Outpatient Ketamine Prescribing Practices in Psychiatry in the United States:

A Nationwide Survey Study

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Abstract

Background: Ketamine is an increasingly popular tool for the treatment of psychiatric disorders. Initially available in controlled studies at academic institutions, it is now being offered widely in the community, but little is known about how treatment is actually being delivered and if there are undetermined safety concerns. The aim of this study is to assess ketamine prescribing practices among clinics across the United States.

Methods: An online survey was sent to all community-based ketamine clinics with publicly available email addresses collected from 4 ketamine clinic databases (n = 484) between September and November 2023. Public ketamine clinic websites (n = 473) were also reviewed for information regarding the credentials of prescribers in June 2024.

Results: A total of 126 (26% response rate) of the clinics responded to the survey request, and 119 were included in analyses. All included respondents (100%) report utilizing ketamine for treatment-resistant depression, with many also prescribing ketamine for treatment naive (72.3%), bipolar (78.9%), and subclinical depression (59.7%) in addition to nondepressive conditions at significant rates. Over 80% of clinics utilize maintenance ketamine treatment, with a substantial portion doing so for prolonged periods. A variety of ketamine formulations are regularly prescribed, and over 40% of clinics provide ketamine for at-home use. Based on website review, fewer than 30% of ketamine clinics reviewed are run by psychiatric physicians and over 25% are run by nonphysician providers.

Conclusions: There is significant variability in ketamine treatment in the community including indications for therapy, duration of treatment courses, formulation of ketamine prescribed, and setting of use. There is a need for increased oversight and more specific practice guidelines to ensure ketamine is being used safely, appropriately, and effectively.

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Ketamine has become an increasingly popular pharmacologic tool in treating psychiatric illness in recent years. A dissociative anesthetic with consciousness-altering properties, ketamine has been approved for use in the US for anesthesia and procedural sedation since 1970, with interest in potential use for treating psychiatric illness emerging in the 1990s.[1] Following initial clinical trials beginning in the early 2000s that demonstrated promising results in patients with treatment-resistant depression (TRD),[2,3] academic and community-based outpatient ketamine clinics have opened across the US, and it is estimated that there are now at least 500 clinics offering this treatment nationwide for a variety of diagnostic indications.[4] In 2019, intranasal esketamine was approved for TRD and major depressive disorder (MDD) with acute suicidal ideation.[5] This is currently the only formulation approved by the US Food and Drug Administration (FDA) for psychiatric use. Off-label ketamine prescribing is common practice, but little is known about how treatment is actually being delivered in the community. There are some guidelines available to help direct clinical care, but the evidence base remains fairly limited given the relative novelty of this treatment in psychiatry. While judicious use of intravenous (IV) racemic ketamine and its FDA-approved enantiomer, intranasal esketamine, for TRD has proven both safe and effective in research settings,[6–9] concerns have been raised about the increasing availability of ketamine from clinics in the community and telehealth services, often advertising to treat conditions for which ketamine has minimal data supporting efficacy. While there is benefit in increasing access to treatment, questions have been raised about the risk of unregulated prescribing and potential delivery of substandard and possibly unsafe care.[10–12]

Clinical Points

- Currently, little is known about the delivery of ketamine treatment in community clinics across the US. Ketamine can be a highly effective treatment, but it is necessary to determine if it is being utilized appropriately.
- Findings suggest that there are multiple areas of concern regarding delivery of ketamine treatment in the community. Development of specific treatment guidelines and establishment of a ketamine registry could provide additional patient safeguards.
- Psychiatrists should advocate for involvement in the care of patients receiving this treatment for mental illness and should provide evidence-based education to patients who are considering pursuing this treatment option.

Despite these unknowns, there has not been a systematic investigation into the delivery of ketamine treatment in the community. The aim of this study was to assess current ketamine prescribing practices at outpatient ketamine clinics across the US to better characterize how this treatment is being used to treat patients.

This study was approved by the University of Michigan Institutional Review Board. Some of the data from this survey have been previously published on the topic of reproductive concerns in the context of ketamine treatment for psychiatric illness.[13]

METHODS

The American Society of Ketamine Physicians, Psychotherapists and Providers (ASKP3) online clinic directory was used to obtain publicly available information about community ketamine prescribers across the US. Clinics included in this review were those with active websites including sufficient information about prescribers listed in the directory as of June 2024. Clinic websites were reviewed for information about the education, training, and credentials of the primary ketamine prescriber at the practice. Those without a listed website or insufficient information to determine the prescriber's primary specialty were excluded from analysis.

