levels of depression. Of the participants 19.8% indicated no sign of distress, 26% mild distress, 37.3% average distress and 16.9% high depression. There was no statistical association of distress between female and male students (P=0.198). However, significant associations were Sedative drugs, parents level and occupation, Study Field, Future Career and Financial situation with depression (P<0.05).

**Conclusions:** Overall, the prevalence of depression was higher among students compared with general population. Providing programs for improving student's mental health is suggested.

**Keywords:** Student; Depression; Beak test; Isfahan

## EPP0530

## How effective are ketamine or esketamine in treatment-resistant depression?

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**Introduction:** Globally, depression affects millions of individuals. A third of depression patients meet the criteria for treatment-resistant depression (TRD). The N-methyl-D-aspartate receptor antagonist, ketamine, improved depressive symptoms in a span of 24-hours. Recently, the FDA approved esketamine, an enantiomer of ketamine for TRD.

**Objectives:** To determine the effectiveness of ketamine and esketamine in TRD, and observe their role in suicidality.

**Methods:** Individual systematic searches were conducted on the PubMed database following the PRISMA protocol (Figure 1). Inclusion criteria included randomized clinical trials (RCT). Search strings were (i) "ketamine" OR "esketamine" AND "treatment-resistant depression" (ii) "ketamine" OR "esketamine" AND "suicide." Eleven studies were included for depression and five studies for suicidality (Table 1). Comparison analysis for suicide appeared trivial because of only one inclusion eligible esketamine RCT. This review was submitted for registration at PROSPERO. Randomized odds ratios, 95% confidence interval (CI), and heterogeneity were obtained.

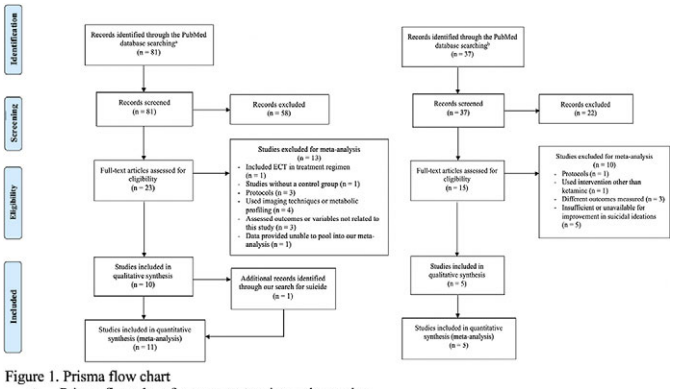


Figure 1. Prisma flow chart
a. Prisma flow chart for treatment resistant depression
b. Prisma flow chart for suicide

**Results:** The comprehensive meta-analysis, version 3.0, was used for analysis. Ketamine improved TRD symptoms and reduced suicidality by a nine-fold and three-fold odds, respectively (OR 9.01, CI 4.89–16.6, p<0.001 and OR 2.9, CI 1.67–5.06, p<0.001). Esketamine also improved TRS symptoms (OR= 2.61, 95% CI= 1.56–4.37, p<0.001). The heterogeneity ranged from 11% to 60% between the three groups. Sensitivity analysis did not alter the results.

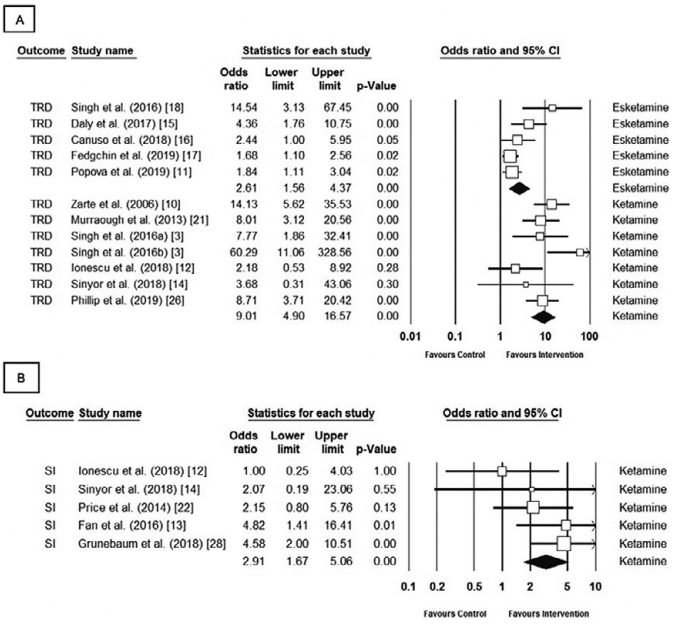


Figure 2. Forest plot analysis
A. Ketamine and esketamine impact on treatment resistant depression
B. Ketamine's impact on reducing suicidal ideations

