquiry into electronic health records. The completion of point five included the evaluation of all psychiatric prescribers who received the evidence-based pharmacogenetics testing education ordering practices both two years before and four months following the educational intervention (White et al., 2016). During the evaluation phase of the evidence-based SIP, a survey was administered to all psychiatric prescribers prior to implementing the intervention to evaluate knowledge, beliefs, and barriers of psychiatric prescribers in relation to the use of pharmacogenetic testing for patients with MDD. Following the intervention, the review of the electronic health records of patient charts who received pharmacogenetic testing was completed to assess for the potential impact of the intervention. Trends were assessed comparing and contrasting the number of pharmacogenetic tests ordered pharmacogenetic testing pre and post-intervention.

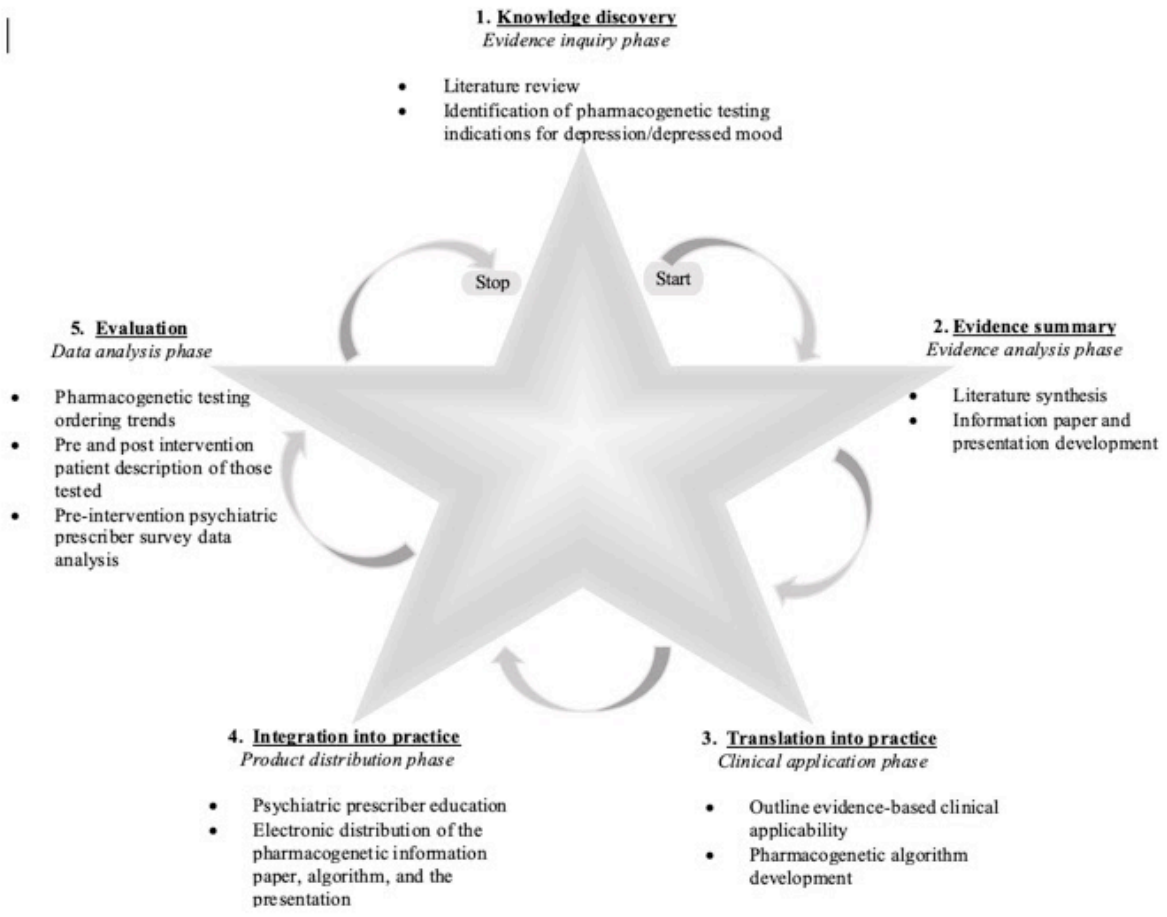

Figure 1. The academic center for evidence-based practice (ACE) star model of knowledge transformation. Adapted from *Translation of evidence into nursing and health care* (2nd ed.) p.17-18, by K. White, S. Dudley-Brown, S., & M. Terhaar, 2016, Springer. Copyright 2016 by Springer Publishing Company.

Change Theory. The Lewin's Force Field Analysis was selected to guide the process of organizational change required for the SIP (*See Figure 2*). Lewin asserts that there are opposing and driving forces of change within an organization (White et al., 2016). According to Lewin, there are mechanisms that can assist or prevent change from occurring (White et al., 2016). The driving forces of change of the Lewin Force Field Analysis addressed the changes needed across multiple departments, changes to typical and expected clinical antidepressant management, and organizational recommendations to support positive forces for change. Understanding the

driving forces working for or against the desired end-state was key to the effective implementation of the SIP. The desired end-state of the project was to improve psychiatric prescriber awareness of pharmacogenetic testing as it pertains to evidence-based pharmacotherapy clinical practices for patients with depression or depressed mood. Ultimately, improved awareness of pharmacogenetic testing may lead to improved patient outcomes through the application of precision medicine (Barsanti-Innes, 2020).

Unfreezing the current state, during phase one of the theory, required promoting positive forces while reducing opposing forces for change. Positive forces for change included educating, informing and promoting the use of evidence-based pharmacogenetic testing indications through the use of an information paper and a clinical practice algorithm. Creating a stepped approach reduced the potential opposing forces. These steps included informing the laboratory department key stakeholders, including the supervisor for the department of pathology and the supervisor for pathology support services. Working with stakeholders further eased potential barriers through techniques such as identifying psychiatric pharmacogenetics laboratory order sets already built within the electronic health record system. Surveys and evaluation of patient electronic medical records were integral to the second phase of the Lewin's force field analysis, and organizational moving or changing towards the desired end-state. The surveys informed us of potential challenges to SIP implementation due to perceived barriers by psychiatric prescribers as well as the current level of knowledge of the prescribers related to the topic. The review of patient electronic health records may highlight improvements to patient outcomes to include any improvements to depression symptoms.

The data-informed the effectiveness of the unfreezing phase and ensured that the efforts progressed towards the desired end-state. Performing assessments also allowed for the

evaluation of the power of each driving force to adjust as needed throughout each phase, including the final phase entitled refreezing. Refreezing the sustainment of change throughout the organization, bolstered by adjustments made based on assessment results, further assisted in instilling the tenants of the theory. Trust building was encouraged by a new way of thinking and point of view as well as the integration of new ideas in order to affect organizational change. As stated in previous sections, all assessments occurred two years pre and four months post-intervention. Administration of surveys and appropriate electronic medical record assessments drove the efforts that moved forces towards the refreezing, sustainment phase.

Lewin's Force Field Analysis pairs well with the organizing framework for the SIP. The ACE Star Model's driving force of the clinical application phase allows for the intervention to be translated into everyday practice while avoiding subjective barriers to change (Houser & Oman, 2010). The triphasic approach of the Lewin's theory also flowed with the compact nature of the EBP model and allowed for quick adaptation.

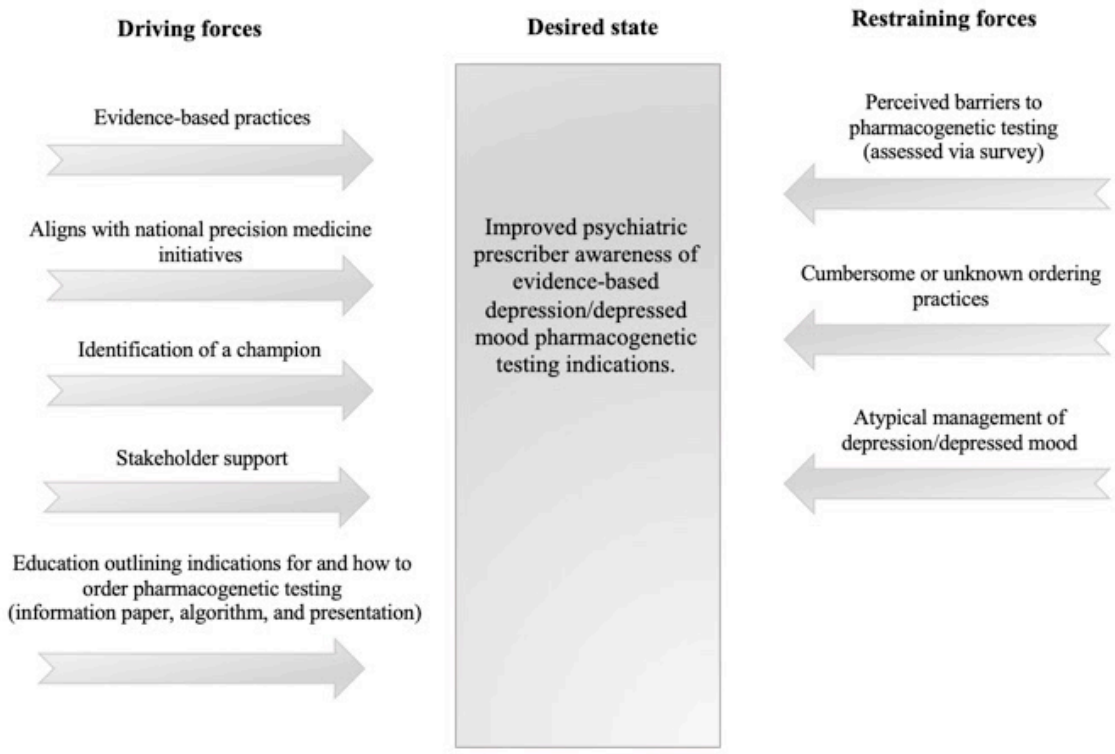

Figure 2. Lewin's force field analysis change theory. Adapted from *Translation of evidence into nursing and health care* (2nd ed.) p.58-59, by K. White, S. Dudley-Brown, S., & M. Terhaar, 2016, Springer. Copyright 2016 by Springer Publishing Company.

Project Design

General Approach

This project reported the effect of providing evidence-based pharmacogenetic testing education to psychiatric prescribers at two MTFs within MHS and the impact of the educational intervention on the ordering of pharmacogenetic testing by psychiatric prescribers in treating patients with MDD. This comparison of ordering frequency between MTFs was twofold. First, the comparison was completed for the purpose of understanding the historic ordering practice of pharmacogenetic testing by psychiatric prescribers at both MAMC and WBAMV. The comparison between sites was also completed to better understand the effect of the SIP

intervention on pharmacogenetic testing ordering practices by psychiatric prescribers. The intent of the project was that by increasing prescriber awareness of pharmacogenetic testing for patients with MDD, there would be a reflected increase of test order post-intervention.

Setting

The population for this project is licensed behavioral health prescribers who are credentialed prescribers at both MAMC and WBAMC. Psychiatric prescribers include all employed active duty and government service psychiatrist, psychiatric-mental health advanced practice nurse practitioners and psychologists credentialed to prescribe medications. The intervention is an educational/ awareness toolkit accessible via a link to a hypertext market language (HTML) page with multiple embedded hyperlinks to the individual educational toolkit items. The educational/ awareness toolkit consists of pre-recorded presentations, uploaded to YouTube, overviewing what is and the evidence-based use of pharmacogenetic testing for depression and depressed mood, and how-to order the testing in both MHS Genesis and AHLTA/CHCS, an information paper, and an algorithm summarizing the literature for evidence-based use of pharmacogenetic testing in clinical practice.