A request for participation in a 20-question survey available via an online distribution platform (Qualtrics) was sent via email to 484 outpatient ketamine clinics in the US. This cohort of clinics was not identical to the cohort above, but there was significant overlap. Four online community ketamine clinic databases (ASKP3 Directory, Ketamine Directory, Ketamine Clinic Directory, and Find Ketamine Directory) were used to obtain clinic contact information. Responses were collected between September and November 2023. All responding clinics identified as offering ketamine treatment for a psychiatric indication were included in the analysis of results. Academic centers that administer ketamine were not included in the survey cohort as we chose to focus on community clinics because this is where the majority of patients actually receive this care and to exclude information from research studies that is unlikely to represent clinical practice in the community at large. Survey questions were designed to ascertain information about general ketamine prescribing practices including routes of treatment indications, medication formulations utilized, treatment course duration, and telehealth practices among other information. The survey included a combination of question types including those indicating to select all that apply with an option for an additional free-response and multiple choice questions allowing for the selection of a single response. The full survey instrument is available in Supplementary Appendix 1. Respondents were given the option to provide an email address for entry into a drawing for a $50 Amazon gift card, but this was not required for participation.

RESULTS

Of the 488 clinics listed in the ASKP3 directory at the time of website review, 473 (96.9%) had websites with publicly available information about prescriber credentials. Fifteen clinics did not have a listed website or their website lacked necessary information. Of the included clinics (n = 473), 27.7% are run by physicians with postgraduate training in psychiatry. Anesthesia-trained physicians account for 19.5% of prescribers. Nonphysician providers account for 26% of prescribers with 13.5% trained as nurse practitioners and 12.5% as certified registered nurse anesthetists. The distribution of the remainder of prescriber specialties is listed in Table 1.

Of the 484 clinics contacted, survey responses were received from 126 outpatient ketamine clinics in the US (response rate 26%).[13] Seven responses were excluded from reported results as they did not indicate that the clinic prescribed ketamine for a psychiatric indication (they reported prescribing ketamine for pain or other conditions, or did not answer this question). The adjusted response rate based on 119 included responses is 24.6%. 16.1% of respondents reported that their clinic was in the Northeast, 22.6% in the Midwest, 35.5% in the South, and 25.8% in the West. Survey respondents estimated cumulatively treating 7,480 individual patients in a 30-day period.[13]

Of the included responses (n = 119), TRD was the most commonly reported indication with 100% of clinics prescribing ketamine for this condition, followed by posttraumatic stress disorder (PTSD) at 94.1% and

generalized anxiety disorder (GAD) at 82.3%. Clinics also reported prescribing ketamine for treatment-naive depression, bipolar depression, and unspecified depressive symptoms at rates of 73.2%, 78.9%, and 59.7%, respectively. All reported indications are detailed in Table 2. Eighty-two percent of responding clinics reported prescribing maintenance ketamine treatment, and over half of these prescribe maintenance ketamine for at least half of their patients.[13] Additional details about maintenance ketamine courses are listed in Table 3.

The most commonly prescribed route of administration was intravenous (IV), which is reportedly used at 90.8% of clinics, followed by sublingual (52.9%), intramuscular (52%), intranasal (IN) esketamine (32.8%), and IN racemic ketamine (21.8%). Over 40% of prescribers indicate providing ketamine for at-home use as shown in Figure 1. 87% of clinics require at least 1 in-person evaluation during the course of treatment.

Table 1.

Clinics by Prescriber Specialty (n = 473)[a]

Prescriber specialty	
Psychiatry	27.7% (n = 131)
Anesthesia	19.5% (n = 92)
Nurse practitioner	13.5% (n = 64)
Certified registered nurse anesthetist	12.5% (n = 59)
Emergency medicine	11.4% (n = 54)
Family medicine	4.7% (n = 22)
Internal medicine and subspecialties	4.4% (n = 21)
Combination and other	6.3% (n = 30)

[a]Per ketamine clinic websites available via ASKP3 database in June 2024.

DISCUSSION

As ketamine is increasingly utilized as a treatment for psychiatric illness, there is a need to better understand how it is being prescribed to patients in the community as there is a general lack of available practice standards to ensure both medical and psychiatric safety. The results of this study indicate several areas of concern about how this treatment modality is being used in clinical practice, including potential prescribing for inappropriate indications, frequent use of ongoing maintenance treatment, and utilization of potentially unsafe ketamine formulations among other concerns.

