AN EDUCATIONAL INTERVENTION ON THE EFFICACY OF KETAMINE-ASSISTED PSYCHOTHERAPY FOR ANXIETY

by

Allison Elizabeth Meaux

A DNP Project Submitted to the Faculty of the

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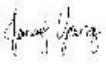
As members of the DNP Project Committee, we certify that we have read the DNP project prepared by Allison Elizabeth Meaux, titled An Educational Intervention on the Efficacy of Ketamine-Assisted Psychotherapy for Anxiety, and recommend that it be accepted as fulfilling the DNP project requirement for the Degree of Doctor of Nursing Practice.



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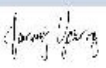
I hereby certify that I have read this DNP project prepared under my direction and recommend that it be accepted as fulfilling the DNP project requirement.



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LAND ACKNOWLEDGEMENT

We respectfully acknowledge the University of Arizona is on the land and territories of Indigenous peoples. Today, Arizona is home to 22 federally recognized tribes, with Tucson being home to the O'odham and the Yaqui. Committed to diversity and inclusion, the University strives to build sustainable relationships with sovereign Native Nations and Indigenous communities through education offerings, partnerships, and community service.

DEDICATION

I dedicate this manuscript to all who believe healing and peace are beyond their reach. May we hold space for you and your journey to wellness.

"Between stimulus and response, there is a space. In that space is our power to choose our response. In our response lies our growth and freedom."

- Victor Frankl

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ABSTRACT

Purpose: This quality improvement project was designed to educate mental health care professionals (MHCPs) regarding the literature-informed efficacy of utilizing ketamine-assisted psychotherapy (KAP) as a treatment modality for patients with a diagnosis of generalized anxiety disorder (GAD) that has been unresponsive to prior treatments.

Background: Generalized anxiety disorder is a highly prevalent comorbid diagnosis among those with mental health concerns. Individuals with GAD can experience poor treatment responses to first-line intervention recommendations. Therefore, MHCPs must identify and utilize efficacious alternate treatments for this patient population. A southern Arizona outpatient clinic identified that GAD is frequently comorbid among their clients receiving KAP services for both major depressive disorder (MDD) and post-traumatic stress disorder (PTSD); clinic staff may benefit from receiving further information regarding the efficacy of KAP for GAD.

Methods: Prior to the educational intervention's implementation, a survey of MHCPs at the project's implementation site was conducted to assess the prevalence of KAP use for patients with GAD. Mental health care providers at a southern Arizona outpatient clinic providing mental health services were recruited through convenience sampling for the prevalence survey and an asynchronous educational presentation presenting the literature-informed efficacy of KAP for GAD. To assess the outcomes of the educational intervention, participants completed pre-intervention and post-intervention surveys which evaluated their knowledge of KAP for GAD and their intention to incorporate KAP for GAD into their care recommendations. Descriptive statistics, bar graphs, and paired t-tests were used to analyze and interpret the survey data.

Results: Four MHCPs participated in the educational intervention. Analysis of the participants' results indicated improved knowledge regarding the literature-identified efficacy of KAP for GAD and increased intent to utilize KAP for GAD.

Conclusions: The results of this quality improvement project indicated that an asynchronous educational intervention can influence MHCP's knowledge regarding the current literature-identified efficacy of KAP for patients with GAD and increase participants' intention to recommend KAP for patients with GAD.

Keywords: generalized anxiety disorder, ketamine-assisted psychotherapy

INTRODUCTION

Generalized anxiety disorder (GAD) has been identified as a frequently comorbid diagnosis among individuals with many mental health disorders. It has lasting impacts on not only an individual's well-being but society's as well. In the context of a poor response to first-line treatment recommendations for GAD and comorbid diagnoses, mental health care professionals must seek alternate treatments that can fulfill this need for their patients. This Doctor of Nursing Practice (DNP) project sought to identify literature supporting ketamine-assisted psychotherapy for the treatment of GAD and presented these findings to a local mental health clinic in Southern Arizona, which has been providing KAP to individuals with treatment-resistant depression and posttraumatic stress disorder (PTSD) that are often comorbid with GAD.

Background Knowledge and Significance

The American Psychiatric Association's (2022) *Diagnostic and Statistical Manual of Mental Health Disorders 5th Edition Text Revision* (5th ed.; *DSM-5-TR*) defines the mental and physical symptoms constituting a diagnosis of GAD. These must include the following: excessive anxiety and worry about different events or activities that are difficult to control and must occur more days than not for at least six months (American Psychiatric Association [APA], 2022). Stein and Sareen (2019) note that with GAD, worry is not limited to a singular topic; it is multifocal, and the worries are pervasive, all-encompassing of the individual and their mental capacities. Additional specific diagnostic symptoms of GAD include feeling restless or on edge, fatiguing easily, difficulties with concentration, irritability, muscle tension, and sleep disturbances (APA, 2022). Physical symptoms may also present, such as sweating, nausea, diarrhea, an exaggerated startle response, irritable bowel symptoms, and headaches (APA, 2022).

An individual with GAD is impacted by not only psychological symptoms but physical ones as well, contributing to the functional impact of this diagnosis.

The development of GAD is associated with many risk factors. When faced with unexpected adverse life events, an individual's environment, temperament, and the parenting approach used during childhood can play a role in their response to these stimuli (Newman et al., 2013). These factors cultivate the heightened worry state associated with the GAD diagnosis. It is thought that this mental state is a maladaptive strategy used by individuals with GAD to decrease contrasting negative emotional states when presented with threats (Newman et al., 2013). Compared to individuals who do not habitually engage in negative cognitive processes, those who repeatedly contemplate worse-case scenarios may pre-emptively condition cognitive responses. This may result in a diminished shift in mental negativity in unfavorable circumstances. As a result, the individual with GAD may experience less distress during an isolated difficulty, but the impact of this constant state of mental negativity, or neuroticism, is profound.

Impact of Generalized Anxiety Disorder (GAD)

Generalized anxiety disorder significantly impacts the diagnosed individual and societal well-being. Revicki et al. (2012) report that individuals with GAD have significantly impaired health-related quality-of-life outcomes, including psychosocial functioning, role functioning, general health status, and work productivity. Notably, impaired role functioning is highly concerning as this impacts an individual's ability to manage home life and work responsibilities and maintain a healthy social life with fulfilling close relationships. Ruscio et al. (2017) document that individuals with GAD experienced 41.2 days out of role due to GAD in the past

year. GAD-related role impairment is the same as individuals with chronic medical conditions, and GAD-related disability is greater than substance use disorders, other anxiety disorders, and personality disorders (Alonso et al., 2011; Grant et al., 2005). GAD profoundly impacts an individual and their ability to function in their day-to-day life. Furthermore, untreated GAD becomes an expensive burden to society due to increased medical service use (primary care, specialty clinic, and emergency room services) and impacts workplace performance (Fogarty et al., 2008; Hoffman et al., 2008). GAD has been associated with higher care costs in the primary care setting (Olfson & Gameroff, 2007; Rovira et al., 2012). However, a study found that while the direct costs of GAD were not significantly different from those without GAD, the indirect costs associated with work impairment were higher for those with GAD (Toghanian et al., 2014). The cost of GAD to an individual's quality of life, the loss of productivity within workplaces due to GAD, and the significant healthcare expenditures associated with treating GAD are substantial.

Prevalence of Generalized Anxiety Disorders

The significance of GAD's impact on individuals, workplaces, and the healthcare system is made more profound, given the prevalence of GAD. One study reports a global lifetime prevalence of GAD to be as high as 3.7% (Ruscio et al., 2017). In the United States (US), 5.7% of adults are reported to have experienced GAD at some point in their lives, with an estimated 22.8% with serious impairment and 33.7% with moderate impairment (National Institute of Mental Health, n.d.). There is a strong likelihood that these numbers are increasing given that Mental Health America's Online Screening Program tracked a 93% increase in the total number

of anxiety screens taken from January 2020 to September 2020 compared to the 2019 total number of anxiety screens (Mental Health America, 2021).

Treatments for Generalized Anxiety Disorders and Efficacy

Treatment guideline recommendations from the Federation of Societies of Biological Psychiatry, the German guidelines for the treatment of anxiety disorders, and the National Institute for Health and Care Excellence designate antidepressant medications selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) as the first-line pharmacological treatments for GAD (Borwin Bandelow et al., 2023; Bandelow et al., 2022; National Institute for Health and Care Excellence, 2022). A Canadian clinical practice guideline recommends agomelatine, pregabalin, SSRIs, and SNRIs as first-line pharmacological treatments for GAD (Katzman et al., 2014). In addition to first-line pharmacological treatment recommendations, cognitive behavioral therapy (CBT) is a preferred psychological treatment due to the highest level of evidence of efficacy for anxiety disorders (Bandelow et al., 2022; Katzman et al., 2014; Szuhany & Simon, 2022).

Although GAD treatment guidelines recommend SSRIs and SNRIs, their efficacy is backed by small to medium effect sizes (Szuhany & Simon, 2022). When there is limited relief of anxiety symptoms in the context of first-line treatments, these patients are often labeled as "non-responders." Taylor et al. (2012) define non-responders "as people who might have experienced some degree of symptom reduction, but either failed to attain clinically significant improvement or respond to treatment to such an extent that their target symptoms at the end of treatment were still clinically significant." Studies of anxiety disorders indicate that proportionally, non-responders range from 34% to 36% for CBT and 30% for SSRIs;

additionally, there are notable treatment dropout rates for CBT and serotonin reuptake inhibitors, and complete recovery is uncommon (Taylor et al., 2012).

Patient adherence to medication treatment may contribute to the efficacy of first-line treatment recommendations for GAD. Adherence to medication treatment is influenced by various factors, including a provider's availability to establish and maintain a therapeutic relationship, the patient's beliefs regarding the treatment and their openness to change, as well as aspects attributable to a specific medication such as treatment side effects, duration, and alignment with the patient's lifestyle (Zalta et al., 2015). Particular to the first-line recommended treatments, SSRIs and SNRIs can negatively affect appetite, sexual function, and sleep, which can influence a patient's adherence to the medication (Ferguson, 2001). One study reports that 57% of those with anxiety disorders treated with antidepressants are non-adherent at six months (Stein et al., 2006). When first-line medications are ineffective, other pharmacologic recommendations as monotherapies and augmentation therapies include benzodiazepines, tricyclic antidepressants, buspirone, hydroxyzine, and antipsychotics; however, the evidence for these interventions is less robust than that supporting SSRIs and SNRIs (Borwin Bandelow et al., 2023; Katzman et al., 2014).

With remission of symptoms as the ideal goal in the treatment of anxiety disorders, it is worth noting that comorbid depression has resulted in lower rates of remission, higher symptom severity, and poorer treatment responses (Dold et al., 2017; Springer et al., 2018). Rates of comorbid GAD and MDD are reported to be substantial, with one study identifying 59.1% of all 12-month GAD cases also fulfilling MDD criteria (Carter et al., 2001). Given the current first-line treatment recommendations, the high rate of nonresponse and nonadherence to medication

for anxiety disorders, as well as the frequent comorbidity of generalized anxiety disorder (GAD) and major depressive disorder (MDD), there are significant risks for GAD patients who do not respond to initial treatments. Alternative treatments are needed to minimize the severe impact of symptoms. One such alternative is ketamine-assisted psychotherapy (KAP), which will be explored as an effective intervention for GAD.

Ketamine Assisted Psychotherapy (KAP)

Ketamine is a non-competitive N-methyl-D-aspartate receptor (NMDAR) antagonist that has a broad safety profile, allowing it first to be used as a shorter-acting sedative agent; ketamine has since expanded in use within psychiatry due to its discovered rapid-acting antidepressant actions (Johnston et al., 2024). Ketamine NMDAR antagonistic actions affect the glutamate system in the brain, which has a role in fear extinction; the decrease in glutamatergic neurotransmission is thought to produce fast antidepressant and anxiolytic effects (Gupta & Prabhavalkar, 2021). Ketamine also increases α- amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPAR) transmission, which increases brain-derived neurotrophic factor (BDNF) expression (Johnston et al., 2024). Brain-derived neurotrophic factor plays a crucial role in neuroplastic changes related to learning and memory and is neuroprotective (Miranda et al., 2019). Ketamine's mechanism of action is believed to be a key reason for achieving clinical efficacy among multiple neuropsychiatric disorders (Johnston et al., 2024).

Like many medications, ketamine's effects are dose-dependent. A consequence of ketamine's pharmacological effects on the human body can result in an altered state of consciousness. Ketamine-assisted psychotherapy capitalizes on this altered state of

consciousness and increased BDNF through the utilization of a trained KAP professional to support an individual through ketamine's out-of-body effects. This guided experience can be particularly impactful for individuals living in a state of survival, where it has been challenging to connect with parts of oneself (Wolfson & Vaid, 2024). Ketamine-assisted psychotherapy provides patients the ability to experience a time absent of negative emotions, temporarily detach from their usual identity, and reduce external sensations, enhancing an individual's ability to engage in psychotherapy meaningfully (Dore et al., 2019). These experiences can be healing and renewing for patients. Some KAP clinic professionals guide their patients through different levels of trance through dose escalation, where a full out-of-body experience can be experienced (Dore et al., 2019). Due to the debilitating and pervasive nature of worries that patients with GAD experience, this could be especially important for those unresponsive to other treatments. Combining ketamine's neuromodulation of glutamatergic neurotransmission, increased BDNF expression, and the facilitated state of openness provided to the individual engaging in KAP offers theoretical support for KAP and its use in treating patients with GAD.

Ketamine Assisted Psychotherapy Research

Currently, the United States Federal Food and Drug Administration (USFDA) warns about the potential risks associated with the use of compounded ketamine products, including oral formulations (USFDA, 2023). USFDA especially warns about the risks associated with these products for at-home use without a trained provider's supervision (USFDA, 2023). Further, the USFDA emphasized that compounded ketamine products do not have a USFDA-approved use and do not have significant clinical research supporting the efficacy and safety of these products (USFDA, 2023). This lack of research on ketamine's use for psychiatric disorders may

be attributable to pharmaceutical company incentives for funding research to support additional USFDA-approved uses. As an unpatented generic medication, ketamine's price has been competitively driven down by market competition, making it affordable. However, a generic medication holds little incentive for a pharmaceutical company to invest funds for clinical research supporting additional USFDA-approved indications (Robinson, 2022). Patented medications are protected from market competition for a certain period and are profitable for a pharmaceutical company, resulting in further innovation investment (Robinson, 2022). Unfortunately, once the patent-protected period ends, a pharmaceutical company has little to no incentive to conduct research for further indications for the medication (Robinson, 2022). With this current trend in investment in pharmacological treatments, there is concern that generic medications, like ketamine, have unlocked potential for helping patients with conditions like GAD that can be unresponsive to USFDA-approved options.

Local Problem

In October 2019, the National Center for Health Statistics (NCHS) reported that 7.8% of adults reported having anxiety symptoms associated with the diagnosis of GAD (National Center for Health Statistics, 2021). For comparison, the Household Pulse Survey conducted by The National Center for Health Statistics (NCHS) and the Census Bureau included questions about adults' symptoms of anxiety associated with a diagnosis of GAD. This survey found that in 2023, from October 18 through October 30, 29.5% of adults in the US reported symptoms of anxiety, and 29% of adults in Arizona reported symptoms of anxiety during the same period (NCHS, 2023). According to the Healthcare Cost and Utilization Project, in Arizona, in 2020, there were 4,402 emergency department visits for depressive disorders and 13,868 visits for

anxiety and fear-related disorders (Agency for Healthcare Research and Quality [AHRQ], n.d.). It is evident that symptoms of anxiety are prevalent and appear to be increasing, indicating a need for effective treatment given the devastating impact that anxiety can have.

A mental health clinic in southern Arizona provides clinician-administered KAP to qualifying clients. Before initiating this treatment modality, this clinic comprehensively evaluates each KAP-interested client for contraindicated mental health and medical conditions. Once clients are cleared for KAP participation, they are typically recommended to complete six sessions. This series of sessions consists of a preparatory session where a therapist reviews what can be expected and the KAP sessions themselves, followed by an integration session two days after each KAP experience. During this integration, the KAP experience is processed with the support of a KAP-trained therapist. Integration sessions capitalize on ketamine's effects on neuroplasticity through previously discussed glutamatergic and BDNF modulation. The goal of KAP for this clinic is to integrate the KAP experience with the client's life experience to facilitate healing. Currently, clients who qualify for treatment have a history of MDD or PTSD and have not responded to two other treatment methods (such as medication, psychotherapy, or lifestyle changes). Many of the clinic's clients also have GAD alongside these conditions. Due to existing research limitations on alternative uses of ketamine, the clinic staff are interested in understanding the evidence-based support for KAP in treating GAD. To effectively assist their patients and make the best use of KAP, clinic staff must comprehend the current literature regarding the efficacy of KAP for GAD. A deeper understanding of this evidence-based efficacy aligns closely with the goal of upholding a clinical practice rooted in solid evidence and is the focus of this project.

Intended Improvement

Project Purpose

Quality improvement is the ongoing effort to enhance healthcare quality to improve patient outcomes, system performance, and professional development (Batalden & Davidoff, 2007; Centers for Medicare & Medicaid Services [CMS], 2023). This systematic improvement is driven by specific methodologies that allow proposed changes to be continuously evaluated in real-time, informing further adjustments in practice and empowering staff to participate in improvements (Backhouse & Ogunlayi, 2020). Furthermore, quality improvement focuses on customizing initiatives to specific environments and expanding use based on their effectiveness in additional settings (Backhouse & Ogunlayi, 2020). This DNP project's quality improvement initiative sought to demonstrate to stakeholders that using KAP for GAD has mixed evidence concerning the modality's proposed efficacy. By engaging stakeholders in education, their knowledge was expected to increase, inform their clinical judgment on whether to recommend KAP for their patients with GAD, and improve their confidence in their clinical decision-making. For this project and the remainder of this paper, GAD will refer to a generalized anxiety disorder that has not responded to two trials of alternate therapies. With a quality improvement approach, these goals will be evaluated through specific and measurable objectives that will be analyzed and used to further an understanding of the following project question.

Project Question

The question guiding this DNP project was: Will an educational presentation on the effectiveness and prevalence of ketamine for generalized anxiety disorder increase participants'

knowledge and influence their intention to recommend ketamine-assisted psychotherapy for patients with generalized anxiety disorder in a private mental health clinic?

Project Objectives

I. Measure the prevalence of mental health care professionals (MHCPs) recommending KAP among patients with GAD.

II. Implement an educational presentation for MHCPs to increase knowledge and awareness of the current literature-informed efficacy of KAP for patients with GAD.

III. Evaluate the MHCPs' pre- and post-intervention attitudes towards recommending KAP for patients with GAD.

IV. Assess MHCPs' intentions to recommend KAP for GAD within their mental health practices.

V. Analyze how MHCPs' intentions to recommend KAP for GAD relate to their attitudes toward providing KAP for patients with GAD after participating in an educational intervention regarding the literature-informed efficacy of KAP for GAD.

Theoretical Framework

The theory of planned behavior (TPB) guided the development of this quality improvement project. Icek Ajzen (1991) developed this theory as an extension of the theory of reasoned action (TRA) due to its limitations in addressing incomplete voluntary control over certain behaviors (Ajzen, 1991). Central to this theory is that an individual's intention to perform a given behavior is influenced by their perception of their behavioral control of performing the identified behavior (Ajzen, 1991). The theory assumes that the stronger a person's intention to engage in an identified behavior, the more likely engagement in the behavior will follow (Ajzen,

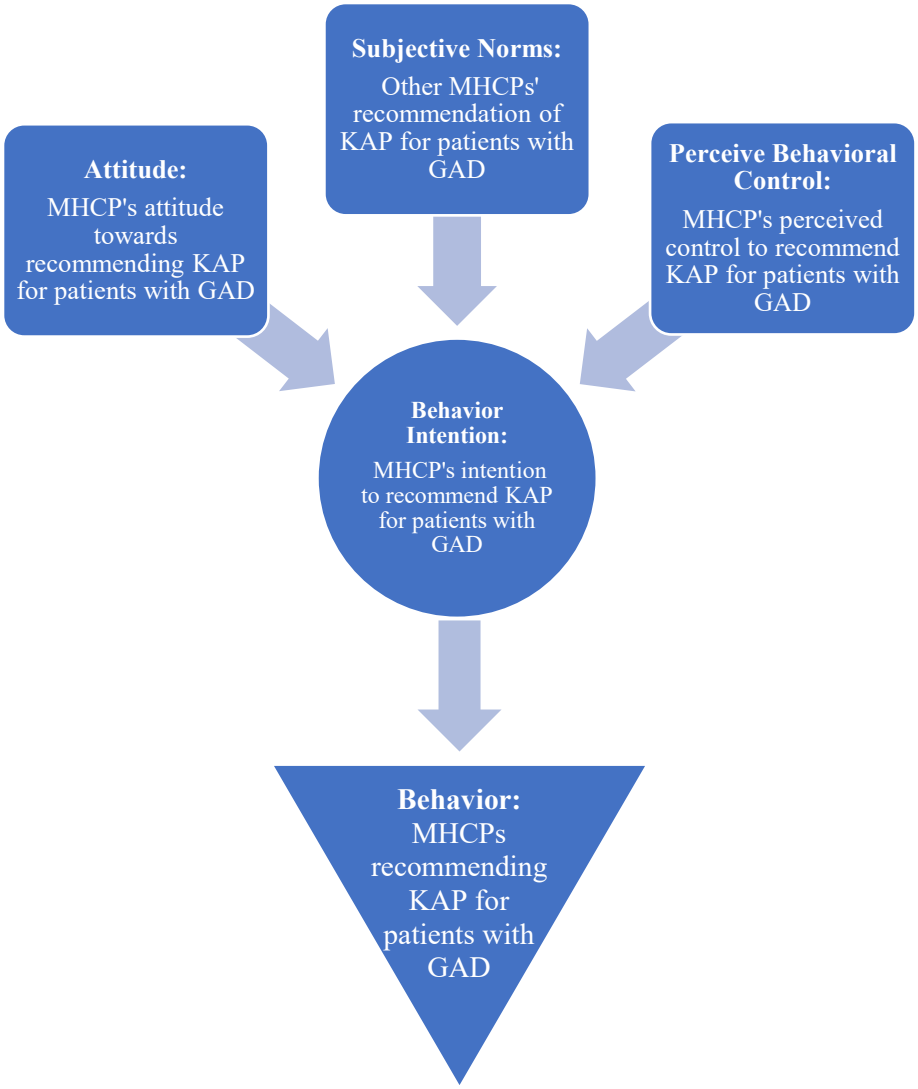
2020). For this project, the TPB informs an understanding of the MHCPs' intentions to recommend KAP for GAD. Furthermore, it implies how likely MHCPs are to recommend KAP for GAD based on the educational information provided to them.

