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**Visualizing Depressive Symptom Improvement: Implementing the 17-Item
Hamilton Depression Rating Scale**

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2012

A dissertation submitted to the Graduate School at the University of Missouri- St. Louis
in partial fulfillment of the requirements for the degree

Doctor of Nursing Practice

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Abstract

Problem

Depression, a mental health diagnosis, has affected about 18.5% of adults (Villarroel & Terlizzi, 2020). Ketamine, a medication initially used as an anesthetic, has improved depressive symptoms in individuals struggling with treatment-resistant depression.

Method

This quality improvement (QI) project used the 17-item Hamilton Depression Rating Scale questionnaire to assess depressive symptom changes in patients receiving intramuscular ketamine for treatment-resistant depression. The questionnaire was administered to patients pre-and post-intramuscular ketamine administration. The data was collected on injections one, three, and six on each participant's set schedule of injections and participation period. The primary outcomes measured were the questionnaire scores before and after the administration of ketamine intramuscularly and the sum of the depressed mood questions (1-3), insomnia questions (4-6), physical symptoms questions (9-11, 16), anxiety questions (9-11, 15), and insight question (17). Paired-samples t-testing analyses were performed on the collected data.

Results

The data showed that week one's participants' (n=14) scores significantly reduced the following categories: depressed mood and thought, anxiety, and physical symptoms. Week three's (n=13) and week six's (n=8) data showed a significant reduction in depressed mood and thought and anxiety categories.

Implications for Practice

This QI project provided encouraging data examining depression severity changes after the administration of intramuscular ketamine for patients with major depressive disorder or bipolar disorder. The results provide reassuring objective information for providers concerned about possible medication tolerance or misuse during treatment while ensuring providers that ketamine can be used to effectively improve depressive symptoms.

Visualizing Depressive Symptom Improvement: Implementing the 17-Item Hamilton Depression Rating Scale

Depression is a serious and common medical illness that negatively affects feelings, thoughts, and actions (American Psychiatric Association [APA], 2013). In 2019, the Centers for Disease Control (CDC) reported that about 60 million, or approximately 18.5% of adults over 18, experience depressive symptoms (Villarroel & Terlizzi, 2020). Of these individuals, 11.5% experience mild symptoms, 4.2% have moderate symptoms, and 2.8% suffer from severe symptoms (Villarroel & Terlizzi, 2020).

The Diagnostic and Statistical Manual of Mental Disorders (DSM-5) requires individuals have five or more symptoms associated with depression before being diagnosed with depression (APA, 2013). One of the symptoms must either be anhedonia or depressed mood, while the remaining secondary symptoms are categorized as somatic (physical) and non-somatic (psychosocial or behavioral) (APA, 2013). Patients who do not respond to depression treatment are referred to as having treatment-resistant depression (Agency for Healthcare Research and Quality [AHRQ], 2016). The AHRQ (2016) stated treatment-resistant depression often presents in the diagnoses of major depressive disorder (MDD) or bipolar disorder. Treatment remission is the goal for depressed patients, achieved about 30% of the time, which leaves the other 70% of patients with little to no depressive symptom relief (Trivedi et al., 2006). Fortunately, ketamine, a medication used initially for anesthesia, was found to help patients with treatment-resistant depression (Li & Vlisides, 2016).

The N-methyl-D-aspartate (NMDA) receptor is a cellular channel found on the dendritic spines of the postsynaptic neurons, the presynaptic axon terminals, interneurons in the brain, and on glial cells in the brains of mammals (Conti, 1997). Glutamate, a neurotransmitter, activates the NMDA receptor, which then creates synaptic changes; these changes play a role in learning and memory (National Center for Biotechnology Information, 2021). Researchers have found that individuals diagnosed with depression do not have the central nervous system capability to effectively use glutamate (The Mount Sinai Hospital / Mount Sinai School of Medicine, 2017). Ketamine is a noncompetitive NMDA receptor antagonist that prevents glutamate neurotransmitters from binding to NMDA receptors (Zorumski, 2016). Ketamine in subanesthetic doses improves depressive symptoms by blocking the NMDA receptor by changing either the receptor's electric charge or shape (Zorumski, 2016).

Ketamine has two isomer forms, S (+) and R (-). Racemic ketamine is the title given to ketamine that has both isomer forms, which can be administered intravenously (IV), intramuscularly (IM), subcutaneously (SQ), and orally (Andrade, 2017; Molero et al., 2018). Although the oral administration of ketamine is more convenient, IV, IM, and SQ ketamine are more bioavailable (Andrade, 2017; Molero et al., 2018). The higher the bioavailability of a medication route, the quicker the medication reaches a body's circulatory system. Ketamine IV and IM are, respectively, with onsets of action of mere seconds and four minutes, both ideal for ketamine clinic use (Rosenbaum et al., 2021). Despite the onset of action difference between IV and IM ketamine, researchers have found IM ketamine to be just as successful in decreasing depressive symptoms (Chilukuri et al., 2014; Fond et al., 2014; Harihar et al., 2013; Rot et al., 2012; Xu et al., 2015). Fond

et al. (2014), Ghasemi et al. (2014), and Kheirabadi et al. (2014) reported ketamine not only reduces depressive symptoms quicker, but the medication can also significantly reduce suicidal ideations in patients with treatment-resistant depression while having fewer cognitive side effects compared to electroconvulsive therapy.

Provider determination of the diagnosis of depression differs based on the instrument used for assessment. While the PHQ-9 can provide a diagnosis of depression, only the Hamilton Depression Rating Scale (HDRS) enables providers to apply a level of severity to the diagnosis of depression (Wittkamp et al., 2009).

