Ketamin for Treatment resistant depression

Review information

Authors

[Empty name][1]

[1][Empty affiliation]

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Contact person

[Empty name]

Dates

Assessed as Up-to-date:	
Date of Search:	
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Last Citation Issue:	Not specified

What's new

Date / Event	Description

History

Date / Event	Description

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Characteristics of studies

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Ionescu 2019

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** 0.5 mg/kg R/S-ketamine hydrochloride (2 infusions pr week for 3 weeks) normal saline (placebo) (2 infusions pr week for 3 weeks) Overall **Included criteria:** (1) 18–65 years old; (2) Primary diagnosis of current major depressive disorder (MDD), based on SCID;(3) HDRS-28 score ≥ 20 at screening; (4) History of ≥ 3 failed antidepressant treatment trials of adequate dose and duration during the current episode (ATHQ); (5) SI for ≥ 3 months (as measured by ≥ 1 on the ColumbiaSuicide Severity Rating Scale (C-SSRS) SI scorewithout the requirement for immediate hospitalization, and have a HDRS suicide item score ≥ 2 (current SI, thoughts of own death) at screening or one of the other two pre-infusion phase visits; (6) Ability to remain on an adequate, stable antidepressant regimen for ≥ 4 weeks prior to infusions; (7) Ability to secure a reliable adult chaperone after ketamine infusion days; and (8) Maintain a treating psychiatrist in agreement with study participation **Excluded criteria:** (1) pregnancy; (2) unstable medical illness; (3) bipolar disorder; (4) past multiple adverse drug reactions; (4) psychotic illness; (5) substance use disorder within the past year; (6) positive urine toxicology; (7) past history of ketamine abuse; (8) SI requiring immediate hospitalization or indicating immediate risk. In addition, although patients were maintained on their stable outpatient medication regimens prior to the start of the study and during infusions, certain medications were exclusionary due to risk of interactions: St. John's wort, theophylline, tramadol, and any use of illicit narcotics or barbiturates within the previous six months. **Pretreatment:** Placebo group had first depressive episode at a younger age - else no difference

Interventions	**Intervention Characteristics** 0.5 mg/kg R/S-ketamine hydrochloride (2 infusions pr week for 3 weeks) normal saline (placebo) (2 infusions pr week for 3 weeks)
Outcomes	*Depressionssymptomer* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Scale**: HDRS ● **Direction**: Lower is better *Remission* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: n ● **Direction**: Higher is better ● **Notes**: Defineret som <= 7 HDRS *Respons* ● **Outcome type**: DichotomousOutcome ● **Scale**: n ● **Direction**: Higher is better ● **Data value**: Change from baseline ● **Notes**: defineret som >= 50% forbedring i HDRS score *Funktionsniveau* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Not reported ● **Data value**: Change from baseline *Livskvalitet* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Not reported ● **Direction**: Higher is better *Adverse event - indlæggelse* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Partially reported *Selvmordsforsøg* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported ● **Notes**: Der rapporteres på selvmordstanker - og give score herfor *Misbrug ketamin/eskatemin* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported *Øvrige bivirkninger* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported *Remission - længste follow up* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Direction**: Higher is better *Frafald* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Direction**: Lower is better
Identification	**Sponsorship source:** This work was supported by the American Foundation for Suicide Prevention (AFSP), the Clinical Research Center at Massachusetts General Hospital, and the Department of Psychiatry, Massachusetts General Hospital, Boston, Massachusetts to Cristina Cusin (P.I.). The project was also funded by grant number 8UL1TR000170-05, Harvard Clinical and Translational Science Center, from the National Center for Advancing Translational Science **Country:** United States of America **Setting:** Out-patient **Comments:** No comment **Authors name:** Dawn F. Ionescu **Institution:** Depression Clinical and Research Program, Department of Psychiatry, Massachusetts General Hospital, Boston, MA, United States **Email:** ccusin@mgh.harvard.edu **Address:** (C.Cusin) Depression Clinical and Research Program, Massachusetts General Hospital, 1 Bowdoin

	Square, 6th Floor, Boston, MA 02114, United States
Notes	*Claus Sørensen* on 11/11/2019 07:42 **Select** Relevant definition af TRD, relevante data . placebokontrolleret RCT

Risk of bias table

Bias	Authors' judgement	Support for judgement
Allocation concealment	Low risk	Judgement Comment: patienter, klinikere og rater var blindet.
Sequence generation	Low risk	Judgement Comment: computer genereret alogoritme
Blinding of participants and personnel for All outcomes	Low risk	Judgement Comment: patienter, klinikere og rater var blindet
Incomplete outcome data for All outcomes	Unclear risk	Judgement Comment: De rapporterer på det de har beskrevet. Både i aktiv og i placebo grupper er det 69% som gennemfører, øvrige dropper ud på et tidspunkt. man har data på 24/26 for første infusion og rating bagefter
Selective outcome reporting	Low risk	Judgement Comment: rapporteret data svarer til hvad der beskrives at ville undersøges Der foreligger en protokol som kan rekvireres - ligger ikke på ClinicalTrials.gov
Other sources of bias	Unclear risk	Judgement Comment: 3 år til inclusion er lang tid. 30% droppet ud indenfor 3 uger. 3/13 i palcebogrupper stopper efter første behandling, fordi de troede de fik placebo
Blinding of outcome assesors for All outcomes	Low risk	Judgement Comment: rater var blindet

