

Аналіз психіатричних протипоказань до застосування кетаміну як допоміжного засобу в психотерапії

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Актуальність та мета. Депресія є дуже поширеним захворюванням, і 30–60 % пацієнтів не реагують належним чином на стандартну терапію. Кетамін-асистована психотерапія є перспективним підходом, проте психіатричні протипоказання до неї досі не стандартизовані. Метою цього дослідження було систематизувати протипоказання до кетамін-асистованої психотерапії, пов'язані з психічним здоров'ям.

Матеріал і методи. Ми проаналізували 74 публікації, відібрали 15 ключових клінічних настанов та оглядових статей для складання уніфікованого переліку психіатричних протипоказань, а потім проаналізували 126 цільових досліджень для оцінки ризиків кожного стану. Кожне протипоказання було класифіковано як таке, що залишається в переліку, вилучене або підтверджене недостатніми доказами.

Результати. Стани було розділено на три групи. Шизофренія, шизоафективний розлад, депресія з психотичними симптомами, психотичні симптоми, делірій, манія, біполярний розлад I типу, когнітивні порушення та розлади харчової поведінки із соматичною декомпенсацією повинні залишатися протипоказаннями. АСД, ОКР та нелікована апное сну можуть бути виключені зі списку, тоді як докази щодо розладів особистості кластера В залишаються недостатніми. Ця структурована система може покращити відбір пацієнтів та безпеку терапії.

Висновки. У цьому дослідженні пропонується трирівнева класифікація психіатричних протипоказань до КАП на основі клінічного ризику. Хоча розлади високого ризику повинні залишатися обмеженими, деякі стани можна переглянути з метою виключення. Потрібні подальші масштабні дослідження для уточнення стратифікації ризику та стандартизації протоколів безпеки.

Ключові слова: кетамін, кетамін-асистована психотерапія, резистентна до лікування депресія, психічні розлади, протипоказання, безпека лікування.

Introduction

Depression is one of the most common mental disorders in the world and a leading cause of disability. According to estimates by the World Health Organization, approximately 280–350 million people worldwide suffer from depression, accounting for about 3.8–5% of the population (Chiriță et al., 2015; Marcus et al., 2012; Stringaris, 2017; Sultana et al., 2023). Depression is 1.5–3 times

more common in women than in men (Sultana et al., 2023). Each year, about 1 in 20 people report an episode of depression (Marcus et al., 2012; Praghlapati 2020). In the worst cases, depression can lead to suicide. Each year, approximately 800,000 people die by suicide, making it the second leading cause of death among people aged 15 to 29 (Machado et al., 2024). Thus, depression is the leading cause of disability worldwide (Marcus et al., 2012; Reddy, 2010; Stringaris, 2017).

There is confirmed evidence of a trend toward increasing prevalence of depression that cannot be explained solely by changes in research methods (Goodwin et al., 2022; Moreno-Agostino et al., 2021). The prevalence of depression has increased particularly since 2020, when over 53 million additional new cases were recorded; this is linked to the COVID-19 pandemic (Sultana et al., 2023). The gap between the number of people who need treatment for depression and those who seek help ranges from approximately 16% to 84% across different countries. The global average rate of untreated depression is about 56%. In other words, more than half of people diagnosed with depression do not seek help and do not receive professional care (Magaard et al., 2017). Therefore, actual prevalence rates may be significantly higher. Depression affects hundreds of millions of people worldwide, and its prevalence continues to rise. It is a serious public health problem that requires attention and effective support and treatment measures.

Pharmacotherapy using antidepressants and psychotherapy are currently the primary methods of treating depression. Antidepressants are widely used to treat depression, and numerous large-scale studies show that they are statistically more effective than placebos. However, complete remission is achieved in far from all patients. Response to antidepressants is a significant challenge in the treatment of depression: between 30% and 60% of patients do not achieve an adequate response to antidepressant therapy (Fanelli et al., 2020; Fava, 2003; Feltes et al., 2017; Mojtabai et al., 2021). This underscores the need for an individualized approach and the search for new therapeutic strategies.