Before 1960, existing scales only provided information to help a provider determine if a patient suffered with depression. Recognizing the limitations of the existing scales, Hamilton (1960) created the Hamilton Depression Rating Scale (HDRS) to determine the severity of depression symptoms in depressed patients. The original HDRS Hamilton created was a 21-item questionnaire which he shortened to 17-items. After a depression diagnosis, the administration of the HDRS provides patient-rated data to assess and define symptom severity (Sharp, 2015). The scale asks patients to self-assess and rate the severity of their depressed mood, suicidal ideations, insomnia, agitation, anxiety, and motivation levels. At the time of development, Hamilton (1960) found the HDRS to be especially effective at assessing treatment results.

The American Psychiatric Nurses Association (APNA) encourages administering a depressive symptom scale before and after ketamine administration for all depression diagnoses (Bolton et al., 2021). The purpose of this proposed quality improvement project was to implement the use of the HDRS for the evaluation of treatment for treatment-resistant depression patients receiving ketamine administered intramuscularly

in a midwestern ketamine clinic. The aim of the project was to increase the amount of 17-item HDRS scales used in the clinic to evaluate treatment-resistant depression by 15%. The primary outcome measured was the HDRS ratings before and after intramuscularly administered ketamine on treatment appointments one, three, and six. The secondary outcomes measured were age, gender, race, and diagnosis. A study question was created to help guide the literature search: In patients with treatment-resistant depression receiving an IM ketamine injection, does the use of the 17-item HDRS before and after IM ketamine administration effectively track improvements in depressive symptoms?

Literature Review

A literature search was conducted to determine what version of the HDRS would help provide the best measurement of depressive symptom improvement in patients receiving IM ketamine for treatment-resistant depression. The following search engines were used: PubMed, Summon, and Google Scholar. Key search terms included *Hamilton Depression Rating Scale, HDRS, ketamine, intramuscular ketamine, depression, and treatment-resistant depression*, which yielded 6,915 results. Search settings included: peer-reviewed journals, randomized controlled trials (RCT), research articles, systematic reviews, and meta-analyses written in English from 1/1/2013 to 9/10/2021. Any article written before 2013 was excluded, except for three pertinent articles. Duplicates were then removed, and a review of inclusion criteria focusing on the age of participants, type of depressive screening tool used, and use of racemic ketamine administration articles were reduced to a total of 53. The abstracts were read, and eight articles were selected for review.

Depressive Symptom Rating Scales

In 2006, a physician-researcher named Per Bech created a 6-item HDRS. Bech (2006) compared 47 articles to provide a microanalysis of the 17-item HDRS to his 6-item HDRS. The HDRS 6-item questionnaire asked patients how they were feeling overall in the past three days. The 6-item scale asked about mood, self-satisfaction, interest in activities, fatigue, mental slowing, and anxiety. The narrative review reported the 6-item HDRS to be more sensitive in determining if a medication treatment improved a patient's depressive symptoms. Bech (2006) encouraged other researchers to compare his 6-item HDRS to the original 21-item HDRS for a more accurate reliability conclusion for in-practice use.

A meta-analysis was performed by Trajković et al. (2011) to determine the reliability of the various HDRS questionnaires. A total of 409 articles were used. The researchers concluded the original 21-item and modified HDRS questionnaires appeared beneficial for healthcare professionals by helping provide quantitative data in patients reporting the severity of their depressive symptoms. The team discovered a good internal consistency between the HDRS scales. Inter-rater reliability was calculated with 14 articles with a total of 449 subjects. The results found the inter-rater reliability to be the highest with "insomnia-early", "suicide", and "depressed mood," while the weakest inter-rater reliability was "loss of insight" Trajković et al. (2011) also calculated the test-retest reliability of the scales by using 11 articles totaling 729 participants. This analysis revealed the longer the HDRS questionnaires were used between two researchers, the lower the test-retest reliability. It was concluded the HDRS remains a reliable measurement in patients with depression, and further research comparing the sensitivity of the six and 17-item HDRS should be performed (Trajković et al., 2011).

Dunlop et al. (2019) completed a post hoc analysis to compare the sensitivity of the 6-item and 17-item HDRS. The study included 1,541 patients in a 24-week trial conducted within 60 primary care and psychiatry specialty clinics in the United States. Patients were enrolled if they were diagnosed with MDD and reported an inadequate response to previous depressive treatments. A randomized control trial was created that compared two different prescribing methods for patients struggling with MDD. Both methods were found to be beneficial by using the 6-item and 17-item HDRS questionnaires. Furthermore, the study's analyses found the 6-item scale more beneficial in gauging the improvement of depressive symptoms through pharmacological use. However, since the 6-item scale uses the past three days as a time frame, the 17-item Hamilton scale provides better information on how a rapid treatment improves depressive symptoms. The researchers recommended the HDRS scales be compared to other depressive symptom scales to determine which scale is more reliable (Dunlop et al., 2019).

Carrozzino et al. (2020) performed a comprehensive review of 203 articles to determine which versions of the HDRS were more reliable, valid, and sensitive to change than other depressive symptom scales. When the HDRS 17-item scale was compared to the Beck Depression Inventory (BDI), results showed the 17-item HDRS was more sensitive to depression symptom changes than the BDI. The HDRS 6-item scale was more sensitive to symptom change than the Montgomery-Asberg Depression Rating Scale (MADRS). The HDRS scales were determined to be valid, sensitive, and reliable if researchers structured the scales. Structured scales use the same questions for every

patient. The researchers concluded the 17-item HDRS should be used to differentiate levels of severity and depressive symptoms of patients throughout a specific treatment. In contrast, the 6-item HDRS should be used when determining the efficacy of active treatment compared to placebo (Carrozzino et al., 2020).

Incorporation of HDRS with Ketamine Therapy

Several studies have validated the use of the HDRS for clinician use in measuring ketamine therapy results. The HDRS can help clinicians identify rapid changes in a patient's depression symptoms. Additionally, with the APNA's encouragement of using a depressive symptom scale before and after administering ketamine, use of the HDRS for ketamine therapy is a viable strategy for depression treatment (Berman et al., 2000; Carrozzino et al., 2020; Chilukuri et al., 2014; Ghasemi et al., 2014; Harihar et al., 2013; Katalinic et al., 2013; Kheirabadi et al., 2020).

