



Review article

The use of repetitive transcranial magnetic stimulation (rTMS), electroconvulsive therapy (ECT), ketamine, and esketamine in reducing suicidality in major depressive disorder: A comprehensive narrative review

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ABSTRACT

Background: Although repetitive transcranial magnetic stimulation (rTMS), electroconvulsive therapy (ECT), ketamine, and esketamine have established antidepressant effects, their effects on suicide outcomes are less reported. This comprehensive narrative review aims to analyze the antisuicidal effects of these interventions in individuals with major depressive disorder (MDD).

Methods: Search terms for this review included words related to the interventions of interest, suicidality, and depression. Databases included PubMed, OVID, and Google Scholar, with the search occurring from inception to June 19, 2025. Screening of studies, data extraction, and quality assessment of studies using NIH tools were performed.

Results: 108 studies met the eligibility criteria and were included in the review, with 30 studies investigating the effects of rTMS, 9 for ECT, 53 for ketamine, and 24 for esketamine. Some studies investigated the use of multiple interventions. All interventions were effective in reducing suicidality ($p < 0.05$), particularly in the suicidal ideation (SI) dimension, with variations in the time of onset and duration of antisuicidal effects. rTMS and ECT demonstrated the longest-lasting effects in reducing SI and suicidal behavior while treatment with ketamine and esketamine resulted in the fastest reductions in measures of suicidality.

Conclusion: Ketamine, esketamine, rTMS and ECT are associated with reductions in SI in persons with MDD, with the strongest evidence from randomized controlled trials supporting rapid, short-term effects, particularly for ketamine and esketamine. Further characterization and differentiation of the durability of antisuicidal effects of the aforementioned interventions requires investigation in large-scale, adequately-controlled clinical trials. In addition, whether reductions in SI following administration of these agents reduces the severity of aspects of suicidal behavior should be evaluated.

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1. Introduction

Suicidality is a multi-faceted domain encompassing suicidal behavior (e.g., self-harm, suicide attempts), suicidal ideation (SI), and completed suicide, with the experience of self-harm or SI being important risk factors for completed suicide (Cai et al., 2021; Cawley et al., 2019). Major depressive disorder (MDD) is among the most prevalent mental health disorders, with reported SI affecting 32.3 % to 43.4 % of these individuals (Cai et al., 2021; Le et al., 2025).

First-line treatments for persons living with MDD include psychotherapy (e.g., cognitive behavioral therapy) and monoamine-based pharmacotherapies (e.g., selective serotonin reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors) (Simon et al., 2024). Notwithstanding, approximately 44 % of MDD patients inadequately respond to two or more antidepressant treatments regimens, and are described as having treatment-resistant depression (TRD) which is associated with a greater risk of suicide (Bergfeld et al., 2018; Le et al., 2025; McIntyre et al., 2023). Consequently, it is critical to identify interventions that are safe and display both rapid-acting, acute and long-term efficacy for persons with MDD and TRD experiencing suicidality (Jiang et al., 2021; Kern et al., 2021; Lewitzka et al., 2015; Mann et al., 2021). Furthermore, depression and SI are only moderately correlated, indicating that they are distinct constructs. Therefore, treatments that are effective in reducing overall depression severity may not significantly improve suicidality severity (Keilp et al., 2012; Weissman et al., 2021).

Among patients with TRD and/or those presenting with severe symptoms (e.g., SI), alternative interventions such as neurostimulation and mechanistically-novel pharmacotherapies have been investigated (Holtzheimer & Nemeroff, 2008; McIntyre et al., 2024a). Repetitive transcranial magnetic stimulation (rTMS) and electroconvulsive therapy (ECT) are U.S. Food and Drug Administration (FDA) approved and effective neurostimulation therapies for adults with TRD (U.S. Food and Drug Administration, 2011; U.S. Food and Drug Administration, 2018). Separately, ketamine and esketamine (i.e., N-methyl-D-aspartate receptor antagonists) are novel pharmacotherapies that have demonstrated rapid antidepressant and antisuicidal effects in adults with TRD, and have also been associated with improvements in quality of life and functional outcomes. (Cheng et al., 2025; McIntyre et al., 2023). Although esketamine is approved by the FDA for the treatment of depressive symptoms in persons with TRD as well as persons with MDD at a current risk of suicide, treatment with ketamine is yet to be approved (Calder et al., 2024; McIntyre et al., 2021; McIntyre & Jain, 2024; U.S. Food and Drug Administration, 2025; Vekhova et al., 2025).

Notwithstanding replicated evidence supporting the antidepressant efficacy of rTMS, ECT, ketamine, and esketamine, their effects on aspects of suicide-related outcomes have not been systematically synthesized in recent analyses. Herein, we aimed to systematically evaluate the efficacy of rTMS, ECT, ketamine and esketamine in reducing suicidality in individuals with MDD, as well as characterize the onset and duration of their antisuicidal effects.

2. Methods

2.1. Search and selection strategy

A comprehensive literature search was conducted on online databases, including PubMed, OVID, and Google Scholar, from inception until July 12, 2024, with an updated search being conducted on June 19, 2025 to ensure currency. The databases were searched using the following Boolean search strings to identify studies reporting on the efficacy of the four interventions of interest in improving suicidality severity outcomes: (("Transcranial Magnetic Stimulation" OR "TMS") AND ("suicidality" OR "suicidal ideation" OR "suicide" OR "self-harm") AND ("Depression" OR "TRD" OR "Treatment-resistant Depression")), (("Electroconvulsive Therapy" OR "ECT") AND ("suicidality" OR

"suicidal ideation" OR "suicide" OR "self-harm") AND ("Depression" OR "TRD" OR "Treatment-resistant Depression")), and (("ketamine" OR "esketamine") AND ("suicidality" OR "suicidal ideation" OR "suicide" OR "self-harm") AND ("Depression" OR "TRD" OR "Treatment-resistant Depression"))).

Three reviewers (T.M., A.L., A.A.) independently screened articles using Covidence (Covidence systematic review software, 2025). Once duplicate articles were removed, an initial screening of study titles and abstracts was conducted. After potentially relevant studies were identified, the same reviewers performed full-text screening. Any conflicts regarding article screening between reviewers were resolved through discussion. Articles deemed to be relevant according to eligibility criteria were included for data extraction.

2.2. Eligibility criteria

Studies were eligible for inclusion if they included adults between the ages of 18–65 years with a primary diagnosis of MDD, who were being treated with one of the interventions of interest, although some studies included participants slightly out of this age range (below 18 and over 65). Both primary and post-hoc analyses were included.

Studies were excluded if they primarily focused on adolescent participants or geriatric participants, included participants with bipolar depression, psychosis, or another primary diagnosis, or involved the initiation of multiple new interventions. Review papers (e.g., systematic reviews, narrative reviews) and meta-analyses were also excluded. Lastly, studies were excluded if they were not written in English.

2.3. Data extraction process

Data extraction was conducted by four independent reviewers (T.M., A.L., A.A., C.D.). The extracted data included 1) authors and publication year, 2) study design, 3) primary diagnosis/inclusion criteria, 4) dosage/the specific type of intervention, 5) treatment duration, 6) control condition (if applicable), 7) study sample size, 8) age range of participants, 9) suicidality assessment tool(s), and 10) significance based on p-values, or the primary outcome measure defined by the authors when p-values were not reported.

2.4. Risk of bias assessment

Study quality was assessed by two reviewers independently (T.M., A.L.), using the National Institute of Health's quality assessment tools (NIH, 2021). The Quality Assessment of Controlled Intervention Studies, the Quality Assessment of Systematic Reviews and Meta-Analyses, the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies, the Quality Assessment of Case-Control Studies, the Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group, and the Quality Assessment Tool for Case-Series Studies were all used.

3. Results

3.1. Study results and selection

The initial search using PubMed and OVID databases retrieved 15,192 publications (Fig. 1). Once duplicates were removed, 7282 studies remained for title and abstract screening. Subsequently, 1212 studies were deemed eligible for full-text screening, of which 108 studies were included in this narrative review. Studies were excluded due to outcomes irrelevant to the research questions of interest (n = 629), incorrect study design (e.g., a systematic review or narrative review; n = 260), incorrect patient population (e.g., patients did not have a primary diagnosis of MDD; n = 136), not being published in English (n = 42), incorrect intervention (e.g., an intervention other than one of our interventions of interest was used; n = 23), no full-text availability (n =

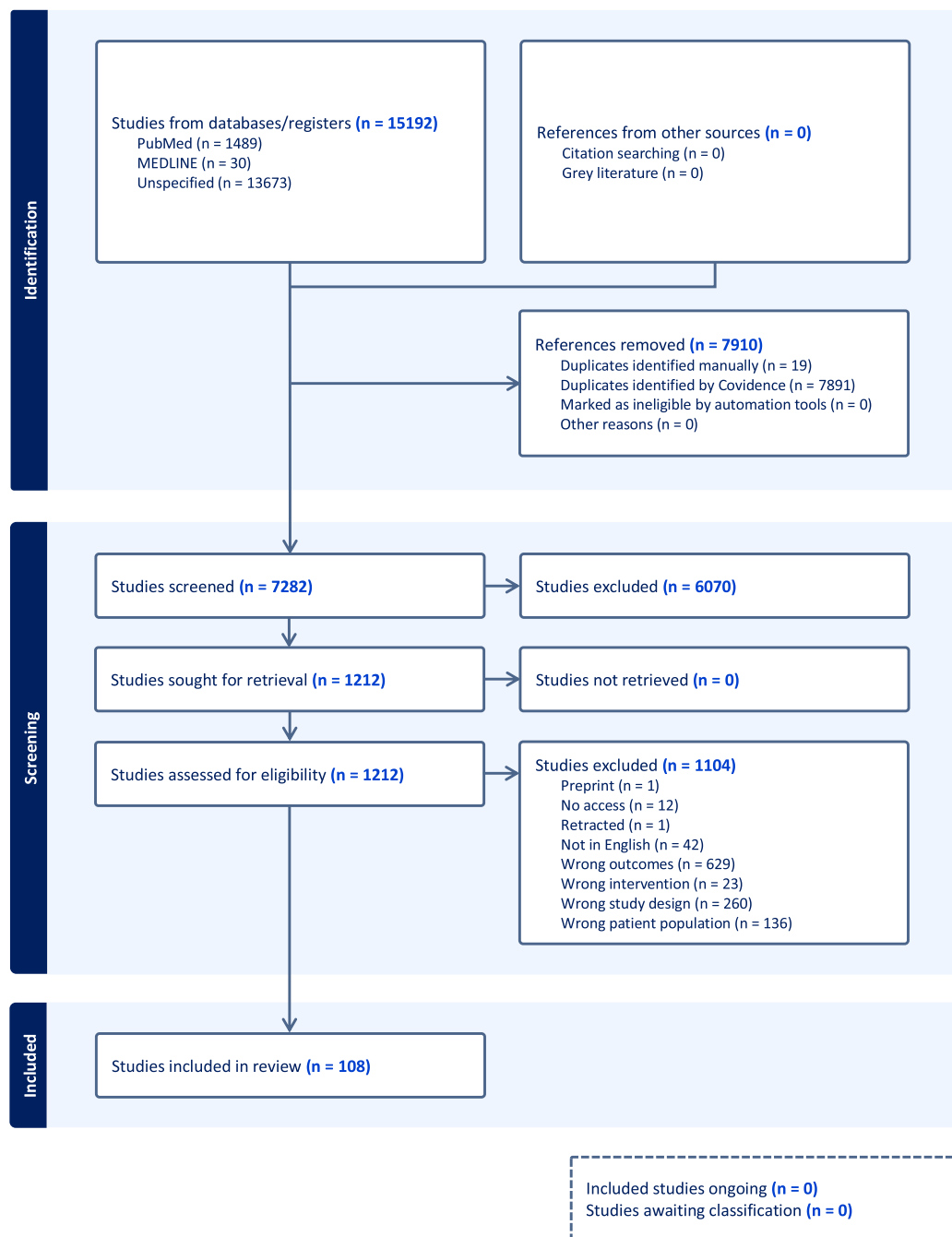


Fig. 1. PRISMA Flow Diagram.

12), or because it was a preprint (n = 1) or redacted (n = 1).

3.1.1. Risk of bias assessment

All included studies received a risk of bias assessment of either “good” or “fair”. Detailed risk of bias assessment tables are available in the supplementary materials (Table S1-S5).

3.2. Literature findings

3.2.1. Repetitive transcranial magnetic stimulation

Thirty of the included studies assessed the use of rTMS in reducing SI, and less commonly suicidal behavior, in individuals with MDD (Baeken et al., 2019; Barredo et al., 2021; Bozzy et al., 2020; Chen et al., 2022a; Davila et al., 2019; Desmyter et al., 2014; Desmyter et al., 2016; Fujita & Koga, 2005; Holtzheimer et al., 2010; Huang et al., 2025; Keshtkar et al.,

2011; Kong et al., 2023; Leuchter et al., 2015; Mehta et al., 2022a; Ozcan et al., 2020; Pan et al., 2020; Pan et al., 2023; Ramasubbu et al., 2024; Stapper et al., 2025; Tang et al., 2021; Terpstra et al., 2023; Wang et al., 2022; Wang et al., 2024; Weissman et al., 2018; Wilkening et al., 2022; Yesavage et al., 2018; Zapf et al., 2024; Zhan et al., 2024; Zhang et al., 2021; Zhao et al., 2024). In all studies specifying the stimulation target, rTMS was directed to the dorsolateral prefrontal cortex (DLPFC), with one study also targeting the left visual cortex (VC; Kong et al., 2023). Treatment duration varied between studies, with some studies administering multiple sessions of rTMS per day, and some administering the sessions over days or weeks, up to a maximum of eight weeks (Barredo et al., 2021). The scales used to assess suicidality primarily included the Beck Scale for Suicidal Ideation (BSI), Patient Health Questionnaire 9 (PHQ-9), Scale for Suicide Ideation (SSI), Hamilton Depression Rating Scale (HAMD/ HDRS), Montgomery–Åsberg Depression Rating Scale

(MADRS), and Columbia Suicide-Severity Rating Scale (CSSRS).

Mixed findings were observed regarding the acute efficacy of rTMS in reducing SI severity (Table 1). Twenty-five studies observed significant improvements in SI scores post-TMS (Barredo et al., 2021; Bozzy et al., 2020; Chen et al., 2022a; Davila et al., 2019; Desmyter et al., 2016; Fujita & Koga, 2005; Holtzheimer et al., 2010; Huang et al., 2025; Keshtkar et al., 2011; Kong et al., 2023; Mehta et al., 2022a; Ozcan et al., 2020; Pan et al., 2020; Pan et al., 2023; Ramasubbu et al., 2024; Stapper et al., 2025; Tang et al., 2021; Terpstra et al., 2023; Wang et al., 2022; Wang et al., 2024; Weissman et al., 2018; Zapf et al., 2024; Zhan et al., 2024; Zhang et al., 2021; Zhao et al., 2024), whereas nonsignificant between-group differences in SI severity post-rTMS compared to control conditions were reported in five studies (Baeken et al., 2019; Desmyter et al., 2014; Leuchter et al., 2015; Wilkening et al., 2022; Yesavage et al., 2018).

The studies that investigated the effects of rTMS over time reported persistence of reduced SI following treatment in individuals with MDD/TRD; however, these findings were primarily derived from observational or follow-up designs (Chen et al., 2022a; Holtzheimer et al., 2010; Pan et al., 2020; Ramasubbu et al., 2024; Stapper et al., 2025; Wang et al., 2024). Participants exhibited reductions in SI following stimulation (as soon as the day after), with further reductions being observed throughout the treatment course if maintenance treatments were provided. However, there may be a limit to the benefits that additional treatments provide, with one study reporting a plateau in SI symptom improvements following 22 sessions (Stapper et al., 2025). Generally, improvements observed early in treatment were maintained at the end of the treatment phase. For example, one study delivering rTMS to patients for seven consecutive days reported reductions in scores to be maintained from day three to day seven (Pan et al., 2020). Several studies with a follow-up period reported that reductions in SI and suicidal behavior were maintained once treatment was discontinued as well, with improvements remaining significant for weeks post-treatment (Ramasubbu et al., 2024; Holtzheimer et al., 2010; Wang et al., 2024) and even up to 3 months in one study (Chen et al., 2022a).

Notably, head-to-head comparisons reported differential efficacy associated with the different types of rTMS. For example, Chen et al. (2022a) found 10 Hz rTMS to have weaker antisuicidal effects than intermittent theta-burst stimulation (iTBS; $p=0.002$). Moreover, Stapper et al. (2025) also found 18 Hz deep TMS to be less effective than TBS. Additionally, Zhao et al. (2024) found continuous theta-burst stimulation (cTBS) to result in greater reductions in SI than iTBS ($p=0.04$), with more patients who received cTBS exhibiting remission of SI during the follow-up period than patients receiving iTBS ($p=0.007$). Weissman et al. (2018) also found bilateral rTMS to be more effective than unilateral rTMS in reducing dimensions of suicidality such as SI and suicidal behavior.

3.2.2. Electroconvulsive therapy

Nine included studies investigated the use of ECT in individuals with MDD and assessed multiple domains of suicidality, including SI, suicidal behavior, self-harm, and suicide mortality (Çakir & Çağlar, 2017; Isometsä et al., 1996; Jørgensen et al., 2020; Kellner et al., 2005; Keshtkar et al., 2011; Kheirabadi et al., 2020; Liang et al., 2018; Lin et al., 2020; Salagre et al., 2022; Table 1). Six of these studies reported that ECT was effective in reducing certain dimensions of suicidality, including self-harm, suicidal behavior, and SI (Kellner et al., 2005; Keshtkar et al., 2011; Kheirabadi et al., 2020; Liang et al., 2018; Lin et al., 2020; Salagre et al., 2022). The manner in which ECT was delivered varied between studies, with three studies not specifying how treatment was conducted (Jørgensen et al., 2020; Liang et al., 2018; Salagre et al., 2022). Suicidality outcomes were measured using the HDRS, self-harm, suicide attempts and completed suicide, BSI, and Beck's Depression Inventory (BDI).

Overall, ECT was associated with significant reductions in SI and in some studies, suicidal behavior, even when compared to other

treatments such as rTMS and pharmacotherapy (e.g., fluoxetine; Keshtkar et al., 2011; Liang et al., 2018; Lin et al., 2020). For example, one study demonstrated that 80.9 % of patients experienced full remission of suicidal intent following nine ECT sessions (Kellner et al., 2005). However, observational studies with a long-term follow-up period found that many patients relapsed over time. For example, Salagre et al. (2022) reported that suicide-related events significantly decreased up to one year after the first ECT session, but the decrease in events were no longer significant at the two-year follow-up period. Similarly, other studies reported that patients who initially responded to treatment were found to relapse during the follow-up period with no ECT treatment, which was 1 year in Çakir and Çağlar (2017) study and 3 months in Isometsä et al.'s (1996) study.

3.2.3. Ketamine

There were fifty-three studies included that investigated the effect of ketamine on SI and suicidal behavior in individuals with MDD (Ahmed et al., 2023; Arango-Posada, 2024; Averill et al., 2022; Beaudequin et al., 2020; Beaudequin et al., 2021; Burger et al., 2016; Chaudhary et al., 2023; Chen et al., 2019; Chen et al., 2020; Chen et al., 2022a; Chen et al., 2022b; Chen et al., 2023; Chen et al., 2024; d'Andrea et al., 2024; De la Salle et al., 2022; Domany & McCullumsmith, 2022; Di Vincenzo et al., 2021; Fava et al., 2020; Feeney, et al., 2021; Galusko-Wegielnik et al., 2021; Gilbert et al., 2020; Grunebaum et al., 2018; Grunebaum et al., 2021; Gutierrez et al., 2024a; Gutierrez et al., 2022b; Hossein et al., 2025; Ionescu et al., 2016; Ionescu et al., 2019; Kaur et al., 2023; Keilp et al., 2021; Kheirabadi et al., 2020; Li et al., 2023; Lin et al., 2023; Nikayin et al., 2022a; Pan et al., 2024; Phillips et al., 2020; Price et al., 2009; Price et al., 2014; Rodrigues et al., 2024; Seraj et al., 2025; Singh et al., 2016a; Sinyor et al., 2018; Su et al., 2023; Thakurta et al., 2012; Tu et al., 2025; Uyar & Gunes, 2024; Vieira et al., 2021; Vidal et al., 2018; Wang et al., 2017; Zheng et al., 2019; Ziegler et al., 2021; Zolghadriha et al., 2024; Table 1). All studies assessed SI, while select studies also reported on suicidal behavior. The scales most commonly used to assess suicidality included the BSI, PHQ-9, SSI, HAMD, MADRS, CCSSRS, and Quick Inventory of Depressive Symptomatology scale (QIDS). The most common route of ketamine administration was intravenous (IV; $n=45$), followed by oral ($n=5$), intranasal ($n=2$) and intramuscular ($n=1$). Across the studies, an IV ketamine dose of 0.5 mg/kg, administered over 40 min, was most commonly investigated.

Ketamine treatment was associated with significant reductions in SI severity in persons with MDD/TRD (Ahmed et al., 2023; Arango-Posada, 2024; Averill et al., 2022; Beaudequin et al., 2021; Beaudequin et al., 2020; Burger et al., 2016; Chaudhary et al., 2023; Chen et al., 2019; Chen et al., 2020; Chen et al., 2022a; Chen et al., 2022b; Chen et al., 2023; Chen et al., 2024; d'Andrea et al., 2024; De la Salle et al., 2022; Domany & McCullumsmith, 2022; Di Vincenzo et al., 2021; Galusko-Wegielnik et al., 2021; Gilbert et al., 2020; Grunebaum et al., 2018; Grunebaum et al., 2021; Gutierrez et al., 2024a; Gutierrez et al., 2022b; Hossein et al., 2025; Ionescu et al., 2016; Kaur et al., 2023; Keilp et al., 2021; Kheirabadi et al., 2020; Li et al., 2023; Lin et al., 2023; Nikayin et al., 2022a; Pan et al., 2024; Phillips et al., 2020; Price et al., 2009; Price et al., 2014; Rodrigues et al., 2024; Seraj et al., 2025; Singh et al., 2016a; Sinyor et al., 2018; Su et al., 2023; Thakurta et al., 2012; Tu et al., 2025; Uyar & Gunes, 2024; Vieira et al., 2021; Vidal et al., 2018; Wang et al., 2017; Zheng et al., 2019; Ziegler et al., 2021; Zolghadriha et al., 2024). Only three studies observed non-significant between-group differences in SI severity post-ketamine compared to placebo treatment (Fava et al., 2020; Feeney, et al., 2021; Ionescu et al., 2019).

