Spring 5-12-2022

The Effect of VMAT2 Inhibitors on Tardive Dyskinesia Symptoms in patients with Schizophrenia

Ada Kelly

THE EFFECT OF VMAT2 INHIBITORS ON TARDIVE DYSKINESIA SYMPTOMS IN PATIENTS WITH SCHIZOPHRENIA

by

Ada Kelly

A Doctoral Project
Submitted to the Graduate School,
the College of Nursing and Health Professions
and the School of Leadership and Advanced Nursing Practice
at The University of Southern Mississippi
in Partial Fulfillment of the Requirements
for the Degree of Doctor of Nursing Practice

Approved by:

Dr. Carolyn Coleman, Committee Chair
Dr. Marti Jordan, Committee Member

May 2022

Published by the Graduate School

ABSTRACT

Prior to the FDA approval of VMAT2 inhibitors for the treatment of tardive dyskinesia (TD), few concrete treatment options were available for TD. The most common management strategy would include switching a patient from an FGA to an SGA while discontinuing any anticholinergic medications the patient was currently taking. Other options included changing, decreasing, or discontinuing the antipsychotic. Augmenting stable antipsychotic regimens, however, may not be feasible in the management of schizophrenia as antipsychotics are foundational in the treatment of schizophrenia. A retrospective chart review was performed on 70 records that were chosen through a convenience sample of patients being treated by one physician and two nurse practitioners. The main intervention was the initiation of a VMAT2 inhibitor for the treatment of TD, therefore no records were identified for comparison with the intervention of initiation of a VMAT2 inhibitor. AIMs scores at four, eight, and twelve weeks after VMAT2 initiation were identified. Fifteen (N=15) records were identified to meet inclusion criteria for the DNP project. All records included patients between the ages of 25 to 65 on an approved VMAT2 inhibitor for at least 90 days, with a diagnosis within the DSM-V Schizophrenia Spectrum and other Psychotic Disorders of either schizophrenia, schizophreniform disorder, schizotypal disorder, delusional disorder, or schizoaffective disorder. The data from this DNP project shows that VMAT2 inhibitors are very effective in reducing tardive dyskinesia symptoms based on the AIMS scale scores and a statistically significant mean 4.27% decrease in AIMS scale scores overall in the 12-week period, which is comparable to results obtained by previous studies.

ACKNOWLEDGMENTS

I would like to express my sincere gratitude to Dr. Carolyn Coleman, my committee chair who has been gracious, supporting, and encouraging throughout this process to help me complete this DNP project. Her guidance and expertise were paramount throughout this process as she took time out of her busy schedule to help me anytime I called her, for words of wisdom or clinical direction, and for that, I will always be grateful. I would also like to thank my other committee member, Dr. Marti Jordan for all the feedback, input, and support provided during this process.

I would also like to acknowledge how grateful and thankful I am for Dr. Maxi Gordon, not only for allowing me to utilize his clinic to conduct my DNP project but also for taking a personal interest in my growth and my individual success. His knowledge, support, insight, and encouragement have helped bring this DNP project to completion. I would also like to thank my mentor, Dr. Deidra Thompson, for her feedback, preceptorship, input, expertise, and support throughout this journey.

DEDICATION

I would like to first and foremost, Thank God for carrying me and my family throughout this process and getting me where I am today. Without God, none of this could have been possible, and this dream would have never become a reality. I would like to dedicate this to my husband and my children who have stuck by me tirelessly throughout this process. I thank my husband Patrick, who has not missed a beat in caring for our two children as I pursued this dream. Your strength, support, and love show me that I can conquer anything. To my beautiful children Jaydan and Jordyn, thank you for all your support and understanding through the late nights, missed movie nights, and Saturday outings with daddy that mommy could not participate in because I was doing homework, or reading. To my parents, thank you for always supporting our dreams and pushing us to be a better version of ourselves. Thank you both for always encouraging me when I wanted to give up. To my Church family and Pastor, thank you all for your constant prayers and for always supporting me and my family. Finally, to my sister-in-law Gail, the Impetus for it all, thank you. I miss you, and I love you.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF ILLUSTRATIONS

LIST OF ABBREVIATIONS

AAN	American Association of Neurology
ADL	Activities of Daily Living
AIMS	Abnormal Involuntary Movement Scale
ANOVA	Analysis of Variance
APA	American Psychiatric Association
BID	Bis In Die (Twice a Day Dosing)
DNP	Doctor of Nursing Practice
DSM	Diagnostic and Statistical Manual of Mental Disorders
EPS	Extrapyramidal side effects
FDA	Food and Drug Administration
FGA	First Generation Antipsychotic
HRQoL	Health Related Quality of Life
ICD	International Classification of Disease
IRB	Institutional Review Board
KTA	Knowledge to Action
MD	Medical Doctor
NP	Nurse Practitioner
PA	Physician Assistant
PI	Principal Investigator
PMHNP	Psychiatric Mental Health Nurse Practitioner
PRN	Pro re nata (As Needed)

QOL	Quality of Life
SGA	Second Generation Antipsychotic
TD	Tardive Dyskinesia
VMAT2	Vesicular Monoamine Transporter-2
USM	The University of Southern Mississippi

CHAPTER I - INTRODUCTION

Throughout the six editions of the Diagnostic and Statistical Manual of Mental Disorders (DSM), the definition of schizophrenia has changed, yet three components have remained the same. The three components that have remained within the root of all the DSM editions are: (a) avolition, (b) the view that dissociative pathology is primary and fundamental, and (c) the stress on reality distortion (Tandon et al., 2013). Schizophrenia is a clinically diagnosed brain disorder with the hallmark symptom of psychosis, which incorporates auditory hallucinations and delusions (American Psychiatric Association [APA], 2013). According to the American Psychiatric Association (2013), diagnostic criteria for schizophrenia is six-fold but must "include two or more of the following: delusions, hallucinations, disorganized speech, grossly disorganized or catatonic behavior, and negative symptoms such as a diminished emotional expression or avolition; with each being present for a significant portion of time during a one-month period" (p. 99), with the specification that either delusions, hallucinations, or disorganized speech must be present (APA, 2013). Once the diagnosis of schizophrenia has been determined, and the decision to initiate treatment has been determined, treatment usually involves an antipsychotic medication.

Antipsychotics have been effectively used since the 1950s to treat schizophrenia, however, these medications have various side effects, including movement disorders like tardive dyskinesia (Bergman & Soares-Weiser, 2018). Tardive dyskinesia (TD) is a movement disorder that commonly affects the lips, tongue, jaw, face, periorbital areas, trunks, and limbs (Ricciardi et al., 2019). According to the American Psychiatric Association (2013), these symptoms generally develop in response to use of a neuroleptic

medication for at least a few months, persists despite discontinuing or changing the medication, and must remain present for one month after discontinuation of the medication, so as not to confuse TD with neuroleptic withdrawal emergent dyskinesia, which usually lasts less than four to eight weeks and occurs after discontinuation, dosage reduction, or medication change (Ward & Citrome, 2018). Several studies have identified disruptions in dopamine D2 receptors as well as oxidative damage as potential causes of TD, and although the literature indicates that second-generation antipsychotics (SGAs) are less likely to precipitate TD than first-generation antipsychotics (FGAs), the literature is still controversial (Ricciardi et al., 2019). As noted by Ricciardi et al., (2019), "equal rates of TD have been reported for SGA and FGA treatments in randomized controlled trials" (p. 389). According to Vasan and Padhy (2021), the average prevalence of TD is 20% of all individuals treated with FGAs, which differs significantly from the mean prevalence rates noted by Ricciardi et al. (2019), of 21% for patients being treated with an SGA and 30% for patients being treated with an FGA. According to the American Academy of Neurology (AAN, 2013), the prevalence of TD in outpatients with schizophrenia being treated with neuroleptics is 30%. According to Carroll and Irwin (2019) "In 2017, the global mean prevalence of TD among all patients taking antipsychotics was estimated to be 25.3%" (p. 811). Carroll and Irwin (2019) also note that the incidence rate for adults receiving FGAs or SGAs ranges from less than 1% to 42% annually with elderly patients being five times more likely to get TD than younger patients. These differing prevalence rates bring to the forefront the reality that all antipsychotics can be associated with TD development, and the recommended treatment guidelines suggesting withdrawal of antipsychotic medications or reduction in dosage,

are not clinically possible for patients with schizophrenia as these medications are integral for controlling their psychotic symptoms and preventing relapse (Bergman et al., 2017).

As noted by Ward and Citrome (2018), the American Academy of Neurology recently updated their TD treatment guidelines, and based on available evidence an A rating, which corresponds to established efficacy was awarded to two vesicular monoamine transporter-2 (VMAT2) inhibitors. Fortunately for patients suffering from TD, such as patients with schizophrenia unable to discontinue or augment their antipsychotic regimen, Valbenazine and Deutetrabenazine were both approved in 2017 for the treatment of TD by the United States Food and Drug Administration (Ward & Citrome, 2018). As studies are being conducted on the efficacy and safety of these VMAT2 inhibitors in treating TD among patients taking antipsychotics for various mood disorders, such as bipolar disorder, major depressive disorder, schizophrenia, and other psychiatric disorders, this specific DNP project focuses on patients diagnosed with schizophrenia. Research exists indicating that the impact of TD on health-related quality of life (HRQoL) for patients with bipolar disorder, major depressive disorder, and schizophrenia indicates that patients with schizophrenia and TD scored significantly lower on both mental and physical health-related quality of life measures (McEvoy et al., 2019).

Background

Tardive dyskinesia is classified as a hyperkinetic movement disorder that can be irreversible with localized or widespread involuntary movements (McEvoy et al., 2019). TD was first documented in 1957 after orofacial movements were noted with the

antipsychotic chlorpromazine and persisted after discontinuation or withdrawal (Caroff et al., 2018). Despite the available literature on the management of TD since TD was initially documented, guidelines on the management of TD remain inconsistent, difficult to understand, and appear geared towards the expert

care provider to decipher the intricacies (Vasan & Padhy, 2021). Some studies have shown improvement when the antipsychotic is decreased or discontinued, yet others have not. Some studies suggested using more potent antipsychotics, which is not supported by the American Academy of Neurology (2013), as neuroleptic agents cause TD and can mask symptoms rather than treat the symptoms. As noted by Carroll and Irwin (2019), "among patients with TD, healthcare utilization increased significantly in the 12 months after diagnosis compared with the 12 months before diagnosis, which included an overall increase in inpatient admissions, emergency room visits, and outpatient visits" (p. 815).

The approval of the VMAT2 inhibitors for the treatment of TD offers a solution to a problem previously riddled with inconsistent, unsatisfactory answers. For a patient diagnosed with schizophrenia, it is not clinically feasible to discontinue his antipsychotic and if the patient's psychotic symptoms are stable, switching antipsychotics generally would not be in the best interest of the patient, especially if the patient is tolerating his current medication regimen. As noted by Ricciardi et al. (2019) "the strongest current evidence for TD treatment is the use of the VMAT2 inhibitors, deutetrabenazine, and valbenazine" (p. 396). Available literature indicates that the VMAT2 inhibitors are effective for the treatment of TD with more favorable side effects; however, VMAT2 inhibitors are not widely available, they are expensive, they are not formulary, and there

is minimal long-term safety data available about the use of these inhibitors. If VMAT2 inhibitors are truly effective at treating TD, additional studies with data quantifying the effectiveness would be beneficial to the body of literature to help establish evidence-based guidelines for the management of TD that can be easily followed by primary care providers as well as psychiatric healthcare providers.