The use of ketamine within the framework of ketamine-assisted psychotherapy (KAP) or as a standalone pharmacological agent is one of the new methods for treating depression that is currently receiving significant attention and for which high hopes are pinned. Esketamine (the S-enantiomer of ketamine), known under the brand name Spravato, is used as a pharmacological agent outside of KAP for the treatment of depressive disorders. It was officially approved by the FDA for the treatment of treatment-resistant depression in March 2019 as an adjunct to antidepressants (combination therapy) (Vekhova et al., 2024). In December 2019, the FDA and the European Medicines Agency (EMA) added the indication of treatment-resistant depression (TRD) for Spravato. In January 2025, the FDA approved changes allowing Spravato to be used as monotherapy for the treatment of treatment-resistant depression (TRD) (Rahrig et al., 2025). At the same time, ketamine in the form of a racemic mixture is used off-label by specialized clinics as an innovative treatment for treatment-resistant mental disorders, including depression, post-traumatic stress disorder (PTSD), anxiety disorders, and other mental disorders. Ketamine has a rapid antidepressant effect, particularly in patients with suicidal thoughts, making it an important tool in modern psychopharmacotherapy (Berman et al., 2000; Krystal et al., 2019).

The widespread use of ketamine for the treatment of depressive disorders necessitates an understanding of the drug's safety profile. It is well known that depression has a high rate of comorbidity with other mental disorders, some of which may preclude the use of ketamine for the treatment of depression. A review of the current literature indicates the absence of a unified classification of psychiatric contraindications to ketamine use, which complicates clinical decision-making. For this reason, it is important to conduct a systematic analysis of the available scientific data to create a structured system of psychiatric contraindications. It also makes sense to conduct a critical analysis of each of these contraindications to assess the validity of including a given psychiatric condition in the list of contraindications.

Materials and methods

To achieve this objective, we conducted a systematic review and critical analysis of the scientific literature. In the initial stage, we analyzed 74 publications, including clinical protocols of various levels, practical guidelines and recommendations, consensus statements from expert groups, meta-analyses, and systematic reviews that provided clinical recommendations. From the publications reviewed, we selected 15 that contained clear lists of contraindications or exclusion criteria related to the patient's mental health prior to ketamine administration. After a detailed review of the aforementioned 15 publications, we systematized the contraindications and exclusion criteria listed therein and compiled a unified list of mental health-related contraindications.

In the next stage of the study, we selected and analyzed scientific publications dedicated to the use of ketamine in relation to each of the psychiatric conditions included in the list we had compiled. For this purpose, 126 publications were selected and analyzed. Thus, we critically evaluated each of the identified psychiatric contraindications for actual risk to the life and health of patients, taking into account new data from scientific studies specific to each of the listed contraindications.

After reviewing and critically evaluating each contraindication on the list, we formulated a recommendation for each one, choosing one of three options:

- keep it on the list of contraindications,
- remove it from the list of contraindications,
- insufficient information to formulate a recommendation.

Results

The contraindications for ketamine-assisted therapy that we identified after analyzing the sources are presented in Table 1.

Contraindications		Sources
Current episode or history of schizophrenia		Galecki et al., 2024; Texas Health and Human Services [TX HHS], n.d.; Tham et al., 2021; VA PBM, 2022b; VA Pharmacy Benefits Management Services et al. [VA PBM], 2022a; VHA Office of Integrated Veteran Care, 2025
Current episode or history of schizoaffective disorder		Galecki et al., 2024; Tham et al., 2021; TX HHS, n.d.; VA PBM, 2022a; VA PBM, 2022b; VHA Office of Integrated Veteran Care, 2025
Depressive disorder with psychotic symptoms		VA PBM, 2022b
Psychotic symptoms	Active	Beaglehole et al., 2023; Chrenek et al., 2024; Cohen et al., 2018; Galecki et al., 2024; McInnes & Yu, 2020; McIntyre et al., 2021; Schwenk et al., 2018; Swainson et al., 2020; Tees, Esk and Wear Valleys NHS Foundation Trust [TEWV], 2023; Tham et al., 2021; TX HHS, n.d.
	History of:	TEWV, 2023; Tham et al., 2021; TX HHS, n.d.
Delirium	Acute:	VA PBM, 2022a; VA PBM, 2022b; Tham et al., 2021; VHA Office of Integrated Veteran Care, 2025; Cohen et al., 2018
	Within the last 7 days:	VA PBM, 2022a; VHA Office of Integrated Veteran Care, 2025
	Within the last 30 days:	VA PBM, 2022b
Symptoms of mania	Manic symptoms:	TX HHS, n.d.