Some studies aimed to compare the effect of route of administration and/or dosage of ketamine on outcomes of suicidality in persons with MDD/TRD. For example, Chen et al. (2022b) and Chen et al. (2019) both reported that participants receiving 0.5 mg/kg of ketamine exhibited greater reductions in suicidal symptoms than those receiving a dose of 0.2 mg/kg. Kheirabadi et al. (2020) found that both intramuscular and oral routes of administration were similarly effective in reducing scores

Table 1
Study Characteristics and Results.

Author(s)	Study Type	Primary Diagnosis	Dosage/Specific Intervention	Duration	Control	Sample Size	Age Range	Measure	Outcomes of Interest
rTMS									
Baeken et al., 2019	Randomized double-blind sham-controlled trial	MDD, stage 1 treatment-resistance	-Accelerated intermittent TBS (aiTBS) -Left DLPFC targeted -5 sessions/day -Patients received 1620 pulses/session in 54 triplet bursts with a train duration of 2 s and intertrain interval of 8s -Pause of 15 min between each session	20 sessions spread over 4 days	Magnetism 70-mm Double Air Film sham coil used, identical to active variant except without stimulation	n=21 received active treatment in the first week, sham in the second; n=24 followed reverse order	M=44	BSI	Wilcoxin-paired <i>t</i> -tests revealed that 4 days of sham aiTBS resulted in a significant decrease in BSI scores ($z=-2.24$, $p=0.03$), but 4 days of active aiTBS resulted in a barely-significant decrease in score ($z=-1.89$, $p=0.06$) The change in scores after 1 week of active stimulation was not significantly different from the change after 1 week of sham aiTBS ($p=0.53$). Similarly, the change in score during the second week after active stimulation was not significantly different from the change after sham stimulation ($p=0.62$).
Barredo et al., 2021	Open label trial	MDD and PTSD	5 Hz to DLPFC Intensity: 120 % of motor threshold. Pulse Range: 3000–4000 pulses/session	Up to 40 sessions over 8 weeks	N/A	n=25	M = 52.4	IDS-SR	65 % of participants ($n = 11$) experienced a reduction in suicidality (IDS-SR Item 18 decreased by ≥ 1 point). Mean reduction in suicidality scores across all participants: 42.6 % ($p < 0.00001$). 12 % of participants ($n = 3$) experienced an increase in suicidal ideation post-treatment.
Bozzy et al., 2020	Retrospective Review	MDD	All veterans received 5 or 10 Hz rTMS delivered to the left dorsolateral prefrontal cortex at 120 % of motor threshold for up to 40 sessions ($M = 31.5$, $SD = 6.93$, Range = 15–40)	At least 15 sessions, up to 40 sessions	N/A	n=43 veterans	27–73	PHQ-9	Paired <i>t</i> -tests indicated that suicidal ideation improved after stimulation ($t(40) = 3.82$, $p < 0.001$) Groups with baseline SI: ($n = 29$), patients showed reduced SI following TMS ($F(1,27) = 8.63$, $p < 0.01$, $\eta^2 = 0.12$)
Chen et al., 2022a	Post-hoc pooled analysis of two RCTs	TRD	Low-Dose Ketamine Group: A single intravenous infusion of 0.5 mg/kg ketamine. (rTMS) Groups: 10 sessions of intermittent theta-burst stimulation (iTBS) or 10-Hz rTMS monotherapy.	Single infusion of ketamine 10 sessions of TMS or TBS	Saline infusion Sham stimulation	n=48 for ketamine n=105 for rTMS	Ketamine: M=48.46; Saline: M=48.63; rTMS: M=47.14; Sham: M=47.06	HDRS	Significant reduction in HDRS Item 3 (Suicide) scores for ketamine and iTBS. Ketamine's effect was prominent by Day 7 ($p < 0.001$) but diminished by Day 28. iTBS exhibited a gradual, sustained antisuicidal effect, lasting up to 3 months ($p = 0.002$). 10-Hz rTMS showed weaker antisuicidal effects compared to

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Table 1 (continued)

Author(s)	Study Type	Primary Diagnosis	Dosage/Specific Intervention	Duration	Control	Sample Size	Age Range	Measure	Outcomes of Interest
rTMS									
Davila et al., 2019	Retrospective review	MDD	-rTMS treatment consisted of single daily 37-min sessions -Coil was positioned at the DLPFC -Using Neurostar and MagVenture stimulators	A period of 6 weeks, up to a maximum of 30 treatments	N/A	n=247	18–80	PHQ-9	ketamine and iTBS (p < 0.002 when comparing across groups). 80 % of those reporting a prior suicide attempt achieved complete remission, compared to 67 % of participants not reporting suicide attempts, p=0.03. This was achieved after 3.1±1.0 weeks of rTMS.
Desmyter et al., 2016	Randomized, sham-controlled trial	Therapy-resistant unipolar depression	-Intermittent TBS -Site of stimulation was the DLPFC -An iTBS session consisted of 54 trains of 10 bursts of 3 stimuli, applied in a 50 Hz frequency and repeated every 200ms -1620 stimuli/session -Two groups: one group received active stimulation during the first week and sham the second, and vice versa	-20 sessions delivered at 5 sessions/day over 4 days -4 timepoints: baseline (T1), after the first week of stimulation (T2), after the second week of stimulation (T3), and 2 weeks after the last stimulation (T4)	For the sham condition, a specially designed sham coil was used	n=32	M=41.90	BSI	There was a significant decrease in BSI scores from T1 to T2 (p<0.01). There was no significant effect of the order of treatment (p=0.66). Overall, there was a significant decrease of BSI scores from T1 to all subsequent timepoints (p<0.05).
Desmyter et al., 2014	Randomized, sham-controlled, cross-over pilot study	Unipolar depression	-Accelerated intermittent theta burst stimulation (TBS) targeting the left dorsolateral prefrontal cortex. -Active Stimulation: 1620 pulses per session (total of 32,400 pulses).	-20 sessions over 4 days (5 sessions per day).	-Sham Stimulation: Identical setup without active stimulation.	n=12	22–61	SSI HDRS	Significant decrease in SSI scores over time (baseline to T3), irrespective of active or sham stimulation. (p < 0.01) No statistical difference between active and sham groups. Reduction in depressive severity (HDRS) was noted but was unrelated to changes in suicidal ideation.
Fujita & Koga, 2005	Open-label study	Major depression	-Five stimuli at each site at 6–10 s intervals for a total of 20 stimuli/day	5 consecutive days	N/A	n=23	22–74	HAMD	Comparison of scores between 2 days before TMS and 1 day after showed a significant decrease in the scores for feelings of suicide, p<0.01.
Holtzheimer et al., 2010	Open-label study	TRD	Single-pulse TMS positioned at lowest motor threshold for right first dorsal interosseous or abductor pollicis brevis muscle Left DLPFC treatment 5.5 cm anterior from MT	15 sessions, 5 sessions on day 1, 10 consecutive, with 10 Hz rTMS in 5 sec with 25 s interval at 100 % intensity Total: 1500 rTMS over 2 days	N/A	N=14 (12 completed)	20–74	BDI, HDRS	Two patients discontinued, one due to increased suicidal ideation Mean HDRS24 decreased by 47 % on day 3, 55 % by week 6 HDRS24 = baseline 24.6(5.6) at 3 days: 13.0(6.1) and 6 weeks: 11.1(7.7). Study suggests efficacy.

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Table 1 (continued)

Author(s)	Study Type	Primary Diagnosis	Dosage/Specific Intervention	Duration	Control	Sample Size	Age Range	Measure	Outcomes of Interest
rTMS									
Huang et al., 2025	Sham-controlled trial	MDD	-Stimulation over the left DLPFC -rTMS: 10 Hz TMS at a resting motor threshold of 100 %, with each patient receiving 3000 pulses of 25 min -iTBS: 80 % resting motor threshold, delivered as 50 Hz trains (600 pulses over 3 min 9 s)	15 days of TMS	Sham TMS	MDD: n=63 (rTMS:n=25; iTBS: n=15; sham TMS: n=22); HC: n=40	rTMS: M=21.08; iTBS: M=19.93; sham: M=21.68	BSI-CV BDI HAMD-17	Both rTMS and iTBS mitigated SI symptoms from baseline to posttreatment ($p<0.001$) in MDD patients. There were improved scores after 15 days of rTMS ($p<0.001$) and iTBS ($p=0.002$), not sham treatment ($p>0.05$).
Kong et al., 2023	Randomized, double-blind non-inferiority trial	MDD	-Intermittent theta burst stimulation (iTBS) targeted to the left DLPFC or left VC (varied based on group) -Triplet 50 Hz bursts, repeated at 5 Hz -2 s on and 8 s off -600 pulses/session with a total duration of 3 min 9 s	Performed twice daily with a minimum 2 hour interval, 14 consecutive days	N/A	n=38 in left DLPFC group; n=37 in left VC group	18–55	Beck Scale for Suicidal Ideation Chinese Version (BSI-CV), item 3 of HAMD-17, item 10 of MADRS	Suicidal ideation scores decreased significantly in both groups after iTBS. The BSI-CV and item 3 of HAMD-17 scores were lower in the VC group following treatment. Following treatment, the DLPFC group had a higher mean BSI-CV score (M=2.0) than the VC group (M=0.0). Both scores were significantly lower than baseline scores ($p=0.01$). Both groups had a mean score of 0.0 for HAMD-17 item 3 and MADRS item 10, however only the HAMD-27 scores were significantly lower than baseline scores ($p=0.02$).
Leuchter et al., 2015	Double-blind sham-controlled trial	MDD	-Low-field sTMS -Device had a surface field of 0.64 T, positioned in the sagittal line	-Participants received daily treatments 5 days/ treatment week for 5 weeks, for a maximum of 30 treatments	Sham device was indistinguishable from the active device, other than being inactive (non-magnetic rotating metal shaft)	sTMS: n=103; sham: n=99	22–65	C-SSRS	There was no significant difference in the rates of suicidal ideation between participants in the active treatment and sham at baseline ($p=0.10$) or at the end of treatment ($p=0.64$). The only suicide attempt during the study occurred in a sham-treated subject.
Mehta et al., 2022a	Post-hoc of data from THREE-D trial	TRD	-rTMS delivered to the dlPFC -10 Hz rTMS: (120 % RMT stimulation intensity; 10 Hz frequency; 4 s on and 26 s off; 3000 pulses per session; total duration of 37.5 min). iTBS was delivered at the same site and intensity (120 % RMT, triplet 50 Hz bursts, repeated at 5 Hz; 2 s on and 8 s off; 600 pulses per session; total duration of 3 min 9 s)	-Five sessions per week for a total of 20 sessions	N/A	10 Hz rTMS (n=205) iTBS (n=209)	18–65	HDRS-17	HRSD-17 scores improved from 23.5 (SD 4.4) to 13.4 (7.8) in the 10 Hz rTMS group and from 23.6 (4.3) to 13.4 (7.9) in the iTBS group ($p=0.0011$), which indicated non-inferiority of iTBS.

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Table 1 (continued)

Author(s)	Study Type	Primary Diagnosis	Dosage/Specific Intervention	Duration	Control	Sample Size	Age Range	Measure	Outcomes of Interest
rTMS									
Ozcan et al., 2020	Open label study	TRD	20 Hz stimulation, intensity: 100 % of motor threshold to DLPFC. Total pulses per session: 1000 magnetic pulses (2 s per train with a 30-second interval between trains).	5 sessions per week for 4–6 weeks	N/A	n=30	18–65	SIS, C-SSRS, MADRS	Reduction in Suicidal Ideation SIS (Suicidal Ideation Scale): Pre-treatment mean score: 10.41 ± 2.31 . Post-treatment mean score: 4.30 ± 2.67 . Significant reduction ($t = -4.47$, $p < 0.001$). C-SSRS Severity of Ideation Subscale: Pre-treatment mean score: 2.36 ± 1.34 . Post-treatment mean score: 0.7 ± 0.78 . Statistical Change: Significant reduction ($t = -4.45$, $p < 0.001$). Reduction in Depression Severity (MADRS) Pre-treatment mean score: 35.48 ± 7.39 . Post-treatment mean score: 15.89 ± 8.06 . Statistical Change: Significant reduction ($t = 9.31$, $p < 0.001$).
Pan et al., 2020	Double-blind, randomized, sham-controlled trial	MDD	-Each rTMS session comprised 120 trains of 5 s at 5 Hz, with inter-train intervals of 15 s -The coil was placed over the DLPFC -An eight-figured coil was used	-TMS treatment was given for 7 consecutive days	Sham rTMS: parameters were the same as those in the active group, except the coil was turned 90 degrees with only one wing in contact with the scalp	rTMS: n=21; sham: n=21	13–45	BSI	The active rTMS group showed a significantly greater BSI score reduction compared to the sham group on day 3 ($p < 0.001$), and this significant difference was maintained on day 7 as well ($p < 0.001$).
Pan et al., 2023	Randomized sham-controlled trial	Treatment-resistant MDD	-rTMS with an eight-figured coil was delivered to each participant's left DLPFC -Each session included 6000 stimuli/day delivered in 120 trains of 5 s at 10 Hz with 15 s inter-train intervals	-Each subject received 7 daily sessions of rTMS -Outcomes were assessed at baseline, day 3, and day 7	Sham rTMS: coil turned 90 degrees with only 1 wing in contact with the scalp	Active: n=31; sham: n=28	13–45	BSI	The active rTMS showed a significantly greater BSI score reduction than the sham group at day 7 ($p < 0.001$).
Ramasubbu et al., 2024	Open-label pilot study	MDD	-All participants received TBS 5 times/day with an inter-session interval of 15 min -In each treatment, participants first received iTBS over the left DLPFC followed by cTBS over the right DLPFC -iTBS consisted of 600 pulses/session delivered in 20 trains of 10 triplet bursts at 50 Hz with a train duration of 2 s (5 Hz) on and 8 s off -cTBS consisted of	-Treatment over 5 consecutive days -Assessments were administered daily after treatment, and 2 weeks after treatment.	N/A	n=25	18–65	C-SSRS	With treatment, there were significant decreases in suicidal ideation and behavior ($X^2(2) = 17.522$, $p < 0.001$) with posthoc significance at 2 weeks after treatment compared to baseline ($z = -2.62$, $p = 0.027$) and in the intensity of ideation ($X^2(2) = 12.640$, $p = 0.002$)

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Table 1 (continued)

Author(s)	Study Type	Primary Diagnosis	Dosage/Specific Intervention	Duration	Control	Sample Size	Age Range	Measure	Outcomes of Interest
rTMS									
Stapper et al., 2025	Retrospective review	MDD-TRD	600 pulses delivered in 200 triplet bursts at 50 Hz in a single train with a duration of 40 s. Either unilateral or bilateral TBS, 18 Hz deep TMS, or TBS with a deep TMS coil	Unilateral/bilateral TBS: M=38.9 sessions; deep TMS: M=35.5 sessions; TBS with deep TMS coil: M=38.4 sessions	N/A	Unilateral/bilateral TBS: N=67; deep TMS: N=53; TBS with deep TMS coil: N=10	M=55.9	Suicide item on PHQ-9 or BDI-II	Symptoms of SI decreased from baseline to post-rTMS treatment ($p<0.001$). Following TMS, 48 % of patients achieved SI remission and 61 % achieved SI-response. More specifically, 55 % of patients who received TBS and 40 % of patients who received 18 Hz TMS achieved SI remission. There were greater improvements in SI symptoms for the TBS and TBS deep TMS coil groups than the 18 Hz TMS group ($p=0.003$ and $p=0.016$). There was a near-linear decrease in SI symptoms for the first 22 sessions, and then a subsequent plateau. Patients showed a significant reduction in BSI-CV scores ($p<0.001$), item 3 of HAMD ($p<0.001$), and item 10 of MADRS ($p<0.001$) following treatment. 53.33 % of patients were in remission according to the BSI-CV scale after 5 days of treatment. Remission rates met 80 % 30 days after treatment.
Tang et al., 2021	Open-label study	MDD with suicidal ideation	-Left DLPFC targeted -Individual target TMS was used -50 iTBS sessions of 1800 pulses per session	-10 daily sessions over 5 consecutive days	Healthy controls	Patients: n=15; HCs: n=15	18–60	BSI-CV HAMD item 3 MADRS item 10	Patients showed a significant reduction in BSI-CV scores ($p<0.001$), item 3 of HAMD ($p<0.001$), and item 10 of MADRS ($p<0.001$) following treatment. 53.33 % of patients were in remission according to the BSI-CV scale after 5 days of treatment. Remission rates met 80 % 30 days after treatment.
Terpstra et al., 2023	Open label clinical trial	TRD	Low frequency (LF)-rTMS: 1 Hz 30 min sessions with 1800 pulses	5 sessions/week for four weeks	N/A	n=55	18–80	MADRS CHRT	CHRT Total Score: Mean decrease of 8.4 points ($p < 0.001$) from baseline to week 17. CHRT Propensity Score: Mean decrease of 6.8 points ($p < 0.001$). CHRT Risk Score: Mean decrease of 0.8 points ($p = 0.004$) Mean MADRS score decreased from 29.0 at baseline to 19.7 at week 5 ($p < 0.001$).
Wang et al., 2022	Open-label Study	TRD with suicidal ideation	-rTMS, scalp position of L-DLPFC 5.5 cm anterior in the mid-sagittal plane 60 trains of 50 pulsations, 3.33 s stimulation, 26	25 sessions lasting 30 mins, 5 sessions per day for 5 consecutive days and evaluated 4 weeks after	N/A	n=31	18–60	C-SSRS HAM-D-17	The remission rate of suicidal ideation was 87.09 % at day 5 and at 4 weeks was 77.42 %. Treatment was tolerated by all patients, no serious

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Table 1 (continued)

Author(s)	Study Type	Primary Diagnosis	Dosage/Specific Intervention	Duration	Control	Sample Size	Age Range	Measure	Outcomes of Interest
rTMS									
Wang et al., 2024	Open-label study	MDD-TRD	intervals 110 % rMT intensity, 3000 pulses at 15 Hz -Accelerated rTMS -15 Hz stimulation over the left DLPFC -A total of 3000 pulses	25 sessions, each lasting 30 min -Five sessions per day for 5 consecutive days	N/A	n=119	18–60	C-SSRS HAM-D-17	adverse effects except for dizziness. A significant effect of treatment on depression and suicide ideation was achieved by day 5 and maintained through 4 weeks ($p<0.01$), scores at all follow-up time points were significantly improved compared to baseline ($p<0.01$). Suicidal ideation resolved in 40.4 % of participants who received bilateral rTMS, 26.8 % of those who received left unilateral rTMS, and 18.8 % of those who received sham rTMS. The difference in resolution of suicidal ideation between bilateral and sham rTMS was statistically significant ($p=0.02$), but there was no significant difference between left unilateral and sham rTMS ($p=0.33$).
Weissman et al., 2018	Post-hoc analysis of 2 RCTs	Treatment-resistant major depression	-Bilateral rTMS, unilateral rTMS, and sham rTMS	-15 sessions over 3 weeks	Sham condition	n=156 Sham rTMS: n=48; unilateral rTMS: n=56; bilateral rTMS: n=52	18–84	HDRS-17 item 3	For all subjects, 62 % showed a decrease in suicide score, 21 % showed no change, 17 % showed an increase. Suicide score was reduced by 24.61 % on average. Comparing the change in suicidality between active and sham stimulation groups showed no significant differences, $t(80) = -0.07$, $p = 0.94$. Bonferroni-adjusted pairwise comparisons revealed significantly greater suicidality reductions from week 1 to all other weeks (2–6). The suicidality score between week 1 and week 6 showed a significant difference $t(80) = 3.46$, $p = 0.001$, effect size of $d = 0.39$.
Wilkens et al., 2022	Quadruple-blind sham-controlled crossover RCT	MDD, ongoing moderate or severe depressive episode	-iTBS, stimulation ON for 2 s followed by 8 s of stimulation OFF, performed 60 times in a session -1800 stimuli applied with a frequency of 5 Hz or 50 Hz to the left DLPFC over a session - One daily visit: 4 sessions of 10 min, each followed by at least a 20 min pause	20 sessions/week over 2 weeks of stimulation and 6 weeks of observation	Sham condition: the same coil was blindly flipped 180 degrees; electrical stimulation delivered to mimic stimulation	n=81; treatment=40, sham=41	18–60	HAMD item 3, MADRS item 10, BDI-II item 9	No significant effect of treatment on suicidality was found at the end of the treatment phase.
Yesavage et al., 2018	Double-blind, sham-controlled RCT	MDD (TRD)	-Participants were randomized to either left prefrontal rTMS treatment (10 Hz, 120 % motor threshold, 4000 pulses/session) or sham rTMS	-Between 20 and 30 sessions of rTMS -Treatment was delivered in 5 session blocks over 5 to 12 days	Sham rTMS treatment	Treatment group: n=60; sham: n=65	18–80	BSI, CSSRS	No significant effect of treatment on suicidality was found at the end of the treatment phase.