Berman et al. (2000) conducted a study comparing patients receiving ketamine to others receiving saline. The researchers used the HDRS to determine how each treatment reduced depressive symptoms. This randomized, double-blind trial included seven subjects diagnosed with major depression. Three participants who received saline and three of the four participants who received ketamine were included in the data collection due to one participant not completing both ketamine administrations. Measurements of treatment, time after administration, and medication efficacy were analyzed. On average, the HDRS scores of the patients who received ketamine were reduced by about 50% compared to no reduction made in the patients who received saline. In addition, the HDRS was able to provide researchers with statistically significant information on what categories improved after ketamine administration. It was concluded that ketamine is an

effective way to reduce depressive symptoms; however, due to the small population, the researchers encouraged others to explore the benefits and efficacy of ketamine (Berman et al., 2000).

Chilukuri et al. (2014) created a study “to compare the safety, tolerability, and efficacy of intramuscular versus intravenous ketamine in major depression”. This randomized parallel study had a total of 27 subjects. All subjects had MDD as a diagnosis and were separated into three groups of nine. Ketamine was administered to each group in a dose of either 0.5mg/kg IV, 0.5mg/kg IM, or 0.25mg/kg IM. The HDRS was used before administration, two hours after administration, and four days after administration to assess the tolerability and efficacy the three groups had with ketamine. The researchers graded patients as non-responders (an HDRS score less than 25% from baseline), partial responders (if the HDRS score was reduced between 26 and 49% from baseline), and responders (an HDRS score reduction of 50% or more from baseline). Results showed that by using the HDRS, researchers were able to determine that all groups were responders to the ketamine 0.5mg/kg IV, 0.5mg/kg IM, or 0.25mg/kg IM treatment with a reduction of the HDRS scores at 58.86%, 60.29%, and 57.36%, respectively. With IM ketamine being just as effective, the smaller IM dosage provides a safer dosage amount for providers to administer while achieving the same depressive symptom reduction benefits as IV ketamine (Chilukuri et al., 2014).

Katalinic et al. (2013) performed a comprehensive narrative review to determine the safety and efficacy of subanesthetic doses of ketamine to treat depression. Eleven of the 20 studies reviewed used the HDRS to determine subjects’ symptomatic improvement. The HDRS was able to show researchers how ketamine can significantly

reduce depressive symptoms by quantifying qualifiable data. Unfortunately, not everyone responded to ketamine treatment. According to the review, 70 to 80% of patients reported ketamine as a successful treatment for their depression. Although ketamine provided rapid relief for these successful treatments, the maximum amount of time reported for ketamine to help was one month unless ketamine administrations were repeated to maintain patients' symptomatic improvement. Frequently repeated ketamine administrations occurred. Although IM administration of ketamine has not been providers' top choice for patients struggling with depression, it has improved depressive symptoms, which can be shown by HDRS questionnaire scores administered before and after treatment. Future research was encouraged to focus on identifying predictors of response, such as clinical, genetic, and environmental, examining various routes and dosing regimens, and strategies to maintain the antidepressant response (Katalinic et al., 2013).

Similarly, Kheirabadi et al. (2020) created a pilot study to compare oral and IM ketamine treatment efficacy to electroconvulsive therapy in patients diagnosed with major depressive disorder. Forty-five participants, 22 males and 23 females between 20 and 70 years of age, were divided equally into three groups. Each group received either 0.5mg/kg of IM ketamine, 1mg/kg of oral ketamine, or electroconvulsive therapy. Each treatment lasted six to nine sessions for three weeks. The HDRS and Beck Scale for Suicidal Ideations (BSSI) were used at baseline, 24 hours, one week, two weeks, and three weeks within the intervention to measure depressive symptoms and suicidal ideation. The researchers reported the HDRS scores were reduced in every group and did not go back to baseline after the treatment and each treatment significantly reduced the

BSSI and HDRS scores from baseline. Despite each group showing a significant reduction in depressive symptoms, the researchers did not see a significant difference between the IM ketamine, oral ketamine, and electroconvulsive therapy treatments. While ketamine can be easily administered to help improve depressive symptoms and suicidal ideations, the long-term effects of this medication for the treatment of treatment-resistant depression are unknown. Providers should be aware of the risks and benefits of any treatment offered to patients struggling with treatment-resistant depression and are encouraged to take appropriate measures to care for them in a safe environment (Kheirabadi et al., 2020).

Research shows the 17-item HDRS is a reliable screening tool to help provide quantitative data for qualitative information and can assess rapid changes in depressive symptoms. Since ketamine can rapidly improve depressive symptoms, the 17-item HDRS is the questionnaire of choice to assess these improvements. Therefore, the APNA's recommendations of administering a depressive symptom scale before and after ketamine administration for all depression diagnoses can be implemented using the HDRS.

Methods

Design

This descriptive study QI project used prospective data collection. The data collection contained patients' HDRS scores before and after IM ketamine administration. Data collection occurred from February 9, 2022, through March 31, 2022.

Setting

The setting was in one of the six ketamine clinics/healthcare offices caring for urban and rural individuals in a Midwestern state. A little over 300,000 people live in the

area. Five employees work in the clinic: two physicians, one registered nurse, and two office assistants. The clinic screens patients for any suicidal thoughts with a modified Columbia-Suicide Severity Rating Scale before their IM treatment; however, it does not have any depressive symptom severity scales to administer before and after patients' IM ketamine treatment.

Sampling

The sample was composed of patients receiving IM ketamine for severe depression using a convenience sampling method. The inclusion criteria were adult patients from ages 18 through 70 with a diagnosis of major depressive disorder or bipolar disorder. Exclusion criteria included individuals younger than 18 years of age, inmates, and pregnant women. Weekly, the clinic administered IM ketamine to about 15 patients, the desired size.