Singh 2016

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** 0.20 mg/kg Esketamine IV single dose 0.40 mg/kg Esketamine IV single dose normal saline (placebo) IV single dose Overall **Included criteria:** men and women 18–64 years old who met DSM-IV-TR diagnostic criteria for recurrent MDD without psychotic features, based on clinical assessmentand confirmed by the Mini-International NeuropsychiatricInterview. Based on the conventional definition of TRD, patients were required to have had an inadequate response to at least one antidepressant drug in their currentdepressive episode and an inadequate response to at least one other antidepressant either in their current or in a previousdepressive episode, as assessed by the Massachusetts General Hospital Antidepressant Treatment Response Questionnaire. At screening and on day 21, patients were also required to have a total score of at least 34 on the Inventory of Depressive Symptomatology–Clinician Rated, 30-Item (mild,12–23; moderate, 24–36; severe, 37–46; very severe, 47–84). **Excluded criteria:** Exclusion criteria included any primary DSM-IV-TR diagnosis of active generalized anxiety disorder, panicdisorder, obsessive-compulsive disorder, posttraumatic stressdisorder, anorexia nervosa, or bulimia nervosa; patientswere also excluded if they had been acutely suicidalor homicidal requiring hospitalization in the past 12 months or had a history of previous nonresponse to ketamine or esketamine **Pretreatment:** none
Interventions	**Intervention Characteristics** 0.20 mg/kg Esketamine IV single dose 0.40 mg/kg Esketamine IV single dose normal saline (placebo) IV single dose
Outcomes	*Depressionssymptomer* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Scale**: MADRS ● **Range**: 0-60 ● **Direction**: Lower is better ● **Data value**: Change from baseline *Response* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Direction**: Higher is better ● **Data value**: Endpoint

	Remission ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported ● **Data value**: Endpoint *Funktionsniveau* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Not reported *Livskvalitet* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Not reported *Adverse event - indlæggelse* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported *Adverse event - selvmordsforsøg* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported *Øvrige bivirkninger* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported ● **Data value**: Endpoint *Misbrug esketamin* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported *Frafald* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Data value**: Endpoint ● **Notes**: 1 er udgået af aktiv-gruppen grundet AE, men det er ikke muligt at sige hvilken af dem.
Identification	**Sponsorship source:** This work was supported by Janssen Research & Development.We thank Dr. Harry Ma (Janssen Research & Development) for writingassistance. The investigators and the sponsor thank all the patients andtheir families who took part in this study **Country:** Belgien, Tyskland, Polen - ifl protokol **Setting:** Multicenter out-patient **Comments:** Medicinal industri **Authors name:** Jaskaran B. Singh **Institution:** Janssen Research& Development **Email:** jsingh25@its.jnj.com **Address:** Janssen Research& Development, LLC, 3210 Merryfield Row, San Diego, CA 92121; USA
Notes	*Aake Packness* on 21/11/2019 19:05 **Study Design** RCT DB m placebo indtil til 2. randomisering på 4. dagen. Data er relevant for os i perioden med reel placebo - altså 4 dage hvor forløbet er parallelt og før krydsningerne *Aake Packness* on 25/11/2019 23:14 **Outcomes** Ikke outcomes på længste follow up på depressionssymptomer eller remission - *Claus Sørensen* on 27/11/2019 22:57 **Outcomes** For øvrige bivirkninger er flere perioder blandet sammen. Kan ikke se bivirkninger alene for dobbelt-blind periode

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement Comment: computer genereret,permuterede blokke.
Allocation concealment (selection bias)	High risk	Judgement Comment: unblinded pharmacist gav behandling og viste hvad pt fik
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: Fremgår at patienter og investigarorer var blindet. Pharmacist som gav behandling var ikke

Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: Fremgår at patienter og investigarorer var blindet. Pharmacist som gav behandling var ikke
Blinding of outcome assessment (detection bias)	Low risk	Judgement Comment: Behandlingsteam blindet i blindingsfasen (dag 1 og 4) Efter 2. dosering ophører blinding
Blinding of outcome assessment (detection bias)	Low risk	
Incomplete outcome data (attrition bias)	High risk	Judgement Comment: flere sekundære outcomes ikke raporrteret, diskrepans mellem primært outcome madrs baseline vs dag 2, og f.eks sekundært outcome cgi-s baseline vs dag 7 af 42 screenet blev 30 randomiseret, 1 udgår grundet bivirkninger3 går ud af åben-fase-forløbet grundet transportproblemer(Jeg kan ikke få flowchart frem der viser bortfaldet fra 42 - til 30). Et eksklusionskriterie er at man ikke tidligere har responderet på ketamin eller eskatemin - hvor mange den gruppe udgør er ikke synligt
Incomplete outcome data (attrition bias)	High risk	Judgement Comment: flere sekundære outcomes ikke raporrteret, diskrepans mellem primært outcome madrs baseline vs dag 2, og f.eks sekundært outcome cgi-s baseline vs dag 7 af 42 screenet blev 30 randomiseret, 1 udgår grundet bivirkninger3 går ud af åben-fase-forløbet grundet transportproblemer(Jeg kan ikke få flowchart frem der viser bortfaldet fra 42 - til 30). Et eksklusionskriterie er at man ikke tidligere har responderet på ketamin eller eskatemin - hvor mange den gruppe udgør er ikke synligt
Selective reporting (reporting bias)	High risk	Judgement Comment: flere sekundære outcomes ikke raporrteret
Selective reporting (reporting bias)	High risk	Judgement Comment: flere sekundære outcome sikke raporrteret
Other bias	High risk	Judgement Comment: Designet gør kun den indledende del af studiet egnet for os. Det krydsover og eksklusionskriterieret at man ikke tidligere har kunnet tåle ketamin/esketamin - og ikke kan se hvor mange der udelukkkes på det kriterium virker mærkelig.Randomiseringen ophører tidligt. Patienter med angstlidelser ikke med, ikke indlagt for suicidalitet seneste 12 mdr. Primær endpoint madrs efter 1 dag. Generaliserebarhed?
Other bias	High risk	Judgement Comment: Designet gør kun den indledende del af studiet egnet for os. Det krydsover og eksklusionskriterieret at man ikke tidligere har kunnet tåle ketamin/esketamin - og ikke kan se hvor mange der udelukkkes på det kriterium virker mærkelig.Randomiseringen ophører tidligt. Patienter med angstlidelser ikke med, ikke indlagt for suicidalitet seneste 12 mdr. Primær endpoint madrs efter 1 dag. Generaliserebarhed?