As illustrated in Figure 1, behavioral intention is determined by three factors: the attitude towards the behavior, the subjective norm concerning the behavior, and the perceived behavioral control (Ajzen, 2020). An individual's attitude toward a behavior encompasses believing that performing the behavior will lead to a particular outcome (Ajzen, 2020). The subjective norm influences behavioral intention by shaping an individual's perception of others' expectations regarding the behavior. This includes the individual's belief about whether others expect them to perform the behavior or whether these influential individuals engage in it, thereby creating social pressure to conform to the expected action (Ajzen, 2020). Finally, perceived behavioral control considers factors that facilitate or impede behavior performance, such as insufficient time, money, resources, and lack of skills (Ajzen, 2020). The degree of actual behavioral control (ability to overcome barriers and presence of facilitating factors) is thought to moderate the intention of engagement in behavior, and perceived behavioral control moderates the influence of attitude and subjective norms on intention (Ajzen, 2020). Most studies rely on perceived behavioral control as a proxy for actual control; it is often assessed by having participants rate their ability to perform a behavior and how much it is under their control (Ajzen, 2020). The theory of planned behavior has been used as a theoretical basis for understanding and predicting clinician behavior (Godin et al., 2008; Perkins et al., 2007). Given that this quality improvement project aims to assess MHCPs' intent to recommend KAP for GAD, TPB is an appropriate theoretical framework to guide this project.

The TPB framework, illustrated in Figure 1, informed this project's guiding question and aims. As depicted in Figure 1, the project determined the prevalence of MHCPs recommending KAP as a treatment option for patients with GAD. The educational intervention included this information, a subjective norm, influencing the MHCPs' behavioral intentions. Additionally, as indicated in objective III, the participant's perceived behavioral control and attitudes toward recommending KAP for patients with GAD were evaluated before and after the intervention. These three components of the TPB framework were used to guide the development of the pre-intervention and post-intervention survey questions (Ajzen, 2019). These factors may have influenced the change in MHCPs' intentions to recommend KAP for patients with GAD. Assessing this change in intention provided an analysis of how the intervention influenced the participants' perceived behavioral control and attitudes toward recommending KAP to patients with GAD. Ultimately, this informed stakeholders how this educational intervention may influence a MHCP's intention to recommend KAP for patients with GAD and, based on the TPB framework, anticipatory MHCP engagement in recommending KAP for patients with GAD.

Figure 1

Theory of Planned Behavior for Recommending KAP for Patients with GAD



Literature Synthesis

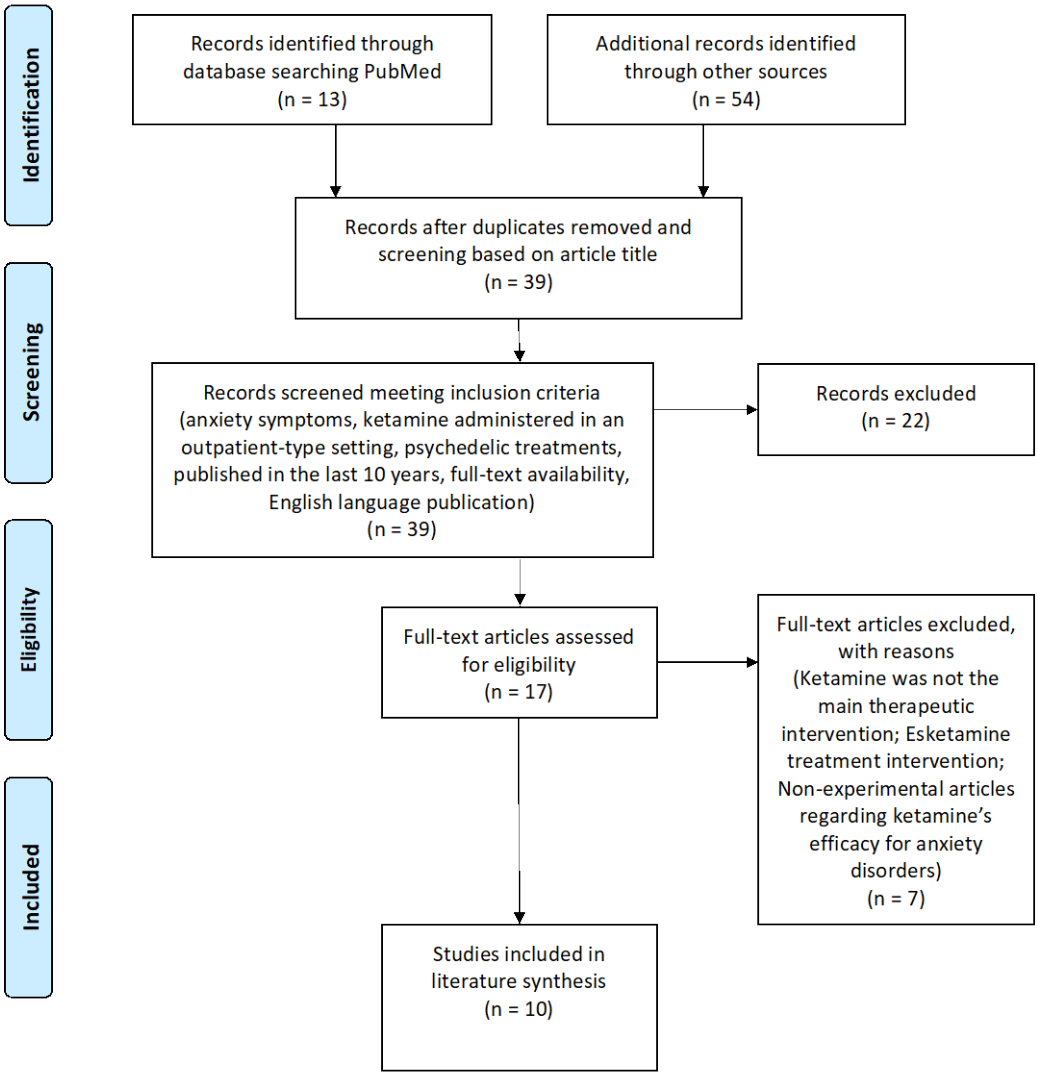
Evidence Search

With the assistance of a research librarian, an initial systematic literature search with the electronic database PubMed was completed. The following MeSH keywords were utilized: "Anxiety Disorders" OR "general anxiety disorder" AND "Psychotherapy" AND "Ketamine" OR

"Esketamine." This search resulted in 13 articles not specific to KAP for GAD treatment. However, the reference list from Sartori and Singewald (2019) was scanned for possible articles, resulting in 54 articles. Additionally, PubMed's similar article lists for two articles were screened for applicable literature (B. Bandelow et al., 2023; Glue, Medlicott, et al., 2020). Due to the minimal literature discovered within PubMed, Google Scholar, PsychINFO, and Embase were also searched using search terms similar to those used in the PubMed search, including "ketamine," "ketamine-assisted psychotherapy," and "anxiety." Some article reference lists were used to identify additional literature. Figure 2 depicts this literature synthesis's article search process using a PRISMA flow diagram (Moher et al., 2009). Ultimately, ten articles were chosen for inclusion in this literature review based on publication within the last ten years, full-text availability, publication in the English language, the inclusion of anxiety diagnoses among the study population, the use of ketamine in an outpatient setting, and ketamine administered via oral or intramuscular routes. In particular, the outpatient setting and defined administration routes were essential to this author because they most closely resemble how the local clinic administers ketamine for KAP interventions.

Figure 2

PRISMA Flow Diagram



Comprehensive Appraisal of Evidence

Many studies retained for this literature synthesis were of low quality and included retrospective descriptive cohort, descriptive, uncontrolled open-label exploratory, and case series (Ahuja et al., 2022; Dore et al., 2019; Glue et al., 2017; Glue, Medlicott, et al., 2020; Glue et al., 2018; Robison et al., 2022; Yermus et al., 2023). Due to the few studies that were specific to

KAP for anxiety disorder, a recent, non-peer-reviewed study was included in the literature synthesis (Yermus et al., 2023). Among the ten articles contained in this literature synthesis, the following themes emerged: (a) KAP and its efficacy in anxiety disorders; (b) the efficacy of ketamine on anxiety symptoms and participant functionality; (c) the effects of ketamine in the context of anxiety with other comorbidities; (d) the use of ketamine in an outpatient setting; and (e) ketamine's side effects among patients with anxiety (Appendix G).

Ketamine-Assisted Psychotherapy and Efficacy in Anxiety Disorders

Three articles were focused on KAP and its use in patient populations diagnosed with anxiety disorders (Dore et al., 2019; Robison et al., 2022; Yermus et al., 2023). Longer durations of treatment were associated with significant improvements in depression and anxiety among study participants (Dore et al., 2019). However, one study did show that two patients experienced clinically significant improvement in anxiety symptoms when comparing their pre-dose ketamine anxiety score to the score 24 hours following the fourth weekly ketamine dosing session (Robison et al., 2022). While patients may experience more significant benefits with a longer duration of treatment, patients with anxiety may benefit from KAP interventions as soon as 24 hours following the ketamine administration.

The literature also suggests that among patients with depression and anxiety, those with developmental trauma experience greater improvement in anxiety and depression symptoms (Dore et al., 2019). Symptomatic improvements after engagement in KAP may include sustained reduction in anxiety, depression, and PTSD for as many as five months after the last KAP session (Yermus et al., 2023). Results of the KAP process were attributed to both sublingual and intramuscular administration of ketamine, suggesting that these may be effective methods for

administering ketamine during KAP for GAD (Dore et al., 2019; Robison et al., 2022; Yermus et al., 2023).

While there is limited literature explicitly studying the effects of KAP on GAD treatment outcomes, Glue et al. (2018) suggest that non-specific factors may have improved mood and functionality among study participants receiving clinic-administered ketamine for treatment-resistant anxiety. These patients received weekly ketamine doses, which were followed by a two-hour session with a psychiatrist or registered nurse (Glue et al., 2018). Given the previously identified positive symptomatic outcomes of KAP among patients with anxiety symptoms, it seems plausible that even among ketamine interventions that do not have an explicit psychotherapy intervention component, engagement with the treatment team may contribute to ketamine's therapeutic effects. This effect remains unexplored in most ketamine administration for anxiety symptoms studies but may further contribute to ketamine's efficacy in treating GAD.

Ketamine's Effects on Anxiety Symptoms and Functionality

Ketamine not only affects symptoms of anxiety but positively affects an individual's functionality as well. Administration of ketamine is notable for the rapid onset of anxiolytic effects persisting anywhere from three days to two weeks (Glue et al., 2017; Glue, Neehoff, et al., 2020; Hartland et al., 2023; Tully et al., 2022). Individuals can experience a 50% reduction in anxiety symptoms following subcutaneous ketamine administration as tracked by Fear Questionnaire (FQ) and Hamilton Anxiety Scale-A (HAMA) ratings (Glue et al., 2017; Glue et al., 2018; Hamilton, 1959; Marks & Mathews, 1979). However, in studies that did not include a designated psychotherapy component with the intervention, these rapid anxiolytic effects and improved anxiety ratings were remitted within three days to two weeks after the administration

(Glue et al., 2017; Glue, Neehoff, et al., 2020; Glue et al., 2018; Hartland et al., 2023; Tully et al., 2022). In contrast, a study exploring KAP's effects identified the impact of sustained reductions in anxiety, depression, and PTSD to extend as much as five months after the last KAP session (Yermus et al., 2023). In addition to improvements in anxiety symptoms, enhancements in functionality were also observed, such as returning to employment, enrollment in educational programming, and reduced social avoidance (Glue, Medlicott, et al., 2020; Glue et al., 2018). Further beneficial effects of ketamine include the correlation of additional treatments with larger decreases in depression and suicidal ideation (Ahuja et al., 2022). The rapid anxiolytic effects, improvements in functionality, and additional beneficial effects following ketamine administration may be able to be extended through the addition of intentional psychotherapy sessions.

Patient Demographics

Patient demographics, including age, comorbid psychiatric diagnoses, concurrent treatment with multiple psychiatric medications and psychotherapy, and previous failed treatment trials, appear to support the selection of individuals who may benefit from KAP for GAD. Among individuals with treatment-resistant GAD who are not currently depressed, ketamine administration produces anxiolytic effects, suggesting that ketamine may be effective for GAD with or without a history of depression (Glue et al., 2017; Glue, Neehoff, et al., 2020). However, ketamine is also effective in decreasing depression and anxiety among patients with multiple psychiatric comorbidities and diagnoses, including major depressive disorder, complex post-traumatic stress disorder, attention deficit hyperactivity disorder, post-traumatic stress

disorder, generalized anxiety disorder, other anxiety disorders, other mood disorder, substance use disorder, and obsessive-compulsive disorder (Ahuja et al., 2022; Dore et al., 2019).

Among patients receiving a KAP-specific intervention, participants displayed pre-intervention moderate depression and anxiety as well as significant Adverse Childhood Event (ACE) scores; however, those with more severe symptoms, including current suicidality and a higher ACE score, tended to benefit the most (Dore et al., 2019). This implies that while patients with moderate anxiety symptoms may benefit from KAP interventions, patients with more severe symptoms may benefit more from KAP intervention. Additionally, the literature identified patients ages 22 to 43 as possibly benefiting from KAP intervention (Dore et al., 2019; Robison et al., 2022; Yermus et al., 2023). Ketamine administration studies that did not include a psychotherapy component expanded this age range from 18 to 55, indicating that a broader age range may benefit from this therapeutic modality (Ahuja et al., 2022; Glue et al., 2017; Glue, Medlicott, et al., 2020; Glue, Neehoff, et al., 2020).

Regarding treatments concurrently administered with ketamine, the literature supports efficacy in the context of patients remaining on current medication regimens and continued psychotherapy (Glue et al., 2017; Glue, Neehoff, et al., 2020; Glue et al., 2018). However, the literature does not account for the difference in patients participating in concurrent psychotherapy and those who are not participating when evaluating the effects of ketamine on anxiety without a KAP treatment component. Furthermore, patients who are taking antidepressants or taking more than one medication and failed to respond to prior medication or psychotherapy trials may respond well to ketamine interventions (Dore et al., 2019; Glue et al., 2017; Glue, Medlicott, et al., 2020; Glue, Neehoff, et al., 2020; Robison et al., 2022; Yermus et

al., 2023). The articles in this literature synthesis demonstrate the use of ketamine among diverse patient populations that present with the clinical complexity of taking multiple medications, failing prior treatments, and having mental health comorbidities.

Use of Ketamine in Outpatient Settings for Anxiety Disorders

The literature discusses the use of ketamine in outpatient settings for anxiety symptoms or diagnoses. Settings, where ketamine was administered, included a university clinic, a private outpatient psychiatric clinic network in the US, three private general psychiatric practices, and 11 field trip health clinics in North America (Ahuja et al., 2022; Dore et al., 2019; Glue et al., 2018; Yermus et al., 2023). Within the outpatient settings, ketamine has been noted to achieve anxiolytic effects through the following administration routes: subcutaneous injections into the upper arm, an oral extended-release tablet formulation, intramuscular injection, and intravenous administration (Ahuja et al., 2022; Glue et al., 2017; Glue, Neehoff, et al., 2020; Glue et al., 2018; Tully et al., 2022). Typical ketamine dosing used among patients with anxiety symptoms and disorders includes subcutaneously administered 1 milligram (mg) per kilogram (kg), sublingual dosing of 200 mg to 500 mg, and intramuscular dosing of 25 mg to 100 mg (Dore et al., 2019; Glue et al., 2018; Yermus et al., 2023). Per this literature, ketamine administered for its anxiolytic effects, both with and without explicit psychotherapy, has been effective in outpatient settings.

Overall, ketamine administration in outpatient settings was tolerated well. For subcutaneously administered ketamine, blood pressure increases were noted at 30 minutes, which may be dose-related (Glue et al., 2017; Glue, Neehoff, et al., 2020; Glue et al., 2018). Additionally, heart rate increases at 15 to 30 minutes after administration may be related to

subcutaneous ketamine doses as well (Glue et al., 2017; Glue, Neehoff, et al., 2020). Other side effects reported for subcutaneously administered ketamine included nausea, vomiting, dizziness, blurred vision, and sleepiness, none of which resulted in sentinel events (Glue, Neehoff, et al., 2020; Glue et al., 2018; Yermus et al., 2023). Intramuscular ketamine administration in the outpatient setting did result in additional panic attacks, hallucinations, confusion, potentially unsafe movement, and bladder pain, but all side effects resolved before the patient left the clinic (Ahuja et al., 2022). An extended-release ketamine tablet formulation may be the most tolerable for the outpatient setting due to side effects limited to dizziness and headache with no reported blood pressure or heart rate changes (Glue, Medlicott, et al., 2020).

Strengths of Evidence

Of the limitedly available research on ketamine for generalized anxiety disorder, only two identified studies were systematic reviews, the highest level of evidence, where at least two authors independently screen data (Hartland et al., 2023; Tully et al., 2022). Select studies had a substantial number of participants, including Ahuja et al. (2022) with 452 patients, Dore et al. (2019) with 235 patients, and Yermus et al. (2023) with 1,806 adult patients. All studies that were not systematic reviews utilized validated evaluation tools to collect data on patient anxiolytic responses to ketamine treatment; these included the Hamilton Anxiety Scale-A (HAMA), Fear Questionnaire (FQ), and the Generalized Anxiety Disorder (GAD-7) survey (Ahuja et al., 2022; Dore et al., 2019; Glue et al., 2017; Glue, Medlicott, et al., 2020; Glue, Neehoff, et al., 2020; Glue et al., 2018; Hamilton, 1959; Marks & Mathews, 1979; Robison et al., 2022; Spitzer et al., 2006; Yermus et al., 2023). One study replicated a previous study included in this literature synthesis. This replication study increased the rigor by establishing

double-blinding and a psychoactive control group (Glue, Neehoff, et al., 2020). All studies, except for Yermus et al. (2023), were peer-reviewed, reflecting academic rigor. Despite not being peer-reviewed, the Yermus et al. (2023) study was included due to the paucity of literature analyzing KAP specifically for treating anxiety disorders in an outpatient setting.

Weaknesses of Evidence

Seven of the ten studies retained for this review were lower levels of evidence, and while six were peer-reviewed, one was not (Ahuja et al., 2022; Dore et al., 2019; Glue et al., 2017; Glue, Medlicott, et al., 2020; Glue et al., 2018; Robison et al., 2022; Yermus et al., 2023). An additional weakness included the frequently limited number of participants (Glue et al., 2017; Glue, Medlicott, et al., 2020; Glue, Neehoff, et al., 2020; Glue et al., 2018; Robison et al., 2022). One of these studies was not adequately powered or structured to determine the duration of the anxiolytic benefits of KAP (Robison et al., 2022). Many of the studies did not include specifics regarding racial and educational demographics; however, Ahuja et al. (2022) evaluated 452 patients receiving IM ketamine treatment; 95% were white, non-Hispanic, and non-Latinx, and of the patients 25 years and older, 86% had engaged in post-secondary education. A significant weakness of the studies included in this literature synthesis is the lack of generalizability of the results due to the limited participants, poorly identified patient demographics, and limited inclusivity of the few identified demographics. A weakness regarding identifying the long-term effects of KAP on anxiety is a poor response rate for follow-up assessments after the KAP intervention completion, further limiting the conclusions that can be drawn concerning KAP's lasting effects on anxiety (Yermus et al., 2023).

Gaps and Limitations

Due to the relatively novel nature of using KAP specifically for GAD, there is an understandable paucity of strong research to draw critical conclusions supporting KAP as an effective treatment modality for GAD. Few studies considered KAP specifically for GAD. These studies did not identify specific psychotherapy protocols used in the treatment intervention. Additionally, none of these studies were randomized controlled trials or systematic reviews. While a handful of studies examined the effects of ketamine's anxiolytic properties, there were not any studies that compared a KAP intervention to a non-KAP ketamine administration intervention and the resulting treatment outcomes for patients with anxiety. Additionally, many studies included participants who continued their prior ketamine intervention medication and psychotherapy. This was not accounted for in the analysis, and it is worth noting that engagement with established psychotherapy or close follow-up with study clinicians may have impacted the treatment outcomes while not being formally integrated psychotherapy. Additionally, there is a gap in the literature for evidence-based recommendations for providing KAP for patients with GAD, limiting the ability of MHCPs to provide KAP for patients with GAD that aligns with published positive patient outcomes.

Overall, the literature should be regarded as preliminary for recommending KAP for GAD that has been non-responsive to prior mental health treatments such as pharmacotherapy or psychotherapy. Considering the difficulties experienced by MHCPs treating patients with GAD who are non-responsive to first-line treatment recommendations, the potential benefits of KAP for GAD should be strongly considered by MHCPs as administration of ketamine in the outpatient setting is relatively safe, and there are rapid anxiolytic effects that could prove most

efficacious in the KAP treatment setting. Mental health care providers who desire to incorporate patients with a primary diagnosis of GAD into their KAP practice might consider following already established guidelines for protocols for alternate diagnoses such as MDD and PTSD, as many studies had participants with multiple comorbidities. Ultimately, MHCPs must remember that KAP is not fully supported as a therapeutic modality for GAD and use their best clinical judgment in working with their clients to guide them through the most appropriate treatment plan.

METHODS

Project Design

This quality improvement project was designed to inform MHCPs of the current, literature-informed efficacy of recommending KAP for patients with GAD and assess how this educational intervention influences a MHCP's intent to recommend KAP for patients with GAD. A descriptive, quantitative approach determined the educational intervention's effectiveness and informed key stakeholders of pertinent MHCP insight into whether current literature supports using KAP for GAD. Self-report data was obtained through pre- and post-survey questionnaires due to effectiveness in determining the strength of an intervention's effects (Alessandri et al., 2017). The following outcomes evaluated this project's purpose:

1. The educational intervention will increase participant knowledge regarding the literature-informed efficacy of KAP for GAD in an outpatient setting.
2. The educational intervention will impact the participants' perceived behavioral control and attitudes toward recommending KAP for patients with GAD.