Data was collected using a unique alphanumeric identifier which was created and applied to each patient for de-identification purposes. The identifier combined the two-digit month (01), two-digit year (22), and three successive letters of the alphabet: ABC to each patient chart creating a unique seven-digit identifier. A master list of coded identifiers and patient names were stored in a password-protected file on the clinic's computer. Data collected was entered on an Excel spreadsheet and stored on the student investigator's password-protected laptop.

Recruitment strategies for the project included asking patients if they would be willing to participate in a quality improvement project upon making their appointment or right before receiving their injection. going back for their injection. Informed consent was given to the patients who were interested in participating. A consent form was signed,

and a \$5 Amazon gift card was gifted to the individuals who completed each pre-IM administration HDRS questionnaire, for a total of \$15.

Procedure

Implementation of the HDRS versus current practice without screening was a QI project selected by the healthcare organization, which the student primary investigator (PI) led. The 17-item HDRS was administered just prior to the scheduled IM administration time via a paper handout completed by the patient. The IM injection was administered by a physician in a private room. After the patient came out of their dissociative state, about 20 to 30 minutes after the injection, each HDRS question was read by the physician and the HDRS questionnaire was offered to the patient via a laminated sheet. The interviewer requested and recorded patient responses by circling the correlating numbers to the answers provided on the paper 17-item HDRS administered before IM ketamine administration. The pre-administration and post-administration HDRS scores and totals for each depressive symptom segment were calculated and documented on the final data collection sheet by the PI.

Data Collection/Analysis

The primary outcomes measured were the HDRS scores before and after the administration of ketamine intramuscularly and the sum of the depressed mood questions (1-3), insomnia questions (4-6), physical symptoms questions (9-11, 16), anxiety questions (9-11, 15), and insight question (17). The 17-item HDRS scores were collected on injections one, three, and six on each participant's set schedule of injections and period of participation. The secondary outcomes measured were gender, race, age, and

diagnosis. The analysis used was the paired-samples t-test, as this analysis can assess for significant changes in the pre- and post-HDRS and categorical scores.

Approval Process

Formal, written approval was received from the participating clinic's founders. Before implementation, further approval was obtained from the University of Missouri-St. Louis Institutional Review Board. Risks of this QI project included the HDRS questionnaire asking the patients to reveal sensitive information, possibly causing distress when reporting. Healthcare professionals were available to monitor the patients, and the participants could have opted out of the QI project at any time. The benefits of this QI project included the provision of an additional evaluation tool to measure changes in depressive symptoms for patients receiving IM ketamine, and the dissemination of this data could support ketamine as a treatment in patients with treatment-resistant depression for wary providers.

Results

Demographics

Out of 24 patients receiving IM ketamine, 15 participants participated in this QI project; however, one participant was dropped from the QI project related to pregnancy, making 14 participants ranging between the ages of 25 and 68 ($M = 45$, $SD = 12.15$). A total of nine females (64.3%), three males (21.4%), and two in the other identifying (14.3%) participated. African American ($n=1$), American Indian ($n=1$), and Caucasian ($n=12$, 85.7%) were the participants' specified races. Participants who received IM ketamine were being treated for depression ($n=12$, 85.7%) and bipolar ($n=2$, 14.3%). All participants received IM ketamine from this ketamine clinic before this QI project started,

see Figure 1 to view what identifying gender percentages are associated with treatment diagnosis. A total of 14 participants completed week one pre- and post-HDRS questionnaires. While 13 participants completed week three and eight participants were able to complete the pre- and post-HDRS questionnaires though week six. Only calculating the participants who completed all six questionnaires, the eight participants make up 30% of the patients, surpassing the aim by 15%.

Results of the HDRS Before and After Ketamine Therapy

A paired-samples t-test was conducted to evaluate participants' depressive symptom severity total and categorical totals before and after IM ketamine administration. The 17-item HDRS questionnaire scores were totaled for a pre- and post-IM administration score, and each question in the HDRS was separated into five different categories. Questions were separated based on what depressive symptom category with which they were correlated. Category one was depressed mood and thought (questions 1 - 3). Category two was insomnia containing questions 4 through 6. Questions 7, 8, 12 through 14, and 16 were in category three of physical symptoms and activities of daily living (ADL). Anxiety questions 9 through 11 and 15 were in category four, and insight, question 17, was in category five. The paired-samples t-test compared each pre- and post-17-item HDRS score and question category week by week since there were at least seven days between injections, creating a washout period. A washout period is a duration in which research participants do not receive any treatment, and the effects of the previous treatment are presumed to be eliminated (Segen, 2011).

The literature review above indicated ketamine was a successful treatment in patients with treatment-resistant depression. It also mentioned how the 17-item HDRS

scale was the best depression symptom severity scale assessment for a specific treatment while being a more reliable tool, especially when the tool is administered by one provider. Only the provider, who administered the IM ketamine, administered the post-HDRS to each participant making the QI data more reliable. The results within this QI project show many relational results compared to what the literature showed. Tables 1 through 4 in the appendix provide this information while Figure 2 provides a comparison of each category within the pre- and post-total scores on weeks 1, 3, and 6.

When week one's total pre- and post-HDRS scores were compared, there was a significant decrease in the total depressive scores from before ($M = 18.21$, $SD = 8.997$) to post ($M = 10.71$, $SD = 5.312$) IM ketamine was administered with $p = <.001$ (two-tailed) (Table 1). In scoring the HDRS, the higher the HDRS score is, the more severe the participant's depression is therefore, the IM ketamine reduced depression severity in HDRS total scores by almost 50%. Similarly, participants' depressed mood and thought and anxiety scores were reduced by about 50%. While physical symptoms and ADL scores were significantly reduced the first week with $p = 0.007$ (two-tailed), they were not as significant as the pre- and post-total depressed mood and thought (category one) and anxiety scores (category four).

