The Bipolar Crash: Treating Bipolar Depression

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Abstract

Bipolar Disorder (BD), in the depressive phase is among the most common mental disorder diagnosed in patient's I treated based on the insight gained after completing a 10-day reflective practice log at Emergence Health Network, outpatient services. In my clinical practice, I noticed that when patients with bipolar depression were on certain antipsychotics, i.e., Aripiprazole, their bipolar disorder, depressive phase symptoms were not improving. Bipolar depression is a debilitating mental disorder and if effective treatment is not implemented, the disease can provoke a suicide death. After an intensive literature review, I found the following guidelines for the effective treatment of bipolar depression The application of the Canadian Network for Mood and Anxiety (CANMAT) and the International Society for Bipolar Disorder (ISBD) 2018 guidelines in treating bipolar depression improved and alleviated bipolar depression symptoms within two weeks. Ten patients were included in this quality improvement of the Doctor of Nursing Practice (DNP) Project nine reported symptom improvements and confirmed that the treatment improved their quality of life.

Keywords: Bipolar Disorder, Bipolar Depression, Aripiprazole, CANMAT

Introduction

Bipolar disorder (BD) is a highly debilitating psychiatric mental disorder that affects 1 out 25 individuals (Miklowitz & Johnson, 2008). BD has its onset in adolescence age and individuals who suffer from this disorder have mood swings ranging from very high highs, meaning mania, and very low lows meaning depression (Miklowitz & Johnson, 2008). Bipolar depression has major challenges because it can lead to instability of the patient's mental health and other critical medical conditions. Patients with BD face a high risk of committing suicide. If untreated, the risk factors are 20 times greater than other major psychiatric conditions (Baldessarini, Vázquez, & Tondo, 2020). Increased depression is the most prevalent phase for somebody who suffers from BD (Baldessarini, Vázquez, & Tondo, 2020). Clinical challenges that make these symptoms difficult to treat include fear of reporting, reluctance to seek help, and patients taking more medications to manage their BD (Baldessarini, Vázquez, & Tondo, 2020). BD can lead to loss of job, make patients lag in their academic achievements, and be unsuccessful in their employment owing to constant absence from work (Baldessarini, Vázquez, & Tondo, 2020). BD can lead to a high risk of myocardial infarction, strokes, obesity, increased smoking, a decrease in patients' longevity If not treated quickly (Baldessarini, Vázquez, & Tondo, 2020). Evidence demonstrates that the use of antipsychotics and/or the use of anticonvulsants, short-term or long-term treatments of BD can assist in obtaining stability and mental well-being (Baldessarini, Vázquez, & Tondo, 2020).

A 10-day reflective practice log on my place of work at Emergence Health Network revealed that it took over 2 weeks of outpatient services to maintain proper

documentation of patients. The log included a plan of care, diagnosis, assessments, age, and sex of the patient. After analyzing the complete reflective practice log, I gained insight into all phases of patients' mental disorders, which was the most prevalent disease diagnosed. During the care of patients with BD, I explored the quality of their improvement during the depressive phase since their symptoms failed to improve while on Aripiprazole.

Previous studies were reviewed to explore a quality improvement associated with the treatment of bipolar depression. I preferred the Canadian Network for Mood and Anxiety Treatments (CANMAT) to treat patients BD depressive phase as it collaborated with the International Society for Bipolar Disorder (ISBD) 2018 guidelines. Moreover, CANMAT/ISBD 2018 guidelines is preferable because its evidence-based information is the most recent for treating bipolar depression as its step-by-step guidelines are easy to follow. The treatment procedures of BD follow evidence-based recommendations. The CANMAT/ISBD 2018 guidelines used years of research and available first, second, and third evidence from randomized control trials to suggest guidelines for treatment (Yatham, et al., 2018). The CANMAT guidelines were available in 2005 and updated in 2013. The CANMAT's latest update was in 2018, in collaboration with ISBD, which continue to use the highest level of research for random control trials. The CANMAT/ISBD 2018 guidelines assist in managing the bipolar depression phase, bipolar mania phase, and maintenance of the BD. The CANMAT/ISBD 2018 guidelines represent important advances in the psychiatric care of the mental disorder, which includes psychological and pharmacological treatments as they have been making significant updates since its first publication in 2005 (Yatham, et

al., 2018). The guidelines are comprehensive and easy to follow as their recommendations are based on clinical experience and evidence-based practice for a line of treatment. Moreover, the guidelines are safe for patients because it is based on clinical outcome research (Yatham, et al., 2018). The CANMAT/ISBD 2018 guidelines describe bipolar depression, according to the DSM-5 diagnostic criteria such as status of symptom, change in appetite, sleep, low mood, fatigue, lack of interest, and decrease concentration (Yatham, et al., 2018). The guidelines assess the severity of the symptoms and the ability to adhere to treatment (Yatham, et al., 2018). Depending on the type of BD the patient may be suffering from, the CANMAT/ISBD 2018 guidelines offer the best treatment to manage and improve symptoms. Table 1 presents type 1 and 2 depressive phases for the treatment of BD. Before considering medication, the guideline recommends assessing any previous medication taken and either maximizing the current medication, considering adjunctive medication with current medication, or switching to another medication recommended according to the BD phases. The strategy will assist in alleviating symptoms and enhancing bipolar disorder stability (Yatham, et al., 2018). Electroconvulsive therapy (ECT) is recommended as a second line of treatment for patients requiring rapid response treatment, especially patients with severe bipolar depression and symptoms of death wishes (Yatham, et al., 2018). The clinical evidence from the CANMAT/ISBD shows that rapid treatment relief, Quetiapine relief, and Lurasidone (Latuda) may improve symptoms in approximately one week as this is the first-line monotherapy or adjunctive treatment (Yatham, et al., 2018). In my reflective practice log, the numbers of female patients treated for bipolar mental health disorder are higher than male patients. The CANMAT/ISBD 2018 guidelines offer