3. The educational intervention will change participants' intention to recommend KAP for GAD within their practices.
4. The educational intervention will influence participants' opinions regarding the literature-informed efficacy of providing KAP for GAD.
5. Participants will report feeling more confident about their clinical decision-making regarding whether to recommend KAP for GAD.

Model for Implementation

This DNP quality improvement project's implementation was guided by the Institute for Healthcare Improvement's (IHI) Model for Improvement (MFI), which consists of the practical implementation model, Plan-Do-Study-Act (PDSA) (Institute for Healthcare Improvement [IHI], n.d.-a). Initially, the MFI directs healthcare improvement interventions by explicitly identifying the following: what is trying to be accomplished, what will signify that the change has resulted in improvement, and what change can be made that will result in the desired improvement ([IHI], n.d.-a). By identifying what is trying to be accomplished, this project identified the following aim: increase MHCP knowledge regarding the literature-informed efficacy of KAP for GAD to inform their clinical judgment on recommending KAP for patients with GAD. To identify the impact of the proposed quality improvement, pre- and post-test survey questionnaires were used to quantify changes in participant knowledge and participant intent to recommend KAP for patients with GAD. Finally, the change proposed to impact a participant's intent to recommend KAP for patients with GAD was an educational presentation identifying the current prevalence of MHCPs recommending KAP for GAD and the literature-informed efficacy of KAP for GAD.

The Model for Improvement's Plan-Do-Study-Act guided the implementation of this project's proposed change (Figure 2). The Plan-Do-Study-Act (PDSA) model consists of four stages: planning the intervention, doing the intervention, studying the results of the intervention, and acting on the results such that changes to future implementations are made to increase the effectiveness of the intervention ([IHI], n.d.-b). These stages allow improvement initiative teams to rapidly test change on a small scale and evaluate and refine the change for further effectiveness on a broader scale ([IHI], n.d.-b). The Model for Improvement's PDSA cycle helped to establish whether the proposed educational intervention increased MHCPs' knowledge of and influenced their intent to recommend KAP for GAD at a local clinic providing KAP services.

Planning for improvement implementation consists of understanding the questions the improvement is being designed to answer, identifying the predicted outcomes, and developing the plan to test the improvement ([IHI], n.d.-b). For this project, the planning stage consisted of developing an educational presentation, creating pretest and posttest surveys for participants in the educational intervention, and generating a survey to assess the prevalence of MHCPs utilizing KAP for GAD. Planning also included coordination with implementation site staff for the intervention's distribution, identification of a mode of data collection regarding the intervention's effectiveness, and outlining how the data would be analyzed and distributed to key stakeholders.

The plan synthesized in the first phase of PDSA is implemented in the second phase, "Do" (IHI, n.d.-b). For this project, the prevalence of using KAP for GAD was assessed, and participants were recruited and engaged in the educational intervention. Results on the

intervention's effectiveness were obtained through pre-survey and post-survey assessments. Analysis of the collected data, evaluation of the results compared to predicted outcomes, and reflection on what was learned comprise the third stage, "Study" (IHI, n.d.-b). During this stage, the results of this project's intervention were synthesized into a deliverable format so that key stakeholders could understand the impact of the educational intervention and the MHCP's intent to recommend KAP for patients with GAD. In the final stage, "Act," the results deliverable informed key stakeholders of how further educational interventions may support MHCP decision-making for recommending KAP for patients with GAD.

Setting and Stakeholders

This quality improvement project's setting was a southern Arizona outpatient mental health clinic that provides KAP services to patients with treatment-resistant depression and post-traumatic stress disorder. This clinic is a private group practice setting offering various outpatient therapy and medication management interventions, including KAP. Ketamine-assisted psychotherapy interventions provided at this clinic include individual, relationship, and group sessions. Clinic clients who are approved for KAP treatment must meet specific criteria and undergo a comprehensive evaluation with a psychiatric mental health provider to determine eligibility for this therapy. Clinicians providing KAP at this clinic have received training from either the Multidisciplinary Association for Psychedelic Studies or the California Institute of Integrative Studies. This clinic has also intentionally chosen to contribute to future KAP clinician education by creating a clinician training protocol for KAP. Mental health care professionals recommending KAP services or providing information about KAP services in the outpatient setting will be invited to participate in this quality improvement project's intervention. Given the

clinic's dedication to delivering KAP for patients and educating future KAP-offering clinicians, this clinic was an appropriate setting to implement this quality improvement project.

Critical stakeholders for this quality improvement project included the clinic's organizational leadership, the MHCPs recommending KAP to patients, and MHCPs providing information about KAP services and, ultimately, the patients. Patients were expected to benefit from this intervention due to the anticipated impact on MHCP decision-making regarding recommending KAP to patients with GAD. Mental health care professionals were expected to benefit as their knowledge of the literature-informed efficacy of KAP for GAD was expected to increase, and their intent to recommend KAP to patients with GAD was expected to be better informed. Mental health care professionals providing and recommending KAP services are responsible for identifying patients who may benefit from this treatment. They are vested in acquiring more knowledge about the effectiveness of expanding eligible diagnoses to facilitate the healing of more patients. It was anticipated that the MHCP's enhanced knowledge would lead to better patient outcomes in providing KAP for GAD, benefiting clinic leadership as well.

Planning the Intervention

Following the establishment of a need to inform this clinic's MHCPs of the current literature-informed efficacy of KAP for GAD, this quality improvement project was approved by the site's organizational leadership (Appendix A). Project implementation followed an identified timeline (Appendix F). Due to the paucity of literature regarding the efficacy of KAP for GAD specifically, the prevalence of KAP recommendations among patients with GAD was assessed. A 2-question survey was sent via email to the implementation clinic's MHCPs and evaluated the prevalence of their recommending KAP to patients with a primary diagnosis of GAD (Appendix

D**)**. This information was included in the intervention presentation slides to help inform intervention-participating MHCPs. In addition, educational presentation materials consisted of the identified need for effective treatments for GAD that is unresponsive to first-line therapies and relevant themes regarding the literature-informed efficacy of KAP for GAD identified during the literature synthesis of this project (Appendix E). Themes included KAP and its effectiveness in anxiety disorders; the efficacy of ketamine on anxiety symptoms and participant functionality; the effects of ketamine in the context of anxiety with other comorbidities; the use of ketamine in an outpatient setting; and ketamine's side effects among patients with anxiety.

Due to this author's residence outside of the state of project implementation and to ensure that all participants received the same material and increased participation, the educational content was presented via a 15-minute, recorded presentation. Clinic leadership shared a recruitment email containing a link to the educational intervention. This link enabled participants to easily complete the pre-survey, educational intervention, and post-survey in a single process. The seamless experience was supported by Qualtrics software. Participants had 12 days to engage with this material and complete both the brief pre-survey and post-survey, which identified their knowledge of the efficacy of KAP for GAD and their intent to recommend this intervention to patients (Appendix D). To incorporate expert feedback in this intervention's development, this project's committee approved all survey materials and the educational intervention before implementation.

Participants and Recruitment

Project participants were recruited from a population of licensed psychotherapists, masters-level interns, administrative staff, and medical providers. However, the specific

demographics of each participant were not obtained to maintain participant confidentiality, and due to the overall lack of relevance of this data for determining the success of this quality improvement project. Demographic data collection was not part of the desired outcomes.

Convenience sampling was used to survey the prevalence of MHCPs reporting their recommendation of KAP for patients with GAD. Participation was voluntary among survey respondents. As identified in the consent to participate (Appendix B), it was assumed that the participants self-identified as eligible. In further establishing consent to participate, participants could only proceed with the survey if they agreed to the consent in Qualtrics. Eligibility criteria included mental health care professionals recommending KAP services to patients over 18 years of age, the ability to read English, and the ability to provide consent. This project's author requested the assistance of the implementation clinic's leadership to send an email drafted by the project's author to recruit participants for participation in the prevalence survey (Appendix C).

Similar convenience sampling was used among participants in the educational intervention. They were also recruited via an email drafted by this project's author and delivered by the clinic's organizational leadership (Appendix C). These participants were eligible to participate based on their MHCP role at the implementation site. Their self-identification as eligible was assumed with their consent to participate (Appendix B). As done in the prevalence survey, participants could not proceed with the intervention if they did not agree to the consent in Qualtrics. Eligibility criteria included involvement in recommending patients to KAP services or providing information to patients regarding KAP services, being over 18 years of age, having the ability to read English, and having the ability to provide consent. The anticipated sample size was 10 participants. The recruitment emails had two notification periods, including the day the

content was accessible and once more before the day of content closure. It was anticipated that this email reminder schedule would help mitigate non-response and increase MHCP participation.

Consent and Ethical Considerations

Consent

Obtaining consent from individuals who participated in this educational intervention was a core component of the project's implementation. The participants were informed with an electronically provided risk disclosure and asked to consent to participate before starting any intervention materials, including the pre-survey (Appendix B). Participant responses to the questionnaires were obtained through Qualtrics, an encrypted software tool that collects secure and blinded participant responses. This data collection method was expected to negate the need for personal information protection or deidentification and contributed to the project proposal approval from the Institutional Review Board (IRB) at the University of Arizona (Appendix D). In addition to the IRB review process, the project proposal was reviewed for approval by a three-person DNP project committee, further supporting the implementation's ethical competency.

Ethical Considerations

Three principles are well-known in guiding human subject research. Principles include respect for human dignity, justice, and beneficence (Mihajlovic-Madzarevic, 2010). Maintaining the principle of respect for human dignity requires researchers to acutely protect participant autonomy through voluntary participation after receiving adequate information regarding the intervention (Mihajlovic-Madzarevic, 2010). For this project, participant autonomy was upheld throughout the intervention by providing participants with informed consent and the option to

discontinue participation at any time. Another principle guiding this project's design was beneficence, the obligation to maximize benefits while minimizing harm (Mihajlovic-Madzarevic, 2010). Participation in this intervention was not expected to pose any physical risks or consequences for the participants due to the informative and educational nature of the presentation. The potential risk of impeding patient care due to MHCP participation in this intervention was minimized due to the asynchronous deliverable format, allowing MHCPs to complete the material at a time that integrated appropriately into their daily workflow. Overall, the benefit of educating MHCPs regarding the literature-identified efficacy of KAP for GAD was expected to outweigh the potential risk of MHCP participation. The third ethical principle influencing this quality improvement project's development was justice. In human subject research, justice refers to determining how the benefits and burdens of participation in research are applied (Mihajlovic-Madzarevic, 2010). To align with this principle, participants were invited to participate based upon direct relation to the problem being studied. This ensured that participants likely to be burdened by study participation or those who may not benefit from participation were not chosen.

Data Collection

Data from the pre-surveys and post-surveys was collected through Qualtrics software. Multiple choice and Likert-style questions were used to assess participants' intention to provide KAP for GAD, attitude towards recommending KAP for GAD, behavioral control of recommending KAP for GAD, MHCP knowledge regarding literature-informed efficacy of recommending KAP for GAD, and MHCP confidence in clinical decision making regarding recommending this treatment modality. An open-ended question was provided as an optional

response for participants to indicate further opinions regarding recommending KAP for patients with GAD. Participants were sent an email link to the Qualtrics-facilitated intervention materials. Email invitations to participate were done for both the prevalence of KAP for GAD data collection and during the educational intervention data collection periods. A recorded educational presentation for the educational intervention was embedded in the Qualtrics survey. Immediately following the educational presentation, the post-survey questions were available to the participants within the same Qualtrics survey. Data collection for the prevalence of KAP for GAD was done over one week. Data collection for the educational intervention was completed over 12 days. Data analysis followed the educational intervention's implementation period.

Data Analysis

Descriptive statistics and paired t-tests were used to analyze survey data extracted from Qualtrics into an Excel file on a password-protected computer. A comparison of pre-intervention and post-intervention surveys was expected to demonstrate possible changes in MHCP attitudes toward recommending KAP for patients with GAD and their intent to recommend this therapeutic modality in treating patients diagnosed with GAD. This analysis was presented in bar graphs to facilitate visual interpretation of the results in an easily understandable format. Statistically significant changes in pre- and post-survey responses were determined with paired t-tests. The post-survey's final, open-ended question identified themes among MHCP opinions regarding barriers to recommending KAP for GAD. Paraphrased verbiage was used to present these thematic findings. Both thematic findings and pre-survey and post-survey data comparisons were used to examine the alignment of the results with intervention-predicted outcomes. Additionally, this information was used to inform the project implementation's effectiveness.

Finally, this project's successful results were used to inform key stakeholders of the intervention's impact.

RESULTS

The DNP quality improvement project was implemented in September 2024. The educational intervention and the pre-survey and post-survey (Appendix D & E), were available for 12 days. Four participants completed the educational intervention and the pre-survey and post-survey. All four participants consented to the intervention, as consent was required before the survey questions and intervention would appear in Qualtrics. All participants reported participating in at least one of the activities: determining patient eligibility, recommending patients to, or providing information regarding KAP. Further demographic information was not obtained during the intervention implementation to maintain the anonymous integrity of this DNP project as there was an expected small sample size of 4 participants.

Outcomes

Prevalence of MHCPs Recommending KAP Among Patients with GAD

The first objective of the DNP project was to measure the prevalence of MHCPs recommending KAP among patients with GAD. The prevalence survey results are presented in the educational presentation, which can be found in Appendix E. The data was presented to the MHCPs who participated in the educational intervention, as this was expected to provide intervention participants with knowledge of what their colleagues are doing concerning recommending KAP for patients with a primary diagnosis of GAD. All seven prevalence survey respondents reported that they recommend KAP to patients; among these seven, three reported recommending KAP to patients with a primary diagnosis of GAD. Four participants reported not

recommending KAP specifically for GAD, though many of their patients presented with a comorbid diagnosis of GAD.

Educational Intervention Results

The following is a report of the pre-survey and post-survey data analysis findings. Descriptive statistics were used to analyze the Likert items and the multiple-choice and true and false questions were analyzed with paired t-tests. The final free-response question was examined for themes and commonalities.

Provider Intention to Recommend KAP for GAD

The DNP project's objectives to assess mental health care practitioners' attitudes toward recommending and intentions to recommend KAP for patients with GAD after participating in an educational intervention were assessed with the pre-survey and post-survey Likert questions. Below is a table of all measured values, and pre-survey and post-test mean results are included in Figure 3.

Table 1

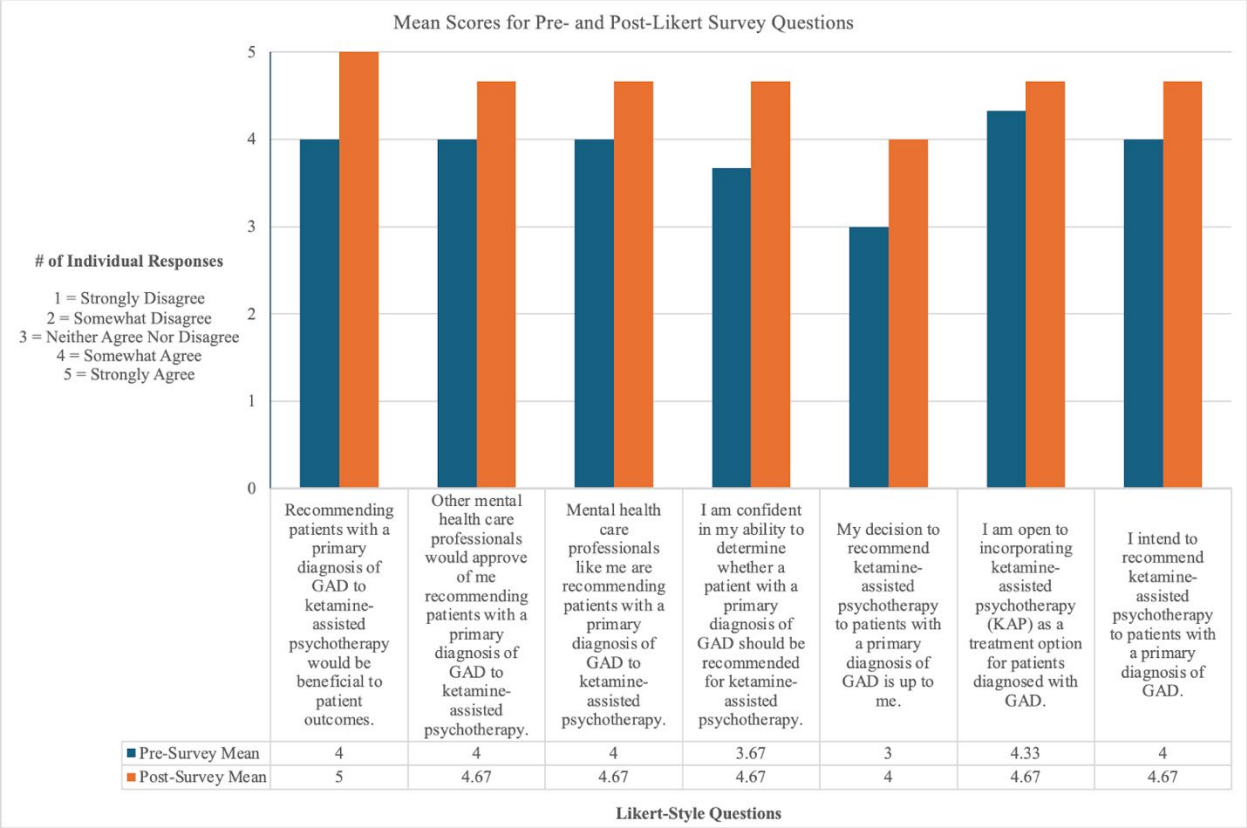
Descriptive Statistics for Pretest and Posttest: Likert Statements

	Pre (n=4)		Post (n=8)	
	Mean (sd)	**Median (min,max)**	**Mean (sd)**	**Median (min,max)**
Recommending patients with a primary diagnosis of GAD to ketamine-assisted psychotherapy would be beneficial to patient outcomes.	4 (1)	4 (3,5)	5 (0)	5 (5,5)
Other mental health care professionals would approve of me recommending patients with a primary diagnosis of GAD to ketamine-assisted psychotherapy.	4 (1)	4 (3,5)	4.67 (0.58)	5 (4,5)
Mental health care professionals like me are recommending patients with a primary diagnosis of GAD to ketamine-assisted psychotherapy.	4 (1)	4 (3,5)	4.67 (0.58)	5 (4,5)
I am confident in my ability to determine whether a patient with a primary diagnosis of GAD should be recommended for ketamine-assisted psychotherapy.	3.67 (1.15)	3 (3,5)	4.67 (0.58)	5 (4,5)
My decision to recommend ketamine-assisted psychotherapy to patients with a primary diagnosis of GAD is up to me.	3 (1.73)	2 (2,5)	4 (1.73)	5 (2,5)
I am open to incorporating ketamine-assisted psychotherapy (KAP) as a treatment option for patients diagnosed with GAD.	4.33 (1.15)	5 (3,5)	4.67 (0.58)	5 (4,5)
I intend to recommend ketamine-assisted psychotherapy to patients with a primary diagnosis of GAD.	4 (1)	4 (3,5)	4.67 (0.58)	5 (4,5)

Likert Statement Scale: 1=strongly disagree, 2=somewhat disagree, 3=neither agree nor disagree, 4=somewhat agree, 5=strongly agree

Figure 3

Mean Scores for Pre- and Post-Likert Survey Questions



	Recommending patients with a primary diagnosis of GAD to ketamine-assisted psychotherapy would be beneficial to patient outcomes.	Other mental health care professionals would approve of me recommending patients with a primary diagnosis of GAD to ketamine-assisted psychotherapy.	Mental health care professionals like me are recommending patients with a primary diagnosis of GAD to ketamine-assisted psychotherapy.	I am confident in my ability to determine whether a patient with a primary diagnosis of GAD should be recommended for ketamine-assisted psychotherapy.	My decision to recommend ketamine-assisted psychotherapy to patients with a primary diagnosis of GAD is up to me.	I am open to incorporating ketamine-assisted psychotherapy (KAP) as a treatment option for patients diagnosed with GAD.	I intend to recommend ketamine-assisted psychotherapy to patients with a primary diagnosis of GAD.
Pre-Survey Mean	4	4	4	3.67	3	4.33	4
Post-Survey Mean	5	4.67	4.67	4.67	4	4.67	4.67

As these questions were guided by the Theory of Planned Behavior, attitude, subjective norms, perceived behavioral control, and intent to engage in behavior were all assessed with the Likert questions. Participant attitudes toward recommending KAP for GAD were assessed with the following statement: *"Recommending patients with a primary diagnosis of GAD to KAP would be beneficial to patient outcomes."* The pre-survey mean and median response was '4' somewhat agree, and the post-survey mean and median response was '5' strongly agree. Notably, the post-survey minimum was '5,' and the maximum was '5,' indicating that after the

intervention, participants all strongly agreed that recommending patients with a primary diagnosis of GAD to KAP would benefit patient outcomes.

The impact of participants' perceived subjective norms was assessed with the following Likert statements: *"Other MHCPs would approve of me recommending patients with a primary diagnosis of GAD to KAP"* and *"MHCPs like me are recommending patients with a primary diagnosis of GAD to KAP."* The pre-survey results for the statement *"Other MHCPs would approve of me recommending patients with a primary diagnosis of GAD to KAP"* included a mean of '4' somewhat agree and a median of '4' somewhat agree with a range of '3' neither agree nor disagree to '5' strongly agree. The post-survey results included a mean of '4.67' and a median of '5' strongly agree with a range of '4' to '5.' The changes in the mean and median indicate participants' increased positive perceptions of other MHCPs' approval of them recommending patients with a primary diagnosis of GAD to KAP. Similarly, for the statement *"MHCPs like me are recommending patients with a primary diagnosis of GAD to KAP,"* the pre-survey and post-survey results indicate an increased positive perception of the subjective norms of recommending KAP for GAD (Table 1).

