Sustaining Depression Remission:

Integrating Mindfulness-Based Modalities and Ketamine Infusion Therapy

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Abstract

Major depressive disorder contributes to a growing disease burden globally, with limiting or inadequate treatment options available to patients and healthcare providers. Traditional medications to treat the disorder demonstrate modest efficacy while best outcomes are seen when psychotherapy is implemented adjunctively. Barriers to delivering optimal treatment can lead to relapse, diminished psychosocial functioning, and suicide, a leading cause of death in the United States. The purpose of this paper is to examine the rapid antidepressant effects of ketamine combined with nurse-delivered mindfulness-based cognitive therapy to help reduce depression severity and support remission. Research differentiating ketamine's mechanism of action from traditional anti-depressants and the efficacy of mindfulness-based interventions to reduce depression, have led this evidence-based project integrating these modalities.

Keywords: major depressive disorder, ketamine, mindfulness-based, remission, mind-body interventions, yoga

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Untreated depression can lead to a lifetime of despair, comorbid illness and even death. Falling within a spectrum of mood disorders, major depressive disorder (MDD) is characterized by reported feelings of sadness, emptiness and hopelessness, accompanied by a loss of interest or pleasure in daily activities. These and other symptoms, ultimately lead to a significant impairment in social and occupational functioning with a high risk of suicide (American Psychiatric Association [APA], 2013). Current data from The National Epidemiological Survey on Alcohol and Related Conditions (NESARC) reported a lifetime prevalence of major depression at 13.2% in the United States, while World Mental Health (WMH) surveys report a 12.85% lifetime prevalence in 18 countries globally (Sadock, Sadock & Ruiz, 2017). With a treatment goal of achieving remission and improvement in function, current first-line anti-depressant agents achieve only a 30-40% response rate taking up to 6-8 weeks for therapeutic effect. This has inspired a growing body of research to support the rapid and sustainable effects of ketamine combined with mindfulness-based therapy in the treatment of major and treatment resistant depression.

Problem Statement

In the year 2020, MDD has been estimated as the second largest cause of disability contributing to enormous public health cost and morbidity. In the United States alone, 17.7 million adults age 18 years and older had witnessed at least one major depressive episode (MDE) in 2018, with 11.5 million experiencing severe impairment in various life domains (Substance Abuse and Mental Health Services Administration [SAMHSA], 2019).

The strong correlation between MDD and suicide adds to the urgency to search for more effective treatment pathways in supporting patients, families and communities along this debilitating disorder. In 2017 over 47,000 people died by suicide in the United States alone (Centers for Disease Control and Prevention [CDC], 2018, as cited in SAMSHA, 2019). This global cry for help places the responsibility on each of us to recognize the signs and symptoms of depression and to pursue innovative evidence-based modalities to better treat the disorder and help sustain remission.

Purpose and Rationale

Nurses, social workers, primary care physicians, therapists and mental health providers all play a powerful role in identifying both acute and progressive signs of depression. The question soon becomes, how do we move forward with treatment planning at various stages of illness to best mitigate worst case outcomes and improve quality of life. Assisting patients through multi-disciplinary approaches in healing can involve a combination of psychopharmacology, therapy, nutrition and complementary and alternative medicine (CAM) all of which have been demonstrated to support symptomology. While a combination of these modalities can be supportive in episodic and some chronic conditions of depression, ketamine infusion therapy alone is demonstrating strong evidence in mitigating suicidality and treatment resistant depression after a single treatment.

The purpose of this paper will be to summarize current literature that demonstrates the efficacy of ketamine infusion therapy in the treatment of depression and suicidality, and to support the use of mindfulness-based interventions (MBIs) grounded in psychotherapy as an adjunctive approach to treatment.

Background/Significance

The escalating burden of disease secondary to depression comes at a high cost. Decreased quality of life and the high risk of suicide is impacting over 300 million people globally with an estimated 200-billion-dollar financial burden in the United States alone (Bratsos & Saleh, 2019). MDD has been directly associated with accelerated cellular aging and contributes to a decline in neuroplasticity, cognition, somatic health and a mortality risk of 60-80% globally (Tolahunase et al., 2018). The limitations surrounding current first-line antidepressants such as selective serotonin reuptake inhibitors (SSRIs) has demonstrated that delayed onset of action and failed response rates contributes to this burden. As an alternative approach, a growing body of research is targeting the brain's glutamate system where depression may actually have its origins.

Patient Receiving Ketamine for Depression

Ketamine was approved by the U.S. Food and Drug Administration in 1970 for use as an anesthetic medication typically utilized in operating room procedures. Its affinity for blocking excitatory glutamate receptors in the brain, contributes to its mechanism of action that imparts its calming and dissociative effects (Grunebaum, 2018). The antidepressant effects of ketamine are believed to be achieved through the antagonism of N-methyl-D-aspartate (NMDA) receptors which then increase glutamate transmission at α-amino-3-hydroxy-5-4-isoxazole propionic acid (AMPA) receptors. When this happens, an increase of hippocampal brain-derived neurotropic factor (BDNF) is made available and produces an antidepressant response (Bratsos & Saleh, 2019). Current literature is now demonstrating ketamine's ability to deliver antidepressant qualities within hours of a subanesthetic dose via intravenous infusion or intranasal spray. This rapid relief of symptoms can provide an acute treatment alternative in emergency departments helping to avoid lengthy admissions and non-therapeutic patient experiences. Ketamine infusion

therapy can also serve as a safe and effective intervention in the outpatient setting supporting patients with other chronic major depressive disorders leading to a decline in function or death.

Domany, Shelton & McCullumsmith, (2019) recently conducted a randomized clinical trial in the emergency department setting for patients meeting criteria with major depression, bipolar depression, depression NOS (not otherwise specified), or dysthymia and identified with clinically significant suicidal ideation. Short-term remission from suicidal ideation in this study was noted at 88% in the ketamine group, compared to 33% in a group receiving only saline, after 90 minutes following the infusion. While this study demonstrated the rapid effects of subanesthetic ketamine for suicidality, it did not appreciate a reduction in overall depressive symptoms long-term. This may be secondary to the study's episodic nature.

Longer-term remission rates were examined in another randomized control trial (RCT) that tested ketamine at varying single doses of 1.0mg/kg, 0.5mg/kg and 0.1mg/kg. Salloum et al., (2020) did identify a correlation with stronger remission rates at the higher doses after 3 days. Of all the patients in the study, only 53% sustained remission at 7 days, 26% at 14 days and 21% at 30 days. Singh et al., (2016) studied the sustainability of depression remission over a 15-day period after 0.5mg/kg ketamine infusions vs. placebo in twice and thrice-weekly dosing groups. A similar reduction in depression scores was noted in each of dosing group vs. placebo. While these studies continue to support short-term efficacy, they lack the inclusion of adjunctive interventions to help sustain ketamine's supportive effects.

Mindfulness-based Cognitive Therapies

Yoga, meditation and mindfulness are scientific mind-body interventions supporting wellbeing and disease management. Current research is demonstrating that mindfulness-based interventions rooted in Eastern philosophy and practice, are leading to evidence-based treatments

for psychiatric disorders including depression. Tolahunase et al., (2018) noted that consistent yoga and mindfulness practitioners demonstrated a reduction in age-related gray matter decline, which is correlated with neuroplasticity secondary to increased BDNF production. The central nervous system's ability to adapt and reorganize in response to external and internal stimuli is the biological manifestation of neuroplasticity. The hippocampus and other central nervous system regions become highly vulnerable to plasticity and neurodegeneration as a result of MDD, suggesting they are equally susceptible to positive intervention (Tolahunase et al., 2018). One of the key biomarkers of neuroplasticity is BDNF and is implicated in the positive pharmacodynamic effects of ketamine on depression. Tolahunase et al., (2018) demonstrated a significant increase in BDNF in a study comparing participants engaging in a yoga and meditation-based lifestyle intervention (YMLI) to a control group.

The psychological flexibility cultivated through mindfulness is the goal of the emerging evidenced-based modality Acceptance and Commitment Therapy (ACT), empirically shown to treat a number of psychiatric illnesses including depression. ACT increases psychological flexibility through deepening awareness in six interrelated processes including; *acceptance, contact with the present moment, self as context, cognitive diffusion, committed action and personal values* (Bai et al., 2020). A recent systematic review and meta-analysis demonstrated that ACT significantly reduced depressive symptoms in adults with mild depression at 3-month follow-ups compared to TAU (Bai et al., 2020). While this study was unable to demonstrate a reduction in severe depression symptomology on its own, ACT can provide effective coping tools to manage depression over time. The process helps patients change their relationship with their thoughts and somatic experiences through mindfulness exercises, helping them align with more closely with personal values and important aspects of life (Bai et al., 2020).

Integrating this type of psychotherapeutic based intervention as adjunctive support with current ketamine treatment-as-usual practice, aligns more closely with evidence-based recommendations for MDD that integrate both medication management and nurse facilitated therapeutic modalities.

Treatment as Usual

Current clinical standards for receiving ketamine infusion in the treatment of MDD, include a weight-based subanesthetic dose of ketamine up to 0.5mg/kg delivered over a 40-minute infusion. Treatment is typically provided twice a week for 4-5 weeks. Vital signs, level of consciousness, symptoms of toxicity, and dissociative effects are monitored. Patient education is provided to both caregivers and patients. Caregivers providing transportation are arranged post-treatment and an emergency response system is established (American Psychiatric Nurses Association, 2019). This process typically does not currently include the integration of a MBI or other psychotherapeutic modalities.

Desired Outcomes

In a RCT, Hamidian et al., (2016) found that severity of depression and the ability to regulate emotion, improved significantly in patients with chronic depression after combined mindfulness-based interventions and pharmacotherapy. This study identified mindfulness-based skills as a viable modality that may be integrated with pharmacotherapeutic agents such as ketamine, in the treatment of MDD where emotional regulation has a central role. Developing and teaching skills that extend the positive effects of ketamine infusion beyond the clinical environment is a targeted goal of this work.

This discussion has identified ketamine infusion therapy as a safe and effective pharmacological treatment for MDD. Its ability to generate a significant biological effect upon

the brain's glutamate system has been shown to quickly relieve depressive and suicidal symptomology in controlled clinical settings. To extend the benefits of ketamine's effect on glutamate and BDNF, MBIs have been shown to support neuroplasticity, BDNF production and reduction of depression. Sustaining MDD symptomology and remission through the integration of MBI with ketamine infusion therapy, may help to inspire a significant practice change within this paradigm.