This project will contain three different types of analytical data. The data analysis will include statistical analysis of pre and post-intervention psychiatric prescriber ordering practices, analysis of pre-intervention survey data, and qualitative descriptors of patients who received pharmacogenetic testing. Statistically significant differences between psychiatric prescriber pharmacogenetic testing practice two years pre and four months post-intervention will be analyzed via t-tests, utilizing SAS software to analyze deidentified data collected in Microsoft Excel, by averaging the monthly number of psychiatric prescribers ordered pharmacogenetic tests. Analyzing the monthly average of pharmacogenetic testing will account for the potential

limitation of comparing two years to four months of data. Assuming the patient population eligible for pharmacogenetic testing, by psychiatric prescribers, remained relatively consistent two years prior to and four months post educational intervention. Patient descriptors for the type of patient for whom psychiatric prescribers ordered pharmacogenetic testing for, will include the average number of prescribed classes and names of antidepressant medications specifically mentioned in the educational intervention. Qualitative patient description will also include the length of time and number of antidepressant trials used to manage depression and depressive symptoms. Analytical data from Survey Monkey, displayed via histograms, will be used to summarize psychiatric prescribers reported attitudes, beliefs, and potential barriers towards pharmacogenetic testing.

Procedural Steps

The initial steps in completing this project began prior to the arrival of both Doctor of Nursing Practice (DNP) students at either of the Phase II MTFs. The Phase II Site Directors contacted the WBAMC and MAMC supervisors for clinical laboratory services as well as pathology support services and verified that the ordering of pharmacogenetic testing was possible at both sites.

Upon arrival at their respective assigned MTF, the DNP students coordinated with the regional sales representative at the civilian for-profit clinical laboratory corporation contracted to process, report and store the data for all laboratory samples referred by the MTF. For this project, both MTFs had contracts for laboratory services with LabCorp. The LabCorp regional sales representatives were able to provide the DNP students with all of the patients who had undergone genetic testing within the past two years for CYP450 2D6, CYP450 2C19,

methylenetetrahydrofolate reductase and catechol-o-methyltransferase at both MAMC and WBAMC.

After receiving the information related to all pharmacogenetic testing ordered by any provider at both MTF within the past two years, both DNP students completed an extensive chart review. This chart review was completed utilizing the MHS Genesis and Armed Forces Health Longitudinal Technology Application (AHLTA) on every pharmacogenetic test ordered during the two years and determined which tests had been ordered by psychiatric prescribers. Of those tests ordered by psychiatric prescribers during the two year period, for every patient the age, gender, military rank, psychiatric diagnoses, number and length in weeks of antidepressant medication trials, as well as which of the 4 pharmacogenetic tests had been ordered was tracked by the DNP students. All patient specific identifiers, including names, date of birth, department of defense identification number, or social security numbers, were not compiled, and the data remained de-identified for the entirety of the DNP project.

In addition to the review of all pharmacogenetic testing applicable to the SIP at both MAMV and WBAMC, the DNP students created an evidence-based algorithm and information paper outlining pharmacogenetic testing evidence for psychiatric prescriber use in medication selection to effectively manage patients with treatment resistant MDD. Aims for this outcome were to review the literature, determine the best supporting practices in the development of the algorithm and information paper. The overarching outcome of this project was to increase awareness of pharmacogenetic testing among MHS psychiatric prescribers at MAMC and WBAMC to inform treatment options for patients with depressed mood. The next outcome was to integrate pharmacogenetic testing into psychiatric prescribing practices. Aims for this outcome include developing an evidence-based algorithm. This evidence-based algorithm would

serve as clinical decision support aids to remind prescribers of pharmacogenetic testing options. Psychiatric prescribers received education on the clinical decision support aids, disseminated electronically.

This project employed multiple methodologies to analyze outcomes. To reduce the likelihood of opposing force (White et al., 2016), phase II leadership at both sites and subject matter experts vetted and approved the algorithm and information paper. Vetting and approval by the MAMC and WBAMC phase II site directors of the algorithm and information paper were vital to analysis as they both are the crux of the SIP. Electronically disseminated surveys to psychiatric prescribers at MAMC and WBAMC assessed awareness, knowledge and beliefs of pharmacogenetic testing among psychiatric prescribers. The survey was disseminated prior to the educational intervention. Evaluation of electronic health records two-year pre-intervention and four months post-intervention of patients empaneled to the psychiatric prescribers at MAMC and WBAMC provided further data of post-intervention practices. All data collection was devoid of personally identifiable information and maintained on electronic spreadsheets.

Project analysis data will drive recommendations for sustainment. Survey data will assist in determining needs to shift change. Differentiating between a lack of awareness and negative attitudes towards pharmacogenetic testing will inform sustainment efforts. If the analysis indicates a continued lack of awareness among psychiatric prescribers, then sustainment towards improving awareness via education will occur. Evaluating barriers to performing pharmacogenetic testing, such as the inability to find order sets or minimal belief of added benefit to clinical practice, will inform recommendations to sustain intervention efforts. Coordinating education from clinical subject matter experts and meeting with phase II laboratory and technical stakeholders assisted in reducing reluctance towards change.

A parallel top-down approach was employed to distribute the project. All communication begins with engaging both clinical phase II site directors at MAMC and WBAMC for oversight and assistance. Most of the communication efforts before arrival at both sites relied on an electronic or telephonic correspondence between applicable clinical leadership at both locations. The information paper, pre-recorded video, algorithm and surveys were disseminated by the authors of this paper following their arrival at their respective Phase II sites. Monthly analytical data informing recommendations for sustainment and the need for further efforts to effect change was shared with key stakeholders. These stakeholders included the leadership staff for the Department of Behavioral Health at both MAMC and WBAMC. As stakeholders, the behavioral health leadership at both MTFs supported and highly encouraged psychiatric prescriber education intervention engagement. Psychiatric prescribers at both WBAMC and MAMC appeared to be seemingly interested in the topic of pharmacogenetic testing and evidence-based methods for incorporating the testing into practice.

HIPPA Considerations

This SIP requires identifying the pharmacogenetic testing trends of psychiatric prescribers assigned to behavioral health clinics at both MAMC and WBAMC. The students completed a chart review of behavioral health patients who had received pharmacogenetic testing two years prior to the intervention and the three months following the intervention. This review required the DNP students to analyze de-identified information derived from the AHLTA and MHS Genesis medical records. By reviewing these electronic health records, the DNP students accessed Health Insurance Portability and Accountability (HIPAA) protected patient information. The process of completing the SIP was not research. The SIP did not warrant a recommendation by the Office of Human Research Protection for either an expedited

Institutional Review Board (IRB), or a traditional IRB (Hernandez, 2016). There was no requirement for an IRB by either MTF. As a covered entity, there is a HIPAA mandate to protect patient information associated with this DNP project (Strauss, 2017). The SIP tracker was completely de-identified. The de-identified data ensured constant fidelity of patient-specific information (Wofford, n.d.). Every step of this process protected any specific patient health information, which was consolidated to derive the ordering practices of the prescriber. Throughout the process, prescribers were not identified by name. Since all de-identified information derived by the chart audits was only utilized to compile data trends, the principles of safe harbor were ensured, and there was no need for an expert determination (Strauss, 2017). Prior written consent by patients was not necessary since this compiled data only analyzed trends and was not individualized to any specific patient (Butera, 2002).

Project Results

The project resulted in some unexpected findings and opportunities for improving psychiatric provider comfortability with utilizing evidence-based pharmacogenetic testing in clinical practice. The pre-intervention survey responses (*See figure 3*) identified potential areas to strengthen prescriber confidence with and address barriers to utilizing pharmacogenetic testing in their clinical practice. There was a total of 13 responses to the pre-intervention survey, nine of which came from MAMC psychiatric prescribers and four from WBAMC. A substantial number, 83% of psychiatric prescriber respondents agreed that pharmacogenetic testing is a resource that should be used in the selection of psychopharmaceutic treatment. However, nearly 70% of respondents reported that they lack confidence in knowing how to order pharmacogenetic testing. A large number of nearly 38% replied neutrally, 31% replied as disagreed, and 8% strongly disagreed with feeling confident about knowing when to order

pharmacogenetic testing. The most significant barriers to pharmacogenetic testing noted by respondents were lack of clinical guidelines, resources, and access and the perceived costs of conducting the tests.

Psychiatric prescribers at both MTFs infrequently used pharmacogenetic testing in their clinical practice, in fact, none were ordered in 2017, and three were ordered in 2018. There was a total of two pharmacogenetic tests ordered post-intervention in 2019, and one in 2020 (*See table 1*). The majority of the patients who received pharmacogenetics testing by their psychiatric prescribers had a history of greater than one trial of antidepressants (*See tables 2 and 3*). All but one of the patients who received testing at either MTF were Active Duty males (*See table 4*). Overall testing practices varied across both MTFs, between 2017 until June 2018, no tests were done at either site. Then from June 2018 until the time of the intervention, two patients were tested at MAMC, and one patient was tested at WBAMC. Post-intervention two patients were tested at MAMC one in October and another in November, and one patient received testing in March 2020 at WBAMC (*See table 1*).

Figure 3. Psychiatric prescriber pre-intervention survey data.

Psychiatric Prescriber Ordered Pharmacogenetic Tests (per patient) by Month and Year

	MTF	MTHFR	CYP450			COMT
			2D6	2C19	2D6/2C19	
Pre-intervention	**JBLM**	Jun 2018	None ordered	None ordered	Jun 2018	Jun 18
	JBLM	Jun 2018	None ordered	None ordered	Jun 2018	Jun 18
	WBAMC	None ordered	None ordered	Sep 2018	None ordered	None ordered
Total		*2*	*0*	*1*	*2*	*2*
Post-intervention	**JBLM**	None ordered	None ordered	None ordered	Oct 2019	None ordered
	JBLM	None ordered	None ordered	None ordered	Nov 2019	None ordered
	WBAMC	Mar 2020	None ordered	None ordered	Mar 2020	Mar 2020
Total		*1*	*0*	*0*	*3*	*1*
Total number of tests ordered		*3*	*0*	*1*	*5*	*3*

Table 1. Psychiatric prescriber ordered tests.

Pre-intervention Patients Who Received Pharmacogenetic Testing

	MDD Diagnosis Yes/No	**Other Psychiatric Diagnosis/Problems**	**Ordered Psychiatric Tests**	**Medication Trials**
Patient 1	Yes	ADHD/Insomnia	MTHFR, CYP450 2D6/2C18, and COMT	x1 TCA for ~6 months
Patient 2	Yes	ADHD/ Adjustment Disorder, with depressed Mood, High risk patient	MTHFR, CYP450 2D6/2C18, and COMT	x4 SSRIs for ~2 years x1 SNRI for ~1 month x1 TCA for ~2 months -NRDI for ~7 months
Patient 3	No	Dysthymic Disorder	CYP450 2C19	x1 SSRI for ~3 months

Table 2. Pre-intervention pharmacogenetic tested patient demographics.

Post-intervention Patients Who Received Pharmacogenetic Testing

	MDD Diagnosis Yes/No	**Other Psychiatric Diagnosis/Problems**	**Ordered Psychiatric Tests**	**Medication Trials**
Patient 1	No	General Anxiety Disorder, Insomnia	CYP450 2D6/2C18	x2 SSRIs for ~4 months x1 SNRI for ~3 months
Patient 2	Yes	Anxiety, NOS	CYP450 2D6/2C18	x1 SSRI for ~2 months x1 SNRI for ~4 months -NRDI for ~2 months
Patient 3	Yes	Adjustment Disorder, mixed with anxiety and depressed mood	MTHFR, CYP450 2D6/2C18, and COMT	x3 SSRIs ~3 years x1 SNRI ~2 weeks -NRDI ~2 months

Table 3. Pre-intervention pharmacogenetic tested patient demographics.

Patients Demographics
Number of those in each category of those who received pharmacogenetic testing

Rank:	E-1 to E-4: 1	E-5 to E-8: 2	CW1 to O-6: 2	Family members: 1
Gender:	Male: 5	Female: 1		
Age:	20 to 30 years of age: 3	30 to 40 years of age: 2	40 to 50 years of age: 1	

Table 4. Psychiatric prescriber ordered pharmacogenetic testing patient demographics.