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Table 1 (continued)

Author(s)	Study Type	Primary Diagnosis	Dosage/Specific Intervention	Duration	Control	Sample Size	Age Range	Measure	Outcomes of Interest
rTMS									
Zapf et al., 2024	Secondary analysis	MDD	treatment -rTMS administered using a MagPro R30 device -1200 pulses/day of both active and sham stimulation -Active stimulation over the left DLPFC -a single iTBS session was delivered at 120 % resting motor threshold in bursts of 3 pulses at 50 Hz, repeated at 5 Hz for 600 pulses. -There was a once-daily and twice-daily iTBS group	-30 treatment days corresponding to 60 sessions -Assessed at baseline, after 10 days, and after 30 days	Sham stimulation	Once-daily: n=82; Twice-daily: n=76	18–59	HDRS-17 QIDS MADRS BDI-II	After 10 days of treatment, 15 (18.3 %) of participants in the once-daily group and 19 (25 %) of participants in the twice-daily group remitted from SI. After 30 days, 27 (32.9 %) in the once-daily group and 30 (39.5 %) participants in the twice-daily group achieved remission. There was a significant main effect of time ($p<0.001$), but no significant effect of group ($p=0.501$). SI scores showed a mean reduction score of 9.1 from baseline to post-treatment. The percentage decrease was 32.5 %. 60 % of participants showed improvements in SI. 64.9 % achieved remission of SI (HAMD-SI score = 0) after 2 weeks of treatment.
Zhan et al., 2024	Secondary analysis of an open-label trial	MDD (TRD)	-Participants received rTMS over the right DLPFC -1200 pulses/session	-20 overall sessions -Treatment delivered once daily on weekdays across 4 weeks	N/A	n=55	M=42.8	CHRT-SR	HF Left DLPFC: 76.7 % remission rate (33/43 participants). Greater efficacy in reducing SI than LF Right DLPFC: (55.6 % remission rate (30/54 participants)). BSI scores at all follow-up time points were significantly lower than baseline scores ($p<0.001$). There was a larger reduction in suicidal ideation in the cTBS group compared to the iTBS group ($p=0.04$). During the 4-week follow-up, 72.73 % of patients in the cTBS group achieved remission of suicidal ideation compared to 31.82 % of patients in the iTBS group ($p=0.007$).
Zhang et al., 2021	Open label trial	MDD	HF: 10 Hz rTMS to left DLPFC, 80 trains of 30 pulses LF: 1 Hz rTMS to left DLPFC, 2 trains of 700 pulses	5 session per week for 2 weeks	N/A	n=146	10–80	HAMD	HF Left DLPFC: 76.7 % remission rate (33/43 participants). Greater efficacy in reducing SI than LF Right DLPFC: (55.6 % remission rate (30/54 participants)). BSI scores at all follow-up time points were significantly lower than baseline scores ($p<0.001$). There was a larger reduction in suicidal ideation in the cTBS group compared to the iTBS group ($p=0.04$). During the 4-week follow-up, 72.73 % of patients in the cTBS group achieved remission of suicidal ideation compared to 31.82 % of patients in the iTBS group ($p=0.007$).
Zhao et al., 2024	Active-comparator randomized controlled trial	Treatment-resistant major depression	-Targeted the left DLPFC -iTBS cycles comprised 10 bursts of 3 pulses at 50 Hz, delivered in 2-second trains, with an 8-second intertrain interval and a total duration of 10 min	-Treatment sessions were administered hourly 10 times a day, for a total of 18,000 pulses/day for 5 consecutive days -Clinical assessments at week 1, 3, and 5	-cTBS: continuous delivery of 50 Hz triplets at 5 Hz for a total of 1800 pulses	n=22 in each group (total: n=44)	13–40	BSI	BSI scores at all follow-up time points were significantly lower than baseline scores ($p<0.001$). There was a larger reduction in suicidal ideation in the cTBS group compared to the iTBS group ($p=0.04$). During the 4-week follow-up, 72.73 % of patients in the cTBS group achieved remission of suicidal ideation compared to 31.82 % of patients in the iTBS group ($p=0.007$).
ECT									
Çakır & Çağlar, 2017	Naturalistic observation	MDE	-ECT was applied to all patients with a standardized modality -Initial stimulus energy	-ECT was delivered 3 times/week -The number of	N/A	n=30 with unipolar depression	18–65	HDRS	Nine patients had a suicide attempt during the follow-up period, $p=0.004$.

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ECT									
			determined by an age-based method adjusted for gender -Energy delivered was between 20 and 120 %; charge delivered was between 108 and 648 mC -Electrodes placed bitemporally Series of ECTs comprising of 5 unilateral treatments with convulsion times of 40–55 s	ECT sessions was determined by the primary physician -The follow-up occurred one year after the last ECT session.					
Isometsä et al., 1996	Case report	Major depression		N/A	N/A	Total n=2; n=1 with non-psychotic depression	49	Completed suicide	Subject was discharged after seemingly responding to treatment, but died of overdose 3 months after the final ECT session due to experiencing a relapse.
Jørgensen et al., 2020	Observational study based on data from the Danish National Patient Registry	Single episode or recurrent unipolar depression	Not specified	Median number of ECT sessions was 10	Patients not treated with ECT	Total N=92,895; n=5004 treated with ECT	≥10	Suicide attempts and suicide	ECT was associated with a higher risk of suicidal behavior, but with lower all-cause mortality. 3653 patients not treated with ECT had a suicide attempt and 495 committed suicide. 270 patients treated with ECT had a suicide attempt and 103 attempted suicide.
Kellner et al., 2005	Multisite, collaborative study	MDD	-Stimulus dosing was at 1.5 times the seizure threshold -Standard brief-pulse ECT with bitemporal electrode placement	-Thrice weekly ECT sessions -6-month continuation phase following remission: ECT weekly for 4 weeks, biweekly for 8 weeks, and monthly for 2 months	N/A	n=131	18–85	HAMD item 3	15.3 % of patients with high expressed suicidal intent experienced remission of suicidal intent after 1 ECT session, 38.2 % after 3 ECT sessions, 61.1 % after 6 ECT sessions, and 76.3 % after 9 ECT sessions. 80.9 % of these patients experienced full remission overall.
Keshtkar et al., 2011	Randomized parallel-group	MDD	-rTMS view magnetic stimulator, 408 stimulations per session, left DLPFC -ECT brief-pulse, square-wave, constant current (1.4 ms, for 1.25 s 80 Hz) with thiopental as anesthetic	rTMS: 10 day course with repeated pulses ECT: 10 sessions, 3 weekly	N/A	n=75, 40 ECT 35 rTMS	34	BDI and HDRS	Significant decrease in the BDI suicidal subscale score, with ECT (mean[SD] = 1.4[1.0] to 0.5[0.7] after intervention), decreasing more than rTMS (mean [SD] = 1.5[0.8] to 1.2[0.9] after intervention) ECT (mean[SD] = 2.3 [1.1] to 0.3[0.5] after treatment) decreased the score for the suicidal subscale of HDRS more than rTMS (mean = 1.9[1.3] to 1.3[1.2] after treatment). Overall ECT more effective than rTMS in reducing suicidal behavior in the short-term.

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ECT									
Kheirabadi et al., 2020	Pilot study	MDD	-ECT: electrodes were placed bifrontotemporally and the electrical stimulus was first set at 20 J and then titrated based on the duration of the seizure -intramuscular ketamine: 0.5mg/kg of racemic ketamine in the gluteus medius site -Oral ketamine: 1mg/kg of racemic ketamine	-ECT: individuals received 6–9 sessions over the 3 weeks -IM ketamine: 6–9 injections over 3 weeks -Oral ketamine: 6–9 sessions over 3 weeks	N/A	ECT: n=12; oral ketamine: n=12; IM ketamine: n=15	20–70	BSI	BSI scores significantly reduced for all 3 groups following treatment ($p<0.001$). The greatest reduction in BSI scores occurred 24 hours after the first intervention and did not return to baseline even one month after (all $p<0.001$). Significantly lower suicide scores were seen for both the oral and IM ketamine groups compared to the ECT group, especially on the first day ($p=0.045$), and second week ($p=0.033$), suggesting that the antisuicidal effects of ketamine may be superior to ECT.
Liang et al., 2018	Retrospective cohort study	Unipolar depression and bipolar depression	Not specified	-Mean hospital stay for the ECT group was 22.8 days and 16.4 days for the non-ECT group -ECT group mean follow-up period: 4.4 years, and 2.76 for non-ECT group	Control: non-ECT cohort of people who received psychopharmacotherapy instead	Of those with unipolar depression, ECT group: n=319, non-ECT group: n=1276	ECT group: M=38.5; non-ECT group: M=39.2	Not specified	In patients with unipolar depression, ECT patients showed a significantly lower cumulative incidence of suicide than non-ECT recipients ($p<0.001$).
Lin et al., 2020	Data analysis of 2 open-label trials	MDD	-Standard bilateral frontotemporal and modified ECT was performed -Seizure duration was at least 20 s	Treatment was given 3 times a week at first, and then 2 times a week for a maximum of 12 treatments (for a total of 6 weeks)	Control: fluoxetine at a dose of 20mg/day for 6 weeks	ECT group: n=111; fluoxetine: n=114	ECT: M=46.5; fluoxetine: n=45.6	HAMD-17 item 3	After treatment, both groups had significantly improved suicide item scores (both $p<0.001$), however, the effect was greater for the ECT group. At endpoint, the ECT group exhibited significantly lower suicide item scores than the fluoxetine group ($p<0.001$).
Salagre et al., 2022	Observational study based on nationwide data from Danish registers	Unipolar depression, bipolar disorder, psychotic disorder, personality disorder	Not specified	Median number of ECT sessions for patients with unipolar depression was 10, with the median admission length being 43 days	Comparison group: patients not receiving ECT matched on age, sex, and diagnostic category	ECT unipolar depression group: n=8843; Non-ECT comparison group: 43,107	ECT unipolar depression group: M=56.1	Intentional self-harm and suicide attempts	For patients with unipolar depression, the number of events decreased significantly from before the first ECT session to 1, 2, 3, 6 months, and 1 year after the first ECT session (all $ps<0.001$). However, there was no longer a significant reduction at 2 years ($p=0.465$). For the non-ECT group, there were no significant

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ECT									
Ketamine									reductions in number of events at all time points (all ps>0.001).
Ahmed et al., 2023	Double-blind randomized controlled trial	Treatment-resistant MDD	-Two infusions of IV ketamine hydrochloride (0.5mg/kg ketamine in 50 ml saline)	One infusion each week for 2 consecutive weeks	Placebo: saline 50ml	n=18 in each group	18–65	Suicide Probability Scale (SPS)	SPS scores dropped significantly from before treatment to after the first infusion (p=0.085) and after both infusions (p=0.009) for the ketamine group. However, scores did not drop significantly from before treatment to after the first infusion (p=0.673) or after both infusions (p=0.767) for the placebo group. The day after the infusion, the patient reported better mood and said the suicidal thoughts had almost completely disappeared. Eleven months following the infusion the suicidal thoughts still had not returned.
Arango-Posada, 2024	Case report	Major depression	Single IV infusion of 1.5mg/kg of ketamine diluted in 250 ml saline over 25h	Patient discharged 4 days after infusion, frequent follow-ups for 12 weeks	N/A	n=1	55	PHQ-9	Ketamine significantly reduced suicidal severity: MADRS (p<0.0001), QIDS (p=0.005), BSS (p=0.002). Antisuicidal effects peaked at day 1 post-treatment, and were maintained at week 1. Compared to baseline scores, the antisuicidal effects lost statistical significance by week 2 for MADRS (p=0.10) and QIDS (p=0.08), but not BSS (p=0.013). BSI scores significantly decreased from baseline (pre-ketamine) to follow-up (p<0.001)
Averill et al., 2022	Secondary analysis of a double-blind placebo-controlled study	MDD (current episode)	-0.5mg/kg IV ketamine -Prior to ketamine: placebo on one infusion day, and 6 mg of oral rapamycin on the other infusion day	-Infusions were administered over 40 min. The two infusions were at least 2 weeks apart	Placebo (not specified)	N=20	21–65	MADRS item 10, QIDS item 12, BSI	BSI scores significantly decreased from baseline (pre-ketamine) to follow-up (p<0.001)
Beaudequin et al., 2021	Secondary analysis	MDD	-Oral ketamine at an initial dose of 0.5mg/kg, and then titrated up by 0.2–0.5mg/kg or down by 0.2–0.7mg/kg at each treatment depending on participant	One dose/week during a 6-week treatment phase, and then a 4-week follow-up phase	N/A	n=30	≥18	BSI	BSI scores significantly decreased from baseline (pre-ketamine) to follow-up (p<0.001)

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Ketamine									
Beaudequin et al., 2020	Secondary analysis	MDD and chronic suicidal thoughts	tolerance. -The maximum dose at the last treatment session was 3.0mg/kg -Oral ketamine at an initial dose of 0.5mg/kg, and then titrated up by 0.2–0.5mg/kg or down by 0.2–0.7mg/kg at each treatment depending on participant tolerance. -The maximum dose at the last treatment session was 3.0mg/kg	One dose/week during a 6-week treatment phase, and then a 4-week follow-up phase	N/A	n=30	≥18	BSI	At follow-up, 50 % of participants were assessed as being responders (≥50 % improvement from pre-treatment BSI). 33 % of participants were assessed as being in full remission (BSSI=0, no more suicidal ideation).
Burger et al., 2016	Double-blind, randomized, placebo-controlled pilot study	Acute depression + suicidal thinking	-infusion of 0.2mg/kg over 2 mins	240 mins stay in the emergency department	Placebo = normal saline for 2 mins	n=10, 7 in placebo, 3 in ketamine	18–65	BSI BHS	Study terminated early 67 % of ketamine users showed improvement in hopelessness and suicidality. Significant time x group interaction in BHS score and BHS score were statistically different at discharge (p < 0.05) but not at follow-up (p > 0.05).
Chaudhary et al., 2023	Retrospective data analysis	MDD	-IV ketamine infusions given at a dose ranging from 0.4–0.7mg/kg	-Infusion over 50 min -6 sessions over 2 weeks -Outcomes assessed at 2 h, 7 days, and 1 month post-treatment	N/A	n=10	22–49	C-SSRS	Ketamine significantly reduced C-SSRS scores following the first dose and remained reduced throughout all assessments. 9/10 reported no SI following the first dose, which was sustained for 30 days. There were no suicide-related adverse events.
Chen et al., 2024	Reanalysis of previous clinical trials	TRD-SI (with and without melancholic features)	0.5 mg/kg ketamine or 0.045 mg/kg midazolam single infusion	7-day time period	N/A	n=84 n=42 (ketamine n= 42 midazolam	35.57 (12.75 is SD)	MADRS, CSSRS, PANSI; HDRS	Antisuicidal effect noted in non-melancholic TRD individuals on MADRS item 10 scale: (4.18 [0.38]) better than in melancholic TRD (4.33[0.48]). Patients without melancholic features had better antisuicidal effects based on PANSI-NSI score after ketamine but scored higher in the ketamine group than midazolam in patients with melancholic

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Ketamine									
									features, significance at day 2 but not at other time points. The antisuicidal effect of a single infusion persisted for 5 days on MADRS, CSSR-ISS and 7 days on self reported scores. On day 3 post-infusion, the ketamine group had significantly lower HDRS (p=0.029) and MADRS (p=0.004) scores than the midazolam group. The CSSRS-ISS scores did not significantly differ between groups (p=0.053).
Chen et al., 2023	Randomized controlled trial	MDD (TRD)	Single infusion of 0.5mg/kg ketamine	Patients were assessed 2, 3, 5, 7, and 14 days post-infusion	Control: 0.045mg/kg of midazolam	n=48; n=24 in each group	20–64	MADRS item 10, HDRS, CSSRS-ISS	
Chen et al., 2022b	Double-blind, randomized placebo-controlled study	Treatment resistant double depression (major depression and persistent depressive disorder)	Patients in ketamine groups either received 0.2mg/kg or 0.5mg/kg of IV ketamine	Patients assessed prior to treatment, 40 and 240 min posttreatment, and on days 1–7 and 14 following the treatment	Placebo: IV saline infusion	0.2mg/kg ketamine: n=11; 0.5mg/kg ketamine: n=12; placebo: n=12	0.2mg/kg ketamine: M=42.36 0.5mg/kg ketamine: M=53.58; Placebo: M=47.33	HDRS item 3	The 0.5mg/kg ketamine group exhibited significant reduction in HDRS item 3 scores (p=0.033) compared to the 0.2mg/kg ketamine and placebo groups. Changes in suicidal symptoms did not differ between 0.2mg/kg ketamine and placebo groups. Ketamine administered before increased ECT effect, by reducing sessions needed for SI reduction. SI scores were reduced to 19 from 21 patients in study group, but no statistically significant difference in rate of SI reduction between control group (P > 0.05). Significant difference (p = 0.044) in median number of ECT sessions required to achieve SI reduction (3.0 +/- 0.75 in study 6.0 +/-1.19 in control).
Chen et al., 2020	Randomized, placebo-controlled double-blind study	MDD	ECT: bitemporal, intensity determined as half patients age, under propofol anesthesia, discontinued when outcome reached or no response Ketamine: 0.03mg/kg before ECT	3 times a week until discontinued when outcome reached or no response during 2 sessions	n=66, received isovolumetric dose of saline with ECT	n=66	18–65	HDRS	
Chen et al., 2019	Randomized, placebo-controlled double-blind study	TRD	- IV administered for 40 min - 0.5mg/kg ketamine	Single infusion, with follow-up 40, 80, 120, 240 min post-infusion, and	Saline	n=71	21–64	HAMD MADRS	For HAMD scores, there was a significant group (p = 0.007) and time (p = 0.004)

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Table 1 (continued)

Ketamine									
			- 0.2mg/kg ketamine	sequentially on days 2–7 and day 14					effect on reducing suicidal symptoms. The group that was administered 0.5mg/kg of ketamine reported a significantly lower score in item 3 (suicidal ideation and behavior) of HAMD than the group that received 0.2mg/kg of ketamine or placebo. For the MADRS scores, there was a significant group effect ($p = 0.002$) on reducing suicidal symptoms. For those with baseline item 3 of HAMD ≥ 2 or item 10 of MADRS ≥ 2 , both infusions were effective in reducing suicidal symptoms. With baseline item 3 of HAMD ≥ 2 or item 10 of MADRS ≥ 4 , 0.5mg/kg was more effective than 0.2mg/kg and placebo.
d'Andrea et al., 2024	Retrospective, post-hoc pooled analysis	Unipolar TRD	-IV ketamine -First 2 infusions were administered at 0.5mg/kg and infused in 40 min -Patients with a suboptimal response were then offered a dose of 0.75mg/kg -Intranasal esketamine -Starting dose of 56mg Modified dose of 28 mg for patients 65+ -Patients demonstrating a suboptimal response following the first dose were offered 84mg	-4 ketamine infusions over 2 weeks -Esketamine was administered biweekly	N/A	n=171 in ketamine group n=140 in esketamine group	≥ 18	QIDS-SR ₁₆ item-12	Suicidal symptoms were significantly reduced 1 month following ketamine treatment (T0: M=1.29, T1: M=0.75, $p<0.001$). Suicidal symptoms were significantly reduced 1 month following esketamine treatment (T0: M=2.17, T1: M=1.07, $p<0.001$), similar to IV ketamine.
De la Salle et al., 2022	Multi-phase clinical trial	MDD (TRD)	-0.5mg/kg of IV ketamine hydrochloride diluted in 0.9 % saline -30µg/kg of midazolam diluted in saline	Medications were administered over 40 min	Control: 30µg/kg of midazolam	n=24	18–65	MADRS	Pre-infusion, the ketamine group's mean SI score was 2.75. Two hours post-infusion, their mean score was 1.2, at one day it was 1.2, and at one week it was 1.8. Pre-infusion, the midazolam group's mean SI

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Table 1 (continued)

Ketamine									
									score was 2.6. Two hours post-infusion, their mean score was 2.2, at one day it was 1.8, and at one week it was 2.5 Overall, the response rate to a single ketamine infusion at 2 h was 16.7 % and 25 % at one day post-infusion. The response rate for the midazolam group was 0 % at all time points. 4 hrs after administration there was a reduction of suicidal symptoms measured by MADRS-SI (mean difference between groups is 1.267, reduction in ketamine group is 4.89 +/- 0.4 compared to placebo 3.35 +/- 0.5). BSS - showed a reduction of 17.4 +/- 9.4 points in the ketamine group compared to 10.5 +/- 8.21 in the placebo (not statistically significant, p = 0.086). 12/15 patients in the ketamine group went into remission four hours after administration compared to 5/15 in the placebo group. Ketamine group had 5 days of hospitalization whereas it was 9 days for the placebo.
Domany & McCullumsmith, 2022	Randomized controlled clinical trial	Suicidal ideation with psychiatric hospitalization	-intranasal mucosal application of 4 administrations for 40 mg total (single fixed dose)	application in each nostril separated by 10 min, once and monitored for 4 hrs after	Placebo - normal saline (0.1 ml)	N=30 (15 placebo 15 ketamine)	18–65	BSI C-SSRS MADRS-SI	
Di Vincenzo et al., 2021	Retrospective, observational analysis	MDD (TRD)	-At each session, patients received IV ketamine hydrochloride diluted in a 0.9 % saline solution, administered over a 45 min infusion period -Dosage at first 2 infusion was 0.5 mg/kg, those who did not experience a benefit increased dose to 0.75 mg/kg	-A total of infusions were administered over 1 or 2 weeks, based on scheduling and availability	N/A	n=181 received ketamine adjunctly to an oral antidepressant; n=39 received ketamine as a monotherapy	≥18	QIDS-SR item 12	Bonferroni pairwise comparisons revealed a significant reduction in the SI subscore from baseline to all subsequent time points (p<0.001), from post-infusion 1 to post-infusions 3 and 4 (p<0.01), and from post-infusion 2 to post-infusion 3

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Table 1 (continued)

Ketamine									
									(p<0.05). Those in the ketamine monotherapy group reported a mean subscore reduction of 0.91, while the ketamine adjunct group's mean reduction was 0.37. Overall, the ketamine monotherapy group exhibited greater reduction in SI.
Fava et al., 2020	Double-blind, placebo-controlled study	MDD (TRD), current MDE	single dose of IV ketamine 0.1mg/kg, or 0.2mg/kg, or 0.5mg/kg, or 1.0mg/kg	Study assessments performed at days 0, 1, 3, 5, 7, 14, 30	Placebo: single dose of midazolam 0.045mg/kg	Ketamine: 0.1mg/kg: n=18, 0.2mg/kg: n=20, 0.5mg/kg: n=22, 1.0mg/kg: n=20 Placebo: n=19	18–70	C-SSRS	During treatment, 32.1 % of participants in a ketamine group experienced suicidal ideation, while 44.4 % of participants in the midazolam group experienced suicidal ideation. Although less participants in the ketamine groups had suicidal ideation, this finding was non-significant, p=0.32.
Feeney, et al., 2021	Post-hoc analysis of a randomized double-blind, multi-site, placebo-controlled trial	TRD	-single infusion of IV ketamine 0.1mg/kg, or 0.2mg/kg or 0.5mg/kg or 1.0mg/kg	-single dose then 30 day follow-up, assessments done at 0,1,3,5,7,4 and 30 days	-1 placebo arm of midazolam (0.045mg/kg)	n=56 18–20 per treatment/control group	18–70	MADRS - suicidal ideation	Of patients with ≥ 2 at baseline, 31 had a drop in MADRS suicide score at day 3 but at 30 days the suicide item score did not differ between the placebo and ketamine group (p > 0.10). Placebo or treatment did not differ significantly in survival probability after 30 days. 10 of the 22 participants with baseline ≥ 2 MADRS suicide scores had a recurrence of significant suicide ideation. Overall, a ketamine single dose may have a small benefit in reducing suicide ideation, but effects diminish rapidly.
Galuskzo-Wegielnik et al., 2021	Case Report	TRD + somatic comorbidity	0.5 mg/kg of ketamine hydrochloride over 40 mins (as add-on care)	2 or 3 series, with 8 infusions twice weekly	N/A	n=5	51, 56, 43, 63, 60	MADRS-Sigma, CSSRS	4/5 patients achieved remission after one series and 3/5 had remission after the second