Internal Evidence

While no hard data has currently been made available, a community-based ketamine infusion clinic in Southern California, has identified a need to examine interventions that would support remission rates, improve patient experience and outcomes. The short-term clinical efficacy of ketamine to help mitigate symptoms of suicidality and MDD have been appreciated in this establishment through treatment as usual practices. The clinic's medical director, a board-certified emergency medicine physician. He is an advocate for integrative medicine and recognizes an opportunity to implement an innovative evidence-based approach within this practice.

PICOT

This inquiry has led to the clinically relevant PICOT question, "In patients receiving ketamine infusion therapy for depression (P), how does the integration of mindfulness-based therapy (I), support disorder severity and remission (O), compared to treatment as usual (C)."

Search Strategies

A thorough literature review was conducted to support relevant components of the PICOT question. The two significant paradigms of medicine and mindfulness led to initial searches utilizing academic databases PsycINFO, PubMed and CINAHL. These databases were selected for their robust contributions in the areas psychiatry, medicine and nursing where the integration of these disciplines aligns with this project. Additionally, a grey literature search included government agencies of the CDC, SAMHSA and WHO, providing supporting data related to current MDD prevalence and ketamine protocols.

The initial search included key terms *ketamine, depression* and *cognitive therapy* and yielded 65 results utilizing PsycINFO. This was then narrowed by limiting the search to articles published in the last five years with a return of 47 results. A review of article titles and their abstracts was conducted to exclude literature that may have fallen out of the scope of this project. A secondary search conducted through PubMED included the key terms *meditation, depression,* and *randomized clinical trial* to support high-level literature. This search yielded 235 articles and was then limited to publication dates within the last five years, returning 99 articles. A review of this work was then reduced by exclusion criteria where depression was secondary to another comorbid illness. An additional search within PubMED was conducted to help support a revision of the intervention for this project which included key terms *guided meditation* or *yoga* and *major depression* and *remission,* yielding 11 articles for review. A final search in CINAHL included key terms *mindfulness, depression* and *RCT,* resulting in a yield of 45 articles. After narrowing this search to the last five years, 34 articles were maintained for review. Inclusion criteria was narrowed to articles where mindfulness effected MDD.

The narrowed results from the three databases led to 22 final articles that were critically appraised with priority given to high-level studies. The reference lists of these articles were reviewed for further relevant literature and led to the inclusion of an additional randomized clinical trial (RCT). This process resulted in 10 final studies including six RCTs, two meta-analysis (MA), and a systematic review (SR) supporting the efficacy of ketamine infusion and mindfulness for MDD. Studies included in the review appropriately related to the PICOT constructs supporting the use of ketamine, yoga, and MBI in treating MDD (see Appendix A, Table 1).

Critical Appraisal and Synthesis

The final 10 chosen studies were of high-quality reporting level of significance (*P*), effect size (ES), confidence interval (CI) standard deviations (SD) and included Hedges *g* measuring effect sizes (see Appendix A, Table 1). Across all studies, a clinical diagnosis of MDD was identified as inclusion criteria for all independent variables. Studies were heterogeneous in their country of origin and interventions were largely delivered in outpatient settings in the English language. Collectively, participants ranged from 18-75 years old, were largely balanced in gender, adding to the generalizability of findings. Of the 7 RCTs, participants were blinded in 6 studies and double-blinded in 2. A low incidence of bias was noted across a majority of the RCTs. Data findings within the MAs and SR were largely homogeneous but carried a risk of bias, secondary to limited allocation concealment or self-reporting measures. This indicated an awareness for this project to address in its study design helping to increase validity.

Primary outcomes in all studies demonstrated the reduction of depression severity utilizing similar clinically recognized self-reporting measures (see Appendix A, Table 2). Conceptual framework among MBI studies were heavily based in Mindfulness and Cognitive

Behavioral Theoretical models. A common weakness among RCTs and within MA studies, were noted small sample sizes. Finally, an increase in mindfulness was seen in 3 of 6 MBI studies with depression remission noted in 5 of the overall collection (see Appendix A, Table 2).

The evidence suggests that independently, both ketamine infusion therapy and MBIs are safe and effective resources to help reduce the severity of depressive symptoms in patients with MDD. While remission of depression had been witnessed in a number of studies, it did not extend beyond 7 days in ketamine trials, despite its rapid relief of symptomology. However, remission appears to be more sustainable in MBIs studies, with additional evidence demonstrating long-term efficacy in yoga-based modalities. This identifies a community-based, outpatient opportunity to integrate MBIs with ketamine infusion services to help extend remission. The behavioral and physiological effects that have been appreciated in the evidence may provide long-term recovery, decreased disease burden and overall well-being to patients and communities impacted by MDD.

Theoretical Application

The Theory of Self-Transcendence developed by Dr. Pamela G. Reed, provides the framework for this project. It's core purpose is to inspire inquiry and practices promoting well-being in the face of life-limiting illness or difficult life situations (Smith & Liehr, 2014). Largely developed during Reed's work in psychiatric-mental health care, she recognized that well-being and mental health arose from an understanding of a patient's developmental process. Empirical evidence has demonstrated that developmental change continues beyond childhood and across the lifespan. This may be attributed to the pandimensionality of humans and the inherent potential for healing and wellness (Smith & Liehr, 2014).

The chronic complexities faced by patients with MDD, do in fact progress across the lifespan contributing to developmental changes that impact overall quality of life and raise fear for the future. The concepts of the self-transcendence theory assume that humans are integral and coextensive with their environment, and able to expand awareness beyond temporal and physical confines (Smith & Liehr, 2014). This develops through practices that deepen one's connection to the self, others, or higher spiritual awareness as with meditation and other MBIs. The second assumption of the theory states that self-transcendence is a developmental imperative, and a resource that must be expressed through participation ultimately leading to well-being. This is where nursing plays a role in helping to facilitate this participation through evidence-based modalities that expand the patient's boundaries and mediate the relationship between well-being and vulnerability. A model of this theory demonstrates the relationships between these concepts as shown in Appendix B, Figure 1.

Research has shown that interpersonal, intrapersonal and transpersonal strategies grounded in self-transcendence, are effective in promoting well-being while reducing negative outcomes in practice settings. These strategies may include nurse-facilitated meditation, visualization, self-reflection or prayer that helps to connect the patient with a power and purpose greater than the self (Smith & Liehr, 2014). Implementing a nurse facilitated MBI as the primary independent variable in the current project aligns with the framework of this theory. Developing, teaching and monitoring practices to expand self-boundaries, regulate vulnerability, and navigate developmental changes may lead to longer MDD remission periods and overall well-being.

Implementation Framework

The ACE (Academic Center for Evidence-based Practice) Star Model draws from empirical research as a framework to support knowledge transformation, guiding practice change

and improving direct patient care at the bedside (Keele, 2011). This model was selected for its strong focus on knowledge discovery and integration, that may be easily implemented through teaching and training interventions outlined in this project. The model follows a 5-point process of knowledge transformation including; *Knowledge discovery, Evidence summary, Translation into practice, Integration into practice, and Evaluation,* as shown in Appendix B, Figure 2.

The theme of discovery supports both the self-transcendence theoretical framework of this project as well as a clinician inspired willingness to search for new ways in treating MDD. A synthesis of evidence supporting the efficacy of MBIs and ketamine's ability to reduce depressive symptoms has opened an unchartered pathway to merge these two interventions for clinical evaluation. This model is well suited for the small organizational structure of the project's practice setting and its patient population, allowing for a methodical integration and close evaluation of MBI with current treatment methods.

Potential Outcomes

This project combines innovations in psychopharmacology with emerging approaches in mindfulness therapy to support a unique psychiatric nurse-driven practice change. Outcomes will align with Office of Disease Prevention and Health Promotion (ODPHP, 2020) objective, Mental Health and Mental Disorders (MHMD)-4.2, to reduce the proportion of adults 18 years and older who experience major depressive episodes. The holistic approach outlined in this project provides patients with a transformative and sustainable life skill beyond the clinical setting. With the self-transcendence theory as a working paradigm, teaching MBI will help to decrease vulnerability to depressive episodes and offer patients an ongoing platform for self-healing. Finally, the union between ketamine and therapeutic MBI, echoes current best practice treatment where medication and therapy are most efficacious.

Delivering these interventions in succession, provides a fully integrative approach, minimizing therapeutic disruptions and promoting continuity in care. This single location, multidisciplinary design, may lead to improved therapeutic rapport, increased patient compliance, sustained remission and inspire other practice improvements in psychiatric care.

Methods

Ethical Considerations

The Arizona State University Internal Review Board (IRB) approved this project on July 31, 2020 for human subjects via distance implementation on the Zoom platform in response to COVID-19 restrictions. Participants self-selected into the study as current patients of a private outpatient ketamine infusion clinic owned and operated by a board-certified emergency medicine physician in Southern, California. Patients receiving ketamine infusion services were offered a recruitment flyer and directed to the clinic's website outlining the opportunity to participate between August 1, 2020 and December 2, 2020.

Informed Consent

Patients selecting into this study contacted the project administrator, a psychiatric registered nurse via phone or email to complete an initial assessment. In response, to Covid-19 pandemic restrictions, Zoom video calls were scheduled for participants to facilitate screening and to develop therapeutic rapport. Participants meeting inclusion criteria for unipolar depression without a history of bipolar disorder, were provided informed consent regarding risks, intervention procedures and the voluntary nature of the project outlined in the approved IRB consent form. Completion of the (PHQ-9) measurement tool was considered consent for this study after assigning a unique identification number to each participant.

Intervention Description

The clinical site for this project employs certified medical assistants and registered nurses supporting ketamine infusion services. Responsibilities including patient intake, administrative tasks, data collection, comfort measures, and discharge support. Beyond the clinical staff, and the community at large, key stakeholders include patients who are referred for treatment of depression, anxiety, post-traumatic stress disorder and chronic pain.