Two Likert statements assessed participants' perceived behavioral control in recommending KAP to patients with GAD. The statement *"I am confident in my ability to determine whether a patient with a primary diagnosis of GAD should be recommended for KAP"* resulted in a pre-survey mean of '3.67,' a median of '3' neither agree nor disagree, and a range of '3' neither agree nor disagree to '5' strongly agree. Post-survey results showed an increased mean of '4.67,' median of '5' strongly agree, and a range of '4' somewhat agree to '5' strongly agree. This indicates participants increased confidence in recommending patients with a primary

diagnosis of GAD to KAP, which would indicate greater belief in their perceived behavioral control in this recommendation after participating in the educational intervention. The statement *"my decision to recommend ketamine-assisted psychotherapy to patients with a primary diagnosis of GAD is up to me"* also assessed perceived behavioral control, however, the results were not as indicative of an increase in perceived behavioral control and showed a wide range in variability of perceived behavioral control. The pre-survey results included a mean of '3' neither agree nor disagree, a median of '2' somewhat disagree, and a range of '2' somewhat disagree to '5' strongly agree. Post-survey results included a mean of '4' somewhat agree, a median of '5' strongly agree, and a range of '2' somewhat disagree to '5' strongly agree.

The final two Likert statements assessed participant intent to recommend KAP for patients with GAD. The statement *"I am open to incorporating KAP as a treatment option for patients diagnosed with GAD"* resulted in pre-survey results of a mean of '4.33,' a median of '5' strongly agree, and a range of '3' neither agree nor disagree to '5' strongly agree. Post-survey results indicated a slight increase in intent to recommend, with a mean of '4.67,' a median of '5' strongly agree, and a range of '4' somewhat agree to '5' strongly agree. The final statement showed an increase in intention to recommend KAP to patients with a primary diagnosis of GAD. Pre-survey results included a mean of '4' somewhat agree, a median of '4' somewhat agree, and a range of '3' neither agree nor disagree to '5' strongly agree. Post-survey results included a mean of '4.67,' a median of '5' strongly agree, and a range of '4' somewhat agree to '5' strongly agree. The frequency results for each of the four participants are presented in Figures 4 through 10.

Figure 4

Pre- and Post-Survey Data: Likert Statement 1 – Individual Participant Responses

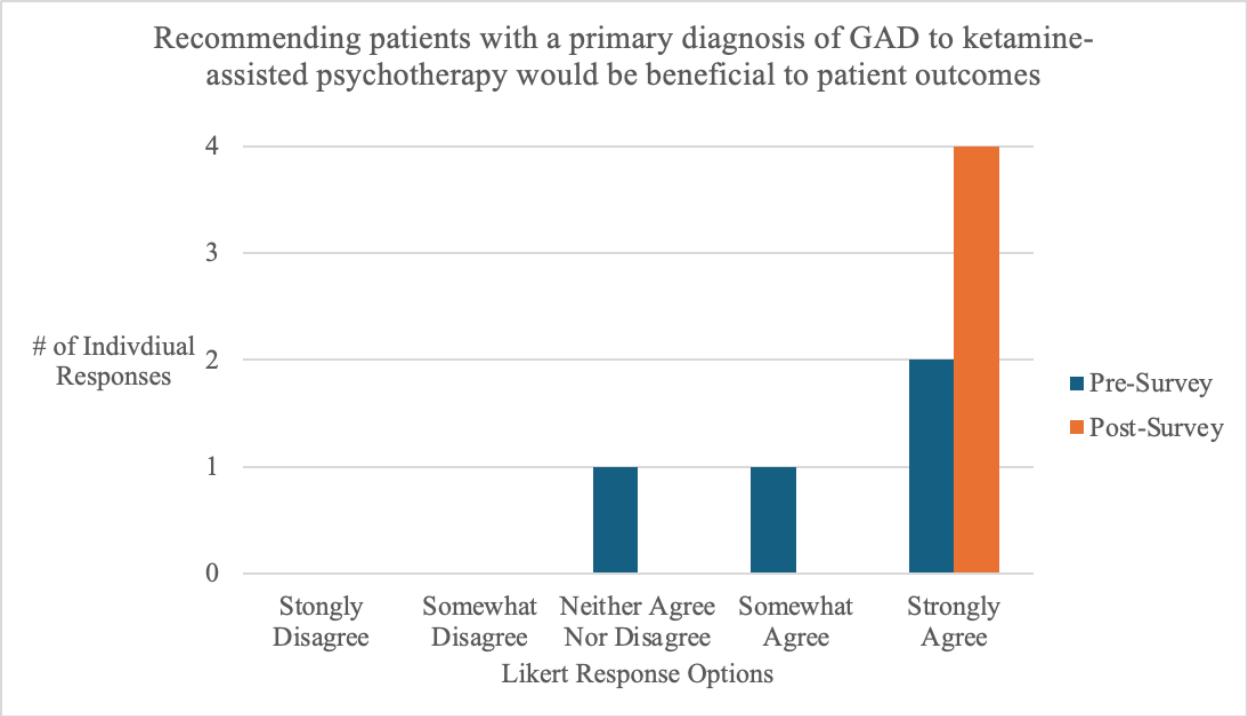


Figure 5

Pre- and Post-Survey Data: Likert Statement 2 – Individual Participant Responses

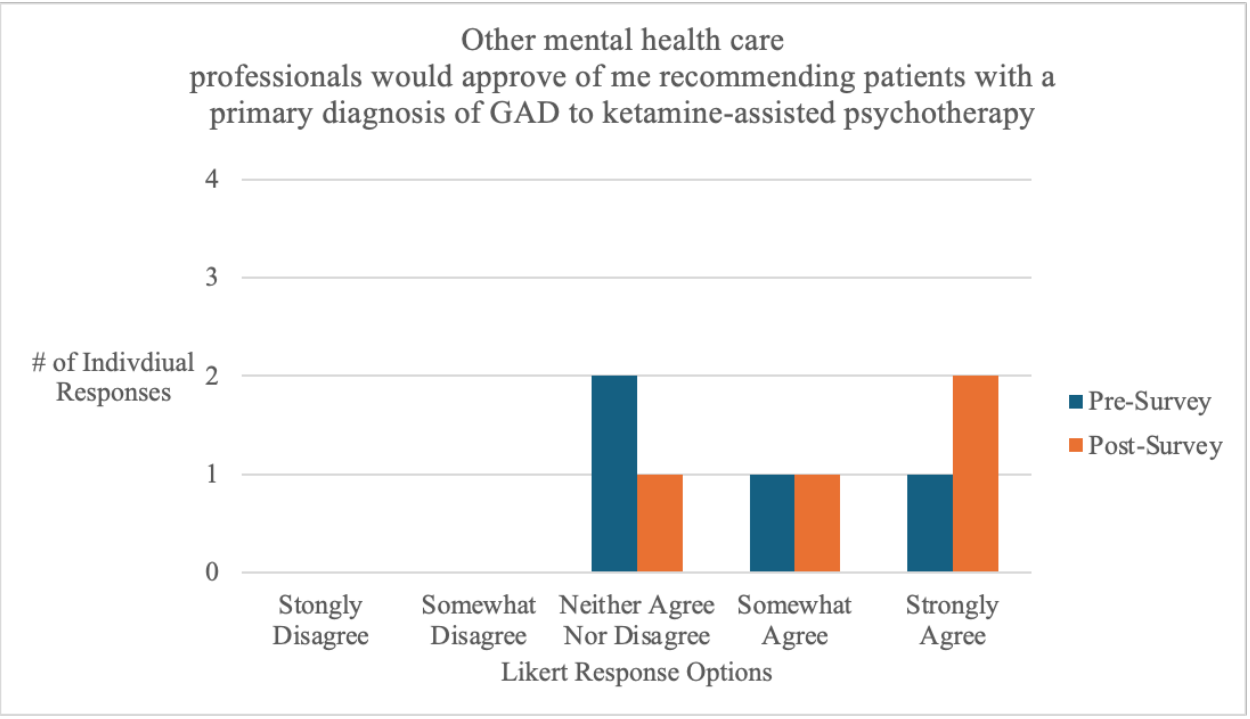


Figure 6

Pre- and Post-Survey Data: Likert Statement 3 – Individual Participant Responses

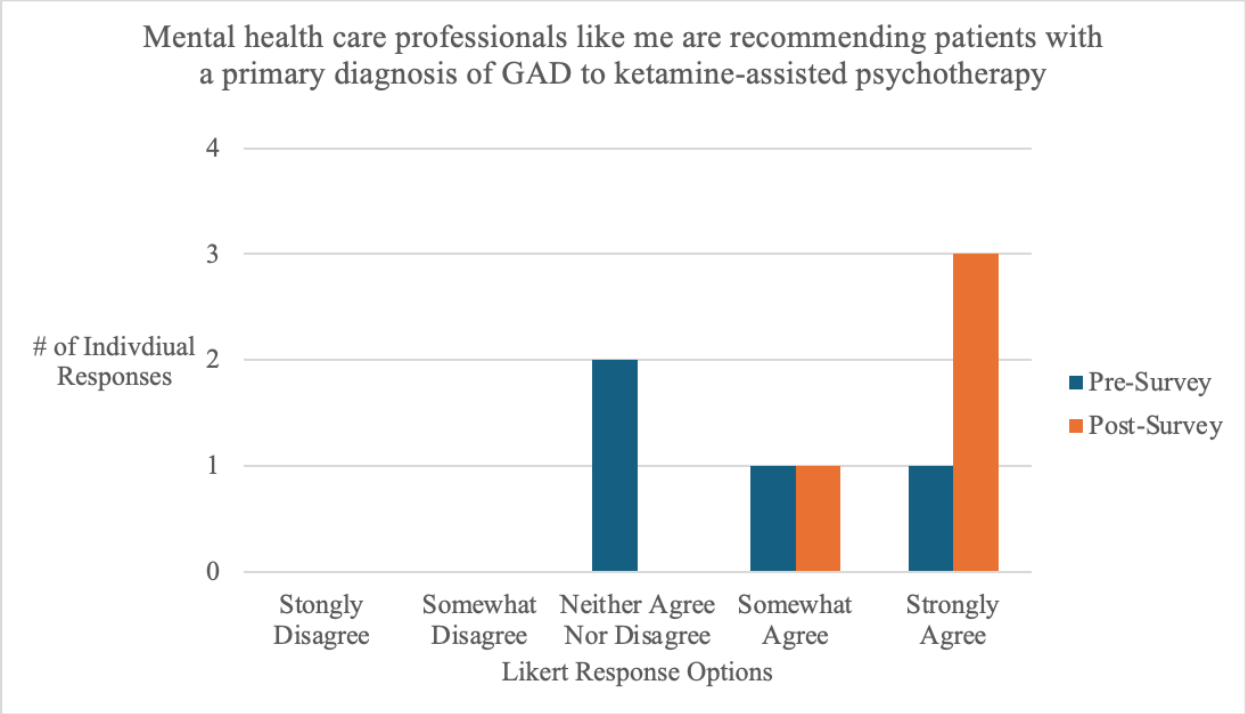


Figure 7

Pre- and Post-Survey Data: Likert Statement 4 – Individual Participant Responses

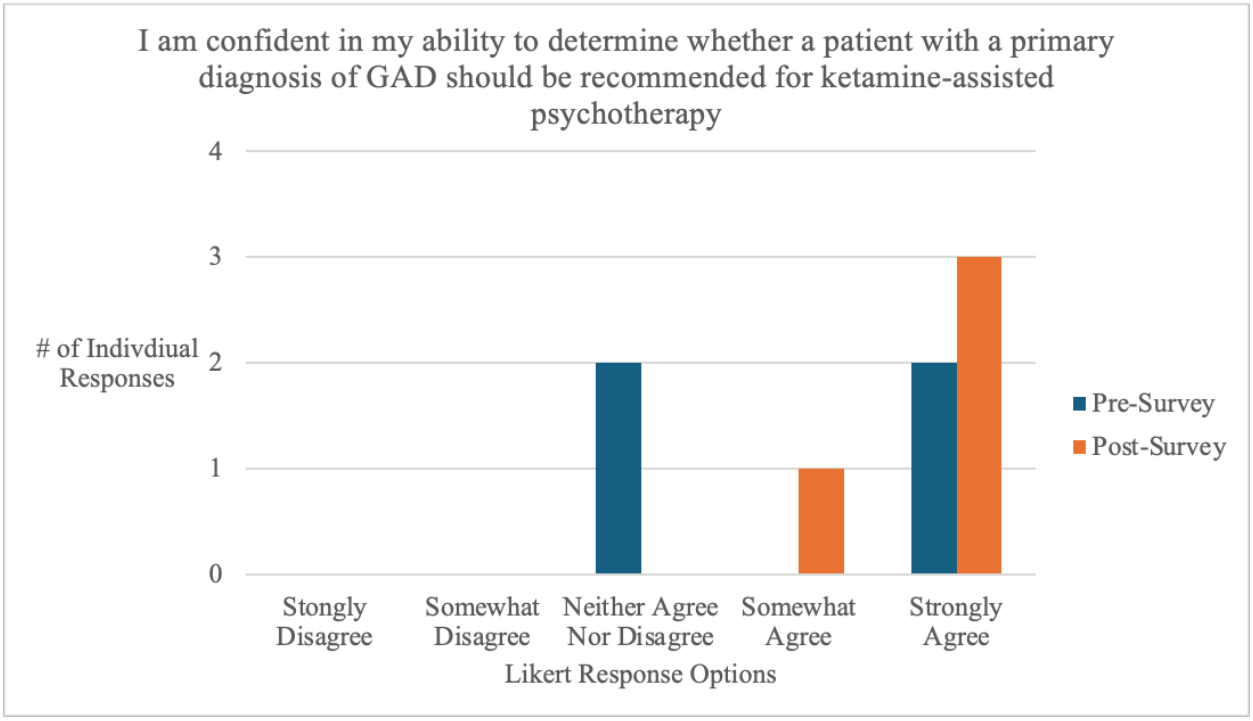


Figure 8

Pre- and Post-Survey Data: Likert Statement 5 – Individual Participant Responses

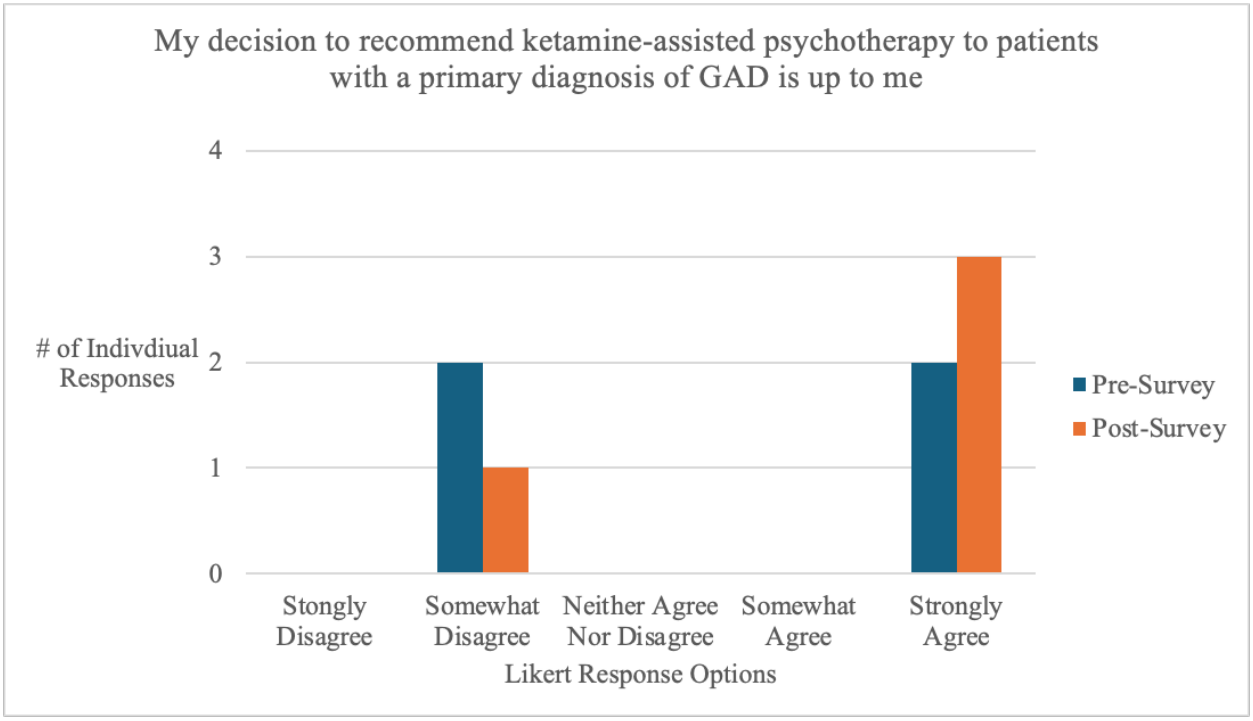


Figure 9

Pre- and Post-Survey Data: Likert Statement 6 – Individual Participant Responses

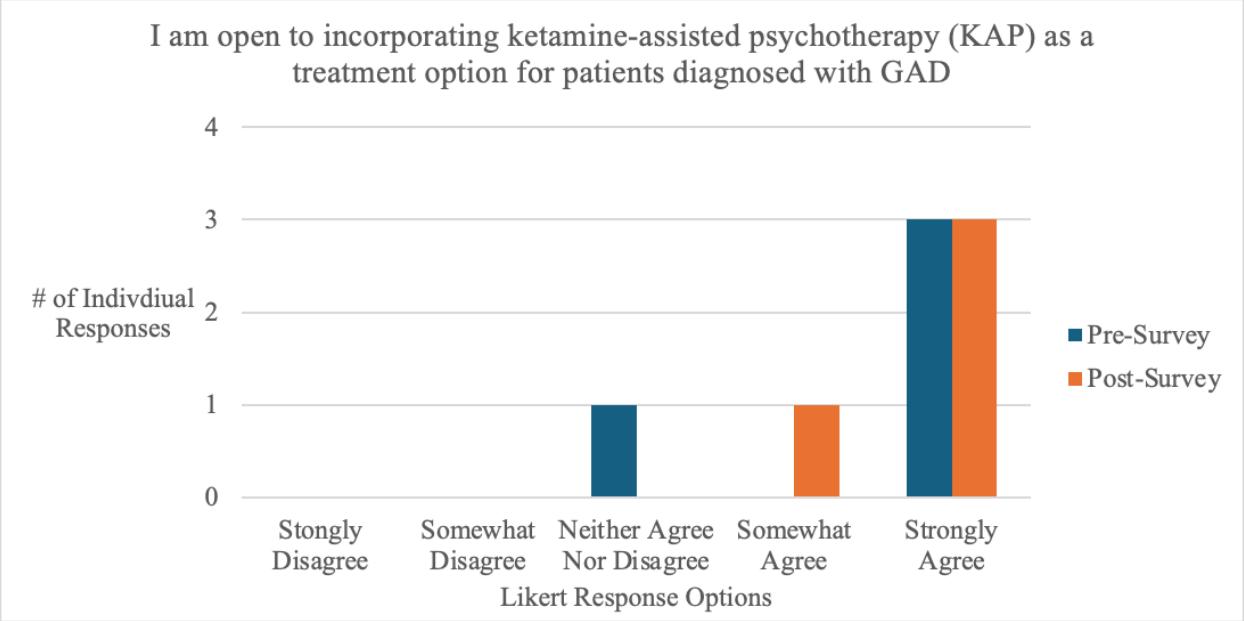
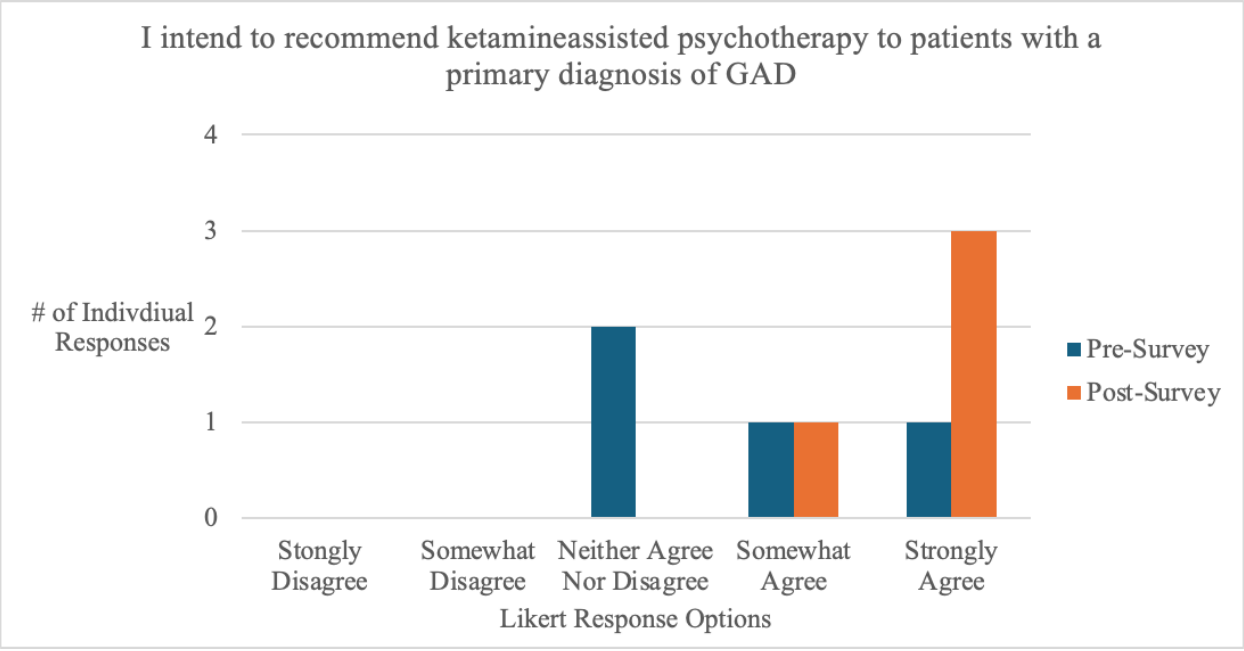


Figure 10

Pre- and Post-Survey Data: Likert Statement 7 – Individual Participant Responses



Provider Knowledge and Awareness

A primary objective of this DNP project was to increase MHCP's knowledge and awareness of the current literature-informed efficacy of KAP for patients with GAD. This was assessed in both the pre-survey and post-survey. The first question was a true or false statement testing the participants' knowledge of ketamine's anxiolytic effects without additional psychotherapy. All participants answered correctly for both the pre-survey and post-survey, as seen in Figure 11. Similarly, the true and false statement *"Among the research studies exploring the administration of ketamine for GAD, a notably significant association has been identified between positive study outcomes of increased participant functionality and continuing participants' pre-intervention medication regimens or psychotherapy treatments"* resulted in all participants answering correctly with 'True' for both the pre-survey and post-survey as shown in Figure 12. As both questions resulted in unchanged responses after the intervention, no statistics were completed.