Analysis of Results

The results from the implementation of the SIP identified opportunities to strengthen psychiatric prescriber use of pharmacogenetic testing at both MAMC and WBAMC. The last time psychiatric prescribers ordered pharmacogenetic testing on any patient pre-intervention was September 2018. Three patients received testing post-intervention. The pharmacogenetic education intervention seemingly had some effect on testing practices. Psychiatric prescribers reported believing pharmacogenetic testing can be beneficial; however, barriers may persist influencing their use of testing into their practices. This aligns with the literature, which found that hesitation with pharmacogenetic testing exists due to a lack of knowledge and experience with patient pharmacogenetic testing (Peterson et. Al., 2016). The majority of the patients had a diagnosis of MDD with additional psychiatric conditions. Patients received, on average, 15 months of treatment and with a mean of three antidepressant trials prior to receiving

pharmacogenetic testing. Of the patients who were tested, prescribers chose to limit testing to one test, CYP450 2D6/2C19, for two patients and conducted all of the recommended tests for only one patient. The patients tested also have a history of either extended length of time on an anti-depressant or a history of multiple anti-depressant trials. Psychiatric provider's belief regarding when to test, as indicated as neutral on the pre-intervention survey may also influence their pharmacogenetic testing practices. Psychiatric prescribers may be ambivalent as to when patients may receive the most benefit from pharmacogenetic testing. The results identify opportunities for increasing psychiatric provider comfort with the use of pharmacogenetic testing.

The recommended practice is to initiate pharmacogenetic testing after at least one failed and before three failed antidepressant trials (Fabbri, & Serretti, 2020; Perez et al., 2017), which varied greatly across each MTF. Pharmacogenetics testing continues to be ordered at both MTFs for only the very complicated cases of patients with chronic MDD and several failed antidepressant medication trials. The psychiatric prescribers at both MTFs who had ordered pharmacogenetic testing within the past two years averaged less than ten years' experience as credential providers. This trend may indicate that less experienced psychiatric prescribers had greater exposure to the concepts of pharmacogenetics in their psychiatric residencies.

When considering the psychiatric prescribers at both MTFs, prescribers at MAMC ordered pharmacogenetics testing for patients only after an average of over four failed trials of antidepressant medications and prescribers at WBAMC ordered testing after an average of three failed trials. The utilization of pharmacogenetic testing following multiple medication failures indicates a knowledge deficit at both MTFs related to both the correct use of pharmacogenetic testing as well as the potential benefits of pharmacogenetic testing. The use of pharmacogenetic

testing more broadly within local MTFs can lower the overall cost of health care through precision medicine providing earlier relief from symptoms and reducing complication associated with prolonging of symptoms (Frieling & Tadic, 2013; Lynch et al., 2016; Perlis et al., 2018).

Limitations

Some significant limitations of this project include a survey by The Joint Commission (TJC) at WBAMC in November 2019, shortly before the holiday season, and the COVID-19 response at both installations. Behavioral health leadership focused on ensuring clinical staff and the environment was well prepared for TJC visit, distracting from the ability to re-engage prescribers. The COVID-19 global pandemic response affected both installations impacting all clinical services. Another potential limitation is the explicit instruction from the WBAMC behavioral health leadership to ensure participating psychiatric prescribers were well aware the survey was voluntary and not necessary to receive the educational intervention.

Impact

Organizational Impact

The results of this project at both MTFs indicated that increased awareness of the availability and capability of pharmacogenetic testing can result in trends of increased utilization of pharmacogenetic testing. This increased utilization aligns with the review of literature indicating a future of precision medicine in prescribing practices for determining the dosing of medication in the treatment of patients with MDD (Barsanti-Innes, 2020; Frieling & Tadic, 2013). Increased awareness of the benefits of pharmacogenetic testing through more widespread implementation of the SIP may result in more use of pharmacogenetic testing by MHS behavioral health prescribers for the treatment of patients with MDD. Dialogue and engagement between individuals are key to adult learning (Gravani, 2019). Antidotally, the implementation

of the SIP led to several discussions between prescribers related to the potential benefits of pharmacogenetic testing for treating patients with MDD.

For a sustainable change in the prescriber's awareness, repetition of the information in numerous settings can elicit a relational response to the information presented by the SIP leading to the integration of experiences with the result of increased knowledge by adult learning (Halls, 2014). To that end, the next step in the rollout of the SIP could include a post-intervention survey for psychiatric prescribers, as well as, presenting on the SIP to a forum of prescribers that includes primary care. One opportunity for the way ahead at MAMC is listing pharmacogenetic testing as one of the order sets included in the standardized training on how to utilize MHS Genesis to order and review patient labs.

Implications to Practice & Policy

There is a growing perception by a significant majority of psychiatric prescribers that the use of pharmacogenetic testing to aid in medication decision making is beneficial and will ultimately become the standard of practice (Thompson, Hamilton, & Hippman, 2015; Walden et al., 2015). Similar to the results from those surveyed for this DNP project, studies have demonstrated that the majority of psychiatric prescribers are still unsure of when it is appropriate to refer patients for pharmacogenetic testing (Drozda, Muller & Bishop, 2014; Selkirk, Weissman, Anderson, & Hulick, 2013; Thompson et al., 2015).

Both clinical practice and regulatory policy are based upon the utilization of scientific data in creating evidence-based decision making (Schuck et al., 2016). The inclusion of recommendations for pharmacogenetic testing as well as pharmacogenetic information related to the pharmacodynamic and pharmacokinetic properties should be included within both physical prescription labeling and prescription labeling embedded within electronic medical records

(Drozda et al., 2014; Schuck et al., 2016). If the FDA utilize policy changes to ensure the inclusion of pharmacogenetic properties of medication, prescribers will have an increased understanding of when it is appropriate to screen MDD patients using pharmacogenetic testing as well as how to interpret the results of the tests (Schuck et al., 2016)

Future Direction for Research and Practice

While the relationship between a patient's DNA variations and the effectiveness of antidepressant medication continues to be studied, there is sufficient scientific evidence supporting the correlation between an individual genetic variability and their response to medication within the body (FDA, 2018; FDA, 2020). In February of 2020, the FDA created a collaboration between its Center for Drug Evaluation and Research and Center for Devices and Radiological Health and Center for Drug Evaluation to better inform the public and healthcare providers related to the most current science of pharmacogenetics (FDA., 2020; Shuren, & Woodcock, 2020). The FDA published a table of medications shown to present with altered drug metabolism for patients with specific genetic variants or variant-inferred phenotypes (FDA, 2020; Shuren, & Woodcock, 2020). This table includes many medications used in treating depression. This information was made available to reduce the risk of adverse events for certain patients with altered drug metabolism (FDA, 2020).

The efficacy of pharmacogenetic testing in the treatment of depression will continue to improve as research identifying genetic biomarkers of psychiatric illnesses continues to develop (Limandri, 2019). As the benefits of pharmacogenetic testing become more widely understood, testing will be incorporated more broadly in clinical guidelines for standardized treatments of behavioral health diagnoses (Burke, Love, Jones, & Fife, 2016; Limandri, 2019). Since an individual's pharmacogenetic results remain throughout their lifetime, a global database can be

established for results to be accessed by both primary care prescribers and specialty care prescribers (Burke et al., 2016; Murfin, 2019). Ensuring this database is accessible through the patient's electronic medical record at both MTFs and civilian medical facilities might increase provider's use of pharmacogenetic testing for a more personalized medication decisions based upon patient-specific genotyping (Burke et al., 2016; Murfin, 2019). This database would also help to reduce the cost burden by preventing the ordering of redundant pharmacogenetic testing in both the MHS and Veterans Health Administration (Burke et al., 2016, Schuck et al., 2016).

By continuing to incorporate pharmacogenetic testing for the treatment of MDD in primary care, prompter symptom management can result (Parve et al., 2019). Both primary care and behavioral health prescribers should embrace the advancements afforded by pharmacogenetic testing to assist in medication and dosing determinations for patients with MDD (Barsanti-Innes, 2020; Burke et al., 2016; Parve et al., 2019).

Conclusion

The results of the survey conducted prior to the implementation of the SIP demonstrated that many of the behavioral health prescribers at both WBAMC and MAMC reported a lack of confidence in understand how to order pharmacogenetic testing, or when ordering of testing for patients with MDD was appropriate. The outcomes from the implementation of the SIP WBAMC and MAMC was increased awareness of the best evidence for pharmacogenetic testing for the treatment of MDD as well as the availability of testing at both MTFs for psychiatric prescribers. The information provided by the SIP intervention will remain accessible electronically and could be incorporated into a broader disseminated training utilized throughout the MHS and nested with the most recent FDA guidance.

References

Abul-Husn, N., Obeng, A., Sanderson, S., Gottesman, O., & Scott, S. (2014). Implementation and utilization of genetic testing in personalized medicine. *Pharmacogenomics and Personalized Medicine*, *13*(7), 227-40. doi: 10.2147/PGPM.S48887

Al-Harbi, K. (2012). Treatment-resistant depression: Therapeutic trends, challenges, and future directions. *Patient Prefer Adherence*, *6*, 369–388. doi: 10.2147/PPA.S29716

Altar, C. A., Carhart, J., Allen, J. D., Hall-Flavin, D., Winner, J., & Dechairo, B. (2015). Clinical utility of combinatorial pharmacogenomics-guided antidepressant therapy: Evidence from three clinical studies. *Molecular Neuropsychiatry*, *1*(3), 145-155. doi: 10.1159/000430915

American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). Washington DC: Author.

Anxiety and Depression Association of America. (n.d.). Facts and statistics. Retrieved from https://adaa.org/about-adaa/press-room/facts-statistics

Army Recovery Care Program. (2019). *Depression*. Retrieved from https://wct.army.mil/modules/soldier/s5-depression.html

Bagg, M. R., Covey, D. C., & Powell, E. T. (2006). Levels of medical care in the Global War on Terrorism. *Journal of American Academy of Orthopedic Surgeons*, *14*(10), S7-S9. doi: 10.5435/00124635-200600001-00003

Barsanti-Innes, B. (2020). Precision medicine is here, but are we ready for it?. *University of Toronto Medical Journal*, *97*(1), 25-26. Retrieved from http://utmj.org/index.php/UTMJ/article/view/1233

Blakeley, K. & Jansen, D. (2013). Post-traumatic stress disorder and other mental health problems in the military: Oversight issues for Congress. *Congressional Research Service*. Retrieved from https://fas.org/sgp/crs/natsec/R43175.pdf

Bousman, C. A., Arandjelovic, K., Mancuso S., G., Eyre, H., A., & Dunlop B. W. (2019). Pharmacogenetic tests and depressive symptom remission: A meta-analysis of randomized controlled trials. *Pharmacogenomics*, *20*(1), 37-47. doi: 10.2217/pgs-2018 0142

Bradley, P., Shiekh, M., Mehra, V., Vrbicky, K., Layle, S., Olson, M., ... & Lukowiak, A. (2018). Improved efficacy with targeted pharmacogenetic-guided treatment of patients with depression and anxiety: A randomized clinical trial demonstrating clinical utility. *Journal of Psychiatric Research*, *96*, 100-107. doi: 10.1016/j.jpsychires.2017.09.024

Burke, E., Love, R., Jones, P., & Fife, T. (2016). Pharmacogenetic testing: Application in mental health prescribing. *Journal of American Psychiatric Nurses Association*, *22*(3), 185-191. doi: 10.1177/1078390316641488

Butera, A. (2002). HIPAA preemption implications for covered entities under state law. *Tort & Insurance Law Journal*, *37*(4),1181-1211. Retrieved from https://www-jstororg.vlib.excelsior.edu/stable/25763590