Significance

The symptoms of TD can have a significant effect on a patient's HRQoL as even subtle involuntary facial movements can have a significantly negative social and emotional correlation (McEvoy et al., 2019). McEvoy et al. (2019) estimated that the prevalence of TD is expected to increase due to the increased incidence of early-onset schizophrenia. Studies have shown that individuals with schizophrenia have higher mortality rates (McEvoy et al., 2019). For patients with schizophrenia, antipsychotics remain the best option for treating psychotic symptoms despite awareness that all FGAs and SGAs have the potential to cause TD (Jackson et al., 2021). Patients with TD can display impairments in several body systems, impacting their ability to carry out activities of daily living (ADLs). TD can affect gait and stability, speech, fine motor skills, and range of motion, creating challenges with psychosocial functioning (Strassnig et al., 2018). With so much focus on involuntary movements caused by TD, it is easy to forget that TD goes beyond involuntary movements and often affects patients socially, biologically, and psychologically. As noted by Jackson et al. (2021) "TD can have a profound negative impact on patient's day to day functioning and may lead to negative physical, cognitive, and psychosocial outcomes" (p. 1590). To assess the overall impact of TD on an individual, the social, physical, vocational, psychological, and psychiatric

domains must be assessed (Jackson et al., 2021) at each visit. Now that the FDA has approved 2 VMAT2 inhibitors for the treatment of TD, patients with schizophrenia do not have to alter their antipsychotic regimen to obtain relief from the debilitating symptoms of TD. Adding a VMAT2 inhibitor to the medication regimen has shown efficacy in modulating the symptoms of TD, however according to Stahl (2018) this inhibition is reversible and can be affected by changes in psychosis, mood, and other factors that also affect dopamine levels, therefore clinicians must be skilled in the ability to balance these factors when initiating VMAT2 inhibitors to ensure optimal patient outcomes. Effectively assessing the impact of VMAT2 inhibitors on TD symptoms through statistically significant improvements in assessment tools such as the Abnormal Involuntary Movement Scale (AIMS) can help generate best practice recommendations for TD treatment for healthcare providers.

Significance to Healthcare and Advanced Nursing Practice

The DNP-prepared advanced practice practitioner's role entails the ability to discern nuances in research to translate those findings into ways to improve patient care and clinical practice (Zaccagnini & Pechacek, 2021). The skill of translating research into practice requires the ability to address a complex clinical problem, identify evidence-based interventions to address the problem, and incorporative leadership skills during the implementation and evaluation of the outcomes with the overall goal of using new evidence obtained to improve health outcomes, patient outcomes, and clinical processes (Zaccagnini & Pechacek, 2021). Antipsychotics are a necessary component of schizophrenia treatment; however, prolonged use increases an individual's risk for extrapyramidal side effects (EPS) such as tardive dyskinesia (Othman et al., 2013). The

involuntary movements associated with tardive dyskinesia (TD) can affect a patient's mouth, lips, tongue, jaws, eyes, upper extremities, lower extremities, upper trunk, or any muscle in the body, with the likelihood of TD increasing the longer a patient takes antipsychotics (Othman et al., 2013). The physical disabilities, as well as the social and psychological implications of TD, can affect a patient's quality of life (QOL). According to Othman et al. (2013), QOL is an important health outcome measure that includes life satisfaction, social functioning, activities of daily living, and physical health. QOL has been utilized as an important measure of how well patients with schizophrenia can function and according to Othman et al. (2013), the severity of TD is negatively associated with quality of life which is consistent with prior studies indicating patients with schizophrenia have a poor quality of life and TD is one of the contributing factors to poor quality of life. As a healthcare provider and DNP-prepared advanced practice practitioner with a goal to improve patient outcomes, these findings outline the importance of recognizing and treating TD as efficiently as possible to improve the quality of life for patients.

Problem Statement

Tardive dyskinesia (TD) can have a major impact on multiple functional domains. The physical impact can impair communication by affecting swallowing, eating, gait, posture, and ADLs like self-care (Jackson et al., 2021). The physical effects that patients experience from TD can then affect their social relationships and affect them emotionally and psychologically, eventually affecting their quality of life (Othman et al., 2013). Jackson et al. (2021) note that "many patients and caregivers describe emotional and social impacts of TD as the most debilitating features of this disease" (p. 1593). Patients

describe unwanted attention from people staring at them as a culprit for feelings of self-consciousness and embarrassment, which can also worsen underlying psychiatric symptoms for patients already being treated for a mental health disorder. Some patients can become depressed and isolated, leading to further declines in quality of life (Jackson et al., 2021).

Available Knowledge

Current guidelines recommend the prevention of TD as the most important concern in clinical practice. Healthcare providers are cautioned to follow best practice guidelines when prescribing antipsychotics, which includes limiting prescription to specific indications, prescribing the minimal effective dose, and minimizing the duration of therapy when possible (Ricciardi et al., 2019). According to Correll et al. (2017; as cited in Citrome, 2018), there are many different risk factors for TD such as older age, antipsychotic exposure, female sex, African American ethnicity, prior mood disorder, cognitive disorder, history of alcohol abuse, diabetes, being HIV positive, use of lithium or antiparkinsonian agents, and use of FGAs. Education should be provided to patients about modifiable risk factors to prevent TD. Avoiding antipsychotics and other dopamine receptor blocking agents (DRBAs) is not possible in the management of schizophrenia as antipsychotics are the only foundational treatment currently available for schizophrenia (Citrome, 2018).

Before the FDA approval of VMAT2 inhibitors for the treatment of TD, few concrete treatment options were available for TD. The most common management strategy would include switching a patient from an FGA to an SGA while discontinuing any anticholinergic medications the patient was currently taking (Citrome, 2018). If no

improvement was noted in the TD, the patient would be switched to an alternate SGA, then switched to Clozapine if there was still no improvement in TD symptoms (Citrome, 2018). Suppression therapy was an additional consideration for severe, potentially life-threatening cases of TD, as was the case when TD interfered with breathing due to diaphragm muscle involvement. Suppression therapy entailed masking the TD by adding a potent first-generation antipsychotic medication (Citrome, 2018). In 2013, the American Academy of Neurology (AAN) introduced guidelines stating that there was insufficient data to support stopping the medication associated with TD to suppress symptoms, as well as the strategy of switching from an FGA to an SGA (AAN, 2013). The AAN also noted there was insufficient evidence to support or refute treatment of TD with vitamin E, buspirone, electroconvulsive therapy, reserpine, and deep brain stimulation, along with other strategies that have been posited throughout the years.

Needs Assessment

Attention to this issue at the local level was noted while working as a PMHNP-DNP student in a community-based outpatient psychiatric care clinic in central Mississippi. This healthcare facility provides comprehensive mental and physical health services, ranging from psychiatry to internal medicine. Several patients with the diagnosis of schizophrenia were noted with symptoms consistent with TD and required a change in their medication regimen. Some patients were often prescribed alternate antipsychotics, while others were noted on VMAT2 inhibitors. Some patients on VMAT2 inhibitors often were unable to tolerate one VMAT2 inhibitor and were subsequently switched to another VMAT2 inhibitor to control TD symptoms. I wondered how much of a change in the patients' TD symptoms could be expected from adding the VMAT2

inhibitors to their medication regimen, as opposed to simply switching their antipsychotic medication. American Psychiatric Association (APA, 2013) guidelines recommend TD monitoring every 6 months for patients treated with FGAs and every 12 months for patients on SGAs. For patients who are at high risk for TD, more frequent evaluations are indicated using a rating scale such as the AIMS scale to gauge improvements in involuntary movements associated with TD. The psychiatrist making the changes to the medication regimens had the knowledge to do so, which led me to also wonder if there were any guidelines available for treating TD with VMAT2 inhibitors in schizophrenic patients for other healthcare disciplines to reference in clinical practice. The FDA approved two VMAT2 inhibitors for the treatment of TD in 2017, valbenazine and deutetrabenazine. Given the emergence of these two drugs, the development of a treatment algorithm for TD management with VMAT2 inhibitors in patients with Schizophrenia is merited (Scorr &Factor, 2018) to guide collaboration across the disciples of psychiatry, neurology, and primary care. As a DNP student, implementing an evidence-based DNP project will add to the body of knowledge needed for the development of a TD treatment algorithm. I developed a data collection tool that would be utilized for this retrospective DNP project and discussed the findings with the medical director and approval was obtained to determine if the addition of a VMAT2 inhibitor compared to stopping, decreasing, or changing antipsychotics significantly decreases tardive dyskinesia symptoms after 90 days of initiation in schizophrenic patients with TD due to antipsychotic medication use.

PICOT

Among patients diagnosed with schizophrenia and started on antipsychotic medications, does the addition of a VMAT2 inhibitor, compared to stopping/decreasing or changing antipsychotics significantly decrease tardive dyskinesia symptoms after 90 days?

Purpose and Objectives

The purpose of this doctoral DNP project is to determine if VMAT2 inhibitors are more effective at treating tardive dyskinesia than previous alternatives in a real-world experience. The objective is to identify a statistically significant decrease in tardive dyskinesia symptoms for patients on VMAT2 inhibitors utilizing the AIMs to establish a clinically significant reduction in TD severity (Stacy et al., 2019). The aim is to increase the knowledge base of the healthcare profession on the use of VMAT2 inhibitors to treat TD and to add to the body of knowledge required to eventually increase access and availability of VMAT2 inhibitors to all patients, decrease costs of VMAT2 inhibitors to help establish them as available options on healthcare formularies and to establish evidence-based guidelines for the development of a treatment algorithm/protocol for TD management with VMAT2 inhibitors in patients with Schizophrenia.

Concepts

Abnormal Involuntary Movement Scale (AIMS)

The abnormal involuntary movement scale (AIMS) is a screening tool used to monitor symptoms of abnormal movement related to antipsychotic medication use (Stacey et al., 2019).

First Generation Antipsychotics (FGAs)

The earliest effective treatment for schizophrenia and other psychotic illnesses is also called conventional antipsychotics, classical antipsychotics, or typical antipsychotics (Stahl, 2018).

Health-Related Quality of Life (HRQoL)

Health-related quality of life (HRQOL) is an individual's or a group's perceived physical and mental health over time (Centers for Disease Control and Prevention [CDC], 2021).

Neuroleptics

Antipsychotic drugs used to treat psychiatric disorders (Carroll & Irwin, 2019)

Quality of Life (QOL)

Similar to Health-Related Quality of Life.

Second Generation Antipsychotic (SGAs)

Second-generation antipsychotics (SGAs), also known as atypical antipsychotics, generally have a lower risk of extrapyramidal side effects and tardive dyskinesia compared with first-generation antipsychotics (Stahl, 2019).

Tardive Dyskinesia (TD)

A hyperkinetic movement disorder is defined by abnormal involuntary movements that occur most often in the orofacial area but can occur in the neck, trunk, upper and lower extremities, and any muscles (Jackson et al., 2021).

Vesicular Monoamine Transporter 2 (VMAT2) Inhibitors

The vesicular monoamine transporter type 2 (VMAT2) inhibitors are agents that cause a depletion of neuroactive peptides such as dopamine in nerve terminals and are

used to treat chorea due to neurodegenerative diseases, or dyskinesias due to neuroleptic medications (Stahl, 2018).

Theoretical Framework

This DNP project will utilize a portion of The Theory of Unpleasant Symptoms as a foundational guide. The Theory of Unpleasant Symptoms, which was developed in 1995 presents three main elements: the symptoms that the patient is experiencing; the factors that influence those symptoms, and the consequences of that experience (Gomes et al., 2019). Experienced symptoms are the central focus of the model, described as indicators of change in the health status of the individual, which often occurs multiple times and simultaneously. The theory outlines four dimensions: intensity, time, suffering, and quality; as well as three categories of these dimensions which are the physiological, psychological, and situational factors that relate to each other beyond their individual relationships with the symptoms (Gomes et al., 2019). The final component of the Theory is the consequence that reflects the functional and cognitive responses given to the experience of the symptoms (Gomes et al., 2019). As noted by Gomes et al. (2019), the Theory of Unpleasant Symptoms is very useful in research "because the theory provides the identification of the dimensions of the symptoms and their relationships, which can be used as a starting point for the development of clinical instruments and research, since it is sufficiently precise in its theoretical framework" (p. 7).

The Knowledge to Action Framework will also be utilized as a conceptual framework for the implementation of this DNP project. According to Field et al. (2014), conceptual frameworks are broad and provide a frame of reference for organizing thinking and provide a guide for action and interpretation. The Knowledge to Action

Framework (KTA Framework), “is a conceptual framework intended to help those concerned with knowledge translation deliver sustainable, evidence-based interventions” (Field et al., p. 2). The KTA Framework was developed by Dr. Ian Graham and colleagues in Canada in the 2000s as a response to the multitude of terms used to describe the process of moving knowledge into action (Field et al., 2014). The KTA Model Framework is composed of two components, Knowledge Creation and the Action Cycle with each component having several phases that overlap. The Action phases can be conducted simultaneously, and knowledge phases impact the action phase (Field et al., 2014). The Action Cycle describes the process representing the activities needed for knowledge to be applied to practice, whereas knowledge is adapted to the local content allowing for barriers and facilitators of its use to be assessed (Field et al., 2014). For this DNP project, application of the “Action” cycle will entail the activities during the implementation portion of this DNP project as I collect data on patients via retrospective chart reviews utilizing the data collection tool. The results obtained will be utilized to decipher the specific knowledge obtained from the DNP project, which will then be utilized to help establish if the results will be disseminated as “Knowledge into Action” into the healthcare environment.