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Table 1 (continued)

Ketamine									
									series of ketamine infusions. Percentage of change in the MADRS score was lower after the second series than the first. Patient 1 - achieved remission after 8 ketamine infusions. Patient 2 - achieved remission of 7 months after 8 ketamine infusions but did not respond to second treatment. Patient 3 - achieved 9 months of remission and then sustained remission for 12 months after the second series. Patient 4 - 8 ketamine infusions with no response but 40 % reduction of MADRS score, then 8 more infusions but no response. Patient 5 - short-term remission only lasting 3 weeks, second series remission lasted 13 months.
Gilbert et al., 2020	Secondary analysis of a double-blind, placebo-controlled study	MDD (TRD)	0.5mg/kg of IV ketamine	Outcomes were assessed before infusion and 40, 80, 120, and 230 min, as well as on days 1, 2, 3, 10, and 11 after infusion	Placebo saline infusion	n=29	18–65	SI was assessed based on an exploratory factor analysis across multiple assessments of depression, including the MADRS, HDRS, Snaithe-Hamilton Pleasure Scale, and BDI	There was a significant reduction in SI factor score following ketamine compared with baseline ($p<0.05$), but not for placebo.
Grunebaum et al., 2018	Randomized controlled trial	MDD	-0.5mg/kg of IV racemic ketamine hydrochloride	-Infused over 40 min	0.02mg/kg of midazolam	n=40 in each group	18–65	SSI	The average SSI score was 4.96 points lower in the ketamine group than the midazolam group 1 day after infusion ($p<0.001$). The decrease in suicidal ideation at 230 min was also greater in the ketamine group ($p=0.001$).
Grunebaum et al., 2021	Assay sensitivity pilot study, parent RCT	MDD, in a current major depressive episode	-0.5mg/kg of IV racemic ketamine hydrochloride	-Infused over 40 min -6-week study	0.02mg/kg of midazolam	Ketamine: n=9; midazolam: n=11	18–65	SSI, CAT-SS	SSI score for ketamine patients decreased by an average of 5.67

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Table 1 (continued)

Ketamine									
									points from baseline to day 1 post-infusion (to a score of 5.88). For midazolam patients, the score decreased by an average of 7.00 points from baseline to day 1 post-infusion (to a score of 10.44). The drug by day interaction was 1.33, indicating slightly less change with ketamine ($p=0.62$). For the CAT-SS, the drug by day interaction was -5.98, indicating a 54 % greater decrease in suicidal ideation for ketamine compared to midazolam ($p=0.44$). Scores of midazolam-treated patients decreased by 10.98 points (to 57.12), and the score of ketamine-treated patients decreased by 16.96 points (to 48.22).
Gutierrez et al., 2024a	Retrospective cohort analysis	MDD-TRD	-IV ketamine at a dose of 0.5mg/kg, administered over 40 min	-Bi-weekly sessions for 4 weeks	N/A	n=71	18–75	BDI-II item 9, MADRS item 10	Patients experienced a statistically significant reduction in suicidal ideation from baseline to endpoint. BDI-II (Q9): $p=0.0014$; MADRS (Q10): $p=0.0019$. Of the patients who were experiencing SI before starting treatment, 55.88 % reported a reduction in SI and 44.12 % reported no SI at endpoint.
Hosseini et al., 2025	Secondary analysis of a randomized, controlled trial	TRD	Single dose of IV ketamine, 0.5mg/kg over 40 min	Participants completed at a minimum baseline and 24h	IV saline placebo	Ketamine: n=103; Placebo: n=49	M=34.3	MADRS C-SSRS	On day 1, there were no between-group differences regarding suicidal thoughts ($p=0.38$). A significant difference in suicidal thoughts was found on post-infusion day 21 ($p<0.05$), such that the ketamine group experienced a

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Ketamine								
Ionescu et al., 2016	Secondary analysis of an open-label study	Treatment-resistant MDD	-IV ketamine -0.5mg/kg for the first 3 infusions -0.75mg/kg for the last 3 infusions	-2 infusions/week for 3 weeks -Patients assessed once every 2 weeks for 3 weeks	N/A	n=14	18–65	C-SSRS HDRS ₂₈ -SI greater improvement, but no significant differences were found at any other time point. There was a significant decrease in C-SSRS ideation scores over time ($p<0.001$), such that scores decreased by an average of 0.27 per patient following each infusion. There was no significant effect of dose ($p=0.58$). There was also a significant decrease in the C-SSRS intensity scores over time ($p<0.01$). Again, there was no significant effect of dose on intensity scores ($p=0.67$). HDRS ₂₈ -SI scores also significantly decreased over time ($p<0.001$), with no significant effect of dose ($p=0.63$). Of the 7 patients who achieved C-SSRS suicidal ideation remission at the end of the treatment phase, 2 patients maintained remission at the end of follow-up.
Ionescu et al., 2019	Randomized, double-blind, placebo-controlled trial	Treatment-resistant MDD	-0.5mg/kg of IV ketamine	-Six 45 min IV infusions over 3 weeks -Outcomes were assessed four hours post-infusion -Follow-ups occurred every other week for 3 months after all the infusions	Placebo: saline	Ketamine: n=13; placebo: n=13	18–65	C-SSRS After the final infusion, 42 % of patients in the ketamine group met the criteria for absence of SI, while 25 % met the criteria in the placebo group. The difference was statistically insignificant ($p>0.05$).
Kaur et al., 2023	Open label uncontrolled study	MDD	Oral ketamine administered in a fixed dose of 150 mg in a volume of 50 ml of water	Patients were instructed to sip the solution over 10–15 min	N/A	n=30	22–56	MSSI All patients had severe suicidal ideation at baseline (MSSI>20), but at day 6 two-thirds of the sample had scores in the mild to moderate range (9–20), 4 of which had scores <9. Overall, MSSI scores significantly

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Ketamine								
Keilp et al., 2021	Randomized controlled trial	MDD and clinically significant suicidal ideation	-0.5mg/kg of IV racemic ketamine	-40 min infusion -Participants were reassessed approximately 24 hours post-infusion	0.02mg/kg midazolam IV infusion	Ketamine: n=39; midazolam: n=39	Ketamine: M=37.2; midazolam: M=39.6	SSI decreased from baseline to day 6 (p<0.001). SSI scores improved in both groups (p<0.001), but to a greater degree for the ketamine group compared to the midazolam group (p=0.008). On day 3 postinfusion, the ketamine group had significantly lower MADRS item 10 scores than the midazolam group (p=0.019), meaning that the ketamine group had lower suicidality scores. The rate of full remission of suicidal symptoms significantly differed between groups from day 1, 240 min post-infusion (p=0.001) to day 5 (p=0.044), such that the ketamine group experienced a higher rate of remission. The remission rate did not differ between groups after day 7.
Li et al., 2023	Randomized, double-blind placebo-controlled trial	Unipolar TRD	-single infusion of 0.5 mg/kg of ketamine	Outcomes assessed at 240 min post-infusion, and on days 2, 3, 5, 7, and 14	Control: 0.045 mg/kg midazolam	n=24 in each group	20–64	Item 10 of MADRS, CSSRS-ISS The rate of full remission of suicidal symptoms significantly differed between groups from day 1, 240 min post-infusion (p=0.001) to day 5 (p=0.044), such that the ketamine group experienced a higher rate of remission. The remission rate did not differ between groups after day 7.
Lin et al., 2023	Post-hoc analysis of two randomized, double-blind, placebo-controlled trials	Treatment-resistant MDD	-Single IV infusion of 0.5mg/kg of ketamine	Outcomes assessed 240 min post-infusion, and on days 2, 3, 5, and 7 post-infusion.	0.045mg/kg of midazolam or normal saline	Total: Ketamine group: n=33; Control group: n=32	Ketamine: M=37.03; Control: M=38.16	HDRS item 3, MADRS item 10, CSSRS-ISS The rate of full remission of suicidal symptoms significantly differed between groups from day 1, 240 min post-infusion (p=0.001) to day 5 (p=0.044), such that the ketamine group experienced a higher rate of remission. The remission rate did not differ between groups after day 7.
Pan et al., 2024	Retrospective cohort study	MDD	Prescription of ketamine	Study population followed between January 2019–January 2023; outcomes of interest analyzed up to 270 days after drug prescription	Patients prescribed common antidepressants such as fluoxetine and mirtazapine	N=21,372 in each cohort	Ketamine: M=50; Comparison: M=50.6	One or more encounter diagnoses of suicidal ideation The prescription of ketamine was associated with significant decreases in SI at 1 day - 7 days, 1 day - 30 days, 1 day - 90 days, 1 day - 180 days, and 1 day - 270 days (all ps<0.05).
Phillips et al., 2020	Secondary analysis	MDD (TRD)	- IV infusion of 0.5 mg/kg ketamine diluted in 0.9 % saline - IV infusion of midazolam 30 µg/kg diluted in saline	Administration occurred over 40 min -Phase 1: up to 2 infusions of either ketamine or midazolam -Phase 2: 6 infusions thrice weekly over a 2 week period -Phase 3: once-weekly infusions for 4 weeks	Control: midazolam (30 µg/kg diluted in saline)	n=37	Mean age: 39.5	MADRS-SI, QIDS-SR, QIDS-SI Phase 1: Participants treated with ketamine had lower MADRS-SI scores than those treated with midazolam at 2 h (p=0.03) and 7 days (p<0.001) post-infusion. There was no significant difference at 24 h (p=0.90). Phase 2: There were significant cumulative decreases in

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Ketamine								
								MADRS-SI scores from the start of Phase 2 to 3 successive infusions and each infusion after ($p<0.001$). Phase 3: During the maintenance phase, there was no change in MADRS-SI scores during maintenance infusions ($p=0.94$). A single infusion of ketamine significantly reduced MADRS-SI scores at 24 hours post-infusion ($p<0.001$), with 81 % of patients scoring 0 or 1. In patients receiving repeated doses of ketamine, the first infusion also significantly reduced MADRS-SI scores ($p<0.001$), with 90 % of patients receiving a rating of 0. Reductions were maintained throughout the 12-day treatment period ($p=0.001$). SI scores reduced 24 hrs post-infusion compared to midazolam (53 % of the ketamine group scored 0 on all scales, 24 % in control). Ketamine reduced implicit suicide-related associations. 86.1 % of the ketamine group had below 4 on the BSS score at 24 hrs and 61.9 % in midazolam.
Price et al., 2009	Open-label study	MDD (TRD)	-IV infusion of racemic ketamine hydrochloride at a dose of 0.5mg/kg, diluted in saline -A subset of ketamine responders received up to 5 additional infusions	-Administered over 40 min and assessed over 24 hours	N/A	n=26	M=48.2	MADRS-SI
Price et al., 2014	Double-blind randomized control trial	TRD	-single IV infusion of ketamine hydrochloride (0.5mg/kg) or midazolam (2:1)	- 40 min and overnight stay	Control - midazolam (0.045mg/kg)	n= 54	Mean = 48.6 (11.4)	MADRS QIDS-SR BSI Implicit Association Test
Rodrigues et al., 2024	Naturalistic, retrospective study	Treatment-resistant MDD	-IV ketamine -First 2 infusions dosed at 0.5mg/kg and last two flexibly dosed between 0.5mg/kg and 0.75mg/kg based on clinical response and tolerability	4 infusions	N/A	n=84	18–65	QIDS-SR ₁₆ SI

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Ketamine								
Seraj et al., 2025	Randomized, double-blind, midazolam-controlled trial	MDD	Single dose of oral ketamine (3mg/kg dissolved in 50 ml of water)	Assessments conducted at baseline, 4 h after administration, day 3, day 7	Oral midazolam (0.3mg/kg dissolved in 50 ml of water)	Ketamine: n=40; 18–60 midazolam: n=40	HAMD MSSI	MSSI scores were significantly lower in the ketamine group at all 3 assessment points (4 h, day 3, day 7; all $p < 0.001$).
Singh et al., 2016a	Multicenter, double-blind RCT	Recurrent MDD (TRD)	-2 ketamine groups -0.5 mg/kg of IV ketamine, either 2 or 3 times a week (based on group), administered over 40 min	-Maximum study duration was 13 weeks, with 4 weeks allocated to the double-blind treatment phase	-2 placebo groups -0.9 % of IV sodium chloride 2 or 3 times a week (based on group), administered over 40 min	-Placebo 2 times/ week: n=16 -Placebo 3 times/ week: n=16 -Ketamine 2 times/week: n=18 -Ketamine 3 times/week: n=17	C-SSRS	Placebo 2 times/ week: at baseline, 12 participants were experiencing suicidal ideation or behavior. Following treatment, 8 participants were, demonstrating an overall improvement. Placebo 3 times/ week: at baseline, 13 participants were experiencing suicidal ideation or behavior. Following treatment, 8 participants were, also demonstrating an overall improvement. Ketamine 2 times/ week: at baseline, 10 participants were experiencing suicidal ideation or behavior. Following treatment, 4 participants showed an improvement in suicidality. Ketamine 3 times/ week: at baseline, 10 participants were experiencing suicidal ideation or behavior. Following treatment, 4 were, also showing an improvement in suicidality. Overall, an improvement in suicidality was observed in all treatment groups, but more so for the ketamine groups.
Sinyor et al., 2018	Single-site, double-blind, pilot RCT	MDD, current MDE	-0.5 mg/kg of ketamine, in 100 ml normal saline infused over 40–50 min -Treatment delivered on 6 separate occasions	-Treatment delivered over 12 days, 3 times weekly until participants received six infusions -Study visits at baseline, each infusion day, day 14, day 42 after treatment	Control: 0.045 mg/kg of midazolam, administered in the same manner as ketamine	Ketamine: n=5; 18–65 Midazolam: n=4	SSI C-SSRS MADRS item 10	In the ketamine group, SSI scores reduced by 84 % at baseline (14.0 ± 4.5) to endpoint (2.2 ± 2.5). MADRS item 10 (suicidal ideation) scores also reduced by 68 % from baseline (3.8 ± 0.45) to

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Ketamine									
									endpoint (1.2 ± 0.84). In the midazolam group, SSI scores reduced by 37 % from baseline (19.8 ± 9.5) to endpoint (12.5 ± 15.0). MADRS item 10 scores reduced by 29 % from baseline (3.5 ± 1.7) to endpoint (2.5 ± 3.0). Overall, SI reduction in the ketamine group was larger, more robust, and longer-lasting than reduction seen in the midazolam group.
Su et al., 2023	Randomized, double-blind, controlled trial	Treatment-resistant MDD	-Single IV infusion of 0.5mg/kg ketamine	Outcomes assessed at 40, 80, and 240 min post-infusion, and on days 2, 3, 5, 7, and 14 post-infusion	0.045mg/kg of midazolam	20–64	n=42 in each group (total: n=84)	MADRS item 10 CSSRS-ISS	More patients receiving ketamine achieved full remission of suicidal ideation from day 2 ($p=0.015$) to day 5 ($p=0.038$) compared to those receiving midazolam.
Thakurta et al., 2012	Single-center, prospective, 4-week, open-label, single-arm pilot study	TRD	Single IV infusion of ketamine hydrochloride (0.5 mg/kg diluted in 0.9 % saline), administered over 40 min	Assessed at baseline, 40, 80, 120, and 230 min post-infusion, 1 and 2 days post-infusion	N/A	18–5	n=27	HDRS SSI	(SSI): Significant reduction in SSI scores was observed. Baseline mean Score: 4.85 ± 5.37. 40 Minutes Post-Infusion: 0.78 ± 1.48 (an 80 % reduction; $P = 0.001$). The change in scores remained statistically significant at all time points from 40 to 230 min post-infusion. By Day 1, scores began to approach baseline, and by Day 2, the change was not significant compared to baseline ($P = 0.534$). (HDRS-SI): Baseline Mean Score: 1.37 ± 1.33. 40 Minutes Post-Infusion: 0.41 ± 0.57 (a 70 % reduction; $P = 0.001$). The change in scores remained statistically

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Ketamine									
Tu et al., 2025	Post-hoc analysis of two randomized, double-blind, placebo-controlled trials	MDD-TRD	Single infusion of 0.5mg/kg or 0.2mg/kg of ketamine	Assessed prior to infusion, at 40, 80, and 240 min postinfusion, and on days 2, 3, 5, 7, and 14 postinfusion	Normal saline or 0.045mg/kg midazolam	Trial 1: 0.5mg/kg: n=16; 0.2mg/kg: 16; saline: n=16 Trial 2: 0.5mg/kg: n=24; midazolam: n=24	Trial 1: M=46.15; Trial 2: M=32.35	MADRS HAMD PANSI	significant from 40 to 230 min post-infusion. By Day 1, the reduction was no longer statistically significant. In trial 1, the normal saline group did not statistically differ from the ketamine infusion group on any of the clinical measure reductions ($p>0.05$). In trial 2, patients with 0.5mg/kg ketamine had greater reduction rates on MADRS, HAMD item 3, and MADRS item 10 scores at day 3 compared to the midazolam group (all $ps<0.05$), but total HAMD and PANSI scores did not differ ($p>0.05$). There was a statistically significant difference between the MADRS suicide item scores of all participants before the ketamine infusion (3.88 ± 1.38) and at 4 h (2.52 ± 1.28) and 24 h (1.80 ± 1.08) following the infusion, $p<0.001$. Reductions were greater at 24 h than at 4 h. This study demonstrates the rapid and significant antidepressant and antisuicidal effects of a single ketamine infusion. Significantly reduced depression severity as early as 40 mins after injection ($p < 0.001$) and the HDRS decreased from baseline significantly 40 mins past injection although BDI-II did not have statistical significance after
Uyar & Gunes, 2024	Retrospective study	MDD	Single IV infusion of 0.5mg/kg over 40 min	Assessed before treatment and 4 h and 24 h after treatment	N/A	N=120	M=35.35	CGI MADRS	
Vidal et al., 2018	Open-label longitudinal Study	MDD	Single 0.5mg/kg 1 min IV injection	4 week follow-up	N/A	N = 10	25–65	MADRS SSI HDRS BDI-II	

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Table 1 (continued)

Ketamine									
									day 3. Statistically significant decrease from suicidality on days 1 (p = 0.002) and 7 (p = 0.003), suicidal thoughts decreased over time and change in suicidal ideation significantly correlated with the changes in severity of depression. Prior to ketamine treatment, score was 11. At 40, 80, 120, and 230 min after injection, BSI scores were consistently under 5. At the follow-up 2 weeks after discharge, it seemed as though his symptoms had disappeared.
Wang et al., 2017	Case report	Recurrent depressive disorder, current MDE	Ketamine IV injection, dose of 70 mg (<1 mg/kg) (first dose), later given 40 mg (0.5 mg/kg)	Injected every other day, 3 times total	N/A	n=1	27	BSI-CV	After the first infusion, there were significant reductions in the mean SSI score, which decreased from 3.5 to 1.5, p<0.001. Four hours after the first treatment, the suicide item showed a significant reduction (a score of 4 before beginning treatment, and 0 after) improvement and the patient reported no suicidality. After the 3rd and last treatment (day 13), the patient was deemed to be in remission. On days 14–17 following treatment, the patient continued to deny any feelings of suicidality. After the intervention, the ketamine group experienced a significantly greater decrease in suicidal ideation than the control group (p<0.001).
Zheng et al., 2019	Open-label study	MDD	0.5mg/kg of IV ketamine over 40 min	6 infusions administered over the course of 12 days	N/A	n=77	18–65	SSI-part 1	
Ziegler et al., 2021	Case report	MDD	Patient received intranasal ketamine at a dose of 50 mg/day (10 mg/spray), with 5 min between sprays	Ketamine was administered for 3 days, over a 5 day period, starting on day 9 upon admission, with the last dose given on day 13.	N/A	n=1	49	HAMD-6 suicide item	
Zolghadriha et al., 2024	Randomized controlled clinical trial	Treatment-resistant MDD	Trial group: 0.5mg/kg of IV ketamine	Outcomes were assessed up to 2 months post-injection	Control group received normal saline	n=64; n=32 in each group	25–60	BSI Scale	

Esketamine									
Arrighi et al., 2023	Case report	Treatment-resistant MDD	Esketamine nasal spray introduced at 56 mg, and increased to 84 mg twice a week	20 weeks of twice-weekly administrations	N/A	n=1	31	MADRS	The first clinical signs of response to the treatment were seen at week 6, with a reduction in the intensity and frequency of the suicidal thoughts. After the 20 weeks of treatment, the patient described a complete remission of symptoms, including suicidal ideation. Patient continued esketamine upon discharge at a reduced frequency for 6 months; after discontinuation there has been no relapse for 2 years.
Brendle et al., 2022	Retrospective observational cohort study	MDD	-Patients who received esketamine nasal spray -Patients received between 1 to 71 treatments	Data from July 2019 to June 2021 was collected	N/A	n=140	≥18; M=36	PHQ-9	When comparing all patients, suicidal ideation scores significantly decreased from baseline to last available treatment, ($p<0.001$). Specifically, patients with 31–71 treatments experienced the most significant decline ($p=0.012$) when compared to patients with 2–5 treatments ($p=0.603$), patients with 6–10 treatments ($p=0.071$), patients with 11–15 treatments ($p=0.043$), and patients with 16–30 treatments ($p=0.227$).
Canuso et al., 2021	Post-hoc analyses of pooled data from double-blind, randomized, placebo-controlled multicenter trials	MDD	-84 mg of esketamine nasal spray and standard of care -Dose could be adjusted during the first 2 weeks of treatment if needed	Twice weekly for 4 weeks	Matching placebo nasal spray and standard of care	Esketamine: n=229; placebo: n=227	18–64	CGI-SS-r	Patients in both groups experienced a significant reduction in the severity of their suicidality. However, the difference between groups was not statistically significant. From baseline to 24 hours after the first dose, CGI-SS-r scores decreased by a mean of 1.5 points in the esketamine group and a mean of 1.3 points in the placebo group. Severity of suicidality also improved in both groups at the end of the treatment. Resolution of suicidality was achieved by 33.2 % of esketamine patients and 20.0 % of placebo patients at 4 hours after the first dose, 34.5 % and 32.9 % respectively at 24

