

## Attitudes and Perceptions of Portuguese Psychiatrists and Psychologists on the Clinical Use of Ketamine

### Atitudes e Perceções dos Psiquiatras e Psicólogos Portugueses sobre o Uso Clínico de Cetamina

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#### ABSTRACT

**Introduction:** Ketamine has garnered attention for its rapid efficacy in alleviating depressive symptoms in treatment-resistant depression, offering a novel mechanism as a non-monoaminergic agent. Despite its potential, limited research has explored mental health professionals' perspectives on its use. This study assesses the attitudes, knowledge, and concerns of Portuguese psychiatrists and psychologists regarding the clinical application of ketamine in treatment-resistant depression.

**Methods:** A cross-sectional survey study was conducted from June 2022 to January 2024 among Portuguese psychiatrists and psychologists. The anonymous online questionnaire assessed perceptions of ketamine's therapeutic utility, risks, and knowledge sources. Statistical analyses examined subgroup differences by age, sex, profession, and prior psychedelic use.

**Results:** Among 156 participants (mean age = 37.2; 68.6% female), 53.8% were psychologists, and 46.2% were psychiatrists or trainees in Psychiatry. Only 35.9% reported substantial knowledge of ketamine's therapeutic potential, while 59% were open to integrating it clinically. The majority expressed interest in training, though 73% raised concerns about inadequate professional training. Significant differences emerged, with psychiatrists reporting higher knowledge levels and openness to ketamine compared to psychologists, while younger professionals showed greater interest in training and usage.

**Conclusion:** There was a favorable attitude toward ketamine use among Portuguese psychiatrists and psychologists, yet substantial educational gaps remain. Customized training addressing age, sex, and professional background is essential for safe and effective clinical integration of ketamine in treatment-resistant depression. Further studies should focus on longitudinal outcomes of ketamine treatment under standardized protocols to ensure efficacy and safety in clinical practice.

**Keywords:** Attitude of Health Personnel; Depressive Disorder, Treatment-Resistant/drug therapy; Ketamine/therapeutic use; Surveys and Questionnaires

#### RESUMO

**Introdução:** A cetamina é um fármaco que tem despertado um maior interesse devido à sua eficácia rápida na atenuação dos sintomas depressivos na depressão resistente ao tratamento, oferecendo um mecanismo inovador enquanto agente não monoaminérgico. Apesar do seu potencial, há uma escassez de investigação sobre as perspetivas dos profissionais de saúde mental relativamente à sua utilização. Este estudo avalia as atitudes, o conhecimento e as preocupações dos psiquiatras e psicólogos portugueses quanto à aplicação clínica da cetamina na depressão resistente ao tratamento.

**Métodos:** Foi realizado um estudo transversal através de um inquérito entre junho de 2022 e janeiro de 2024, abrangendo psiquiatras e psicólogos portugueses. O questionário, anónimo e online, avaliou perceções sobre a utilidade terapêutica, os riscos e as fontes de conhecimento sobre a cetamina. As análises estatísticas examinaram diferenças entre subgrupos segundo idade, sexo, profissão e experiência prévia com psicadélicos.

**Resultados:** Entre os 156 participantes (média de idade = 37,2 anos; 68,6% do sexo feminino), 53,8% eram psicólogos e 46,2% eram psiquiatras ou médicos internos de Psiquiatria. Apenas 35,9% relataram ter um conhecimento substancial sobre o potencial terapêutico da cetamina, enquanto 59% demonstraram abertura para a sua integração na prática clínica. A maioria mostrou interesse em obter formação específica, embora 73% tenham expressado preocupações quanto à insuficiência da formação profissional disponível. Observaram-se diferenças significativas: os psiquiatras reportaram níveis de conhecimento e abertura superiores aos dos psicólogos, enquanto os profissionais mais jovens mostraram maior interesse na formação e utilização da cetamina.

**Conclusão:** Pareceu existir uma atitude favorável à utilização da cetamina entre psiquiatras e psicólogos portugueses; no entanto, persistem lacunas educacionais significativas. A formação personalizada, considerando idade, sexo e contexto profissional, é essencial para uma integração clínica segura e eficaz da cetamina no tratamento da depressão resistente ao tratamento. Estudos futuros deverão focar resultados longitudinais do tratamento com cetamina sob protocolos padronizados, garantindo eficácia e segurança na prática clínica.

**Palavras-chave:** Atitude do Pessoal de Saúde; Cetamina/uso terapêutico; Inquéritos e Questionários; Perturbação Depressiva Resistente a Tratamento/tratamento farmacológico

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## KEY MESSAGES

- Ketamine shows promise as a treatment for depression, with rapid antidepressant effects and potential benefits for treatment-resistant cases.
- Most participants expressed openness to using ketamine clinically, with 78.9% seeking further training and 79.4% advocating for more research.
- Significant knowledge gaps were evident, as only 35.9% of participants reported good understanding of ketamine's therapeutic potential.
- Concerns about safety included inadequate training, risk of psychosis, and potential for misuse, emphasizing the need for structured protocols.
- Strengths of the study include its diverse sample and comprehensive insights, while limitations include self-selection bias and reliance on self-reported data.