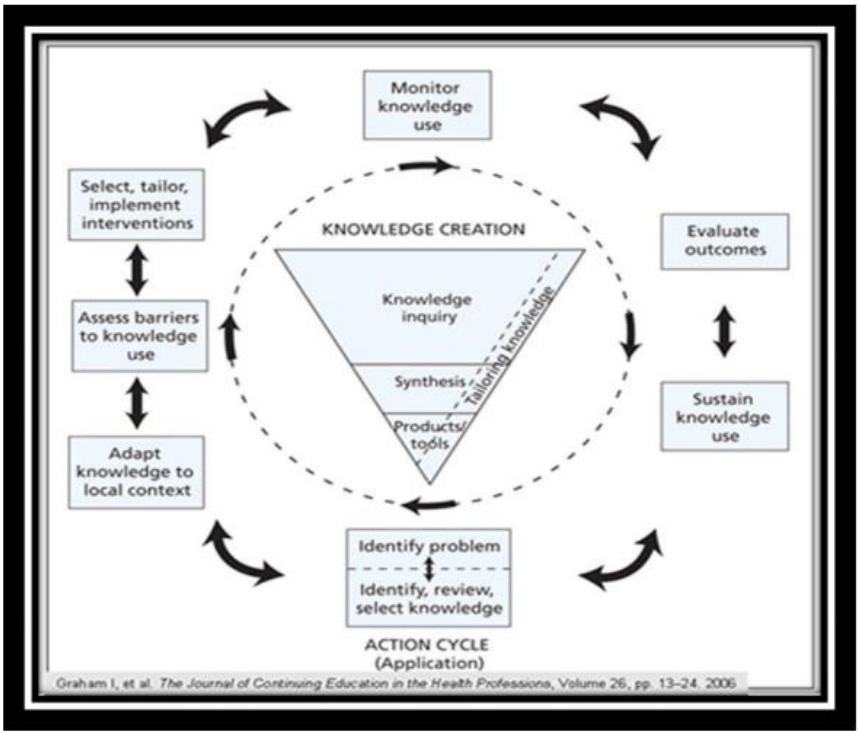


FIGURE 1. Knowledge to action cycle.

Figure 1. Knowledge to Action Cycle.

(Graham et al., 2006, pp. 24).

Synthesis of Evidence

A literature search was conducted on the following databases: CINAHL, MEDLINE, PsychINFO, PubMed, Google Scholar, Cochrane Database, and Science Direct. Key terms used in the review of literature were: tardive dyskinesia, schizophrenia, evidence-based treatment, VMAT2 inhibitors, screening for tardive dyskinesia, abnormal involuntary movement scale, Secondary terms were “social function for schizophrenia”, “antipsychotic screening for tardive dyskinesia,” “tardive dyskinesia management and schizophrenia,” “treatment of tardive dyskinesia,” “VMAT2 inhibitors and schizophrenia,” “abnormal involuntary movement scale,” “health-related quality of life,” “knowledge to action framework,” “frameworks.” Filters included full-text articles

written between the years 2012 to 2021. The search yielded over 900 articles. These articles were narrowed down based on whether they included the main criteria which were information about 5 specific topics: tardive dyskinesia, schizophrenia, antipsychotics, the AIMS, and VMAT2 inhibitors. Articles were excluded that focused on "movement disorders, as opposed to specifically on tardive dyskinesia. From the articles reviewed, 30 were selected for a critical appraisal for inclusion in the DNP project.

Prevention of Tardive Dyskinesia

Tardive dyskinesia is a hyperkinetic disorder that affects patients' orofacial muscles, neck muscles, neck and trunk muscles as well as upper and lower extremity muscles (Jackson et al., 2021). Consensus in the literature is that prevention of TD is the most important consideration in the management of TD, therefore clinicians should be cautious to ensure they are following best practice guidelines when prescribing antipsychotics, utilizing minimal effective dosages, and minimizing the duration of therapy when possible (Ricciardi, 2019). As noted by Strassnig et al. (2018), there are patients prescribed antipsychotics who have no diagnosis of a condition that would require antipsychotics. Antipsychotics are also being prescribed off-label to allay symptoms unrelated to psychosis. Healthcare providers should identify alternative treatment options for these patients when considering the risk/benefit analysis. Citrome (2018) also notes that ideally, it is best to prevent TD by identifying modifiable risk factors and working with patients to eliminate those risk factors such as alcohol and substance abuse.

Tardive Dyskinesia Causes Decline in Quality of Life

TD can have a significant negative impact on a patient's daily functioning, leading to negative physical, cognitive, and psychosocial outcomes. Even mild physical impairments can cause anxiety and problems with activities of daily living (Jackson et al., 2021). Healthcare professionals must assess patients with TD for impairments in social functioning, physical functioning, vocational functioning (job duties, employment), psychological functioning, as well as for worsening of their psychiatric disorders, as these impairments can worsen due to insufficient control or relapse (Jackson et al., 2021). As noted by McEvoy et al. (2019), patients with TD and schizophrenia had the lowest scores on all health-related quality of life indicators indicating that TD has a major impact on the physical health burden for patients already experiencing the burden of mental illness. According to Caroff et al. (2018) “studies have shown correlations between impaired cognition, poor response to treatment, greater risk of relapse, longer hospital stays, lower quality of life and functioning, a progressive course, and increased mortality” (p. 3). As noted by Othman et al. (2013), quality of life is an important health outcome measure that includes life satisfaction, social functioning, activities of daily living, and physical health, and is an important indicator of how well patients with schizophrenia are functioning. Otthman et al. (2013) found that the severity of TD was negatively correlated with quality of life.

FGAs and SGAs May Have Similar TD Risk

The literature shows that TD can occur during or after stopping treatment with a dopamine receptor antagonist or partial agonist, which includes both FGAs and SGAs (Jackson et al., 2021). The literature also indicates that although SGAs were identified as

having a lower likelihood of causing TD, the research on SGA's is inconsistent as there are as many studies to refute the efficacy as there are to corroborate the claims. Ward and Citrome (2018), note that more studies will be necessary to determine the impact of atypical antipsychotics/SGAs on TD risk, citing a real-world prospective DNP project which noted that the adjusted TD incidence rate for patients on SGAs alone versus FGAs alone was only 0.68 with a 95% confidence interval of 0.29 to 1.64 which suggests that there may be little to no difference between the two classes of antipsychotics as it relates to TD risk.

VMAT2 Inhibitors are Effective Treatments for Tardive Dyskinesia

The use of deutetrabenazine and valbenazine has been proven to be effective in the treatment of TD, although further studies are needed to solidify the safety and efficacy of these drugs due to their new nature (Ricciardi, 2019). Caroff, Aggarwal, and Yonan (2018) documented the clinical effectiveness of valbenazine in the treatment of TD in larger, more rigorously designed studies. Stahl (2018), also noted the effectiveness of VMAT2 inhibitors in treating TD, but also noted that this inhibition is reversible and the degree of VMAT2 inhibition needed for a specific patient depends on several factors and can be affected by mood as well as psychosis status (Stahl, 2018). Ward and Citrome (2018) note that Level A evidence for efficacy exists for VMAT2 inhibitors, and there are no additional FDA-approved medications for the treatment of TD.

Summary of Evidence

The use of deutetrabenazine and valbenazine has been proven to be effective in the treatment of TD, although further studies are needed to solidify the safety and efficacy of these drugs due to their new nature (Ricciardi, 2019). Caroff et al. (2018)

documented the clinical effectiveness of valbenazine in the treatment of TD in larger, more rigorously designed studies. Stahl (2018), also noted the effectiveness of VMAT2 inhibitors in treating TD, but also noted that this inhibition is reversible and the degree of VMAT2 inhibition needed for a specific patient depends on several factors and can be affected by mood as well as psychosis status (Stahl, 2018). Ward and Citrome (2018) note that Level A evidence for efficacy exists for VMAT2 inhibitors, and there are no additional FDA-approved medications for the treatment of TD.

DNP Essentials

At the culmination of this DNP project, the DNP essentials have been met. The DNP Essentials outlined in this DNP project establish mastery of the advanced practice nurse practitioner discipline. Essential I: Scientific Underpinnings for Practice (American Association of Colleges of Nursing (AACN), 2006) was fulfilled by integrating the science of nursing using analytical approaches to evaluate current processes for implementing guidelines for the management of tardive dyskinesia with VMAT2 inhibitors in patients with schizophrenia. Knowledge obtained was analyzed and organized to develop an algorithm for the management of tardive dyskinesia for patients with schizophrenia. Essential II: Organizational and Systems Leadership for Quality Improvement and Systems Thinking (AACN, 2006), was met by utilizing advanced communication processes throughout the implementation of this DNP project to gain collaborative knowledge on the subject matter from doctors, nurse practitioners, as well as executive pharmaceutical representatives to improve patient safety and analyze the cost-effectiveness of VMAT2 inhibitor use for the treatment of tardive dyskinesia.

Essential III: Clinical Scholarship and Analytical Methods for Evidence-Based Practice (AACN, 2006) was met by applying relevant findings to develop a treatment protocol for the management of tardive dyskinesia with VMAT2 inhibitors in patients with schizophrenia. Essential VI: Interprofessional Collaboration for Improving Patient and Population Health Outcomes (AACN, 2006) was met by using leadership skills with interprofessional collaboration to create change in the process for managing tardive dyskinesia (TD). Essential VII: Clinical Prevention and Population Health for Improving the Nation's Health (AACN, 2006), was met using statistical measures to analyze the DNP project population. Essential VII was also met by statistical measures to synthesize concepts from the population to evaluate data results and provider interventions to identify outcomes. Essential VIII: Advanced Nursing Practice (AACN, 2006) was met through the comprehensive assessment of management practices of providers in a rural health clinic. Advanced levels of clinical judgment, systems thinking and evaluating evidence-based care to improve patient outcomes were demonstrated throughout the implementation of the DNP project. An algorithm for the management of TD with VMAT2 inhibitors in patients with schizophrenia was developed to educate healthcare professionals to improve patient outcomes and minimize interruptions in patients' stable antipsychotic regimens.

Summary

Tardive dyskinesia is a treatable side-effect of antipsychotic medications. The increasing use of antipsychotic drugs and the implications this increased use has for tardive dyskinesia monitoring raises concerns. As antipsychotics are being used to treat more than just schizophrenia, health-related quality of life has the potential to decrease.

The emergence of VMAT2 inhibitors provides the opportunity for patients on antipsychotics to remain on their medication regimens when tardive dyskinesia symptoms emerge; however, healthcare providers in areas unrelated to mental health need readily available resources to help them gain familiarity with VMAT2 inhibitors and how to initiate and manage them. The literature indicates VMAT2 inhibitors are effective at controlling TD symptoms. Several DNP essentials will be utilized to implement a DNP project to gauge how efficiently the VMAT2 inhibitors are able to control TD symptoms in patients with schizophrenia.

CHAPTER II - METHODS

Setting

The setting for this DNP project with be mainly in a rural healthcare clinic that provides holistic care to patients. The clinic provides general medicine, psychiatric services as well as professional counseling and psychosomatic care to the patient population served. The clinic utilizes a comprehensive approach to mental wellness that meets patients where they are to get them where they need to be. This is a privately owned clinic located in an urban Metropolitan area. The clinic accepts all types of health insurance; however, a majority of the patients utilize Medicare and Medicaid. Uninsured patients are also accepted at this facility and are billed for services based on a self-pay system. Demographic data for the location of this clinic indicates that the population base consists of 54.77% females and 45.23% males. The racial make-up of the population served by this rural health clinic consists of 53% Caucasians, 39% African American, 5% Asian, and 3% other races.