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Table 1 (continued)

Esketamine									
Canuso et al., 2018	Double-blind multi-center, proof of concept	MDD	Nasal spray administered 14 mg per 100uL, self-administered but supervised to each nostril 5 mins apart. Days 1,4,8,11,15,18,22 and 25	24–48 hrs of screening then 4 weeks of double-blind treatment and then 8 weeks of posttreatment follow-up	Matching placebo	N=66 and 44 completed + followup	19–64	MADRS	hours, and 61.9 % and 54.7 % at day 25.. MADRS improved (decreased) from baseline to 4 hrs (mean = -13.4, SD = 9.03) after a dose greater than placebo (mean = -9.1, SD = 8.38), over 4 week phase. Significant improvement in depressive symptoms in esketamine between 24 hours after the dose (p = 0.002), day 3 and day 11 but in the posttreatment follow-up, the improvement was not statistically greater than placebo. Esketamine had greater improvement in MADRS suicidal thoughts 4 hrs after treatment but not 24 hrs after the first dose. Results support the idea that esketamine is a good treatment for the rapid reduction of symptoms of imminent risk of suicide.
Fu et al., 2020	Double-blind randomized, placebo-controlled, multicenter study	MDD, active suicidal ideation	-84 mg of intranasal esketamine (in addition to standard of care) -After day 1, a single dose reduction from 84 mg to 56 mg was permitted	-4 weeks of treatment followed by 9 weeks of follow-up -Drug was administered twice weekly for the 4 weeks	Placebo nasal spray (in addition to standard of care)	Esketamine: n=112; Placebo: n=112	18–64	CGI-SS-r	At 24 hours post-first dose, patients in both groups demonstrated improvement in the severity of their suicidality, but there was no significant difference between groups (p=0.107).
Fu et al., 2023	Post-hoc analysis using data pooled from two double-blind, randomized, placebo-controlled, multicenter, phase 3 studies	MDD, current suicidal ideation with intent	-Intranasal esketamine at a dose of 84 mg (in addition to standard of care) -After the first dose, a one-time dose reduction to 56 mg was allowed for tolerability issues	-4 weeks of the treatment phase, followed by a 9-week post-treatment follow-up phase	Placebo nasal spray (in addition to standard of care)	Esketamine: n=226; placebo: n=225	18–64	CGI-SS-r	Time to achieving a suicidality score ≤ 1 was significantly shorter in the esketamine group (median: 16 days) versus the placebo group (median: 25 days, p=0.003). Time to achieving a suicidality score ≤ 1 for two consecutive visits was significantly shorter in the esketamine group (median: 25 days) than the placebo group (median: 52 days) as well (p=0.020).
Gutierrez et al., 2024b	Multi-centre observational prospective cohort study	MDD-TRD	IV ketamine (0.5mg/kg over 40 min) or intranasal esketamine (56 mg for first treatment and 84 mg for the rest of the treatments)	Twice a week sessions for 4 weeks	N/A	Ketamine: n=26; Esketamine: n=27	18–75	MADRS	Patients receiving ketamine and esketamine both experienced a statistically significant reduction in SI severity from baseline to post-treatment. At

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Table 1 (continued)

Esketamine									
									treatment endpoint, 46.15 % responded to ketamine and 58.82 % responded to esketamine. The SI remission rate was 30.78 % for ketamine and 23.53 % for esketamine.
Hong et al., 2023	Post-hoc analysis of a randomized phase 3 study	MDD	-Intranasal esketamine at a dose of 84 mg in addition to standard of care treatment	-Administered twice a week for 25 days	A placebo group was included	Esketamine asian subgroup: n=26; esketamine total group: n=111; placebo asian subgroup: n=27; placebo total group: n=112	18–64	CGI-SS-r	CGI-SS-r scores improved from baseline to 4 hours post-first dose, and continued to improve through day 25 in both groups. However, the treatment difference was greater for the esketamine group.
Ionescu et al., 2021	Phase 3, double-blind, randomized study	MDD	-84 mg esketamine nasal spray and standard of care -After the first dose, a one-time dose reduction from 84 mg to 56 mg was allowed	Self-administered twice weekly for 4 weeks	Placebo nasal spray and standard of care	Esketamine: n=114; placebo: n=113	18–64	CGI-SS-r,	Patients in both groups experienced rapid reductions in the severity of their suicidality from baseline to 24 hours post-first dose, the between-group difference was not statistically significant (p=0.379). Among patients who completed the double-blind treatment phase and entered the follow-up phase, 86.3 % of patients in the esketamine group and 76.6 % of patients in the placebo group had a score of 0 or 1 at day 90.
Lopes et al., 2024	Secondary analysis of an open-label study	Unipolar TRD	-0.5mg/kg of subcutaneous esketamine -Could be escalated to 0.75mg/kg or 1mg/kg if needed	8 weekly administrations	N/A	n=24	M=33.05	BSI MADRS-SI	A significant reduction in BSI scores was observed 24 h after the first session and was maintained over the following sessions. There was no significant difference between the mean BSI observed at 24 h and 7 days after each session, indicating that each dose had a sustained effect. The effect was maintained throughout the 6 months of follow-up, such that BSI scores during follow-up were significantly lower than baseline scores (p<0.0001).
Martinotti et al., 2022	Observational, retrospective and multicentric study	treatment-resistant depression (TRD)	-esketaamine nasal spray, started on the 56 mg dosage, with some switching to the 84 mg dosage after the first month -done along with existing medications	Anamnestic data and psychometric assessments were collected at baseline (T0), 1 month (T1), and 3 months (T2) after treatment began	N/A	n=116	M = 50 ± 12 years; >18	MADRS, HAM-D-21	Significant reduction in depressive symptoms at 1 month (p<0.0001) and 3 months (p<0.0001) compared to baseline. 3-month response rate of 64.2 % and remission rate of 40.6

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Table 1 (continued)

Esketamine									
									%.
									Most 3-month remitters were not responders at 1 month, indicating a later response to esketamine.
McIntyre et al., 2024b	Open-label, rater-blinded, RCT	MDD (TRD)	-Esketamine nasal spray, flexibly dosed per label -Each participant received at least 1 dose -In combination with an ongoing SSRI/SNRI	Week 8 was the primary endpoint, but the entire study lasted 32 weeks	-Quetiapine extended release, flexibly dosed per label -Each participant received at least 1 dose -In combination with an ongoing SSRI/SNRI	Esketamine: n=336; quetiapine: 334	18–74	N/A	Treatment-emergent suicidal ideation was reported in 5 (1.5 %) of patients treated with esketamine, and in 7 (2.1 %) patients treated with quetiapine. Treatment-emergent suicide attempts were reported in 2 (0.6 %) of patients treated with esketamine, and in 1 (0.1 %) patient treated with quetiapine.
Nikayin et al., 2022a	Comparative analysis	MDD (current episode)	Intranasal esketamine (56 or 84 mg)	Multiple treatments each ≤7 days apart for up to 8 total treatments	IV ketamine (0.5mg/kg) over 40 min	Esketamine: n=81; ketamine: n=129	Esketamine: M=46.7; ketamine: M=49.9	MADRS, QIDS-SR	There were no group differences in MADRS or QIDS-SR suicidal ideation scores between the esketamine and ketamine groups.
Pepe et al., 2023	Open-label study	MDD (TRD), current MDE	Esketamine oral spray administration, first administration was 28 or 56 mg, then increased to 56 or 84 mg based on clinical judgement and tolerability	Twice a week for the first month, then once a week for the following 8 weeks (overall treatment of 3 months)	N/A	n=25	M=55.1	Sub-item 10 of MADRS and subitem 9 of BDI	Clinicians' evaluations reported significant reductions in suicide starting in the first month of treatment, but reduction compared to baseline score was only statistically significant at month 1 and 3: (1 month: p=0.007, 2 months: p=0.178, 3 months: p=0.01). Patients rated reductions in suicide starting at one month, which became statistically significant at endpoint (1 month: p=0.076, 2 months: p=0.48, 3 months: p=0.039).
Pompili et al., 2023	Case reports	MDD (TRD)	-Intranasal esketamine -Induction (first month): 56 mg administered twice a week -Maintenance (second month): 56 mg administered once a week -Maintenance (third month): 56 mg administered once ever 2 weeks	3+ months	N/A	n=2	Case 2: 52; Case 3: 28	C-SSRS	Case 2: The C-SSRS highlighted suicidal ideation with intent. After 23 esketamine administrations there was no more suicidal ideation (full recovery and symptom resolution). Subsequent follow-ups revealed the same results. Case 3: At intake suicide risk was high, suicidal ideation and intent for most of the day were reported. After 13 administrations, a significant improvement, especially in reducing

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Esketamine									
Singh et al., 2016b	Double-blind, double-randomized, placebo-controlled study	MDD (TRD)	Esketamine was either administered intravenously, at a dose of 0.20mg/kg, or 0.40 mg/kg depending on group membership -Received over 40 min	-Screening: up to 2 weeks -Treatment: 7 days -Posttreatment: 4 weeks	Control: placebo (0.9 % saline solution) -Received over 40 min	Esketamine 0.20mg/kg: n=9; esketamine 0.40mg/kg: n=11; placebo: n=10	18–64	C-SSRS	suicide risk was observed (treatment ongoing). No patients had treatment-emergent suicidal ideation or suicidal behavior. Generally, suicidal ideation scores either improved or were maintained from screening to posttreatment.
Smith-Apeldoorn et al., 2024	Multicenter, double-blind, randomized, placebo-controlled, parallel-group trial	TRD (unipolar), current MDE	-Participants took capsules containing esketamine 3 times a day -During the first 3 days, doses were gradually increased from 30 mg/day to 90 mg/day -During the last 3 days, dosages were decreased from 90 mg/day to 30 mg/day	-42 consecutive days of treatment, followed by 4 weeks of posttreatment wash-out	Control: placebo capsules containing microcrystalline cellulose and magnesium stearate	Treatment: n=57; placebo: n=56	18–80	HDRS item 3	In both groups, one participant committed suicide - in the first week of treatment for the placebo group, and in the fourth week of treatment for the esketamine group.
Surjan et al., 2022	Retrospective real-word study	Treatment-resistant MDD or BD	-Subcutaneous esketamine injections -Doses varied from 0.5mg/kg to 1mg/kg	-Outcomes were assessed at baseline, 24 hours, and 7 days after each administration	N/A	n=39 in the MDD group	16–70	MADRS item 10	Significant effects for time on item 10 MADRS scores were found (p<0.0001), such that the score significantly decreased from baseline to the end of the study. Significant reductions in the suicidality score were observed from 24 hours after the first administration (p<0.001), and there were further reductions with repeated administrations.
Tomy et al., 2025	Case series	MDD	56 mg or 86 mg of intranasal esketamine	Weekly or twice weekly treatments for 4 weeks and then weekly or biweekly treatments Patient 1: 56 weeks Patient 2: 52 weeks Patient 3: 32 weeks	N/A	n=3	Patient 1: 52; QIDS-SR- Patient 2: 56; 16 Patient 3: 39		Patient 1: At 2 weeks following treatment initiation, he no longer reported SI and had a marked reduction in his score. At 7 weeks, he remained without SI, although he had worsening depressive symptoms. Patient 2: At 2 weeks following initiation, he no longer experienced SI. At week 24, he had worsening depressive symptoms but did not develop SI. Even over a year later, he had no SI. Patient 3: At 2 weeks, she no longer had SI and experienced an overall improvement in mood. She never experienced worsening symptoms throughout the course of treatment or

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Esketamine									
Turkoz et al., 2022	Post hoc analysis of a pooled data set	MDD	-Patients self-administered intranasal esketamine (84 mg) twice weekly	- 24 hour to 48 hour screening period -4 weeks double-blind treatment phase -9-week follow-up phase	Placebo nasal spray	Esketamine: n=182; placebo: n=180	18–64	CGI-SS-r	when esketamine was discontinued. Patients in both treatment groups experienced a rapid reduction in suicidality severity at 24 hours after the first dose. There was no significant difference between groups
Vieira et al., 2021	Randomized, double-blind clinical trial	Treatment-resistant major depression	Single IV infusion of 0.5mg/kg of ketamine over 40 min. Single IV infusion of 0.25mg/kg of esketamine over 40 min.	Assessed at baseline, 24 h, 72 h, and 7 days post-infusion	N/A	N=59 Ketamine: N=9 Esketamine: N=30	≥18	MADRS	The effect of both ketamine and esketamine in reducing suicidal ideation from baseline to all time points was statistically significant (p<0.001). There was no significant difference between time points following infusion and between treatment groups at each point.
Zaki et al., 2023	Ongoing phase 3, open-label, multicenter, long-term extension study	MDD (TRD)	-Starting dose of esketamine nasal spray was 28 mg for those 65+, and 56 mg or 84 mg for others, as a flexible dose	-Therapy twice a week for 4 weeks	N/A	n=1148	≥18	C-SSRS	Overall, 5.6 % of participants experienced 1 or more events related to suicidality. One participant died by suicide, 4 days after the most recent dose. In the C-SSRS assessment, 49 participants (4.3 %) without history of suicidal ideation reported occurrences of suicidal ideation during the study. 10 participants (0.9 %) reported new suicidal behavior, 9 of whom had a previous history. Improvement in suicidality severity from baseline to post-baseline occurred in 160 participants (14 %).
Zhang et al., 2022	Case report	MDD (TRD)	-IV esketamine infusions (0.4 mg/kg), over 40 min	12 infusions	N/A	n=1	26	HAMD	Prior to treatment with esketamine, the patient had severe suicidal ideation. Following the 12 infusions, he reported a complete remission of suicidality. There was no recurrence of symptoms at a 6-month follow-up.

rTMS: Repetitive transcranial magnetic stimulation; ECT: electroconvulsive therapy; MDD: Major depressive disorder; TRD: treatment-resistant depression; M: Mean; SD: Standard deviation; N/A: Not applicable; TBS: theta-burst stimulation; DLPFC: dorsolateral prefrontal cortex; BSI: Beck Scale for Suicidal Ideation; IDS-SR: Inventory of Depressive Symptomatology Self-Report; PHQ-9: Patient Health Questionnaire 9; HDRS/HAMD: Hamilton Depression Rating Scale; MADRS: Montgomery-Åsberg Depression Rating Scale; SSI: Scale for Suicidal Ideation; SIOSS: Self-Rating Idea of Suicide Scale; BDI: Beck Depression Inventory; C-SSRS: Columbia-Suicide Severity Rating Scale; SIS: Suicidal Ideation Scale; CHRT: Concise Health Risk Tracking Self-Report; QIDS: Quick Inventory of Depressive Symptomatology; BHS: Beck Hopelessness Scale; PANSI: Positive and Negative Suicide Ideation Inventory; CAT-SS: Computerized Adaptive-Suicide Scale; MSSI: Modified Scale for Suicidal Ideation; CGI-SS: Clinical Global Impressions scale for Severity of Suicidality.

of SI; however, ketamine was associated with greater reductions in SI compared to ECT ($p=0.045$). Similarly, another study comparing rTMS to a single ketamine infusion (Chen et al., 2022a) also reported greater reductions following treatment with ketamine compared to a treatment course with rTMS ($p=0.002$).

The frequency of ketamine treatment may also affect the magnitude of reductions in suicidality. Although significant improvements are observed following a single ketamine infusion, multiple infusions seem to provide a greater benefit than a single infusion. For example, Phillips et al. (2020) and Ionescu et al. (2016) reported that successive infusions of ketamine resulted in additional decreases in SI scores. Similarly, Price et al. (2009) found that more participants who received multiple infusions experienced a greater reduction in scores of suicidality than those who only received a single infusion. However, there seems to be a limit to the cumulative improvements seen with additional ketamine treatments, with maintenance infusions following the main treatment phase not resulting in additional improvements (Ionescu et al., 2016). Also, Singh et al. (2016a) did not observe significant differences between outcomes for ketamine administered twice weekly and ketamine administered thrice weekly, demonstrating that there are some conflicting findings regarding the importance of frequency of administration.

Moreover, several studies reported rapid reductions in SI following ketamine administration, with improvements being observed as soon as 40 minutes following an infusion (Thakurta et al., 2012; Vidal et al., 2018). However, the rapid improvements seem to be transient, with suicide symptoms returning approximately one week after a single infusion (Lin et al., 2023), and in one study, patients returned to baseline scores of SI just one day after the infusion (Thakurta et al., 2012). Once again, there are some conflicting findings, with a controlled trial reporting that ketamine's antisuicidal effect diminished 28 days following a single infusion (Chen et al., 2022a), and in a case report, suicidal thoughts had not returned even eleven months after a single infusion (Arango-Posada et al., 2024). Notwithstanding, studies examining the effects of multiple ketamine infusions suggest that reductions in SI may persist for longer periods than with a single infusion, typically ranging from two weeks (Averill et al., 2022), to 1 month (Chaudhary et al., 2023; d'Andrea et al., 2024).

3.2.4. Esketamine

There were twenty-four studies included that assessed the efficacy of esketamine in reducing SI, and in some cases, suicidal behavior, in patients with MDD (Arrighi et al., 2023; Brendle et al., 2022; Canuso et al., 2018; Canuso et al., 2021; d'Andrea et al., 2024; Fu et al., 2020; Fu et al., 2023; Gutierrez et al., 2024b; Hong et al., 2023; Ionescu et al., 2021; Lopes et al., 2024; Martinotti et al., 2022; McIntyre et al., 2024b; Nikayin et al., 2022a; Pepe et al., 2023; Pompili et al., 2023; Singh et al., 2016b; Smith-Apeldoorn et al., 2024; Surjan et al., 2022; Tomy et al., 2025; Turkoz et al., 2022; Vieira et al., 2021; Zaki et al., 2023; Zhang et al., 2022; Table 1). The scales most commonly used to assess suicidality included the HAMD, MADRS, CCSSRS, and the Clinical Global Impression of Severity of Suicidality (CGI-SS) scale. Most of the studies used a nasal spray to administer esketamine, most commonly at a dose of 56 mg to 84 mg, with seven studies administering the esketamine either subcutaneously, orally, or intravenously (Lopes et al., 2024; Pepe et al., 2023; Singh et al., 2016b; Smith-Apeldoorn et al., 2024; Surjan et al., 2022; Vieira et al., 2021; Zhang et al., 2022).

Eighteen studies found esketamine to be effective in reducing SI severity (Arrighi et al., 2023; Brendle et al., 2022; Canuso et al., 2018; d'Andrea et al., 2024; Fu et al., 2023; Gutierrez et al., 2024b; Hong et al., 2023; Lopes et al., 2024; Martinotti et al., 2022; Nikayin et al., 2022a; Pepe et al., 2023; Pompili et al., 2023; Singh et al., 2016b; Surjan et al., 2022; Tomy et al., 2025; Vieira et al., 2021; Zaki et al., 2023; Zhang et al., 2022), with six studies reporting that treatment with esketamine did not result in improvements that were significantly different from control treatments (Canuso et al., 2021; Fu et al., 2020; Ionescu et al., 2021; McIntyre et al., 2024b; Smith-Apeldoorn et al., 2024; Turkoz et al., 2022). Studies comparing the efficacy of ketamine and esketamine (Gutierrez et al., 2024b; Nikayin et al., 2022a; Vieira et al., 2021) found them to have comparable antisuicide effects ($p>0.05$), such that they both significantly reduced suicidal symptoms (d'Andrea et al., 2024; $p<0.001$).

Improvements in SI and suicidal behavior were found to occur rapidly in a number of studies, as soon as 4 hours following administration (Canuso et al., 2018; Hong et al., 2023; Surjan et al., 2022; Vieira et al., 2021), though some studies report it taking upwards of 1 month to observe clinical improvements when multiple treatments were given

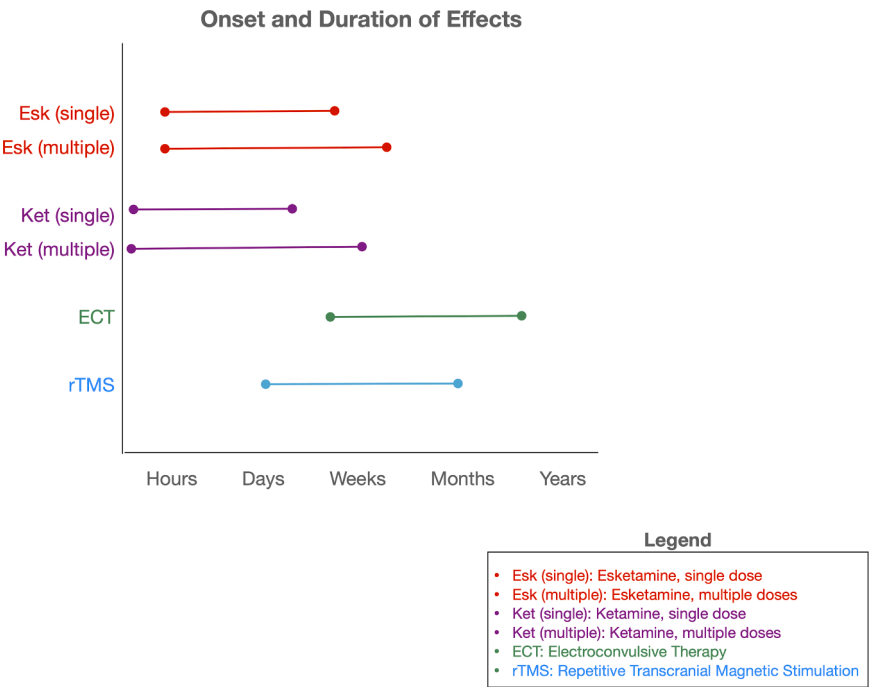


Fig. 2. Summary of Reported Onset and Duration of Antisuicidal Effects Across Interventions.