Consented participants were administered a guided MBI from the Accept, Connect Embody (ACE) script, a model developed by Dr. Rosalind Watts shown in Appendix C, Figure 1. The ACE script is based in the psychological flexibility model of Acceptance and Commitment Therapy (ACT) and its experiential processes of mindfulness shown in Appendix C, Figure 2. The ACE script was originally developed for use in psychedelic assisted therapy aligning with the constructs of this project. The MBI was delivered through Zoom video conference following each ketamine infusion by a psychiatric registered nurse, certified as an experienced registered yoga teacher (E-RYT 200) with added training in mindfulness and ACT. A digital audio version of the MBI was developed and provided to participants for daily home use between measurement intervals.

Clinical and IRB restrictions secondary to the COVID-19 pandemic resulted in modification of the intervention to a fully virtual implementation setting, a departure from its original face to face design. This helped to demonstrate the feasibility of an integrative approach in supporting patients with depression while offsetting barriers to accessibility. Connecting patients who receive ketamine infusion with skilled therapists for adjunctive services may help to inspire a practice change in this clinic and across the paradigm. Observing the impact of MBI's

delivered with ketamine's dissociative and neurogenic effects, may help contribute to a growing body of knowledge in the treatment of depression and other mental health disorders.

Instrumentation and Data Collection

The Patient Health Questionnaire (PHQ-9), which is closely correlated with the DSM-V criteria for depressive disorders and widely accepted in the literature as a valid and reliable tool, was employed for this project. Responses to the 9-item questionnaire are based on a 0-3 Likert scale assessing depression severity and remission of symptoms. A baseline PHQ-9 was administered in the clinic by the attending physician at the first integration of ketamine infusion with the MBI. Subsequent measures were collected prior to the third and final intervention in the series of six. Completed PHQ-9 forms were placed in sealed envelopes coded with the unique participant identification number and collected by the project administrator at the end of the study.

Results

The implementation phase of this project occurred at the height of the Covid-19 pandemic, yielding five patients who met inclusion criteria at this project site. From this group, one patient self-selected to participate in the study. This patient was a 78-year-old female with a 15-year history of resistant major depressive disorder. Prior treatment included electroconvulsive therapy (ECT), psychopharmacology and psychotherapy over the course of her illness. An initial consultation and informed consent were obtained via Zoom session on August 23, 2020 with both the patient and spouse. It was noted at this meeting the patient demonstrated significant hopelessness surrounding her condition but was willing to move forward and was found to be well supported by family.

The patient was seen at the project site for the initial series of six ketamine infusions on August 28, 2020, where a PHQ-9 score of 12 (moderate depression) was obtained by the attending physician. Following infusion recovery, the psychiatric nurse delivered the virtual ACE intervention via a scheduled Zoom call in compliance with Covid-19 restrictions and project modifications. The patient was then emailed an MP3 version of the intervention as noted in the methods section and instructed to engage daily between ketamine infusion sessions.

This process was repeated over the course of 4 more ketamine infusion appointments with a PHQ-9 score of 12 after the third infusion. Unfortunately, the patient only completed 5 of the six scheduled infusions with a PHQ-9 score of 13 (moderate depression) at the last visit. While there was no improvement in the PHQ-9 score, there are some qualitative findings worth noting. The patient did endorse using the provided MP3 mindfulness-based intervention on a daily basis and was able to identify committed action steps that support her well-being. This was noted by her motivation to engage the MP3 daily at bedtime, take walks with her spouse, and prepare meals. Following the third infusion, the patient demonstrated PHQ-9 stability and mentioned that she had attended a social outing which had been previously avoided for many months. Perhaps most importantly, the patient appeared engaged in the therapeutic relationship and participated with strong effort in the nurse delivered interventions.

This is an impactful outcome that correlates with the project's theoretical nursing framework of self-transcendence. Beyond quantitative analysis, lies the commitment of both nurse and patient working together in service of the patient's values and wellness. Over the course of this patient relationship, there were glimpses of hope and motivation that may help to diminish depressive symptomology. This demonstrates the value of nurse driven

psychotherapeutic integration as a valuable asset to ketamine and other interdisciplinary care teams.

Discussion

This project offers timely insight in regard to the feasibility of taking an integrative approach to treating patients with major depression and other potential mental health diagnoses. The Covid-19 pandemic has hastened the need for medical communities to adapt care models, expand patient outreach, and to supplement treatment with interdisciplinary resources through virtual platforms. The modification of this project's design to accommodate pandemic restrictions, demonstrates a strong collaborative effort from all stakeholders.

While the Covid-19 pandemic did serve as a limitation to this project in terms of decreased patient census and patient engagement, the mindfulness-based cognitive therapy intervention was implemented with noted advantages. Scheduling the virtual home interventions at convenient times for the patient following ketamine infusion recovery, helped to support patient comfort and improved clinical flow patterns. This modification was congruent with current literature that supports post-infusion antidepressant onset between 2-24 hours with response lasting up to 3-17 days (Singh et al., 2016). It was important that the intervention remained within these parameters as an integrative approach, synchronistic with the mechanism of action related to ketamine discussed earlier in this paper. Having some flexibility around intervention delivery times may also help to inform future practice environments that need to accommodate provider location, availability and schedules.

There is a growing body of research emerging to support the expanded use of ketamine beyond IV infusion to treat depression and other mental health disorders. Ketamine assisted psychotherapy (KAP) is being widely studied with promising results utilizing intramuscular,

intranasal, sublingual and oral delivery routes. The KAP sessions can be lengthy up to three hours and are adapted from a range of psychotherapeutic modalities. Similar to this project's intervention, the fundamentals of KAP are rooted upon an inward journey free of emotional constraints and of deep meditative states. Dore et al, (2019) conducted a study of 235 patients receiving KAP sessions both in office and at home using various ketamine administration methods based on the patient's location. For patients with major depressive disorder in this study, there was an 11.24 point drop in Beck Depression Inventory (BDI) scores from initial intake, placing them at a mild depression rating.

Evidence-based research continues to generate new frontiers in psychiatric treatment. The moment is now for mental health nurses to integrate skills at the full scope of practice as a holistic care imperative. The union of fundamental nursing theories that promote relationship, empathy, healing, and self-transcendence, coupled with strong clinical acumen, positions advanced practice nurses as unique contributors in the field. Psychiatric nurse driven efforts to expand and develop cognitive-based therapeutic skills, can offer depth to mental health treatment when integrated with medication management. Future work in this paradigm should focus on cultivating and employing these therapeutic skills in an effort to support the growing mental health crisis in our nation. The psychiatric nurse community must continue to be inspired by innovation, collaboration and a true commitment to restoring and promoting well-being for all that we serve.

References

American Psychiatric Association, & American Psychiatric Association (Eds.). (2013). *Diagnostic and statistical manual of mental disorders: DSM-5* (5th ed). American Psychiatric Association.

American Psychiatric Nurses Association. (2020). Ketamine infusion therapy. https://www.apna.org/i4a/pages/index.cfm?pageID=6603

Bai, Z., Luo, S., Zhang, L., Wu, S., & Chi, I. (2020). Acceptance and Commitment Therapy (ACT) to reduce depression: A systematic review and meta-analysis. *Journal of Affective Disorders*, *260*, 728–737. https://doi.org/10.1016/j.jad.2019.09.040

Bratsos, S., & Saleh, S. N. (2019). Clinical efficacy of ketamine for treatment-resistant depression. *Cureus*. https://doi.org/10.7759/cureus.5189

Centers for Disease Control and Prevention, National Center for Injury Prevention and Control. (2018). *National Violent Death Reporting System (NVDRS): About NVDRS, NVDRS overview fact sheet*. https://www.cdc.gov/violenceprevention/datasources/nvdrs/

Chen, M.-H., Li, C.-T., Lin, W.-C., Hong, C.-J., Tu, P.-C., Bai, Y.-M., Cheng, C.-M., & Su, T.-P. (2018). Persistent antidepressant effect of low-dose ketamine and activation in the supplementary motor area and anterior cingulate cortex in treatment-resistant depression: A randomized control study. *Journal of Affective Disorders*, *225*, 709–714. https://doi.org/10.1016/j.jad.2017.09.008

Cramer, H., Lauche, R., Langhorst, J., & Dobos, G. (2013). YOGA FOR DEPRESSION: A SYSTEMATIC REVIEW AND META-ANALYSIS: Review: Yoga for Depression: A Meta-Analysis. *Depression and Anxiety*, *30*(11), 1068–1083. https://doi.org/10.1002/da.22166

Domany, Y., Shelton, R. C., & McCullumsmith, C. B. (2019). Ketamine for acute suicidal ideation. An emergency department intervention: A randomized, double-blind, placebo-controlled, proof-of-concept trial. *Depression and Anxiety*. https://doi.org/10.1002/da.22975

Dore, J., Turnipseed, B., Dwyer, S., Turnipseed, A., Andries, J., Ascani, G., Monnette, C., Huidekoper, A., Strauss, N., & Wolfson, P. (2019). Ketamine Assisted Psychotherapy (KAP): Patient Demographics, Clinical Data and Outcomes in Three Large Practices Administering Ketamine with Psychotherapy. *Journal of Psychoactive Drugs*, *51*(2), 189–198. https://doi.org/10.1080/02791072.2019.1587556

GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. (2018). Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. The Lancet. https://doi.org/10.1016/S0140-6736(18)32279-7

Grunebaum, M. F., Galfalvy, H. C., Choo, T.-H., Keilp, J. G., Moitra, V. K., Parris, M. S., Marver, J. E., Burke, A. K., Milak, M. S., Sublette, M. E., Oquendo, M. A., & Mann, J. J. (2018). Ketamine for Rapid Reduction of Suicidal Thoughts in Major Depression: A Midazolam-Controlled Randomized Clinical Trial. *American Journal of Psychiatry*, *175*(4), 327–335. https://doi.org/10.1176/appi.ajp.2017.17060647

Han, Y., Chen, J., Zou, D., Zheng, P., Li, Q., Wang, H., Li, P., Zhou, X., Zhang, Y., Liu, Y., & Xie, P. (2016). Efficacy of ketamine in the rapid treatment of major depressive disorder: A meta-analysis of randomized, double-blind, placebo-controlled studies. *Neuropsychiatric Disease and Treatment*, *Volume 12*, 2859–2867. https://doi.org/10.2147/NDT.S117146

Haukaas, R. B., Gjerde, I. B., Varting, G., Hallan, H. E., & Solem, S. (2018). A Randomized Controlled Trial Comparing the Attention Training Technique and Mindful Self-Compassion for Students With Symptoms of Depression and Anxiety. *Frontiers in Psychology*, *9*. https://doi.org/10.3389/fpsyg.2018.00827

Keele, R. (2011). *Nursing research and evidence-based practice: Ten steps to success*. Jones & Bartlett Learning.