Castro, M. & Turner, C. (2017). Military genomics: a perspective on the successes and challenges of genomic medicine in the Armed Services. *Molecular Genetics and Genomic Model*, *5*(6), 617-620. doi. 10.1002/mgg3.335

Caudle, K. E., Gammal, R. S., Whirl-Carrillo, M., Hoffman, J. M., Relling, M. V., & Klein, T. E. (2018). Evidence and resources to implement pharmacogenetic knowledge for precision

medicine. *American Journal of Health-System Pharmacy*. *73*(23), 1977-1985. doi: 10.2146/ajhp150977

Culpepper, L., Muskin, P. R., & Stahl, S. M. (2015). Major depressive disorder: Understanding the significance of residual symptoms and balancing efficacy with tolerability. *The American Journal of Medicine*, *128*(9a), S1-S15. doi: 10.1016/j.amjmed.2015.07.001

Department of Veterans Affairs Department of Defense. (2016). *VA/DoD Clinical Practice Guideline for the Management of Major Depressive Disorder*. Retrieved from https://www.healthquality.va.gov/guidelines/MH/mdd/MDDCPGClinicianSummaryFINAL1.pdf

Dingle, R. S. (2019, December 5). Lieutenant General R. Scott Dingle, the Surgeon General, United States Army before the House Committee on the Armed Services Subcommittee on the Armed Services Subcommittee on Military Personnel. *U.S. House of Representatives Document Repository*. Retrieved from https://docs.house.gov/meetings/AS/AS02/20191205/110182/HHRG-116-AS02-Wstate-DingleS-20191205.pdf

Drozda, K., Müller, D. J., & Bishop, J. R. (2014). Pharmacogenomic testing for neuropsychiatric drugs: Current status of drug labeling, guidelines for using genetic information, and test options. *Pharmacotherapy*, *34*(2), 166-184. doi: 10.1002/phar.1398

Espadaler, J., Tuson, M., Lopex-Ibor, J. M., Lopez-Ibor, F., & Lopez-Ibor, M. I. (2016). Pharmacogenetic testing for the guidance of psychiatric treatment: A multicenter retrospective study. *CNS Spectrums*, *22*(4), 325-324. doi: 10.1017/S1092852915000711

Fabbri, C., & Serretti, A. (2020). Genetics of treatment outcomes in major depressive disorder: Present and future. *Clinical Psychopharmacology and Neuroscience*, *18*(1), 1-9. doi: 10.9758/cpn.2020.18.1.1

Fatunde, O. A., & Brown, S. (2020). The role of CYP450 drug metabolism in precision cardio oncology. *International Journal of Molecular Sciences*, *21*, 604. doi:10.3390/ijms21020604

Food and Drug Administration. (2018, November 1). The FDA warns against the use of many genetic tests with unapproved claims to predict patient response to specific medication: FDA safety communication. *FDA.GOV*. Retrieved from https://www.fda.gov/medical-devices/safety communications/fda-warns-against-use-many-genetic-tests-unapproved-claims-predict patient-response-specific

Food and Drug Administration. (2020, February 25). The table of pharmacogenetic associations. *FDA.GOV*. Retrieved from https://www.fda.gov/medical-devices/precision-medicine/table pharmacogenetic-associations

Freund, C. L., & Gregory, D. F. (2004). Evaluating pharmacogenetic tests a case example. *Archives of Pediatrics and Adolescent Medicine*, *158*(3), 276-279. doi:10.1001/archpedi.158.3.276

Frieling, H., & Tadic, A. (2013). Value of genetic and epigenetic testing as biomarkers of response to antidepressant treatment. *International Review of Psychiatry*, *25*(5), 572-8. doi: 10.3109/09540261.2013.816657

Gallagher, S., Insel, K., Badger, T., & Reed, P. (2018, June 2nd). Antidepressant adherence in the United States active duty Army soldiers: A small descriptive study. *Archives in Psychiatric Nursing*, *32*(6), 793-801. doi: 10.1016/j.apnu.2018.06.002

Gaynes, B., Warden, D., Trivedi, M., Wisniewski, S., Fava, M., & Rush, A. (2009). What did STAR*D teach us? Results from a large-scale, practical, clinical trial for patients with depression. *Psychiatric Services*, *60*, 1439-1445. doi: 10.1176/appi.ps.60.11.1439

Gillis, N., & Innocenti, F. (2014). Evidence required to demonstrate clinical utility of pharmacogenetic testing: The debate continues. *Clinical Pharmacology & Therapeutics*, *96*(6), 655-657. doi: 10.1038/clpt.2014.185

Gravani, M. N. (2019). Learner-centred education as a tool for enhancing adult learning in distance learning universities. *Journal of Adult and Continuing Education*, *25*(2), 198. doi: 10.1177/1477971419858689

Groessl, E., Talley, S., Hillery, N., Maciel, A., & Garces, J. (2018). Cost-effectiveness of a pharmacogenetic test to guide treatment for Major Depressive Disorder. *Journal of Managed Care and Specialty Pharmacy*, *24*(8), 726-734. doi: 10.18553/jmcp.2018.24.8.726

Haga, S. B., & LaPointe, M. N. (2013). The potential impact of pharmacogenetic testing on medication adherence. *Pharmacogenomics Journal*, *13*(6), 481-483. doi: 10.1038/tpj.2013.33

Hall-Flavin, D. K., Winner, J. G., Allen, J. D., Carhart, J. D., Proctor, J. M., Snyder, B.,… Mrazek, D. (2013). Utility of integrated pharmacogenomics testing to support the treatment of major depressive disorder in a psychiatric outpatient setting. *Pharmacogenetics and Genomics*, *23*(10), 535-548. doi: 10.1097/FPC.0b013e3283649b9a

Halls, J. (2014). Memory and cognition in learning. *Infoline*, *31*(1405). Retrieved from https://eds-a-ebscohost com.vlib.excelsior.edu/eds/ebookviewer/ebook/bmxlYmtfXzgwMjIzMV9fQU41?sid=0243fa4-3d48-4d7e-97aa-8b1dcb860145@sessionmgr4008&vid=3&format=EB&rid=16

Han, C., Sheng-Min, W., Won-Myong, B., Soo-Jung, L. Patkar, A. S., Masand, P. S.,… Serretti, A. (2018). A Pharmacogenomic-based antidepressant treatment for patients with Major Depressive Disorder: Results from an 8-week, randomized, single-blinded clinical trial. *Clinical Psychopharmacology of Neuroscience*, *16*(4), 469-480. doi: 10.9758/cpn.2018.16.4.469

Harper, C. C., Philip, E., Robinowitz, M., & Gutman, S. I. (2005). FDA perspectives on pharmacogenetic testing. *Expert Review of Molecular Diagnostics*, *5*(5), 643-648. doi: 10.1586/14737159.5.5.643

Hernandez, J. (2016). What should you know about IRB review of research? *US Department of Health and Human Services*. Retrieved from https://www.hhs.gov/ohrp/education-and-outreach/online-education/videos/webinar-what-you-should-know-about-irb-review-research/index.html

Houser, J., & Oman, K. S. (2010). *Evidence-based practice*. Jones & Bartlett Publishers

Kapoor, R., Tan-Koi, W. C., & Teo, Y. (2016). Role of pharmacogenetics in public health and clinical health care: A SWOT analysis. *European Journal of Human Genetics*, *24*, 1651-1657. doi: 10.1038/ejhg.2016.114

Komaroff, A. L. (1982). Algorithms and the 'art' of medicine. *American Journal of Public Health*, *72*(1), 10-12. doi: 10.2105/AJPH.72.1.10

Kathleen, B. S. (2015). Clinical implications of pharmacogenetic and microarray testing for advanced practice nurses. *Journal of the American Association of Nurse Practitioners*. *27*(5), 246. doi: 10.1002/2327-6924.12237

Kredo, T., Bernhardsson, S., Machingaidze, S., Young, T., Louw, Q., Ochodo, E., & Grimmer, K. (2016). Guide to clinical practice guidelines: The current state of play. *International Journal of Quality Health Care*, *28*(1), 122-128. doi: 10.1093/intghc/mzv115

Limandri, B. J. (2019). Pharmacogenetic testing: Why is it so disappointing. *Journal of Psychosocial Nursing and Mental Health Services*. *57*(4), 9-12. doi: 10.3928/02793695-20190312-0p1

Lui, S. T., & Shuch, B. (2019). Genetic testing in kidney cancer patients: Who, when, and how?. *European Urology Focus*, *5*(6), 973-976. doi: 10.1016/j.euf.2019.09.005

Lynch, J., DuVall, S. L., Berse, B., Whatley, A., St. Pierre, C., Oloruntoba, O,… Hunt, C. M. (2016). Implementation of pharmacogenetic testing within the Veterans Health Administration from 2011 to 2013. *Military Medicine*, *181*(10), 1375-1381. doi: 10.7205/MILMED-D-15-00523

Lynn, D. C., Lesemann, R. K. & Detro, J. F. (2014). Employment of the “Role 2-Plus”: Lessons Learned in a Time of High OPTEMPO. *Military Medicine*, *79*(12), 1412-1418. doi: 10.7205/MILMED-D-14-00099

Mingote, S., Masson, J., Gellman, C., Thomsen, G. M., Lin, C., Merker, R. J.,… Rayport, S. (2015). Genetic pharmacotherapy as an early CNS drug development strategy: Testing glutaminase inhibition for schizophrenia treatment in adult mice. *Frontiers in Systems Neuroscience*, *9*, 165. doi: 10.3389/fnsys.2015.00165

Murfin, M. (2019). Using pharmacogenetics in primary care. *Journal of the American Academy of PAs*, *32*(8), 17-21. doi: 10.1097/01.JAA.0000569772.68575.ac

Naifeh, J. A., Herberman, H. B., Stein, M. B., Fullerton, C. S., Kessler, R. C., & Ursanol. R. J. (2018). The Army study to assess risk and resilience in servicemembers (Army STARRS): Progress toward understanding suicide among soldiers. *Molecular Psychiatry*, *24*, 34-48. doi: 10.1038/s41380-018-0197-z

Nock, M., Stein, M., & Heeringa, S. (2014). Prevalence and correlates of suicidal behavior among soldiers results From the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS). *JAMA Psychiatry*, *71*(5), 514-22. doi: 10.1001/jamapsychiatry.2014.30

Nock, M., Ursano, R., Heeringa, S., Stein, M., Jain, S., Raman, R., ... & Colpe, L. (2015, January 26). Mental disorders, comorbidity and pre-enlistment suicidal behavior among new soldiers in the US Army: results from the Army Study to Assess Risk and Resilience in Service members (Army STARRS). *Suicide Life Threat Behaviors*, *45*(5), 588-599. doi: 10.1111/sltb

Parve, J. , Carlile, J. & Parve, J. (2019). Pharmacogenetic testing in primary care. *The Nurse Practitioner*, *44*(10), 44–49. doi: 10.1097/01.NPR.0000580780.66980.85.