## INTRODUCTION

Over the last decades, ketamine – a glutamatergic modulating drug with psychedelic properties, formally approved as an anesthetic – has stood out in the scientific literature and psychiatric clinical practice due to its rapid onset of action and effectiveness in relieving depressive symptoms.<sup>1</sup> Its mechanism of action is unique, being a non-monoaminergic agent with proven efficacy in major depression.<sup>2</sup> A single infusion of ketamine in sub-anesthetic doses demonstrates a rapid antidepressant effect, with a peak effect within 24 hours, and which remains superior to placebo for up to 10 - 12 days.<sup>1</sup> Meta-analytic evidence reveals that repeated administrations of ketamine sustain the antidepressant response, an effect observed up to four weeks after the last treatment applied.<sup>1</sup>

Scientific support for the off-label use of ketamine in psychiatric disorders – mainly in treatment-resistant depression (TRD) – relies on more than 20 years of research through placebo and active-treatment-controlled clinical trials, systematic reviews with meta-analysis, and real-world evidence.<sup>3</sup> Positive results from more than 40 randomized controlled trials led to the recent recognition of intravenous ketamine as level 1 evidence (higher quality of evidence), supporting its integration as a second-line treatment in the management of TRD in a recent update of the international treatment guidelines for depression from The Canadian Network for Mood and Anxiety Treatments (CANMAT), which are among the most widely used by psychiatrists around the world.<sup>4</sup> The intravenous administration of ketamine (0.5 - 1.0 mg/kg) is therefore no longer considered an “experimental treatment” according to the guidelines authors, but now appears as one of the options to be considered after failure of treatment with antidepressants, together with other equally established treatments with level 1 evidence such as lithium, quetiapine or intranasal esketamine (one of the enantiomers of ketamine, and therefore possessing similar effects).<sup>4</sup>

Furthermore, despite lingering questions about the ther-

apeutic value of ketamine's subjective experience, several studies suggest that the presence of psychedelic experiences promotes greater benefits and may improve mental health and well-being.<sup>5</sup> This has generated a lot of debate about its subjective effects and also uncertainty about how its use can be optimized or which model of approach is safer and more effective to be used in patients with psychiatric disorders. Preliminary data also suggest ketamine holds potential for treating alcohol and other substance use disorders in combination with structured behavioral therapy.<sup>6-8</sup>

Over the past decade, some researchers have examined mental health professionals' attitudes and beliefs about integrating psychedelic substances into clinical practice. Studies in the United States provided important insights into these perspectives. Barnett *et al* found that psychiatrists generally viewed psychedelics as dangerous and supported keeping them illegal for recreational use.<sup>9</sup> However, a follow-up study published in 2024 showed a significant shift, with many psychiatrists now recognizing the therapeutic benefits of psychedelics and planning to use psychedelic-assisted therapy in their practice if approved, with younger psychiatrists being particularly optimistic.<sup>10</sup> Similarly, a survey with clinical psychologists found generally favorable attitudes toward psychedelic-assisted therapy, although they remained cautious about potential psychiatric and neurocognitive risks.<sup>11</sup> The survey also revealed a significant lack of education and training about psychedelics. Most of these studies, however, only integrated perspectives from mental health professionals concerning classic psychedelic substances [such as psilocybin and lysergic acid diethylamide (LSD)] and 3,4-methylenedioxymethamphetamine (MDMA), which still lack sustained scientific evidence that could result in their approval for clinical use. On the other hand, professional perspectives regarding the clinical use of ketamine have not been explored as much, despite being a more common and widespread practice worldwide. However, a study conducted by Levin *et al* included the

perspectives of psychiatrists on different psychedelic substances, including ketamine, with participants rating psilocybin and ketamine as safer and with greater therapeutic potential than substances like alprazolam.<sup>12</sup> Overall, these findings highlight the need for comprehensive educational programs to prepare healthcare professionals to safely and effectively use psychedelic-assisted therapies.

In Portugal, the antidepressant properties of ketamine sparked interest in Portuguese psychiatric services. Since 2021, ketamine treatments have been made available according to different protocols in both public and private institutions, most of them taking advantage of its psychedelic effects, and usually with psychological support before, during and after ketamine administration. Despite that, data regarding the efficacy and safety of this approach in any of these institutions have not yet been published. Taking these recent developments into account, it is timely to assess the knowledge, attitudes, and perceptions of Portuguese psychiatrists and psychologists regarding ketamine and its therapeutic potential for psychiatric disorders. This assessment is crucial to understand the readiness and receptivity of healthcare providers to integrate new treatments with psychedelic drugs into their clinical practice. It will also identify educational gaps and inform the development of specific training programs to ensure that healthcare professionals are well-equipped to use psychedelic therapies safely and effectively.