Week three's pre- and post-total HDRS, depressed mood and thought, and anxiety scores paired-samples t-test all had a significant decrease in score totals with $p = 0.001$, 0.006 , and <0.001 , respectively, and about a 50% reduction in each category's total score (Table 2). Physical symptoms and ADL scores before ($M = 4.77$, $SD = 3.086$) to after ($M = 4.31$, $SD = 2.626$) IM ketamine administration decreased slightly, but not significantly ($p = 0.165$).

The paired-samples t-test completed on week six's pre- and post-total HDRS, depressed mood and thought, and anxiety scores also had a significant decrease in score totals with p ranging between 0.003 and 0.014 with close to about a 50% reduction in scores after the administration of IM ketamine (Table 3). Similarly, the sixth week's total in physical symptoms and ADL scores did not significantly decrease with $p = 0.118$.

After assessing the total scores of weeks one, three, and six, it was determined that week one's pre- and post-total HDRS scores differed from week six's pre- and post-total HDRS scores. A paired-samples t-test was used to determine if there was a significant difference (Table 4). There was a significant decrease when week one's pre ketamine total HDRS scores ($M = 20.25, SD = 6.519$) were compared to week six's pre ketamine total HDRS scores ($M = 16.63, SD = 6.927$) with $t(7) = 4.396$ and $p = 0.036$ (two-tailed). Every week's pre- and post-score analysis of insomnia and insight could not be performed due to no change in the reporting data as participants did not have a chance for insomnia reassessment in the hour they were at the clinic and the insight about their condition was stable.

Discussion

The clinic's founders wanted to begin an assessment of depressive symptom severity for patients receiving IM ketamine to provide best patient practice while assessing a patient's depressive symptoms on a weekly basis. This six-week QI project provided encouraging data examining depression severity changes after the administration of IM ketamine for patients with major depressive disorder or bipolar disorder. The literature evidence of ketamine improving depressive symptoms and the QI data coincided with each other, despite the project's participants having prior treatment

establishment. The results provide reassuring objective information for providers who are concerned about possible medication tolerance or misuse during treatment. Although the data above provided encouraging information, there were many limitations of this project which included: time frame of project, sample size, and type of questionnaire.

Due to the university's institutional review board needing to review this project in depth related to sensitive matter, this project started a month later than anticipated. Between the later start date and the completion date preventing six participants from completing all data collection dates based on the participants own ketamine schedule. If the project's time-period had the planned three months to complete the project, each data point would have had the same sample size in each calculation.

Unfortunately, the largest limitation of this project was the sample size. Overlooking the small population receiving IM ketamine in the clinic, a total of 14 participants were included in this study. Of the 14 participants, only 13 completed week three's questionnaires due to the clinic being busier and a questionnaire was forgotten about. Due to time constraints, only eight participants were able to complete every questionnaire. Small population sizes can impact effect size by skewing data results, creating a false data correlation with the pre and post IM ketamine 17-item HDRS scores.

Although the questionnaire chosen for this project due to the literature results comparing the 17-item HDRS to other scales assessing depressive symptom severity, the 17-item HDRS was originally created for a clinician tool during inpatient assessments. The 17-item HDRS was a tool created in the 1960's and uses medical terminology that is not patient friendly (i.e., retardation, somatic, and hypochondriasis). Recalling the methods portion of this project, participants completed the pre HDRS questionnaire while

a provider interviewed the patient post IM ketamine administration. Despite the questionnaire being a successful tool in assessing depressive symptom severity in an inpatient setting, the 17-item HDRS ultimately made more work for the provider as medical terminology and the questionnaire's inpatient intended use was not ideal for this outpatient QI project or patient participation.

Conclusion

This QI project provides practice information and encouraging data for any ketamine clinic who does not perform pre and post surveys assessing depressive symptom severity in patients receiving ketamine for major depressive disorder or bipolar disorder. Assessing depressive symptom severity by turning something subjective into objective data, providers can determine the success of depression treatment while following encouraged guidelines from associations like the APA and APNA.

The Doctor of Nursing Practice (DNP) degree track can prepare practitioners to easily assess areas of improvement and create a plan, do, study, act (PDSA) cycle to ultimately improve patient care and practice settings. Any QI project turns evidence-based practice information into quality practice data and creates learning opportunities in healthcare. This project provided the opportunity to collaborate with other healthcare providers while gaining more insight on an interesting treatment to complex but common diagnoses.

Future research recommendations would be to compare the reliable inpatient 17-item HDRS scale with outpatient depressive symptom scales in patients receiving ketamine and to perform a quality improvement project assessing a patient-orientated

outpatient depressive symptom severity scale such as the Quick Inventory of Depressive Symptomatology- Self Report questionnaire.

References

- American Psychiatric Association. (2013). *Diagnostic And Statistical Manual Of Mental Disorders* (5th ed.). American Psychiatric Publishing.
- Agency for Healthcare Research and Quality (AHRQ). (2016). *Treatment-resistant depression: A narrative and systematic review of definitions and methods in clinical research studies*.
<https://www.ahrq.gov/sites/default/files/wysiwyg/research/findings/ta/topicrefinement/trdepression-protocol-amendment.pdf>
- Andrade, C. (2017). Ketamine for depression, 4: In what dose, at what rate, by what route, for how long, and at what frequency? *The Journal of Clinical Psychiatry*, 78(7). <https://doi.org/10.4088/jcp.17f11738>
- Bech, P. (2006). Rating scales in depression: Limitations and pitfalls. *Dialogues in Clinical Neuroscience*, 8(2), 207–215.
<https://doi.org/10.31887/dcns.2006.8.2/pbech>
- Berman, R. M., Cappiello, A., Anand, A., Oren, D. A., Heninger, G. R., Charney, D. S., & Krystal, J. H. (2000). Antidepressant effects of ketamine in depressed patients. *Biological Psychiatry*, 47(4), 351–354. [https://doi.org/10.1016/s0006-3223\(99\)00230-9](https://doi.org/10.1016/s0006-3223(99)00230-9)
- Bolton, P., Carbray, J., Mitchell, R., & Nihart, M. (2021). *Ketamine infusion therapy treatment considerations*. American Psychiatric Nurses Association.
<https://www.apna.org/ketamine-infusion-therapy/>.
- Bonnet, U. (2015). Long-term ketamine self-injections in major depressive disorder: Focus on tolerance in ketamine's antidepressant response and the development of

ketamine addiction. *Journal of Psychoactive Drugs*, 47(4), 276–285.