Perez, V., Salavert, A., Espadaler, J., Tuson, M., Saiz-Ruiz, J., Saez-Navarro, C.,… Menchon, J. M. (2017). Efficacy of prospective pharmacogenetics testing in the treatment of major depressive disorder: Results of a randomized, double-blind clinical trial. *BMC Psychiatry*, *17*(1), 250. doi: 10.1168/s12888-017-1412-1

Perlis, R., Mehta, R., Edwards, A., Tiwari, A., & Imbens, G. (2018, February 10th). Pharmacogenetic testing among patients with mood and anxiety disorders is associated

with decreased utilization and cost: A propensity-score matched study. *Depression and Anxiety*, *35*(10), 946-952. doi: 10.1002/da.22742

Peterson, J., Field, J., Shi, Y., Schildcrout, J., Denny, J., McGregor, T., & Clayton, W. (2016). Attitudes of clinicians following large-scale pharmacogenomics implementation. *Pharmacogenomics Journal*, *16*(4), 393-398. doi: 10.1038/tpj.2015.57

Pompili, M., Serafini, G., Innamorati, M., Ambrosi, E., Giordano, G., Girardi, P.,… & Lester, D. (2010). Antidepressants and suicide risk: A comprehensive overview. Pharmaceuticals, 3(9), 2861-2882. doi: 10.3390/ph3092861

Schuck, R. N., Marek, E., Rogers, H., & Pacanowshi, M. (2016). Clinical and regulatory considerations in pharmacogenetic testing. *American Journal of Health-System Pharmacy*, *73*(23), 1999-2006. doi: 10.2146/ajhp160476

Simon, G. (2019). Unipolar major depression in adults: Choosing initial treatment. *UpToDate.com*. Retrieved from https://www.uptodate.com/contents/unipolar-major depression-in-adults-choosing-initial-treatment

Selkirk, C. G., Weissman, S. M., Anderson, A., & Hulick, P. J. (2013). Physicians' preparedness for integration of genomic and pharmacogenetic testing into practice within a major healthcare system. *Genetic Testing and Molecular Biomarkers*, *17*(3), 219-225. doi: 10.1089/gtmb.2012.0165

Shuren, J. E., & Woodcock, (2020). FDA announces collaborative review of scientific evidence to support associations between genetic information and specific medications. *FDA.gov*. Retrieved from https://www.fda.gov/news-events/press-announcements/fda-announces collaborative-review-scientific-evidence-support-associations-between-genetic

Solomon, V., Cates, K. W., & Li, K. J. (2019) Does obtaining CYP2D6 and CYP2C19 pharmacogenetic testing predict antidepressant response or adverse drug reactions?. *Psychiatry Research*, *271*, 604-613. doi: 10.1016/j.psychres.2018.12.053

Strauss, L. (2017). De-identifying protected health information: De-identification allows growth and development of health care while protecting individual privacy. *Journal of Health Care Compliance*, *19*(6), 51-54. Retrieved from https://eds-b-ebscohost com.vlib.excelsior.edu/eds/pdfviewer/pdfviewer?vid=3&sid=9a1f9e25-af5e-41a5-a6df 58a86dd99e8a%40sessionmgr120

Tanner, J. A., Davies, P. E., Voudouris, N. C., Shahmirian, A., Herbert, D., Braganza, N.,… Kennedy, J. (2018). Combinatorial pharmacogenomics and improved patient outcomes in depression: Treatment by primary care physicians or psychiatrists. *Journal of Psychiatric Research*, *104*, 157-162. doi: 10.1016/j.jpsychires.2018.07.012

The Center for Evidence-Based Medicine. (n.d.). *CEBM.net*. https://www.cebm.net/2014/06/critical-appraisal/

The White House. (2015). *Fact sheet: President Obama's precision medicine initiative*. Retrieved from https://obamawhitehouse.archives.gov/the-press-office/2015/01/30/fact sheet-president-obama-s-precision-medicine-initiative

Thompson, C., Hamilton, S. P., & Hippman, C. (2015). Psychiatrist attitudes towards pharmacogenetic testing, direct-to-consumer genetic testing, and integrating genetic counseling into psychiatric patient care. *Psychiatry Research*, *226*(1), 68-72. doi: 10.1016/j.psychres.2014.11.044

Torrellas, C., Carril, J. C., Cacabelos, R. (2017). Optimization of antidepressant use with pharmacogenetic strategies. *Current Genomics*, *18*(5), 442-449. doi: 10.2174/1389202918666170426164940

U.S. Department of Health and Human Services. (2015). *National ambulatory medical care survey: 2015 state and national summary tables*. Retrieved from https://www.cdc.gov/nchs/data/ahcd/namcs_summary/2015_namcs_web_tables.pdf

US CENTCOM. (2019). *PPG-Tab A: Amplification of the minimal standards of fitness for deployment to the CENTCOM AOR; to accompany MOD thirteen to USCENTCOM individual protection and individual/unit deployment policy*. Retrieved from https://www.tam.usace.army.mil/Portals/53/docs/UDC/medical-disqualifiers.pdf

Walden, L., Brandl, E., Tiwari, A., Cheema, S., Freeman, N., Braganza, N., ... & Muller, D. (2018). Genetic testing for CYP2D6 and CYP2C19 suggests improved outcome for antidepressant and antipsychotic medication. *Psychiatry Research*. Retrieved from doi: 10.1016/j.psychres.2018.02.055

Walden, L. M., Brandl, E. J., Changasi, A., Sturgess, J. E., Soibel, A., Notario, J. F. Cheema, S.,… Muller, D. (2015). Physicians' opinions following pharmacogenetic testing for psychotropic medication. *Psychiatry Research*, *229*(3), 913-918. doi: 10.1016/j.psychres.2015.07.032

White, K., Dudley-Brown, S., & Terhaar, M. (2016). *Translation of evidence into nursing and health care* (2nd ed.). New York, NY: Springer.

Winner, J. G., Carhart, J. M., Altar, C. A., Allen, J. D., & Dechairo, B. M. (2013). A prospective, randomized, double-blind study assessing the clinical impact of integrated

pharmacogenomic testing for major depressive disorder. *Discovery Medicine*, *16*(89), 219-227. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/24229738

Wofford, K. (n.d.). Legal and ethical issues (PowerPoint Slides). Retrieved from https://drive.google.com/file/d/0B-1eScB2RqTVOUNXazJfaVV6ajA/view

World Health Organization. (2018). Depression. Retrieved from http://www.who.int/news-room/fact-sheets/detail/depression

Xue, C., Zhang, X., & Cai, W. (2018). Prediction of drug-drug interactions with bupropion and its metabolites as CYP2D6 inhibitors using a physiologically-based pharmacokinetic model. *Pharmaceutics*, *10*(1). doi: 10.3390/pharmaceutics10010001

Appendix A


CITI CERT_1.pdf
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Fit to page
Page view
Read aloud
Add notes
CITI PROGRAM
Completion Date 26-Aug-2017
Expiration Date 25-Aug-2020
Record ID [redacted]
This is to certify that:
Dennis Flynn
Has completed the following CITI Program course:
OUSD P&R Human Research (Curriculum Group)
Biomedical Investigators and Research Study Team (Course Learner Group)
1 - Basic Course (Stage)
Under requirements set by:
Office of the Under Secretary of Defense (Personnel and Readiness)
Verify at www.citiprogram.org/verify/?w8747935d-d1f0-451b-8f58-896452f8fffd-24324927


CITI Biomedical _ Resea
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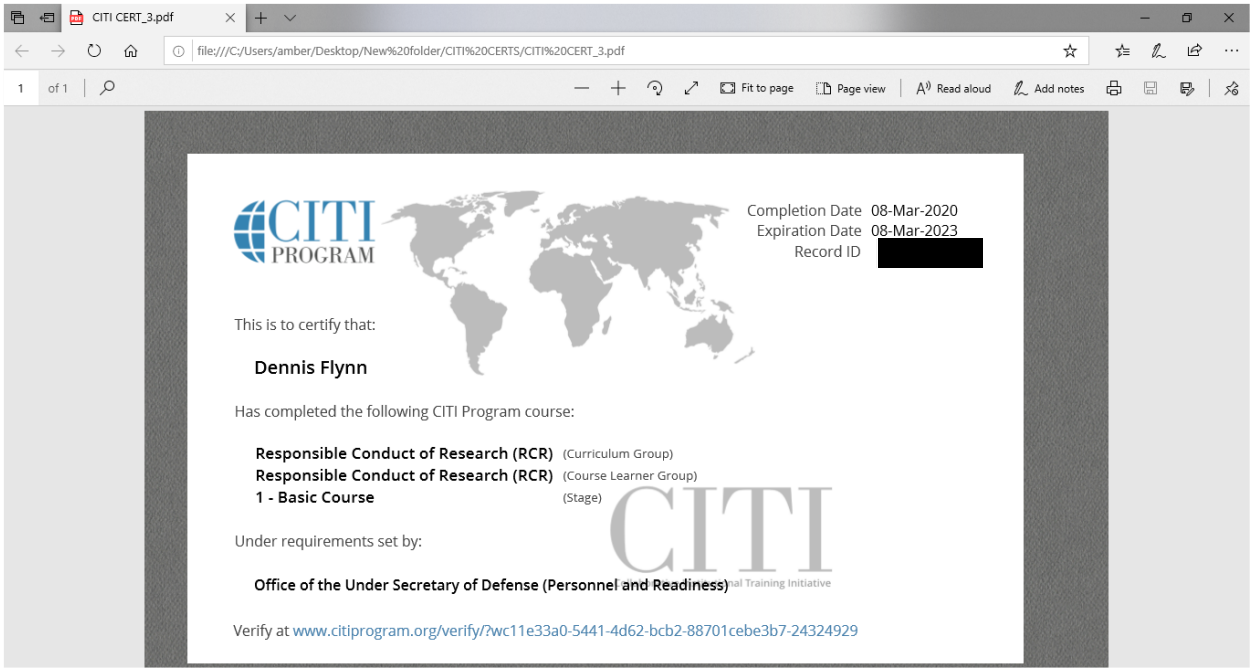
Fit to page
Page view
Read aloud
Add notes
CITI PROGRAM
Completion Date 28-Aug-2017
Expiration Date 27-Aug-2020
Record ID [redacted]
This is to certify that:
Jasmine Peterson-Ware
Has completed the following CITI Program course:
OUSD P&R Human Research (Curriculum Group)
Biomedical Investigators and Research Study Team (Course Learner Group)
1 - Biomedical Investigators (Stage)
Under requirements set by:
Office of the Under Secretary of Defense (Personnel and Readiness)



CITI CERT_3.pdf

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CITI PROGRAM

Completion Date 08-Mar-2020
Expiration Date 08-Mar-2023
Record ID [redacted]

This is to certify that:

Dennis Flynn

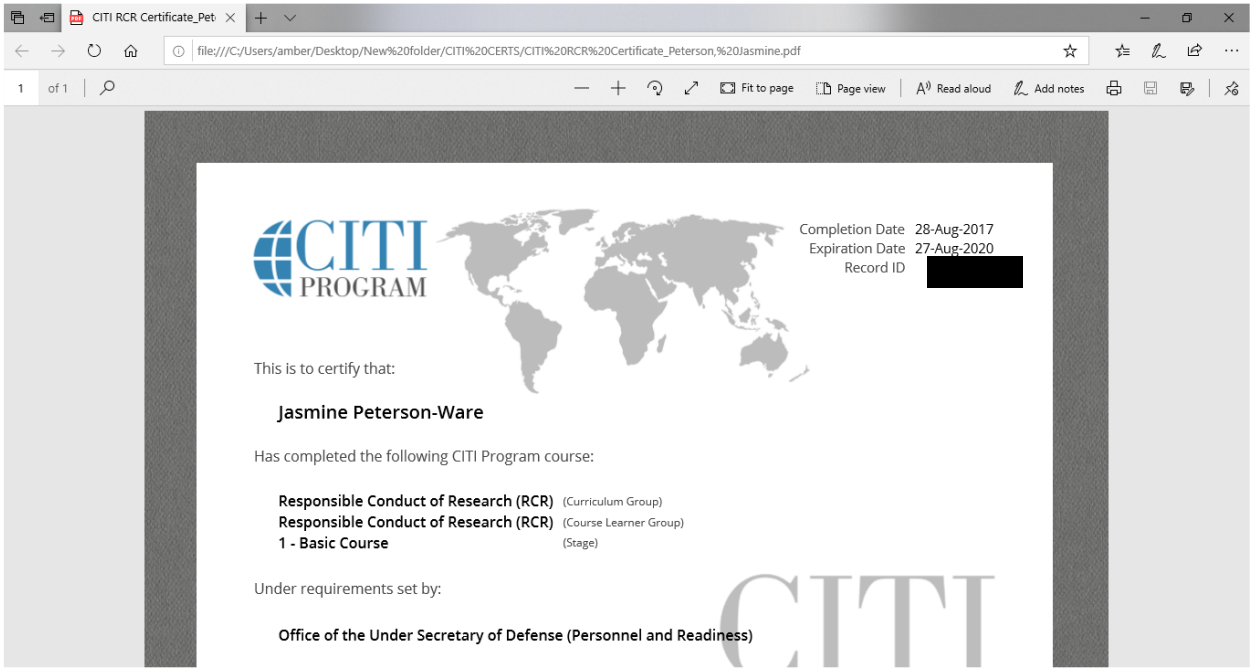
Has completed the following CITI Program course:

Responsible Conduct of Research (RCR) (Curriculum Group)
Responsible Conduct of Research (RCR) (Course Learner Group)
1 - Basic Course (Stage)

Under requirements set by:

Office of the Under Secretary of Defense (Personnel and Readiness)

Verify at www.citiprogram.org/verify/?wc11e33a0-5441-4d62-bcb2-88701cebe3b7-24324929



CITI RCR Certificate_Pet

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1 of 1 | Fit to page | Page view | Read aloud | Add notes

CITI PROGRAM

Completion Date 28-Aug-2017
Expiration Date 27-Aug-2020
Record ID [redacted]

This is to certify that:

Jasmine Peterson-Ware

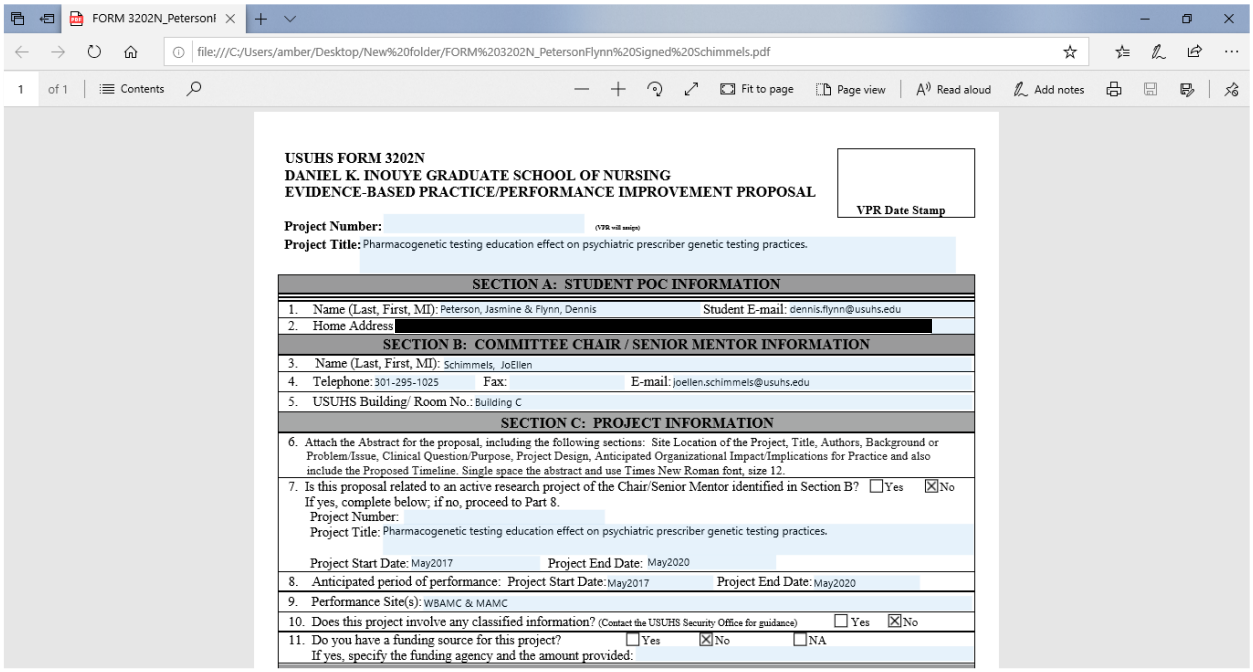
Has completed the following CITI Program course:

Responsible Conduct of Research (RCR) (Curriculum Group)
Responsible Conduct of Research (RCR) (Course Learner Group)
1 - Basic Course (Stage)

Under requirements set by:

Office of the Under Secretary of Defense (Personnel and Readiness)

Appendix B



FORM 3202N_Personi

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1 of 1 | Contents | Fit to page | Page view | Read aloud | Add notes

USUHS FORM 3202N
DANIEL K. INOUYE GRADUATE SCHOOL OF NURSING
EVIDENCE-BASED PRACTICE/PERFORMANCE IMPROVEMENT PROPOSAL

VPR Date Stamp

Project Number: (VPR will assign)
Project Title: Pharmacogenetic testing education effect on psychiatric prescriber genetic testing practices.

SECTION A: STUDENT POC INFORMATION

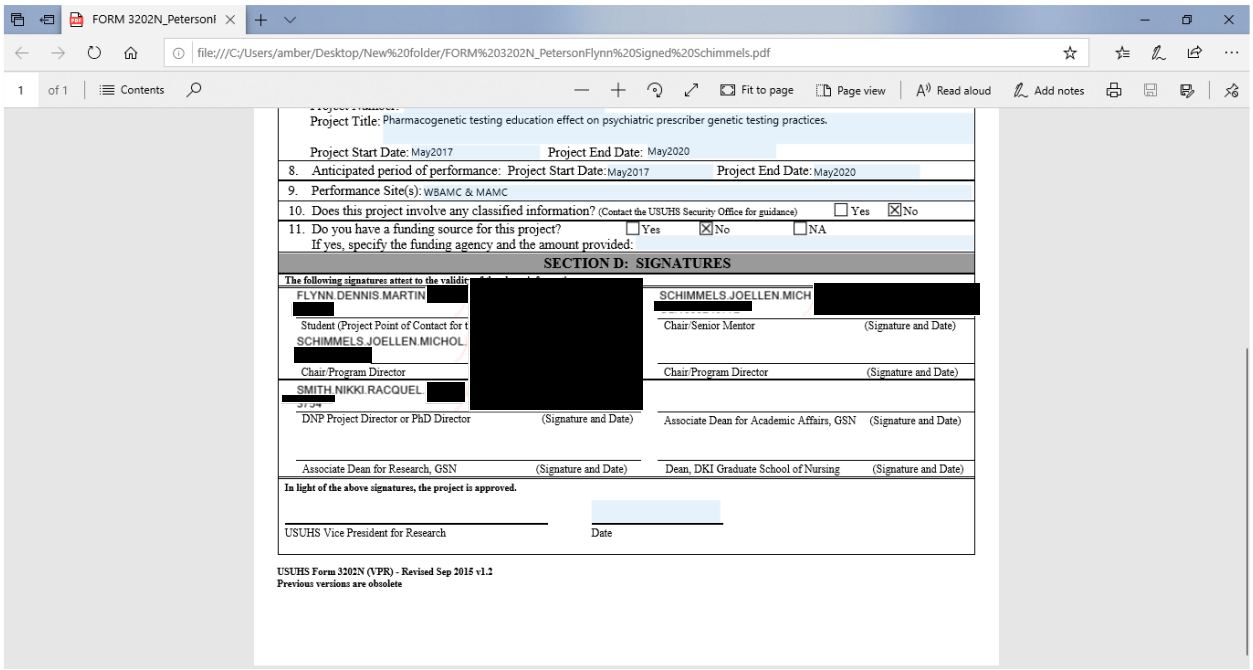
1. Name (Last, First, MI): Peterson, Jasmine & Flynn, Dennis — Student E-mail: dennis.flynn@usuhs.edu
2. Home Address [redacted]

SECTION B: COMMITTEE CHAIR / SENIOR MENTOR INFORMATION

3. Name (Last, First, MI): Schimmels, JoEllen
4. Telephone: 301-295-1025 — Fax: — E-mail: joellen.schimmels@usuhs.edu
5. USUHS Building/ Room No.: Building C

SECTION C: PROJECT INFORMATION

6. Attach the Abstract for the proposal, including the following sections: Site Location of the Project, Title, Authors, Background or Problem/Issue, Clinical Question/Purpose, Project Design, Anticipated Organizational Impact/Implications for Practice and also include the Proposed Timeline. Single space the abstract and use Times New Roman font, size 12.
7. Is this proposal related to an active research project of the Chair/Senior Mentor identified in Section B? ☐ Yes ☒ No
   If yes, complete below; if no, proceed to Part 8.
   Project Number:
   Project Title: Pharmacogenetic testing education effect on psychiatric prescriber genetic testing practices.
   Project Start Date: May2017 — Project End Date: May2020
8. Anticipated period of performance: Project Start Date: May2017 — Project End Date: May2020
9. Performance Site(s): WBAMC & MAMC
10. Does this project involve any classified information? (Contact the USUHS Security Office for guidance) ☐ Yes ☒ No
11. Do you have a funding source for this project? ☐ Yes ☒ No ☐ NA
    If yes, specify the funding agency and the amount provided:



FORM 3202N_Personi

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1 of 1 | Contents | Fit to page | Page view | Read aloud | Add notes

Project Title: Pharmacogenetic testing education effect on psychiatric prescriber genetic testing practices.
Project Start Date: May2017 — Project End Date: May2020
8. Anticipated period of performance: Project Start Date: May2017 — Project End Date: May2020
9. Performance Site(s): WBAMC & MAMC
10. Does this project involve any classified information? (Contact the USUHS Security Office for guidance) ☐ Yes ☒ No
11. Do you have a funding source for this project? ☐ Yes ☒ No ☐ NA
    If yes, specify the funding agency and the amount provided:

SECTION D: SIGNATURES

The following signatures attest to the validity [redacted]

FLYNN.DENNIS.MARTIN [redacted] — SCHIMMELS.JOELLEN.MICH [redacted]
Student (Project Point of Contact for t — Chair/Senior Mentor (Signature and Date)

SCHIMMELS.JOELLEN.MICHOL [redacted]
Chair/Program Director — Chair/Program Director (Signature and Date)

SMITH.NIKKI.RACQUEL [redacted]
DNP Project Director or PhD Director (Signature and Date) — Associate Dean for Academic Affairs, GSN (Signature and Date)

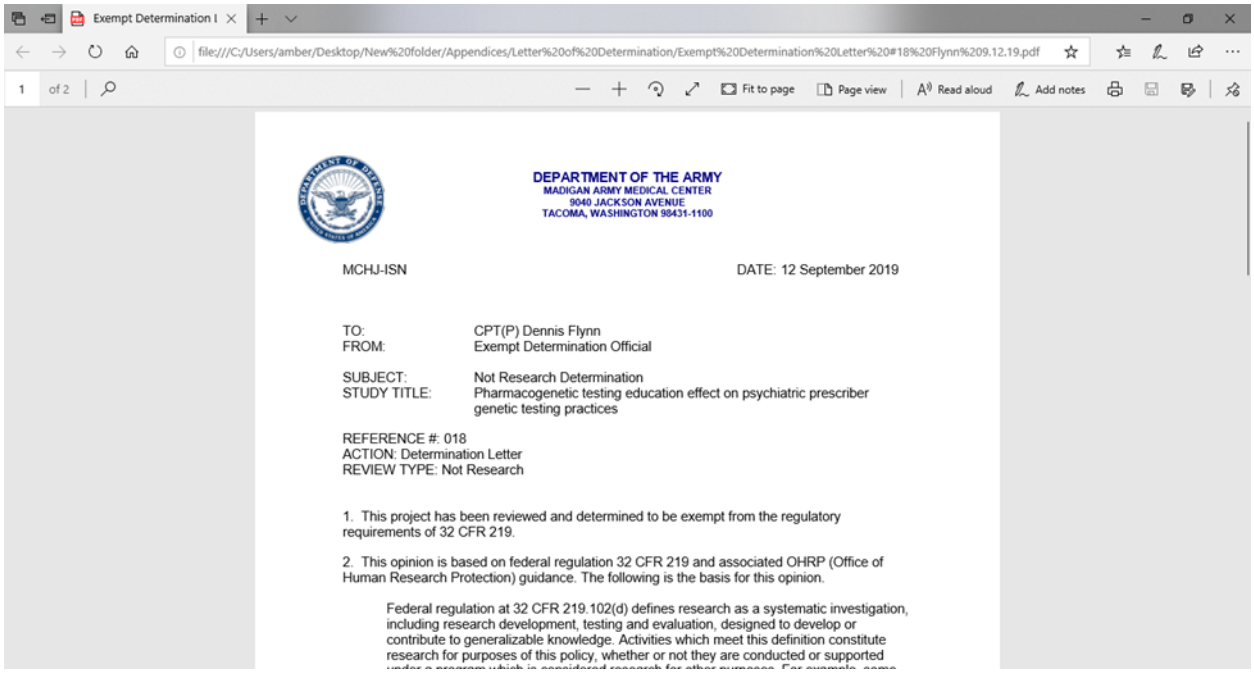
Associate Dean for Research, GSN (Signature and Date) — Dean, DKI Graduate School of Nursing (Signature and Date)

In light of the above signatures, the project is approved.