	History of manic episodes caused by drugs or medications	TEWV, 2023
Current episode or history of bipolar disorder		VA PBM, 2022a; VA PBM, 2022b; VHA Office of Integrated Veteran Care, 2025
Obsessive-compulsive disorder		VA PBM, 2022b
Personality disorders according to DSM-5		Beaglehole et al., 2023; Tham et al., 2021; VA PBM, 2022b
Cognitive impairments	Major Neurocognitive Disorders (Dementia)	Beaglehole et al., 2023; Galecki et al., 2024; Tham et al., 2021; VA PBM, 2022a; VA PBM, 2022b; VHA Office of Integrated Veteran Care, 2025
	Intellectual Disability	VA PBM, 2022b
Autism		VA PBM, 2022b
Active eating disorders. Anorexia nervosa or bulimia nervosa within the past 12 months		Galecki et al., 2024
Untreated sleep apnea		McInnes & Yu, 2020

Table 1. *Psychiatric Contraindications for Ketamine*

Current episode or history of schizophrenia

Ketamine is widely used as a pharmacological model of psychosis in schizophrenia because its action as an NMDA receptor antagonist induces temporary positive, negative, and cognitive symptoms in healthy individuals that are similar to those observed in patients with schizophrenia (Frohlich & Van Horn, 2013; Kruse & Bustillo, 2022; Lahti, 2001; Vollenweider et al., 1997).

Studies show that ketamine can reproduce characteristic changes in brain activity, particularly hyperfrontality and impaired connections between the thalamus and the cortex, which are also found in patients with schizophrenia (Abram et al., 2022; Vollenweider et al., 1997).

A number of studies emphasize that ketamine causes an exacerbation of psychotic symptoms in patients with schizophrenia, particularly positive symptoms such as hallucinations, delusions, and thought disorders (Beck et al., 2020; Evanoff et al., 2023; Lahti et al., 1995; Lahti, 2001; Malhotra, 1997).

At the same time, an analysis of 9 studies (pilot and clinical reports) involving a total of 41 patients concluded that short-term ketamine treatment may be safe and effective in patients with depression who have a history of or current psychotic symptoms. Side effects were generally mild and resolved spontaneously (Veraart et al., 2021). A review of individual clinical cases suggests that a single intravenous administration of ketamine may be a safe and promising option for treating catatonia in patients with schizophrenia who do not respond to standard therapy (Siddiqui, 2024).

It must be acknowledged that the available data are limited, and the findings of studies are contradictory. Further research is needed to categorize patients by risk levels and to develop specialized clinical protocols.

Given this, at this stage, we consider it appropriate to retain the criterion “Current episode or history of schizophrenia” in the list of contraindications for PAT.

Current episode or history of schizoaffective disorder

Currently, there is a lack of sufficient research on the safety of ketamine use in patients with schizoaffective disorder. However, there are isolated reports describing the successful use of ketamine to treat treatment-resistant depression or catatonia in cases where other methods have proven ineffective; with no exacerbation of psychotic symptoms observed (Brown et al., 2017; Gonzales et al., 2005; Gregor & Zheng, 2023; Ribeiro et al., 2015; Turkia, 2024).

A systematic review of clinical cases and small studies has shown that short-term use of ketamine in patients with psychotic symptoms (current or in history) may be safe and effective for treating depression, and side effects are usually mild and transient (Veraart et al., 2021). However, it should be noted that this review did not focus exclusively on patients with schizoaffective disorder.

It must be acknowledged that the available data are limited. Further research is needed to categorize patients by risk level and to develop specialized clinical protocols.

Given this, at this stage, we consider it appropriate to retain the criterion “Current episode or history of schizoaffective disorder” in the list of contraindications for PAT.

Depressive disorder with psychotic symptoms

A systematic review of existing clinical studies and an analysis of several individual clinical cases have shown that short-term use of ketamine in patients with depression and psychotic symptoms can be both effective and safe: side effects were mild and transient, and no exacerbation of psychotic symptoms was observed (Gałuszko-Węgielnik et al., 2023; Veraart et al., 2021).

In the general population of patients with depression, ketamine demonstrates a rapid and pronounced antidepressant effect; however, it may cause transient psychotomimetic phenomena, which typically do not progress to persistent psychosis (Corriger & Pickering, 2019; McGirr et al., 2015; Short et al., 2017).

At the same time, most studies of ketamine for depression have excluded patients with psychosis, so the available data remain limited, and larger-scale studies are needed to draw definitive conclusions (Veraart et al., 2021; Zhang & Ho, 2016).

It must be acknowledged that the available data are limited; therefore, further research is needed to categorize patients by risk level and develop specialized clinical protocols.

Given this, at this stage, we consider it appropriate to retain the criterion “Depressive disorder with psychotic symptoms” in the list of contraindications for ECT.