specific suggestions for treating women during their reproductive cycles (Yatham, et al., 2018).

Table 1 (Yatham, et al., 2018)

	Bipolar Disorder Type 1 Depressive State	Bipolar Disorder Type 2 Depressive State
First Line of Treatment	• Quetiapine Monotherapy • Lurasidone+Lithium or Divalproex • Lithium Monotherapy • Lamotrigine Monotherapy • Lurasidone monotherapy • lamotrigine adjunctive	• Quetiapine
Second Line of Treatment	• Divalproex monotherapy • SSRI/Bupropion adjunctive • Cariprazine monotherapy • Olanzepine+Fluoxetine • ECT (Electroconvulsive Therapy)	• Lithium monotherapy • Lamotrigine monotherapy • Bupropion Adjunctive • ECT • Sertraline • Venlafaxine
Third Line of Treatment	• Aripiprazole adjunctive • Armodafinil adjunctive • Carbamazepine monotherapy • light therapy	• Bupropion adjunctive • Divalproex • Fluoxetine • Ziprasidone • TMS (Transcranial Magnetic Stimulation) therapy

The latest collaboration between the CANMAT and the ISBD goal is to publish efficacious evidence and a range of interventions in improving BD all phases for symptom relief.

The change model from Kurt Lewin provided insight in implementing the Doctor of Nursing Practice (DNP) Project. The change model is implemented in three steps: the unfreezing, moving, and refreezing stages approach used to manage changes (Burnes, 2020). This theoretical framework model is straightforward for processing change, during the unfreezing change. The theoretical framework also allows the flexibility necessary for changes since it helps learners to gain knowledge about the upcoming changes and equips them in identifying problems associated with changes (Burnes, 2020). During the moving stage, changes arising from the intended purpose and forces in change are greater than the individual who resists change (Burnes, 2020). The final stage, the freezing process, reinforcing the change, stabilizing the change is implemented to find equilibrium and decrease the risk of regression (Burnes, 2020). By reducing the individuals opposing changes and reinforcing the desire to achieve a better outcome, one can achieve change for more positive outcomes. Using the CANMAT/ISBD 2018 guidelines for treating BD, Lewin's model of change implements the guidelines for quality improvement. Once the steps have been completed, the process will be re-evaluated, and changes will be done to incorporate the quality improvement *Plan*, *Do*, *Study*, *Act* (PDSA) model. This model will facilitate the guidelines and their effectiveness (AHRQ, 2020). The *Plan* stage identifies the patients who qualify for the DNP Program; the *Do* stage is used to identify the best approach in change or augmentation of medication; the *Study* stage evaluates any adverse side

effects. Improvement in the patient's symptoms and finally *Act* stage determined the successful guidelines and standardized implementation for improving symptoms of bipolar depression.

Technique in measuring the effectiveness of the treatment is by using the subjective and objective data from the patient's history and using the numeric rating scale to measure pain. The rating scale for pain is modified to serve my purpose in rating the depressive state of the patient before and after the medication change. The scale of 0 represents no depressive symptoms and 10 represents highest the bipolar depressive state. The patient rates their bipolar depressive mood from 0-10. The numeric rating scale has been validated as it correlates with the patient's pain symptoms (Lazariduo, et al., 2018) and will be used to measure bipolar depression. A Patient-Reported Outcome is an outcome measurement tool that provides direct reporting of the patient's response and provides a reliable measurement for symptoms to improve patient's quality of life (Weldring, Smith, 2013). The 0-10 rating scale is used to measure patient's health outcomes and provides insight into the patient's treatment (Weldring, Smith, 2013). There will be a numeric count of the patients who meet the DNP Project criteria.