This clinic consists of two providers that can prescribe medications: one psychiatrist (Doctor of Medicine), and one dually certified Family Nurse Practitioner/Psychiatric Mental Health Nurse Practitioner, as well as rotating Nurse Practitioner students and rotating Physician Assistant students. The psychiatrist and nurse practitioner at this facility also have prescribing privileges at four different clinic locations as well as three group homes. Data from the medical records will be collected from all these locations. This practice was selected as the source for gathering information because the principal investigator (PI) spent clinical time in these clinics and had the opportunity to interact with patients taking psychotropic medications that caused

tardive dyskinesia and noted a significant number of these patients had a diagnosis of schizophrenia. A letter of support from the clinic director was obtained before implementing the DNP project.

Population

The population for this DNP project includes a convenience sample of mental health patients between the ages of 20 to 75 years of age that have been diagnosed with schizophrenia and started on antipsychotic medications and subsequently initiated on a VMAT2 inhibitor for the presence of tardive dyskinesia symptoms. This DNP project entails a retrospective review of medical records and progress notes completed by prescribing providers (MD, NP, PA). The 10th version of the International Classification of Disease (ICD-10) was used to identify diagnosis codes for inclusion in this DNP project. The fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) was also utilized to identify diagnosis codes for inclusion in this DNP project. All psychiatric diagnoses identified by DSM-V to fall under the schizophrenia spectrum and other psychotic disorders were reviewed for inclusion in this DNP project. The DSM-V diagnoses chosen for inclusion in this DNP project are identified within ICD-10 codes F20 through F29, specifically F20.9 (Schizophrenia), F20.81(Schizophreniform disorder), F21 (schizotypal disorder), F22 (Delusional Disorder), F25.0 (schizoaffective disorder, bipolar type, and F25.1(schizoaffective disorder, depressive type). Additional ICD-10 codes pertinent for inclusion in this project include G24.01 (Drug-Induced Subacute Dyskinesia), and G24.4 (Orofacial Dyskinesia).

Design

This DNP project is a descriptive study. The DNP project will include a retrospective chart review of medical records and progress notes entered by prescribers to determine if the use of VMAT2 inhibitors, compared to decreasing, stopping, or changing antipsychotics, significantly decreases tardive dyskinesia symptoms after 90 days. Data collected from the chart reviews were recorded on the data collection tool developed specifically for this DNP project. The data collection tool allowed for patients to be assigned a random identification number with no identifying information on the form. Data collected was then transferred to an Excel spreadsheet and SPSS was utilized to analyze the data and make interpretations for the DNP project results.

Procedures

After obtaining USM IRB approval (protocol # 21-307), a retrospective chart review will be conducted to identify patients that meet inclusion criteria for this DNP project. The medical records of those patients will be reviewed to determine the prescribing providers' course of action after the diagnosis of tardive dyskinesia has been identified or documented. Specifically, the medical records will be reviewed to identify those patients initiated on VMAT2 inhibitors versus those patients in whom the prescribing provider chose to either decrease, stop, or change the antipsychotic deemed responsible for the tardive dyskinesia symptoms. The medical records will also be reviewed to identify the AIMS score utilized to document the baseline assessment, as well as the AIMS scores documented to assess TD symptom improvement. The data extractor is a part-time/PRN prescriber and family nurse practitioner (FNP) at the rural healthcare clinic.

Progress notes and medical records will be accessed by the data abstractor. Records from the timeframe of January 01, 2020, through the present day, will be abstracted for inclusion criteria which include males and females between the ages of 20 to 75 years with a diagnosis identified within the schizophrenia spectrum and other psychotic disorders which includes “schizophrenia, schizotypal disorder, and other psychotic disorders, which are identified based on abnormalities in one or more of the five domains of delusions, hallucinations, disorganized thinking or speech, grossly disorganized or abnormal motor behavior, and negative symptoms” (APA, 2013, p. 87).

For the patients that meet inclusion criteria, I will identify those that were initiated on VMAT2 inhibitors, those whose antipsychotic was stopped, and those whose antipsychotic was changed to a different antipsychotic. I will then compare the initial AIMS score from when Tardive Dyskinesia (TD) was first diagnosed with the AIMS scores at 30 days, 60 days, and 90 days follow-up to determine what impact each had on the AIMS scores. The goal is to determine if VMAT2 inhibitors have a more profound effect on the AIMS score. The long-term goal is to help add to the literature to establish VMAT2 inhibitors as a credible treatment for patients with tardive dyskinesia in hopes of making these medications more widely available, formulary, and establishing them as 1st line treatment for TD.

Data Collection

A retrospective record review will be done by the principal investigator (PI) to collect data regarding Tardive Dyskinesia Symptoms. A data collection form has been developed for utilization in this DNP project. No identifying information will be on the data collection form. The data collected on the data collection tool will include a few

basic demographics, whether there is a diagnosis of schizophrenia, and if the patient was started on antipsychotics. The specific data collected will include age, sex, race, Schizophrenia diagnosis, whether the patient was started on an antipsychotic, whether the patient has a documented diagnosis of tardive dyskinesia, the date TD was first documented, initial AIMS score, prescribing provider's intervention (whether initiated on a VMAT2 inhibitor, or whether the antipsychotic was stopped, changed, or decreased), and the AIMS score at 30 days, 60 days, and 90 days post provider intervention. Information from the data collection tool will then be transferred to an excel spreadsheet. Data will then be analyzed and reported in a de-identified, aggregate form.

Protection of Human Subjects

Participants' anonymity and confidentiality will be maintained. IRB approval for this DNP project was requested through the University of Southern Mississippi's Institutional Review Board (IRB) and approval was granted through Protocol Number 21-307. To protect the confidentiality, data will be recorded on a password-protected spreadsheet on an encrypted file, using only a unique study number. Data will be analyzed and reported in a de-identified, aggregate form. DNP project records will be stored on the investigator's identity authenticated, secure firewall-protected, personal computer. Every effort will be made to maintain the confidentiality of DNP project records. Information collected during the DNP project will be identified by a unique DNP project number. Information from the medical record will be recorded on a password-protected spreadsheet on an encrypted file. Data were analyzed and reported in a de-identified, aggregate form. Investigational records from this DNP project will be maintained in a confidential manner. Consistent with IRB retention requirements, the

DNP project records will be maintained for six years after completion of the DNP project. Thereafter, paper and electronic records will be destroyed or erased using data overwriting software per USM policy and confidential methods. Subsequent analyzed aggregate data will be maintained to enable retrieval if requested during consideration for publication. The DNP project is no greater than minimal risk and will have no direct impact on patients' rights, welfare, or clinical care. Identified measures were implemented to minimize the risk of a breach of confidentiality during record review and data collection.

Ethical Considerations

According to Chism (2019), the Belmont Report states that "if there is any element of research in an activity, that activity should undergo review for the protection of human subjects" (p. 111). The Belmont Report identifies three principles for human subject research which include: respect for persons, beneficence, and justice. These principles, discussed in further detail below are utilized to analyze and resolve ethical concerns in healthcare issues related to human subjects.

Respect for Persons

Respect for persons, as noted by Chism (2019) involves maintaining an individual's capacity for autonomous choice, respecting the privacy of individuals, protecting confidential information, obtaining consent for interventions, and helping individuals make important decisions when asked. This DNP project is a retrospective chart review. I am obtaining data from records in existence at the time of this submission. The DNP project involves no prospectively collected data so there is no access to patients or opportunity to seek informed consent. A waiver of consent will be sought from the

USM IRB as recontacting these patients to obtain informed consent would be impracticable and would hinder this researcher's ability to conduct the study. Although the principal investigator will know who the patients are initially while conducting chart reviews of the medical records, anonymity will be maintained beyond this point via de-identification and the use of codes that cannot be used to identify the patients.

Beneficence

As noted by Chism (2019), the principle of beneficence entails the obligation to act for the benefit of others. A general requirement for beneficence is knowing the values, beliefs, and cultural practices of individuals to act in their best interest. This DNP project consists of a retrospective chart review based on documented information already present in the patients' medical records and progress notes. There is no direct contact with these patients and no opportunity to delineate their values, beliefs, or cultural practices unless previously documented in the records. No harm will be inflicted on participants as this is a retrospective chart review. The principle of beneficence is noted in this DNP project by the long-term goals of the study. The long-term goal is to help add to the literature to establish VMAT2 inhibitors as a credible treatment for patients with tardive dyskinesia in hopes of making these medications more widely available, formulary, and establishing them as 1st line treatment for TD. There are no direct benefits for the patients enrolled in this DNP project. Rather, future patients requiring treatment for tardive dyskinesia may benefit from knowledge gained from this DNP project.

Justice

The principle of justice entails treating people without prejudice and incorporates the equitable distribution of benefits as well as burdens (Chism, 2019). The privacy of

patients selected for this DNP project based on inclusion criteria will be maintained and all data from the selected patients will be treated fairly and equally. Although the sampling for this DNP project involves a convenience sample, selected patients will be chosen based on meeting all inclusion criteria without prejudice.

Summary

The methods used to implement this DNP project followed the office of Research Integrity guidelines ensuring risk to subjects was minimized and the data collected was monitored to ensure the safety of the patients. Patient privacy and data confidentiality were maintained by using a carefully designed plan that allowed for patients to be assigned random identification numbers with no identifying information. Although this was a retrospective review, ethical principles such as respect for persons, beneficence, and justice were utilized in the data collection process. Ensuring proper procedures are implemented during the data gathering process, improves the reliability of the results.

CHAPTER III – RESULTS

The purpose of this DNP project was to determine if VMAT2 inhibitors are more effective at treating tardive dyskinesia than previous alternatives in a real-world experience. A retrospective chart review was performed on 70 records that were chosen through a convenience sample of patients being treated by one physician and two nurse practitioners. An exhaustive chart review was conducted on each record for DNP project inclusion criteria. Each chart was reviewed to determine if the patient had the required DSM-V Schizophrenia Spectrum and related disorders diagnosis, and if so, the earliest date noted for when the patient was diagnosed was also identified. The date the patient was started on an antipsychotic for schizophrenia was also identified, along with any documentation of tardive dyskinesia symptoms, or suspected tardive dyskinesia symptoms. If there was documentation of tardive dyskinesia (TD) present, the date the patient's tardive dyskinesia symptoms first started was noted. The intervention the healthcare provider planned to implement was also identified and noted along with the date the intervention was implemented. The charts were also reviewed to ensure that AIMs scores were present.

Within the 70 charts reviewed, when patients were noted to show positive signs of tardive dyskinesia that met treatment guidelines, there was no documentation of the healthcare providers changing the patients' antipsychotics, stopping their antipsychotics, or decreasing their antipsychotics. The main intervention was the initiation of a VMAT2 inhibitor for the treatment of TD, therefore no records were identified for comparison with the intervention of initiation of a VMAT2 inhibitor. The date the patient was started on the VMAT2 inhibitor was identified along with the initial AIMs score when the

intervention was implemented. AIMs scores were identified for the patients at four weeks, eight weeks, and twelve weeks after the VMAT2 inhibitor was initiated, along with the dates when these AIMs scores were obtained. The current VMAT2 inhibitor that the patient was on was also noted at four, eight, and twelve weeks.

Fifteen (N=15) records were identified to meet inclusion criteria for the DNP project. All records included in this DNP project are for patients between the ages of 25 to 65 on an approved VMAT2 inhibitor for at least 90 days, with a diagnosis within the DSM-V Schizophrenia Spectrum and other Psychotic Disorders of either: (a) schizophrenia (F20.9), (b) schizophreniform disorder (F20.81), (c) schizotypal disorder (F21), (d) delusional disorder (F22), or (e) schizoaffective disorder (F25.0). The data from the reviews was logged on the data collection tool created by the principal investigator, and the data were analyzed using SPSS to conduct a Repeated Measures Analysis of Variance (ANOVA) on the data. All of the patients that met inclusion criteria were male (N=15; 100%). Over half of the patients were African American males (N= 8; 53.3%), 40% (N=6) were Caucasian, and 6.7% (N=1) were Asian. Forty percent of the patients (N=6) were between the ages of 56-65, another 40% (N=6) were between the ages of 46-55, an additional 13.3% (N=2) were between the ages of 36-45, and 6.7% (N=1) were between the ages of 25-35.