Figure 11

Pre- and Post-Survey Knowledge Data: Ketamine's Anxiolytic Effects Without Psychotherapy Individual Participant Responses

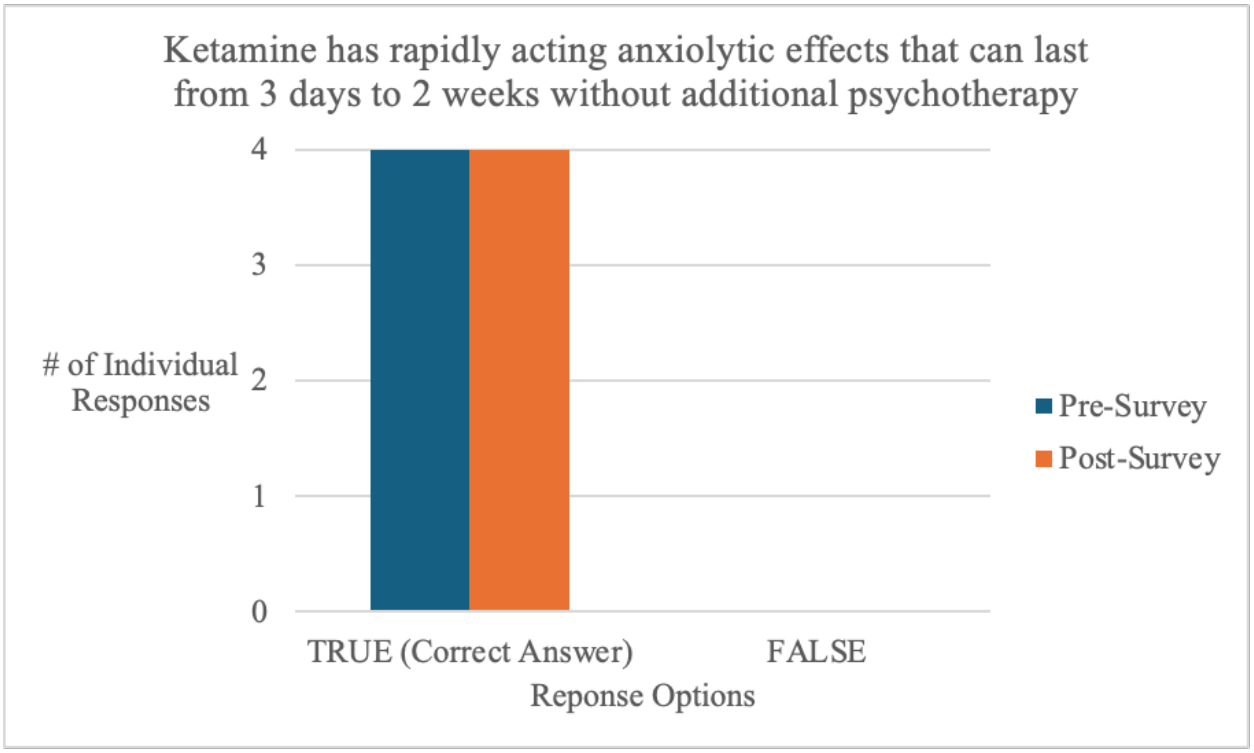
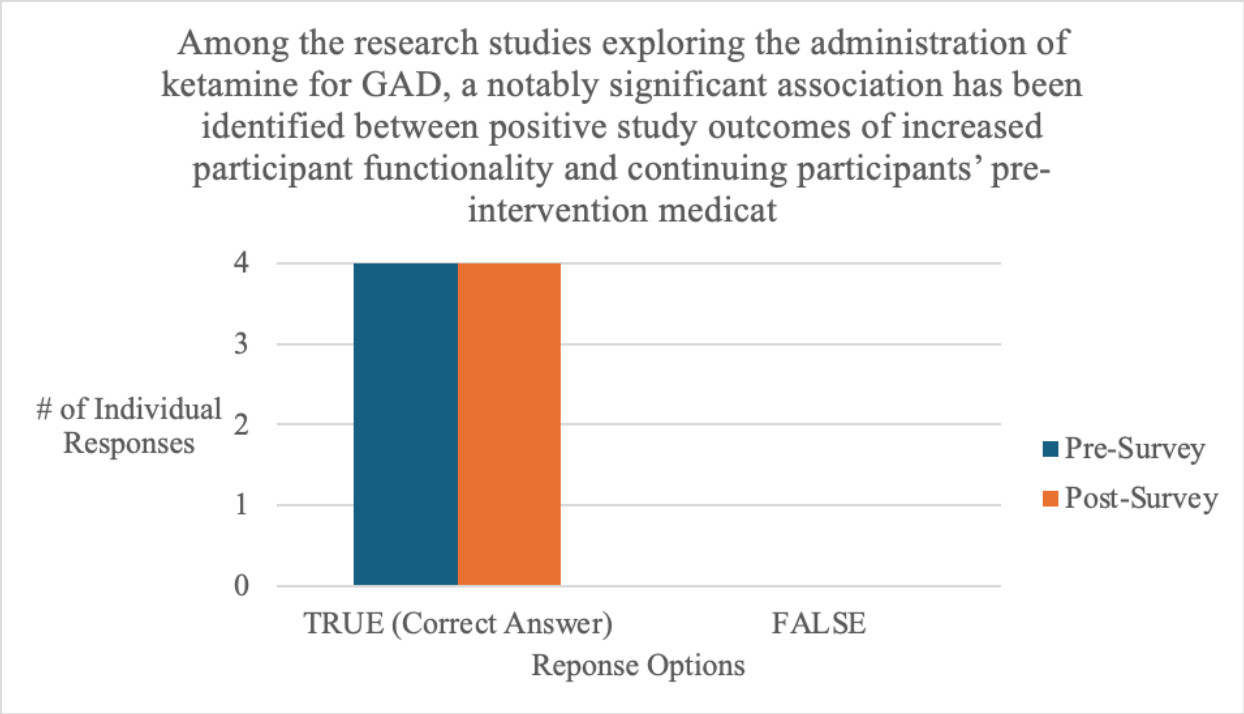


Figure 12

Pre- and Post-Survey Knowledge Data: Continuing Pre-Intervention Medication Regimens



Paired t-test results for the remaining knowledge assessment questions and the participant belief in the literature-supported efficacy of KAP for GAD question are displayed in Table 2. Response frequencies are noted in the visual displays, Figures 13 through 15. Based on the paired t-test results, the mean differences between the pre-survey and post-survey responses were not statistically significant.

Table 2

Paired T-Test Results

	t-statistic	p-value	alpha
Ketamine-assisted psychotherapy (KAP) has produced sustained reductions in anxiety, depression, and PTSD symptoms for as many as months after the last KAP session.	-0.52	0.64	0.05
Patients with more severe pre-treatment anxiety symptoms may benefit the most from KAP.	1	0.39	0.05
Within the outpatient setting, there are serious and dangerous side effects associated with administering ketamine among patients with GAD.	-1	0.39	0.05
Do you believe there is literature-supported efficacy in providing KAP for patients with a primary diagnosis of GAD?	1	0.39	0.05

Figure 13

Pre- and Post-Survey Knowledge Data: KAP Sustained Reductions

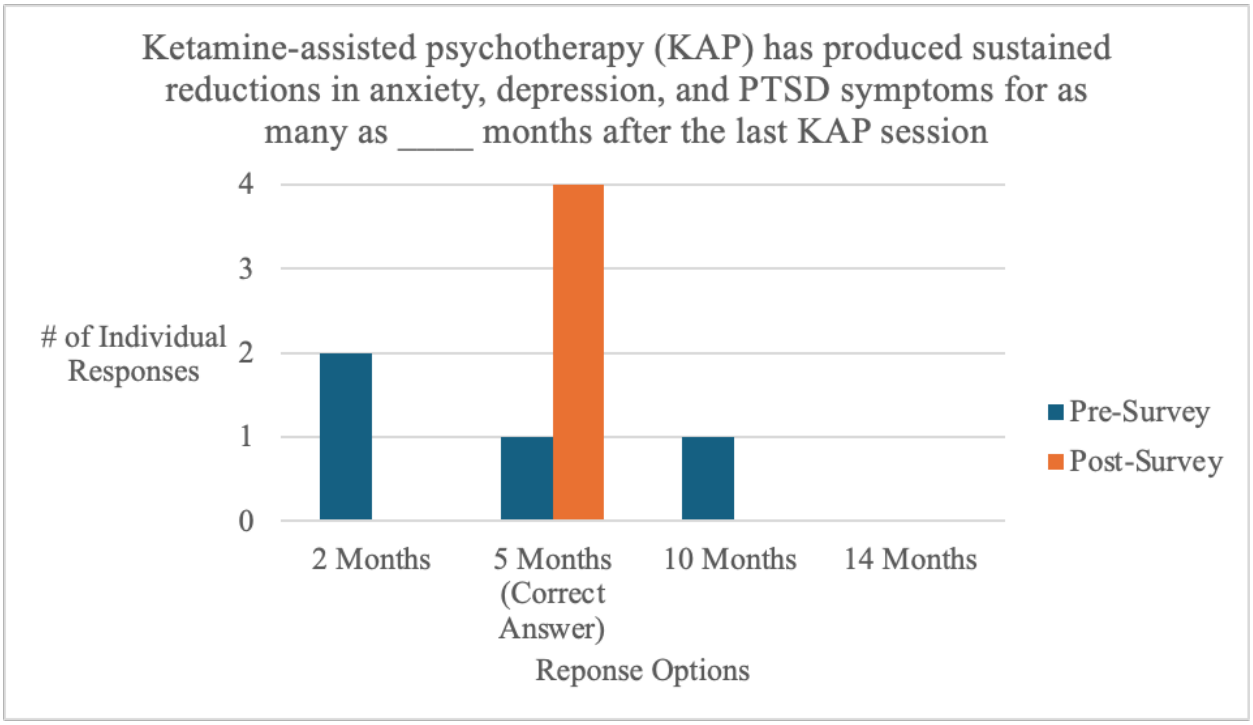


Figure 14

Pre- and Post-Survey Knowledge Data: Pre-Treatment Anxiety Symptoms and KAP

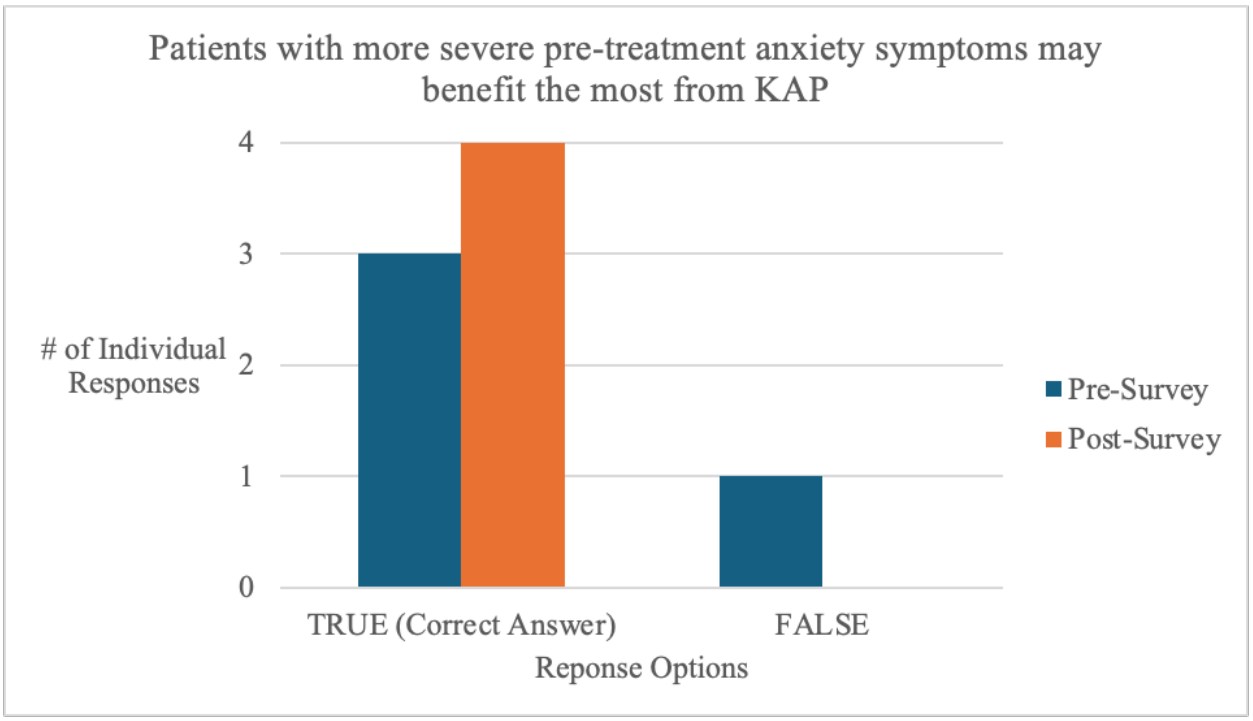
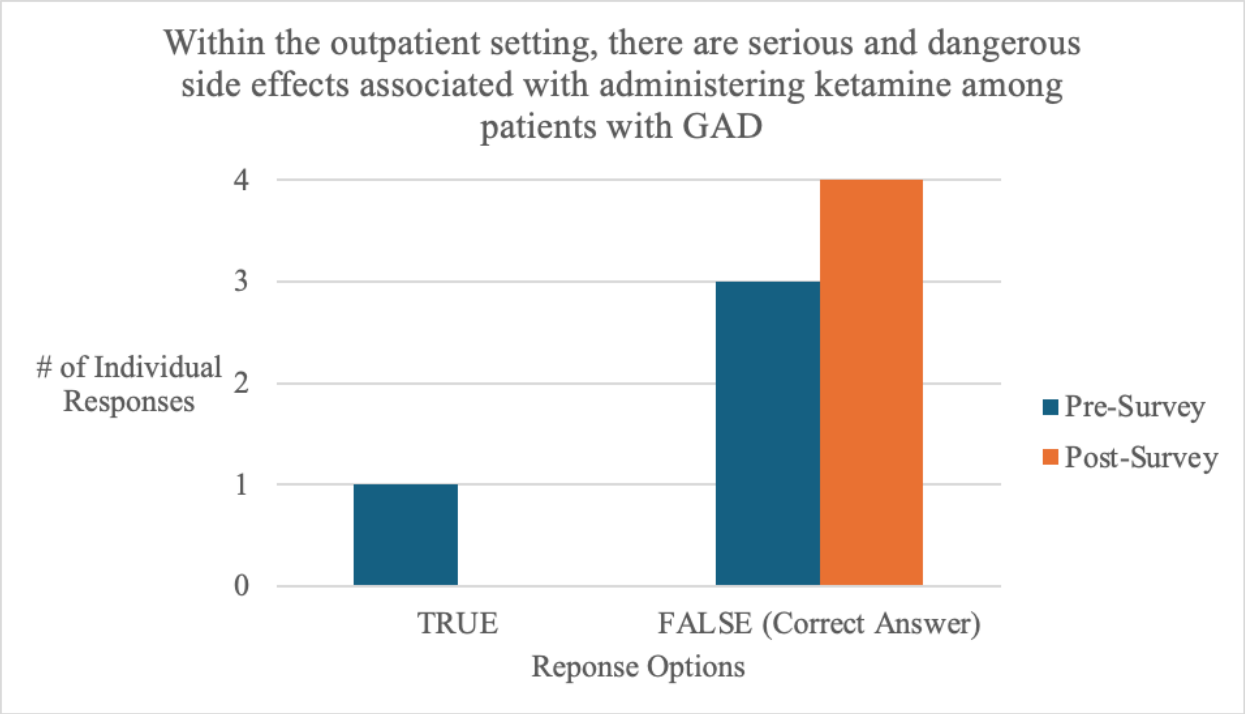


Figure 15

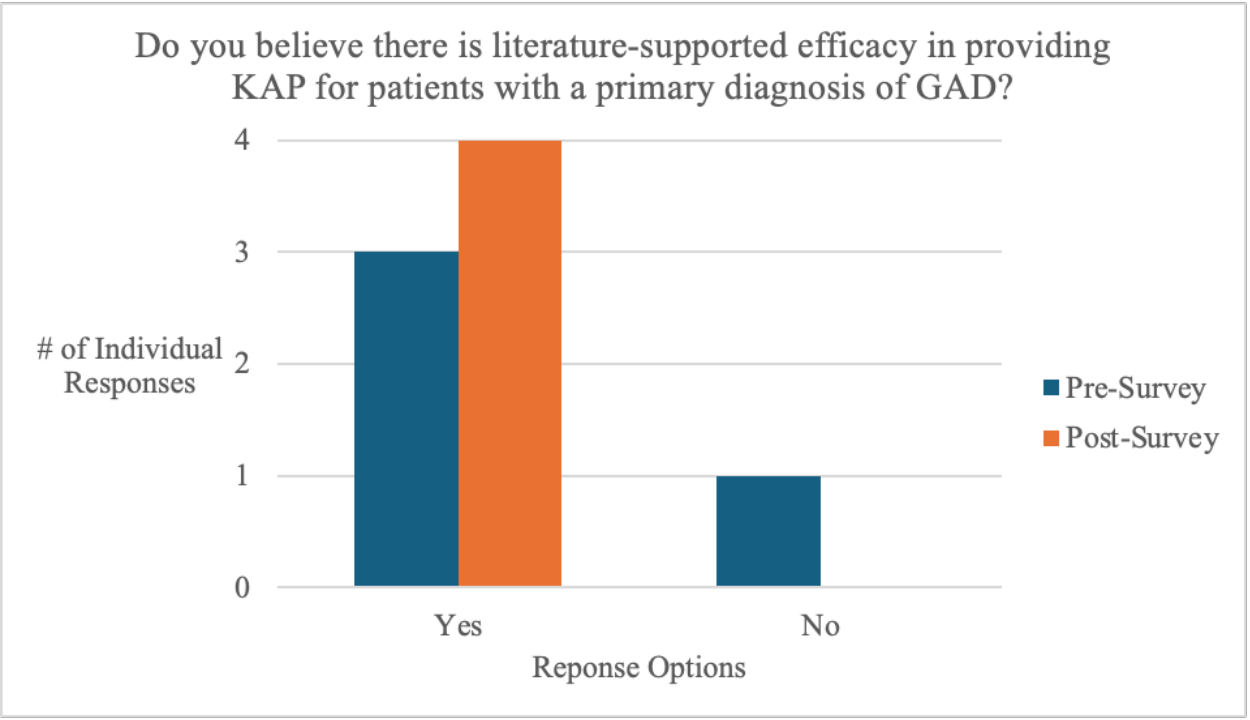
Pre- and Post-Survey Knowledge Data: Side Effects of KAP



Figures 13, 14, and 15 each indicate participants' increased knowledge regarding providing KAP for GAD. During the post-surveys, all participants chose the correct answers to these questions. After the educational intervention, all participants responded that they believed there is literature-supported efficacy in proving KAP for patients with a primary diagnosis of GAD. Before the educational intervention, one participant did not share this belief, as displayed in Figure 16.

Figure 16

Pre- and Post-Survey Data: Belief of Literature-Supported Efficacy



Barriers to Providing KAP for GAD

The final question of the post-survey was not included in the pre-survey. This question's objective was to assess the participants' perceived barriers to recommending KAP to patients with a primary diagnosis of GAD that has been unresponsive to two prior therapies. Three themes were identified in this free-response question. One theme included articulating the limited awareness and education of KAP's potential benefits in GAD among patients and MHCPs. More psychoeducation is needed for patients regarding the benefits of KAP for GAD and how comorbidities may play a role in the treatment's effectiveness. Regulatory approval was identified as another potential barrier to recommending KAP for GAD. The final theme identified was patient hesitancy to engage in KAP, possibly due to negative press coverage

resulting in misconceptions or fears regarding KAP and the perceived focus on KAP benefits for MDD and PTSD, but not GAD. These themes highlight the multifaceted nature of the barriers, ranging from regulatory issues to public perception and educational needs. They suggest addressing these barriers might require improved public education, professional training, and potentially more research or formal recognition of KAP's applicability to GAD treatment.

DISCUSSION

Summary

This DNP project's purpose was to inform MHCPs of the current, literature-informed efficacy of recommending KAP for patients with GAD and assess how this educational intervention influences a MHCP's intent to recommend KAP for patients with GAD. Due to the limited efficacy of current FDA-approved treatments for GAD, their relatively poor treatment outcomes, and the vast impacts of symptomatic GAD, it is crucial that MHCPs explore alternative treatment modalities that may have greater efficacy. Given the efficacy of KAP among patients with MDD and PTSD and the often frequently comorbid diagnosis of GAD, MHCPs who recommend KAP services should be aware of the current literature-informed efficacy of KAP among patients with GAD.

Based on a comprehensive literature search, evidence of KAP's efficacy among patients with GAD was synthesized to meet this educational need at a private mental health clinic in Southern Arizona. Literature findings were presented to the clinic's staff as an optional, asynchronous educational intervention. Anonymous pre-intervention and post-intervention surveys were used to identify participant changes in attitudes toward recommending KAP for

patients with GAD and assess knowledge changes. The results were analyzed with descriptive statistics and a paired-t-test was used when appropriate to determine statistical significance.

Interpretation

Overall, this quality improvement DNP project did meet the objectives assessed with the project's evaluative outcomes. Among the participating MHCPs, the results analyses demonstrated more positive attitudes toward and greater intent to recommend KAP for patients with GAD (Figure 3). Participants also reported increased confidence in their clinical decision-making regarding this recommendation (Figure 3). Participant knowledge about the literature-informed efficacy of KAP for GAD was improved following the educational intervention as all participants responded with the correct answers for knowledge-based questions (Figures 11 through 15). Finally, results did indicate that the educational intervention influenced participant opinions regarding the literature-informed efficacy of providing KAP for GAD, as all participants agreed that the literature supports recommending KAP for patients with GAD (Figure 16).

Strengths of this project included the assessment of behavioral intent to engage in recommending KAP for GAD to better inform key stakeholders of participating MHCPs' intentions. Additionally, the free-response questions identified a need for continued educational interventions to increase KAP recommendations among patients with GAD. Mental health care providers and patients need continued education regarding the efficacy of KAP for GAD.