It is notable that a minority of ketamine clinics are staffed by board-certified psychiatrists, as most patients seeking ketamine treatment are those with complex, refractory mental health conditions. Of the 473 clinics with available provider credential information in the ASKP3 directory as of June 2024, fewer than 30% were staffed by an MD or DO with postgraduate training in psychiatry. While physicians with anesthesia, emergency medicine, or other training are well-equipped to ensure medical safety, a thorough psychiatric assessment by a trained specialist is indicated when weighing the suitability of various treatment options. Nuanced initial and ongoing evaluations are standard of care for any complex psychiatric presentation, especially if interventional methods are being considered, and this is an important step in determining if ketamine is an appropriate treatment for an individual patient. Even when patients presenting for ketamine treatment report relatively straightforward symptoms consistent with a diagnosis for which there is good or emerging evidence such as TRD or PTSD, there is the possibility that other pathology or comorbidity could be missed.[14,15] A less-experienced clinician may overlook subtle signs of psychosis, substance misuse or personality pathology which might indicate that ketamine is not an appropriate treatment option. While off-label medication prescribing is common in treating psychiatric illness, this is typically done by psychiatric specialists who are actively assessing patients, are providing ongoing monitoring, and have the expertise to manage complex psychopharmacologic problems. It is unclear to what degree psychiatrists are included in the care of patients receiving treatment for mental illness at clinics run by other providers; however, psychiatric specialists should advocate to be very involved in the evaluation and ongoing management of these potentially vulnerable patients.

Survey respondents report prescribing ketamine for a wide variety of indications, which suggests ketamine is being used much more broadly than for TRD alone. The Canadian Network for Mood and Anxiety Treatments Task Force evidence-based recommendations for racemic ketamine prescribing indicate that IV ketamine should be considered a third-line intervention for depression in patients who "exceed minimum criteria for TRD" based on a comprehensive systematic review of available evidence.[16] Despite this, 72% of clinics reported prescribing ketamine for treatment-naive depression and 60% for unspecified depression not meeting full criteria for a major depressive episode. Use of ketamine for unspecified depressive symptoms, in addition to the other conditions detailed in Table 1, indicates that the patient population considered by these clinics to be eligible to receive this intervention may be much larger than previously considered. The efficacy of ketamine for many other conditions (listed in Table 2) has not been well-established, though a significant number of clinics report prescribing ketamine for these indications. The most studied conditions include PTSD, anxiety disorders, OCD, and alcohol use disorder, and preliminary evidence suggests possible efficacy for these conditions; however, a recent extensive review and meta-analysis asserts that "evidence on the effects of ketamine on psychiatric disorders other than MDD remains insufficient."[17(pg.359)] While it is not known how treatment indications differ based on specialty of clinic prescribers, psychiatric expertise is especially important when using ketamine for conditions for which supporting data are limited or

Table 2.

Diagnostic Indications for Ketamine Treatment (n = 119 Survey Respondents)

Indication	
Treatment-resistant depression[a]	100% (n = 119)
Treatment naive depression[b]	72.3% (n = 86)
Bipolar depression[c]	78.9% (n = 92)
Unspecified depression/depressive symptoms[d]	59.7% (n = 71)
Generalized anxiety disorder, social anxiety disorder, or panic disorder	82.4% (n = 98)
Obsessive-compulsive disorder	65.5% (n = 78)
Posttraumatic stress disorder	94.1% (n = 112)
Substance use disorders	44.5% (n = 53)
Personality disorders	16.8% (n = 20)
Suicidal ideation	76.5% (n = 91)

[a]A depressive episode meeting *DSM-5* criteria for major depressive disorder that has not remitted with adequate trials of 2 or more antidepressant medications.
[b]A depressive episode meeting *DSM-5* criteria for major depressive disorder for which the patient has not received at least 2 antidepressant trials medications during the current episode.
[c]A depressive episode that meets full *DSM-5* criteria for a major depressive episode in a patient with a history of a bipolar spectrum disorder or manic/hypomanic episodes.
[d]Depressive symptoms that do not meet full *DSM-5* criteria for major depressive disorder.