The guideline's extensive evidence-based clinical practice and the quality improvement DNP Project tools are used in treating bipolar depression and improving the mental health of my patients as well their quality of life. The CANMAT/ISBD 2018 guidelines are tools to improve symptoms and provide patient's stability globally (Yatham, et al., 2018). A study published in The International Journal of Neuropsychopharmacology identified 583 guidelines and treatment algorithms

(Fountoulakis & Vieta, 2008). Of those 583 articles, 32 randomized control trials studies demonstrated structural guidelines for the treatment of bipolar depression. A meta-analytical study in this article found that Aripiprazole as a monotherapy strategy offers excellent treatment using for acute mania phase BD compared to a placebo at 15-30 mg per day. Aripiprazole also provided negative endpoints when compared with placebo in treating acute bipolar depression (Fountoulakis & Vieta, 2008). In another meta-analysis of random control trial, an article published in the International Journal of Neuropsychopharmacology recommended Quetiapine or Lurasidone (Latuda) and cognitive behavioral therapy as the first-line treatment for bipolar depression. However, the article suggests avoiding using cognitive behavioral therapy monotherapy (Konstantinos, et al., 2017). The World Journal of Biological Psychiatry also suggested Lurasidone (Latuda) as more effective compared to Aripiprazole and Ziprasidone in treating bipolar depression (Ostacher, et al., 2018). Lurasidone (Latuda) compared to Quetiapine was also effective, it was less sedative and offered similar benefits (Ostacher, et al., 2018). The Journal of Psychopharmacology suggested using effective guidelines and the evidence-based clinical experience supported by research ranging from level I, the highest hierarchy levels, to level IV, for treatment of BD (Goodwin, et al., 2016). These guidelines offer standards of care based on evidence to improve the BD symptoms, especially for the DNP Project, Bipolar Depression. However, Aripiprazole, as a monotherapy treatment, has not been effective compared to a placebo in treating bipolar depression; but it is the first line of treatment for bipolar mania (Yatham, et al., 2018). The Current Psychiatry Reports, published in 2021, revealed that oral Aripiprazole as monotherapy was not effective in improving acute

bipolar depressive symptoms (Keramatian, et al., 2021). Table 2 presents a PICOT question format for the quality improvement project. Three PICOT questions were developed and the one mentioned was my first choice. Patients who met inclusion criteria are those who currently use Aripiprazole and have bipolar depressive symptoms. After patient identification, evidence-based literature from the CANMAT/ISBD 2018 guidelines is used to improve and alleviate bipolar depressive symptoms. Before proceeding with my DNP project for Quality Improvement (QI), a QI project proposal was developed, and an approval letter was received from the Institutional Review Board (IRB) of The University of Texas at El Paso to proceed with my worksite at Emergence Health Network outpatient clinic. A code of conduct is assumed to be the utmost standard of care in treating my patients and in providing quality improvement for the DNP Project. I am a certified PMHNP (Psychiatric Mental Health Nurse Practitioner), which is within my scope of practice and allows me to practice, assess, diagnose, treat, and evaluate patients. The privacy of the patients will be maintained by following the standards of the HIPPA (Health Insurance Portability and Accountability) act.

Table 2 PICOT

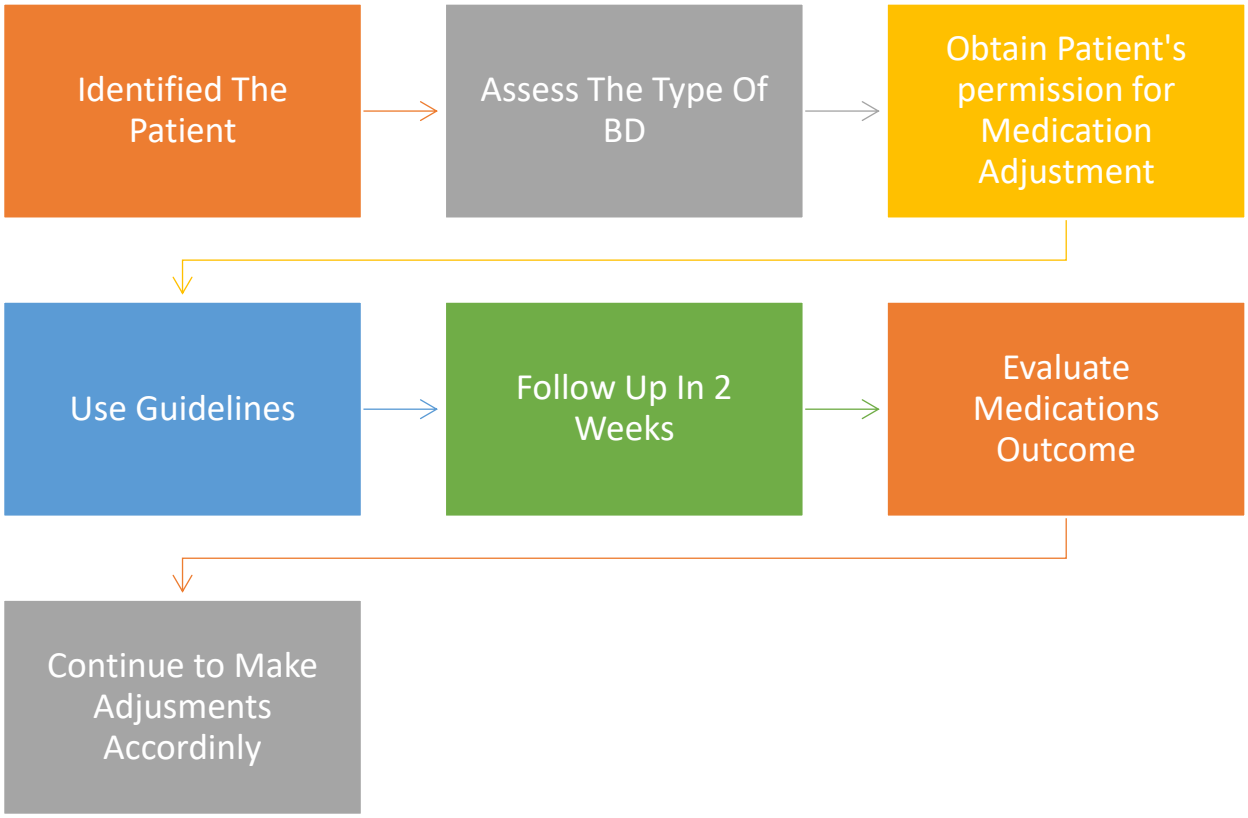
○ ***Population:*** **Patients 21 to 65 years old with bipolar disorder with continued bipolar depression**
○ ***Interventions:*** **Use CANMAT/ISB 2018 Bipolar Depression Guidelines**
○ ***Current practice:*** **Using Oral Aripiprazole 10 mg QHS**
○ ***Outcome:*** **Desire outcome it to alleviate bipolar depression symptoms**
○ ***Time:*** **4 weeks**