Table 1 identifies the AIMS scale scores for each of the 15 patients as well as the medication each was initiated on for the treatment of TD. Eighty percent (N=12) of the patients have initiated on Ingrezza 40mg and 20% (N=3) of the patients were initiated on Austedo 6mg BID. The AIMS scale scores ranged from 11 to 18 which is clearly depicted in Figure 2. Table 1 however, provides more insight on the percentage of

patients taking each medication with the corresponding AIMS scores, as 66.7% (N=2) of the patients that were started on Austedo were noted to have an initial AIMS score of 14. After 30 days of being on the VMAT2 inhibitors, these patients were generally titrated to the next dose by this 30-day period as Ingrezza can be increased from 40mg to 80mg after one week and Austedo is usually initiated at 6mg twice a day and titrated up by 6mg weekly as tolerated by the patient to a maximum dose of 48 milligrams daily in equally (24 mg BID) divided doses (Stahl, 2019). Two of the patients' medications were switched before they reached the 30-day period. One patient was initially started on Austedo 6mg but was switched to Ingrezza secondary to either no improvement or worsening symptoms. This information was unclear from the documentation in the patient's chart. The other patient was taken off Ingrezza 40mg secondary to a possible allergic reaction however the patient was switched to Austedo 6mg without any problems weeks later.

Table 1

*Initial AIMs Test Score * Initial VMAT2 Inhibitor Initiated Crosstabulation*

		Medication@Initial					
		Ingrezza 40mg		Austedo 6mg BID		Total	
		N	%	N	%	N	%
Initial AIMs	11	1	8.3%	0	0.0%	1	6.7%
	12	2	16.7%	0	0.0%	2	13.3%
	13	3	25.0%	0	0.0%	3	20.0%
	14	1	8.3%	2	66.7%	3	20.0%
	15	2	16.7%	0	0.0%	2	13.3%
	16	2	16.7%	1	33.3%	3	20.0%
	18	1	8.3%	0	0.0%	1	6.7%
Total		12	100.0%	3	100.0%	15	100.0%

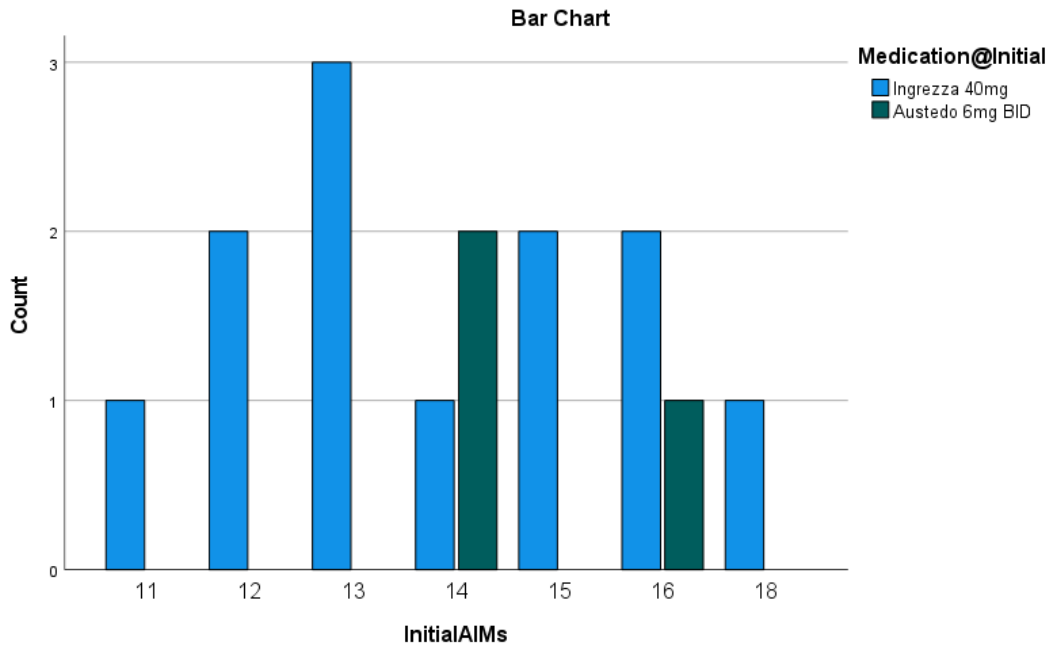


Figure 2. Graph by Medication of AIMs Scores for all Patients when VMAT2 Inhibitor Initiated

As noted in Table 2, the AIMS scale scores have decreased from a previous range of 11-18 to 9-15 after the patients have been on the VMAT2 Inhibitors for at least 30 days. At this stage, the patients are on four different doses of VMAT2 inhibitors as 60 % (N=9) of the patients have been titrated to the 80mg dose of Ingrezza, and 20% (N=3) are still on Ingrezza 40mg. In addition to this 13.3% (N=2) have been titrated up to the 12 mg twice a day dosing of Austedo and there is one patient that is on Austedo 6mg twice a day. As noted in Figure 3, of the nine patients on Ingrezza 80mg, 55.5% (N=5) of them still have an AIMS score of 13 or above.

Table 2

*Initial AIMs Test Score * Medication After 30 Days Crosstabulation*

		Medication@30Days									
		Ingrezza 40mg		Ingrezza 80mg		Austedo 12mg BID		Austedo 6mg BID		Total	
		N	%	N	%	N	%	N	%	N	%
AIMSat30Da	9	0	0.0%	1	11.1%	0	0.0%	0	0.0%	1	6.7%
ys	11	1	33.3%	2	22.2%	0	0.0%	0	0.0%	3	20.0%
	12	1	33.3%	1	11.1%	1	50.0%	0	0.0%	3	20.0%
	13	0	0.0%	3	33.3%	0	0.0%	1	100.0%	4	26.7%
	14	0	0.0%	1	11.1%	1	50.0%	0	0.0%	2	13.3%
	15	1	33.3%	1	11.1%	0	0.0%	0	0.0%	2	13.3%
Total		3	100.0%	9	100.0%	2	100.0%	1	100.0%	15	100.0%

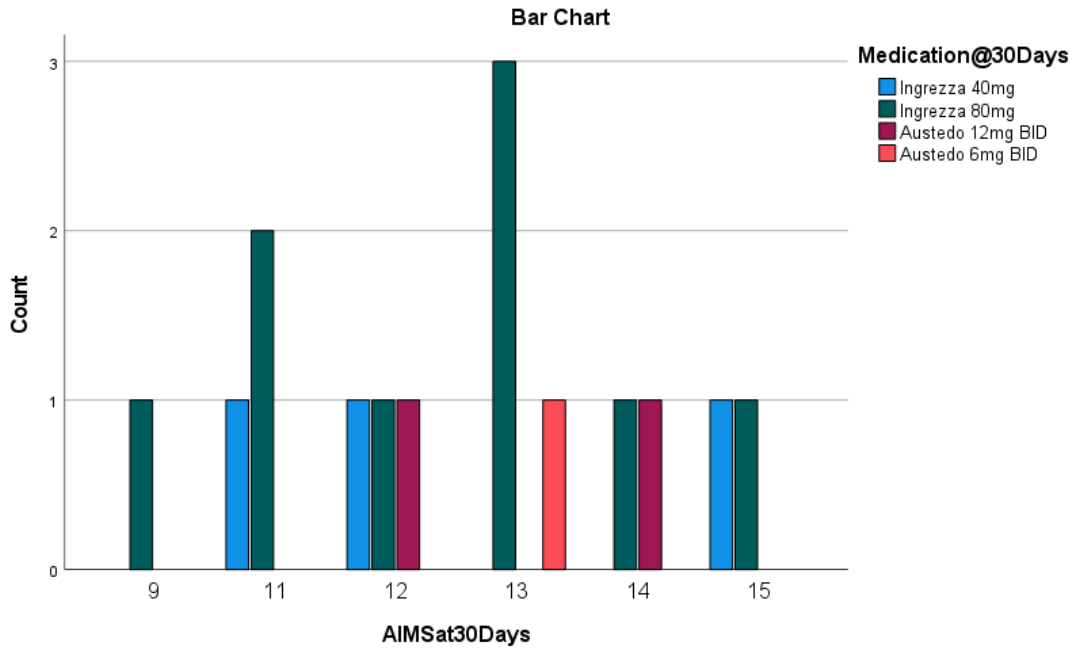


Figure 3. Graph of AIMS Scores for all Patients after 30 Days of VMAT2 Inhibitors Use by Medication

After 60 days of VMAT2 Inhibitor use, 66.6% (N=10) of the patients had documented AIMS scale scores of 10 to 11, as noted in Table 3 with a mean AIMS score

of 11.13% at this time. During this timeframe, all patients had transitioned to Ingrezza 80mg or Austedo 12 mg with significant drops noted in some of the AIMS scale scores for some patients, with one patient's score being documented as 5 at this point and only 13.4% (N=2) of patients AIMS scores still above 12. Figure 4 again shows the AIMS score counts by the medication the patient is currently taking after 8 weeks.

Table 3

*Initial AIMs Test Score * Medication after 60 Days Crosstabulation*

		Medication@60Days					
		Ingrezza 80mg		Austedo 12mg BID		Total	
		N	%	N	%	N	%
AIMS@60Days	5	1	8.3%	0	0.0%	1	6.7%
	10	2	16.7%	0	0.0%	2	13.3%
	11	4	33.3%	1	33.3%	5	33.3%
	12	3	25.0%	2	66.7%	5	33.3%
	13	1	8.3%	0	0.0%	1	6.7%
	14	1	8.3%	0	0.0%	1	6.7%
Total		12	100.0%	3	100.0%	15	100.0%

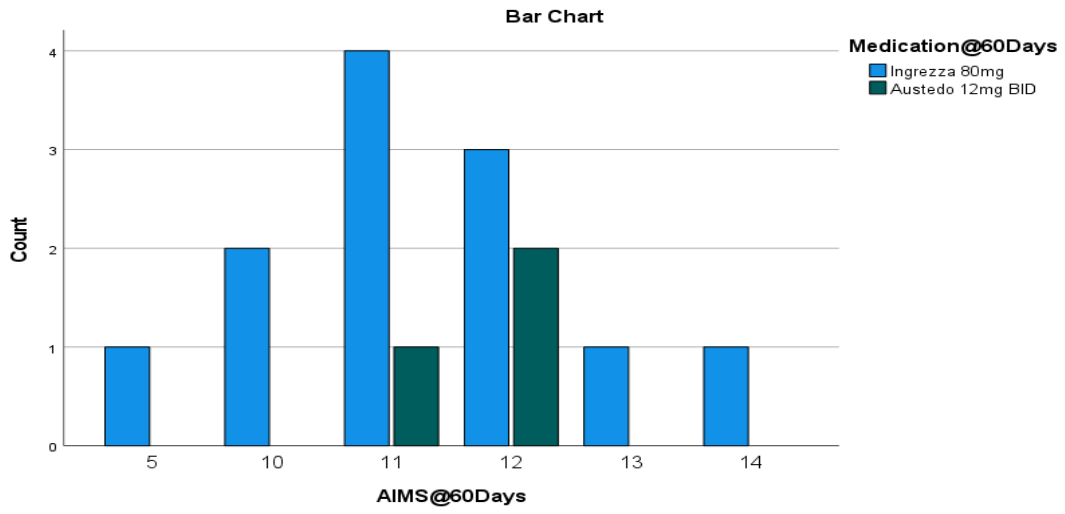


Figure 4. Graph of AIMS Score for All Patients after 60 Days of VMAT2 Inhibitors Use by Medication.

After 12 weeks, 80% (N=12) of the patients remained on Ingrezza 80 mg and 20% (N=3) remained on Austedo 12mg. The mean AIMS scale scores were 9.87% and, the range of AIMS scale scores was from five to 13 as noted in Table 4 and Table 5. Figure 4 shows the minimum and maximum point decrease in the AIMS total score for all 15 patients that met inclusion criteria. According to these results three patients had a two-point total decrease in their initial AIMS score, three patients had a three-point total decrease in their initial score, one patient had a four-point decrease in his initial AIMS score, four patients had a five-point total decrease in their AIMS scores, three patients had a six-point total decrease in their initial AIMS score, and one patient had a seven-point total decrease in his AIMs scale score over the 12-week study.