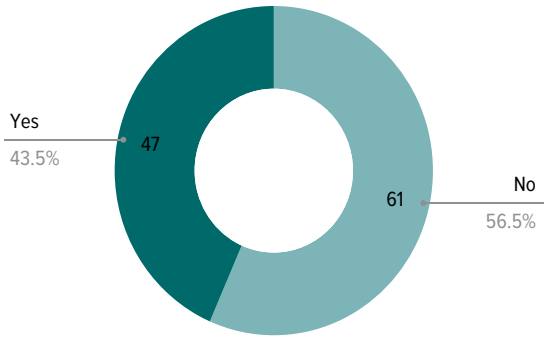
Table 3.

Maintenance Ketamine Prescribing (n = 88 Survey Respondents)

Percentage of patients receiving maintenance treatment	
Less than 25%	15% (n = 13)
25%–50%	28% (n = 24)
51%–75%	36% (n = 31)
76%–100%	22% (n = 19)
Duration of maintenance treatment	
Less than 3 mo	9% (n = 8)
3–6 mo	22% (n = 19)
6–12 mo	24% (n = 21)
Longer than 12 mo	44% (n = 38)

Figure 1.

Ketamine Prescribing for At-Home Use (n = 108 Survey Respondents)



nonexistent. More rigorous study is needed to establish safety and efficacy, especially before this is marketed broadly to patients and utilized widely in clinical practice as an early-line or routine treatment option.[18]

There are some guidelines to help direct the initial course of ketamine treatment,[19] but the durability of response and symptomatic remission following an initial course can be highly variable. Evidence suggests that ongoing maintenance treatment with racemic ketamine for depression is likely effective in preventing relapse and relatively safe,[7] and long-term outcomes involving maintenance esketamine treatments indicate the same.[6] Despite this, there is minimal, if any, information available to guide clinicians with the selection of appropriate patients for ongoing treatment, determination of appropriate dosing frequency and duration, the use of additional psychotropic medications in combination with ketamine for optimal symptomatic control, relapse prevention planning in the context of eventual ketamine taper and discontinuation, or the consideration of indefinite treatment. Over three-quarters of responding clinics are prescribing maintenance treatment, with over half of these doing so for at least half of their patients. Reported treatment durations are often prolonged, with nearly half of clinics prescribing maintenance ketamine doing so for 12 months or longer. While there are certainly cases for which maintenance ketamine can be beneficial, this should be considered carefully on an individual basis taking into account a variety of patient factors as more study is needed to determine how maintenance treatment can be delivered most effectively including if and when it is appropriate to incorporate long-term or indefinite ketamine treatment into routine practice. Given this, maintenance treatment should likely be reserved for use by highly experienced practitioners in patients who have exhausted other treatment options until more evidence is available to support the efficacy and safety of long-term ketamine use.[9]

Research has demonstrated that ketamine is relatively safe in studied populations, but it is not free of

risk. Largely treated in academic settings with rigorous inclusion and exclusion criteria, study populations may not be representative of the actual patients who are receiving ketamine treatment in the community, and underrepresented and special patient populations may be vulnerable to risks that are not yet apparent. For instance, there is a known risk of ketamine abuse and dependency, which is likely minimal when used in appropriately controlled clinical settings. However, there are increasing concerns about possible misuse of ketamine in nonclinically supervised settings and potentially serious medical and psychiatric adverse effects associated with the use of compounded ketamine formulations.[20–22] The majority of responding clinics reported prescribing a compounded formulation of ketamine including over 50% providing oral/sublingual ketamine and over 20% utilizing intranasal racemic ketamine. There is significant variability in the quality and consistency of these products, as well as inconsistent absorption, which can have profound impacts on the effective doses patients are receiving and potential adverse reactions. The evidence for efficacy of non-IV racemic ketamine formulations remains limited, and its use is not widely recommended. Likewise, an optimal treatment setting has not been established; however, available evidence currently only supports the administration of this treatment with supervision.[9] Despite this, nearly half of clinics report prescribing ketamine for at-home use, though almost 90% require an in-person evaluation at least once during the treatment course.