Singh 2016a

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Ketamine 3 times a week 0.5 mg/kg IV Placebo 3 times a week IV Ketamine 2 times a week 0,5 mg/kg IV Placebo 2 times a week IV Overall **Included criteria:** 8 to 64 years of age who met DSM-IV-TR criteria for recurrent major depressivedisorder without psychotic features, confirmed by MINI. Additional inclusion criteria were qualifying valid depressive episodes,as assessed with the SAFER criteria (12) (defined as state versus trait, assessability, face validity, ecological validity, and rule of three Ps—pervasive, persistent, and pathological); inadequate response to at least two antidepressants (with at least one antidepressant failure in the current episode), assessed by medication history and the Massachusetts GeneralHospital Antidepressant Treatment Response Questionnaire(13); and a score$34 on the 30-item Inventory of DepressiveSymptomatology–Clinician Rated(14, 15) at screening and pre-infusion assessment on day 1. Independent SAFER raters fromMassachusetts General Hospital verified that all randomizedpatients met the SAFER criteria, had treatment-resistant depression documented on the Antidepressant Treatment Response Questionnaire, and manifested the required depression severity. **Excluded criteria:** A primary DSM-IV diagnosis of OCD, PTSD, anorexia nervosa, or bulimia nervosa or a prior historyor current diagnosis of a psychotic disorder, bipolar disorder, mental retardation, borderline personality disorder, mooddisorder with postpartum onset, or somatoform disorders. Or history of previous non-response of depressive symptoms to ketamine, clinically significant suicidal or homicidal ideation (imminent risk ofharm), and substance abuse or dependence within the year preceding the screening visit. **Pretreatment:** Agree

Interventions	**Intervention Characteristics** Ketamine 3 times a week 0.5 mg/kg IV Placebo 3 times a week IV Ketamine 2 times a week 0,5 mg/kg IV Placebo 2 times a week IV
Outcomes	*Depressionssymptomer* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Partially reported ● **Scale**: MADRS ● **Range**: 0 - 50 ● **Unit of measure**: interger ● **Direction**: Lower is better ● **Data value**: Change from baseline *Remission* ● **Outcome type**: DichotomousOutcome ● **Scale**: n ● **Direction**: Higher is better ● **Data value**: Endpoint ● **Notes**: Remission defineret som MADRS score <=10 *Respons* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Partially reported ● **Scale**: MADRS ● **Range**: 0- 50 ● **Unit of measure**: n ● **Direction**: Higher is better ● **Data value**: Endpoint ● **Notes**: Defineret som antal pt med >= 50 reduktion i symptomscore i MADRS *Funktionsniveau* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Not reported *Adverse event - indlæggelse* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported ● **Direction**: Lower is better *Adverse events - selvmordsforsøg* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported *Misbrug ketamin/esketamin* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported *Øvrige bivirkninger* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Data value**: Endpoint *Frafald* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Data value**: Endpoint
Identification	**Sponsorship source:** Janssen Research and Development, which alsoprovided a formal review of the manuscript **Country:** United States of America **Setting:** Outpatient **Comments:** Medical industri **Authors name:** Jaskaran B. Singh **Institution:** Janssen Research and Development, Titusville, N.J. USA **Email:** jsingh25@its.jnj.com **Address:** Janssen Research and Development, Titusville, N.J., and Beerse,Belgium; the Departments of Psychiatry and Neuroscience, Icahn Schoolof Medicine at Mount Sinai, New York, N.Y
Notes	*Aake Packness* on 25/11/2019 22:10 **Outcomes** Depressionssymptomer længste follow up er ikke relevant, da randomisseringen ophører efter to ugerTilsvarende for Remission længste follow up

Risk of bias table

Bias	Authors' judgement	Support for judgement
Sequence generation	High risk	Judgement Comment: Det er uklart hvorfor 97 sorteres fra fiorud for randomiseringen - det er ikke beskrevet - et af eksklusionskriterierne er tidligere manglede respons ved ketamin administration på depressionssymptomer Computergereneret allokering
Sequence generation	High risk	
Blinding of participants and personnel for All outcomes	Low risk	Judgement Comment: patienter, behandlere og investigatorer var blindet
Blinding of outcome assessors for All outcomes	Low risk	Judgement Comment: investigatorer var blindet
Incomplete outcome data for All outcomes	Low risk	Judgement Comment: Da det kun er dag 1-15 som reelt dobbelt blindt behandling, er de data som skal indgå
Selective outcome reporting	Low risk	Judgement Comment: Data synes at svare til beskrivelse i metode
Other sources of bias	Unclear risk	Judgement Comment: pt med OCD, ptsd, spiseforstyrrelse, psykotisk depression, postpartum depression og misbrug indenfor det sidste år ikke med. Betydning for generaliserbarhed
Allocations concealment	Low risk	Judgement Comment: patienter, behandlere og invstigatorer var blindet

Su 2017

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** 0.5 mg/kg R/S-ketamine hydrochloride IV single dose 0.2 mg/kg R/S-ketamine hydrochloride IV single dose normal saline (placebo) IV single dose Overall **Included criteria:** DSM IV criteria for major depressive disorder,recurrent without psychotic features on the basis of the MINI, and who had failed to respond to more than two adequate antidepressant trials. The evaluation of the adequacy of prior antidepressant trials and the inadequacyof clinical response was determined on the basis of asemistructured patient interview and review of the medicalrecord. **Excluded criteria:** A history of bipolar disorder, psychotic symptoms, substance dependence other than nicotine, and mild symptoms HAMD-17 score o18 at screening or o13 before study entry;. Patients with active medical disease were excluded on the basis of medical screening that included history, physical examination, laboratory tests **Pretreatment:** NS **alle taiwanesere:** Taiwanees
Interventions	**Intervention Characteristics** 0.5 mg/kg R/S-ketamine hydrochloride IV single dose 0.2 mg/kg R/S-ketamine hydrochloride IV single dose normal saline (placebo) IV single dose
Outcomes	*response* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Partially reported ● **Unit of measure**: n ● **Direction**: Higher is better ● **Data value**: Endpoint ● **Notes**: Response >= 50 reduktion i HAMD-score.HAMD baseret på telefon interview *Depressionssymptomer* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Scale**: HAMD-17 ● **Data value**: Endpoint ● **Notes**: Reported as least square means visualiseret i hver sin graf (fig 2) *Remission* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported ● **Direction**: Higher is better *Funktionsniveau*