Klainin-Yobas, P., Oo, W. N., Suzanne Yew, P. Y., & Lau, Y. (2015). Effects of relaxation interventions on depression and anxiety among older adults: A systematic review. *Aging & Mental Health*, *19*(12), 1043–1055. https://doi.org/10.1080/13607863.2014.997191

Lent, J., Arredondo, A., Pugh, M., & Austin, P. (2019). Ketamine and treatment-resistant depression. *AANA Journal, 87*(5), 411-419.

López-Díaz, Á., & Fernández-González, J. L. (2018). Ineffectiveness of repeated intravenous ketamine infusions in treatment-resistant depression after a post–ketamine relapse: Time for a rethink? *Journal of Clinical Psychopharmacology, 38*(5), 534-536.

Office of Disease Prevention and Health Promotion. (2020). Mental health and mental disorders. In *Healthy People 2020*. U.S. Department of Health and Human Services. https://www.healthypeople.gov/2020/topics-objectives/topic/mental-health-and-mental-disorders

McGirr, A., Berlim, M. T., Bond, D. J., Fleck, M. P., Yatham, L. N., & Lam, R. W. (2015). A systematic review and meta-analysis of randomized, double-blind, placebo-controlled trials of ketamine in the rapid treatment of major depressive episodes. *Psychological Medicine*, *45*(4), 693–704. https://doi.org/10.1017/S0033291714001603

Reavy, K. (2016). *Inquiry and leadership: A resource for the DNP project*. F. A. Davis Company.

Sadock, B. J., Sadock, V. A., & Ruiz, P. (Eds.). (2017). *Kaplan & Sadock's comprehensive textbook of psychiatry* (Tenth edition). Wolters Kluwer.

Salloum, N. C., Fava, M., Hock, R. S., Freeman, M. P., Flynn, M., Hoeppner, B., Cusin, C., Iosifescu, D. V., Trivedi, M. H., Sanacora, G., Mathew, S. J., Debattista, C., Ionescu, D. F., & Papakostas, G. I. (2020). Time to relapse after a single administration of intravenous ketamine augmentation in unipolar treatment-resistant depression. *Journal of Affective Disorders*, *260*, 131–139. https://doi.org/10.1016/j.jad.2019.09.017

Singh, J. B., Fedgchin, M., Daly, E. J., De Boer, P., Cooper, K., Lim, P., Pinter, C., Murrough, J. W., Sanacora, G., Shelton, R. C., Kurian, B., Winokur, A., Fava, M., Manji, H., Drevets, W. C., & Van Nueten, L. (2016). A double-blind, randomized, placebo-controlled, dose-frequency study of intravenous ketamine in patients with treatment-resistant depression. *American Journal of Psychiatry*, *173*(8), 816–826. https://doi.org/10.1176/appi.ajp.2016.16010037

Smith, M. J., & Liehr, P. R. (Eds.). (2014). *Middle range theory for nursing* (3rd ed). Springer.

Strauss, C., Cavanagh, K., Oliver, A., & Pettman, D. (2014). Mindfulness-Based Interventions for People Diagnosed with a Current Episode of an Anxiety or Depressive Disorder: A Meta-Analysis of Randomised Controlled Trials. *PLoS ONE*, *9*(4), e96110. https://doi.org/10.1371/journal.pone.0096110

Substance Abuse and Mental Health Services Administration. (2019). *Key substance use and mental health indicators in the United States: Results from the 2018 National Survey on Drug Use and Health* (HHS Publication No. PEP19-5068, NSDUH Series H-54). Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. https://www.samhsa.gov/data/

Sundquist, J., Palmér, K., Memon, A. A., Wang, X., Johansson, L. M., & Sundquist, K. (2019). Long-term improvements after mindfulness-based group therapy of depression, anxiety and stress and adjustment disorders: A randomized controlled trial. *Early Intervention in Psychiatry*, *13*(4), 943–952. https://doi.org/10.1111/eip.12715

Tolahunase, M. R., Sagar, R., Faiq, M., & Dada, R. (2018). Yoga and meditation-based lifestyle intervention increases neuroplasticity and reduces severity of major depressive disorder: A randomized controlled trial. *Restorative Neurology and Neuroscience*, *36*(3), 423–442. https://doi.org/10.3233/RNN-170810

Watts, R., & Luoma, J. B. (2020). The use of the psychological flexibility model to support psychedelic assisted therapy. *Journal of Contextual Behavioral Science*, *15*, 92–102. https://doi.org/10.1016/j.jcbs.2019.12.004

Appendix A

Table A1

Evaluation Table for Quantitative Studies

Citation	Theory/ Conceptual Framework	Design/ Method	Sample/ Setting	Major Variables & Definitions	Measurement/ Instrumentation	Data Analysis (stats used)	Findings/ Results	Level/Quality of Evidence; Decision for practice/ application to practice
Chen, et al., (2018). Persistent antidepressant effect of low-dose ketamine and activation in the supplementary motor area and anterior cingulate cortex in treatment-resistant depression: A randomized control study. **Bias:** None noted	Inferred to be the Health Belief Model.	**Design:** Quantitative RCT **Purpose:** To demonstrate that a persistent increase in the SUVs of glucose metabolism in the SMA and dACC may contribute to the persistent antidepressant effects of ketamine.	**N:** 24 **n:** 8 (EG 1) **n:** 8 (EG 2) **n:** 8 (CG) **Setting:** Intervention performed Taipei Veterans General Hospital. **Baseline HDRS-17:** EG1: 24.00 EG2: 27.13 CG: 24.63	**IV:** 0.5mg/kg ketamine infusion, 0.2mg/kg ketamine infusion or normal saline over 40 minutes. **DV1:** HDRS scores **DV2:** SUVs of glucose metabolism.	**Imaging:** F-FDG positron-emission tomography (PET) using 3.0 GE Discovery 750 whole-body high-speed imaging device. **Depression severity:** HDRS-17	One-way ANOVA for continuous variables and Fisher's chi-square for clinical data among three subgroups. P< 0.05 was used to indicate statistically significant. Changes of SUV were a result of the interaction between time (before and after ketamine) and	**Depression severity:** Significant decrease at 240 minutes *0.5mg/kg* -42.7%, *0.2mg/kg* -15.9%, *saline* ± 9.8%. P< 0.001. After 1 day: *0.5mg/kg* -50% *0.2mg/kg* -23.3% *Saline* -11.5% P 0.001	**LOE: II** **Strengths:** Findings supported hypothesis; activation of the SMA and dACC could persist one day after ketamine infusion via increased SUV of glucose. Significant decrease in depressive symptoms after 1

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Funding: Ministry of Science and Technology, Taipei Veterans General Hospital and trhe Kung-Po Soo Medical Foundation. **Country:** Taiwan			**IC:** Ages 21-65 with a diagnosis of MDD who failed three antidepressant treatments. **EC:** Major medical or neurological illness or history of alcohol or substance abuse.			ketamine group, two-way repeated measures ANOVA was conducted. Interaction between group and time and main effect of group and time reported $p<0.05$, 2-sided corrected by family wise errors.	**SUV:** PET scan showed no significant main effect of the group. Post-hoc showed 05mg/kg increased SUV P=0.014 in SMA and dACC vs. 0.2mg/kg. this was negatively correlated with depressive symptoms after one day.	ketamine infusion up to one day post infusion. **Weaknesses:** Patients were continued on regularly prescribed psychotropic medications. Not uncommon with ketamine therapy, results may be combined or regulatory effect. Small sample size of 24 may decrease statistical power. **Conclusions:** 0.5mk/kg

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								ketamine infusion had rapid and persistent antidepressant effects. Effects mediated by increased glucose metabolism in the dACC and SMA facilitating glutamatergic neurotransmission extending benefits of ketamine beyond its half-life. **Feasibility/ Applicable to population:** The major findings in this study support the application of ketamine in decreasing

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								depressive symptoms in patients with MDD and aligns with the population chosen in this projects PICO.
Cramer et al., (2013). Yoga for depression: A systematic review and meta-analysis. **Bias:** Attrition bias was high in most studies. 3 studies low risk of bias. **Funding:** Rut- and Klaus-Bahlsen Foundation	Yoga and Mindfulness theoretical foundations.	**Design:** Quantitative MA **Purpose:** Assess the effectiveness and safety of different yoga forms in patients with depressive disorders.	**N:** 12 **n:** 619 **Databases Searched:** Medline/PubMed, Scopus, Cochrane Library, PsychInfo, IndMED. **IC:** RCT, Dx depression, yoga modalities as intervention, quantitative design.	**IV:** Yoga MBI interventions. **DV:** Severity of depression.	BDI, HAMD, Cornell Dysthymia Scale, Centers for Epidemiology Studies Depression Scale, the Zung Depression Scale.	SMD I^2 X^2 test Funnel plots	**DV: Severity** (SM= -0.69; 95% CI -0.99 to -0.39; $P < .001$ Heterogeneity; I^2 =86%; X^2 = 28.81; $P < .001$)	**LOE:** I **Strengths:** MA design. No language restrictions. **Weaknesses:** Low methodological quality, the exclusion of MBSR & MBCT RCTs which fall within the category of MBI.