| Author | Design | Sample Size[a,b,c,d] | Intervention Regimen | Control Regimen[e] | Concomitant Therapy[f] | Primary Endpoint | Diagnosis[h] | Assessment Scale[i] |
|---|---|---|---|---|---|---|---|---|
| **Ketamine** | | | | | | | | |
| Zarte et al. (2006) [10] | Cross-over | 17 | 0.5 mg/kg IV | Placebo | None | 110 minutes[g] | TRD | 21 item HAM-D |
| Murrough et al. (2013) [21] | Parallel | I: 47 C: 25 | 0.5 mg/kg IV | Midazolam | None | 24 hours | TRD | MADRS |
| Price et al. (2014) [22] | Parallel | I: 36 C: 21 | 0.5 mg/kg IV | Midazolam | Information not provided. | 24 hours | Anti- suicidal effect | BSS |
| Fan et al. (2016) [13] | Parallel | I: 20 C:17 | 0.5 mg/kg IV | Midazolam | Information not provided. | 24 hours | Anti- suicidal effect | BSI |
| Singh et al. (2016) [3] | Parallel | 2w: I: 16 C: 15 3w: I: 13 C: 16 | 0.5 mg/kg IV | 0.9% Sodium Chloride IV | Antidepressants | 15 days | TRD | MADRS |
| Ionescu et al. (2018) [12] | Parallel | 26 | 0.5 mg/kg IV | Saline | None | 21 days[g] | TRD; Anti-suicidal effect | 28 item HAM-D; C-SSRS |
| Sinyor et al. (2018) [14] | Parallel | I: 5 C: 4 | 0.5 mg/kg IV | Midazolam | TAU | 42 days | MDD; Anti-suicidal effect | C-SSRS; SSI; MADRS |
| Grunebaum et al. (2018) [28] | Parallel | I: 40 C: 40 | 0.5 mg/kg IV | Midazolam | Antidepressants | 24 hours | Suicidal Ideation | SSI |
| Phillip et al. (2019) [26] | Cross-over | 41 | 0.5 mg/kg IV | Midazolam | Antidepressants | 24 hours | TRD | MADRS |
| **Esketamine** | | | | | | | | |
| Singh et al. (2016) [18] | Parallel | I: 20[b] C: 10 | 0.20 mg/kg or 0.40 mg/kg IV | Placebo | Information not provided. | 24 hours | TRD | MADRS |
| Daly et al. (2017) [15] | Parallel | I:34[c] C: 33 | 28 mg, 56, and 84 mg | Placebo | Antidepressants | 8 days | TRS | MADRS |
| Canuso et al. (2018) [16] | Parallel | I: 34 C: 31 | 84 mg | Placebo | Antidepressants | 4 hours | TRS; Anti-suicidal effect | MADRS; MADRS-SI |
| Fedgchin et al. (2019) [17] | Parallel | I: 209[d] C: 108 | 56 mg or 84 mg | Placebo | Antidepressants | 28 days | TRS | MADRS |
| Popova et al. (2019) [11] | Parallel | I: 101[d] C: 100 | 56 or 84 mg | Placebo | Antidepressants | 28 days | TRS | MADRS |

Table 1. Characteristics of Included Randomized Clinical Trials of Ketamine and Esketamine for TRD and Suicidality.
a. I=Intervention group sample size; C=control group sample size; 2w= two-week group; 3w= three-week group
b. Esketamine 0.20 mg/kg IV sample size = 9; Esketamine 0.40 mg/kg IV sample size = 11. Results were combined for our analysis.
c. Esketamine 28 mg/kg sample size = 11; Esketamine 56 mg/kg sample size = 11; Esketamine 84 mg/kg sample size = 12. Results were combined for our analysis.
d. Results were reported as combined findings (56 mg plus 84 mg).
e. Midazolam was chosen as the active placebo agent
f. TAU= Treatment as usual, participants were allowed to continue current medications any contraindicated medications; participants were allowed to continue their previous antidepressants
g. Authors of the study did not indicate the primary end point. Thus, the authors of this study selected these primary end points. 21 days was taken for Ionescu et al. (2018), which is at the sixth infusion.
h. TRD= treatment resistant depression; MDD= Major depressive disorder
i. HAM-D= Hamilton Depression Rating Scale; MADRS= The Montgomery–Asberg Depression Rating Scale; BSS/BSI= Beck's Scale for Suicide Ideation; C-SSRS= Columbia Suicide Severity Rating Scale; SSI= Scale of Suicide Ideation; MADRS-SI= The Montgomery–Asberg Depression Rating Scale-Suicidal Ideation

**Conclusions:** Findings must be cautiously interpreted as the primary endpoint differed. The primary endpoint was set at 24-hours and 28-days for ketamine and esketamine, respectively. Esketamine's effectiveness over 28 days appears promising for TRD. Current aim should consist of structured guidance for clinicians in esketamine administration.

**Keywords:** TRD; Ketamine; treatment-resistant depression; esketamine