At the same time, we consider it necessary to emphasize that it is the symptoms of psychosis in this case that constitute an obstacle to enrolling patients in PAT programs. Therefore, this criterion can be viewed as an illustration of psychotic disorders in general as a contraindication to therapy.

Psychotic symptoms (current or past)

Psychotic symptoms constitute a broad and diverse group of mental phenomena characteristic of a wide range of psychiatric disorders and conditions. Therefore, the term “psychotic symptoms” as one of the contraindications for CAP cannot be viewed as a single, isolated phenomenon and cannot be subject to an unambiguous critical assessment regarding the validity of its inclusion in the relevant list. This issue requires further elaboration and a separate examination of the various types of psychotic symptoms.

Ketamine is used as a model of psychosis in healthy volunteers because, at high doses, it can induce transient psychotic symptoms similar to those of schizophrenia (Bentaleb et al., 2023; Lahti, 2001; Powers et al., 2015). In patients with schizophrenia, ketamine may exacerbate positive psychotic symptoms, and in healthy individuals, it may induce schizophrenia-like manifestations, making it a valuable tool for studying the neurobiology of psychosis (Beck et al., 2020; Bentaleb et al., 2023; Lahti, 2001; Malhotra, 1997; Okada et al., 2020; Zorumski et al., 2016). Chronic ketamine abuse in some cases leads to the development of persistent psychosis with cognitive impairments resembling the clinical picture of schizophrenia (Cheng et al., 2018). Furthermore, data from functional neuroimaging studies confirm that ketamine induces changes in brain networks similar to those

observed in schizophrenia; this further underscores its significance as an experimental model of psychosis (Bentaleb et al., 2023; Zorumski et al., 2016).

At the same time, the clinical use of ketamine to control aggression or psychomotor agitation carries a risk of exacerbation (worsening) of psychotic symptoms, especially in vulnerable individuals (Evanoff et al., 2023). However, recent reviews indicate that short-term use of ketamine for the treatment of depression in patients with psychotic symptoms does not necessarily lead to a worsening of psychosis, and side effects are predominantly mild and transient (Perbet et al., 2018; Veraart et al., 2021). Research findings also show that the presence of psychotic symptoms is not an absolute contraindication to the therapeutic use of ketamine, although further studies are needed to confirm its safety in this patient group (Costa et al., 2023; Evanoff et al., 2023; Veraart et al., 2021). Thus, although ketamine is a powerful tool for studying psychosis, its use in patients with psychotic disorders requires considerable caution and further research (Cheng et al., 2018; Costa et al., 2023; Evanoff et al., 2023; Lahti, 2001; Veraart et al., 2021).

It must be acknowledged that the available data remain limited. Further research is needed to categorize patients by risk level, to specify the types of psychotic symptoms within the context of specific psychiatric nosologies or conditions, and to develop specialized clinical protocols.

In light of this, at this stage, we consider it appropriate to retain the criterion “Psychotic symptoms (active or in history)” in the list of contraindications for PAT.

Delirium

The use of ketamine for the prevention or treatment of delirium remains a matter of debate. Large randomized trials have shown that a single administration of a sub-anesthetic dose of ketamine during surgery does not reduce the incidence of postoperative delirium in elderly patients, and in some cases may even cause adverse psychiatric effects, including hallucinations and nightmares (Avidan et al., 2017; Hollinger et al., 2020; Hovaguimian et al., 2018). At the same time, there are studies whose authors reach the opposite conclusion: the intraoperative use of S-ketamine in thoracic surgery in predominantly elderly patients has the potential to effectively prevent postoperative delirium (Chen et al., 2025).

Other studies and retrospective analyses indicate that low doses of ketamine may reduce the incidence and duration of delirium in intensive care unit patients, particularly when mechanical ventilation is used (Faisal et al., 2024; Li et al., 2019; Perbet et al., 2018). Some studies confirm that the use of ketamine under strictly regulated protocols is safe for the management of psychomotor agitation or delirium (Mo et al., 2020; O'Brien et al., 2024). In contrast, other observations suggest that the use of ketamine for sedation in the intensive care unit may be an independent risk factor for the development of delirium, although these findings require further confirmation (Wu et al., 2021).

Studies in animal models demonstrate that (R)-ketamine is capable of reducing neuroinflammation and cognitive impairments associated with delirium; however, these results have not yet been confirmed in humans (Zhang et al., 2021). Thus, current information from scientific sources regarding the use of ketamine for the prevention and treatment of delirium-like disturbances of consciousness is characterized by diametrically opposed conclusions.