Table 4

*Initial AIMs Test Score * Medication After 90 Days Crosstabulation*

		Medication@90Days					
		Ingrezza 80mg		Austedo 12mg BID		Total	
		N	%	N	%	N	%
AIMS@90Days	5	1	8.3%	0	0.0%	1	6.7%
	9	1	8.3%	2	66.7%	3	20.0%
	10	7	58.3%	0	0.0%	7	46.7%
	11	2	16.7%	1	33.3%	3	20.0%
	13	1	8.3%	0	0.0%	1	6.7%
Total		12	100.0%	3	100.0%	15	100.0%

Table 5

Descriptive Statistics for AIMS Scale Scores

	N	Range	Minimum	Maximum	Sum	Mean	Std. Deviation	Variance
Initial AIMs	15	7	11	18	212	14.13	1.885	3.552
AIMSat30Days	15	6	9	15	188	12.53	1.642	2.695
AIMS@60Days	15	9	5	14	167	11.13	1.995	3.981
AIMS@90Days	15	8	5	13	148	9.87	1.685	2.838
Valid N (listwise)	15							

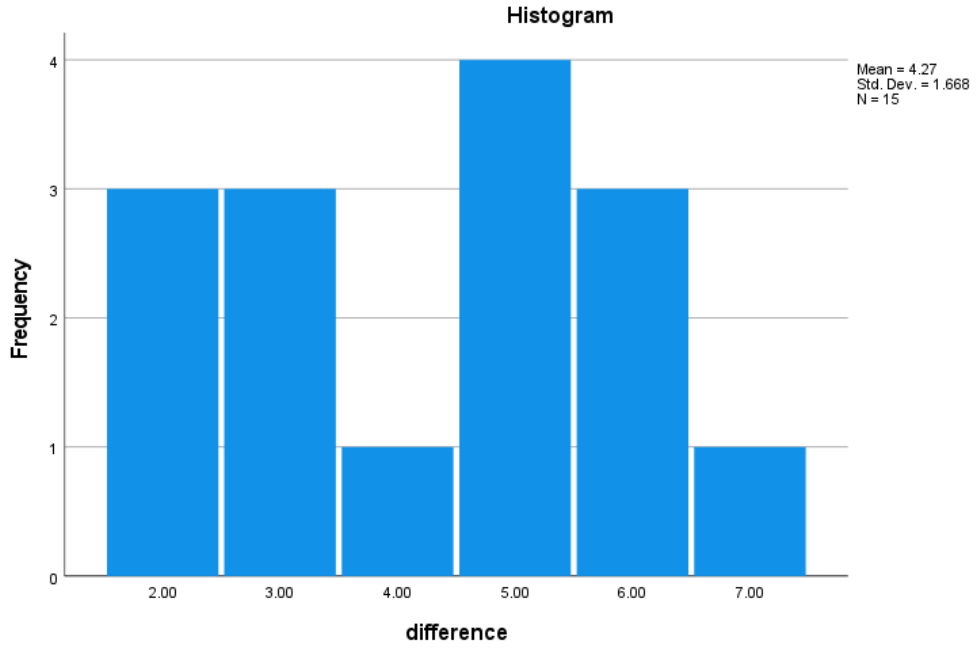


Figure 5. Bar Graph Showing Minimum to Maximum Point Decrease in the AIMS Total Score.

Summary

The data from this DNP project shows that VMAT2 inhibitors are effective in reducing tardive dyskinesia symptoms based on the statistically significant decrease in AIMs scale score. The data also showed that healthcare providers in this study setting

chose to implement VMAT2 inhibitors as opposed to stopping, changing, or decreasing current antipsychotics in patients with schizophrenia. Although researcher was unable to compare any patients on VMAT2 inhibitors with patients whose antipsychotic was adjusted, the researcher was still able to compare AIMS scale scores over time for the patients on VMAT2 inhibitors over a 90-day period. The study was able to determine after analyzing the AIMS scale scores of the patients on VMAT2 inhibitors, that the addition of a VMAT2 significantly decreased TD symptoms after 90 days.

CHAPTER IV – DISCUSSION

The purpose of this DNP project was to identify a statistically significant decrease in tardive dyskinesia symptoms for patients on VMAT2 inhibitors utilizing the AIMS scale score to establish a clinically meaningful reduction in tardive dyskinesia severity based on a 2-point decrease in AIMS total scores. The goals of the DNP project were to determine if VMAT2 inhibitors had a more profound effect on the AIMS score than stopping, changing, or decreasing antipsychotic medications, however, no patients were found to meet these criteria during exhaustive charge reviews of the patient population. Additional goals included increasing the knowledge base of the healthcare profession on the use of VMAT2 inhibitors to treat tardive dyskinesia in patients with schizophrenia and to develop a treatment algorithm for TD management with VMAT2 inhibitors in patients with schizophrenia. The data from this DNP project shows that VMAT2 inhibitors are very effective in reducing tardive dyskinesia symptoms based on the AIMS scale scores and a statistically significant 2-point decrease in AIMS total scores for all the patients in this DNP project which is comparable to results obtained by previous studies (Factor et al., 2017).

Interpretation

The effects of tardive dyskinesia can be physically, emotionally, and socially limiting which can exacerbate any underlying mental health condition an individual already has. VMAT2 inhibitors have been approved for the treatment of these symptoms for patients who choose to receive treatment. Understanding the effects of VMAT2 inhibitors and how they affect various demographic populations in various settings will help healthcare providers gain insight into best practices for caring for their patients.

Although the initial direction of this DNP project was to gauge how much more effective VMAT2 inhibitors are at augmenting TD symptoms than the other alternatives of discontinuing, changing, or decreasing antipsychotic medications for patients with schizophrenia, the available records did not identify patients that met these parameters. Perhaps, the healthcare providers caring for the current patient population have already adopted the recommendations of the AAN and APA to initiate "a reversible VMAT2 inhibitor as first-line treatment for moderate to severe or disabling tardive dyskinesia secondary to antipsychotic therapy" (Keepers et al., 2020, p. 869). In patients with mild TD, the APA notes that VMAT2 Inhibitors may be considered based on patient preference, impairment, and impact on psychological functioning. A comparison population would have added strength to the results; however, with the current patient population of patients with schizophrenia who also have TD, augmenting the antipsychotic therapy for these patients whose schizophrenia regimen is stable to correct another issue could lead to further declines in quality of life for these patients. As noted by McEvoy et al. (2019), TD is not a nuisance side effect, it impacts the well-being of patients and can worsen the stigma associated with their underlying condition so choosing treatment options for TD can be co-administered with the current antipsychotic regimen is warranted.

Limitations

One of the main limitations of this DNP project is the AIMS scale scores. The AIMS is designed to measure abnormal involuntary movements in patients on neuroleptic medications. There are 12 items on the AIMS that the healthcare provider scores. The total score from items one through seven is calculated to represent observed movements

on a severity scale from zero, indicating none to four, indicating severe (Stacy et al., 2019). The problem is the subjectivity of the AIMS scale as two different providers may rate movements differently and what one provider deems is severe may be deemed as mild to moderate to the next provider. Without knowing who scored the AIMS scales in the retrospective DNP project, it is difficult to correct this limitation. The small sample size may also be a limitation. A longer time frame and the ability to review records from other facilities would have yielded a larger sample size, however, the data collected from the current sample size showed a mean 4.27% decrease in AIMS scale scores overall in the 12 weeks. Another limitation noted in this DNP project was the lack of completed AIMS scale scores for patients that met all other inclusion criteria for this DNP project, which excluded those patients from the DNP project as an AIMS scale was a major requirement for this DNP project.

Implications for Practice

The implications for practice are to increase awareness for the evidence-based practice guidelines recommending the use of VMAT2 inhibitors for the treatment of tardive dyskinesia when treatment is indicated. Providers must become comfortable and familiar with this drug class to ensure they offer these medications to patients when they present with troubling symptoms of TD that can be managed. The results of this DNP project will be shared with the key stakeholders of the facility with the recommendation to improve documentation of the AIMS scale scores for patients on antipsychotics with positive symptoms of TD to gauge the effectiveness of the VMAT2 inhibitors being prescribed to determine what changes need to be implemented.

Recommendations for Future Research

Future research ideas include studying the effect of tardive dyskinesia on antipsychotic medication adherence. In addition, to this, Carroll (2019) noted that healthcare utilization increased in the 12 months following TD diagnosis than in the 12 months prior to the diagnosis, additional research into the cause for this would be beneficial in reducing healthcare expenditure and improving health-related quality of life measures for these patients. Future research into antipsychotic medications that do not cause tardive dyskinesia would also be beneficial by conducting additional research to try to identify such medications.

Conclusion

This DNP project shows that VMAT2 inhibitors are effective at treating tardive dyskinesia for patients with schizophrenia on antipsychotic medications and are unable to discontinue these medications when TD symptoms become problematic. This DNP project also determined that a statistically significant decrease in tardive dyskinesia symptoms can be established based on the utilization of the AIMS scale for these same patients. A clinically meaningful reduction in tardive dyskinesia severity was established by a mean 4.27% decrease in AIMS scale scores overall in the 12 weeks. Schizophrenia is a serious disorder that affects the daily functioning of those diagnosed with this condition and requires lifelong management with antipsychotic medications. When these necessary medications compound the physical, behavioral, and psychological impact these patients are experiencing, this increases their risk for worsening psychiatric symptoms. The availability of the VMAT2 inhibitors as an FDA-approved treatment

option for TD is an opportunity for healthcare professionals to provide these patients with an opportunity to improve their quality of life.

APPENDIX A – Data Collection Tool

Identification Number _____

Demographic Information:			
Age:			
Sex			
Race:			
	YES	**NO**	**DATE**
Schizophrenia Diagnosis?			
Started on Antipsychotic?			
Documented Tardive Dyskinesia Symptoms?			
Date First Documented			
Initial AIMS Score:			
PROVIDER'S INTERVENTION			
(1) Initiated VMAT2 Inhibitor			
Drug/Dose:			
(2) Changed Antipsychotic			
Previous Antipsychotic:			
Changed to:			
(3) Stopped Antipsychotic			
AIMS Score 30 days later:			
Med/Dose:			
AIMS Score 60 days later:			
Med/Dose:			
AIMS Score 90 days later:			
Med/Dose:			

APPENDIX B – IRB Approval Letter

Office *of*
Research Integrity

THE UNIVERSITY OF SOUTHERN MISSISSIPPI

118 COLLEGE DRIVE #5116 • HATTIESBURG, MS | 601.266.6756 | WWW.USM.EDU/ORI

NOTICE OF INSTITUTIONAL REVIEW BOARD ACTION

The project below has been reviewed by The University of Southern Mississippi Institutional Review Board in accordance with Federal Drug Administration regulations (21 CFR 26, 111), Department of Health and Human Services regulations (45 CFR Part 46), and University Policy to ensure:

- The risks to subjects are minimized and reasonable in relation to the anticipated benefits.
- The selection of subjects is equitable.
- Informed consent is adequate and appropriately documented.
- Where appropriate, the research plan makes adequate provisions for monitoring the data collected to ensure the safety of the subjects.
- Where appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of all data.

Appropriate additional safeguards have been included to protect vulnerable subjects.
Any unanticipated, serious, or continuing problems encountered involving risks to subjects must be reported immediately. Problems should be reported to ORI via the Incident submission on InfoEd IRB.
The period of approval is twelve months. An application for renewal must be submitted for projects exceeding twelve months.

PROTOCOL NUMBER: 21-307

PROJECT TITLE:INITIAL SUBMISSION FOR VMAT2 INHIBITOR STUDY

SCHOOL/PROGRAM Leadership & Advanced Nursing

RESEARCHERS:PI: Ada Kelly Investigators: Kelly, Ada~Coleman, Carolyn~
IRB COMMITTEE ACTION: Approved

CATEGORY: Expedited Category

PERIOD OF APPROVAL:18-Nov-2021 to 17-Nov-2022

Donald Sacco, Ph.D.
Institutional Review Board Chairperson")

APPENDIX C – Letter of Support

GORDON MEDICAL ARTS

Date: 6/19/2021

RE: Letter of Support for Ada Kelly, MSN, FNP-BC, MPH

Attn: Facility Nursing Research Council Application Process- DNP Student

To: Nursing Research Council Chair and Committee

This letter is in reference to Ada Kelly, MSN, FNP-BC, MPH who is applying for application and approval of her Clinical Doctoral Project. The focus and title of her evidenced-based project is "In patients diagnosed with Schizophrenia and started on antipsychotic medications, does the addition of a VMAT2 inhibitor compared to stopping or changing antipsychotics decrease tardive dyskinesia symptoms after 90 days. " The site is in a community-based outpatient clinic.