Limitations

This quality improvement DNP project had several limitations, primarily due to the limited sample size and the lack of demographic data collected. With only four participants, the

results lack generalizability to a more significant population of MHCPs. The poor response rate may have been related to the voluntary and asynchronous nature of the educational intervention. Participants were asked to engage with the material of their own volition and MHCP clinical commitments may have played a role in their abilities to participate. While the anonymous nature of the data collection was appropriate for protecting participant confidentiality, the lack of demographic information collected may have contributed to the lack of generalizability as all employees (prescribers and non-prescribers) and students at the site of implementation were invited to participate. The four participants could have been all students or all employed MHCPs. Detailed demographic data may have improved the interpretation of the results about who benefited from the educational intervention. The phrasing in this project's surveys and recruitment emails may have also played a role in limiting the number of participants. For example, an administration staff member at the implementation site might have thought they were unable to participate as they do not identify as someone who recommends KAP for GAD. This could also be true for therapists at the site of implementation as well; the act of recommending KAP for GAD may have been interpreted as something that is only for medical practitioners. More inclusive phrasing may have strengthened the quantity of participant responses and demographic data would have helped further interpret these responses. Alternative phrasing to replace "recommending KAP for GAD" could include "referring to appropriate KAP recommending practitioners" to be more inclusive of all possible participants at this implementation site (licensed psychotherapists, masters-level interns, administrative staff, and medical providers). Additionally, there may have been some bias in responses to the answers in both the pre-survey and post-survey. This clinic site has previously participated in DNP projects,

and participants may have intentionally chosen answers to aid in the "success" of the DNP project.

Implications

Practice and Education

The educational intervention for this DNP quality improvement project included synthesized evidence from recent literature regarding KAP's efficacy in treating GAD symptoms that were previously unresponsive to first-line treatment recommendations. Educational topics included the effects of KAP on GAD symptoms, the safety and tolerability of ketamine administration in the outpatient setting among patients with GAD, and the use of ketamine among patients with GAD and other comorbidities. Survey response data indicated an opportunity for improvement in providing both MHCPs and patients with up-to-date education on the efficacy of KAP for GAD. Furthermore, data analysis indicated that an asynchronous educational presentation could increase MHCP knowledge of and intent to recommend KAP for patients with GAD.

This project's design could be used in further quality improvement cycles guided by the PDSA framework. It is recommended that participants be invited to provide input on the selection of topics included in the educational presentation to further participant interest and to gather input from participants regarding the perceived helpfulness and value of the intervention. Further education interventions might consider the inclusion of collecting participant demographic data to inform future educational interventions that are more specific to a targeted population of MHCPs.

Research and Policy

This project has identified a need for further research on the efficacy of KAP for patients with a primary diagnosis of GAD that has responded poorly to first-line treatment recommendations. From the current literature, it is evident that ketamine administration in the outpatient setting is safe and effective in quickly alleviating symptoms of GAD; however, further research is needed to document the longer-term effects of adding psychotherapy to the ketamine administration. As ketamine is a generic medication, it is relatively affordable, and further research could support its use, ultimately decreasing the financial burden on society from uncontrolled symptoms of GAD.

Healthcare policy can enhance the application of KAP for GAD in multiple ways. At the clinical level, policy considerations should include creating stringent protocols for ketamine administration and patient monitoring that align with federal Drug Enforcement Administration (DEA) regulations. Additionally, developing guidelines for ongoing training and competency assessments related to ketamine usage for GAD is recommended, alongside regular updates to clinical policies to incorporate the latest evidence on KAP's safety and efficacy for GAD. State nursing boards can assist by mandating that mental health care providers engaging in KAP for GAD participate in continuing education focused on ketamine administration in outpatient settings. The administration of ketamine for GAD requires careful navigation of a complex array of clinical, state, and federal policies. Ensuring compliance with these regulations is essential for maintaining safety, legal integrity, and ethical responsibility when offering innovative treatments like ketamine.

DNP Essentials Addressed

For nurse practitioner doctoral candidates to complete a DNP program, the American Association of Colleges of Nursing (AACN) has identified critical outcome competencies that candidates must achieve to receive the doctoral degree. These are outlined in the AACN's *Essentials of Doctoral Education for Advanced Nursing Practice* (DNP Essentials) (American Association of Colleges of Nursing [AACN], 2006). This DNP project successfully deployed DNP Essentials I, III, IV, and VII.

DNP Essential I, *Scientific Underpinnings for Practice,* prepares advanced practice nurses to utilize nursing science at a high level to evaluate outcomes in developing new practice approaches based on theories from nursing and other disciplines (AACN, 2006). Utilization of the Theory of Planned Behavior and the PDSA cycle were essential components of the success of this quality improvement project in developing a new practice approach to improving clinician knowledge of KAP efficacy for GAD. DNP Essential III, *Clinical Scholarship and Analytical Methods for Evidence-Based Practice,* builds on DNP Essential I by preparing advanced practice nurses in their ability to critically appraise literature, improve practice through quality improvement, and disseminate findings to improve healthcare outcomes (AACN, 2006). This project utilized the DNP Essential I associated frameworks to support DNP Essential III in guiding a literature review, designing a quality improvement educational intervention, and sharing project findings with key stakeholders. The data analysis from the prevalence survey and the educational intervention further exemplifies this author's successful implementation of DNP Essential III.

DNP Essential IV, *Information Systems/Technology and Patient Care Technology for the Improvement and Transformation of Health Care,* guides advanced nurse practitioner students in developing a refined ability to utilize technology resources when implementing quality improvement initiatives ethically (AACN, 2006). The educational intervention of this DNP project used an advanced data collection software, Qualtrics, with an embedded educational presentation. Additionally, this project's data analyses utilized Excel data analysis tools to generate descriptive statistics, statistical analyses, and data visualizations. The use of technological advances was evident in this DNP project.

DNP Essential VII, *Clinical Prevention and Population Health for Improving the Nation's Health,* requires a DNP program to prepare an advanced nurse practitioner candidate to analyze appropriate scientific data to promote health and prevent disease (AACN, 2006). In developing this project's educational intervention, epidemiological data was utilized to determine its need and relevance.

Conclusions

Generalized anxiety disorder (GAD) is a prevalent comorbid condition among those with mental illness, and first-line treatments often lack reliable efficacy. A private mental health care clinic in Southern Arizona reported providing KAP service to patients with MDD and PTSD and expressed a desire to further understand if there is efficacy for recommending KAP for GAD as this disorder was acknowledged to be a frequent comorbidity among these patients. Currently, a paucity of literature specifically supports KAP's efficacy for GAD; however, there is support for the safety and tolerability of ketamine administration in an outpatient setting among patients with anxiety disorder, resulting in improved functionality and rapidly occurring anxiolytic effects.

Mental health care professionals (MHCPs) participated in an online asynchronous educational intervention that presented the literature findings. They completed pre-intervention and post-intervention surveys to assess changes in participant knowledge and attitudes regarding recommending KAP for GAD. Comparisons of the pre-intervention and post-intervention survey responses indicated overall improvements in participant knowledge of the literature-informed efficacy of KAP for GAD and increased intention to recommend KAP for GAD. Findings also suggested barriers to recommending KAP for a primary diagnosis of GAD that has previously not responded to first-line treatment recommendations, ranging from regulatory issues to public perception and educational needs. Based on this project's findings, it is recommended that the following actions be considered for future implementation: improved public education about the efficacy of KAP for GAD; greater engagement in MHCPs' professional training regarding the efficacy of KAP for GAD; generating a more extensive body of research for KAP for GAD; and consideration of formal recognition of KAP's applicability to GAD treatment.

Plan for Sustainability

The sustainability of quality improvement initiatives is achieved through continuous cycles of maintaining and building upon progress (Institute for Healthcare Improvement [IHI], n.d.-a). There are various elements of sustainability, including supportive management, robust and transparent feedback systems, a shared sense of systems, incorporation of successful changes into redesigned systems, elimination of old processes, ongoing measurement, a culture of continuous improvement, and capacity-building programs (Kumah et al., 2024). Due to the nature of this DNP project's quality improvement initiative, the project was not designed with the intention of continued implementations within the implementation site. However, the

asynchronous nature of the educational video intervention and the creation of the pre-intervention and post-intervention surveys would be able to be utilized for further MHCP's educational needs. If this project were to be implemented with the intention of continued improvement in the educational outcomes of the MHCPs, it is recommended that further surveys request feedback on desired educational topics and improvements in the delivery of the educational material.

Plan for Dissemination

This project's findings, conclusions, and recommendations will be delivered to the implementation site's key stakeholders via a concise executive summary (Appendix H). This will include pre-intervention and post-intervention survey results and the author's data analysis and interpretation. The primary investigator hopes this dissemination will further support the implementation site's dedication to providing clients with the greatest efficacy in treatment options. Project results will also be shared with this project's DNP committee during the final DNP defense. This author may also consider submitting the results to academic journals for possible inclusion in future publications.

APPENDIX A

SITE APPROVAL/AUTHORIZATION LETTER

THE UNIVERSITY OF ARIZONA
Research
Innovation & Impact

University of Arizona IRB
845 N Park Ave., Suite 537A
Tucson, AZ 85719
Fax: 520-621-9810
VPR-IRB@arizona.edu

NOT HUMAN RESEARCH

August 16, 2024

Alli Meaux

Dear Alli Meaux:

On 8/16/2024, the IRB reviewed the following submission:

Type of Review:	Initial Study
Title:	AN EDUCATIONAL INTERVENTION ON THE EFFICACY OF KETAMINE-ASSISTED PSYCHOTHERAPY FOR ANXIETY
Investigator:	Alli Meaux
IRB Submission ID:	STUDY00005115
Sponsor:	None
Prime Sponsor:	None
IND, IDE, or HDE:	None
Documents Reviewed:	• A. Meaux_Advisor Attestation.pdf, Category: Institutional Approval; • Meaux _TCA Site Authorization.pdf, Category: External Site Authorization; • Meaux_IRB Protocol Form, Category: IRB Protocol; • Meaux_IRB_Disclosures and Consents.docx, Category: Consent Form; • Meaux_IRB_Intervention Presentation Outline.docx, Category: Participant Material; • Meaux_IRB_Survey Questions.docx, Category: Data Collection Tool; • Meaux_Participant Recruitment Emails.docx, Category: Recruitment Materials;

The IRB determined that the proposed activity is not research involving human subjects as defined by DHHS and FDA regulations.

THE UNIVERSITY OF ARIZONA
Research
Innovation & Impact

University of Arizona IRB
845 N Park Ave., Suite 537A
Tucson, AZ 85719
Fax: 520-621-9810
VPR-IRB@arizona.edu

IRB review and approval by this organization is not required. This determination applies only to the activities described in the IRB submission and does not apply should any changes be made. If changes are made and there are questions about whether these activities are research involving humans in which the organization is engaged, please submit a new request to the IRB for a determination.

All Covered Individuals must disclose all sponsored and non-sponsored Research Projects to the Office for Responsible Outside Interests (OROI) prior to Conducting Research if the individual is an Investigator. Please visit the OROI website for more information.

We value your feedback and would appreciate you taking the time to complete our survey about your experience with the IRB staff:
https://uarizona.co1.qualtrics.com/jfe/form/SV_ehQ04WxNA06b42i.

If questions arise at any time during your study, please email the general IRB inbox at VPR-IRB@arizona.edu.

Tucson Counseling Associates
125 E Mabel St
Tucson, AZ 85705

February 26, 2024

University of Arizona Institutional Review Board
c/o Office of Human Subjects
1618 E Helen St
Tucson, AZ 85721

Please note that Ms. Allison Meaux, UA Doctor of Nursing Practice student, has permission from Tucson Counseling Associates to conduct a quality improvement project at our facility for her project, "Efficacy and Utilization of Ketamine-Assisted Psychotherapy for Generalized Anxiety Disorder"

The project details are as follows and will be completed by 12/1/24:

Objective: The primary objective of this quality improvement project is to inform and educate clinic staff on best practices for the administration of ketamine in the treatment of generalized anxiety disorder. Enhancing understanding and adherence to established protocols aims to improve patient safety and optimize treatment outcomes.

Project Description: The project will involve developing and delivering educational sessions and informational materials tailored to the clinic staff responsible for administering ketamine therapy for generalized anxiety disorder. These activities will cover key aspects, including patient selection criteria, dosing protocols, monitoring procedures, and emergency response protocols. The project's success will be evaluated through pre- and post-assessments of staff knowledge and practices.

Methods: Conduct educational sessions and workshops for clinic staff. Distribute informational materials outlining best practices for ketamine administration. Administer pre- and post-assessments to evaluate knowledge improvement. Analyze assessment data to measure the effectiveness of the educational interventions.

Ms. Meaux has agreed to provide my office with a copy of the University of Arizona Determination before she recruits participants. She will also present aggregate results to the providers.

If there are any questions, please contact my office.

Signed,
Maureen Milazzo

Maureen Milazzo, LCSW
Licensed Clinical Social Worker
Ketamine Assisted Psychotherapy Operations Director
Clinical Supervisor - Psychotherapist
tcamaureenm@gmail.com
(520) 302-4694
Pronouns: she/her/hers What's this? (https://www.mypronouns.org/)
Tucson Counseling Associates
tucsoncounselingassociates.com

APPENDIX B

CONSENT DOCUMENT (DISCLOSURE AND CONSENT FORM)

Prevalence of Ketamine-Assisted Psychotherapy for GAD - Voluntary Disclosure Consent

Instruction: Please read carefully

This quality improvement project aims to inform mental health care professionals (MHCPs) of the current, literature-informed efficacy of providing ketamine-assisted psychotherapy (KAP) for patients with generalized anxiety disorder (GAD) and assess how an educational intervention influences a practitioner's intent to provide KAP for GAD patients. This survey aims to help inform MHCPs of the prevalence of current MHCPs recommending KAP to patients with GAD.

If you choose to participate in this project, you will be asked to:

1. Participate in a brief survey regarding your recommendation of KAP for patients with GAD.

It will take approximately 2-5 minutes to complete this survey. Responses are anonymous. There are no anticipated risks associated with participation in this survey.

If you choose to participate in this survey, please note that participation is completely voluntary, and you have the right to refuse without penalty. You may withdraw from the survey at any time. When completing the survey, you may skip any question you choose not to answer.

With your participation in this survey, you are indicating:

- You are a mental health care professional and recommend KAP services to patients or provide information regarding KAP services to patients (Note: for the purpose of this survey, KAP is defined as a therapeutic intervention that involves clinician-prescribed ketamine administered in an outpatient clinic under the supervision of mental health care professionals. Integration sessions are completed with a mental health care professional in the days following the ketamine administration session.)
- You are over 18 years of age
- You have the ability to read and understand English
- You provide consent to participate

For questions or concerns regarding this quality improvement project, you may contact:

Allison Meaux, BSN, RN
The University of Arizona DNP-PMHNP Student
Email: aemeaux@arizona.edu

Educational Intervention - Voluntary Disclosure Consent

Instruction: Please read carefully

This quality improvement project aims to inform mental health care professionals (MHCPs) of the current, literature-informed efficacy of providing ketamine-assisted psychotherapy (KAP) for patients with generalized anxiety disorder (GAD) and assess how this educational intervention influences a MHCP's intent to provide KAP for GAD patients. The goal is to improve MHCPs' confidence in their clinical decision-making regarding whether to recommend KAP for patients with a primary diagnosis of GAD that has been non-responsive to prior treatments.

If you choose to participate in this project, you will be asked to:

1. View a brief educational presentation on the literature-informed efficacy of KAP as a treatment for GAD.
2. Take a pre- and post-survey about your knowledge and comfort level regarding the recommendation of KAP for GAD.

It will take approximately 2-10 minutes to complete each pre- and post-survey. Responses to both surveys are completely anonymous. Other than knowledge gained from the educational presentation, you will receive no immediate benefit from your participation. There are no anticipated risks associated with participation in this project.

If you choose to participate in this survey, please note that participation is completely voluntary, and you have the right to refuse without penalty. You may withdraw from the survey at any time. When completing the survey, you may skip any question you choose not to answer.

With your participation in this survey, you are indicating:

- You are a mental health care professional and recommend KAP services to patients or provide information regarding KAP services to patients (Note: for the purpose of this survey, KAP is defined as a therapeutic intervention that involves clinician-prescribed ketamine administered in an outpatient clinic under the supervision of mental health care professionals. Integration sessions are completed with a mental health care professional in the days following the ketamine administration session.)
- You are over 18 years of age
- You have the ability to read and understand English
- You provide consent to participate

For questions or concerns regarding this quality improvement project, you may contact:

Allison Meaux, BSN, RN
The University of Arizona DNP-PMHNP Student
Email: aemeaux@arizona.edu

APPENDIX C

RECRUITMENT MATERIAL (RECRUITMENT EMAILS)

Prevalence Invitation to Participate – Email

Hello, mental health care professionals,

Hopefully, this email finds you all well. As the psychiatry world continues to evolve with increasingly innovative treatment plans for patients with conditions that are unresponsive to traditional treatments, I have chosen to explore the current literature-informed efficacy of providing ketamine-assisted psychotherapy (KAP) for patients with generalized anxiety disorder (GAD) that have not responded to previous treatments.

I am Allison Meaux, a Psychiatric and Mental Health Doctor of Nursing Practice (DNP) Candidate at the University of Arizona. My DNP quality improvement project aims to inform mental health care professionals (MHCPs) of the current, literature-informed efficacy of providing KAP for patients with GAD and assess how an educational intervention influences a MHCP's intent to provide KAP for this patient population. Given the results of my literature synthesis, I have decided that including the prevalence of MHCPs recommending KAP for patients with GAD in the educational presentation would be beneficial. This survey aims to help inform MHCPs of the prevalence of KAP use for patients with GAD.

This email contains a link to an anonymous survey, which can each be completed online in roughly 2-5 minutes. This survey will collect information regarding your recommendation of KAP services.

Participation in the survey is not mandatory; disclosure about the project is available at the start of the survey and via attachment to this email. Participation is completely voluntary; you may choose to skip any of the questions in the survey. If you have any questions or concerns about the project, please do not hesitate to contact me directly. Thank you for your time and consideration.

Link to Survey

Best,

Allison Meaux, BSN, RN
The University of Arizona DNP-PMHNP Student
Phone: 480.249.7446
Email: aemeaux@arizona.edu

Educational Intervention Invitation to Participate - Email

Hello, mental health care professionals,

Hopefully, this email finds you all well. As the psychiatry world continues to evolve with increasingly innovative treatment plans for patients with conditions that are unresponsive to traditional treatments, I have chosen to explore the current literature-informed efficacy of providing ketamine-assisted psychotherapy (KAP) for patients with generalized anxiety disorder (GAD) that have not responded to previous treatments.

I am Allison Meaux, a Psychiatric and Mental Health Doctor of Nursing Practice (DNP) Candidate at the University of Arizona. My DNP quality improvement project aims to inform mental health care professionals (MHCPs) of the current, literature-informed efficacy of providing KAP for patients with GAD and assess how an educational intervention influences a MHCP's intent to recommend KAP for this patient population. I invite you to participate in an educational presentation on the efficacy of KAP for GAD.

The project seeks to assess MHCPs' current knowledge of the literature-informed efficacy of providing KAP for GAD, their intent to recommend KAP for patients with GAD, and their confidence in clinical decision-making in recommending KAP for this patient population. Project participation includes the completion of brief, anonymous surveys before and after the education presentation. This email contains a link to all survey and educational video materials. Both surveys will take roughly 2-5 minutes to complete. Viewing the educational presentation will take about 15 minutes.

Participation in this educational project is not mandatory; disclosure about the project is available at the start of the survey and via attachment to this email. Participation in every project phase is voluntary; you may view the educational presentation but decline to complete the post-survey. If you have any questions or concerns about the project, please do not hesitate to contact me directly. Thank you for your time and consideration.

Link to Surveys and Educational Presentation

Best,

Allison Meaux, BSN, RN
The University of Arizona DNP-PMHNP Student
Phone: 480.249.7446
Email: aemeaux@arizona.edu

APPENDIX D

EVALUATION INSTRUMENTS (PREVALENCE SURVEY, PRE-SURVEY, POST-SURVEY)

Prevalence Survey

Please note that for this survey:

GAD refers to a generalized anxiety disorder that has not responded to two trials of alternate therapies.

KAP is defined as a therapeutic intervention that involves clinician-prescribed ketamine administered in an outpatient clinic under the supervision of mental health care professionals. Integration sessions are completed with a mental health care professional in the days following the ketamine administration session.

1) Do you recommend patients to or provide information about ketamine-assisted psychotherapy?
   a) Yes
   b) No
2) Do you recommend ketamine-assisted psychotherapy services to patients with a primary diagnosis of generalized anxiety disorder?
   a) Yes
   b) No
   c) No, but some of the patients who are recommended to KAP do have comorbid GAD
   d) No, if a patient has GAD, they are not eligible for or recommended to KAP

Pre-Survey for Educational Presentation

1. Do you participate in any of the following activities: determine patient eligibility for, recommend patients to, or provide information regarding ketamine-assisted psychotherapy (KAP)?
    a. Yes
    b. No

Please note that for this survey:

GAD refers to a generalized anxiety disorder that has not responded to two trials of alternate therapies.

KAP is defined as a therapeutic intervention that involves clinician-prescribed ketamine administered in an outpatient clinic under the supervision of mental health care professionals. Integration sessions are completed with a mental health care professional in the days following the ketamine administration session.