Methods

The Emergence Health Network was the DNP project location. The CANMAT/ISBD 2018 guidelines were used to treat the outpatient population with bipolar depression. The participants are the patient and me. My supervising MD was aware of the project and granted full autonomy. He made himself available for consultation. The project barrier was the possibility of the client not returning within the DNP Project timeframe. The DNP Project treatment was individualized and implemented for each patient. The quality improvement was evaluated after the implementation and outcome of the DNP Project. The DNP Project started on January 18, 2022 and aimed at treating bipolar depression using the CANMAT/ISBD 2018 guidelines implementation. Inclusion criteria were females and males subjects aged 18-65 years old; patients who took Aripiprazole and patients diagnosed with bipolar depression. Once the patient was identified and met the criteria for the DNP Project, we started the CANMAT/ISBD 2018 guidelines, proceeded with the recommendations, and started the appropriate treatment. In the first and second weeks, the patients were identified for the DNP Project. Moreover, the patients were assessed, and their depressive symptoms were rated using the rating scale of 0/10. Moreover, I took subjective and objective data from the patients. The next stage was to provide information for treating patient's bipolar depression. With the patient's permission, I will change their medication if possible, or maximized current medication or add other medication by following the CANMAT/ISBD 2018 guidelines. I will assess the patient's current Aripiprazole and if they had any other antipsychotics in the past. If the patient did not take another antipsychotic in the past from the suggested guidelines, I will offer first-line treatment to improve bipolar

depression symptoms. If the patient responded to antipsychotic drugs in the past and as one of the first-line treatments, we offered first-line adjunctive medication or second-line treatment medication if applicable. The same procedure will be implemented for the patient who suffered from BD type 2 depressive phase. While on Aripiprazole, I will start other antipsychotics or continued Aripiprazole based on the guideline's suggestion to the patient and the patient's agreement to proceed. Aripiprazole half-life is 75 hours and is eliminated in 2 weeks after stopping the drug (Keks, Schwartz, Hope, 2019). A cross titration will be conducted by reducing Aripiprazole by 50% and will be stopped after 14 days (Keks, Schwartz, Hope, 2019). I will switch to the recommended medication to be started on Day 1 (Keks, Schwartz, Hope, 2019). I will start the new antipsychotic medication following the recommended dose and increased the medication accordingly. After following the pharmacological CANMAT/ISBD 2018 guidelines, I will follow-up with the patient for two weeks for evaluation purposes. After medication change, the patient will be informed to call the clinic if they experienced any adverse side effects to make any necessary changes before the next follow-up appointments. During the follow-up, I will evaluate the patient's depressive state using the rating scale. In addition, I will assess if the patient tolerates the treatment. Moreover, I will follow the CANMAT/ISBD 2018 guidelines to treat side effects. Importantly, I will take the patient's consideration and respected their right in agreeing or declining change by following the ethical consideration and supporting the patient's decision. However, I do not anticipate any conflict of interest while conducting the quality improvement. Table 3 provides a flowchart for the treatment interventions of the DNP Project. Bipolar depression symptoms should improve after following the implemented guidelines.