I have discussed this topic with Ada Kelly, MSN, FNP-BC, MPH and support and recommend the need for this retrospective chart review of patients that have been on a VMAT2 inhibitor for at least 90 days. After data analysis, I understand that Ada will present her findings to the Dr. Gordon and USM School of Leadership and Advanced Nursing Practice.

I understand that following approval by the Nursing Research Council, she will seek approval from The University of Southern Mississippi Institutional Review Board (IRB) for final approval of her Clinical Doctoral Project proposal. At present, I understand that Ada Kelly, MSN, FNP-BC, MPH is a full-time DNP (Family Nurse Practitioner) student in the Doctor of Nursing Practice Program at the University of Southern Mississippi, Hattiesburg campus.

I am the owner/director/CEO of Gordon Medical Arts Clinic. I am offering this letter of support of the doctoral student Ada Kelly, MSN, FNP-BC, MPH, in her doctoral project as titled above and look forward to hearing her findings.
I understand the planned dates are 30 days from when USM IRB approval is received. I understand that this letter of support will be included in the University of Southern Mississippi Institutional Review Board (IRB) application.

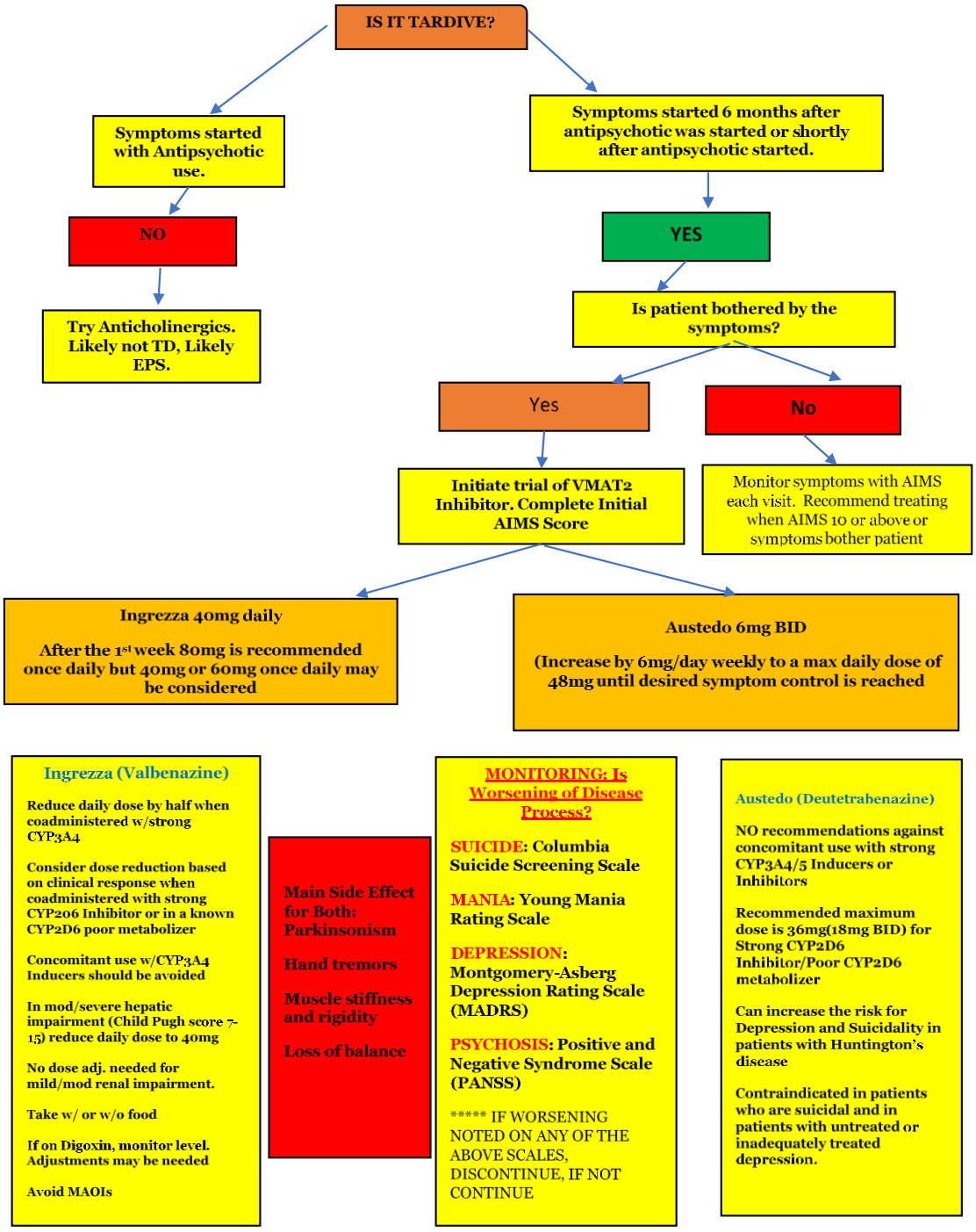
Her Chair contact information is Dr. Carolyn Coleman carolyn.coleman@usm.edu and cell 601 813 6218.

As Director/Chief of Staff at this proposed site, I would like to fully support Ada Kelly, MSN, FNP-BC, MPH to achieve her academic endeavor in this clinical practice project. I look forward to hearing the results of this study and the implications on clinical practice.
If there is any other information you should need, please do not hesitate to contact me.

Sincerely,

Dr. Maxie Gordon
Gordon Medical Arts Clinic

APPENDIX D - Algorithm/Protocol for TD Management with $VMAT_2$ Inhibitors



APPENDIX E – Review of Literature

Author/Year/Title	Design	Sample	Findings
Anderson, K. E., Stamler, D., Davis, M. D., Factor, S. A., Hauser, R. A., Isojärvi, J., ... & Fernandez, H. H. (2017) Deutetrabenazine for treatment of involuntary movements in patients with tardive dyskinesia (AIM-TD): A double-blind, randomized, placebo-controlled, phase 3 trial. *The Lancet Psychiatry*, *4*(8), 595-604.	Double-bling, Placebo-controlled, randomized trial	Patients aged 18-80 years old with tardive dyskinesia	From baseline to week 12 the LS mean AIMS score improved.
Carbon, M., Kane, J. M., Leucht, S., & Correll, C. U. (2018). Tardive dyskinesia risk with first-and second-generation antipsychotics in comparative randomized controlled trials: a meta-analysis. *World Psychiatry*, *17*(3), 330-340	Meta-Analysis	All head to head comparisons of specific antipsychotics in any oral or IM form to any FGA without restriction on age or gender of participants	Mean analysis confirmed a clinically meaningful lower TD risk with SGAs vs FGAs which is not driven b high dose FGA comparators
Caroff, S. N., Aggarwal, S., & Yonan, C. (2018) Treatment of tardive dyskinesia with tetrabenazine or valbenazine: a systematic review. *Journal of Comparative Effectiveness Research*, *7*(2), 135-148.	Systemic Review	487 PubMed/Embase search results/11 studies met the review criteria	Valbenazine appears to have fewer side effects and a more favorable once-daily dosing regimen for TD treatment.
Carroll, B., & Irwin, D. E. (2019) Health care resource utilization and costs for patients with tardive dyskinesia. *Journal of Managed care & Specialty pharmacy*, *25*(7), 810-816.	Retrospective analysis	834 patients diagnosed with TD for the first time between January 1, 2008, and September 30, 2014	Patients with TD have a significantly higher healthcare utilization rate and costs compared with non-TD patients.
Factor, S. A., Remington, G., Comella, C. L., Correll, C. U., Burke, J., Jimenez, R., ... & Christopher, F. O. (2017) The effects of valbenazine in participants with tardive dyskinesia: results of the 1-year KINECT 3 extension study. *The Journal of Clinical Psychiatry*, *78*(9), 0-0. *5*	Double-blind placebo-controlled	Participants with a DSM-IV diagnosis of schizophrenia, schizoaffective disorder, or a mood disorder who completed the 6-week KINECT 3	The long term safety and tolerability of Valbenazine was favorable

McEvoy, J., Gandhi, S. K., Rizio, A. A., Maher, S., Kosinski, M., Bjorner, J. B., & Carroll, B. (2019) Effect of tardive dyskinesia on quality of life in patients with bipolar disorder, major depressive disorder, and schizophrenia. *Quality of Life Research*, *28*(12), 3303-3312.	Cross-sectional survey	Patients at least age 18 with a confirmed diagnosis of BD, MDD, or SZ	Patients with TD have a worse health-related quality of life and social withdrawal than those without.
Othman, Z., Ghazali, M., Razak, A. A., & Husain, M. (2013) The severity of Tardive Dyskinesia and Negative Symptoms are Associated with Poor Quality of Life in Schizophrenia Patients. *International Medical Journal*, *20*(6), 677–680.	Descriptive Analysis	71 clinically stable aged 18 to 65 schizophrenia patients with TD recruited from HUSM or HRPZ.	Quality of life was negatively associated with the severity of TD and negative symptoms.
Ricciardi, L., Pringsheim, T., Barnes, T., Martino, D., Gardner, D., Remington, G., Addington, D., Morgante, F., Poole, N., Carson, A., & Edwards, M. (2019) Treatment recommendations for Tardive Dyskinesia. *Canadian Journal of Psychiatry. Revue Canadienne de psychiatrie*, *64*(6), 388–399.	Systemic Review	Data from Cochrane reviews, AAN guidelines, and individual studies	Data is limited on TD treatment but the best management strategy is prevention.

APPENDIX F – Abnormal Involuntary Movement Scale

Abnormal Involuntary Movement Scale (AIMS) - Overview

- The AIMS records the occurrence of tardive dyskinesia (TD) in patients receiving neuroleptic medications.
- The AIMS test is used to detect TD and to follow the severity of a patient's TD over time.

Clinical Utility

The AIMS is a 12 item anchored scale that is clinician administered and scored

- Items 1-10 are rated on a 5 point anchored scale.
  - Items 1-4 assess orofacial movements.
  - Items 5-7 deal with extremity and truncal dyskinesia.
  - Items 8-10 deal with global severity as judged by the examiner, and the patient's awareness of the movements and the distress associated with them.
- Items 11-12 are yes-no questions concerning problems with teeth and/or dentures, because such problems can lead to a mistaken diagnosis of dyskinesia.

Examination Procedure

The indirect observation and the AIMS examination procedure are on the following two pages.

Scoring[1]

1. A total score of items 1-7 (Categories I, II, III) can be calculated. These represent observed movements.
2. Item 8 can be used as an overall severity index.
3. Items 9 (incapacitation) and 10 (awareness) provide additional information that may be useful in clinical decision making.
4. Items 11 (dental status) and 12 (dentures) provide information that may be useful in determining lip, jaw and tongue movements.

Psychometric Properties

The AIMS is a global rating method. The AIMS requires the raters to compare the observed movements to the average movement disturbance seen in persons with TD. Such relative judgments may vary among raters with different backgrounds and experience.

1. Rush JA Jr., Handbook of Psychiatric Measures, American Psychiatric Association, 2000, 166-168.

AIMS Examination Procedure

Either before or after completing the AIMS on the following page, observe the patient unobtrusively at rest (e.g., in the waiting room).

The chair to be used in this examination should be a hard, firm one without arms.

Questions

1. Ask the patient whether there is anything in his or her mouth (such as gum or candy) and, if so, to remove it.
2. Ask about the *current* condition of the patient's teeth. Ask if he or she wears dentures. Ask whether teeth or dentures bother the patient *now*.
3. Ask whether the patient notices any movements in his or her mouth, face, hands, or feet. If yes, ask the patient to describe them and to indicate to what extent they *currently* bother the patient or interfere with activities.
4. Have the patient sit in chair with hands on knees, legs slightly apart, and feet flat on floor. (Look at the entire body for movements while the patient is in this position.)
5. Ask the patient to sit with hands hanging unsupported -- if male, between his legs, if female and wearing a dress, hanging over her knees. (Observe hands and other body areas).
6. Ask the patient to open his or her mouth. (Observe the tongue at rest within the mouth.) Do this twice.
7. Ask the patient to protrude his or her tongue. (Observe abnormalities of tongue movement.) Do this twice.
8. Ask the patient to tap his or her thumb with each finger as rapidly as possible for 10 to 15 seconds, first with right hand, then with left hand. (Observe facial and leg movements.)
9. Flex and extend the patient's left and right arms, one at a time.
10. Ask the patient to stand up. (Observe the patient in profile. Observe all body areas again, hips included.)
11. Ask the patient to extend both arms out in front, palms down. (Observe trunk, legs, and mouth.)
12. Have the patient walk a few paces, turn, and walk back to the chair. (Observe hands and gait.) Do this twice.