## METHODS

The present study has been developed by the Interdisciplinary Centre for the Study of Human Performance's (CIP-ER) Behavioral Regulation research group at the University of Lisbon, in partnership with the Portuguese Society for Clinical Application of Entheogens (SPACE). It also results from a research partnership with the Johns Hopkins School of Medicine (JHSM) which is conducting a similar study in the United States of America. The study was approved by the Faculty of Human Kinetics Review Board. It represents a cross-sectional study that employed a descriptive online survey from an opportunistic volunteer sample. The target population was currently practicing Portuguese clinical psychologists, psychiatrists and Psychiatry trainees, and registered in their respective professional organizations.

Participants were asked to answer an anonymous and confidential online survey that encompassed professional characterization and their perceptions and attitudes towards the clinical use of ketamine in Psychiatry at a single time point. The survey was originally developed by psychedelic science specialists at JHSM. The measures included are a series of self-constructed items that assess knowledge, perceptions and attitudes on ketamine treatments for which no previous measures were found in the literature.

Topics addressed were: attitudes and beliefs, perceived knowledge, acceptability, concerns, sources of knowledge, trusted sources for future training, secondary effects, and treatment indications. All items were subject to a backtranslation process and were reviewed by bilingual experts to ensure accuracy and cultural relevance.

Data was collected between June 1<sup>st</sup>, 2022 and January 31<sup>st</sup>, 2024, through a secure internet-based survey platform and stored in a password-protected *LimeSurvey* institutional account. The survey was disseminated in social media, institutional newsletters, and survey lists through collaboration with professionals' associations (Portuguese Psychologists Association; The Portuguese Society of Psychiatry and Mental Health and its online platform of the Mental Health Observatory). Preliminary results of this study were presented as part of the official program of the XVI National Congress of Psychiatry, held in November 2022, in order to also foster the engagement of participants.

All analyses were carried out using IBM-SPSS® 29.0 statistical software. Sample characteristics were reported as frequencies and percentages for categorical variables, and as means and standard deviations (SD) for continuous variables. Data were not normally distributed (they deviated from normality sufficiently to affect statistical inference). Differences between groups were assessed with non-parametric tests (Mann-Whitney U test or Kruskal-Wallis test, as appropriate) for continuous variables. Subgroup analyses were conducted according to sex, age groups, and profession. Data are expressed with significance threshold of  $p < 0.05$ .

## RESULTS

A total of 156 Portuguese mental health professionals (68.6% women) completed the questionnaire [mean age = 37.2 (SD = 10.9)]. From this sample, 53.8% were psychologists and 46.2% were medical doctors (15.4% psychiatrists

Table 1 – Descriptive statistics for participant characteristics

| Variable             | Value       |
|----------------------|-------------|
| Age (Mean ± SD)      | 37.2 ± 10.9 |
| Women (%)            | 68.6%       |
| Education Level (%)  |             |
| - Bachelor           | 18.6%       |
| - Masters            | 75.6%       |
| - PhD                | 7.2%        |
| Profession (%)       |             |
| - Medical doctor     | 46.2%       |
| - Psychiatrist       | 15.4%       |
| - Psychiatry trainee | 30.8%       |
| - Psychologist       | 53.8%       |

and 30.8% psychiatrists in training) (Table 1). A minority of the sample (43.6%) declared doing research in some way, and 39.7% of participants reported having had a previous personal experience with a psychedelic substance. Figure 1 and Fig. 2 demonstrates the attitudes of mental health professionals, as well as knowledge and concerns towards ketamine clinical use in Psychiatry.

### Perceptions, attitudes and acceptability

Only 35.9% of participants reported good knowledge on the therapeutic potential of ketamine and only a third (32.7%) reported good knowledge of its risks and side effects. The majority of participants (59%) indicated that they did not have good knowledge of ketamine's pharmacology. A small percentage (13.5%) reported having patients who have used ketamine. Most participants (62.9%) agreed that ketamine is a promising treatment and expressed openness to using ketamine in treating their patients (59.6%). A significant majority (78.9%) desired training on the clinical use of ketamine for psychiatric disorders, and 79.4% believed more research on ketamine was warranted. Only 4.4% disagreed that ketamine can be safely administered in a clinical setting, while 31.4% were undecided. Lastly, 37.4% agreed that health professionals' prior personal experience with ketamine is important for effectively integrating treatment with their patients, with 28.4% remaining neutral.