USUHS Vice President for Research — Date

USUHS Form 3202N (VPR) - Revised Sep 2015 v1.2
Previous versions are obsolete

Appendix C



Exempt Determination l

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1 of 2 | Fit to page | Page view | Read aloud | Add notes

DEPARTMENT OF THE ARMY
MADIGAN ARMY MEDICAL CENTER
9040 JACKSON AVENUE
TACOMA, WASHINGTON 98431-1100

MCHJ-ISN DATE: 12 September 2019

TO: CPT(P) Dennis Flynn
FROM: Exempt Determination Official

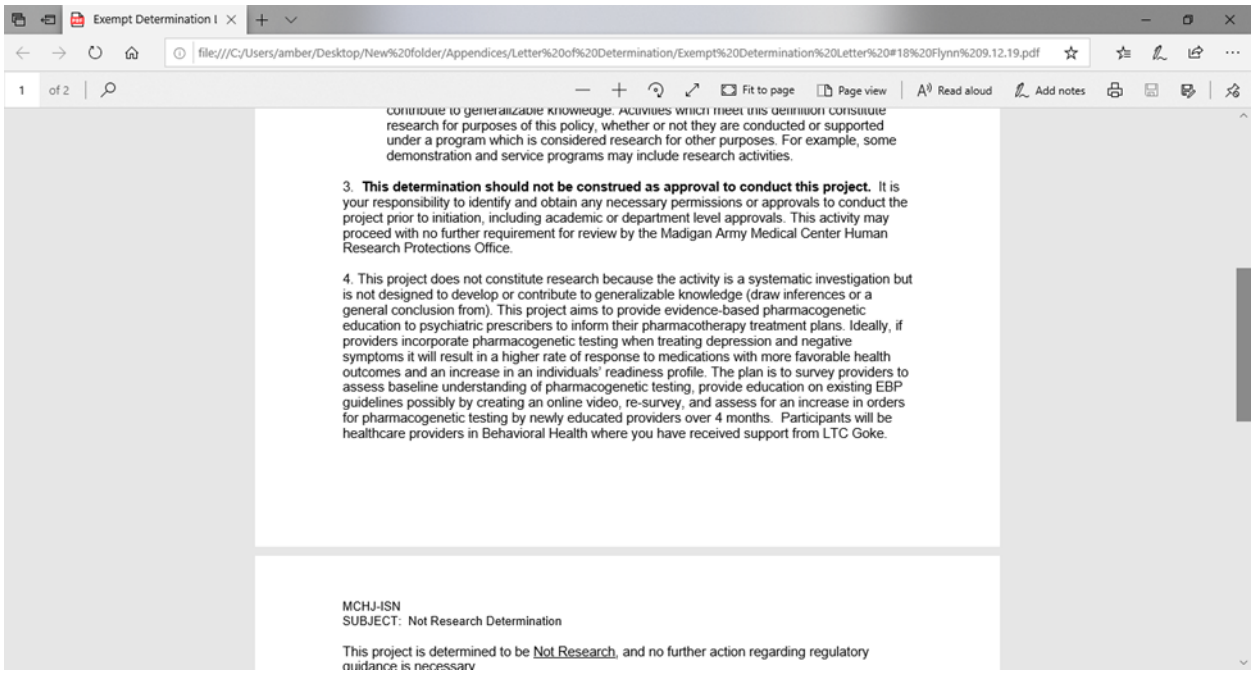
SUBJECT: Not Research Determination
STUDY TITLE: Pharmacogenetic testing education effect on psychiatric prescriber genetic testing practices

REFERENCE #: 018
ACTION: Determination Letter
REVIEW TYPE: Not Research

1. This project has been reviewed and determined to be exempt from the regulatory requirements of 32 CFR 219.

2. This opinion is based on federal regulation 32 CFR 219 and associated OHRP (Office of Human Research Protection) guidance. The following is the basis for this opinion.

Federal regulation at 32 CFR 219.102(d) defines research as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported



Exempt Determination l

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1 of 2 | Fit to page | Page view | Read aloud | Add notes

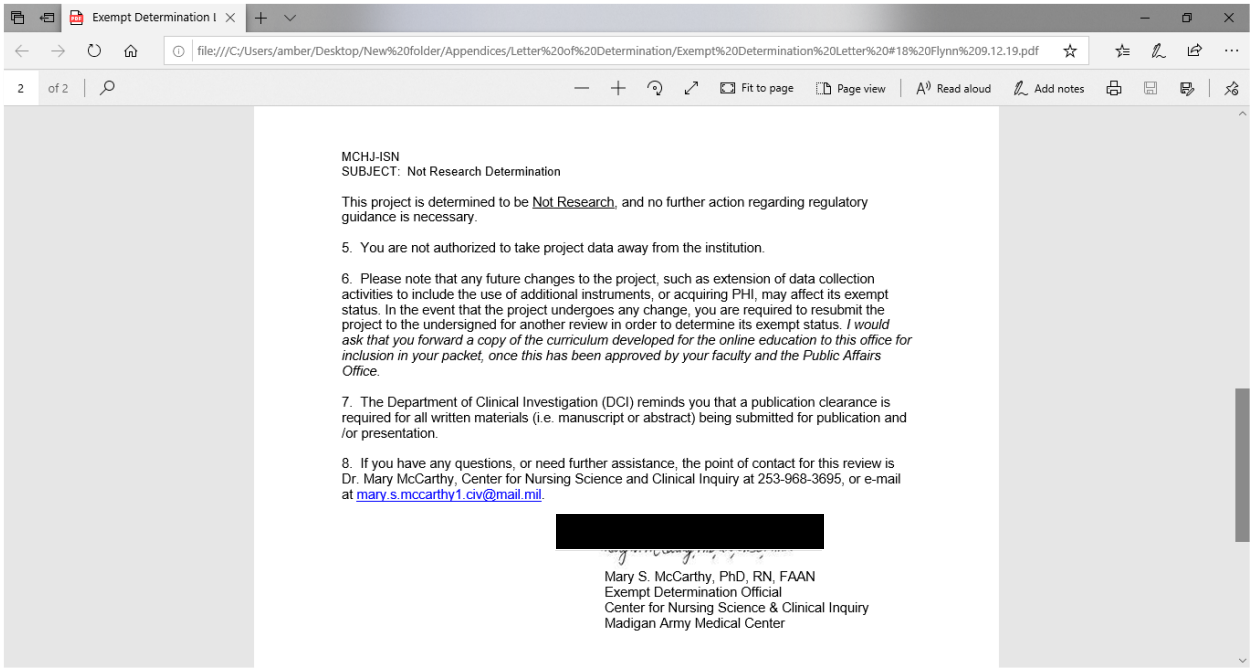
contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.

3. **This determination should not be construed as approval to conduct this project.** It is your responsibility to identify and obtain any necessary permissions or approvals to conduct the project prior to initiation, including academic or department level approvals. This activity may proceed with no further requirement for review by the Madigan Army Medical Center Human Research Protections Office.

4. This project does not constitute research because the activity is a systematic investigation but is not designed to develop or contribute to generalizable knowledge (draw inferences or a general conclusion from). This project aims to provide evidence-based pharmacogenetic education to psychiatric prescribers to inform their pharmacotherapy treatment plans. Ideally, if providers incorporate pharmacogenetic testing when treating depression and negative symptoms it will result in a higher rate of response to medications with more favorable health outcomes and an increase in an individuals' readiness profile. The plan is to survey providers to assess baseline understanding of pharmacogenetic testing, provide education on existing EBP guidelines possibly by creating an online video, re-survey, and assess for an increase in orders for pharmacogenetic testing by newly educated providers over 4 months. Participants will be healthcare providers in Behavioral Health where you have received support from LTC Goke.

MCHJ-ISN
SUBJECT: Not Research Determination

This project is determined to be Not Research, and no further action regarding regulatory guidance is necessary



MCHJ-ISN
SUBJECT: Not Research Determination

This project is determined to be Not Research, and no further action regarding regulatory guidance is necessary.

5. You are not authorized to take project data away from the institution.

6. Please note that any future changes to the project, such as extension of data collection activities to include the use of additional instruments, or acquiring PHI, may affect its exempt status. In the event that the project undergoes any change, you are required to resubmit the project to the undersigned for another review in order to determine its exempt status. *I would ask that you forward a copy of the curriculum developed for the online education to this office for inclusion in your packet, once this has been approved by your faculty and the Public Affairs Office.*

7. The Department of Clinical Investigation (DCI) reminds you that a publication clearance is required for all written materials (i.e. manuscript or abstract) being submitted for publication and /or presentation.

8. If you have any questions, or need further assistance, the point of contact for this review is Dr. Mary McCarthy, Center for Nursing Science and Clinical Inquiry at 253-968-3695, or e-mail at mary.s.mccarthy1.civ@mail.mil.

[redacted]

Mary S. McCarthy, PhD, RN, FAAN
Exempt Determination Official
Center for Nursing Science & Clinical Inquiry
Madigan Army Medical Center

Appendix D

Due to the impact of the COVID19 Pandemic, PAO Clearance was not required.

Appendix E

Pre Antidepressant Pharmacogenetic Testing Education Survey

Survey Purpose: Identifying psychiatric prescribers' perceptions and understanding of the use of pharmacogenetic testing in psychopharmaceutical medication selection, as well as identifying potential barriers in the use of pharmacogenetic testing by psychiatric prescribers.

(Questions 1-3 utilize a Likert scale please select the one answer that most applies.

1. The ordering of genetic testing as a resource to aid in the selection of psychopharmaceutic treatment for patients should be utilized by psychiatric prescribers.

Strongly agree

Agree

Neither agree nor disagree

Disagree

Strongly disagree

2. I am confident about HOW to order genetic testing (to aid in the selection of psychopharmaceutic treatment for patients).

Strongly agree

Agree

Neither agree nor disagree

Disagree

Strongly disagree

3. I am confident about WHEN to order genetic testing (to aid in the selection of psychopharmaceutic treatment for patients).

Strongly agree

Agree

Neither agree nor disagree

Disagree

Strongly disagree

4. Perceived barriers to ordering genetic testing to treat psychiatric patients include (select all that apply):

None

Resources to implement genetic testing into practice.

Comfort with describing/discussing pharmacogenetic information with patients.

Time to utilize genetic testing in practice.

Access to genetic testing.

Genetic testing is not included in clinical practice guidelines for psychiatric drug selection.

Lack of clinical guidelines.

No incentive to perform pharmacogenetic tests for psychiatric drug selection.

Expense to the military treatment facility.

Concern that unauthorized persons may gain access to the results of a patient's genetic testing.

Leadership support to perform pharmacogenectic tests.

Use of genetic testing limits flexibility and individual approach within practice.