Table 3 Flowchart

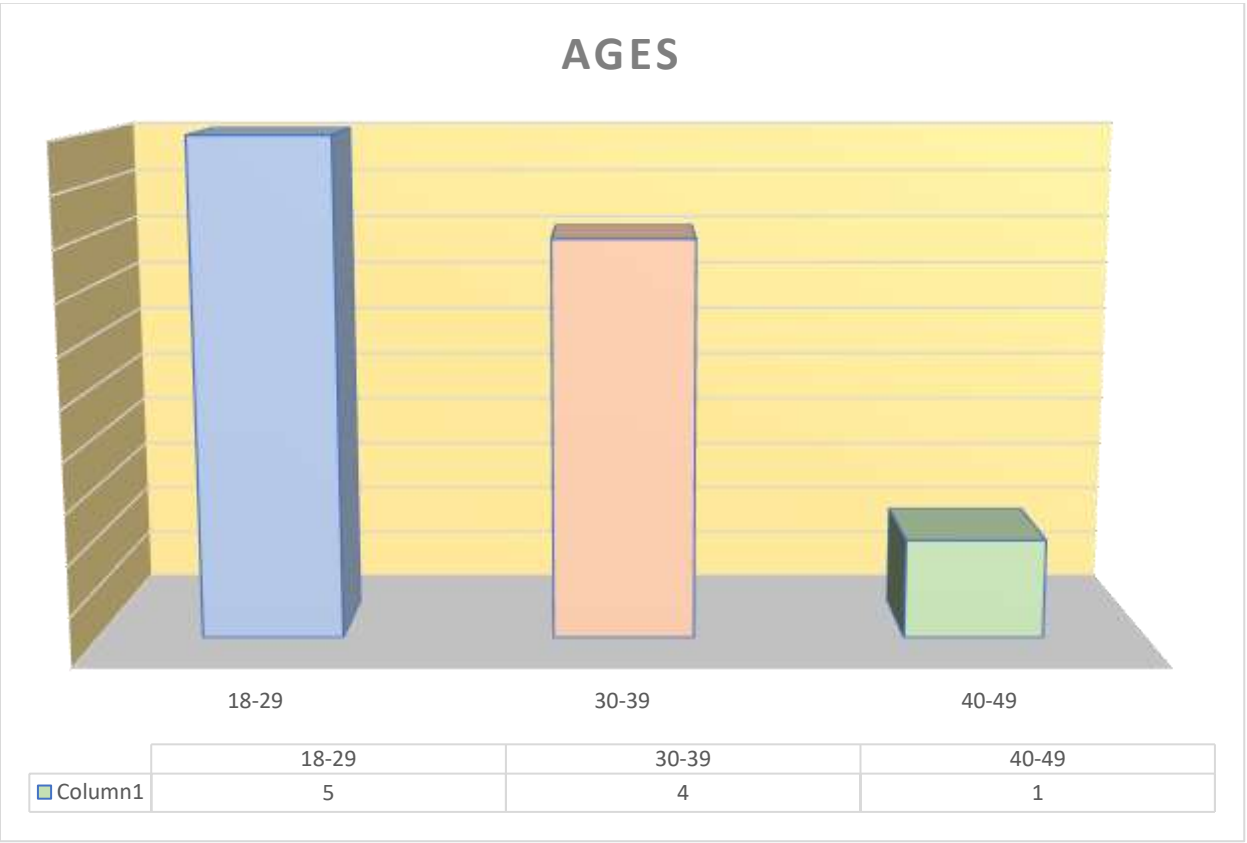


Results

The DNP Project started on January 18, 2022 and ended on February 17, 2022. A total of 160 hours were used for the project and 10 patients who met the inclusion criteria for the DNP Program were identified and treated. The age range of the patients was 22-49 years old. 40% males and 60% females were applicable for DNP project. Three patients had a diagnosis of bipolar two disorder and seven patients had a diagnosis of bipolar one disorder. Table 4a, 4b, and 4c provide patient demographics information. In the first two weeks, 10 patients were identified for the DNP Project. Eight out of ten patients were weaned off Aripiprazole. Some of the patients have taken Aripiprazole for several months or years and experienced more phases of depressive

bipolar disorder compared to manic. Wean off process took 14 days without any adverse effects.