	● **Outcome type**: ContinuousOutcome *Livskvalitet* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Not reported *Adverse events indlæggelse* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported *Adverse event - selvmordsforsøg* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported *Misbrug Ketamin* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported ● **Notes**: Aktiv gruppe rapporteret bivirkninger sammen *Øvrige bivirkninger* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Notes**: Ketamin-gruppen rapporteres fælles mht bivirkninger - det er ikke muligt at adskille dem *Frafald* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported *Depressionssymptomer længste follow up* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Scale**: HAMD ● **Direction**: Lower is better
Identification	**Sponsorship source:** No information **Country:** Taiwan **Setting:** Outpatient **Comments:** None **Authors name:** Tung-Ping Su **Institution:** Division of Psychiatry, Faculty of Medicine, National Yang-Ming University, Taipei, Taiwan; **Email:** tomsu0402@gmail.com **Address:** Department of Psychiatry, TaipeiVeterans General Hospital, No. 201, Section 2, Shih-Pai Road, BeitouDistrict, Taipei 112, Taiwan
Notes	*Aake Packness* on 21/11/2019 23:59 **Outcomes** Der er ikke angivet længeste follow up vedr remission

Risk of bias table

Bias	Authors' judgement	Support for judgement
Allocation concealment	Unclear risk	
Sequence generation	High risk	
Blinding of participants and personnel for All outcomes	Unclear risk	Judgement Comment: beskrives dobbelt blindt - ingen angivelse af hvem og hvordan sikret
Blinding of outcome assessors for All outcomes	Unclear risk	Judgement Comment: beskrives dobbelt blindet - ingen angivelse af hvordan blinding er foregået for investigatorer
Incomplete outcome data for All outcomes	Low risk	Judgement Comment: primært outcome HAMD rapporteret og skundært outcome rapporteret.
Selective outcome reporting	Unclear risk	Judgement Comment: Flere post hoc analyser rapporteret, ingen tilfredstillende beskrivelse af primært outcome. Synes i artiklen at blive til HamD efter 4 dage
Other sources of bias	Unclear risk	Judgement Comment: studiet er på ren kinesisk pop?ulation. Pt måtte ikke være fysisk syge. Generaliserbarhed Data baseres på HAMD telefon-rated. Rapporteres i clusters - fordi observationsperioden er så kort, antageligDer rapporteres på response indenfor 24-96 timer efter infusion. Ikke klinisk relevant

Footnotes

Characteristics of excluded studies

AanHetRotMcharney 2008

Reason for exclusion	Wrong type of publication

Bahr 2019

Reason for exclusion	Wrong type of publication

Berman 2000

Reason for exclusion	Wrong patient population

Canuso 2016

Reason for exclusion	Wrong patient population

Canuso 2017

Reason for exclusion	Wrong patient population

Canuso 2018

Reason for exclusion	Wrong patient population

Chen 2018

Reason for exclusion	Wrong outcomes

Cusin 2012

Reason for exclusion	Wrong type of publication

Daly 2015

Reason for exclusion	Wrong type of publication

Daly 2018

Reason for exclusion	Wrong intervention

Domany 2019

Reason for exclusion	Wrong intervention

Fava 2018

Reason for exclusion	Wrong comparator

Fedgchin 2019

Reason for exclusion	Wrong study design

George 2016

Reason for exclusion	Wrong patient population

George 2017

Reason for exclusion	Wrong patient population

Glvez 2018

Reason for exclusion	Wrong study design

Lapidus 2013

Reason for exclusion	Wrong patient population

Lapidus 2014

Reason for exclusion	Wrong patient population

Llc 2012

Reason for exclusion	Wrong type of publication

Loo 2014

Reason for exclusion	Wrong patient population

Loo 2016

Reason for exclusion	Wrong patient population

Mathew 2013

Reason for exclusion	Wrong study design

Milak 2017

Reason for exclusion	Wrong patient population

Murrough 2012

Reason for exclusion	Wrong comparator

Murrough 2013

Reason for exclusion	Wrong comparator

Murrough 2013a

Reason for exclusion	Wrong comparator

Nash 2017

Reason for exclusion	Wrong outcomes

Perez Esparza 2018

Reason for exclusion	Wrong study design

Phillips 2017

Reason for exclusion	Wrong comparator

Phillips 2019

Reason for exclusion	Wrong comparator

Salloum 2020

Reason for exclusion	Wrong comparator

Sharon 2016

Reason for exclusion	Wrong patient population

Singh 2016b

Reason for exclusion	Wrong patient population

Sos 2013

Reason for exclusion	Wrong patient population

Wan 2015

Reason for exclusion	Wrong study design

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

Summary of findings tables

Additional tables

References to studies

Included studies

Ionescu 2019

Ionescu, Dawn F.; Bentley, Kate H.; Eikermann, Matthias; Taylor, Norman; Johnson-Akeju, Oluwaseun; Swee, Michaela B.; Pavone, Kara J.; Petrie, Samuel R.; Dording, Christina; Mischoulon, David; Alpert, Jonathan E.; Brown, Emery N.; Baer, Lee; Nock, Matthew K.; Fava, Maurizio; Cusin, Cristina; Akeju, Oluwaseun. Repeat-dose ketamine augmentation for treatment-resistant depression with chronic suicidal ideation: A randomized, double blind, placebo controlled trial. Journal of Affective Disorders 2019;243:516-524. [DOI: 10.1016/j.jad.2018.09.037]

Singh 2016

Singh, J. B.; Fedgchin, M.; Daly, E.; Xi, L.; Melman, C.; De Bruecker, G.; Tadic, A.; Sienaert, P.; Wiegand, F.; Manji, H.; et al.,. Intravenous Esketamine in Adult Treatment-Resistant Depression: a Double-Blind, Double-Randomization, Placebo-Controlled Study. Biol Psychiatry 2016;80(6):424-431. [DOI: 10.1016/j.biopsych.2015.10.018]