Our survey did not include companies that provide ketamine exclusively for self-administration via telehealth consultation, but these likely account for thousands of additional patients nationwide. Ketamine has become increasingly available through online services that do not require in-person psychiatric evaluation and may obtain minimal objective medical information during the treatment course, potentially deferring the recommendation for a standard pretreatment workup including vital signs and recommended studies for medical clearance including standard laboratory testing assessing blood counts, electrolytes, metabolic markers, thyroid function, urine drug screen, electrocardiogram, and pregnancy status, or other potentially necessary tests for medically complex patients.[19] A recent study of patients using rapidly dissolving sublingual ketamine at home prescribed via an online platform with a "rigorous telehealth program" demonstrated that ketamine use within a "supportive digital health environment was largely safe and well-tolerated"; however, there were notable limitations to this study. Many clinics likely lack robust telehealth monitoring infrastructure and treat patients that would not meet the strict inclusion criteria for this study, so it is not clear how generalizable these results may be to the wider population of patients who may be utilizing ketamine as an at-home treatment. More investigation is needed to determine the safety of this practice in general.[23] In addition to questions about the quality of the assessment process and monitoring by a qualified psychiatric provider, there are questions regarding how responsibly these treatments are being advertised to potential patients. According to the American Psychiatric Association's 2022 position statement, "information provided to consumers/patients through Direct-To-Consumer-Advertising (DCTA) may be designed to persuade rather than inform. DTCA may not provide the necessary balance and objectivity required for consumers/patients to make informed choices."[24] recent cross-sectional study indicated that a substantial proportion of ketamine clinics were misrepresenting or not disclosing potential risks and the off-label nature of the treatment.[25] This includes the possibility of disappointment and worsening hopelessness in the case of nonresponse to treatment, which can include a substantial subset of patients, and this should likely be introduced as a realistic potential outcome prior to treatment initiation.[26]

Ketamine can be a highly effective treatment for appropriate patients suffering from difficult to treat psychiatric symptoms, but determining if this is an appropriate treatment modality requires a thorough, thoughtful psychiatric assessment, and not all patients are good candidates. The results of this study indicate that ketamine is being prescribed more broadly and less discriminately than the current evidence base supports, routes of administration with less data for efficacy and more potential for safety concerns are being utilized frequently, and psychiatrists are not necessarily involved in the care of patients with complex mental health conditions. These findings suggest that there are significant areas of concern with the delivery of ketamine treatment to patients in the community, including lack of adherence to evidence-based clinical practice, potential ethical violations, and opportunities for patient harm. Establishment of a national ketamine registry to assist with ongoing empirical study and quality improvement efforts would be beneficial for both investigation and patient safety. While ketamine is an important clinical tool and can be life-saving, psychiatrists have a responsibility to ensure this treatment is delivered judiciously and safely.

Strengths, Limitations, and Future Directions

As far as the authors are aware, this is the first study characterizing prescribing trends among community ketamine clinics across the US. The information collected in this survey can help determine what large-scale interventions are potentially needed in this industry, as well as inform decisions made by providers, stakeholders, and policymakers to promote optimal

patient safety and efficient delivery of care. Our results should be taken in the context of the limitations of the study, including, most notably, response bias. There were likely differences between clinics that chose to respond to our survey and those who did not. Likewise, there are potential differences in practice between those listed in the online databases and those that are not. The lack of information about what may differentiate our sample from the total group of clinics currently operational in the US could limit generalizability. There were also responses given in the survey, such as diagnoses, which are unverifiable and likely made at least in some part by patient self-report. As a future direction, it would be prudent to inquire with clinics how diagnoses were made and which objective tools were used for both diagnosis and symptom monitoring. There are numerous additional variables that will be important for future study including, but not limited to, patient referral sources, monitoring practices performed during treatment sessions, incidence of adverse outcomes, safeguards for at-home users, barriers to psychiatric involvement, and avenues for advocacy for the inclusion of psychiatrists in delivering this treatment.

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Supplementary Material

Article Title: Outpatient Ketamine Prescribing Practices in Psychiatry in the United States: A Nationwide Survey Study

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LIST OF SUPPLEMENTARY MATERIAL FOR THE ARTICLE

1. **Appendix 1** Ketamine Clinic Survey Questions

DISCLAIMER

This Supplementary Material has been provided by the authors as an enhancement to the published article. It has been approved by peer review; however, it has undergone neither editing nor formatting by in-house editorial staff. The material is presented in the manner supplied by the author.