On a scale of 1 to 5, please indicate your level of agreement with the following statements. (1 = Strongly Disagree, 5 = Strongly Agree)

2. Recommending patients with a primary diagnosis of GAD to ketamine-assisted psychotherapy would be beneficial to patient outcomes.
    a. Strongly Disagree, Somewhat Disagree, Neither Agree nor Disagree, Somewhat Agree, Strongly Agree
3. Other mental health care professionals would approve of me recommending patients with a primary diagnosis of GAD to ketamine-assisted psychotherapy
    a. Strongly Disagree, Somewhat Disagree, Neither Agree nor Disagree, Somewhat Agree, Strongly Agree
4. Mental health care professionals like me are recommending patients with a primary diagnosis of GAD to ketamine-assisted psychotherapy.
    a. Strongly Disagree, Somewhat Disagree, Neither Agree nor Disagree, Somewhat Agree, Strongly Agree
5. I am confident in my ability to determine whether a patient with a primary diagnosis of GAD should be recommended for ketamine-assisted psychotherapy.

   a. Strongly Disagree, Somewhat Disagree, Neither Agree nor Disagree, Somewhat Agree, Strongly Agree
6. My decision to recommend ketamine-assisted psychotherapy to patients with a primary diagnosis of GAD is up to me.
   a. Strongly Disagree, Somewhat Disagree, Neither Agree nor Disagree, Somewhat Agree, Strongly Agree
7. I am open to incorporating ketamine-assisted psychotherapy (KAP) as a treatment option for patients diagnosed with GAD.
   a. Strongly Disagree, Somewhat Disagree, Neither Agree nor Disagree, Somewhat Agree, Strongly Agree
8. I intend to recommend ketamine-assisted psychotherapy to patients with a primary diagnosis of GAD
   a. Strongly Disagree, Somewhat Disagree, Neither Agree nor Disagree, Somewhat Agree, Strongly Agree
9. Ketamine has rapidly acting anxiolytic effects that can last from 3 days to 2 weeks without additional psychotherapy.
   a. True
   b. False
10. Ketamine-assisted psychotherapy (KAP) has produced sustained reductions in anxiety, depression, and PTSD symptoms for as many as ____ months after the last KAP session.
   a. 2 months
   b. 5 months
   c. 10 months
   d. 14 months
11. Patients with more severe pre-treatment anxiety symptoms may benefit the most from KAP.
   a. True
   b. False
12. Within the outpatient setting, there are serious and dangerous side effects associated with administering ketamine among patients with GAD.

a. True
b. False

13. Among the research studies exploring the administration of ketamine for GAD, a notably significant association has been identified between positive study outcomes of increased participant functionality and continuing participants' pre-intervention medication regimens or psychotherapy treatments.
    a. True
    b. False
14. Do you believe there is literature-supported efficacy in providing KAP for patients with a primary diagnosis of GAD?
    a. Yes
    b. No

Post-Survey for Educational Presentation

1) Do you participate in any of the following activities: determine patient eligibility for, recommend patients to, or provide information regarding ketamine-assisted psychotherapy (KAP)?
    a) Yes
    b) No

Please note that for this survey:

GAD refers to a generalized anxiety disorder that has not responded to two trials of alternate therapies.

KAP is defined as a therapeutic intervention that involves clinician-prescribed ketamine administered in an outpatient clinic under the supervision of mental health care professionals. Integration sessions are completed with a mental health care professional in the days following the ketamine administration session.

On a scale of 1 to 5, please indicate your level of agreement with the following statements. (1 = Strongly Disagree, 5 = Strongly Agree)"

2) Recommending patients with a primary diagnosis of GAD to ketamine-assisted psychotherapy would be beneficial to patient outcomes.
    a) Strongly Disagree, Somewhat Disagree, Neither Agree nor Disagree, Somewhat Agree, Strongly Agree
3) Other mental health care professionals would approve of me recommending patients with a primary diagnosis of GAD to ketamine-assisted psychotherapy
    a) Strongly Disagree, Somewhat Disagree, Neither Agree nor Disagree, Somewhat Agree, Strongly Agree
4) Mental health care professionals like me are recommending patients with a primary diagnosis of GAD to ketamine-assisted psychotherapy.
    a) Strongly Disagree, Somewhat Disagree, Neither Agree nor Disagree, Somewhat Agree, Strongly Agree
5) I am confident in my ability to determine whether a patient with a primary diagnosis of GAD should be recommended for ketamine-assisted psychotherapy.

a) Strongly Disagree, Somewhat Disagree, Neither Agree nor Disagree, Somewhat Agree, Strongly Agree

6) My decision to recommend ketamine-assisted psychotherapy to patients with a primary diagnosis of GAD is up to me.
   a) Strongly Disagree, Somewhat Disagree, Neither Agree nor Disagree, Somewhat Agree, Strongly Agree
7) I am open to incorporating ketamine-assisted psychotherapy (KAP) as a treatment option for patients diagnosed with GAD.
   a) Strongly Disagree, Somewhat Disagree, Neither Agree nor Disagree, Somewhat Agree, Strongly Agree
8) I intend to recommend ketamine-assisted psychotherapy to patients with a primary diagnosis of GAD
   a) Strongly Disagree, Somewhat Disagree, Neither Agree nor Disagree, Somewhat Agree, Strongly Agree
9) Ketamine has rapidly acting anxiolytic effects that can last from 3 days to 2 weeks without additional psychotherapy.
   a) True
   b) False
10) Ketamine-assisted psychotherapy (KAP) has produced sustained reductions in anxiety, depression, and posttraumatic stress disorder symptoms for as many as ____ months after the last KAP session.
   a) 2 months
   b) 5 months
   c) 10 months
   d) 14 months
11) Patients with more severe pre-treatment anxiety symptoms may benefit the most from KAP.
   a) True
   b) False

12) Within the outpatient setting, there are serious and dangerous side effects associated with administering ketamine among patients with GAD.
    a) True
    b) False
13) Among the research studies exploring the administration of ketamine for GAD, a notably significant association has been identified between positive study outcomes of increased participant functionality and continuing participants' pre-intervention medication regimens or psychotherapy treatments.
    a) True
    b) False
14) Do you believe there is literature-supported efficacy in providing KAP for patients with a primary diagnosis of GAD?
    a) Yes
    b) No
15) What are the barriers you see to recommending KAP to patients with a primary diagnosis of GAD that has been unresponsive to two prior therapies?

    _____

    _____

APPENDIX E

PARTICIPANT MATERIAL (EDUCATIONAL POWERPOINT PRESENTATION)

Literature-Informed Efficacy Of Ketamine-Assisted Psychotherapy For Generalized Anxiety Disorder

Allison Meaux, BSN, RN
DNP, PMHNP Candidate, 2024

THE UNIVERSITY OF ARIZONA College of Nursing

1

Introduction

Background on Generalized Anxiety Disorder (GAD)

- Functionally impairment resulting from persistently pervasive worrying with accompanying physical symptoms

Prevalence of GAD

- In the United States, 5.7% of adults are reported to have experienced GAD at some point in their lives

Consequences

- Impaired role functioning, general health status, and work productivity

(Alonso et al., 2011; American Psychiatric Association, 2022; Figueroa et al., 2006; Grant et al., 2005; Hoffman et al., 2008; National Institute of Mental Health, n.d.; Swinkels et al., 2012; Ruscio et al., 2017)

2

Background: GAD Treatment

- First-line medication treatments: second-generation antidepressants SSRIs and SNRIs
- CBT

- Non-responders range from 34% to 36% for CBT and 30% for SSRIs
- 57% of those with anxiety disorders treated with antidepressants are non-adherent at six months
- Comorbid depression has resulted in lower rates of remission

(Bandelow et al., 2015; Bandelow et al., 2016; Katzman et al., 2014; National Institute for Health and Care Excellence, 2022; Springer et al., 2018; Stein et al., 2006; Sruoway & Simon, 2022; Taylor et al., 2012)

3

Background Knowledge: Ketamine-Assisted Psychotherapy

- Experience a time of absent negative emotions
- Temporarily detach from their usual identity
- Experience a reduction in external sensations
- Enhancement of an individual's ability to meaningfully engage in psychotherapy

- Ketamine affects the glutamate system in the brain
- Ketamine promotes brain-derived neurotrophic factor expression and is neuroprotective

(Dorrett et al., 2019; Gupta & Prabhavalkar, 2021; Johnston et al., 2024; Miranda et al., 2019; Newman et al., 2023)

4

Local Problem

- 2023: Roughly 1/3 adults in Arizona with symptoms of anxiety
- 2020: Arizona emergency department visits
  - Depression: 4,402 for depression
  - Anxiety and fear-related: 13,868
- TCA provides KAP for MDD and PTSD
- GAD is frequently comorbid with these disorders

(Agency for Healthcare Research and Quality, n.d.; National Center for Health Statistics, 2021, 2023)

5

Question

Should you be recommending KAP for your clients with a primary diagnosis of GAD?

6

Literature-Informed Efficacy of KAP for GAD

- 10 Studies
- Types of studies:
  - Retrospective descriptive cohort
  - Descriptive
  - Uncontrolled open-label exploratory
  - Case series

- Themes:
  - KAP efficacy in anxiety disorders
  - Ketamine's anxiolytic effects and participant functionality
  - Ketamine in the context of other comorbidities and patient demographics
  - Ketamine administration in the outpatient setting

(Ahuja et al., 2022; Dore et al., 2019; Glue et al., 2017; Glue, Medlicott, et al., 2020; Glue, Neehoff, et al., 2020; Glue et al., 2018; Hartland et al., 2023; Robison et al., 2022; Tully et al., 2022; Yermus et al., 2023)

7

7

KAP and Efficacy in Anxiety Disorders

- Longer durations of treatment were associated with significant improvements in depression and anxiety
- Those with developmental trauma experience greater improvement in anxiety and depression symptoms
- Sustained reductions in anxiety, depression, and PTSD for as many as five months after the last KAP

(Dore et al., 2019; Glue et al., 2018; Robison et al., 2022; Yermus et al., 2023)

8

8

Ketamine's Effects on Anxiety Symptoms and Functionality

Studies with no psychotherapy component:

- Rapid onset of anxiolytic effects persisting anywhere from three days to two weeks
- 50% reduction in anxiety symptoms following subcutaneous ketamine administration
- Enhancements in functionality

Study with psychotherapy component:

- Sustained reductions in anxiety, depression, and PTSD to extend as much as five months after the last KAP session

5

(Glue et al., 2017; Glue, Medlicott, et al., 2020; Glue, Neehoff, et al., 2020; Glue et al., 2018; Hartland et al., 2023; Tully et al., 2022; Yermus et al., 2023)

9

9

Patient Demographics and Comorbidities

- Non-response to prior medication or psychotherapy
- Anxiolytic effects among participants not currently depressed
- Decreased depression and anxiety among multiple comorbidities
- Patients remained on current medication regimens and continued psychotherapy in non-KAP studies

- More severe symptoms of depression and anxiety, higher ACE scores, and current suicidality may benefit most from KAP
- 22 to 43-year-old patients in KAP studies
- 18 to 55-year-old patients in non-KAP studies

(Ahuja et al., 2022; Dore et al., 2019; Glue et al., 2017; Glue, Medlicott, et al., 2020; Glue, Neehoff, et al., 2020; Glue et al., 2018; Robison et al., 2022; Yermus et al., 2023)

10

10

Ketamine Administration in the Outpatient Setting

Administration

- Anxiolytic effects achieved with
  - Subcutaneous injection into the upper arm (1 mg/kg)
  - Oral extended-release tablet formulation (60 mg to 240 mg)
  - Intramuscular injection (2.5 mg to 100 mg)
  - Intravenous injection

Side Effects – subcutaneous

- Possible dose-related blood pressure/heart-rate increase at 15-30 minutes
- Nausea, vomiting, dizziness, blurred vision, sleepiness

Side Effects – intramuscular

- Panic attacks, hallucinations, confusion, potentially unsafe movement, and bladder pain

Side Effects – oral form

- Dizziness and headache

(Ahuja et al., 2022; Dore et al., 2019; Glue et al., 2017; Glue, Medlicott, et al., 2020; Glue, Neehoff, et al., 2020; Glue et al., 2018; Tully et al., 2022; Yermus et al., 2023)

11

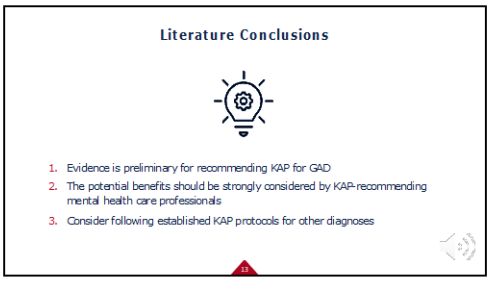
11

Gaps and Limitations of Literature

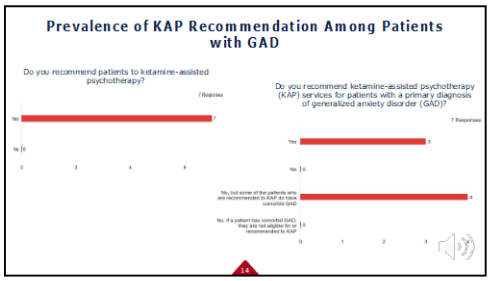
- Few studies considered KAP for GAD specifically
- No identification of psychotherapy protocols
- No randomized controlled trials or systematic reviews
- No comparison of KAP to non-KAP intervention
- No analysis of how continued medication or psychotherapy may have affected non-KAP ketamine administration outcomes
- No evidence-based recommendations for providing KAP for patients with GAD

12

12


Literature Conclusions
1. Evidence is preliminary for recommending KAP for GAD
2. The potential benefits should be strongly considered by KAP-recommending mental health care professionals
3. Consider following established KAP protocols for other diagnoses
13

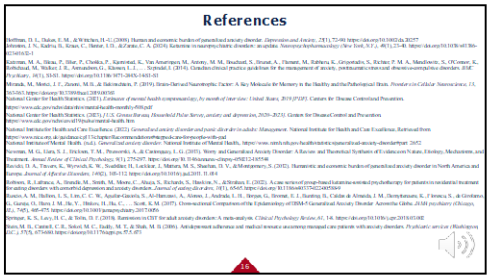
13


Prevalence of KAP Recommendation Among Patients with GAD
Do you recommend patients to ketamine-assisted psychotherapy?
7 Responses
Yes
No
Do you recommend ketamine-assisted psychotherapy (KAP) services for patients with a primary diagnosis of generalized anxiety disorder (GAD)?
7 Responses
Yes
No
No, but some of the patients who are recommended to KAP do have comorbid GAD
No, if a patient has comorbid GAD they are not eligible for or recommended to KAP
14

14


References
15

15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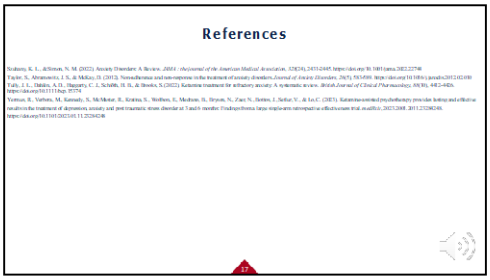
References
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17

APPENDIX F

PROJECT TIMELINE

Completion Date	Planning	Pre-implementation	Implementation	Evaluation
2/26/24	Confirm site-approval with TCA			
5/28/24	Confirm additional committee members for DNP project			
7/12/24	Submission of project proposal to DNP committee chair			
7/22/24	Submission of project proposal to DNP committee members			
8/1/24		Oral Proposal Defense		
8/14/24		Submission of IRB application		
8/16/24		IRB Approval		
9/9/24			Implementation of prevalence survey	Dissemination of prevalence survey
9/15/24			Completion of prevalence survey	Analysis of prevalence survey results
9/23/24			Implementation of Q.I. project at TCA	
10/4/24			Completion of Q.I. project at TCA	
10/14/24				Completion of data analysis
11/15/24				Final Defense

APPENDIX G

LITERATURE REVIEW GRID

Pub. Year; Author's Last Name	Title of Publication	Type of Study	Main Outcomes of Findings	Support for and or Link to Project
(Glue et al., 2017) Ketamine's dose-related effects on anxiety symptoms in patients with treatment refractory anxiety disorders	**Question**: Evaluate the effect of ascending single doses of ketamine on anxiety ratings in patients with treatment-resistant GAD or SAD **Design:** Uncontrolled, open label, exploratory study Ascending single dose study design (0.25, 0.5, 1 mg/kg administered subcutaneously in upper arm) at weekly intervals **Sample:** 12 patients with refractory generalized anxiety disorder and/or social anxiety disorder who were not currently depressed Mean age was 32 years (range 23–55), and duration of their anxiety disorders was 16.5 years (range 5–30). Ten subjects met the criteria for GAD (83%), and nine for SAD (75%) Participants taking antidepressants during the study with non-response to prior trials of antidepressants, group or individual psychotherapy (including CBT) **Setting/method:** monitored in the clinic for 2 h post-dose, with vital signs obtained predose, and 15, 30,	10 of 12 patients (83%) reported a >50% reduction in HAM-A and/or FQ scales after the 0.5 or 1 mg/kg doses Rapid onset of anxiolytic effects after ketamine dose; effects wore off over 3–7 days Duration of anxiolytic effects greatest at 1 mg/kg All subjects reported dissociative symptoms, starting approximately 5 min after each injection, with peak intensity around 20–30 min CADSS scores showed dose-dependent increases at 30 min and were returning towards baseline by 60 min After the 1 mg/kg dose, two subjects rated dissociation as very intense, feeling out of control. **Side effects:** Nausea – transient at 30 min post dose	Dose-dependent efficacy of anxiolytic effects of ketamine administered subcutaneously, effects last 3-7 days and have a rapid onset at administration Evidence that keta- mine improves symptoms of anxiety in patients with treatment refractory GAD and SAD who are not currently depressed, and is safe and well tolerated Peer-reviewed	No documentation of setting where ketamine was administered Only 12 participants Uncontrolled, open label exploratory study

Pub. Year; Author's Last Name	Title of Publication	Type of Study	Main Outcomes of Findings	Support for and or Link to Project
	45, 60, 90, and 120 min post-dosing **Data Collection:** Anxiety assessments: FQ, HAM-A Tolerability assessments: reported adverse events throughout, Clinician Administered Dissociative States Scale **Data Analysis:** Categorical variables reported with counts and percentages	Blood pressure increases (dose-related) – at 30 min Heart rate increases – at 15 minutes		
(Glue et al., 2018) Safety and efficacy of maintenance ketamine treatment in patients with treatment-refractory generalised anxiety and social anxiety disorders	**Question:** evaluate the effect on anxiety ratings, safety and tolerability of 3 months of weekly ketamine in 20 patients with treatment-refractory DSM IV GAD and/or SAD, and subsequent assessment of remission post-treatment **Design:** Uncontrolled, open-label study **Sample:** 20 patients who had been responders in an ascending dose ketamine study 15 patients (75%) met criteria for GAD and 18 (90%) for SAD	One hour after dosing, GQ and HAM-A ratings ratings decreased by ~50% Pre-dose HAMA ratings reached asymptote by 3.5 weeks Progressive decline in pre-dose FQ ratings, reaching asymptote by 7.5 weeks. **Side effects:** mean systolic and diastolic blood pressure increased by ~10 mm Hg at 30 min. The most common adverse events were nausea, dizziness and blurred vision	Benefit of maintenance treatment was seen with improvement in work and social functioning Patients remained on medication treatment and involved in psychotherapy GAD specifically studied in outpatient clinic Peer reviewed	No control identifying if patients participating in psychotherapy experienced greater benefit Small sample size

Pub. Year; Author's Last Name	Title of Publication	Type of Study	Main Outcomes of Findings	Support for and or Link to Project
	Remained on current medication regimens/continue psychotherapy **Setting:** University clinic **Methods:** One or two weekly ketamine doses of 1mg/kg injected subcutaneously for 3 months Participants free from anxiety for 5 days or longer were dosed once weekly Those with shorter duration of response could be dosed twice weekly **Data Collection:** Anxiety: FQ, HAM-A (pre-dose, 1 and 2 hr post-dose) Dissociation: CADSS (pre-dose, 30 and 60 min post-dose Tolerability: reported adverse events throughout study Functionality: Work and Social Adjustment Scale **Data Analysis:** summary statistics, categorical variables reported with counts/percentages, changes in pre-dose mood ratings evaluated through	post-dose dissociative symptoms tended to reduce after repeated dosing CADSS mean scores declined over time, from 20 points at week1 to 8.8 points at week 14 **Functionality Improvement:** *During maintenance treatment:* Patients reported marked improvements in functionality and in their personal lives Of the 20 patients, 18 reported improved social functioning (16/20) and/or work functioning (11/20) during maintenance treatment. 5 patients who were previously unemployed returned to paid employment 3 patients enrolled in tertiary education. Socially, patients reported reduced or minimal social avoidance (i.e. were able to attend parties, go on dates, speak up at meetings/presentations)		

Pub. Year; Author's Last Name	Title of Publication	Type of Study	Main Outcomes of Findings	Support for and or Link to Project
	exponential decay filled using non-linear regression	*After maintenance treatment:* 5 patients – remained well over 3 months of follow-up 8 patients – partial re-emergency anxiety symptoms 5 patients – full re-emergence within 2 weeks last ketamine dose		
(Hartland et al., 2023) A transdiagnostic systematic review and meta-analysis of ketamine's anxiolytic effects	**Question:** Examine the effect of ketamine on symptoms of anxiety at several time points, through synthesizing the findings of blinded, randomised, placebo-controlled trials (RCTs) **Design:** Systematic review and meta-analysis **Sample:** Adult human patients suffering from anxiety disorders of any type (including PTSD and OCD) or in whom anxiety symptoms were measured in the context of mood disorders, chronic pain or palliative care subanesthetic doses of racemic ketamine, S-ketamine or R-ketamine, administered via intravenous, intranasal, oral, subcutaneous, intramuscular or sublin- gual routes	Comparing the 24 h post-administration and 7-14 days post administration there was no significant correlation between peak level dissociation and improvement in anxiety symptoms Anxiolytic effect typically emerged after 3–4h post administration and continued to be significantly superior relative to placebo at 24 h and 7–14 days post-administration Results revealed a significant correlation between mean percentage improvements in depression and anxiety at both the subacute and sustained time points.	Meta-analysis conducted of ketamine's effects on anxiety symptoms across many disorders. Anxiolytic effects emerge rapidly at 3-4 h post-administration and persist for up to 2 weeks Peer reviewed	Exploratory analysis was based on pooled data from multiple studies, authors were unable to control for any covariant effects of mood changes on ketamine's anxiolytic effects. Most studies had high risk of bias; prevalence of unblinding in the included studies Moderate heterogeneity in the meta-analysis of data at the acute time point Meta-analyses consisted of findings from parallel arm and crossover studies – data limited to exclusively first phase of study possible introducing bias