<https://doi.org/10.1080/02791072.2015.1072653>

Carrozzino, D., Patierno, C., Fava, G. A., & Guidi, J. (2020). The Hamilton rating scales for depression: A critical review of clinimetric properties of different versions.

Psychotherapy and Psychosomatics, 89(3), 133–150.

<https://doi.org/10.1159/000506879>

Chilukuri, H., Reddy, N. P., Pathapati, R. M., Manu, A. N., Jollu, S., & Shaik, A. B.

(2014). Acute antidepressant effects of intramuscular versus intravenous

ketamine. *Indian Journal of Psychological Medicine*, 36(1), 71–76.

<https://doi.org/10.4103/0253-7176.127258>

Conti, F. (1997). *Localization of NMDA receptors in the cerebral cortex: A schematic overview*. Brazilian Journal of Medical and Biological Research.

<https://www.scielo.br/j/bjmr/a/m8F5hnCQfBTfT9fm3HsZc3c/?lang=en>

Dunlop, B. W., Parikh, S. V., Rothschild, A. J., Thase, M. E., DeBattista, C., Conway, C.

R., Forester, B. P., Mondimore, F. M., Shelton, R. C., Macaluso, M., Logan, J.,

Traxler, P., Li, J., Johnson, H., & Greden, J. F. (2019). Comparing sensitivity to

change using the 6-item versus the 17-item Hamilton Depression Rating Scale in

the guided randomized controlled trial. *BMC Psychiatry*, 19(1).

<https://doi.org/10.1186/s12888-019-2410-2>

Fond, G., Loundou, A., Rabu, C., Macgregor, A., Lançon, C., Brittner, M., Micoulaud-

Franchi, J.-A., Richieri, R., Courtet, P., Abbar, M., Roger, M., Leboyer, M., &

Boyer, L. (2014). Ketamine administration in depressive disorders: A systematic

review and meta-analysis. *Psychopharmacology*, 231(18), 3663–3676.

<https://doi.org/10.1007/s00213-014-3664-5>

Ghasemi, M., Kazemi, M. H., Yoosefi, A., Ghasemi, A., Paragomi, P., Amini, H., & Afzali, M. H. (2014). Rapid antidepressant effects of repeated doses of ketamine compared with electroconvulsive therapy in hospitalized patients with major depressive disorder. *Psychiatry Research*, 215(2), 355–361.

<https://doi.org/10.1016/j.psychres.2013.12.008>

Hamilton, M. (1960). Hamilton depression rating scale. *SpringerReference*.

https://doi.org/10.1007/springerreference_184614

Harihar, C., Dasari, P., & Srinivas, J. S. (2013). Intramuscular ketamine in acute depression: A report on two cases. *Indian Journal of Psychiatry*, 55(2), 186–188.

<https://doi.org/10.4103/0019-5545.111461>

Kallio, H., Pietilä, A.-M., Johnson, M., & Kangasniemi, M. (2016). Systematic methodological review: Developing a framework for a qualitative semi-structured interview guide. *Journal of Advanced Nursing*, 72(12), 2954–2965.

<https://doi.org/10.1111/jan.13031>

Katalinic, N., Lai, R., Somogyi, A., Mitchell, P. B., Glue, P., & Loo, C. K. (2013).

Ketamine as a new treatment for depression: A review of its efficacy and adverse effects. *Australian & New Zealand Journal of Psychiatry*, 47(8), 710–727.

<https://doi.org/10.1177/0004867413486842>

Kheirabadi, D., Kheirabadi, G. R., Mirlohi, Z., Tarrahi, M. J., & Norbaksh, A. (2020).

Comparison of rapid antidepressant and antisuicidal effects of intramuscular ketamine, oral ketamine, and electroconvulsive therapy in patients with major

- depressive disorder. *Journal of Clinical Psychopharmacology*, 40(6), 588–593.
<https://doi.org/10.1097/jcp.0000000000001289>
- Li, L., & Vlisides, P. E. (2016). Ketamine: 50 years of modulating the mind. *Frontiers in Human Neuroscience*, 10. <https://doi.org/10.3389/fnhum.2016.00612>
- Molero, P., Ramos-Quiroga, J. A., Martin-Santos, R., Calvo-Sánchez, E., Gutiérrez-Rojas, L., & Meana, J. J. (2018). Antidepressant efficacy and tolerability of ketamine and esketamine: A critical review. *CNS Drugs*, 32(5), 411–420.
<https://doi.org/10.1007/s40263-018-0519-3>
- The Mount Sinai Hospital / Mount Sinai School of Medicine. (2017). *Researchers review progress of treating glutamate signalling in depression*. ScienceDaily.
<https://www.sciencedaily.com/releases/2017/03/170317131553.htm>.
- National Center for Biotechnology Information. (2021). *Activation of NMDA receptors and postsynaptic events*. National Center for Biotechnology Information. PubChem Compound Database.
<https://pubchem.ncbi.nlm.nih.gov/pathway/Reactome:R-HSA-442755>.
- Ritter, P., Findeis, H., & Bauer, M. (2019). Ketamine in the treatment of depressive episodes. *Pharmacopsychiatry*, 53(02), 45–50. <https://doi.org/10.1055/a-0991-0582>
- Rot, M., Zarate, C., Charney, D., & Mathew, S. (2012). Ketamine for depression: Where do we go from here? *Society of Biological Psychiatry*, 72(7), 537–547.
<https://doi.org/10.1016/j.biopsych.2012.05.003>
- Segen. (2011). *Washout period*. Segen's Medical Dictionary. Farlex, Inc. <https://medical-dictionary.thefreedictionary.com/washout+period>