Appendix 1.
Survey questions:

- 1. Where is your practice located?
  - Northeast
  - Midwest
  - Southeast
  - Southwest
  - West
- 2. Please select all that you prescribe:
  - Intravenous Ketamine
  - Intramuscular Ketamine
  - Intranasal Ketamine (Spravato)
  - Intranasal Esketamine
  - Sublingual/Oral Ketamine
  - Other
- 3. If other, please describe:
- 4. Please select all conditions for which you prescribe ketamine:
  - Treatment-resistant unipolar depression (A depressive episode meeting DSM-5 criteria for Major Depressive Disorder that has not remitted with adequate trials of two or more antidepressant medications).
  - Unipolar depression (A depressive episode meeting DSM-5 criteria for Major Depressive Disorder for which the patient has not received at least two antidepressant trials medications during the current episode).
  - Unspecified depression (A depressive episode that does not meet full DSM-5 criteria for Major Depressive Disorder)
  - Bipolar depression (A depressive episode that meets full DSM-5 criteria for a Major Depressive Episode in a patient with a history of a bipolar spectrum disorder or manic/hypomanic episodes)
  - Post-traumatic stress disorder or other trauma/stressor related disorders
  - Generalized anxiety disorder, social anxiety disorder or other anxiety disorders
  - Obsessive Compulsive Disorder
  - Substance use disorders
  - Personality disorders
  - Suicidal ideation
  - Other
- 5. If other, please describe:
- 6. Approximately how many patients receive one or more ketamine treatments (administered in the office or via prescription for at-home use) in a 30 day period?
- 7. Approximately what percentage of your patients are premenopausal biological females?*
- 8. Do you prescribe ketamine for at-home use?
- 9. If yes, Does your practice provide treatment exclusively via telemedicine?
  - Yes, all patients are seen exclusively via telemedicine
  - Yes, some patients are seen exclusively via telemedicine
  - No, all patients are seen in-person at least once during a course of treatment

- 10. Do you prescribe long-term or maintenance ketamine regimens?
- 11. If yes, Approximately what percentage of patients at your practice continue receiving ketamine treatment for maintenance after the initial course?
    - 0-25%
    - 25-50%
    - 50-75%
    - 75-100%
- 12. How long is a typical course of maintenance ketamine treatment?
    - 0-3 months
    - 3-6 months
    - 6-12 months
    - 12 months or longer
- 13. Does your practice have a standard process for pregnancy testing and/or screening?*
- 14. If yes, how is this performed?*
    - All patients of childbearing potential are asked about possible pregnancy before ketamine treatment is started.
    - All patients of childbearing potential are offered a pregnancy test prior or during ketamine treatment.
    - All patients of childbearing potential are required to take a pregnancy test prior to ketamine treatment.
    - All patients of childbearing potential are required to take pregnancy tests prior to and during a course of ketamine treatment.
- 15. If yes, Please describe the schedule/frequency of pregnancy testing during a course of ketamine treatment:*
- 16. Please select the choice that most accurately represents your verbal informed consent process:*
    - Pregnancy is not routinely discussed during the informed consent process.
    - All patients of childbearing potential are given a general verbal recommendation to avoid pregnancy while receiving ketamine treatment.
    - All patients of childbearing potential are verbally informed of specific risks related to pregnancy and ketamine exposure.
- 17. Please select the choice that most accurately represents your informed consent documentation:*
    - Informed consent forms do not include language about pregnancy.
    - Informed consent forms include a general recommendation to avoid pregnancy while receiving ketamine treatment.
    - Informed consent forms include language about specific risks related to pregnancy and ketamine exposure.
- 18. Does your practice require or specifically recommend contraception use during a course of ketamine treatment for all patients with the potential to become pregnant?*
- 19. If yes, please select the option that best describes your practice:*
    - Contraception use is required during treatment
    - Specific recommendations about pregnancy prevention are made (i.e. patients are advised to see a primary care physician to discuss options for contraception, or

sexually active patients are counseled to use a reliable birth control method during treatment, etc).
        - A general recommendation to avoid pregnancy is made, but contraception is not discussed specifically.
        - Other
    - 20. If other, please describe:*
    - 21. (OPTIONAL) Enter an email address to be entered in a drawing for a $50 amazon gift card:

*Data from questions denoted by an asterisk was not included in this paper, but has been previously published in “Pacilio, R. M., Lopez, J. F., Parikh, S. V., Patel, P. D., & Geller, J. A. (2024). Safe Ketamine Use and Pregnancy: A Nationwide Survey and Retrospective Review of Informed Consent, Counseling, and Testing Practices. The Journal of clinical psychiatry, 85(3), 24m15293. https://doi.org/10.4088/JCP.24m15293)