### Concerns

The most frequently reported concerns involving ketamine, rated as very or extremely worrying, included the lack of professionals with specialized training (73%), abuse or exploitation of patients (56%), and improper recreational use (58%). Moreover, 50% of the participants were very or extremely concerned about the administration of ketamine to patients with contraindications and 48% were concerned about the potential for psychotic outbreaks. A smaller percentage of participants (44%) expressed concerns related to the potential risk of ketamine addiction.

### Sources of knowledge and training

Participants reported that they primarily obtained information from the scientific and academic literature (51.9%), other health professionals (42.4%), informal conversations (37.3%) and the media (34.8%). When asked about their trusted sources, health professionals favored research centers (84.2%), professional organizations (79.7%), and more experienced colleagues (74.7%) (Table 2).

### Contexts of administration and therapeutic potential

Participants reported that the most suitable places for the clinical administration of ketamine were specialized clinics (67.1%), followed by hospital settings (59.8%) and rehabilitation clinics (43.7%). Some mental health professionals indicated that current evidence suggests ketamine can be

Attitudes and knowledge towards ketamine

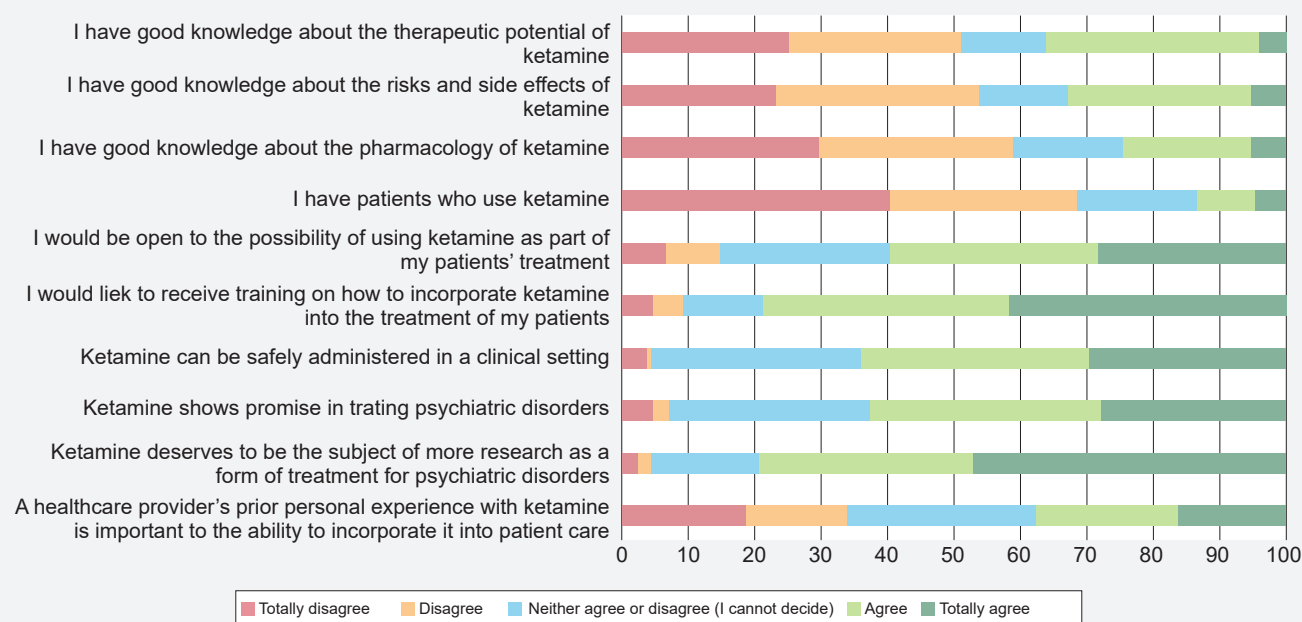
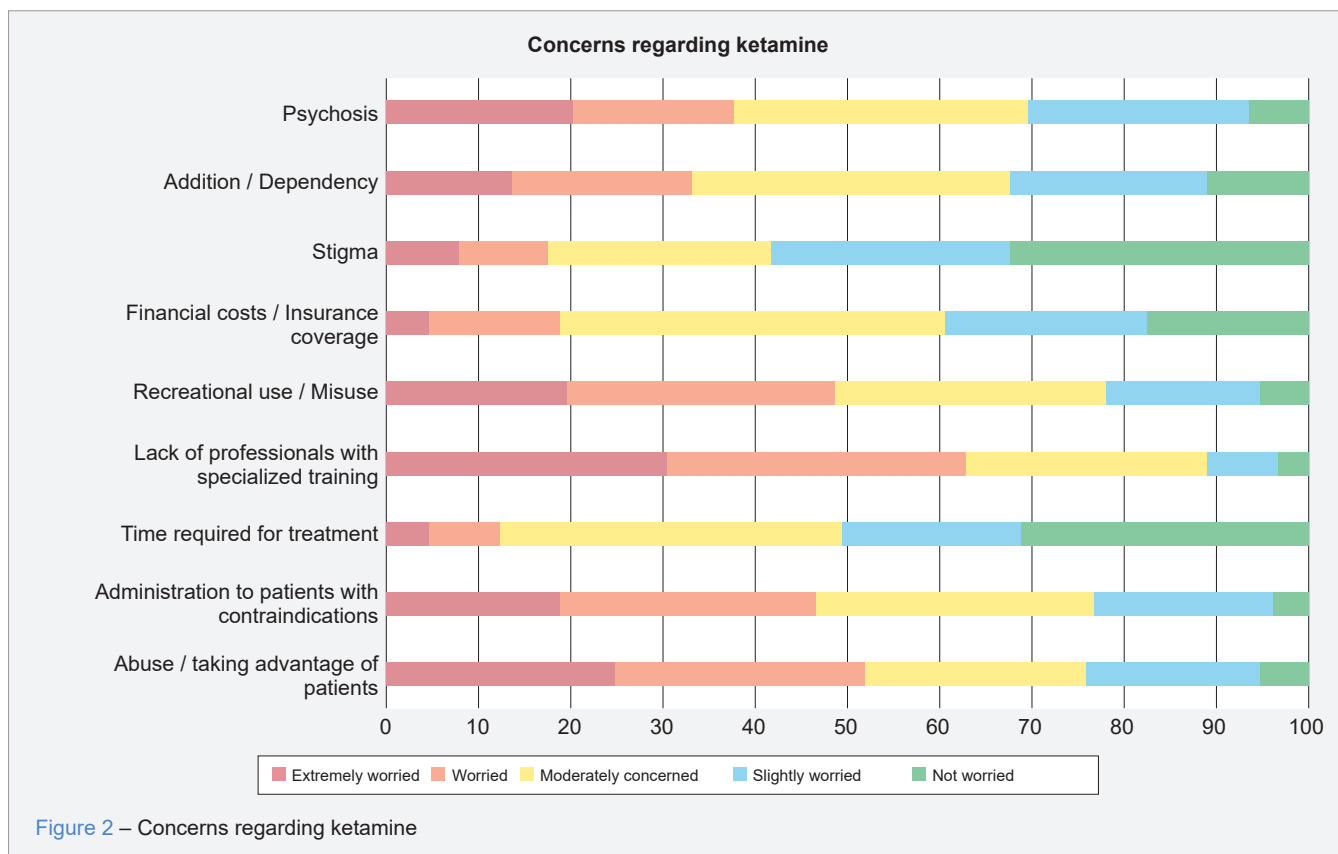