Abnormal Involuntary Movement Scale (AIMS)

Patient Name _____ Date of Visit _____

Code: 0 = None 1 = Minimal 2 = Mild 3 = Moderate 4 = Severe

Movement Ratings:
- Rate highest severity observed in category I, II, III.
- Rate movements that occur upon activation one point less than those observed spontaneously.
- Circle movements as well as code number that applies.

		RATER / DATE	RATER / DATE	RATER / DATE	RATER / DATE
I FACIAL & ORAL MOVEMENTS	**1. Muscles of Facial Expression** e.g. movements of forehead, eyebrows, periorbital area, cheeks, including frowning, blinking, smiling, grimacing	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
	2. Lips and Perioral Area e.g. puckering, pouting, smacking	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
	3. Jaw Biting, clenching, chewing, mouth opening , lateral movement	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
	4. Tongue Rate only increases in movement both in and out of mouth. NOT inability to sustain movement. Darting in and out of mouth	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
II EXTREMITY MOVEMENTS	**5. Upper (arms, wrists, hands, fingers)** Include choreic movements (i.e. rapid objectively purposeless, irregular, spontaneous) athetoid movements. DO NOT INCLUDE TREMOR (i.e. repetitive, regular, rhythmic)	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
	6. Lower (legs, knees, ankles, toes) Lateral knee movement, foot tapping, heel dropping, foot squirming, inversion and eversion of foot	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
III TRUNK MOVEMENTS	**7. Neck, shoulders and hips** Rocking, twisting, squirming, pelvic gyrations	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
IV GLOBAL JUDGEMENT	**8. Severity of abnormal movements overall**	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
	9. Incapacitation due to abnormal movements	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
	10. Patient's awareness of abnormal movements. Rate only patients report: No Awareness = 0 Aware, no distress = 1 Aware, mild distress = 2 Aware, moderate distress = 3 Aware, severe distress = 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
V DENTAL STATUS	**11. Current problems with teeth and/or dentures**	YES NO	YES NO	YES NO	YES NO
	12. Are dentures usually worn	YES NO	YES NO	YES NO	YES NO
	13. Endentia?	YES NO	YES NO	YES NO	YES NO
	14. Do movements disappear with sleep?	YES NO	YES NO	YES NO	YES NO

Available for use in the public domain.

REFERENCES

American Academy of Neurology (AAN). (2013). Summary of evidenced-based guideline for clinicians: Treatment of Tardive Syndromes. www.aan.com.

American Association of Colleges of Nursing. (2006). The essentials of doctoral education for advanced nursing practice. Retrieved from https://www.aacnnursing.org/Portals/42/Publications/DNPEssentials.pdf.

American Psychiatric Association (APA). (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). APA.

Anderson, K. E., Stamler, D., Davis, M. D., Factor, S. A., Hauser, R. A., Isojärvi, J., . & Fernandez, H. H. (2017). Deutetrabenazine for treatment of involuntary movements in patients with tardive dyskinesia (AIM-TD): A double-blind, randomized, placebo-controlled, phase 3 trial. *The Lancet Psychiatry*, *4*(8), 595-604. https://doi.org/10.1016/S2215-0366(17)30236-5

Bergman, H., & Soares-Weiser, K. (2018). Anticholinergic medication for antipsychotic-induced tardive dyskinesia. *Cochrane Database of Systematic Reviews*, (1). https://doi.org/10.1002/14651858.CD000204.pub2.

Bergman, H., Walker, D. M., Nikolakopoulou, A., Soares-Weiser, K., & Adams, C. E. (2017).Systematic review of interventions for treating or preventing antipsychotic-induced tardive dyskinesia. *Health Technology Assessment*, *21*(43), 1-218. https://doi.org/10.3310/hta21430

Bhidayasiri, R., Fahn, S., Weiner, W. J., Gronseth, G. S., Sullivan, K. L., & Zesiewicz, T. A. (2013). Evidence-based guideline: Treatment of tardive syndromes: report of the Guideline Development Subcommittee of the American Academy of

Neurology. *Neurology*, *81*(5), 463-469. https://doi.org/10.1212/WNL.0b013e31829d86b6

Carbon, M., Kane, J. M., Leucht, S., & Correll, C. U. (2018). Tardive dyskinesia risk with first-and second-generation antipsychotics in comparative randomized controlled trials: a meta-analysis. *World Psychiatry*, *17*(3), 330-340. https://doi.org/10.1002/wps.20579

Caroff, S. N., Aggarwal, S., & Yonan, C. (2018). Treatment of tardive dyskinesia with tetrabenazine or valbenazine: a systematic review. *Journal of Comparative Effectiveness Research*, *7*(2), 135-148. https://doi.org/10.2217/cer-2017-0065

Caroff, S. N., Ungvari, G. S., & Owens, D. G. C. (2018). Historical perspectives on tardive dyskinesia. *Journal of the Neurological Sciences*, *389*, 4-9. https://doi.org/10.1016/j.jns.2018.02.015

Carroll, B., & Irwin, D. E. (2019). Health care resource utilization and costs for patients with tardive dyskinesia. *Journal of Managed Care & Specialty Pharmacy*, *25*(7), 810-816.

Centers for Disease Control and Prevention (CDC). (2021). Health-Related Quality of Life. https://www.cdc.gov/hrqol/index.htm

Chism, L. A. (2019). *The doctor of nursing practice: A guidebook for role development and professional issues.*(4th ed.) Jones & Bartlett Learning.

Citrome, L. (2018). Clinical management of tardive dyskinesia: Five steps to success. *Journal of the Neurological Sciences*, *389*, 61-66. https://doi.org/10.1016/j.jns.2017.11.019

Factor, S. A., Remington, G., Comella, C. L., Correll, C. U., Burke, J., Jimenez, R., ... & Christopher, F. O. (2017). The effects of valbenazine in participants with tardive dyskinesia: results of the 1-year KINECT 3 extension study. *The Journal of Clinical Psychiatry*, *78*(9). https://doi.org/10.4088/JCP.17m11777

Field, B., Booth, A., Ilott, I., & Gerrish, K. (2014). Using the knowledge to action framework in practice: a citation analysis and systematic review. *Implementation Science*, *9*(1), 1-14. http://www.implementationscience.com/content/9/1/172

Gomes, L., Oliveira, F., Barbosa, K., Medeiros, A., Fernandes, M., & Nóbrega, D. (2019). Theory of unpleasant symptoms: Critical analysis. *Texto & Contexto-Enfermagem*, *28*. https://www.scielo.br/j/tce/a/kBHmH49RwkkYGkN5wzGXxjP/?format=html&lang=en

Graham, I., Logan, J., Harrison, M., Sharon, E., Tetroe, J., Caswell, W., & Robinson, N. (2006). Lost knowledge translation: Time for a map? *Journal for Continuing Education in Health Professions*, *26*(1), 13-24. Doi: 10.1002/chp.47

Institute for Clinical and Economic Review. (2017). A look at VMAT2 Inhibitors for Tardive Dyskinesia. icer_tardive-dyskinesia_RAAG-122217.pdf

Jackson, R., Brams, M. N., Citrome, L., Hoberg, A. R., Isaacson, S. H., Kane, J. M., & Kumar, R. (2021). Assessment of the impact of tardive dyskinesia in clinical practice: consensus panel recommendations. *Neuropsychiatric Disease and Treatment*, *17*, 1589. https://doi.org/10.2147/NDT.S310605

Keepers, G. A., Fochtmann, L. J., Anzia, J. M., Benjamin, S., Lyness, J. M., Mojtabai, R., ... & (Systematic Review). (2020). The American Psychiatric Association practice

guideline for the treatment of patients with schizophrenia. *American Journal of Psychiatry*, *177*(9), 868-872. https://doi.org/10.1176/appi.ajp.2020.177901

McEvoy, J., Gandhi, S. K., Rizio, A. A., Maher, S., Kosinski, M., Bjorner, J. B., & Carroll, B. (2019). Effect of tardive dyskinesia on quality of life in patients with bipolar disorder, major depressive disorder, and schizophrenia. *Quality of Life Research*, *28*(12), 3303-3312. https://doi.org/10.1007/s11136-019-02269-8

Meyer, J. M. (2018). Future directions in tardive dyskinesia research. *Journal of the Neurological Sciences*, *389*, 76-80. https://doi.org/10.1016/j.jns.2018.02.004

Othman, Z., Ghazali, M., Razak, A. A., & Husain, M. (2013). Severity of Tardive Dyskinesia and Negative Symptoms are Associated with Poor Quality of Life in Schizophrenia Patients. *International Medical Journal*, *20*(6), 677–680. https://content.ebscohost.com/ContentServer.asp?T=P&P=AN&K=94059987&S=R&D=ccm&EbscoContent=dGJyMMTo50SeqLM4xNvgOLCmsEqeprJSr6u4Ta6WxWXS&ContentCustomer=dGJyMPGutk%2BzqrJJuePfgeyx44Dt6fIA

Ricciardi, L., Pringsheim, T., Barnes, T., Martino, D., Gardner, D., Remington, G., Addington, D., Morgante, F., Poole, N., Carson, A., & Edwards, M. (2019). Treatment recommendations for Tardive Dyskinesia. *Canadian Journal of Psychiatry. Revue Canadienne de psychiatrie*, *64*(6), 388–399. https://doi.org/10.1177/0706743719828968

Rush, J.A. (2000). *Handbook of psychiatric measures* (pp. 166-168). APA.

Scorr, L. M., & Factor, S. A. (2018). VMAT2 inhibitors for the treatment of tardive dyskinesia. *Journal of the Neurological Sciences*, *389*, 43-47. https://doi.org/10.1016/j.jns.2018.02.006

Stacy, M., Sajatovic, M., Kane, J. M., Cutler, A. J., Liang, G. S., O'Brien, C. F., & Correll, C. U. (2019). Abnormal involuntary movement scale in tardive dyskinesia: Minimal clinically important difference. *Movement disorders: Official Journal of the Movement Disorder Society*, *34*(8), 1203–1209. https://doi.org/10.1002/mds.27769

Stahl, S. M. (2018). Mechanism of action of vesicular monoamine transporter 2 (VMAT2) inhibitors in tardive dyskinesia: Reducing dopamine leads to less "go" and more "stop" from the motor striatum for robust therapeutic effects. *CNS Spectrums*, *23*(1), 1-6.

Stahl, S.M. (2019). *Stahl's essential psychopharmacology*. (4th edition). Cambridge.

Strassnig, M., Rosenfeld, A., & Harvey, P. D. (2018). Tardive dyskinesia: motor system impairments, cognition, and everyday functioning. *CNS Spectrums*, *23*(6), 370-377. https://doi.org/10.1017/S1092852917000542

Tandon, R., Gaebel, W., Barch, D. M., Bustillo, J., Gur, R. E., Heckers, S., Malaspina, D., Owen, M., Schultz, S., Tsuang, M., Van, J., & Carpenter, W. (2013). Definition and description of schizophrenia in the DSM-5. *Schizophrenia Research*, *150*(1), 3-10. http://dx.doi.org/10.1016/j.schres.2013.05.028

Vasan, S., & Padhy, R.K. (2021, May 3). Tardive Dyskinesia. *StatPearls*. https://www.ncbi.nlm.nih.gov/books/NBK448207/

Ward, K. M., & Citrome, L. (2018). Antipsychotic-Related Movement Disorders: Drug-Induced Parkinsonism vs. Tardive Dyskinesia-key differences in pathophysiology and clinical management. *Neurology and Therapy*, *7*(2), 233–248. https://doi.org/10.1007/s40120-018-0105-0

Zaccagnini, M., & Pechacek, J. M. (2021). *The doctor of nursing practice essentials: A new model for advanced practice nursing*. (4th ed.). Jones & Bartlett Learning.