Other (please specify)

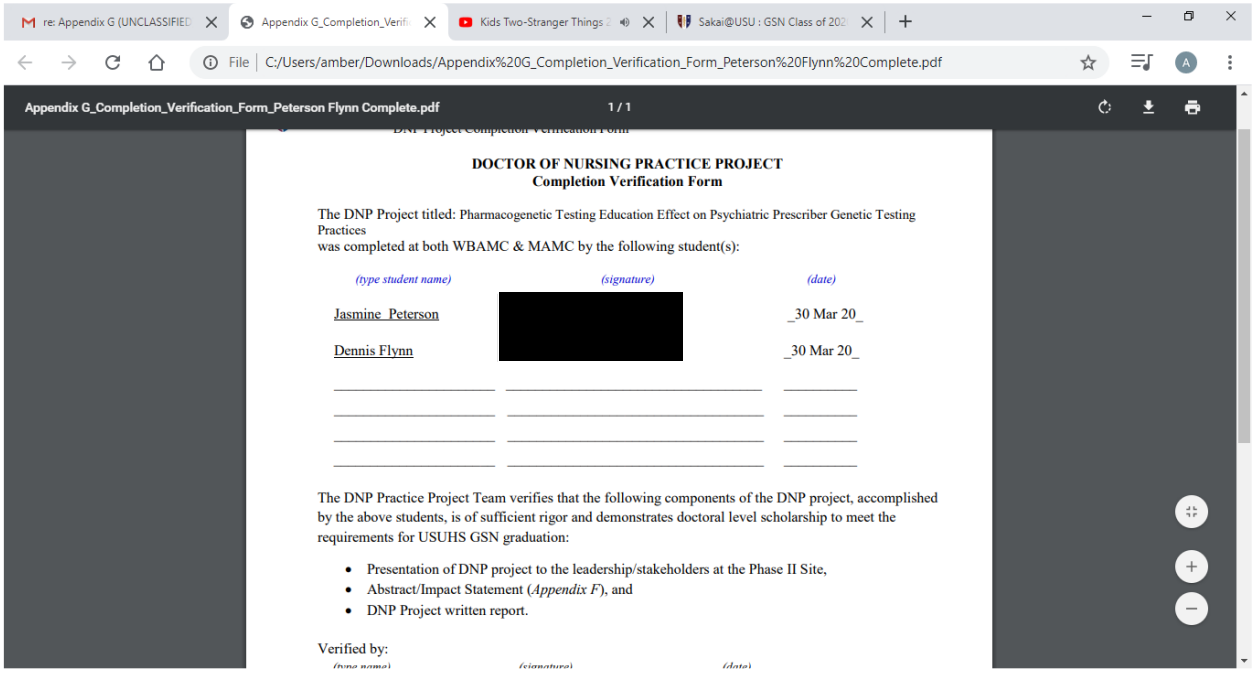
Appendix F

Literature Reference	"Impact of PGT on clinical outcomes", Greden et al. (2019)	"Randomized double-blind study assessing the impact of PGT", Winner et al. (2013)	"Combinatorial PGT and improved patient outcomes", Tanner et al. (2018)	"Improved efficacy with PGT of patients with depression and anxiety", Bradley et al. (2018)	"PGT-based Antidepressant Treatment for Patients with MDD", Han et al. (2018)	"Utility of integrated PGT in treatment of MDD", Hall-Flavin et al. (2013)	"Clinical utility of combinatorial PGT", Alter et al. (2015)	"Does obtaining CYP2D6 and CYP2C19 PGT predict antidepressant response", Solomon et al. (2019)	"PGT for the guidance of psychiatric treatment", Espadaler et al. (2017)	"Efficacy of prospective PGT in the treatment of MDD", Perez et al. (2017)	"PGT and depressive symptom remission", Bousman et al. (2019)	"Optimization of antidepressant use with PGT strategies", Torrellas et al. (2017)
Design Method and Level of Evidence	RCT, Long-Term Blinded - LEVEL II	RCT, Prospective Double Blinded - LEVEL II	Prospective Cohort Study - LEVEL III	RCT, Prospective Double Blinded - LEVEL II	RCT, Blinded - LEVEL II	Prospective Cohort Study - LEVEL III	Meta-Analysis	Systematic Review, MEDLINE/Pubmed - LEVEL I	Comparative Study, Retrospective - LEVEL IV	RCT, Prospective Double Blinded - LEVEL II	Meta-Analysis	Comparative Study, Retrospective - LEVEL IV
Major Variables	IV = PGT in Medication Selection DV = HAM-D17 Scores	IV = PGT in Medication Selection DV = HAM-D17 Scores	IV = PGT in Medication Selection DV = BDI Scores	IV = PGT in Medication Selection DV = HAM-D17 / HAM-A Scores	IV = PGT in Medication Selection DV = HAM-D17 Score	IV = PGT in Medication Selection DV = HAM-D17 Scores	IV = PGT in Medication Selection DV = HAM-D17 Scores	IV = CYP2D6 / CYP2C19 PGT in Medication Selection DV = Depression / Anxiety measurement scales	IV = PGT in Medication Selection DV = CGI-S Scores	IV = PGT in Medication Selection DV = PGI-I Scores	IV = PGT in Medication Selection DV = HAM-D17 Scores	IV = PGT in Medication Selection DV = HDRS Scores
Outcomes Measured	Reduced MDD symptoms	Reduced MDD & DDNOS symptoms	Whether genetically congruent medication selection occurred	Reduced Depressive and Anxiety symptoms	Reduced MDD symptoms	Reduced MDD symptoms	Reduced Depressive Symptoms	Reduced Depressive Symptoms	Reduced Depressive Symptoms	Reduced MDD symptoms	Reduced MDD symptoms	Reduced Depressive Symptoms
Findings	Significant symptom improvement demonstrated by HAM-D17 with respect to control group who were initially prescribed medication incongruent with PGT	Significant Symptoms improvement demonstrated by HAM-D17 with PGT	Significant improvement BDI Score with PGT	Significant Symptoms improvement demonstrated by HAM-D17 with PGT	Significant Symptoms improvement demonstrated by HAM-D17 with PGT	Significant Symptoms improvement demonstrated by HAM-D17 with PGT	Significant Symptoms improvement demonstrated by HAM-D17 with PGT	Significant Symptoms improvement demonstrated by HAM-D17 with PGT	Significant Symptoms improvement demonstrated by CGI-S with PGT	Significant Symptoms improvement demonstrated by PGI-I with PGT	Significant Symptoms improvement demonstrated by HAM-D17 with PGT	Significant Symptoms improvement demonstrated by HDRS with PGT

Symbol Key
PGT = Pharmacogenetic Testing
RCT = Random Controlled Trial
MDD = Major Depressive Disorder
PGI-I = Patient Global Impression of Improvement
CGI-S = Clinical Global Impression of Severity
BDI = Becks Depressive Inventory
DDNOS = Depressive Disorder Not Otherwise Specified
HAM-D17 / HDRS= Hamilton Rating Scale for Depression
HAM-A = Hamilton Rating Scale for Anxiety

Legend	
1. Greden et al. (2019)	7. Alter et al. (2015)
2. Winner et al. (2013)	8. Solomon et al. (2019)
3. Tanner et al. (2018)	9. Espadaler et al. (2017)
4. Bradley et al. (2018)	10. Perez et al. (2017)
5. Han et al. (2018)	11. Bousman et al. (2019)
6. Hall-Flavin et al. (2013)	12. Torrellas et al. (2017)

Appendix G



Appendix G_Completion_Verification_Form_Peterson Flynn Complete.pdf 1 / 1

DOCTOR OF NURSING PRACTICE PROJECT
Completion Verification Form

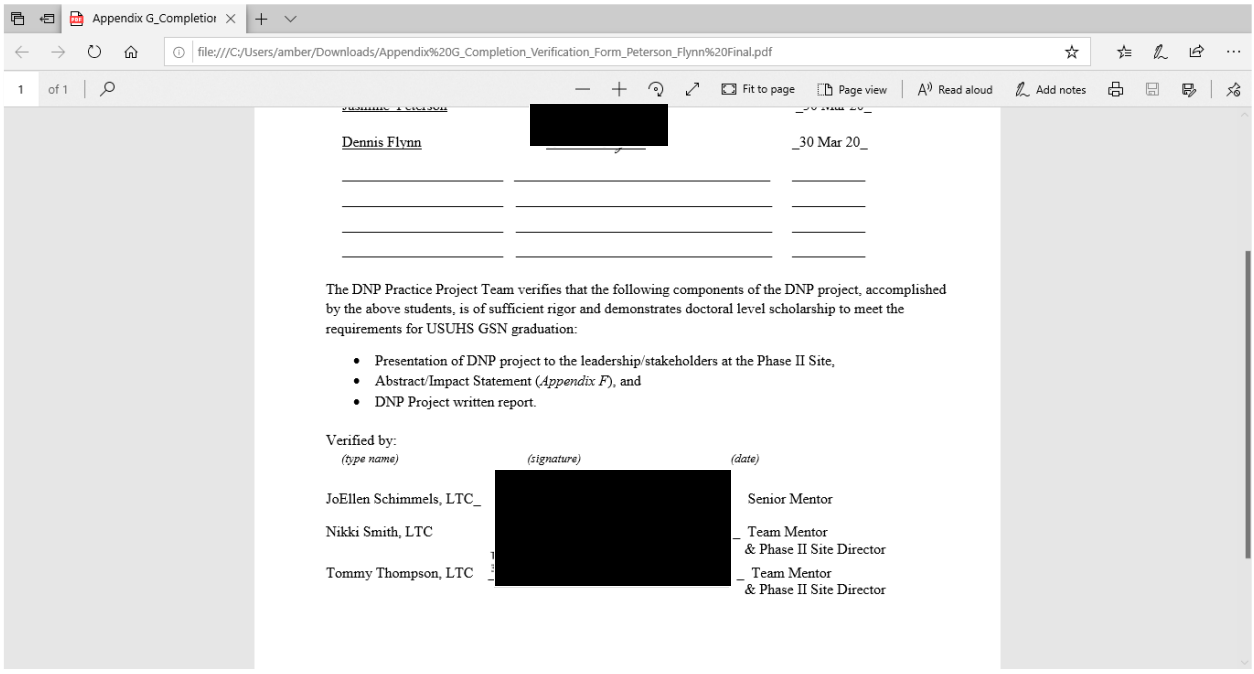
The DNP Project titled: Pharmacogenetic Testing Education Effect on Psychiatric Prescriber Genetic Testing Practices
was completed at both WBAMC & MAMC by the following student(s):

(type student name)	*(signature)*	*(date)*
Jasmine Peterson	[redacted]	_30 Mar 20_
Dennis Flynn		_30 Mar 20_

The DNP Practice Project Team verifies that the following components of the DNP project, accomplished by the above students, is of sufficient rigor and demonstrates doctoral level scholarship to meet the requirements for USUHS GSN graduation:

- Presentation of DNP project to the leadership/stakeholders at the Phase II Site,
- Abstract/Impact Statement (*Appendix F*), and
- DNP Project written report.

Verified by:



Appendix G_Completion_Verification_Form_Peterson_Flynn%20Final.pdf

Dennis Flynn [redacted] _30 Mar 20_

The DNP Practice Project Team verifies that the following components of the DNP project, accomplished by the above students, is of sufficient rigor and demonstrates doctoral level scholarship to meet the requirements for USUHS GSN graduation:

- Presentation of DNP project to the leadership/stakeholders at the Phase II Site,
- Abstract/Impact Statement (*Appendix F*), and
- DNP Project written report.

Verified by:

(type name)	*(signature)*	*(date)*
JoEllen Schimmels, LTC_	[redacted]	Senior Mentor
Nikki Smith, LTC		_ Team Mentor & Phase II Site Director
Tommy Thompson, LTC		_ Team Mentor & Phase II Site Director