Figure 1 – Attitudes and knowledge towards ketamine



useful in the treatment of depression (77.9%) and suicidal ideation (40.9%).

### Influence of training/profession

Psychiatry doctors reported significantly higher perceptions of having good knowledge about ketamine's therapeutic potential ( $p < 0.001$ ), its risks and side effects ( $p < 0.001$ ), and also its pharmacology ( $p < 0.001$ ). They also reported greater openness to integrating ketamine treatments into their clinical practice ( $p < 0.001$ ), receiving specific training ( $p < 0.001$ ), also recognizing that it can be used safely in

clinical settings ( $p < 0.001$ ), and that this is a promising intervention ( $p < 0.001$ ) that should be the target of further future research ( $p = 0.0038$ ). Regarding concerns, there were also significant differences between the two professional categories. Psychologists expressed greater concern about the risk of psychosis ( $p = 0.005$ ), addiction ( $p = 0.028$ ), and misuse of ketamine ( $p = 0.028$ ). They were also more concerned about the lack of properly trained professionals ( $p = 0.044$ ), administration of ketamine to patients with contraindications ( $p < 0.001$ ), and potential for patients' abuse or exploitation ( $p = 0.001$ ).

Table 2 – Sources of knowledge and training

| Sources of knowledge and training  | % (156) |
|--|---------|
| Formal clinical training (e.g., university, private organization, or pre/postgraduate) | 32      |
| Colleagues   | 42      |
| Scientific/academic literature   | 52      |
| Presentations at conferences or workshops  | 34      |
| Media (e.g., books, films, podcasts, social networks, online forums)                   | 35      |
| Informal conversations   | 37      |
| Previous experiences with patients   | 10      |
| Personal experiences   | 7       |
| I have no knowledge  | 19      |