Singh 2016a

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.. A Double-Blind, Randomized, Placebo-Controlled, Dose-Frequency Study of Intravenous Ketamine in Patients With Treatment-Resistant Depression. Am J Psychiatry 2016;173(8):816-26. [DOI: 10.1176/appi.ajp.2016.16010037]

Su 2017

Su, Tung-Ping; Chen, Mu-Hong; Li, Cheng-Ta; Lin, Wei-Chen; Hong, Chen-Jee; Gueorguieva, Ralitza; Tu, Pei-Chi; Bai, Ya-Mei; Cheng, Chih-Ming; Krystal, John H.. Dose-related effects of adjunctive ketamine in Taiwanese patients with treatment-resistant depression. Neuropsychopharmacology 2017;42(13):2482-2492. [DOI:]

Excluded studies

AanHetRotMcharney 2008

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Bahr 2019

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Studies awaiting classification

Ongoing studies

Other references

Additional references

Other published versions of this review

Data and analyses

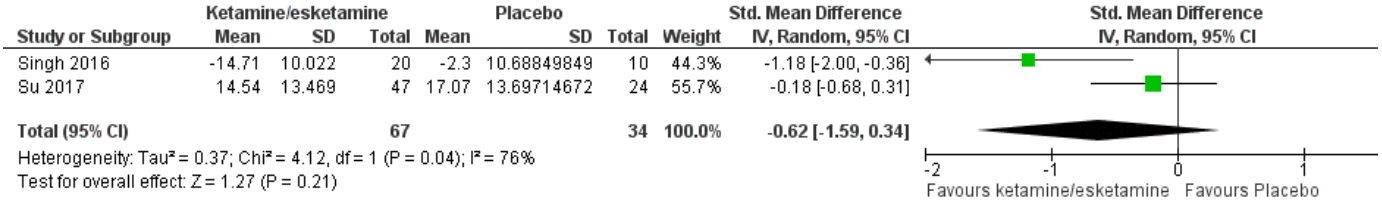
1 IV Ketamin/esketamine versus placebo

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 Depressive symptoms, acute phase	2	101	Std. Mean Difference (IV, Random, 95% CI)	-0.62 [-1.59, 0.34]
1.2 Response, acute phase	2	101	Risk Ratio (IV, Random, 95% CI)	4.17 [1.49, 11.65]
1.3 Depressive symptoms, subacute phase	2	76	Std. Mean Difference (IV, Random, 95% CI)	-1.09 [-2.27, 0.10]
1.3.1 IV 3 times a week	1	29	Std. Mean Difference (IV, Random, 95% CI)	-2.20 [-3.15, -1.25]
1.3.2 IV 2 times a week	2	47	Std. Mean Difference (IV, Random, 95% CI)	-0.57 [-1.66, 0.53]
1.4 Response, subacute phase	2	82	Risk Ratio (IV, Random, 95% CI)	2.74 [0.64, 11.68]
1.4.1 IV 3 times a week	1	29	Risk Ratio (IV, Random, 95% CI)	8.62 [1.21, 61.37]
1.4.2 IV 2 times a week	2	53	Risk Ratio (IV, Random, 95% CI)	1.81 [0.32, 10.42]
1.5 Remission, subacute phase	2	82	Risk Ratio (IV, Random, 95% CI)	4.04 [1.07, 15.21]
1.5.1 IV 3 times a week	1	29	Risk Ratio (IV, Random, 95% CI)	8.50 [0.48, 151.05]
1.5.2 IV 2 times a week	2	53	Risk Ratio (IV, Random, 95% CI)	3.31 [0.74, 14.72]
1.6 Adverse events indlæggelse	2	97	Risk Ratio (IV, Random, 95% CI)	0.33 [0.01, 7.50]
1.7 Adverse event - selvmordsforsøg	2	138	Risk Ratio (IV, Random, 95% CI)	2.68 [0.12, 61.58]
1.7.1 IV 3 times a week	1	33	Risk Ratio (IV, Random, 95% CI)	Not estimable
1.7.2 Single dose	1	71	Risk Ratio (IV, Random, 95% CI)	Not estimable
1.7.3 IV 2 times a week	1	34	Risk Ratio (IV, Random, 95% CI)	2.68 [0.12, 61.58]
1.8 Øvrige bivirkninger	2	138	Risk Ratio (IV, Random, 95% CI)	1.54 [1.07, 2.21]
1.8.1 Single dose	1	71	Risk Ratio (IV, Random, 95% CI)	6.77 [0.40, 115.37]
1.8.2 IV 3 times a week	1	33	Risk Ratio (IV, Random, 95% CI)	1.53 [0.88, 2.67]
1.8.3 IV 2 times a week	1	34	Risk Ratio (IV, Random, 95% CI)	1.48 [0.92, 2.39]

1.9 Frafald	4	194	Risk Ratio (IV, Random, 95% CI)	1.09 [0.46, 2.59]
1.9.1 Single dose	2	101	Risk Ratio (IV, Random, 95% CI)	1.57 [0.07, 35.46]
1.9.2 IV 3 times a week	1	33	Risk Ratio (IV, Random, 95% CI)	8.50 [0.49, 146.29]
1.9.3 IV 2 times a week	2	60	Risk Ratio (IV, Random, 95% CI)	0.84 [0.33, 2.17]

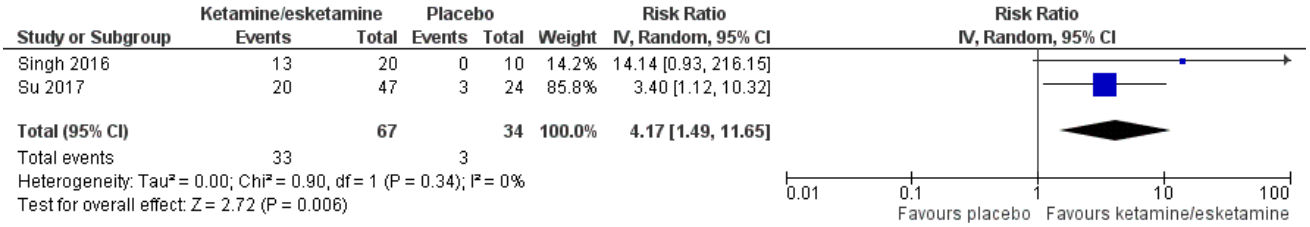
Figures

Figure 1 (Analysis 1.1)