This necessitates further research to categorize patients by risk level and develop specialized clinical protocols. In light of this, at this stage, we consider it appropriate to retain the criterion “Delirium” in the list of contraindications for PAT.

Symptoms of Mania

We were unable to find studies describing the use of ketamine in patients with symptoms of mania

and its direct effect on these symptoms. The use of ketamine in patients in the depressive phase of bipolar disorder is relatively safe; however, in some cases, adverse effects are possible, including the risk of manic or hypomanic switching (Jawad et al., 2023a).

Individual studies analyze clinical cases of mania induced by or associated with ketamine use (Allen et al., 2019; Doernberg et al., 2016; Hu et al., 2021; Lu et al., 2016; Mandyam & Ahuja, 2017; Ricke et al., 2011; Wilkowska et al., 2020). These data suggest the drug's potential to induce symptoms of mania or hypomania. In addition, it is worth noting the lack of scientific information regarding the safety of ketamine use in patients with existing manic symptoms.

Given this, it can be concluded that there are currently insufficient grounds to exclude mania (or hypomania) from the list of contraindications. Therefore, at this stage, we consider it appropriate to retain the criterion "Symptoms of mania" in the list of contraindications for PAT.

At the same time, it should be acknowledged that the available data remain limited; therefore, further research is necessary to categorize patients by risk level and to develop specialized clinical protocols.

Bipolar disorder

The vast majority of the studies we analyzed contain data supporting ketamine's potential as a treatment for reducing depressive symptoms in patients with treatment-resistant bipolar depression (Bahji et al., 2021; Cuomo et al., 2025; Dean et al., 2021; Wilkowska et al., 2020; Wilkowska et al., 2021). Some studies also highlight ketamine's antisuicidal activity in bipolar affective disorder (BAD) (Wilkowska et al., 2020; Wilkowska et al., 2021).

For the most part, the analyzed data indicate an acceptable safety profile and a low risk of mood switching during ketamine use in BAD (Bahji et al., 2021; Cuomo et al., 2025; Fancy et al., 2023; Santucci et al., 2024; Wilkowska et al., 2020; Wilkowska et al., 2021).

Although the use of ketamine is relatively safe, adverse effects are possible in some patients, including the risk of manic or hypomanic switching (Bahji et al., 2021; Fancy et al., 2023; Jawad et al., 2023b). Data from one review (Bahji et al., 2021) indicate that ketamine was generally well-tolerated, although there was a possibility of manic symptoms occurring. In this analysis, which included 6 studies with 135 participants, two cases of manic symptoms were reported: one in the ketamine group and one in the placebo group (Bahji et al., 2021).

Some studies examine specific clinical cases of mania associated with ketamine use (Allen et al., 2019; Wilkowska et al., 2020). At the same time, one study (Wilkowska et al., 2020) provides valuable information on comparing the risks of affective switching in the treatment of major depressive disorder (MDD) with ketamine versus traditional antidepressants. According to its results, the risk of depression switching to a manic or hypomanic state during ketamine treatment was low: only 1.7% (6 out of 235 patients) developed manic symptoms, which is lower than the corresponding rates for traditional antidepressants (3–10%) (Wilkowska et al., 2020).

Overall, the research data indicate an acceptable safety profile and a low risk of affective switching. At the same time, the authors highlight the lack of available information and recommend further research (Bahji et al., 2021; Dean et al., 2021; Jawad et al., 2023b; Santucci et al., 2024; Wilkowska et al., 2020; Wilkowska et al., 2021).

In conclusion, it can be concluded that the CAP method shows potential promise in the treatment of depressive disorders in BAD. Although there are currently insufficient grounds to completely exclude "Bipolar Affective Disorder" from the list of contraindications, there are compelling reasons to discuss narrowing this criterion. At this stage, we consider it appropriate to retain this condition on the list of contraindications for CAP, but in a modified form—"Type I BAD."

However, it must be acknowledged that the available data remain limited; therefore, further research is necessary to categorize patients by risk level and to develop specialized clinical protocols.

Obsessive-Compulsive Disorder

Available data from studies and meta-analyses suggest that ketamine therapy could potentially be considered a treatment for obsessive-compulsive disorder (OCD), as it provides rapid symptom relief and enhances the therapeutic effect when combined with traditional psychotherapy methods. Relevant studies demonstrate promising results (Bandeira et al., 2022; Beaglehole et al., 2024; Bottemanne & Arnould, 2021; Kaltenboeck et al., 2023; Martinotti et al., 2021; Puialto et al., 2024).