### Influence of age

The Kruskal-Wallis test was conducted to determine if there were statistically significant differences in responses between different age groups. The age groups were defined as follows:  $\leq 35$  years, 36 - 49 years, and  $\geq 50$  years. The test results showed statistically significant differences between age groups in the self-assessment of knowledge about the therapeutic potential of ketamine ( $p = 0.001$ ), about its risks and side effects ( $p = 0.0013$ ), and also its pharmacology ( $p = 0.001$ ). Post-hoc comparisons showed that self-perceived knowledge was significantly higher in those three parameters amongst the  $\leq 35$  years group compared to the 36 - 49 years group ( $p = 0.001$ ,  $p = 0.004$  and  $p = 0.001$ , respectively), while the same was true for the  $\geq 50$  years group compared to the 36 - 49 years group regarding knowledge about the therapeutic potential of ketamine ( $p = 0.050$ ), and its pharmacology ( $p = 0.002$ ). Additionally, there were statistically significant differences between group ages regarding willingness to use ketamine as part of treatment for their patients ( $p = 0.001$ ), willingness to receive training ( $p = 0.005$ ) and on the perception that ketamine can be safely administered in clinical settings ( $p = 0.045$ ). Post-hoc comparisons indicated both attitudes were significantly higher for the  $\leq 35$ -year-old group than the 36 - 49-year-old group ( $p = 0.001$ ,  $p = 0.002$ , and  $p = 0.027$ , respectively). About the concerns on the clinical use of ketamine, the Kruskal-Wallis test indicated that there were significant differences between different age categories only regarding the risk of psychosis ( $p = 0.035$ ). Post-hoc comparisons presented that this concern was higher amongst the 36 - 49 years group compared to the  $\leq 35$  years group ( $p = 0.012$ ).

### Influence of gender

The Mann-Whitney test indicated that there were significant differences between gender groups in their attitudes and perceptions. Specifically, men showed significantly more positive perceptions regarding knowledge about ketamine's therapeutic potential ( $p = 0.001$ ), about its risks and side effects ( $p = 0.001$ ), and also its pharmacology ( $p = 0.001$ ). Additionally, men were more willing to use ketamine as part of treatment for their patients ( $p = 0.008$ ) and favored the perceptions that it can be administered safely in clinical settings ( $p = 0.05$ ) and that ketamine is promising for the treatment of psychiatric disorders ( $p = 0.019$ ). Men agreed significantly more often with the perspective that a health-care provider's prior personal experience with ketamine is important to their ability to incorporate it into patient care ( $p = 0.042$ ). There were no significant differences between male and female participants in their levels of concern for any of the aspects regarding its clinical administration.

### Influence of previous psychedelic use

Significant differences were observed in perceptions and attitudes about ketamine between participants who had previously used psychedelic substances compared to those who had not. The results indicated that previous users reported greater interest in considering using ketamine as part of their patients' treatment ( $p = 0.025$ ), desire to receive information on incorporating ketamine into their clinical practices ( $p = 0.001$ ) and agreement with the importance of personal experience with ketamine for health professionals ( $p = 0.003$ ). Significant differences were also observed regarding several concerns, where previous psychedelic users showed that they were less concerned about addiction/dependence ( $p = 0.007$ ), psychosis ( $p = 0.036$ ), and time required for treatment ( $p = 0.002$ ).

### DISCUSSION

Especially during the past decade, there has been a global increase in clinical research on psychedelics. Concurrently, countries with specific regulatory frameworks, such as Switzerland, Australia, and Canada, have progressively integrated psychedelic substances like psilocybin and MDMA into their mental health services.<sup>13-16</sup>

Clinical use of ketamine for psychiatric disorders (mostly depression) has been more significant and widely available, driven by the accumulation of scientific evidence of its efficacy and safety, making it essential that mental health professionals become well informed about this therapeutic approach.<sup>17,18</sup> To our knowledge, this is the first published study that sought to describe attitudes and perspectives of Portuguese psychiatrists and clinical psychologists regarding the use of ketamine for psychiatric disorders. This is important given the availability of ketamine treatment in Portugal. Assessment of Portuguese professionals is also of interest given that Portugal has been an early innovator in drug policy reform. This research provides valuable insights into perceptions, acceptability, concerns, and the influence of demographic factors such as sex, age, and work experience on these attitudes.

According to our findings, there is a general openness among Portuguese mental health professionals towards the clinical use of ketamine for psychiatric disorders. Almost 80% desired further training in ketamine treatment models, as most participants considered ketamine to be a promising treatment and expressed openness to using ketamine in treating their patients. These findings align with previous studies on the clinical use of other psychedelic drugs, which also reported high levels of interest and perceived the need for further research and training among mental health professionals.<sup>10,19,20</sup>