(Arrighi et al., 2023; Martinotti et al., 2022; Pepe et al., 2023). Most studies that administered multiple doses noted that further improvements were observed over time throughout the treatment period (Hong et al., 2023; Surjan et al., 2022). In support of this, an observational study (Brendle et al., 2022) found that patients receiving the highest number of treatments (31–71) experienced the most significant decline in SI scores when compared to those receiving less treatments. Additionally, some studies with follow-up periods—predominantly case series—noted that this reduction lasted for a significant period of time, up to 6 months and even longer in some cases (d'Andrea et al., 2024; Hong et al., 2023; Lopes et al., 2024; Martinotti et al., 2022; Pepe et al., 2023; Pompili et al., 2023; Tomy et al., 2025; Zhang et al., 2022). One case report with a longer follow-up period reported that effects were sustained for years, even after discontinuation of treatment (Arrighi et al., 2023). Notwithstanding, there are some conflicting findings regarding the maintenance of improvements, with some controlled studies indicating that antisuicidal effects may be short-term, such that improvements are lost within a week (Canuso et al., 2018).

4. Discussion

4.1. Implications

The findings of this comprehensive narrative review indicate that rTMS, ECT, ketamine, and esketamine are all associated with reductions in certain dimensions of suicidality, primarily SI, in individuals with MDD. The majority of studies evaluated the effect of the aforementioned interventions on SI, and select studies assessed additional dimensions of suicidal behavior and completed suicide. As a result, the available evidence predominantly supports the efficacy of these interventions in reducing SI, with more limited and lower-certainty evidence regarding the effects on suicidal behavior in persons with MDD/TRD. Although ketamine and esketamine seem to demonstrate similar levels of efficacy according to the studies that compared the two drugs (d'Andrea et al., 2024; Gutierrez et al., 2024b; Nikayin et al., 2022a; Vieira et al., 2021), there is stronger overall evidence in support of ketamine, given the greater consistency of findings across studies. Additionally, studies evaluating the comparative efficacy of ketamine with ECT and rTMS suggest that the antisuicidal effect of ketamine is superior in terms of the onset of the effect and the magnitude of reductions. However, it is important to note that only few studies compared interventions, and as such, the conclusions that can be drawn are limited. Ongoing studies are evaluating the efficacy of interventions such as ECT and ketamine on suicidality in depression to provide deeper insight into their comparative effectiveness (Anand & Hu, 2022).

Most included studies investigating rTMS utilized conventional protocols, including high-frequency and low-frequency stimulation, iTBS, and cTBS, which vary in stimulation parameters, dosing schedules, and targeting approaches. More recently, accelerated protocols such as Stanford Accelerated Intelligent Neuromodulation Therapy (SAINT) have been proposed as iTBS protocols designed to enhance the rapidity and magnitude of antidepressant, and potentially, antisuicidal effects. SAINT employs functional connectivity magnetic resonance imaging (fcMRI) to target a region of the left DLPFC that is most anticorrelated with the subgenual anterior cingulate cortex (sgACC; Cole et al., 2020). Early findings regarding the antidepressant effects of this protocol have been promising, suggesting that it is an innovative and emerging approach to rTMS (Cole et al., 2020; Li et al., 2024). However, the current literature examining the antisuicidal effects of SAINT remains limited and was not a focus of the current review. As such, the antisuicidal effects of accelerated rTMS protocols require more detailed evaluation in future studies.

There are key differences that may inform which intervention is chosen for a patient at risk for suicide. For individuals who require a rapid improvement in SI, ketamine and esketamine may be preferred, as studies suggest that they provide rapid reductions in SI, with some

antidepressant and antisuicidal effects being observed within 24 to 48 hours following a single dose. However, the duration of these effects vary depending on the treatment protocol, with the highest-certainty evidence from controlled trials suggesting that single infusions provide short-term improvements, while multiple or maintenance infusions may result in more sustained improvements. In contrast, rTMS and ECT protocols typically involved multiple sessions over days or weeks, with improvements in SI and suicidal behavior continuing during treatment, and in some observational follow-ups, for several weeks to months after the completion of treatment. As such, rTMS and ECT may be considered for patients who are looking for more sustained effects rather than rapid results. Based on these timelines, ketamine and esketamine appear to provide the fastest reductions in SI following a single treatment, while rTMS and ECT most often require multiple treatment sessions before improvements are observed (Fig. 2). However, these findings reflect the specific treatment protocols and follow-up durations in the included studies, limiting our ability to make comparisons across interventions.

In addition to treatment efficacy, considerations such as safety and the possibility of adverse events may also inform treatment decisions. When administered properly, rTMS is a safe and well-tolerated treatment, with severe adverse effects (e.g., seizures, hearing impairment) being very rare (Mehta et al., 2022b; Taylor et al., 2018). More common side effects are mild, including neck pain and headaches.

ECT is associated with more frequent adverse effects, such as cognitive impairments like disorientation and amnesia after the completion of a treatment course. Other adverse events that are commonly reported with ECT treatment include headaches, muscle aches, and nausea, which are considered mild and transient. More severe events such as cardiovascular complications, prolonged seizures, prolonged apnea, and treatment-induced mania are also possible (Trevino et al., 2010).

Psychiatric, psychomimetic, cardiovascular, neurological, and urinary side effects can all occur with ketamine treatment (Nikayin et al., 2022b; Short et al., 2018). Acute side effects such as headaches, dissociation, elevated blood pressure, and blurred vision seem to occur in many participants following treatment, however, most side effects are resolved shortly after dose administration. Notably, these side effects are most common when ketamine is administered intravenously. Most studies only assess the acute side effects, inviting the need to further evaluate the long-term safety of maintenance ketamine treatment. Similar side effects are observed for treatment with esketamine, with effects on cognition being less common (Nikayin et al., 2022b).

4.2. Strengths and limitations

A notable strength of this study is the inclusion of a wide range of research, allowing for a comprehensive synthesis of findings. However, our results need to be interpreted with several limitations. Although NIH quality assessment tools rated most included studies as “good” or “fair,” it is important to note that the certainty of evidence varied by study design. Randomized controlled designs provided the strongest evidence for reductions in aspects of suicidality, while open-label, observational, and post-hoc analyses offered lower-certainty evidence that weighted less heavily in the interpretation of findings. This distinction is particularly relevant, as changes in suicidality were a secondary outcome in most studies, with changes in general depressive symptoms being the primary outcome of interest. Moreover, the data regarding how measures of suicidality change during and post-treatment with the interventions of interest are limited, with most studies only assessing changes during the treatment course or including a short follow-up period. Studies that did include a post-treatment follow-up period were predominantly observational or case reports, and therefore, provided low-certainty evidence regarding the durability of effects. This highlights the need for future research to examine suicidality as a primary outcome, in order to comprehensively evaluate the sustained effects of these interventions over time, including after treatment

discontinuation.

Additionally, many of the studies used different measures to assess levels of suicidality. Therefore, there could be inconsistencies regarding changes in suicidality between studies as well as the observed domains. Furthermore, due to the inclusion of only patients with MDD, the efficacy of the interventions for other psychiatric disorders could not be determined. Lastly, some studies investigated the use of the interventions of interest on individuals with MDD, while others focused on TRD. Considering that MDD and TRD differ with respect to components such as chronicity, complexity, and treatment response (McIntyre et al., 2023), it is possible that the interpretation of findings may vary due to the heterogeneity of the disorders. As such, this heterogeneity across study populations, designs, treatment protocols, outcome measures, and follow-up durations limited our ability to precisely quantify or draw comparative conclusions regarding the relative onset or durability of antisuicidal effects between interventions. Accordingly, data related to the timing and persistence of effects should be interpreted as descriptive observations of the available literature rather than as conclusive evidence of comparative or sustained efficacy between interventions.

5. Conclusion

Our results indicate that rTMS, ECT, ketamine, and esketamine are associated with reductions in SI, and in some cases suicidal behavior, in individuals with MDD, with some variance with respect to the onset of reductions and duration of observed effects. We did not observe reporting of new onset or the worsening of any aspect of suicidality with any of the interventions (Kwan et al., 2025; McIntyre et al., 2024a). Although each of these interventions are commonly associated with side effects, they are usually mild and resolve quickly (Ceban et al., 2021). The foregoing collection of evidence suggests that these interventions may represent potential options for individuals who fail to respond to first-line treatments, such as antidepressants and psychotherapy. Further research prioritizing suicidality as a primary outcome to assess the long-term effects of these interventions on measures of suicidality and the durability of the effect is required.

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CRediT authorship contribution statement

Trisha Menon: Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Andy Lu:** Writing – review & editing, Investigation, Data curation. **Akhilan Arulmozhi:** Investigation, Data curation. **Christine E. Dri:** Writing – review & editing, Investigation, Data curation. **Sabrina Wong:** Writing – review & editing, Methodology. **Kayla M. Teopiz:** Writing – review & editing. **Gia Han Le:** Writing – review & editing. **Serene Lee:** Writing – review & editing. **Cory R. Weissman:** Writing – review & editing. **Roger S. McIntyre:** Writing – review & editing, Supervision, Conceptualization.

Declaration of competing interest

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Supplementary materials

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References

- Ahmed, G.K., Elserogy, Y.M., Elfadl, G.M.A., Ghada Abdelsalam, K., Ali, M.A., 2023. Antidepressant and anti-suicidal effects of ketamine in treatment-resistant depression associated with psychiatric and personality comorbidities: A double-blind randomized trial. *J. Affect. Disord.* 325, 127–134. <https://doi.org/10.1016/j.jad.2023.01.005>.
- Anand, A., Hu, B., 2022. Comparing Electroconvulsive Therapy and Ketamine in Treating Acute Suicidal Depression [Ongoing Study]. Patient-Centered Outcomes Research Institute. <https://www.pcori.org/research-results/2022/comparing-electroconvulsive-therapy-and-ketamine-treating-acute-suicidal-depression>.
- Arango-Posada, M.D.M., Prada-Escobar, A.I., Marín-Hernández, C., Monsalve-Franco, V., Restrepo-Bernal, D., 2024. Successful treatment for serious depression with suicidal risk in a heart transplant patient. *Rev. Colomb. Psiquiatr.* 53 (2), 210–216. <https://doi.org/10.1016/j.rcpeng.2022.03.001>.
- Arrighi, L., Maakaron, E., Korchia, T., Lancon, C., Richieri, R., 2023. Long-term remission following esketamine nasal spray sessions in a patient with severe and highly treatment-resistant depression: A single-case report. *Int. Clin. Psychopharmacol.* 39 (5), 323–325. <https://doi.org/10.1097/YIC.0000000000000482>.
- Averill, L.A., Averill, C.L., Gueorguieva, R., Fouda, S., Sherif, M., Ahn, K.H., Ranganathan, M., D'Souza, D.C., Southwick, S.M., Sanacora, G., Duman, R.S., Krystal, J.H., Abdallah, C.G., 2022. mTORC1 inhibitor effects on rapid ketamine-induced reductions in suicidal ideation in patients with treatment-resistant depression. *J. Affect. Disord.* 303, 91–97. <https://doi.org/10.1016/j.jad.2022.01.104>.
- Baeken, C., Wu, G.R., van Heeringen, K., 2019. Placebo aiTBS attenuates suicidal ideation and frontopolar cortical perfusion in major depression. *Transl. Psychiatry* 9 (1), 38. <https://doi.org/10.1038/s41398-019-0377-x>.
- Barredo, J., Berlow, Y., Swearingen, H.R., Greenberg, B.D., Carpenter, L.L., Philip, N.S., 2021. Multimodal elements of suicidality reduction after transcranial magnetic stimulation. *Neuromodulation*. 24 (5), 930–937. <https://doi.org/10.1111/ner.13376>.
- Beaudequin, D., Can, A.T., Dutton, M., Jones, M., Galloway, C., Schwenn, P., Yang, C., Forsyth, G., Simcock, G., Hermens, D.F., Lagopoulos, J., 2020. Predicting therapeutic response to oral ketamine for chronic suicidal ideation: A Bayesian network for clinical decision support. *BMC. Psychiatry* 20 (1), 519. <https://doi.org/10.1186/s12888-020-02925-1>.
- Beaudequin, D., Can, A.T., Jones, M., Yang, C., Scherman, J.K., Dutton, M., Schwenn, P., Forsyth, C.G.G., Jensen, E., Hermens, D.F., Lagopoulos, J., 2021. Relationships between reduction in symptoms and restoration of function and wellbeing: outcomes of the oral ketamine trial on suicidality (OKTOS). *Psychiatry Res.* 305, 114212. <https://doi.org/10.1016/j.psychres.2021.114212>.
- Bergfeld, I.O., Mantione, M., Figue, M., Schuurman, P.R., Lok, A., Denys, D., 2018. Treatment-resistant depression and suicidality. *J. Affect. Disord.* 235, 362–367. <https://doi.org/10.1016/j.jad.2018.04.016>.
- Bozzay, M.L., Primack, J., Barredo, J., Philip, N.S., 2020. Transcranial magnetic stimulation to reduce suicidality—A review and naturalistic outcomes. *J. Psychiatr. Res.* 125, 106–112. <https://doi.org/10.1016/j.jpsychres.2020.03.016>.
- Brendle, M., Ahuja, S., Valle, M.D., Moore, C., Thielking, P., Malone, D.C., Robison, R., 2022. Safety and effectiveness of intranasal esketamine for treatment-resistant depression: A real-world retrospective study. *J. Comp. Eff. Res.* 11 (18), 1323–1336. <https://doi.org/10.2217/ce-2022-0149>.
- Burger, J., Capobianco, M., Lovern, R., Boche, B., Ross, E., Darracq, M.A., McLay, R., 2016. A double-blinded, randomized, placebo-controlled sub-dissociative dose ketamine pilot study in the treatment of acute depression and suicidality in a military emergency department setting. *Mil. Med.* 181 (10), 1195–1199. <https://doi.org/10.7205/MILMED-D-15-00431>.
- Cai, H., Jin, Y., Liu, S., Zhang, Q., Zhang, L., Cheung, T., Balbuena, L., Xiang, Y.T., 2021. Prevalence of suicidal ideation and planning in patients with major depressive disorder: A meta-analysis of observation studies. *J. Affect. Disord.* 293, 148–158. <https://doi.org/10.1016/j.jad.2021.05.115>.
- Çakir, S., Çağlar, N., 2017. Electroconvulsive therapy in the treatment of mood disorders: one-year follow-up. *Noro Psikiyatr. Ars.* 54 (3), 196–201. <https://doi.org/10.5152/npa.2016.14845>.
- Calder, C.N., Kwan, A.T.H., Teopiz, K.M., Wong, S., Rosenblat, J.D., Mansur, R.B., Rhee, T.G., Ho, R., Cao, B., McIntyre, R.S., 2024. Number needed to treat (NNT) for ketamine and esketamine in adults with treatment-resistant depression: A systematic review and meta-analysis. *J. Affect. Disord.* 356, 753–762. <https://doi.org/10.1016/j.jad.2024.04.039>.
- Canuso, C.M., Ionescu, D.F., Li, X., Qiu, X., Lane, R., Turkoz, I., Nash, A.I., Lopena, T.J., Fu, D.J., 2021. Esketamine nasal spray for the rapid reduction of depressive symptoms in major depressive disorder with acute suicidal ideation or behavior. *J. Clin. Psychopharmacol.* 41 (5), 516–524. <https://doi.org/10.1097/JCP.0000000000001465>.