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Country: Germany			**EC:** Non RCT, qualitative design, duplicate records, no depression. MBCT& MBSR. **Origins:** Asia, India, Iran, & USA. **Intevention Characteristcs:** Breathing, mindfulness, MBI, asanas, Broota relaxation, Kirtan, Kriya, Sahaj meditation.					**Conclusions:** Included for its effect on depression alone and did support the safe use of multiple yoga modalities in reducing depression severity. Results applicable to vast majority of patients with depressive disorders as patients were recruited from a multiple countries and facilities. **Feasibility/ Applicable to population:** The review concluded that

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								yoga should be considered as a treatment option for affective disorders. A MBI based in yoga's paradigm is supported as safe ancillary tool with ketamine infusion therapy in supporting MDD.
Domany, Shelton, & McCullumsmith, (2019). Ketamine for acute suicidal ideation. An emergency department intervention: A randomized, double-blind, placebo-	Inferred to be Health Belief Model.	Randomized, double-blind, placebo-controlled, proof of concept trial. **Purpose:** Randomly assess the safety, feasibility,	**N: 18** **n:** 9 (EG) **n:** 9 (CG) **Setting:** Emergency department at a university teaching hospital. **Sample Demographics:** Male 44%	**IV1:** 0.2mg/kg ketamine infusion over 5 min. **IV2:** 10ml syringe of normal saline infused over 5 minutes.	BAI BHS BSS MADRS-SI This tool's 10th question provides valid estimation of suicidal ideation.	Kolmogorov test.	**DV1:** 88% reduction in suicidal ideation compared to control (*p<0.5)* **DV2:** 90.7% reduction in hopelessness in the BHS compared to	**LOE: II** **Strengths:** RCT design, no attrition, effect of ketamine on RDoC suicidal constructs. Demonstrates rapid effect of ketamine in acute crisis.

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controlled, proof-of-concept trial. **Funding:** Not listed. **Bias:** None noted **Funding:** Not listed. **Country:** USA		tolerability, and efficacy of single dose ketamine in reducing suicidal ideation. To measure RDoC Constructs for suicidal risk factors including hopelessness and potential threat.	Black 38.9% White 61.1% **IC:** Diagnosis of MDD, bipolar depression, or dysthymia. Clinically significant suicidal ideation. **EC:** Current primary psychotic disorder. Dissociative, developmental, Cognitive disorder, or anorexia. **Attrition:** Not identified.	**DV1:** Suicidal ideation. **DV2:** Suicide related RDoC constructs including Hopelessness and potential threat.			17.5% in control (p<0.5) 82.4% reduction in potential threat in the BAI compared to 47.3% in the control (p<0.5)	**Limitations:** Small sample size secondary to early termination of recruitment. Follow-up was limited and length of hospital stay was not evaluated for long-term ketamine effects. **Conclusions:** This study did emphasize the safety and feasibility of intervention for suicidal patients with effect lasting up to 120 minutes after infusion with

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								noted impact on intent. **Feasibility/ Applicable to population:** The study aligns with current project and supports the use of ketamine in clinical practice for patients with TRD and suicidality. The short duration in action helps to support the need for MBI intervention.
Haukaas et al., (2018). A Randomized Controlled Trial	Meta-Cognitive and Mindfulness	**Design:** RCT **Purpose:** To test	**N:** 81 **n:** 40 ATT (EC1) n: 41 MSC (EC2)	**IV1:** ATT **IV2:** MSC	PHQ-9 GAD-7 SCS-SF DMQ	ANOVA Chi-square	**DV1:** Main effect post intervention.	**LOE:** II **Strengths:** RCT design. Study

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Comparing the Attention Training Technique and Mindful Self-Compassion for Students with Symptoms of Depression and Anxiety. **Bias:** Possible selection bias. **Country:** Norway	theoretical framework.	hypotheses that both interventions will lead to significant reduction in symptoms of depression and anxiety. That both interventions will increase mindfulness, attention flexibility, and self-compassion in treatment responders.	**Sample Demographics:** Norwegian undergraduate and graduate students. 75.3% Female 22.0% Attrition Participants blinded to experimental group. **IC:** Self-reported symptoms of anxiety, depression and stress. **EC:** None noted.	**DV1:** Reduction in Depressive and anxiety symptoms. **DV2:** Increased mindfulness, attention flexibility and self-compassion.	FFMQ		(EC1) PHQ-9 (d=0.53, p<0.001) (EC2) PHQ-9 (d=0.57, p<0.001) (EC1) GAD-7 (d=0.71, p<0.001) (EC2) GAD-7 (d=0.54, p<0.001) **DV2:** (EC1) SCS-SF (d=0.82, p<0.001) (EC2) (d=0.55, p<0.001) (EC1) DMQ (d=0.51, p<0.001) (EC2)	supported both hypotheses. Effect sizes similar or larger for primary outcome measures. MBI from different theoretical frameworks may decrease depression symptoms via common mechanism. **Weaknesses:** Self-report or lack of diagnostic precision. Majority female. Outcome measures were self- reporting yet common in

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							(*d*=0.73, *p*<0.001) (EC1) FFMQ (*d*=0.66, *p*<0.001) (EC2) (*d*=0.53, *p*<0.001)	this area of study. **Conclusion:** Both MSC and ATT were equally significant in reducing depressive symptoms while increasing mindfulness, self-compassion and attention flexibility. Although delivered in small group setting, it is feasible to adapt to individuals. Results of these intervention were maintained at a six-month

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								follow-up and may help to support depression remission techniques. **Feasibility/ Applicable to Population**: This work offers a supportive evidence that MBIs may share a common mechanism in support depression whether self-reported or diagnosed. There were no adverse effects noted making MSC a consideration for

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								this project's population.
Klainin-Yobas et al., (2015). Effects of relaxation interventions on depression and anxiety among older adults: A systematic review. **Funding:** Yong-Loo Lin School of Medicine. **Bias:** Possible selection bias secondary to convivence sampling within studies. **Country:** China	Meta-analysis approach and Cochrane's systematic review.	Quantitative SR **Purpose:** To review the magnitude of effect of relaxation and MBI interventions on depression.	**N:** 15 **Database searched:** Scopus, CINAHL, EMBASE, ERIC, Sociology abstract, PubMed, ScienceDirect, PsyInfo, Mednar, Web of Science Index. **Study origins:** USA, Hong Kong,Singapore, France, France, India & Iceland.	**IV:** Relaxation interventions. 1. Yoga 2. Music 3. Combined relaxation training. 4. PMRT 5. Massage 6. Stress management training. **DV:** Effect of intervention on depression.	Geriatric Depression Scale (GDS) HADS The Center for Epidemiological Depression Scale (CES-D)	Hedges' g Cohen's *d* *z*-test Q and I^2	**DV:** Relevant findings PMRT (g= 1.21, $z = 8.73$, $p < 0.01$). Yoga (g = 0.49, $z = 4.08$, $p < 0.01$). Overall (g = 0.82, $z = 8.85$, $p < 0.00$).	**LOE:** I **Strengths:** SR design, comprehensive literature search reduced publication bias. **Weaknesses:** All English studies, most studies in USA difficult to generalize to other areas. Participants may have simply benefitted from therapist-client relationship which may actually work in favor for this current project.

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			IC: RCTs, reported in English, any gender over age 60, included depression and anxiety variables, efficacy of relaxation interventions, control conditions of TAU. **EC:** Studies with samples of mixed age groups. Online relaxation interventions.					**Conclusion:** This study demonstrated that relaxation and MBI therapies such as yoga may provide adjunctive support to an older population with depression. **Feasibility/ Applicable to population:** The empirical evidence identifies relaxation MBIs as a safe and inexpensive modality when delivered by a certified yoga

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								instructor. This study helps to expand the sample demographic in the current project where an elderly with MDD population may be prevalent.
McGirr et al., (2015). A systematic review and meta-analysis of randomized, double-blind, placebo-controlled trials of ketamine in the rapid treatment of major depressive episodes. **Country:** Canada	Inferred to be the health belief model.	**Design:** Quantitative/ SR & MA of RCT **Purpose:** Assess the efficacy of ketamine in the treatment of major depressive episodes.	**N=**7 **Data Bases Searched:** Medline n=28 EMBASE n=73 CENTRAL=19 PsycInfo=169 **IC:** Study validity; random allocation, allocation concealment, clinician rated	**IV1:** Ketamine Infusion or intranasal ketamine spray. **IV2:** Saline or midazolam. **DV:** Depression scores.	**MADRS HAMD-25 HAMD-21**	**Comprehensive Meta-Analysis Version 2.0** **Egger's regression intercept.**	Ketamine administered intravenously in all but one study that was intranasal. **IV1:** 0.90 (95% CI 0.66-1.13%, z=7.59, p<0.005) indicated significant difference in depression scores favoring	**LOE: I** **Adverse events:** No serious events reported in majority of studies. One study reported n=1refractory hypertension, and n=1 bradycardia & hypertension. One recorded induction of

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Bias: Marginal risk of publication bias assessed with Egger's regression intercept. **Funding:** No sources of funding or industry involvement.			primary outcome measures. Subjects 18-75 years primary diagnosis of MDD. Treatment with ketamine as a single administration. Studies written in English. **EC:** Narrow diagnosis, absence of response or remission rates, ketamine as an Electroconvulsive therapy adjunct.				ketamine vs placebo. Clinical remission after 7 days (95% CI 1.52-10.51, z=2.81, p<0.01) **IV2:** No significant difference between saline and midazolam in depression score/remission (p=0.45).	hypomania with saline infusion noted. No psychotic symptoms noted. **Strengths:** MA study design suggesting ketamine is well tolerated and superior to placebo as an effective and acceptable single dose treatment for MDD. **Weaknesses:** Small samples and crossover designs. Limited duration in follow-up and unable to obtain long-term benefit

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								or cost-effectiveness. **Conclusions, Feasibility & Application to practice:** Ketamine therapy is a safe, effective, and well tolerated for MDD with rapid and clinical remission up to 7 days. This supports PICOT population and the need for interventions to help sustain remission effects.
Singh et al. (2016). A double-blind, randomized,	Quantitative Randomized, double blind placebo-	**N:** 68 **n**: 18 (KG1) **n**: 17 (KG2) **n:** 17 (PG1)	**IV:** 0.5mg/kg ketamine infusion over 40 minutes and	**Efficacy assessment:** MADRS	**Efficacy analysis:** Two-sample t test.	14 patients were required in each group to detect treatment	**LOE:** II **Strengths:** RCT with placebo and