Table 4a Demographics



	18-29	30-39	40-49
Column1	5	4	1

Table 4b Demographic

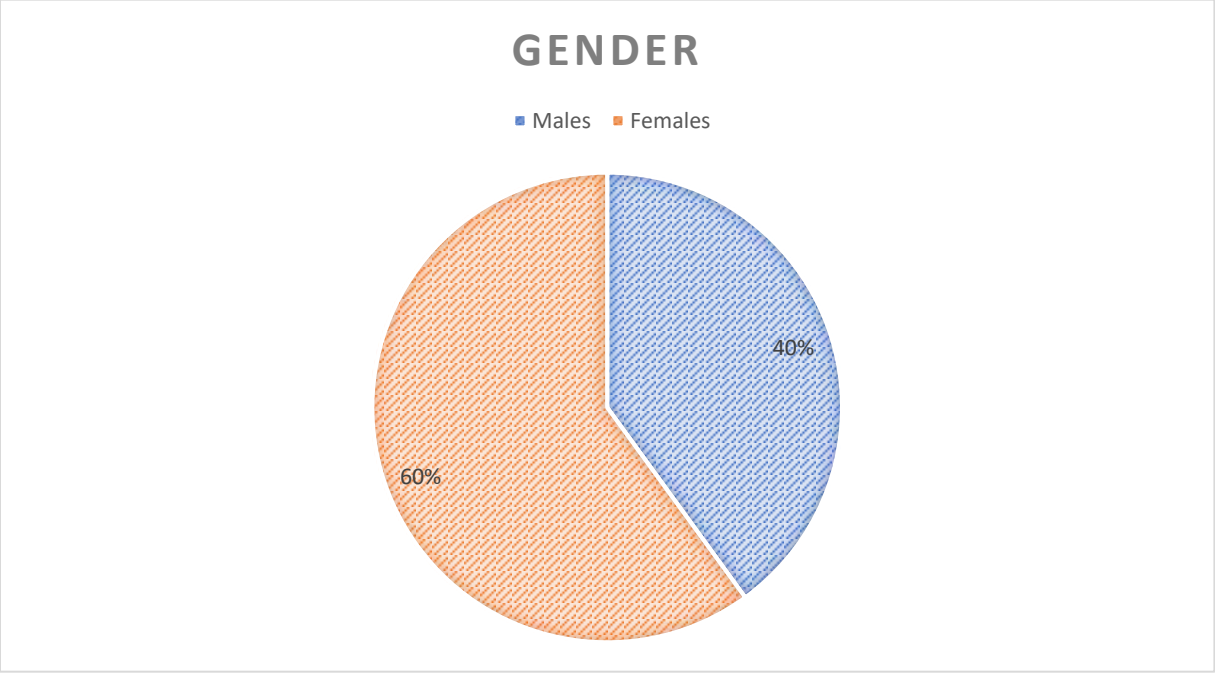
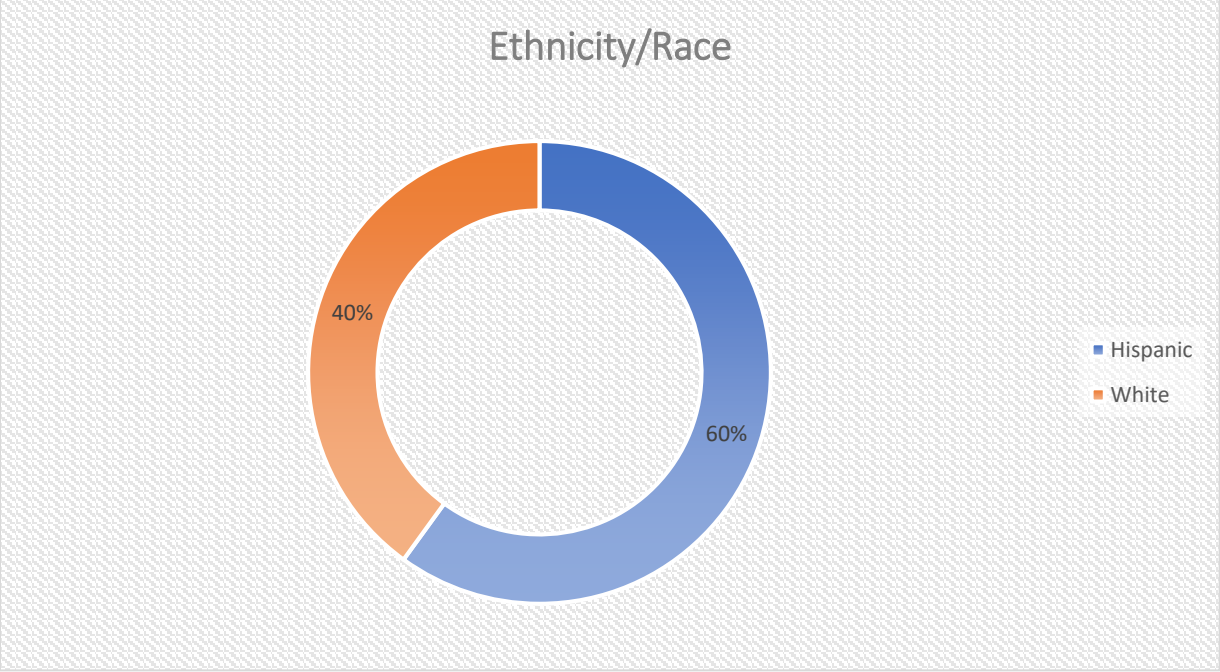


Table 4c Demographics



1 out of 10 patients refused to switch Aripiprazole but was opened to add an adjunctive medication. Another patient out of 10 refused to switch, adjusted current

medication, to add adjunctive medication, and his right was respected. This patient was included in the DNP Project as it met requirements and the patient was followed up for two weeks to see if symptoms continued or if allowed, to opt for a medication change in the follow-up appointment. The patient did not want his medication to be adjusted during initial intervention. Those 10 patients rated their depressive phase 8-10/10 on day one. Four patients were placed on Lurasidone (Latuda); two patients switched to Quetiapine; two patients switched to Cariprazine (Vraylar), and one of the patients who refused to switch added Lamotrigine as an adjunctive. The one patient who refused to change medication, was continued with current dosage as requested. Two of the patients who changed to Lurasidone (Latuda) complained of nausea for 1-2 days. Then, side effects improved. I did not encounter any conflict of interest as foreseen. After the two-week follow-up, assessment and evaluation were done; a rating scale was performed; nine patients reported a 2–5 point decrease in their depressive symptoms and one patient did not experience any change in their depressive symptoms. For those patients reporting 2 points decreased, I considered increasing dose to improve symptoms, of which the patient agreed. Their medication was Lurasidone (Latuda) 20 mg, which was increased to 40 mg per day and to be taken with food. Two other patients who took Lurasidone (Latuda) reported feeling stable at starting dose of 20 mg and continued with the current dosage. One patient who took Quetiapine at 100 mg every night reported feeling stable and had 5 points decrease in their rating scale. Other patients reported 2 points rating scale decrease, recommended medication adjustment and agreed to take 200 mg of Quetiapine at night. The patient who took Cariprazine (Vraylar) had 2-3 points decrease in their rating scale from their starting doses of 1.5 mg