At the same time, the long-term safety and efficacy of ketamine for OCD remain unknown, and there is currently insufficient evidence to recommend it as a standard treatment (Bandeira et al., 2022; Martinotti et al., 2021; Puialto et al., 2024).

Some researchers suggest that combining ketamine with psychotherapy may prolong the positive effect, but this hypothesis requires further study (Bandeira et al., 2022; Bottemanne & Arnould, 2021).

In light of this, it can be concluded that there is currently sufficient grounds to discuss the exclusion of OCD from the list of contraindications for CAP.

However, it must be acknowledged that the available data remain limited; therefore, further research is necessary to categorize patients by risk level and to develop specialized clinical protocols.

Personality Disorders According to the DSM-5

We were unable to find sufficient information in the available scientific literature regarding the use of ketamine in patients with various types of personality disorders as defined by the DSM-5 criteria. Currently, a sufficient body of data exists only regarding the use of ketamine in borderline personality disorder (BPD).

In a pilot randomized trial, ketamine was well tolerated by patients with borderline personality disorder, and side effects were short-lived and did not lead to serious complications (Fineberg et al., 2023). Similar results were obtained in a number of other studies (Chen et al., 2022; Danayan et al., 2023; Olivola et al., 2024). Some publications describe cases of symptom reduction in borderline personality disorder with the use of low doses of ketamine, particularly when administered sublingually (Liestner et al., 2024).

Patients with treatment-resistant depression and comorbid borderline personality disorder who received ketamine demonstrated a significant reduction in the severity of depression and BPD symptoms, as well as a decrease in suicidality and anxiety (Danayan et al., 2023). Significant improvements were achieved in categories of impulsivity (self-harm, suicide attempts, and other types of impulsive behavior) and affective symptoms (inappropriate anger, chronic feelings of emptiness, emotional instability) (Olivola et al., 2024).

At the same time, descriptions of several clinical cases have shown that in patients with borderline personality disorder, impulsive behavior, suicidal thoughts, self-harm, and dissociative symptoms may emerge or intensify during ketamine treatment (Gałaszko-Węgielnik, Jakuszkowiak-Wojten, et al., 2023; Vanicek et al., 2022). In such cases, therapy had to be discontinued due to the development of adverse effects.

Overall, CAP appears to be a promising treatment method for patients with depression and

comorbid borderline personality disorder. However, the potential risk of increased impulsivity and suicidal tendencies necessitates further research to categorize patients by risk level and develop specialized clinical protocols.

It must be acknowledged that the available data remain extremely limited; therefore, at this stage, there is insufficient information to formulate a definitive recommendation regarding this group of disorders.

Cognitive impairments

The professional literature describes several clinical cases demonstrating improvements in mood, cognitive function, and daily activity levels in patients with dementia following ketamine treatment. Specifically, in the case of a 56-year-old woman with early-stage dementia resistant to standard pharmacotherapy, a significant improvement in cognitive abilities, mood, and daily functioning was observed following a two-month course of intravenous ketamine infusions (Tadros et al., 2024).

Another study examines clinical cases of ketamine use for treating depression and managing acute aggression in patients with dementia; no serious side effects were reported. The authors emphasize that ketamine has the potential to treat depression and correct behavioral symptoms in individuals with dementia (Kapoor et al., 2024). The authors of several other review studies reach similar conclusions regarding ketamine's therapeutic potential for treating depression in patients with neurological disorders (Shehata et al., 2022; Wang et al., 2022).

In contrast, studies in animal models show conflicting results:

- on the one hand, long-term ketamine use induces neurodegenerative changes with impaired cognitive function (Fan, 2022; Luo et al., 2020);
- on the other hand, no statistically significant effect of ketamine (whether administered acutely or chronically) has been observed on early behavioral abnormalities associated with Alzheimer's disease (Wright et al., 2025).

A number of other studies emphasize that ketamine's effect on cognitive processes is complex and directly depends on the dose, route of administration, and duration of use. Despite evidence of short-term benefits in improving cognitive function and mood, long-term use of the drug is associated with a risk of developing cognitive deficits (Zhang & Ho 2016).

In summary, it should be noted that the available clinical data are extremely limited, and there are currently no large-scale studies that conclusively confirm the efficacy and safety of ketamine for improving mood, cognitive function, or daily activities in patients with dementia. Further studies are needed to categorize patients by risk level and to develop specialized clinical protocols.