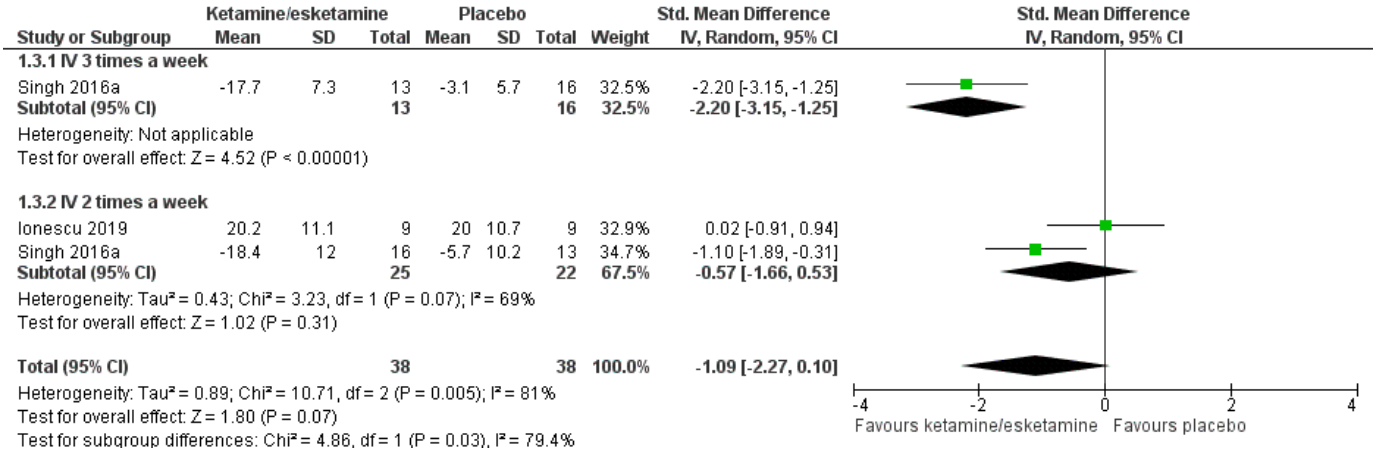
Forest plot of comparison: 13 Ketamin versus placebo, outcome: 13.1 Depressive symptoms, acute phase.

Figure 2 (Analysis 1.2)



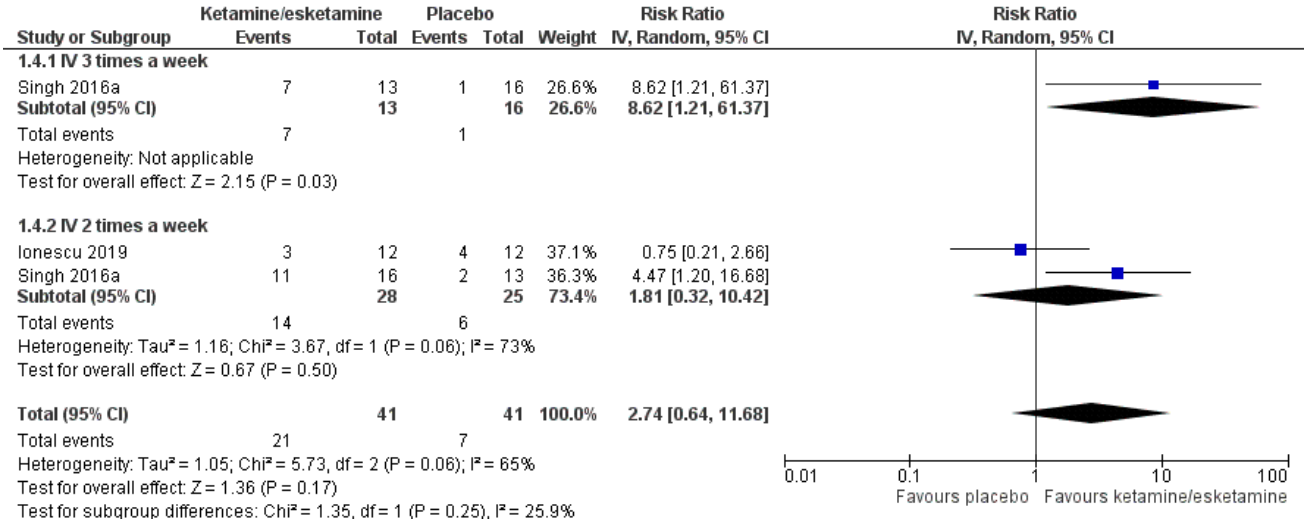
Forest plot of comparison: 13 IV Ketamin versus placebo, outcome: 13.2 Response, acute phase.

Figure 3 (Analysis 1.3)