Despite this, it is worth highlighting that the psychiatrists and psychologists who participated in this survey currently

lacked sufficient knowledge on the therapeutic potential of ketamine and its risks and side effects. However, most participants correctly recognized that ketamine has frequently been studied and used in the treatment of depression and suicidal ideation.<sup>1,21</sup> Considering this, it is relevant to highlight that only about half the sample reported acquiring their knowledge about ketamine primarily through the scientific and academic literature and about a third acquired knowledge or training through formal clinical training. This highlights the need for targeted education and training programs, something which has already been identified in the literature.<sup>11,22</sup> This is particularly relevant because the main concern expressed by the participants in this survey was precisely the administration of ketamine by professionals who are not properly trained, as explored below. Another relevant aspect is related to perceptions of trustworthiness regarding sources of information on the clinical use of ketamine. When asked about their trusted sources, mental health professionals predominantly chose research centers, professional organizations, and more experienced colleagues. It is important to notice that participants were much more reluctant regarding receiving information from private institutions and from pharmaceutical corporations. These findings indicate that professional, formal and peer-reviewed sources are crucial for mental health professionals to access trusted information about ketamine treatments for psychiatric disorders. Therefore, universities, research centers and professional societies should be informed of their important role in educating and training mental health professionals in this specific field.

The present study showed that the main concerns regarding ketamine's clinical use were the lack of trained professionals, the administration to patients with contraindications, and the potential for patient abuse/exploitation. Similar concerns have been highlighted in other studies regarding interventions with psychedelics, indicating a common apprehension about the current readiness of the professional community to manage psychedelic therapies safely.<sup>22</sup> These concerns thus emphasize the need for comprehensive training programs and stringent regulatory frameworks to ensure safe and ethical clinical practices, something that has been highlighted by the recent increase in articles published on this particular topic.<sup>23-29</sup> In this regard, although the offer of professional training in this area is increasing throughout the world, there is a large heterogeneity in training programs and in the skills and background of the trainers.

In Portugal, to date, there has been no training program specifically dedicated to the clinical use of ketamine, so Portuguese professionals currently involved in this practice underwent their training in different international centers. Despite this, SPACE currently provides an online introduc-

tory course on the clinical use of psychedelics and also published a scientific manual on this subject, initiatives that had the scientific support of The Portuguese Society of Psychiatry and Mental Health.<sup>30</sup> A practical guide regarding the clinical use of ketamine aimed at Portuguese mental health professionals was also published, derived from a national collaboration between clinicians with theoretical training and practical experience in administering ketamine for mental health disorders. Some of these experts were responsible for implementing the first ketamine-assisted therapy protocols in the Portuguese National Health Service.<sup>31</sup> Concomitantly, a multidisciplinary group was set up in Portugal, involving several professional societies and the national ethics authority, to anticipate challenges in the regulation of treatments with psychedelics.<sup>32</sup> One of the objectives of this group is to promote ethical and safe practices, having recently proposed practical recommendations in this area, for public discussion.

Participants reported that the most appropriate settings for the clinical administration of ketamine were specialized clinics, followed by hospital settings. The current regulation of ketamine in Portugal requires that it can only be administered in hospitals or similar settings. Over the last few years, ketamine treatment has been made available in Portugal in hospitals and specialized clinics, although each entity has specific protocols approved by the respective ethics and pharmacy committees. No data regarding the efficacy and safety of these interventions have been published yet by any of these clinical teams.

Regarding safety, only a minority of the participants disagreed with the statement that ketamine can be safely administered in a clinical setting, though 31.4% remained undecided. Overall, scientific evidence suggests that the use of ketamine in depression and suicidal ideation is considered a safe and effective treatment.<sup>4,33-35</sup> Recently, CANMAT established a task force to evaluate the evidence on both the efficacy and safety of ketamine in clinical settings.<sup>4</sup> Despite recognizing the effectiveness of this intervention, CANMAT determined that due to potential side effects and feasibility issues, intravenous ketamine (as well as intranasal esketamine) should be considered a second-line treatment for depression.<sup>4</sup> Reported adverse events from ketamine infusions include both psychological symptoms (such as dissociation or anxiety) and physiological effects (more commonly a transient increase in blood pressure). However, the current literature indicates that with basic medical screening, the incidence of serious medical adverse events is very low (~0.1%) when ketamine is used for psychiatric disorders.<sup>4,36</sup> Concerns about the potential for psychotic outbreaks were shared by almost half of our respondents. The development of psychotic symptoms has been described, but primarily in individuals who are

prolonged recreational users of ketamine.<sup>37</sup> Furthermore, most clinical trials have excluded patients with a personal history of psychotic episodes.<sup>38</sup> Despite the theoretical risk of ketamine aggravating psychotic symptoms, several case studies demonstrated that treatment with ketamine not only improved mood, but also improved psychotic symptoms in patients with treatment-resistant depression with psychotic features.<sup>38-40</sup> However, the safety of ketamine in these patients is controversial since ketamine is known to induce psychotomimetic and dissociative effects and further evidence is necessary to establish the efficacy and the safety of ketamine in this population.<sup>38,39</sup>