- Canuso, C.M., Singh, J.B., Fedgchin, M., Alphas, L., Lane, R., Lim, P., Pinter, C., Hough, D., Sanacora, G., Manji, H., Drevets, W.C., 2018. Efficacy and safety of intranasal esketamine for the rapid reduction of symptoms of depression and suicidality in patients at imminent risk for suicide: results of a double-blind, randomized, placebo-controlled study. *Am. J. Psychiatry* 175 (7), 620–630. <https://doi.org/10.1176/appi.ajp.2018.17060720>.
- Cawley, R., Pontin, E.E., Touhey, J., Sheehy, K., Taylor, P.J., 2019. What is the relationship between rejection and self-harm or suicidality in adulthood? *J. Affect. Disord.* 242, 123–134. <https://doi.org/10.1016/j.jad.2018.08.082>.
- Ceban, F., Rosenblat, J.D., Kratiuk, K., Lee, Y., Rodrigues, N.B., Gill, H., Subramaniapillai, M., Nasri, F., Lui, L.M.W., Lipsitz, O., Kumar, A., Lee, J.G., Chau, E.H., Cao, B., Lin, K., Ho, R.C., Mansur, R.B., Swainson, J., McIntyre, R.S., 2021. Prevention and management of common adverse effects of ketamine and esketamine in patients with mood disorders. *CNS. Drugs* 35 (9), 925–934. <https://doi.org/10.1007/s40263-021-00846-5>.
- Chaudhary, P., Shah, P., Mehta, P., 2023. Retrospective data analysis to determine the effectiveness of intravenous ketamine therapy on patients suffering from depression with suicidal ideation. *Ind. Psychiatry J.* 32 (1), 86–92. <https://doi.org/10.4103/ipj.ipj.231.21>.
- Chen, M.H., Bai, Y.M., Wu, H.J., Li, C.T., Lin, W.C., Tsai, S.J., Su, T.P., Tu, P.C., 2023. Role of klotho on antidepressant and antisuicidal effects of low-dose ketamine infusion among patients with treatment-resistant depression and suicidal ideation. *J. Affect. Disord.* 340, 471–475. <https://doi.org/10.1016/j.jad.2023.08.061>.
- Chen, M.-H., Cheng, C.-M., Li, C.-T., Tsai, S.-J., Lin, W.-C., Bai, Y.-M., Su, T.-P., 2022a. Comparative study of low-dose ketamine infusion and repetitive transcranial magnetic stimulation in treatment-resistant depression: A posthoc pooled analysis of two randomized, double-blind, placebo-controlled studies. *Psychiatry Res.* 316, 114749. <https://doi.org/10.1016/j.psychres.2022.114749>.
- Chen, M.H., Lin, W.C., Wu, H.J., Cheng, C.M., Li, C.T., Hong, C.J., Tu, P.C., Bai, Y.M., Tsai, S.J., Su, T.P., 2019. Antisuicidal effect, BDNF Val66Met polymorphism, and low-dose ketamine infusion: reanalysis of adjunctive ketamine study of Taiwanese patients with treatment-resistant depression (AKSTP-TRD). *J. Affect. Disord.* 251, 162–169. <https://doi.org/10.1016/j.jad.2019.03.075>.
- Chen, M.H., Su, T.P., Li, C.T., Lin, W.C., Wu, H.J., Tsai, S.J., Bai, Y.M., Mao, W.C., Tu, P.C., 2024. Effects of melancholic features on positive and negative suicidal ideation in patients with treatment-resistant depression and strong suicidal ideation receiving low-dose ketamine infusion. *Eur. Arch. Psychiatry Clin. Neurosci.* 274 (4), 759–766. <https://doi.org/10.1007/s00406-023-01735-2>.
- Chen, M.-H., Wu, H.-J., Li, C.-T., Lin, W.-C., Tsai, S.-J., Hong, C.-J., Tu, P.-C., Bai, Y.-M., Mao, W.-C., Su, T.-P., 2022b. Low-dose ketamine infusion in treatment-resistant double depression: revisiting the adjunctive ketamine study of Taiwanese patients with treatment-resistant depression. *Hum. Psychopharmacol.* (2), e2820. <https://doi.org/10.1002/hup.2820>.
- Chen, Q., Dong, J., Luo, J., Ren, L., Min, S., Hao, X., Luo, Q., Chen, J., Li, X., 2020. Effects of low-dose ketamine on the antidepressant efficacy and suicidal ideations in patients undergoing electroconvulsive therapy. *J. ECT.* 36 (1), 25–30. <https://doi.org/10.1097/YCT.0000000000000636>.
- Cheng, M.C.H., Dri, C.E., Ballum, H., Valentino, K., Cheung, W., Teopiz, K.M., Wong, S., McIntyre, R.S., 2025. The effects of ketamine and esketamine on measures of quality of life in major depressive disorder and treatment-resistant depression: A systematic review. *J. Affect. Disord.* 382, 438–442. <https://doi.org/10.1016/j.jad.2025.04.119>.
- Cole, E.J., Stimpson, K.H., Bentzley, B.S., Gulser, M., Cherian, K., Tischler, C., Nejad, R., Pankov, H., Choi, E., Aaron, H., Espil, F.M., Pannu, J., Xiao, X., Duvio, D., Solvason, H.B., Hawkins, J., Guerra, A., Jo, B., Raj, K.S., Phillips, A.L., Williams, N. R., 2020. Stanford accelerated intelligent neuromodulation therapy for treatment-resistant depression. *Am. J. Psychiatry* 177 (8), 716–726. <https://doi.org/10.1176/appi.ajp.2019.1907020>.
- Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia. Available at www.covidence.org.
- d'Andrea, G., Pettoruso, M., Di Lorenzo, G., Rhee, T.G., Chiappini, S., Carullo, R., Barlati, S., Zanardi, R., Rosso, G., Di Nicola, M., Andriola, I., Marcatili, M., Clerici, M., Dell'Oso, B.M., Sensi, S.L., Mansur, R.B., Rosenblat, J.D., Martinotti, G., McIntyre, R.S., 2024. The rapid antidepressant effectiveness of repeated dose of intravenous ketamine and intranasal esketamine: A post-hoc analysis of pooled real-world data. *J. Affect. Disord.* 348, 314–322. <https://doi.org/10.1016/j.jad.2023.12.038>.
- Davila, M.C., Ely, B., Manzardo, A.M., 2019. Repetitive transcranial magnetic stimulation (rTMS) using different TMS instruments for major depressive disorder at a suburban tertiary clinic. *Ment. Illn.* 11 (1), 7947. <https://doi.org/10.4081/mi.2019.7947>.
- de la Salle, S., Phillips, J.L., Blier, P., Knott, V., 2022. Electrophysiological correlates and predictors of the antidepressant response to repeated ketamine infusions in treatment-resistant depression. *Prog. Neuropsychopharmacol. Biol. Psychiatry* 115, 110507. <https://doi.org/10.1016/j.pnpbp.2021.110507>.
- Desmyter, S., Duprat, R., Baeken, C., Bijttebier, S., van Heeringen, K., 2014. The acute effects of accelerated repetitive Transcranial Magnetic Stimulation on suicide risk in unipolar depression: preliminary results. *Psychiatr. Danub.* 26 (Suppl 1), 48–52.
- Desmyter, S., Duprat, R., Baeken, C., Van Autreve, S., Audenaert, K., van Heeringen, K., 2016. Accelerated intermittent theta burst stimulation for suicide risk in therapy-resistant depressed patients: A randomized, sham-controlled trial. *Front. Hum. Neurosci.* 10, 480. <https://doi.org/10.3389/fnhum.2016.00480>.
- Di Vincenzo, J.D., Lipsitz, O., Rodrigues, N.B., Lee, Y., Gill, H., Kratiuk, K., Subramaniapillai, M., Mansur, R., McIntyre, R.S., Rosenblat, J.D., 2021. Ketamine monotherapy versus adjunctive ketamine in adults with treatment-resistant depression: results from the Canadian Rapid Treatment Centre of Excellence. *J. Psychiatr. Res.* 143, 209–214. <https://doi.org/10.1016/j.jpsychires.2021.09.002>.
- Domany, Y., McCullumsmith, C.B., 2022. Single, fixed-dose intranasal ketamine for alleviation of acute suicidal ideation. An Emergency department, trans-diagnostic approach: A randomized, double-blind, placebo-controlled, proof-of-concept trial. *Arch. Suicide Res.* 26 (3), 1250–1265. <https://doi.org/10.1080/13811118.2021.1878078>.
- Fava, M., Freeman, M.P., Flynn, M., Judge, H., Hoepfner, B.B., Cusin, C., Ionescu, D.F., Mathew, S.J., Chang, L.C., Iosifescu, D.V., Murrough, J., DeBattista, C., Schatzberg, A.F., Trivedi, M.H., Jha, M.K., Sanacora, G., Wilkinson, S.T., Papakostas, G.I., 2020. Double-blind, placebo-controlled, dose-ranging trial of intravenous ketamine as adjunctive therapy in treatment-resistant depression (TRD). *Mol. Psychiatry* 25 (7), 1592–1603. <https://doi.org/10.1038/s41380-018-0256-5>.
- Feeney, A., Hock, R.S., Freeman, M.P., Flynn, M., Hoepfner, B., Iosifescu, D.V., Trivedi, M.H., Sanacora, G., Mathew, S.J., DeBattista, C., Ionescu, D.F., Fava, M., Papakostas, G.I., 2021. The effect of single administration of intravenous ketamine augmentation on suicidal ideation in treatment-resistant unipolar depression: results from a randomized double-blind study. *Eur. Neuropsychopharmacol.* 49, 122–132. <https://doi.org/10.1016/j.euroneuro.2021.04.024>.
- Fu, D.J., Ionescu, D.F., Li, X., Lane, R., Lim, P., Sanacora, G., Hough, D., Manji, H., Drevets, W.C., Canuso, C.M., 2020. Esketamine nasal spray for rapid reduction of major depressive disorder symptoms in patients who have active suicidal ideation with intent: double-blind, randomized study (ASPIRE I). *J. Clin. Psychiatry* 81 (3). <https://doi.org/10.4088/JCP.19m13191>.
- Fu, D.J., Zhang, Q., Shi, L., Borentain, S., Guo, S., Mathews, M., Anjo, J., Nash, A.I., O'Hara, M., Canuso, C.M., 2023. Esketamine versus placebo on time to remission in major depressive disorder with acute suicidality. *BMC Psych* 23 (1), 587. <https://doi.org/10.1186/s12888-023-05017-y>.
- Fujita, K., Koga, Y., 2005. Clinical application of single-pulse transcranial magnetic stimulation for the treatment of depression. *Psychiatry Clin. Neurosci.* 59 (4), 425–432. <https://doi.org/10.1111/j.1440-1819.2005.01395.x>.
- Galuszko-Wegielnik, M., Włodarczyk, A., Cubala, W.J., Wilkowska, A., Gorska, N., Slupski, J., 2021. Case report: repeated series of ketamine infusions in patients with treatment-resistant depression: presentation of five cases. *Front. Psychiatry* 12 (101545006), 705190. <https://doi.org/10.3389/fpsy.2021.705190>.
- Gilbert, J.R., Ballard, E.D., Galiano, C.S., Nugent, A.C., Zarate Jr., C.A., 2020. Magnetoencephalographic correlates of suicidal ideation in major depression. *Biol. Psychiatry Cogn. Neurosci. Neuroimaging* 5 (3), 354–363. <https://doi.org/10.1016/j.bpsc.2019.11.011>.
- Grunebaum, M.F., Galfalvy, H.C., Choo, T.H., Keilp, J.G., Moitra, V.K., Parris, M.S., Marver, J.E., Burke, A.K., Milak, M.S., Sublette, M.E., Oquendo, M.A., Mann, J.J., 2018. Ketamine for rapid reduction of suicidal thoughts in major depression: A midazolam-controlled randomized clinical trial. *Am. J. Psychiatry* 175 (4), 327–335. <https://doi.org/10.1176/appi.ajp.2017.17060647>.
- Grunebaum, M.F., Mann, J.J., Galfalvy, H.C., Gibbons, R.D., 2021. Computerized-adaptive vs. Traditional ratings of depression and suicidal thoughts: an assay sensitivity pilot study in a. *Ketamine Clin. Trial. Front Psychiatry* 12, 602976. <https://doi.org/10.3389/fpsy.2021.602976>.
- Gutierrez, G., Kang, M.J.Y., Vazquez, G., 2024a. IV low dose ketamine infusions for treatment resistant depression: results from a five-year study at a free public clinic in an academic hospital. *Psychiatry Res.* 335, 115865. <https://doi.org/10.1016/j.psychres.2024.115865>.
- Gutierrez, G., Swainson, J., Ravindran, N., Lam, R.W., Giacobbe, P., Karthikeyan, G., Kowara, A., Do, A., Baskaran, A., Nestor, S.M., Kang, M.J.Y., Biorac, A., Vazquez, G., 2024b. IN Esketamine and IV Ketamine: results of a multi-site observational study assessing the effectiveness and tolerability of two novel therapies for treatment-resistant depression. *Psychiatry Res.* 340, 116125. <https://doi.org/10.1016/j.psychres.2024.116125>.
- Holtzheimer, P.E., Nemeroff, C.B., 2008. Novel targets for antidepressant therapies. *Curr. Psychiatry Rep.* 10 (6), 465–473. <https://doi.org/10.1007/s11920-008-0075-5>.
- Holtzheimer, P.E., McDonald, W.M., Muftic, M., Kelley, M.E., Quinn, S., Corso, G., Epstein, C.M., 2010. Accelerated repetitive transcranial magnetic stimulation for treatment-resistant depression. *Depress. Anxiety.* 27 (10), 960–963. <https://doi.org/10.1002/da.20731>.
- Hong, J.P., Malek, A.Z.A., Li, C.T., Paik, J.W., Sulaiman, A.H., Madriaga, G., Zhuo, J., Siggins, S., Fu, D.J., Ju, P.C., 2023. Efficacy and safety of esketamine nasal spray in addition to standard of care in patients with major depressive disorder who have active suicidal ideation with intent: A subgroup analysis of the Asian cohort of ASPIRE I. *Asia Pac. Psychiatry* 15 (4), e12548. <https://doi.org/10.1111/appy.12548>.
- Hosseini, S., Rengasamy, M., Uzamere, A., Spotts, C., Howland, R.H., Wallace, M.L., Mathew, S.J., Price, R.B., 2025. Effects of ketamine on individual symptoms and symptom networks of depression in a randomised controlled trial of ketamine for treatment-resistant depression. *Br. J. Psychiatry* 1–10. <https://doi.org/10.1192/bjp.2024.276>.
- Huang, X., Xi, C., Fang, Y., Ye, R., Wang, X., Zhang, S., Cui, Y., Guo, Y., Zhang, J., Ji, G.-J., Zhu, C., Luo, Y., Chen, X., Wang, K., Tian, Y., Yu, F., 2025. Therapeutic efficacy of reward circuit-targeted transcranial magnetic stimulation (TMS) on suicidal ideation in depressed patients: A sham-controlled trial of two TMS protocols. *Depress. Anxiety.* (1). <https://doi.org/10.1155/da/1767477>, 2025.
- Ionescu, D.F., Bentley, K.H., Eikermann, M., Taylor, N., Akeju, O., Sweet, M.B., Pavone, K. J., Petrie, S.R., Dording, C., Mischoulon, D., Alpert, J.E., Brown, E.N., Baer, L., Nock, M.K., Fava, M., Cusin, C., 2019. Repeat-dose ketamine augmentation for treatment-resistant depression with chronic suicidal ideation: A randomized, double blind, placebo controlled trial. *J. Affect. Disord.* 243, 516–524. <https://doi.org/10.1016/j.jad.2018.09.037>.
- Ionescu, D.F., Fu, D.J., Qiu, X., Lane, R., Lim, P., Kasper, S., Hough, D., Drevets, W.C., Manji, H., Canuso, C.M., 2021. Esketamine nasal spray for rapid reduction of

- depressive symptoms in patients with major depressive disorder who have active suicide ideation with intent: results of a phase 3, double-blind, randomized study (ASPIRE II). *Int. J. Neuropsychopharmacol.* 24 (1), 22–31. <https://doi.org/10.1093/ijnp/pyaa068>.
- Ionescu, D.F., Sweet, M.B., Pavone, K.J., Taylor, N., Akeju, O., Baer, L., Nyer, M., Cassano, P., Mischoulon, D., Alpert, J.E., Brown, E.N., Nock, M.K., Fava, M., Cusin, C., 2016. Rapid and sustained reductions in current suicidal ideation following repeated doses of intravenous ketamine: secondary analysis of an open-label study. *J. Clin. Psychiatry* 77 (6), e719–e725. <https://doi.org/10.4088/JCP.15m10056>.
- Isometsä, E.T., Henriksson, M.M., Heikkinen, M.E., Lönnqvist, J.K., 1996. Completed suicide and recent electroconvulsive therapy in Finland. *Convuls. Ther.* 12 (3), 152–155.
- Jiang, T., Nagy, D., Rosellini, A.J., Horváth-Puhó, E., Keyes, K.M., Lash, T.L., Galea, S., Sørensen, H.T., Gradus, J.L., 2021. Suicide prediction among men and women with depression: A population-based study. *J. Psychiatr. Res.* 142, 275–282. <https://doi.org/10.1016/j.jpsychires.2021.08.003>.
- Jørgensen, M.B., Rozing, M.P., Kellner, C.H., Osler, M., 2020. Electroconvulsive therapy, depression severity and mortality: data from the Danish National Patient Registry. *J. Psychopharmacol.* 34 (3), 273–279. <https://doi.org/10.1177/0269881119895518>.
- Kaur, S., Parmar, C., Gaur, V., Chauhan, A., Andrade, C., 2023. The efficacy of oral ketamine in severely depressed patients at high risk of suicide. *Asian J. Psychiatr.* 86, 103678. <https://doi.org/10.1016/j.ajp.2023.103678>.
- Keilp, J.G., Grunebaum, M.F., Gorlyn, M., LeBlanc, S., Burke, A.K., Galfalvy, H., Oquendo, M.A., Mann, J.J., 2012. Suicidal ideation and the subjective aspects of depression. *J. Affect. Disord.* 140 (1), 75–81. <https://doi.org/10.1016/j.jad.2012.01.045>.
- Keilp, J.G., Madden, S.P., Marver, J.E., Frawley, A., Burke, A.K., Herzallah, M.M., Gluck, M., Mann, J.J., Grunebaum, M.F., 2021. Effects of Ketamine versus Midazolam on neurocognition at 24 hours in depressed patients with suicidal ideation. *J. Clin. Psychiatry* 82 (6). <https://doi.org/10.4088/JCP.21m13921>.
- Kellner, C.H., Fink, M., Knapp, R., Petrides, G., Husain, M., Rummans, T., Mueller, M., Bernstein, H., Rasmussen, K., O'Connor, K., Smith, G., Rush, A.J., Biggs, M., McClintock, S., Bailine, S., Malur, C., 2005. Relief of expressed suicidal intent by ECT: a consortium for research in ECT study. *Am. J. Psychiatry* 162 (5), 977–982. <https://doi.org/10.1176/appi.ajp.162.5.977>.
- Kern, D.M., Cepeda, M.S., Wiegand, F., 2021. Treatment patterns of patients diagnosed with major depressive disorder and suicidal ideation or attempt: a U.S. population-based study utilizing real-world data. *BMC Psychiatry* 21 (1), 608. <https://doi.org/10.1186/s12888-021-03616-1>.
- Keshtkar, M., Ghanizadeh, A., Firoozabadi, A., 2011. Repetitive transcranial magnetic stimulation versus electroconvulsive therapy for the treatment of major depressive disorder, a randomized controlled clinical trial. *J. ECT* 27 (4), 310–314. <https://doi.org/10.1097/YCT.0b013e318221b31c>.
- Kheirabadi, D., Kheirabadi, G.R., Mirlohi, Z., Tarrahi, M.J., Norbaksh, A., 2020. Comparison of rapid antidepressant and antisuicidal effects of intramuscular ketamine, oral Ketamine, and electroconvulsive therapy in patients with major depressive disorder: A pilot study. *J. Clin. Psychopharmacol.* 40 (6), 588–593. <https://doi.org/10.1097/JCP.0000000000001289>.
- Kong, Y., Zhou, J., Zhao, M., Zhang, Y., Tan, T., Xu, Z., Hou, Z., Yuan, Y., Tan, L., Song, R., Shi, Y., Feng, H., Wu, W., Zhao, Y., Zhang, Z., 2023. Non-inferiority of intermittent theta burst stimulation over the left V(1) vs. Classical target for depression: A randomized, double-blind trial. *J. Affect. Disord.* 343, 59–70. <https://doi.org/10.1016/j.jad.2023.09.024>.
- Kwan, A.T.H., Lakhani, M., Rosenblat, J.D., Mansur, R.B., Rhee, T.G., Teopiz, K.M., Cao, B., Ho, R., Wong, S., Le, G.H., McIntyre, R.S., 2024. A global population-based study on the association between ketamine and esketamine with suicidality using WHO VigiBase. *J. Clin. Psychiatry* 86 (3). <https://doi.org/10.4088/JCP.24m15534>.
- Le, G.H., Wong, S., Au, H., Badulescu, S., Gill, H., Vasudeva, S., Teopiz, K.M., Rhee, T.G., Ho, R., Kwan, A.T.H., Mansur, R.B., Rosenblat, J.D., McIntyre, R.S., 2025. Association between rumination, suicidal ideation and suicide attempts in persons with depressive and other mood disorders and healthy controls: A systematic review and meta-analysis. *J. Affect. Disord.* 368, 513–527. <https://doi.org/10.1016/j.jad.2024.09.118>.
- Leuchter, A.F., Cook, I.A., Feifel, D., Goethe, J.W., Husain, M., Carpenter, L.L., Thase, M. E., Krystal, A.D., Philip, N.S., Bhati, M.T., Burke, W.J., Howland, R.H., Sheline, Y.I., Aaronson, S.T., Iosifescu, D.V., O'Reardon, J.P., Gilmer, W.S., Jain, R., Burgoine, K. S., George, M.S., 2015. Efficacy and safety of low-field synchronized transcranial magnetic stimulation (sTMS) for treatment of major depression. *Brain Stimul.* 8 (4), 787–794. <https://doi.org/10.1016/j.brs.2015.05.005>.
- Lewitzka, U., Severus, E., Bauer, R., Ritter, P., Müller-Oerlinghausen, B., Bauer, M., 2015. The suicide prevention effect of lithium: more than 20 years of evidence—A narrative review. *Int. J. Bipolar. Disord.* 3 (1), 15. <https://doi.org/10.1186/s40345-015-0032-2>. Article.
- Li, K., Bichlmeier, A., DuPont, C., Siegel-Ramsay, J.E., Comfort, A., Logue, E., Stimpson, K.H., Bentzley, B., Williams, N., Reti, I., Almeida, J., Zandi, P., 2024. Fast depressive symptoms improvement in bipolar I disorder after Stanford Accelerated Intelligent Neuromodulation Therapy (SAINT): A two-site feasibility and safety open-label trial. *J. Affect. Disord.* 365, 359–363. <https://doi.org/10.1016/j.jad.2024.08.087>.
- Li, W.C., Chen, L.F., Su, T.P., Li, C.T., Lin, W.C., Wu, H.J., Tsai, S.J., Bai, Y.M., Tu, P.C., 2023. Right dorsolateral prefrontal cortex volumetric reduction is associated with antidepressant effect of low-dose ketamine infusion: A randomized, double-blind, midazolam-controlled PET-MRI clinical trial. *J. Affect. Disord.* 335, 105–110. <https://doi.org/10.1016/j.jad.2023.05.024>.
- Liang, C.S., Chung, C.H., Ho, P.S., Tsai, C.K., Chien, W.C., 2018. Superior anti-suicidal effects of electroconvulsive therapy in unipolar depression and bipolar depression. *Bipolar. Disord.* 20 (6), 539–546. <https://doi.org/10.1111/bdi.12589>.
- Lin, C.H., Chen, C.C., Huang, C.J., 2020. Electroconvulsive therapy versus fluoxetine in suicidal resolution for patients with major depressive disorder. *J. ECT* 36 (4), 234–241. <https://doi.org/10.1097/YCT.0000000000000676>.
- Lin, W.C., Su, T.P., Li, C.T., Wu, H.J., Tsai, S.J., Bai, Y.M., Tu, P.C., Chen, M.H., 2023. Baseline cognitive function predicts full remission of suicidal symptoms among patients with treatment-resistant depression and strong suicidal ideation after low-dose ketamine infusion. *J. Psychopharmacol.* 37 (8), 795–801. <https://doi.org/10.1177/02698811231182107>.
- Lopes, E.I.T.C., Cavalcanti-Ribeiro, P., Palhano-Fontes, F., Gonçalves, K.T.D.C., Nunes, E. A., Lima, N.B.M., Santos, N.C., Brito, A.J.C., de Araujo, D.B., Galvão-Coelho, N.L., 2024. Rapid and long-lasting effects of subcutaneous esketamine on suicidality: an open-label study in patients with treatment-resistant depression. *J. Psychiatr. Res.* 176, 254–258. <https://doi.org/10.1016/j.jpsychires.2024.06.020>.
- Mann, J.J., Michel, C.A., Auerbach, R.P., 2021. Improving suicide prevention through evidence-based strategies: A systematic review. *Am. J. Psychiatry* 178 (7), 611–624. <https://doi.org/10.1176/appi.ajp.2020.20060864>.
- Martinotti, G., Vita, A., Fagioli, A., Maina, G., Bertolino, A., Dell'Osso, B., Siracusano, A., Clerici, M., Bellomo, A., Sani, G., d'Andrea, G., Chiaie, R.D., Conca, A., Barlati, S., Di Lorenzo, G., De Fazio, P., De Filippis, S., Nicolo, G., Rosso, G., di Giannantonio, M., 2022. Real-world experience of esketamine use to manage treatment-resistant depression: A multicentric study on safety and effectiveness (REAL-ESK study). *J. Affect. Disord.* 319 (7906073), 646–654. <https://doi.org/10.1016/j.jad.2022.09.043>.
- McIntyre, R.S., Rosenblat, J.D., Nemeroff, C.B., Sanacora, G., Murrough, J.W., Berk, M., Brietzke, E., Dodd, S., Gorwood, P., Ho, R., Iosifescu, D.V., Lopez Jaramillo, C., Kasper, S., Kratiuk, K., Lee, J.G., Lee, Y., Lui, L.M.W., Mansur, R.B., Papakostas, G.I., Stahl, S., 2021. Synthesizing the evidence for ketamine and esketamine in treatment-resistant depression: an international expert opinion on the available evidence and implementation. *Am. J. Psychiatry* 178 (5), 383–399. <https://doi.org/10.1176/appi.ajp.2020.20081251>.
- McIntyre, R.S., Alsuauidan, M., Baune, B.T., Berk, M., Demyttenaere, K., Goldberg, J.F., Gorwood, P., Ho, R., Kasper, S., Kennedy, S.H., Ly-Usun, J., Mansur, R.B., McAllister-Williams, R.H., Murrough, J.W., Nemeroff, C.B., Nierenberg, A.A., Rosenblat, J.D., Sanacora, G., Schatzberg, A.F., Maj, M., 2023. Treatment-resistant depression: definition, prevalence, detection, management, and investigational interventions. *WPA* 22 (3), 394–412. <https://doi.org/10.1002/wps.21120>.
- McIntyre, R.S., Jain, R., 2024. Glutamatergic regulators for major depression from theory to clinical use. *CNS Drugs* 38 (11), 869–890. <https://doi.org/10.1007/s40263-024-01114-y>.
- McIntyre, R.S., Mansur, R.B., Rosenblat, J.D., Teopiz, K.M., Kwan, A.T.H., 2024a. The association between ketamine and esketamine and suicidality: reports to the Food And Drug Administration Adverse Event Reporting System (FAERS). *Expert. Opin. Drug Saf.* 1–6. <https://doi.org/10.1080/14740338.2024.2368827>.
- McIntyre, R.S., Bitter, I., Buyze, J., Fagioli, A., Godinov, Y., Gorwood, P., Ito, T., Oliveira-Maia, A.J., Vieta, E., Werner-Kiechle, T., Young, A.H., Reif, A., 2024b. Safety and tolerability of esketamine nasal spray versus quetiapine extended release in patients with treatment resistant depression. *Eur. Neuropsychopharmacol.* 85, 58–65. <https://doi.org/10.1016/j.euroneuro.2024.05.009>.
- Mehta, S., Downar, J., Mulsant, B.H., Voineskos, D., Daskalakis, Z.J., Weissman, C.R., Vila-Rodriguez, F., Blumberger, D.M., 2022a. Effect of high frequency versus theta-burst repetitive transcranial magnetic stimulation on suicidality in patients with treatment-resistant depression. *Acta Psychiatr. Scand.* 145 (5), 529–538. <https://doi.org/10.1111/acps.13412>.
- Mehta, S., Konstantinou, G., Weissman, C.R., Daskalakis, Z.J., Voineskos, D., Downar, J., Mulsant, B.H., Blumberger, D.M., 2022b. The effect of repetitive transcranial magnetic stimulation on suicidal ideation in treatment-resistant depression: A meta-analysis. *J. Clin. Psychiatry* 83 (2). <https://doi.org/10.4088/JCP.21r13969>.
- NIH, 2021. Study Quality Assessment Tools. July. National Heart Lung and Blood Institute. <https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools>.
- Nikayin, S., Rhee, T.G., Cunningham, M.E., de Fontnouvelle, C.A., Ostroff, R.B., Sanacora, G., Wilkinson, S.T., 2022a. Evaluation of the trajectory of depression severity with ketamine and esketamine treatment in a clinical setting. *JAMA Psychiatry* 79 (7), 736–738. <https://doi.org/10.1001/jamapsychiatry.2022.1074>.
- Nikayin, S., Murphy, E., Krystal, J.H., Wilkinson, S.T., 2022b. Long-term safety of ketamine and esketamine in treatment of depression. *Expert. Opin. Drug Saf.* 21 (6), 777–787. <https://doi.org/10.1080/14740338.2022.2066651>.
- Ozcan, S., Gica, S., Gulec, H., 2020. Suicidal behavior in treatment resistant major depressive disorder patients treated with transcranial magnetic stimulation (TMS) and its relationship with cognitive functions. *Psychiatry Res.* 286, 112873. <https://doi.org/10.1016/j.psychres.2020.112873>.
- Pan, Y., Gorenflo, M.P., Davis, P.B., Kaelber, D.C., De Luca, S., Xu, R., 2024. Suicidal ideation following ketamine prescription in patients with recurrent major depressive disorder: a nation-wide cohort study. *Transl. Psychiatry* 14 (1), 327. <https://doi.org/10.1038/s41398-024-03033-4>. Article.
- Pan, F., Mou, T., Shao, J., Chen, H., Tao, S., Wang, L., Jiang, C., Zhao, M., Wang, Z., Hu, S., Xu, Y., Huang, M., 2023. Effects of neuronavigation-guided rTMS on serum BDNF, TrkB and VGF levels in depressive patients with suicidal ideation. *J. Affect. Disord.* 323, 617–623. <https://doi.org/10.1016/j.jad.2022.11.059>.
- Pan, F., Shen, Z., Jiao, J., Chen, J., Li, S., Lu, J., Duan, J., Wei, N., Shang, D., Hu, S., Xu, Y., Huang, M., 2020. Neuronavigation-guided rTMS for the treatment of depressive patients with suicidal ideation: A double-blind, randomized, sham-