and continued the dosage as per their request due to reported feeling stable. One patient who opt adjunctive, took Lamotrigine with Aripiprazole, that medication was titrated slow, started at 25 mg in week one and increased to 50 mg in week two due to its risk of adverse reaction of rash, which could lead to Steven-Johnson Syndrome. This treatment was supported by the guidelines (Yatham, et al. 2018). This patient had a 2-point decrease in their initial rating scale, and medication was increased to the target goal at 100 mg based on the patient's agreement to improve symptoms. The rating scale of the patient, who initially refused any change in depressive symptoms, did not change. During day one and follow-up day, the rating scale was 9/10; the patient agreed to increase the dosage of Aripiprazole 15 mg at night. However, he did not want to change his medication. I suggested considering psychotherapy, which was included in the CANMAT/ISBD 2018 guidelines. The patient responded that he would consider this in the future. His medication was adjusted with a two-week follow-up. Those patients who agreed with the medication change were received in two weeks to continue an evaluation of symptoms. Table 5a presents the rating scale of the 10 patients. Table 5b presents their outcomes. The application of the CANMAT/ISBD 2018 guidelines was effective in treating bipolar depression. The guidelines provided step-by-step in treating bipolar depression, which was based on the years of evidence-based clinical validity. The average decrease of the rating scale point was 2.6. The patient reported improvement in symptoms based on medication change. The CANMAT/ISBD 2018 guidelines on medication were well tolerated during their research and were confirmed by my DNP Project as two out of ten patients reported nausea. However, during the last one to two days, no adverse effects were reported. Certain insurances did not approve

brand-name medication currently only sold version of Lurasidone (Latuda) and Cariprazine (Vraylar). Some insurance companies approved Cariprazine (Vraylar) and not Lurasidone (Latuda) and vice versa.

Discussion

The CANAMT/ISBD 2018 guidelines were found to be useful in treating bipolar depression as they did alleviate bipolar depressive symptoms. The bipolar depression symptoms improved in the DNP project timeframe. These CANMAT/ISBD 2018 guidelines can be used for the treatment of the entire bipolar disorder spectrum, not only for bipolar depression phases because these guidelines provide an effective evidence-based clinical experience in the entire BD spectrum (Yatham, et al., 2018). The CANMAT/ISBD 2018 guidelines allowed patients to feel stable and improved their daily activities. More options of antipsychotics are available in treating bipolar one disorder compared to bipolar two disorder as the first line of treatment guidelines stated. Bipolar two has been understudied owing to a long-standing of bipolar one (Yatham, et al., 2018). Quetiapine is the only antipsychotic that FDA approves as the classification to treat bipolar two depressive phase (Yatham, et al. 2018). The CANMAT/ISBD guidelines will need an update due to as of December 2021, Lumateperone (Caplyta) was included as another FDA-approved medication for the treatment of bipolar one and two depressive phases (Sanchez, 2021).

Certain Brand name medications like Lurasidone (Latuda) or Cariprazine (Vraylar) were not approved by insurance. In this project, a patient confirmed that his insurance did not provide Lurasidone (Latuda) coverage but covered Cariprazine (Vraylar), which was not a first-line or not second-line treatment but a third-line

treatment. However, the medication alleviated bipolar depressive symptoms. Some insurances provided brand name medication if the patient failed other generic antipsychotics. Information of previously failed generic antipsychotic medication is provided to insurance companies and sending a prior authorization may be needed. The CANMAT/ISBS 2018 guidelines provide brand only medication and generic antipsychotics which are in most private or federal insurance medication formularies but depends upon the insurance approval of such medication. During this quality improvement, no limitations were encountered because patients who met the DNP project criteria were included. The DNP Project CANMAT/ISBD 2018 guidelines were effective for bipolar depression treatment because they eliminated guessing when it came to treating such depressive phase in the bipolar spectrum. I will incorporate these guidelines in my practice to improve bipolar disorder symptoms, reach patients' stability, and improve patients their quality of life.