Another concern was related to the potential risk for ketamine addiction. Morgan *et al* found that chronic ketamine recreational users (compared to controls) showed more attentional bias (the preferential allocation of attention to cues associated with reward, influencing perception and behavior) to incentive stimuli, consistent with the designation of ketamine as a potentially addictive drug.<sup>41</sup> In this regard, and although a specific withdrawal syndrome has not yet been identified, tolerance to the drug in daily users may develop rapidly.<sup>41</sup> Notably, despite ketamine's potential for recreational use, no studies or reviews to date have reported a transition to illicit use stemming from therapeutic introduction to ketamine, although anecdotally such cases exist.<sup>3</sup> In fact, clinical trials tend to exclude potential patients who have previously abused this substance. Interestingly, it is important to recognize that ketamine has also been studied and used clinically in the treatment of substance use disorders, with therapeutic success reported in studies on different substances, most frequently alcohol.<sup>7,42-45</sup> Future research should continue to monitor this potential adverse effect of ketamine, especially in patients who need maintenance treatments.

### Between group differences in attitudes and concerns

Professional background influenced perceptions and attitudes, with psychiatrists being more familiar with ketamine treatments and showing greater openness. Psychologists seem more concerned about ketamine's possible deleterious effects, which may also be due to lower self-perceived knowledge regarding this treatment. This divergence may reflect differences in training and clinical exposure between these professional groups, suggesting the need for interdisciplinary education and collaboration to harmonize understanding and practices. It may also reflect differences in the scope of professional activities, given that only psychiatrists prescribe medicines. These findings are also consistent with previous studies who also reported varying levels of knowledge and attitudes across different professional groups.<sup>9,19</sup>

Age-related differences also emerged, with younger

professionals ( $\leq 35$  years) showing higher levels of willingness to use ketamine in treatment and a stronger desire for more information compared to older groups. Barnett *et al* (2018) found similar results suggesting that today's trainees and young psychiatrists may encounter more favorable information about psychedelics in both the medical literature and the lay press.<sup>9</sup> In our sample, this trend was statistically significant when comparing the youngest group with the 36 – 49-year-old group, but was not verified when comparing the youngest with the oldest group ( $> 50$  years). This older group also showed significantly greater knowledge of the therapeutic potential of ketamine and its pharmacology when compared to the intermediate age group. These results highlight important asymmetries to be explored in the future and may indicate the group of mental health professionals between 36 - 49 years old as a specific target for education/training.

Regarding differences between men and women, men perceived themselves as more knowledgeable of the therapeutic potential, risks, and pharmacology of ketamine and reported more positive attitudes towards its clinical use, findings that are aligned with those from Grover *et al* (2023).<sup>46</sup>

Significant differences in attitudes were observed based on clinicians' prior psychedelic use, with past users of psychedelics reporting more positive attitudes towards ketamine's clinical use. This suggests that personal experience with psychedelics may influence professional perspectives, a finding supported by different other studies who noted similar trends in the United States of America and Australia.<sup>19,46,47</sup> Currently, there is an open discussion in the scientific and therapeutic community about the role of personal experience in the quality of professional practices in this field.<sup>48</sup>

### Strengths and limitations

This study encompassed different professional groups, having obtained a greater number of participants compared to similar studies in other countries.<sup>46</sup> Secondly, the study expands the existing literature by assessing clinicians' knowledge, current clinical practices, and comfort levels in discussing clinical use of ketamine in psychiatric disorders. This approach includes evaluating the associations between these variables, thereby identifying specific knowledge gaps and targets for future education efforts in Portugal. However, this study also has several limitations, such as the potential for selection bias due to the self-selected nature of this sample. Individuals who are more open to or have strong opinions about psychedelics may have been more motivated to participate, potentially skewing the results. This bias limits the external validity of the findings, as professionals with less openness or more neutral views might be underrepresented. Additionally, while the sample



included almost an equal distribution of psychologists and psychiatrists, this does not reflect the actual proportions in the Portuguese professional landscape, where there are far more psychologists than psychiatrists. Finally, the study relied solely on self-reported data that can be subject to biases such as social desirability or inaccurate recall. Future research should include other professionals (e.g., nurses) and an increased sample size.

## CONCLUSION

This study reveals a generally positive but cautious view among Portuguese mental health professionals regarding the clinical use of ketamine. There is a clear need for more education, training and research to address knowledge gaps and safety concerns, as well as comprehensive training programs to prepare professionals for integrating psychedelic therapies into practice.<sup>25,46</sup> Accordingly, future studies should focus on examining the long-term effects of ketamine treatments for patients with psychiatric disorders under standardized protocols.

## AUTHOR CONTRIBUTIONS

PM: Data collection, writing of the manuscript.

JE, LCC: Statistical analysis, critical review of the manuscript.

CC: Data collection, critical review of the manuscript.

AGR, MWJ, PJT: Survey questionnaire design, critical review of the manuscript.

All authors approved the final version to be published.

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## PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in October 2024.

## DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

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