- controlled trial. *Clin. Pharmacol. Ther.* 108 (4), 826–832. <https://doi.org/10.1002/cpt.1858>.
- Pepe, M., Bartolucci, G., Marcelli, I., Pesaresi, F., Brugnam, A., Caso, R., Fischetti, A., Grisoni, F., Mazza, M., Camardese, G., Di Nicola, M., Sani, G., 2023. The patient's perspective on the effects of intranasal esketamine in treatment-resistant depression. *Brain Sci.* 13 (10). <https://doi.org/10.3390/brainsci13101494>.
- Phillips, J.L., Norris, S., Talbot, J., Hatchard, T., Ortiz, A., Birmingham, M., Owoeye, O., Batten, L.A., Blier, P., 2020. Single and repeated ketamine infusions for reduction of suicidal ideation in treatment-resistant depression. *Neuropsychopharmacol.* 45 (4), 606–612. <https://doi.org/10.1038/s41386-019-0570-x>.
- Pompili, M., Sarli, G., Erbuto, D., Manfredi, G., Comparelli, A., 2023. Clinical experiences with intranasal esketamine for major depressive disorder resistant to treatment and with a psychiatric emergency: case presentations. *Int. Clin. Psychopharmacol.* 38 (3), 195–200. <https://doi.org/10.1097/YIC.0000000000000455>.
- Price, R.B., Iosifescu, D.V., Murrough, J.W., Chang, L.C., Al Jurdi, R.K., Iqbal, S.Z., Soleimani, L., Charney, D.S., Foulkes, A.L., Mathew, S.J., 2014. Effects of ketamine on explicit and implicit suicidal cognition: A randomized controlled trial in treatment-resistant depression. *Depress. Anxiety.* 31 (4), 335–343. <https://doi.org/10.1002/da.22253>.
- Price, R.B., Nock, M.K., Charney, D.S., Mathew, S.J., 2009. Effects of intravenous ketamine on explicit and implicit measures of suicidality in treatment-resistant depression. *Biol. Psychiatry* 66 (5), 522–526. <https://doi.org/10.1016/j.biopsych.2009.04.029>.
- Ramasubbu, R., Brown, E.C., Selby, B., McGirr, A., Cole, J., Hassan, H., McAusland, L., 2024. Accelerated sequential bilateral theta-burst stimulation in major depression: an open trial. *Eur. Arch. Psychiatry Clin. Neurosci.* 274 (3), 697–707. <https://doi.org/10.1007/s00406-023-01648-0>.
- Rodrigues, N.B., Chen-Li, D., Di Vincenzo, J.D., Juneja, A., Pinder, B.D., McIntyre, R.S., Rosenblatt, J.D., 2024. Brain-derived neurotrophic factor Val66Met and CYP2B6 polymorphisms as predictors for ketamine effectiveness in patients with treatment-resistant depression. *J. Psychopharmacol.* 38 (4), 375–381. <https://doi.org/10.1177/02698811241238284>.
- Salagre, E., Rohde, C., Østergaard, S.D., 2022. Self-harm and suicide attempts preceding and following electroconvulsive therapy: A population-based study. *J. ECT.* 38 (1), 13–23. <https://doi.org/10.1097/YCT.0000000000000790>.
- Seraj, A., Reyazuddin, M., Gaur, R.K., Andrade, C., 2025. Oral ketamine for rapid reduction of suicidal ideation in major depressive disorder: A midazolam-controlled randomized clinical trial. *Asian J. Psychiatr.* 106, 104413. <https://doi.org/10.1016/j.jap.2025.104413>. Article.
- Short, B., Fong, J., Galvez, V., Shelker, W., Loo, C.K., 2018. Side-effects associated with ketamine use in depression: a systematic review. *Lancet Psychiatry* 5 (1), 65–78. [https://doi.org/10.1016/S2215-0366\(17\)30272-9](https://doi.org/10.1016/S2215-0366(17)30272-9).
- Simon, G.E., Moise, N., Mohr, D.C., 2024. Management of depression in adults: A review. *JAMA* 332 (2), 141–152. <https://doi.org/10.1001/jama.2024.5756>.
- Singh, J.B., Fedgchin, M., Daly, E.J., De Boer, P., Cooper, K., Lim, P., Pinter, C., Murrough, J.W., Sanacora, G., Shelton, R.C., Kurian, B., Winokur, A., Fava, M., Manji, H., Drevets, W.C., Van Nueten, L., 2016a. A double-blind, randomized, placebo-controlled, dose-frequency study of intravenous ketamine in patients with treatment-resistant depression. *Am. J. Psychiatry* 173 (8), 816–826. <https://doi.org/10.1176/appi.ajp.2016.16010037>.
- Singh, J.B., Fedgchin, M., Daly, E., Xi, L., Melman, C., De Bruecker, G., Tadic, A., Sienaert, P., Wiegand, F., Manji, H., Drevets, W.C., Van Nueten, L., 2016b. Intravenous esketamine in adult treatment-resistant depression: A double-blind, double-randomization, placebo-controlled study. *Biol. Psychiatr.* 80 (6), 424–431. <https://doi.org/10.1016/j.biopsych.2015.10.018>.
- Sinyor, M., Williams, M., Belo, S., Orser, B., Vincent, M., Mah, L., Zarate Jr., C., Castel, S., Levitt, A.J., Schaffer, A., 2018. Ketamine augmentation for major depressive disorder and suicidal ideation: preliminary experience in an inpatient psychiatry setting. *J. Affect. Disord.* 241, 103–109. <https://doi.org/10.1016/j.jad.2018.07.073>.
- Smith-Apeldoorn, S.Y., Veraart, J.K.E., Kamphuis, J., Spijker, J., van der Meij, A., van Asselt, A.D.I., Aan Het Rot, M., Schoevers, R.A., 2024. Oral esketamine in patients with treatment-resistant depression: A double-blind, randomized, placebo-controlled trial with open-label extension. *Mol. Psychiatry* 29, 2657–2665. <https://doi.org/10.1038/s41380-024-02478-9>.
- Stapper, N., Kohn, J., Benster, L., Daniels, H., Tello, V., Patel, A., Oswal, V., Stolz, L., Poorganji, M., Sun, Y., Daskalakis, Z.J., Appelbaum, L.G., Weissman, C.R., 2025. Repetitive transcranial magnetic stimulation for the treatment of suicidal ideation in a naturalistic setting. *Brain Stim.* 18 (1), 141–143. <https://doi.org/10.1016/j.brs.2025.01.005>.
- Su, T.P., Li, C.T., Lin, W.C., Wu, H.J., Tsai, S.J., Bai, Y.M., Mao, W.C., Tu, P.C., Chen, L.F., Li, W.-C., Chen, M.H., 2023. A randomized, double-blind, midazolam-controlled trial of low-dose ketamine infusion in patients with treatment-resistant depression and prominent suicidal ideation. *Int. J. Neuropsychopharmacol.* 26 (5), 331–339. <https://doi.org/10.1093/ijnp/pyad014>.
- Surjan, J., Grossi, J.D., Del Porto, J.A., Delfino, R.S., de Oliveira Cerqueira, R., Lucchese, A.C., Magalhães, E., Del Sant, L.C., Tuena, M.A., Nakahira, C., Fava, V.A.R., Steglich, M.S., Abdo, G.L., Barbosa, M.G., Sarin, L.M., Lacerda, A.L.T., 2022. Efficacy and safety of subcutaneous esketamine in the treatment of suicidality in major depressive disorder and bipolar depression. *Clin. Drug Investig.* 42 (10), 865–873. <https://doi.org/10.1007/s40261-022-01193-z>.
- Tang, N., Sun, C., Wang, Y., Li, X., Liu, J., Chen, Y., Sun, L., Rao, Y., Li, S., Qi, S., Wang, H., 2021. Clinical response of major depressive disorder patients with suicidal ideation to individual target-transcranial magnetic stimulation. *Front. Psychiatry* 12, 768819. <https://doi.org/10.3389/fpsy.2021.768819>.
- Taylor, R., Galvez, V., Loo, C., 2018. Transcranial magnetic stimulation (TMS) safety: a practical guide for psychiatrists. *Australas. Psychiatry* 26 (2), 189–192. <https://doi.org/10.1177/1039856217748249>.
- Terpstra, A.R., Vila-Rodriguez, F., LeMoult, J., Chakrabarty, T., Nair, M., Humaira, A., Gregory, E.C., Todd, R.M., 2023. Cognitive-affective processes and suicidality in response to repetitive transcranial magnetic stimulation for treatment resistant depression. *J. Affect. Disord.* 321, 182–190. <https://doi.org/10.1016/j.jad.2022.10.041>.
- Thakurta, R.G., Das, R., Bhattacharya, A.K., Saha, D., Sen, S., Singh, O.P., Bisui, B., 2012. Rapid response with ketamine on suicidal cognition in resistant depression. *Indian J. Psychol. Med.* 34 (2), 170–175. <https://doi.org/10.4103/0253-7176.101793>.
- Tomy, M., Alexander, W., Gupta, S., Schaefer, D., Case, A.A., 2025. Adjunctive intranasal esketamine for comorbid treatment-resistant depression with suicidal ideation in patients receiving palliative care at a Comprehensive Cancer center: A case series. *J. Palliat. Med.* 28 (1), 131–136. <https://doi.org/10.1089/jpm.2024.0040>.
- Trevino, K., McClintock, S.M., Husain, M.M., 2010. A review of continuation electroconvulsive therapy: application, safety, and efficacy. *J. ECT.* 26 (3), 186–195. <https://doi.org/10.1097/YCT.0b013e3181efa1b2>.
- Tu, P.-C., Chang, W.-C., Su, T.-P., Lin, W.-C., Li, C.-T., Bai, Y.-M., Tsai, S.-J., Chen, M.-H., 2025. Thalamocortical functional connectivity and rapid antidepressant and antisuicidal effects of low-dose ketamine infusion among patients with treatment-resistant depression. *Mol. Psychiatry* 30 (1), 61–68. <https://doi.org/10.1038/s41380-024-02640-3>.
- Turkzo, I., Lopena, O., Salvatore, G., Sanacora, G., Shelton, R., Fu, D.J., 2022. Treatment response to esketamine nasal spray in patients with major depressive disorder and acute suicidal ideation or behavior without evidence of early response: A pooled post hoc analysis of ASPIRE. *CNS. Spectr.* 1–7. <https://doi.org/10.1017/S1092852922000931>.
- U.S. Food and Drug Administration. (2011, July 26). Repetitive transcranial magnetic stimulation (rTMS) systems—Class II special controls guidance for industry and FDA staff. <https://www.fda.gov/medical-devices/guidance-documents-medical-devices-and-radiation-emitting-products/repetitive-transcranial-magnetic-stimulation-rTMS-systems-class-ii-special-controls-guidance>.
- U.S. Food and Drug Administration. (2018, December 21). FDA Brief: FDA takes action to ensure regulation of electroconvulsive therapy devices better protects patients, reflects current understanding of safety and effectiveness. <https://www.fda.gov/news-events/fda-brief/fda-brief-fda-takes-action-ensure-regulation-electroconvulsive-therapy-devices-better-protects>.
- U.S. Food and Drug Administration. (2025, January). SPRAVATO® (esketamine) nasal spray: highlights of prescribing information [Label]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/211243s016bl.pdf.
- Uyar, B., Güneş, M., 2024. An evaluation of the efficacy and side effects of a single dose of ketamine in major depressive disorder. *Postgr. Med J* 101 (1198), 716–722. <https://doi.org/10.1093/postmj/qgae142>.
- Vekhova, K.A., Namiot, E.D., Jonsson, J., Schiöth, H.B., 2025. Ketamine and esketamine in clinical trials: FDA-approved and emerging indications, trial trends with putative mechanistic explanations. *Clin. Pharmacol. Ther.* 117 (2), 374–386. <https://doi.org/10.1002/cpt.3478>.
- Vidal, S., Gex-Fabry, M., Bancila, V., Michalopoulos, G., Warrot, D., Jermann, F., Dayer, A., Sterpenich, V., Schwartz, S., Vutsits, L., Khan, N., Aubry, J.M., Kosel, M., 2018. Efficacy and safety of a rapid intravenous injection of ketamine 0.5 mg/kg in treatment-resistant major depression: an open 4-week longitudinal study. *J. Clin. Psychopharmacol.* 38 (6), 590–597. <https://doi.org/10.1097/JCP.0000000000000960>.
- Vieira, F., Correia-Melo, F.S., Santos-Lima, C., Souza-Marques, B., Leal, G.C., Jesus-Nunes, A.P., Mello, R.P., Caliman-Fontes, A.T., Bandeira, I.D., Marback, R.F., Telles, M., Argolo, F.C., Lins-Silva, D.H., Echeagaray, M.V.F., Beanes, G., Araújo-de-Freitas, L., Silva, S.S., Cardoso, T.A., Kapczynski, F., Quarantini, L.C., 2021. Ketamine and esketamine augmentation for suicidal ideation: A randomized, double-blinded clinical trial. *Gen. Hosp. Psychiatry* 68, 97–99. <https://doi.org/10.1016/j.genhospspsych.2020.12.011>.
- Wang, Q., Huang, H., Li, D., Wang, Y., Qi, N., Ci, Y., Xu, T., 2022. Intensive rTMS for treatment-resistant depression patients with suicidal ideation: an open-label study. *Asian J. Psychiatr.* 74, 103189. <https://doi.org/10.1016/j.jap.2022.103189>.
- Wang, Q., Li, L., Zhao, H., Cheng, W., Cui, G., Fan, L., Dong, X., Xu, T., Geng, Z., 2024. Predictors of response to accelerated rTMS in the treatment of treatment-resistant depression. *Eur. Arch. Psychiatry Clin. Neurosci.* 275, 1725–1736. <https://doi.org/10.1007/s00406-024-01903-y>.
- Wang, S., Qian, M., Li, L., Yang, Q., 2017. A case report of A patient with treatment-resistant depression successfully treated with repeated intravenous injections of A low dosage of ketamine. *Shanghai Arch. Psychiatry* 29 (6), 376–379. <https://doi.org/10.11919/j.issn.1002-0829.217036>.
- Weissman, C.R., Blumberger, D.M., Brown, P.E., Isserles, M., Rajji, T.K., Downar, J., Mulsant, B.H., Fitzgerald, P.B., Daskalakis, Z.J., 2018. Bilateral repetitive transcranial magnetic stimulation decreases suicidal ideation in depression. *J. Clin. Psychiatry* 79 (3). <https://doi.org/10.4088/JCP.17m11692>.
- Weissman, C.R., Hadas, I., Yu, D., Jones, B., Kong, D., Mulsant, B.H., Blumberger, D.M., Daskalakis, Z.J., 2021. Predictors of change in suicidal ideation across treatment phases of major depressive disorder: analysis of the STARD data. *Neuropsychopharmacol.* 46 (7), 1293–1299. <https://doi.org/10.1038/s41386-020-00953-9>.
- Wilkens, J., Wittler, F., Goya-Maldonado, R., 2022. Suicidality and relief of depressive symptoms with intermittent theta burst stimulation in a sham-controlled randomized clinical trial. *Acta Psychiatr. Scand.* 146 (6), 540–556. <https://doi.org/10.1111/acps.13502>.

- Yesavage, J.A., Fairchild, J.K., Mi, Z., Biswas, K., Davis-Karim, A., Phibbs, C.S., Forman, S.D., Thase, M., Williams, L.M., Etkin, A., O'Hara, R., Georgette, G., Beale, T., Huang, G.D., Noda, A., George, M.S., 2018. Effect of repetitive transcranial magnetic stimulation on treatment-resistant major depression in US veterans: A randomized clinical trial. *JAMA Psychiatry* 75 (9), 884–893. <https://doi.org/10.1001/jamapsychiatry.2018.1483>.
- Zaki, N., Chen, L.N., Lane, R., Doherty, T., Drevets, W.C., Morrison, R.L., Sanacora, G., Wilkinson, S.T., Popova, V., Fu, D.-J., 2023. Long-term safety and maintenance of response with esketamine nasal spray in participants with treatment-resistant depression: interim results of the SUSTAIN-3 study. *Neuropsychopharmacol* 48 (8), 1225–1233. <https://doi.org/10.1038/s41386-023-01577-5>.
- Zapf, L., Kaster, T.S., Vila-Rodriguez, F., Daskalakis, Z.J., Downar, J., Blumberger, D.M., 2024. The effect of once-daily vs. twice-daily intermittent theta burst stimulation on suicidal ideation in treatment-resistant depression. *Eur. Arch. Psychiatry Clin. Neurosci.* 275, 1787–1798. <https://doi.org/10.1007/s00406-024-01929-2>.
- Zhan, D., Gregory, E.C., Humaira, A., Wong, H., Klonsky, E.D., Levit, A., Ridgway, L., Vila-Rodriguez, F., 2024. Trajectories of suicidal ideation during rTMS for treatment-resistant depression. *J. Affect. Disord.* 360, 108–113. <https://doi.org/10.1016/j.jad.2024.05.109>.
- Zhang, K., Yang, Y., Yuan, X., Zhang, W., Han, X., Lei, C., Tao, Z., Li, Y., Liu, H., 2022. Efficacy and safety of repeated esketamine intravenous infusion in the treatment of treatment-resistant depression: A case series. *Asian J. Psychiatr.* 68 (101517820), 102976. <https://doi.org/10.1016/j.ajp.2021.102976>.
- Zhang, T., Zhu, J., Wang, J., Tang, Y., Xu, L., Tang, X., Hu, Y., Wei, Y., Cui, H., Liu, X., Hui, L., Li, C., 2021. An open-label trial of adjuvant high-frequency left prefrontal repetitive transcranial magnetic stimulation for treating suicidal ideation in adolescents and adults with depression. *J. ECT.* 37 (2), 140–146. <https://doi.org/10.1097/YCT.0000000000000739>.
- Zhao, H., Jiang, C., Zhao, M., Ye, Y., Yu, L., Li, Y., Luan, H., Zhang, S., Xu, P., Chen, X., Pan, F., Shang, D., Hu, X., Jin, K., Chen, J., Mou, T., Hu, S., Fitzgibbon, B.M., Fitzgerald, P.B., Huang, M., 2024. Comparisons of accelerated continuous and intermittent theta burst stimulation for treatment-resistant depression and suicidal ideation. *Biol. Psychiatry* 96 (1), 26–33. <https://doi.org/10.1016/j.biopsych.2023.12.013>.
- Zheng, W., Zhou, Y.L., Liu, W.J., Wang, C.Y., Zhan, Y.N., Li, H.Q., Chen, L.J., Li, M.D., Ning, Y.P., 2019. Investigation of medical effect of multiple ketamine infusions on patients with major depressive disorder. *J. Psychopharmacol.* 33 (4), 494–501. <https://doi.org/10.1177/0269881119827811>.
- Ziegler, L., Peters, E., Wanson, A., Halpape, K., 2021. Compounded intranasal racemic ketamine for major depressive disorder: A case report. *Exp. Clin. Psychopharmacol.* 29 (6), 750–754. <https://doi.org/10.1037/pha0000437>.
- Zolghadriha, A., Anjomshoa, A., Jamshidi, M.R., Taherkhani, F., 2024. Rapid and sustained antidepressant effects of intravenous ketamine in treatment-resistant major depressive disorder and suicidal ideation: A randomized clinical trial. *BMC. Psychiatry* 24 (1), 341. <https://doi.org/10.1186/s12888-024-05716-0>.