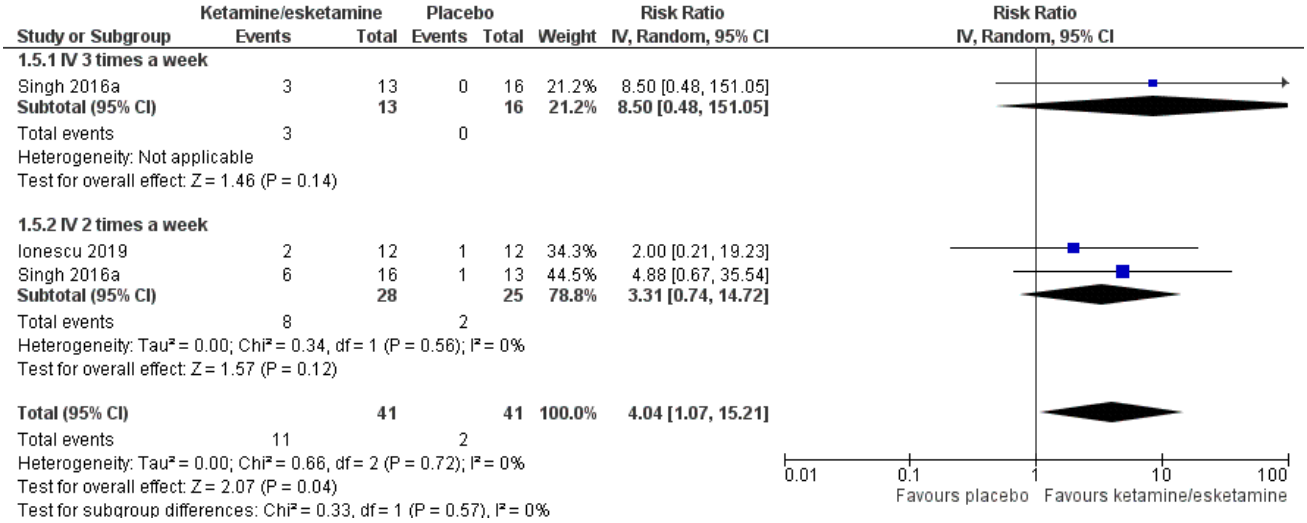
Forest plot of comparison: 13 IV Ketamin versus placebo, outcome: 13.3 Depressive symptoms, subacute phase.

Figure 4 (Analysis 1.4)



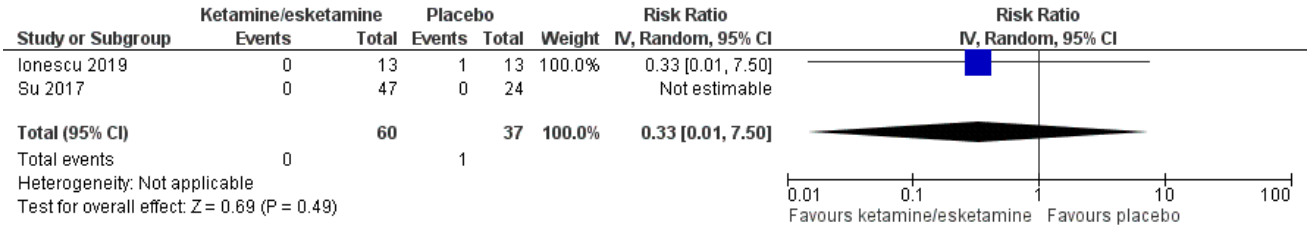
Forest plot of comparison: 13 IV Ketamin versus placebo, outcome: 13.4 Response, subacute phase.

Figure 5 (Analysis 1.5)



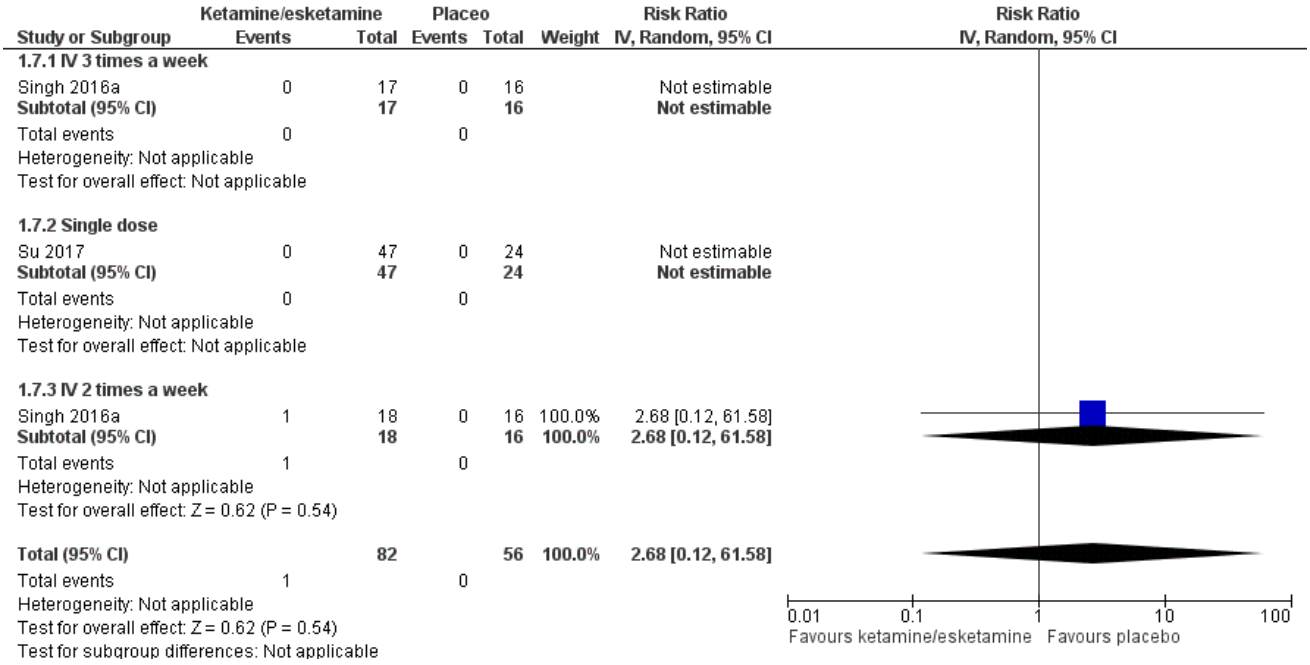
Forest plot of comparison: 13 IV Ketamin versus placebo, outcome: 13.5 Remission, subacute phase.