Furthermore, we question the ability of a patient with severe cognitive impairment to fully understand the terms of treatment within the paradigm of psychedelic-assisted therapy (PAT) and to provide valid, informed consent for the procedure.

In light of this, at this stage, we consider it appropriate to retain the criterion "Cognitive Impairments" in the list of contraindications for ADT.

Autism Spectrum Disorders (ASD)

We found no data in the available scientific literature suggesting that ketamine use leads to a deterioration in the mental or physical condition of patients with autism spectrum disorder (ASD).

One animal study demonstrated the development of symptoms similar to those of the autism

spectrum following ketamine administration in the early postnatal period (Bove et al., 2022). However, this information is of purely theoretical significance to us, as the use of psychedelic-assisted therapy (PAT) in the early postnatal period is clinically irrelevant and unlikely.

Instead, the individual clinical cases reviewed indicate positive changes in ASD symptoms and comorbid mental disorders following the administration of the drug (Harris et al., 2024; Kastner et al., 2016; Özgen & Van Den Brink, 2022). Furthermore, a randomized, double-blind, placebo-controlled study involving 21 patients with ASD demonstrated that ketamine was safe and well-tolerated by patients (Wink et al., 2021).

In light of this, we are inclined to conclude that there is currently sufficient basis to discuss the exclusion of autism (ASD) from the list of contraindications for ECT, provided that the patient is in a stable and controlled mental state.

At the same time, further research is needed to categorize patients by risk level and to develop specialized clinical protocols.

Eating Disorders

The analyzed scientific studies provide grounds for considering CBT a potential treatment for eating disorders, particularly in cases resistant to standard therapy (Escobedo-Aedo et al., 2025; Keeler et al., 2021; Martinotti et al., 2021; Ragnhildstveit et al., 2021; Ragnhildstveit et al., 2022; Robison et al., 2022). Studies indicate significant improvements in mood and a reduction in symptoms in patients with eating disorders when ketamine is used within psychotherapeutic approaches (Keeler et al., 2021; Martinotti et al., 2021; Robison et al., 2022).

In the available literature, we found no data indicating specific adverse effects or increased psychiatric risks associated with the use of ketamine-assisted psychotherapy (KAP) in patients with eating disorders. Based on the information presented, we are inclined to assert that eating disorders should be considered a potential indication for KAP rather than a contraindication.

At the same time, the real danger for this category of patients lies precisely in the somatic complications of AN: somatic instability, electrolyte imbalance, critical deviations in body weight, acute metabolic disorders, and states of “active purging.”

In view of this, at this stage we consider it appropriate to retain the criterion “Eating Disorders” in the list of contraindications for OAT, but to rephrase it in a modified and clinically justified version: “Eating Disorders in a state of somatic decompensation.”

It should be acknowledged that further research is necessary to definitively confirm safety, categorize patients by risk level, and develop specialized clinical protocols.

Obstructive Sleep Apnea Syndrome (OSAS)

Studies involving patients with obstructive sleep apnea syndrome (OSAS) have shown that the use of ketamine during surgical procedures does not improve postoperative respiratory parameters, does not reduce the need for oxygen, and does not decrease pain intensity or the need for opioids. Moreover, the use of high doses of the drug may even prolong the duration of the need for supplemental oxygen therapy (Schreiner et al., 2020).

Some publications describe clinical cases of ketamine use for sedation in critically ill patients; however, this occurred exclusively under close monitoring in intensive care units (Brown, 1986). Thus, the use of ketamine in patients with untreated apnea is generally not recommended due to the risk of respiratory depression; it should only be used under strict medical supervision with readiness to immediately ensure airway patency (Alattas et al., 2022; Driver & Reardon, 2017;

Jonnavithula et al., 2008).

At the same time, it should be emphasized that all the above-mentioned precautions apply to the use of ketamine during surgical procedures or for deep sedation of critically ill patients. In the available scientific literature, we found no information regarding any adverse effects of ketamine use in subanesthetic doses during routine TAC, when the patient does not experience excessive sedation and remains responsive to their surroundings.

In light of this, we take it upon ourselves to question the validity of maintaining “untreated sleep apnea” as a contraindication to TMS. At present, we believe there are sufficient grounds to discuss the exclusion of obstructive sleep apnea from the list of contraindications to TMS.

However, further research is necessary to confirm safety, categorize patients by risk level, and develop specialized clinical protocols. Our recommendations, based on an analysis of the evidence, regarding each contraindication are presented in Table 2.