Pub. Year; Author's Last Name	Title of Publication	Type of Study	Main Outcomes of Findings	Support for and or Link to Project
	14 RCTs were included in qualitative systematic review, 11 articles included in meta-analysis **Methods:** PRISMA guidance, studies screened and evaluated by 3 independent researchers, assessment bias done with Cochrane risk-of-bias assessment tool for randomized trials, each study was double rated by two different reviewers **Data Analysis:** Standard mean differences (SMDs) in anxiety scores between groups receiving ketamine versus placebo less than 12h post-administration (acute), 24 h post-administration (subacute) and 7–14 days post-administration (sustained). Data were pooled across studies to conduct exploratory analyses of the correlation between improvements in anxiety scores post-ketamine and (1) improvements in depression scores post- ketamine and (2) peak CADSS scores using linear regressions			

Pub. Year; Author's Last Name	Title of Publication	Type of Study	Main Outcomes of Findings	Support for and or Link to Project
(Glue, Medlicott, et al., 2020) Safety and efficacy of extended release ketamine tablets in patients with treatment- resistant depression and anxiety: open label pilot study	**Question:** Evaluate efficacy, safety, tolerability, pharmacokinetics of multiple doses of an extended release ketamine tablet formulation in patients with TRD/TRA **Design:** Multiple dose, open-label, flexible dose, uncontrolled study **Methods:** Twice daily dosing increased incrementally based on patient response vital signs, ECGs, safety laboratory tests pre-dose through to 96h post-dose, suicide (CSSRS), dissociation (CADSS), anxiety HAMA and FQ, depression MADRS Plasma ketamine/ norketmaine concentrations, BDNF concentrations up to 96 h post-dose **Sample:** 7 patients with TRD/TRA – all previously demonstrated mood improvement to subcutaneous ketamine, remained on established treatments **Data Collection:** Assessments included ratings of anxiety, depression and	Anxiety/depression ratings improved gradually over 96 hours All patients had > 50% improvements in mood ratings Serum BDNF concentrations did not change during study **Side effects:** dizziness, dissociation (onset 30 min and duration 2 hours during dose increase from 120 mg to 180 mg – none at higher doses), headache Decline in dissociation ratings after oral dosing may reflect relatively lower peak concentrations, which occur some hours after dosing No safety lab test/vital sign, ECG changes of note, no increase suicidal ideation. Extended-release oral formulation used in this study has slow dissolution across the physiological pH range and in ethanolic solution. Taken together with the fact that the tablet is very hard, and potentially difficult	All 7 participants failed to respond multiple prior medication/psychotherapy trials and extensive comorbidity All taking antidepressants Reductions in HAM-A and FQ scores at 48h after oral dosing in this study were comparable to changes 24 h after sub- cutaneous dosing showing that both methods have efficacy in reducing anxiety Support for using oral formulation and anxiolytic effects Peer reviewed	Small sample size No inclusion of psychotherapy or accounting for therapy engagement during study All doses administered within 72 hours, twice daily dosing during the study

Pub. Year; Author's Last Name	Title of Publication	Type of Study	Main Outcomes of Findings	Support for and or Link to Project
	dissociation, safety and tolerability, and blood samples for ketamine pharmacokinetics and BDNF concentrations. **Data Analysis:** Summary statistics were determined for safety laboratory test data, ECG, and ketamine, norketamine, and BDNF concentration data Categorical variables were analyzed using counts and percentage	to crush, this could limit abuse potential.		
(Glue, Neehoff, et al., 2020) Effects of ketamine in patients with treatment-refractory generalized anxiety and social anxiety disorders: Exploratory double-blind psychoactive-controlled replication study	**Question:** Replication of earlier report (Glue et al., 2017) on ketamine's anxiolytic effects in patients with TR-GAD and SAD **Design:** double-blind, psychoactive controlled ascending dose study **Sample:** 12 patients TRA and/or SAD not currently depressed, failed response to at least two antidepressants and psychotherapy Hamilton Anxiety Scale score of ⩾20; Liebowitz Social Anxiety Scale score of ⩾ 60 at screening; Montgomery-Asberg Depression Rating Scale	Improvements in anxiety ratings occurred within an hour of ketamine dosing, and persisted for up to 1 week. 8/12 pts reported >50% reduction HAM-A and FQ after 0.5 and/or 1 mg/kg doses Dose-response profile was noted for anxiolytic effects, dissociative side effects, and changes in blood pressure and heart rate after ketamine dosing Ketamine dosing: 0.25 mg/kg appears to be a threshold dose, and 1 mg/kg has the greatest and most durable anxiolytic effects Midazolam had minor brief effects on anxiety ratings	10 subjects met GAD criteria and all 12 met SAD criteria, two had panic DO All participants were taking antidepressants, 9 had prior MDD but not currently depressed Double-blind with psychoactive control Peer reviewed	Participants remained with psychotherapy, however, the impact of this was not accounted for in results Small sample size

Pub. Year; Author's Last Name	Title of Publication	Type of Study	Main Outcomes of Findings	Support for and or Link to Project
	scores of ⩾20 at screening were excluded Remained on on-going medications/psychotherapy, however, no new treatments started during ketamine treatment **Method:** Ascending doses of ketamine (0.25, 0.5, 1 mg/kg) were administered at weekly intervals, and midazolam 0.01 mg/kg, the control, was randomly inserted into the ketamine dose sequence Weekly, subcutaneous administration **Data Collection:** Ratings of anxiety and dissociation, safety and tolerability, and blood samples for ketamine pharmacokinetics and BDNF concentrations. Anxiety assessments: FQ, HAM-A; Tolerability: AE throughout the study, CADSS (dissociative) **Data Analysis:** Summary statistics and categorical variables	Serum BDNF concentrations declined over time and were similar for all treatments. **Side effects:** Dissociation, blurred vision, sleepiness, nausea, vomiting, most common after 0.5-1 mg/kg dose, dose related increases in blood pressure at 30 min, slight tachycardia at 1 mg/kg dose at 30 min All subjects reported dissociative symptoms, approx. 5 min after each injection with peak intensity 20-30 min Peak ketamine concentrations 15 min post injection (1st sampling point) and then decline; norketamine concentration increased out to 120 min No changes in serum BDNF with ketamine		
(Ahuja et al., 2022) Real-world depression, anxiety and safety outcomes of intramuscular ketamine	**Question:** Describe the clinical characteristics, treatment patterns, clinical outcomes and AEs of outpatients who received	Patients had mean 2.8 psychiatric diagnoses 93% MDD, 54% GAD, 28% PTSD	An acute phase of up to 6 treatments within the span of 1 month, with some patients then receiving less frequent maintenance treatments during the subsequent	No control group, open-label treatment Minimally diverse study population Some missing data

Pub. Year; Author's Last Name	Title of Publication	Type of Study	Main Outcomes of Findings	Support for and or Link to Project
treatment: a retrospective descriptive cohort study	psychiatric IM ketamine treatment. **Design:** Retrospective descriptive cohort study analysis **Sample:** 452 patients with any psychiatric diagnosis; 18 years and older **Setting:** private outpatient psychiatric clinic network in the United States **Methods:** psychiatrist/PA initially recommended/prescribed ketamine and ongoing treatment planning post administration, received ketamine treatment by IM administration only; vitals (BP, pulse), direct observation for at least 60 min by prescribing clinician and medical assistant Ketamine administered while patient was laying in reclining chair in quiet room with dim lights while wearing eye shades and listening to music (relaxing/non-lyrical) through headphones	Baseline pts taking median of 2 psychiatric medications other than ketamine, 78% taking at least one psychiatric medication, most commonly antidepressants Median of 4 IM treatments Significant reductions depression/anxiety scores from baseline to last treatment Additional treatments correlated with larger decrease in depression, SI, and anxiety symptom severity Median PHQ-9 improved 38%, median anxiety scores GAD-7 improved 50% Maintenance ketamine treatments average improvements maintained for over 7 months **Side effects:** occurred during 2.3% of the treatments; Including nausea, vomiting, abnormal vital signs, panic attacks, hallucinations, confusion, potentially unsafe movement, and bladder pain	months or years as determined on a case-by-case basis 452 participants Peer reviewed	No accounting for possible impact of interaction with ketamine administering providers

Pub. Year; Author's Last Name	Title of Publication	Type of Study	Main Outcomes of Findings	Support for and or Link to Project
	Data Collection: Chart review through reports and manual chart review; PHQ-9 and GAD-7 before each session Primary outcomes: changes in cohort's median PHQ-9 and GAD-7 scores from patients' first to last ketamine treatment **Data Analysis:** Descriptive statistics, some missing data (historical questionnaires and some PHQ-9/GAD-7 prior to treatments)	Side effects resolved prior to patients leaving clinic 3 patients had panic attacks 4 of the treatments, 2/3 had history panic attacks		
(Tully et al., 2022) Ketamine treatment for refractory anxiety: A systematic review	**Question:** Systematically examine the restricted number of clinical trials and a case study which show early signs that ketamine is an effective treatment solution for refractory anxiety **Design:** Systematic review **Sample:** Articles were written in English, original studies, human participants, diagnosis of refractory anxiety with or without TRD, excluded OCD and PTSD 18 clinical trials RCTs or a case study, 10 were with	Dissociative symptoms in all cases peak at 30 minutes post-infusion and return to normal 60 minutes post-infusion No data suggest dissociative sensations last longer than 60 minutes Minimizing abuse potential achieved through density of oral tablet form of ketamine inhibiting ability to use it as an intranasal substance. Delivery as oral substrate (dissolved in syrup or injection) reduced potential for abuse.	Most studies used the clinician-administered dissociative state scale (CADSS) Anxiolytic effects are temporary with symptoms returning to baseline after about 2 weeks 513 participants 10 studies with patients with cooccurring treatment resistant depression Peer reviewed	Exclusion of OCD/PTSD diagnoses in the studies included in the systemic reviews No accounting for impact of participants involvement with clinician's part of the studies and the impact this relationship may have on the participants' responses

Pub. Year; Author's Last Name	Title of Publication	Type of Study	Main Outcomes of Findings	Support for and or Link to Project
	TRD and 8 without TRD, total participants 513 8 articles subQ, 8 intravenous, 2 oral dose **Methods:** Data extracted independently by two reviewers, third resolved disputes risk of bias: ROBINS-I tool used and completed by two authors independently **Data Collection:** Included the study design, number patients per trial, type refractory anxiety and depression diagnosis, assessment measurements, ketamine and placebo dosing type and regimen, follow-up period, findings/conclusions **Data Analysis:** Descriptive statistical analysis	Higher doses of ketamine (1 mg/kg weekly) → Greater effects on anxiety across studies, some effects last for a week post-dose Ketamine more potent at reducing anxiety self-report measures than midazolam, lithium, valproate and psychiatric treatment alone		
(Dore et al., 2019) Ketamine Assisted Psychotherapy (KAP): Patient Demographics, Clinical Data and Outcomes in Three Large Practices Administering Ketamine with Psychotherapy	**Question:** Results of three distinct KAP practices, each having matured in consecutive time frames. **Design:** Descriptive **Sample:** 235 patients from 3 private general psychiatric practices in northern California, and Austin, Texas	**Common side effects:** nausea, vomiting, agitation which rarely led to discontinuation of treatment Clinically significant improvements in depression/anxiety in BDI and HAM-A, pts with	Describes outcomes at the three different practices and how this was integrated with psychotherapy Describes trance state vs transformational state Patients were taking on average 2.84 medications	Descriptive study

Pub. Year; Author's Last Name	Title of Publication	Type of Study	Main Outcomes of Findings	Support for and or Link to Project
	Diagnoses of patients in study: MDD, cPTSD, ADHD, PTSD, GAD, other anxiety DO, other mood DO, SUD, OCD **Method:** Average dose SL 200-250 mg and 80-90 mg for IM route; SL dose initiated in clinic then titrated at home to maintain access to trance state; IM dose only administered in clinic **Setting:** 3 private general psychiatric practices, northern California **Data Collection:** Before KAP treatment the following measures used for self-report: Beck Depression Inventory (BDI), HAM-A, PHQ-9, Childhood Resilience Scale (CRS), and Adverse Childhood Event Score (ACE) Follow-up self-report measures from the last available office visit included BDI, HAM-A, PHQ-9, and Levine Depression Scale Ratings	developmental trauma had greatest improvement Patients who have more severe symptoms, including current suicidality, high BDI at intake, and higher ACE score, tend to show the most significant benefit Longer duration of treatment showed greater improvements in depression/anxiety Patient self-reported measures correlated with clinician rater views on visit and termination forms indicating internal consistency between clinician report and patient self-report, p values $p < 0.0001$ Those with rigid personality structures, such as those with severe OCD or personality disorders and perhaps severe PTSD, find entering the trance state difficult and are not able to sustain the benefits they experience during the actual sessions, even if they do indeed experience some relief	(antidepressants, stimulants, mood stabilizers, antipsychotics, sedatives/anxiolytics, other medications) 235 patients included in study Outpatient ketamine administration Description of ketamine protocol: Frequent sessions in the first stage of ketamine's application for depression and TRD (most commonly six sessions in two weeks, which may be repeated until remission is achieved); ketamine administration is done within a psychotherapeutic framework for both in-office sessions and home use Peer reviewed	

Pub. Year; Author's Last Name	Title of Publication	Type of Study	Main Outcomes of Findings	Support for and or Link to Project
	Measures used for rater view of patient response: Change of State, Mystical Experience Questionnaire (MEQ), and Ego Dissolution Index (EDI) (Nour et al. 2016) were used to assess KAP sessions **Data Analysis:** Statistical tests (correlations and moderation analyses)			
(Yermus et al., 2023) Ketamine-assisted psychotherapy provides lasting and effective results in the treatment of depression, anxiety and post traumatic stress disorder at 3 and 6 months: Findings from a large single-arm retrospective effectiveness trial	**Question:** What are the lasting effects of Ketamine-Assisted Psychotherapy on psychological distress? Examine the treatment effects of KAP on anxiety, depression, and PTSD at 1, 3, and 6 months post treatment. **Design:** Retrospective single-arm effectiveness trial **Sample:** 1806 adults with documented history of depression or anxiety that showed lack of adequate response to previous treatment(s) or presented with PTSD **Method:** 4-6 guided ketamine sessions (administered via IM injection or SL lozenge) with psychotherapy-only visits after doses 1 and 2 and then	Large treatment effects at 3 months and sustained at 6 months Sustained reductions in anxiety, depression, PTSD, with symptom improvement lasting well beyond duration of dosing sessions, effects extended as much as 5 months after last KAP session Frequency of missing assessments had a tendency to be negatively correlated with baseline scores on the PHQ Reduction on the GAD-7 at 1 month, d=0.47, which was amplified at 3 months, d=0.86, and remained detectable at 6 months, d=0.73	Includes detailed methods of inclusion/exclusion of participants **Includes dosing information:** Initial dosing via intramuscular injection was of 25-35mg with the option to titrate to 50-70mg at visit 2 and up to 100mg for subsequent visits. The initial dose for lozenges was 200mg with the option to increase by 50-100mg per visit up to 500mg Includes information about set and setting of the KAP Treatment effects demonstrated here are based on those who provided follow-up data. These individuals tended to have more pretreatment distress	Not peer reviewed Poor response rate for follow-up assessments, 18% baseline participants provided 3-month assessment and 5% provided 6-month assessment Lack randomized control group

Pub. Year; Author's Last Name	Title of Publication	Type of Study	Main Outcomes of Findings	Support for and or Link to Project
	after every 2 subsequent doses **Setting:** 11 Field Trip Health clinics in North America **Data Collection:** self-reported outcomes, PHQ-9, GAD-7, PCL-6 **Data Analysis:** Descriptive statistics for the sample and analyze the extent of loss to follow-up; effect size defined by Cohen's d secondary analyses on the effect of doses administered, controlling for age, gender, and site differences. Sensitivity analysis: Expectation- Maximization (EM) and Markov Chain Monte Carlo (MCMC) algorithms to multiply impute missing follow- up data.	Per administered ketamine dose, there was a reduction of 1.2 points on the PHQ-9 and approximately 1 point reductions on the GAD-7 and PCL-6	and may be considered a clinical priority.	
(Robison et al., 2022) A case series of group-based ketamine-assisted psychotherapy for patients in residential treatment for eating disorders with comorbid depression and anxiety disorders	**Question:** Explore depression and anxiety outcomes, safety, and patient satisfaction of group-based KAP (G-KAP) among participants in residential intensive treatment for an ED **Design:** Prospective case series study **Sample:** 5 participants; diagnosis ED with comorbid mood/anxiety disorders,	4 participants showed clinically significant improvement in depression symptoms, while 2 participants showed clinically significant improvement in anxiety symptoms from pre-dose to 24-h follow-up after the fourth ketamine dosing session	IM administered ketamine-assisted-psychotherapy intervention Describes set and setting: Group treatment room included reclining sofas and eyeshades, headphones, and music Individual check-in and support were provided as needed throughout the dosing session. Brief processing	Patients were receiving intensive treatment in residential center and there was no placebo control group, limiting ability to interpret impact of KAP intervention Not adequately powered or structured to determine duration of antidepressant and anxiolytic benefits

Pub. Year; Author's Last Name	Title of Publication	Type of Study	Main Outcomes of Findings	Support for and or Link to Project
	secondary diagnoses MDD with GAD or PTSD, multiple medications (antidepressants SSRIs, SNRIs, second generation antipsychotics, benzos, anxiolytic) **Setting:** Residential treatment center **Methods:** KAP intervention of IM ketamine: groups of four, once a week on Monday mornings over a 4-week period. Staff present were the medical director, and two staff nurses **Data Collection:** GAD-7 and PHQ-9 pre-dose, 4-h post-dose, 24-h post dose **Data Analysis:** Descriptive statistics were used to present and estimate individual change in pre-dose and post-dose PHQ-9 and GAD-7 scores across the study period	Well-tolerated, no serious adverse events reported	took place a group after approximately 90 min post-dosing Described dosing for IM injection Peer reviewed	

APPENDIX H

EXECUTIVE SUMMARY

A Quality Improvement Initiative to Increase Mental Health Care Provider's Knowledge of Ketamine-Assisted Psychotherapy for Generalized Anxiety Disorder

This quality improvement project was designed to educate mental health care professionals (MHCPs) regarding the literature-informed efficacy of utilizing ketamine-assisted psychotherapy (KAP) as a treatment modality for patients with a diagnosis of generalized anxiety disorder (GAD) that has been unresponsive to prior treatments.

Background and Rationale

Generalized anxiety disorder is highly prevalent and significantly functionally impairing; however, first-line treatment recommendations often result in inadequate symptomatic reduction. Ketamine-assisted psychotherapy has been successfully used in outpatient settings to treat disorders such as major depressive disorder and post-traumatic stress disorder, which are frequently comorbid with GAD. An outpatient mental health clinic in southern Arizona providing KAP services to patients with MDD and PTSD has found that GAD is often co-occurring in their patient population and identified a need to understand the efficacy of recommending KAP for patients with a primary diagnosis of GAD that has been unresponsive to prior treatments.

Key Conclusions from Literature Synthesis

- Administration of ketamine (intramuscularly, subcutaneously, and orally) among patients with anxiety has been documented as safe in the outpatient setting.
- Ketamine administered in an outpatient setting among patients with anxiety has rapid anxiolytic effects enhancing their functionality, and studies with an additional psychotherapy component to the study intervention show sustained reduction in symptoms for as many as 5 months after the last KAP session.
- Patients with more severe symptoms of depression and anxiety, higher Adverse Childhood Event scores, and current suicidality may benefit more from KAP.
- Evidence should be considered as preliminary for recommending KAP for GAD due to the gaps and limitations among the literature findings. However, given the potential benefits of KAP for GAD, this treatment modality should still be considered by MHCPs given the difficulties experienced by MHCPs treating patients with GAD non-responsive to first-line treatment recommendations.

Key Project Objectives and Findings

- *Objective: Measure the prevalence of mental health care professionals recommending and providing KAP among patients with GAD.*
    - **Key Finding:** Three of seven prevalence survey participants reported recommending KAP to patients with a primary diagnosis of GAD. Four of seven participants reported not recommending KAP specifically for GAD, though many of their clients present with a comorbid diagnosis of GAD.

- *Objective: Implement an educational presentation for mental health care professionals to increase knowledge and awareness of the current literature-informed efficacy of KAP for patients with GAD.*
    - **Key Finding:** Although not statistically significant, all four educational intervention participants experienced increased knowledge of the literature-informed efficacy of KAP for GAD, and all participants reported believing that there is literature-informed efficacy supporting KAP for GAD.
- *Objectives: Evaluate the mental health care professionals' pre- and post-intervention attitude towards and intention of recommending KAP for patients with GAD; Assess mental health care professionals' intentions to recommend KAP for GAD within their mental health practices*
    - **Key Finding:** Post-intervention results indicated an overall increase in positive attitudes towards recommending KAP, perceived behavioral control of recommending KAP for GAD, more positive perception of peer approval of recommendation of KAP for GAD, and stronger intention to recommend KAP to patients with GAD.
    - **Key Finding:** Barriers to recommending KAP for patients with GAD include: Among both patients and MHCPs, there is limited awareness and education of KAP's potential benefits in GAD; the lack of regulatory approval of KAP for GAD; and patients are hesitant to engage in KAP which may be attributed to both negative press coverage resulting in misconceptions or fears regarding KAP and the perceived focus on KAP benefits for MDD and PTSD, but not GAD.

Discussion

- An asynchronous online presentation may be an effective way to educate MHCPs on the literature-informed efficacy of KAP for GAD.
- This project lacks generalizable results likely related to the following project limitations, including small sample size, possibly due to this intervention's voluntary and asynchronous nature, and the lack of collection of participant demographic data.

Implications for Practice

- Future implementations of similar educational interventions may benefit from survey inclusion of demographic data, in-person intervention dissemination, and participant input on future educational topic inclusions.
- Future research recommendations include the efficacy of KAP for patients with a primary diagnosis of GAD and documentation of the longer-term effects of adding psychotherapy to ketamine administration in an outpatient clinic setting.
- Clinical policy recommendations:
    - Increased alignment with federal drug administration regulations and standardization of protocols for ketamine administration and patient monitoring in the outpatient setting.
    - Ketamine-assisted psychotherapy for GAD guideline development.

Conclusion

This quality improvement project demonstrated the effectiveness of an asynchronous educational intervention's ability to increase both participant knowledge of and intention to recommend KAP for GAD. However, further MHCP education on the efficacy of KAP for GAD may be further supported by increased research on KAP as a treatment modality for GAD and policy development supporting the standardization of KAP for GAD implementation.

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