Figure 6 (Analysis 1.6)



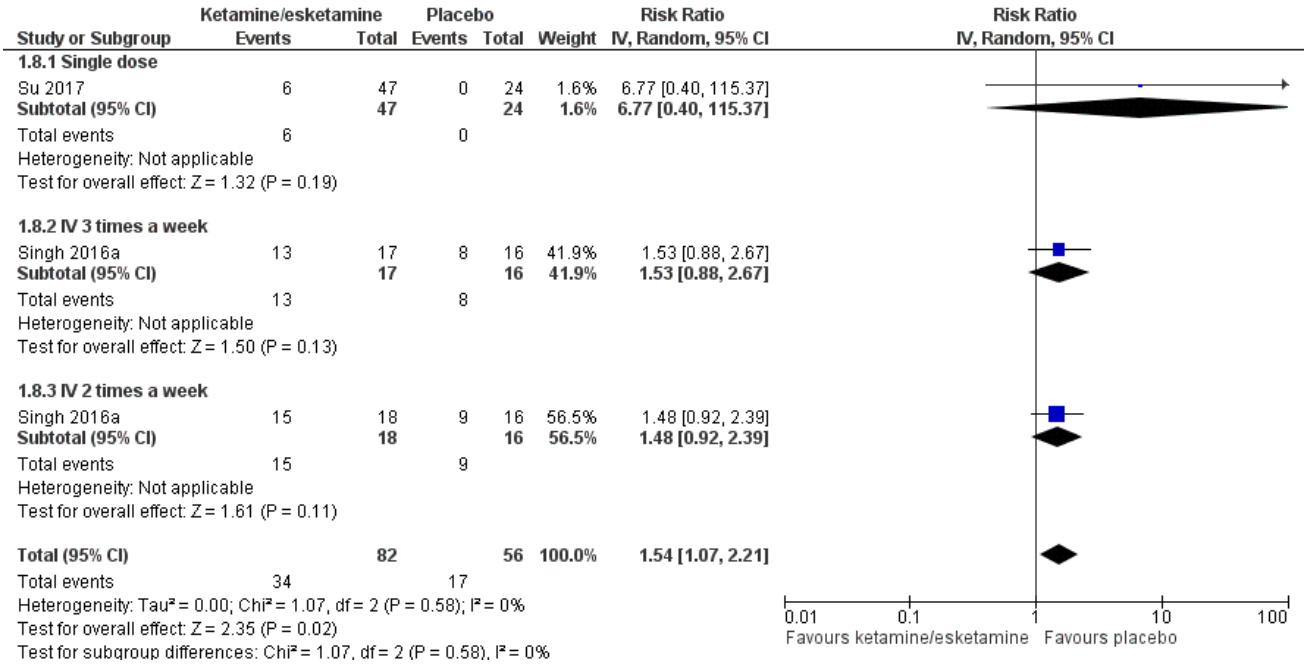
Forest plot of comparison: 13 IV Ketamin versus placebo, outcome: 13.6 Adverse events indlæggelse.

Figure 7 (Analysis 1.7)



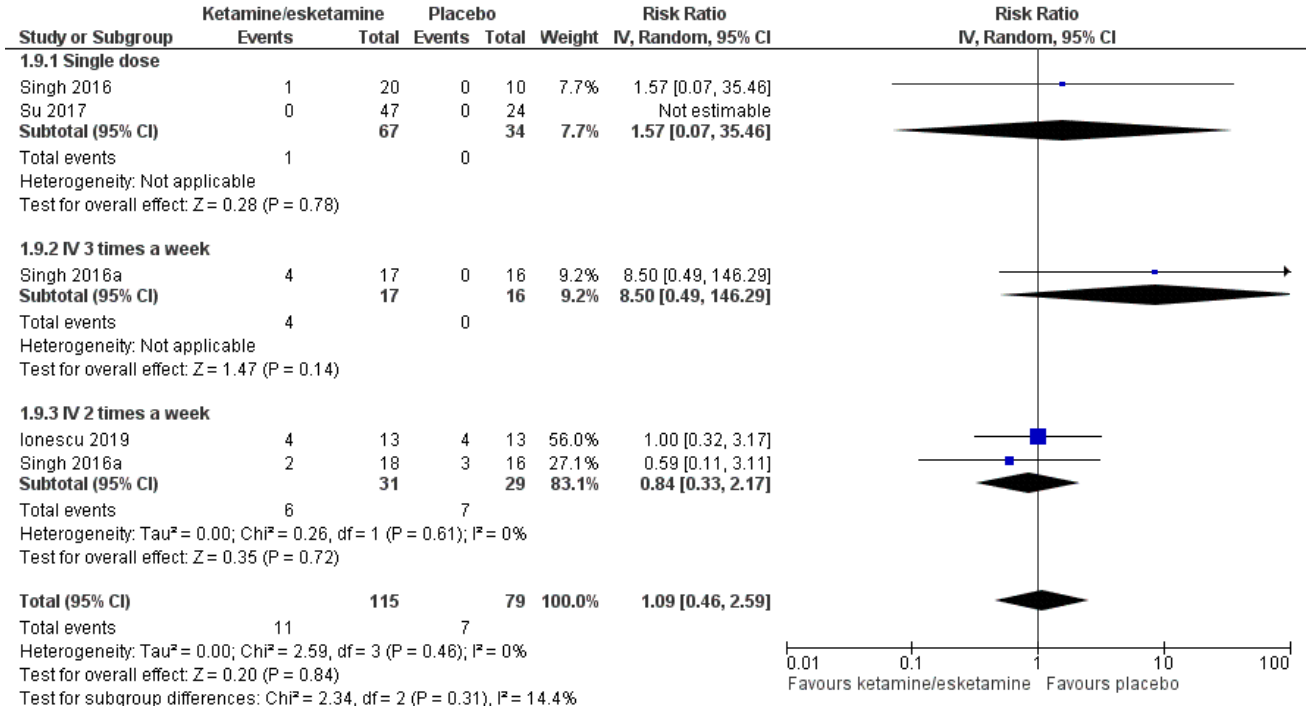
Forest plot of comparison: 13 IV Ketamin versus placebo, outcome: 13.7 Adverse event - selvmordsforsøg.

Figure 8 (Analysis 1.8)



Forest plot of comparison: 13 IV Ketamin versus placebo, outcome: 13.8 Øvrige bivirkninger.

Figure 9 (Analysis 1.9)



Forest plot of comparison: 13 IV Ketamin versus placebo, outcome: 13.9 Frafald.

Sources of support

Internal sources

- No sources of support provided

External sources

- No sources of support provided

Feedback

Appendices