Contraindications	Conclusion
Current episode or history of schizophrenia	Keep in the list of contraindications
Current episode or history of schizoaffective disorder	Keep in the list of contraindications
Depressive disorder with psychotic symptoms	Keep in the list of contraindications
Psychotic symptoms	Keep in the list of contraindications
Delirium	Keep in the list of contraindications
Symptoms of mania	Keep in the list of contraindications
Bipolar affective disorder	There are sufficient grounds to discuss narrowing the definition of the “BAR” criterion and formulating it as “Type I BAR”
Obsessive-compulsive disorder	Remove from the list of contraindications
Personality disorders according to DSM-5	Insufficient information to form a recommendation
Cognitive impairments	Keep in the list of contraindications
Autism spectrum disorders	Remove from the list of contraindications
Active eating disorders. Anorexia nervosa or bulimia nervosa within the last 12 months	Keep it on the list of contraindications, but revise the wording to read: “Eating disorders in a state of somatic decompensation.”
Untreated sleep apnea	Remove from the list of contraindications

Table 2. Study Results

Discussion

This study systematized the available scientific data on psychiatric contraindications to the use of ketamine. The availability of a structured and scientifically grounded list of contraindications is intended to optimize the clinical decision-making process and minimize the risk of adverse complications in patients undergoing ketamine-assisted psychotherapy (KAP). The compiled list was reviewed, and each of the listed contraindications was critically evaluated for actual risk to the life and health of patients, taking into account the latest data from relevant scientific studies.

An analysis of thirteen mental conditions traditionally considered contraindications for ketamine-assisted psychotherapy (KAP) indicates the need to revise current restrictions, as at least three of them are currently being successfully treated off-label in specialized facilities. A substantial body of clinical reports and review articles confirms the experience of using KAP for obsessive-compulsive disorder (OCD), the depressive phase of bipolar affective disorder (BAD), and eating disorders (EDs), making their continued inclusion in the list of contraindications insufficiently justified.

Based on the available data, it is proposed to exclude OCD from this list provided the patient’s condition is stable, as well as to modify the approach to other nosologies: specifically, to narrow the

restrictions regarding BAD, leaving only Type I of the disorder on the list of contraindications. Regarding eating disorders, it is advisable to limit the criterion exclusively to states of somatic decompensation, which will allow for expanded access to therapy for somatically stable patients with anorexia nervosa or bulimia.

Furthermore, the appropriateness of retaining a condition such as “Untreated sleep apnea” on the list is called into question. Since, within the CAP paradigm, ketamine is administered in sub-anesthetic doses that do not result in complete loss of consciousness or disorientation, we recommend removing this condition from the list of contraindications.

We reached a similar conclusion regarding autism spectrum disorders (ASD): current scientific sources indicate the safety of therapy for this category of patients provided their mental state is stable, which provides grounds for recommending the exclusion of ASD from the list of contraindications.

Regarding the criterion “Cluster B personality disorders (according to DSM-5),” the available scientific information is extremely limited, and researchers’ conclusions are inconclusive. Therefore, this condition has been classified as one for which there is currently insufficient data to formulate a clear recommendation.

In contrast, another group of mental conditions is characterized by a high likelihood of complications arising from the use of ketamine. This group includes: schizophrenia (current episode or history), schizoaffective disorder, depressive disorder with psychotic symptoms, presence of psychotic symptoms (active or in history), delirium, symptoms of mania, and cognitive impairments. Based on the current scientific evidence, we strongly recommend retaining these conditions in the list of contraindications.

It is important to emphasize that virtually all of the analyzed psychiatric conditions require further clinical research. This is a necessary prerequisite for accurately categorizing patients by risk level and developing standardized professional clinical protocols.

Conclusion

As a result of this study, a structured list of psychiatric contraindications to the use of ketamine-assisted psychotherapy (KAP) was compiled and critically evaluated for the first time. Based on a systematic review of the scientific literature, all identified conditions were classified into three groups according to the level of established clinical risk and the extent of the available evidence.

An important practical outcome of the study was the identification of a separate group of psychiatric conditions for which there are sound grounds for reconsideration and potential exclusion from the list of contraindications. At the same time, the study confirmed the need to maintain strict restrictions for those disorders that pose a direct threat of exacerbating the patient’s condition during therapy.

Despite the results obtained, available information regarding the safety profile of ketamine in many comorbid mental disorders remains limited. Most of the conditions analyzed require further large-scale clinical studies to accurately stratify risks and develop standardized clinical protocols that will regulate the safe use of ketamine-assisted psychotherapy.

Conflict of interests

The authors declare that there is no conflict of interest.

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