- Sharp, R. (2015). The Hamilton rating scale for depression. *Occupational Medicine*, 65(4), 340–340. <https://doi.org/10.1093/occmed/kqv043>
- Shin, C., Lee, S.-H., Han, K.-M., Yoon, H.-K., & Han, C. (2019). Comparison of the usefulness of the PHQ-8 AND PHQ-9 for screening for major depressive disorder: Analysis of psychiatric outpatient data. *Psychiatry Investigation*, 16(4), 300–305. <https://doi.org/10.30773/pi.2019.02.01>
- Trivedi, M. H., Rush, A. J., Wisniewski, S. R., Nierenberg, A. A., Warden, D., Ritz, L., Norquist, G., Howland, R. H., Lebowitz, B., McGrath, P. J., Shores-Wilson, K., Biggs, M. M., Balasubramani, G. K., & Fava, M. (2006). Evaluation of outcomes with citalopram for depression using measurement-based care in star*d: Implications for clinical practice. *American Journal of Psychiatry*, 163(1), 28–40. <https://doi.org/10.1176/appi.ajp.163.1.28>
- Tolentino, J. C., & Schmidt, S. L. (2018). Dsm-5 criteria and depression severity: Implications for clinical practice. *Frontiers in Psychiatry*, 9. <https://doi.org/10.3389/fpsy.2018.00450>
- Trajković, G., Starčević, V., Latas, M., Leštarević, M., Ille, T., Bukumirić, Z., & Marinković, J. (2011). Reliability of the Hamilton rating scale for depression: A meta-analysis over a period of 49years. *Psychiatry Research*, 189(1), 1–9. <https://doi.org/10.1016/j.psychres.2010.12.007>
- Villarroel, M., & Terlizzi, E. (2020, September 23). *Symptoms of depression among adults: United States, 2019*. Centers for Disease Control and Prevention. <https://www.cdc.gov/nchs/products/databriefs/db379.htm>.

- Wittkamp, K., Ravesteijn, H., Baas, K., Hoogen, H., Schene, A., Bindels, P., Lucassen, P., Lisdonk, E., & Weert, H. (2009). The accuracy of patient health questionnaire-9 in detecting depression and measuring depression severity in high-risk groups in primary care. *General Hospital Psychiatry, 31*(5), 451–459.
<https://doi.org/10.1016/j.genhosppsych.2009.06.001>
- Xu, Y., Hackett, M., Carter, G., Loo, C., Gálvez, V., Glozier, N., Glue, P., Lapidus, K., McGirr, A., Somogyi, A. A., Mitchell, P. B., & Rodgers, A. (2015). Effects of low-dose and very low-dose ketamine among patients with major depression: A systematic review and meta-analysis. *International Journal of Neuropsychopharmacology, 19*(4), 1–15. <https://doi.org/10.1093/ijnp/pyv124>
- Zorumski, C. F., Izumi, Y., & Mennerick, S. (2016). *Ketamine: NMDA receptors and beyond*. *The Journal of neuroscience: the official journal of the Society for Neuroscience*. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5148235/>.

Appendix

Table 1

Week One's Paired-Samples T-Test

Paired test	Mean	Std. Deviation	Paired Difference								eta	
			Mean	Std. Deviation	Std. Error Mean	Lower	Upper	t	df	Sig. (2-tailed)		
HDRS Total Score-Pre	18.21	8.997	7.500	5.155	1.378	4.523	10.477	5.443	1	3	< 0.001	0.695
HDRS Total Score-Post	10.71	5.312										
DMT-Pre	3.14	2.413	2.214	2.326	0.622	0.871	3.558	3.561	1	3	0.003	0.494
DMT-Post	0.93	1.141										
Phy. Sx/ADLs - Pre	6.14	3.527	1.143	1.351	0.361	0.363	1.923	3.166	1	3	0.007	0.435
Phy. Sx/ADLs - Post	5.00	2.660										
Anxiety-Pre	6.00	3.162	4.071	3.050	0.815	2.310	5.832	4.995	1	3	< 0.001	0.657
Anxiety-Post	1.93	1.859										
Insomnia and Insight-Pre/Post			Data unavailable due to no change in the reporting data									

Table 2

Week Three's Paired-Samples T-Test

Paired test	Mean	Std. Deviation	Paired Difference								
			Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference		t	df	Sig. (2-tailed)	eta
HDRS Total Score-Pre	12.54	6.476	4.923	4.153	1.152	2.414	7.432	4.275	12	0.001	0.603
HDRS Total Score-Post	7.62	4.407									
DMT-Pre	2.00	1.683	1.538	1.664	0.462	0.533	2.544	3.333	12	0.006	0.481
DMT-Post	0.46	0.776									
Phy. Sx/ADLs - Pre	4.77	3.086	0.462	1.127	0.312	-	1.142	1.477	12	0.165	0.154
Phy. Sx/ADLs - Post	4.31	2.626									
Anxiety-Pre	3.77	2.315	2.923	2.290	0.635	1.539	4.307	4.603	12	< 0.001	0.638
Anxiety-Post	0.85	1.463									
Insomnia and Insight-Pre/Post			Data unavailable due to no change in the reporting data								