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placebo-controlled, dose-frequency study of intravenous ketamine in patients with treatment-resistant depression. **Multi-site Location:** From and funded by Jassen Research and Development, Titusville, NJ.		controlled, parallel-group design. **Purpose:** Evaluate the efficacy of two dosing protocols, twice and three times a week of intravenous ketamine in sustaining antidepressant effects. Assess onset of antidepressant response and safety of repeated doses.	**n:** 16 (PG2) **Sample demographics:** Overall mean age 43.9, females 45, white 53, black 12, other 2. **Mean baseline MADRS scores:** Overall-35.2 (SD=5.1) (KG) 33.3 (PG1) 35.6 (KG2) 35.4 (PG2) 36.8 **Setting:** 14 clinical sites in the United States. **IC:** Ages 18-24 with MDD and inadequate response to at	placebo of 0.9% sodium chloride infusion over 40 minutes. **DV1:** MADRS scores from baseline. **DV2:** Pharmacokinetic assessment ketamine plasma concentrations (Cmax) and AUCs.	**Pharmacokinetic assessment:** Venous blood samples.	**Pharmacokinetic analysis:** Summarized using descriptive statistics.	difference with a power of 90% with one-sided *p* value of 0.15 **Efficacy Results:** (KG1) -18.4 (PG1) -5.7 $p<0.001$ (KG2) -17.7 (PG3) -3.1 $p<0.001$ Overall mean MADRS scores did not differ between dose frequency. **Pharmacokinetic Results:** (Cmax) ranged from 168 to	time dose variables. No ketamine related adverse effects. Safety established. **Weaknesses:** Short duration 4-6 weeks. Longer study needed to assess is the clinical efficacy of ketamine can be maintained despite dose frequency. **Conclusions, Feasibility & Application to practice:** Identified robust antidepressant effects of ketamine in

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			least 2 antidepressants. **EC:** Extensive range of comorbid psychiatric disorders, previously failed ketamine treatment, current SI or HI. SUD within one year.				219ng/mL across treatment regimes. Mean plasma AUCs similar across treatment groups and study days with a range, 293-342 hng/mL. There was no significant correlation with individual body weight. **Safety:** No deaths reported. 2 patients experienced adverse anxiety event requiring hospitalization. Ketamine as a precipitating factor was ruled.	reducing depressive symptoms at both dose frequencies. It is preferable to reduce the burden of frequent dosing and supports the use of adjunctive interventions such as MBI to help sustain remission.

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Strauss, Cavanagh, Oliver & Pettman (2014). Mindfulness-Based Interventions for people Diagnosed with a Current Episode of an Anxiety or Depressive Disorder: A Meta-Analysis of Randomised Controlled Trials. **Bias:** Publication bias, a slight bias towards publishing small sample size studies for primary symptom severity.	Inferred to be Mindfulness and Cognitive Behavioral theoretical Framework.	**Design:** MA **Purpose:** To analyze the effectiveness of MBIs in RCTs where all participants were diagnosed with a current episode of anxiety or depressive disorder.	**N:** 12 **Database Searched:** MEDLINE, Web of Science, Scopus, ProQuest and PsycINFO. **IC:** RCTs, participants 18yrs or older, mindfulness was a core part of MBI with daily practice encouraged between sessions, studies included psychometrically reliable and valid outcome measures for depression and anxiety, met DSM-5 criteria	**IV:** MBI **DV1:** Primary symptom severity. **DV2:** Primary Symptom effect as function of intervention Mindfulness-based Cognitive Therapy (MBCT) or Mindfulness-based Stress Reduction (MBSR). **DV3:** Effect on depressive or anxiety symptoms irrespective of diagnosis.	HAMD BDI-II	Hedges *g* used to calculate effect size for each study. Forest Plots for post intervention between group effect sizes. Rosenthal's Fails-Safe N for publication bias. Chi-square for heterogeneity. Jadad rating scale to assess quality of each study.	**DV1:** (Hedges *g* =-0.59, 95% CI=-1.06 to -0.12) *p*=0.01 **DV2:** No significant difference between MBI subgroups (*p*=.52). Effect of MBCT (Hedges *g* =0.39, 95% CI=-0.63 to-0.15) *p*<.01 **DV3:** Post-intervention (Hedges *g* =-0.64, 95% CI = -1.00 to -0.28) *p*<.001. Non-significant post MBI differences in anxiety severity.	**LOE: I** **Strengths:** Analysis restricted to RCTs with control. Significant benefits of MBI on depression severity across all studies. **Weaknesses:** Overall evidence-base in MBI effectiveness is somewhat limited in literature resulting in only 12 studies for this analysis.

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Citation	Theory/ Conceptual Framework	Design/ Method	Sample/ Setting	Major Variables & Definitions	Measurement/ Instrumentation	Data Analysis (stats used)	Findings/ Results	Level/Quality of Evidence; Decision for practice/ application to practice
Funding: Authors have no funding or support to report. **Country:** United Kingdom			for MDD, anxiety disorders or hypochondriasis. **EC:** Cognitive impairment, substance misuse, MBI not in group format or in-person, language other than English.					Analysis does not address long term efficacy. **Conclusions:** Significant benefits of MBI for reducing current episodes of depression in MDD. No significant findings for anxiety symptoms for anxiety with no adverse outcomes noted. **Feasibility & Application to practice:** MBI may serve as a viable intervention for this project in

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Citation	Theory/ Conceptual Framework	Design/ Method	Sample/ Setting	Major Variables & Definitions	Measurement/ Instrumentation	Data Analysis (stats used)	Findings/ Results	Level/Quality of Evidence; Decision for practice/ application to practice
								helping to support current depressive symptoms with the opportunity to extend remission.
Sundquist et al., (2019). Long-term improvements after mindfulness-based group therapy of depression, anxiety and stress and adjustment disorders: A randomized controlled trial. **Bias:** None noted. **Country:** Sweden	Inferred to be Mindfulness and Cognitive Behavioral theoretical framework.	**Design:** Quantitative RCT **Purpose:** To compare improvement in psychometric scores after MGT with TAU after intervention in patients diagnosed with depression, anxiety, stress, and	**N:** 215 **n:** 110 (EG) **n:** 105 (CG) **Attrition:** 45% 24 of 150 primary healthcare centers randomly selected. **IC:** Range of ICD-10 depressive or anxiety diagnoses. Ages 26-64	**IV1:** MGT **IV2:** TAU **DV1:** MADRS-S One year from baseline. **DV2:** HADS-D One year from baseline. **DV3:** PHQ-9 One year from baseline. Control group received TAU and may have included pharmacology, CBT, or	MADRS-S HADS-D PHQ-9	Wilcoxon signed-rank test. Student's *t* test.	**DV1:** Wilcoxon *p<0.001* **DV2:** Wilcoxon *p<0.001* **DV3:** Wilcoxon *p<0.001* Differences in baseline characteristics between mindfulness and control at one year: MADRS-S **IV1:** SD(6.7) **IV2:** SD(7.3) HADS-D	**LOE: II** **Strengths:** RCT design with control with one-year follow-up. Interventions can be nurse delivered. 16 primary healthcare centers both urban and rural randomly selected generated

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Citation	Theory/ Conceptual Framework	Design/ Method	Sample/ Setting	Major Variables & Definitions	Measurement/ Instrumentation	Data Analysis (stats used)	Findings/ Results	Level/Quality of Evidence; Decision for practice/ application to practice
		adjustment disorder.	Score cutoffs: MADRS 13-34 HADS-D >7 PHQ-9 >10 Ability to speak and read Swedish **EC:** Severe psychiatric symptoms, risk of suicide, substance misuse, pregnancy, current psychotherapy, thyroid disease.	psychodynamic therapy. Intervention received structured and controlled meditative exercises. 2-hour sessions, once a week for 8 weeks with encouraged daily home practice.			**IV1**: (3.4) **IV2:** (4.1) PHQ-9 **IV1:** (5.6) **IV2:** (5.4)	demographic diversity. **Weaknesses:** Did not included non-Swedish speaking immigrants. Only aspect that was blinded was the randomization. No access to treatment data from non-participating healthcare centers regarding psychotropic therapy. **Conclusion:** The study reveals significant

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Citation	Theory/ Conceptual Framework	Design/ Method	Sample/ Setting	Major Variables & Definitions	Measurement/ Instrumentation	Data Analysis (stats used)	Findings/ Results	Level/Quality of Evidence; Decision for practice/ application to practice
								improvement in psychometric scores with no significant differences between intervention groups. This supports the use of a wide range of MBI in clinical practice for trained healthcare professionals. This study may demonstrate that a long-term follow up intervention may also contribute to improved outcomes.

Key: ANOVA- analysis of variance; **AUCs-** time from 0-6 hours post infusion; **BAI-** Beck Anxiety Index; **BDI-II-** Beck Depression Inventory-II scale; **BDNF-** brain derived neurotropic factor; **BHS-** Beck Hopelessness Scale; **BSS-** Beck Scale for suicidal Ideation; **CBT:** cognitive behavioral therapy; **CI-** confidence interval; **dACC-**dorsal anterior cingulate cortex; **DHEAS-** dehydroepiandrosterone sulfate; **DV**-dependent variable; **EC-**exclusion; **HADS-D:** Hospital Anxiety and Depression Scale; **HAMD/HDRS-** Hamilton Depression Rating Scale; **HI-** homicidal ideation; **IC-**inclusion criteria; **IL-6-** interleukin 6; **IV**- independent variable; **KG1**- intervention receiving ketamine 2 times a week; **KG2-** intervention receiving ketamine 3 times a week; **MA-**meta-analysis; **MADRS-** Montgomery-Asberg Depression Rating Scale; **MBI-** mindfulness-based interventions; **MDD-** major depressive disorder; **MGT-** mindfulness-based group therapy; **N**-number of studies (if SR) or participants in study; **n**- number of participants (if SR) or number of participants in subset; **PG1-** receiving placebo 2 times a week; **PG2-** receiving placebo three times a week;**PHQ-9:** Patient Health Questionnaire; **RCT-**randomized control trial; **RDoC-** Reasearch Domaine Criteria; **ROS-** reactive oxygen species; **SR-**systematic review; **SD-**standard deviation; **SI-** suicidal ideation; **SMA-** supplemental motor area; **SUD-** substance use disorder; **SUV-** Standardized uptake values; **TAU:** treatment as usual; **YMLI-**yoga and meditation-based lifestyle intervention;

Citation	Theory/ Conceptual Framework	Design/ Method	Sample/ Setting	Major Variables & Definitions	Measurement/ Instrumentation	Data Analysis (stats used)	Findings/ Results	Level/Quality of Evidence; Decision for practice/ application to practice
								Feasibility & Application to practice: The long duration of this study may limit feasibility. The MBI is noted to be safe and economical and may be adapted to meet the needs of site-specific settings.
Tolahunase, M. R., Sagar, R., Faiq, M., & Dada, R. (2018). Yoga- and meditation-based lifestyle intervention increases neuroplasticity and reduces severity of major depressive	Inferred to be Yoga science and philosophy.	**Design:** Quantitative RCT **Purpose:** Analyze the effects of a 12-week YMLI on depression severity and biomarkers of	**N:** 58 **n:** 29 (EG) **n:** 29 (CG) **Setting:** Small group YMLI sessions taught at integrated health clinic, New Delhi.	**IV**: 12-week YMLI conducted 5 days a week. **DV1:** BDI-II scores and **DV2:** BDNF marker of neuroplasticity. **DV3:** cortisol. **DV4**: IL-6. **DV5:** DHEAS. **DV6:** ROS	**Measurement of clinical parameters:** BDI-II. **Measurement of blood biomarkers:** Fasting venous blood samples (5ml) divided in two parts. One	Chi-square and Fisher's exact test to compare categorical characteristics at baseline. t-test to compare normally distributed continuous variables.	No harmful effects noted in YMLI. Results displayed as change value from baseline to 12-weeks post intervention Mean CI at 95%. **DV1:** (EG) -5.83	**LOE:** II **Strengths:** RCT design and first to demonstrate yoga's impact on cellular health, neuroplasticity and depression severity.