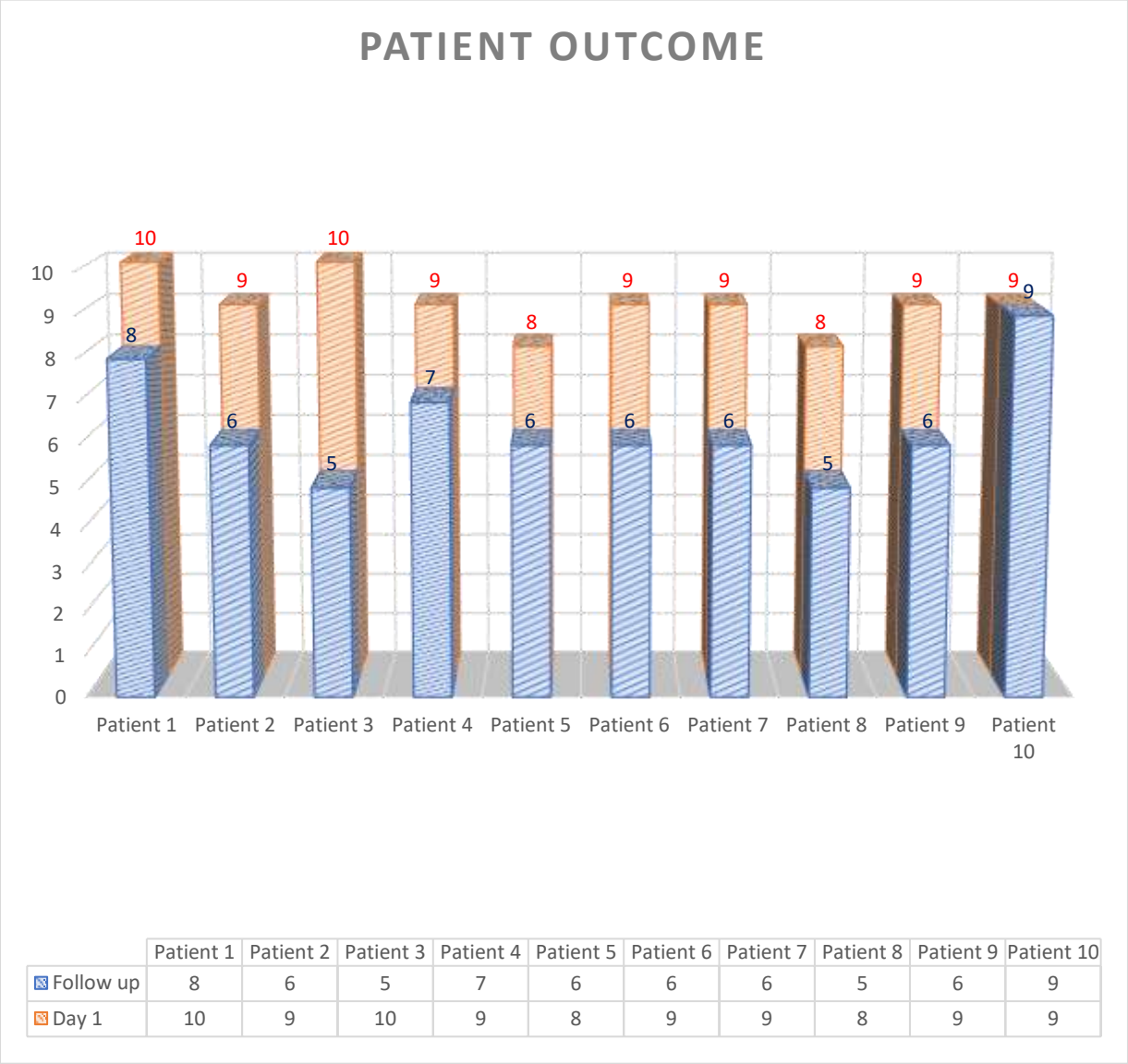
Other Information

I would like to thank my lovely family for their understanding and assistance granted in completing this DNP project. I also thank the Paso Del Norte Health Foundation for providing the program award to complete the Scholarly DNP Project. I would also like to thank Cohort X for all the support they offered during the two-year program at The University of Texas at El Paso. I like to give thank you to Dr. Hector, Morales for his guidance and motivation in completing the DNP Program. The revised standards of quality improvement reporting excellence SQUIRE 2 format were used for this manuscript (SQUIRE, 2020).

Table 5a Patient Outcome

Patients	**Day 1 Rating Scale**	**Follow up Rating Scale**	**Bipolar Disorder Type**
1. Aripiprazole, added Lamotrigine	10/10	8/10 (-2)	Bipolar Disorder Type 1
2. Aripiprazole switch to Lurasidone (Latuda)	9/10	6/10 (-3)	Bipolar Disorder Type 1
3. Aripiprazole & Lamotrigine, switch antipsychotic to Quetiapine	10/10	5/10 (-5)	Bipolar Disorder Type 2
4. Aripiprazole switch to Cariprazine (Vraylar)	9/10	7/10 (-2)	Bipolar Disorder Type 1
5. Aripiprazole switch to Cariprazine (Vraylar) (Lurasidone was not approve by insurance and took Quetiapine in the past)	8/10	6/10 (-2)	Bipolar Disorder Type 1
6. Aripiprazole switch to Lurasidone (Took Quetiapine in the past and did not tolerated side effects)	9/10	6/10 (-3)	Bipolar Disorder Type 1
7. Aripiprazole switch to Quetiapine	9/10	6/10 (-3)	Bipolar Disorder Type 2
8. Aripiprazole switch to Lurasidone (Took Quetiapine in the past and did not tolerated side effects)	8/10	5/10 (-3)	Bipolar Disorder Type 1
9. Aripiprazole switch to Lurasidone	9/10	6/10 (-3)	Bipolar Disorder Type 1
10. Aripiprazole, no switch, no adjunctive medication	9/10	9/10 (0)	Bipolar Disorder Type 1

Figure 5b Patient Outcome



	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10
Follow up	8	6	5	7	6	6	6	5	6	9
Day 1	10	9	10	9	8	9	9	8	9	9

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