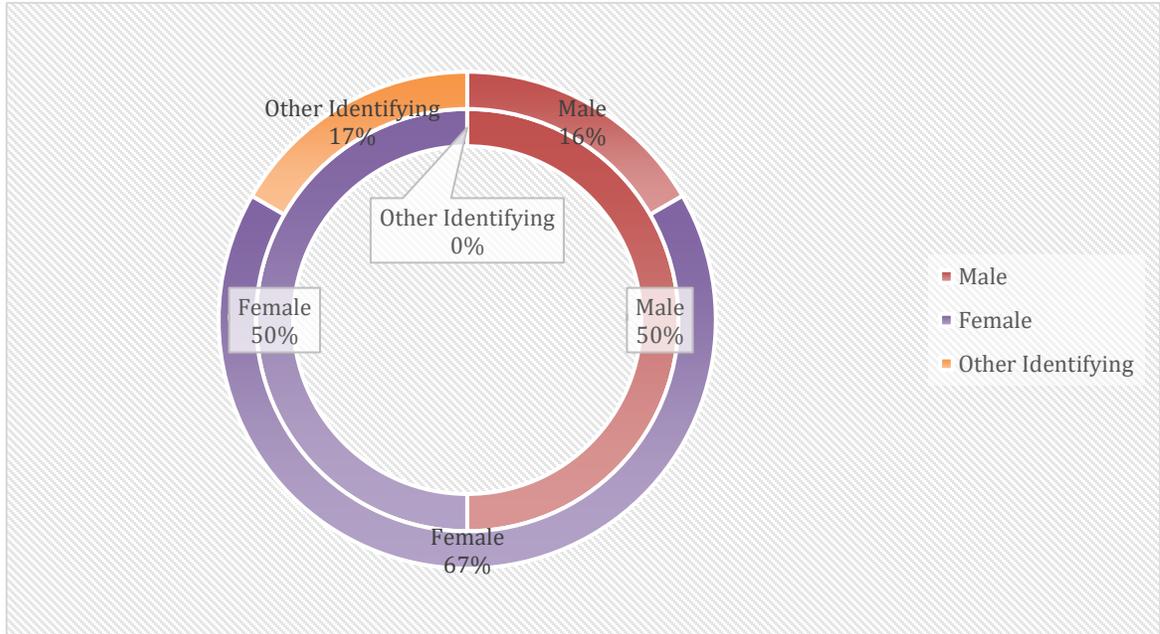
Table 3

Week Six's Paired-Samples T-Test

Paired test	Mean	Std. Deviation	Paired Difference								eta
			Mean	Std. Deviation	Std. Error Mean	Lower	Upper	t	df	Sig. (2-tailed)	
HDRS Total Score-Pre	16.63	6.927	7.000	4.504	1.592	3.235	10.765	4.396	7	0.003	0.734
HDRS Total Score-Post	9.63	4.955									
DMT-Pre	2.88	2.416	1.500	1.309	0.463	0.405	2.595	3.240	7	0.014	0.60
DMT-Post	1.38	2.066									
Phy. Sx/ADLs - Pre	6.63	2.200	1.250	1.982	0.701	-0.407	2.907	1.784	7	0.118	0.312
Phy. Sx/ADLs - Post	5.38	2.200									
Anxiety-Pre	5.25	2.712	3.750	3.012	1.065	1.232	6.268	3.522	7	0.010	0.639
Anxiety-Post	1.50	1.604	0								
Insomnia and Insight-Pre/Post			Data unavailable due to no change in the reporting data								

Figure 1

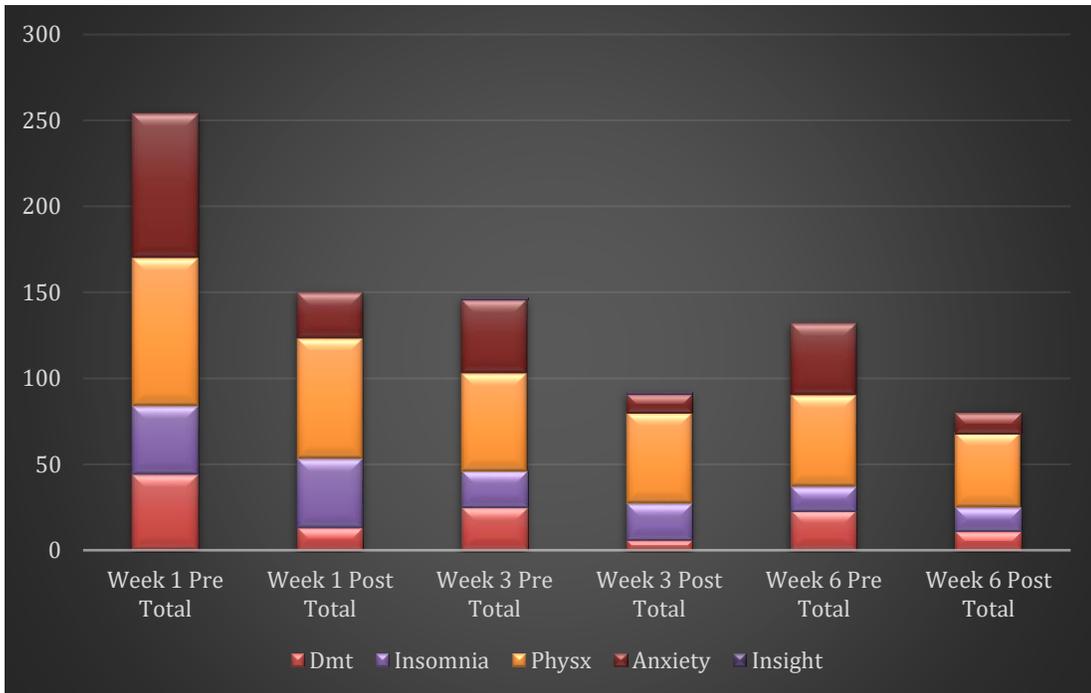
Identifying Gender Percentages in Treatment Diagnoses



Note. The interior circle represents the total percentages of identifying genders receiving treatment for Major Depressive Disorder while the exterior circle provides the total percentages of identifying genders receiving IM ketamine for Bipolar Depression.

Figure 2

Comparing Week 1, 3, and 6 Total Scores and Categories



Note. This figure represents the sum of each participant’s total scores for each week’s pre and post totals. Each color represents one of the five categories which make up the HDRS questionnaire. As a reminder, week one had 14 participants, week three had 13 participants, and week six had 8 participants. The abbreviation Dmt stands for depressed mood and thought, category one.