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Citation	Theory/ Conceptual Framework	Design/ Method	Sample/ Setting	Major Variables & Definitions	Measurement/ Instrumentation	Data Analysis (stats used)	Findings/ Results	Level/Quality of Evidence; Decision for practice/ application to practice
disorder: A randomized controlled trial. **Location:** All India Institute of Medical Sciences. **Country:** India		neuroplasticity in MDD patients on routine drug therapy.	**Sample Demographics:** All adult participants. Mean age 36.94 (EC), 39.10 (CG). Females 16 (EG), 16 (CG). Males 13 (EG), 14 (CG). **BDI-II scores at baseline:** 26.96 (EG), 28.10 (CG). **IC:** Ages 19-50 with DSM-5 diagnosis for MDD on routine drug treatment for six months. **EC**: BDI-II score greater than 45 with comorbid	**DV7:** Deoxyguanosine. **DV8:** telomerase activity.	allowed to clot and separated in 30 minutes, the other heparinized and centrifuged gat 2000g for 15 minutes at -80°C.	Wilcoxon rank-sum test to compare nonparametric continuous data. Wilcoxon signed rank test for continuous variables without normal distributions. ANOVA used to assess gender differences. Multiple regression determined the change in which variables significantly explained associations between	(CG) 1.45 *p<0.001* **DV2:** (EG) 5.48 (CG) 0.02 *p*<0.001 **DV3:** (EG) -165.63 (CG) 28.62 *p*< 0.001 **DV4:** (EG) -0.84 (CG) 0.57 *p*< 0.001 **DV5:** (EG) 11.69 (CG) -1.15 *p* 0.001 **DV6:** (EG) 1066.81 (CG) 123.34 *p*< 0.001 **DV7:** (EG) -96.04 (CG) 35.41 *p*< 0.001 **DV8**: (EG) 8.22 (CG) -0.50 *p*< 0.001	**Weaknesses:** Relatively small sample size, single time-point data interpretation and lack of long-term follow-up. **Conclusions, Feasibility & Application to practice:** Decreased severity in depression increase in neuroplasticity and improved brain physiology. May prevent complications from drug therapy, reduce relapse and

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Citation	Theory/ Conceptual Framework	Design/ Method	Sample/ Setting	Major Variables & Definitions	Measurement/ Instrumentation	Data Analysis (stats used)	Findings/ Results	Level/Quality of Evidence; Decision for practice/ application to practice
			neuropsychiatric and chronic medical conditions including bipolar disorder, hypertension and diabetes.			neuroplasticity and depression.		extend remission. Intervention is safe and may be considered significant component in the prevention and management of MDD. This aligns with PICOT to integrate a YMLI with ketamine infusion services.

Key: ANOVA- analysis of variance; **AUCs-** time from 0-6 hours post infusion; **BAI-** Beck Anxiety Index; **BDI-II-** Beck Depression Inventory-II scale; **BDNF-** brain derived neurotropic factor; **BHS-** Beck Hopelessness Scale; **BSS-** Beck Scale for suicidal Ideation; **CBT:** cognitive behavioral therapy; **CI-** confidence interval; **dACC-**dorsal anterior cingulate cortex; **DHEAS-** dehydroepiandrosterone sulfate; **DV**-dependent variable; **EC-**exclusion; **HADS-D:** Hospital Anxiety and Depression Scale; **HAMD/HDRS-** Hamilton Depression Rating Scale; **HI-** homicidal ideation; **IC-**inclusion criteria; **IL-6-** interleukin 6; **IV**- independent variable; **KG1**- intervention receiving ketamine 2 times a week; **KG2-** intervention receiving ketamine 3 times a week; **MA-**meta-analysis; **MADRS-** Montgomery-Asberg Depression Rating Scale; **MBI-** mindfulness-based interventions; **MDD-** major depressive disorder; **MGT-** mindfulness-based group therapy; **N**-number of studies (if SR) or participants in study; **n**- number of participants (if SR) or number of participants in subset; **PG1-** receiving placebo 2 times a week; **PG2-** receiving placebo three times a week;**PHQ-9:** Patient Health Questionnaire; **RCT-**randomized control trial; **RDoC-** Reasearch Domaine Criteria; **ROS-** reactive oxygen species; **SR-**systematic review; **SD-**standard deviation; **SI-** suicidal ideation; **SMA-** supplemental motor area; **SUD-** substance use disorder; **SUV-** Standardized uptake values; **TAU:** treatment as usual; **YMLI-**yoga and meditation-based lifestyle intervention;

Table A2

Synthesis Table

Studies	Chen et al.	Cramer et al.	Domany et al.	Haukaas et al.	Klainin et al.	McGirr et al.	Sing et al.	Strauss et al.	Sundquist et al.	Tolahunase et al.
Year	2018	2013	2019	2018	2015	2015	2016	2014	2019	2018
Design	RCT	MA	RCT	RCT	SR	MA	RCT	MA	RCT	RCT
Sample										
N/n size	24	N12/n619	18	81	15	7	68	N12/n578	215	58
Location	Taiwan	Germany	USA	Norway	China	Canada	USA	UK	Sweden	India
MDD Diagnosis	X	X	X	X	X	X	X	X	X	X
Setting										
Outpatient		X		X	X	X	X	X	X	X
Inpatient	X		X		X	X				
IV										
Ketamine Infusion	X		X			X	X			
Yoga		X			X					X
MBI		X		X	X			X	X	X
DV										
Depression Severity	X	X	X	X	X	X	X	X	X	X
Measurement Tool										
HAMD/HDRS	X	X			X	X		X	X	
BDI		X	X					X		X
PHQ-9				X					X	
MADRS			X			X	X		X	
FFMQ				X						
Outcomes										
Mindfulness				↑					↑	↑
Depression	↓	↓	↓	↓	↓	↓	↓	↓	↓	↓
MDD Remission	↑	NM	NM	↑	NM	↑	↑	NM	↑	NM

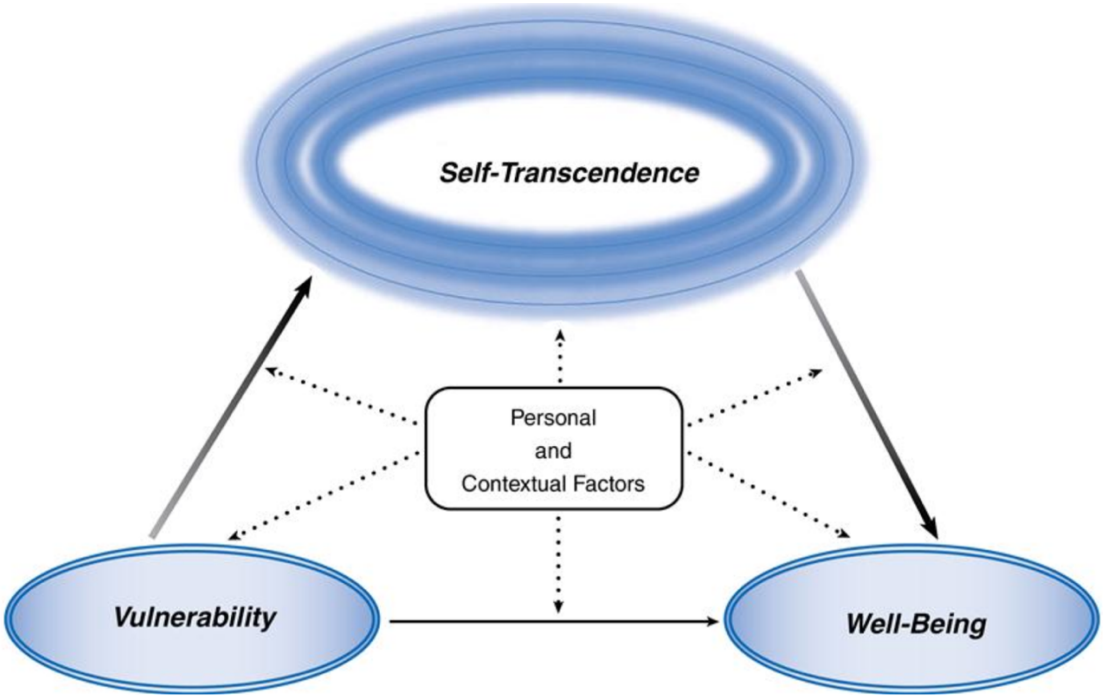
Key: BDI- Beck Depression Inventory scale; **DV**-dependent variable; **FFMQ-**Five Facet Mindfulness Questionnaire; **HAMD/HDRS-** Hamilton Depression Rating Scale; **IV**- independent variable; **MA-**meta-analysis; **MADRS-** Montgomery-Asberg Depression Rating Scale; **MBI-** mindfulness-based interventions; **MDD-** major depressive disorder; **N**-number of studies (if SR) or participants in study; **n**- number of participants; **NM-** not measured; **PHQ-9:** Patient Health Questionnaire; **RCT-** randomized control trial; **SR-**systematic review.

Appendix B

Models and Frameworks

Figure 1

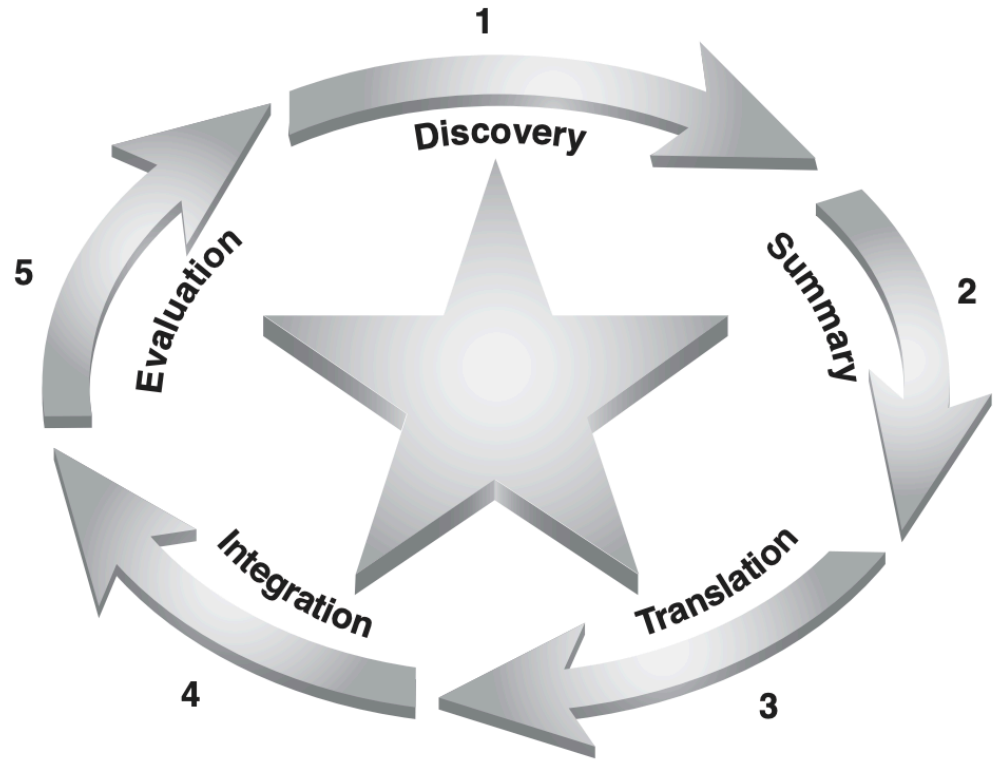
Model of Self-Transcendence Theory



Note: Model of the the Theory of Self-Transcendence. Reprinted from *Middle Range Theory for Nursing* (p.73), by M.J. Smith and P.R. Liehr, 2014, Springer Publishing. Copyright 2014 Springer Publishing Company.

Figure 2

The ACE STAR MODEL



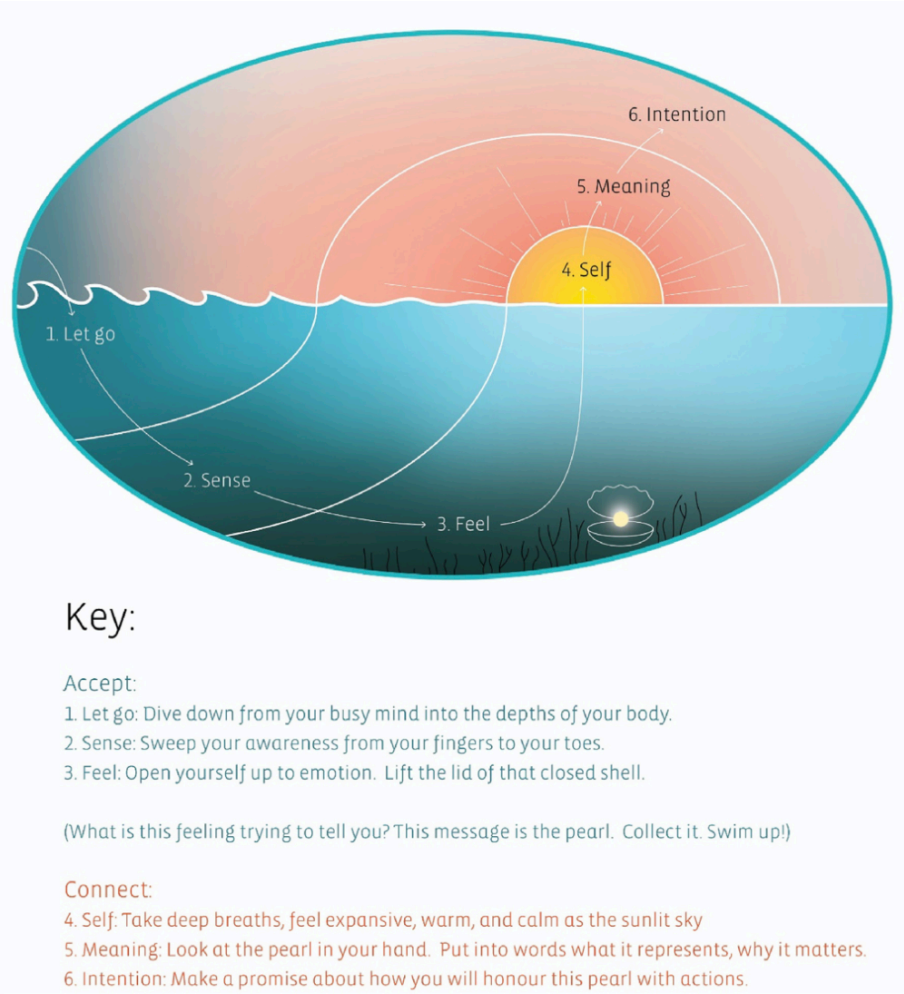
Note: ACE Star Model of EBP: Knowledge Transformation Reprinted from *Nursing Research and Evidence-Based Practice: Ten Steps to Success* (p. 78), by R. Keele, 2011, Jones & Barlett. Copyright by Jones & Barlett Learning, LLC.

Appendix C

ACE Intervention and Framework

Figure 1

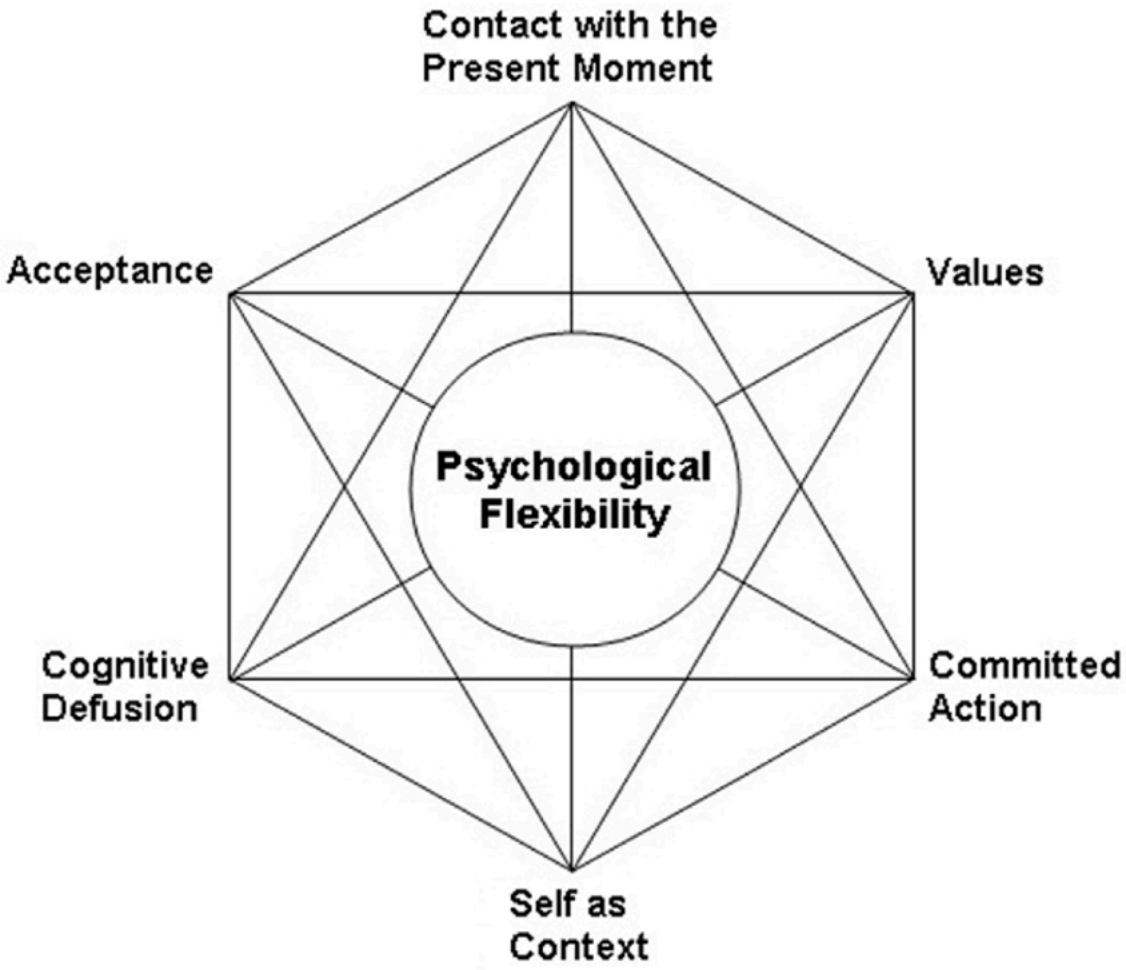
Accept, Connect, Embody Model



Note: The Accept, Connect, Embody (ACE) model used as the framework for psychedelic assisted therapy and guided mindfulness. Adapted from "The Use of the Psychological Flexibility Model to Support Psychedelic Assisted Therapy," by R. W. Watts and J.B. Luoma, 2020, *Journal of Contextual Behavioral Sciences, 15*, p 94. In the public domain.

Figure 2

Acceptance and Commitment Therapy (ACT) Hexaflex Model



Note: The Hexaflex model used as the framework for Acceptance and Commitment Therapy (ACT). Adapted from "The Use of the Psychological Flexibility Model to Support Psychedelic Assisted Therapy," by R. W. Watts and J.B. Luoma, 2020, *Journal of Contextual Behavioral Sciences, 15*, p 94. In the public domain.