Data supplement to Brunoni et al. Transcranial direct current stimulation for acute major depressive episodes: meta-analysis of individual patient data. Br J Psychiatry doi: 10.1192/bjp.bp.115.164715

Search strategy

1. MEDLINE (PubMed)

The following syntax was used, yielding 116 results:

((("depressive disorder" OR "treatment-resistant" OR "treatment resistant" OR "major depression")) AND ("direct current" OR "transcranial direct current stimulation" OR "tDCS”))), limited to 01/01/2015.

2. Embase

The following syntax was used, yielding 316 results:

'depressive disorder'/exp OR 'depressive disorder' OR 'treatment-resistant' OR 'treatment resistant' OR 'major depression'/exp OR 'major depression' AND ('direct current'/exp OR 'direct current' OR 'transcranial direct current stimulation'/exp OR 'transcranial direct current stimulation' OR 'tdcs') NOT [1-1-2015]/sd.

3. ISI - Web of Knowledge

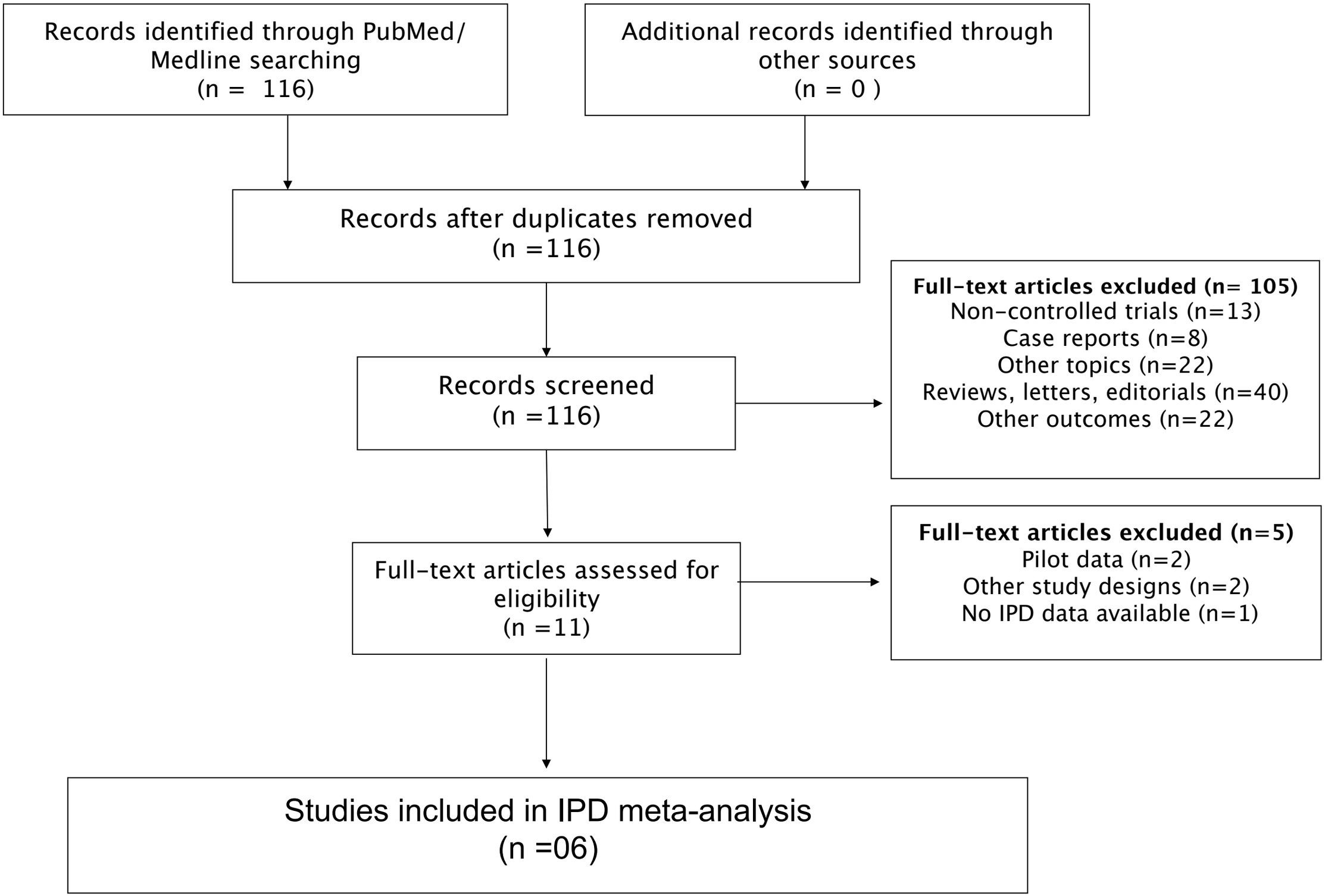
The following syntax was used, yielding 213 results:

TOPIC:(("depressive disorder" OR "treatment-resistant" OR "treatment resistant" OR "major depression") AND ("direct current" OR "transcranial direct current stimulation" OR "tDCS")) **Timespan:** 1864-2014.

4. Scopus

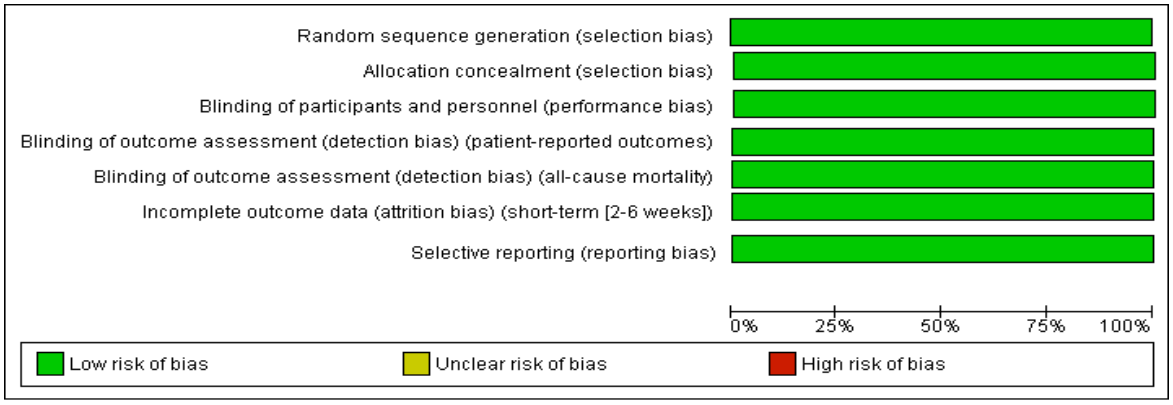
The following syntax was used, yielding 163 results:

TITLE-ABS-KEY ((**"depressive disorder"** OR **"treatment-resistant"** OR **"treatment resistant"** OR **"major depression"**) AND (**"direct current"** OR **"transcranial direct current stimulation"** OR **"tDCS"**)) AND PUBYEAR < **2015**


Records identified through PubMed/ Medline searching (n = 116)
Additional records identified through other sources (n = 0)
Records after duplicates removed (n =116)
Records screened (n =116)
Full-text articles excluded (n= 105)
Non-controlled trials (n=13)
Case reports (n=8)
Other topics (n=22)
Reviews, letters, editorials (n=40)
Other outcomes (n=22)
Full-text articles assessed for eligibility (n =11)
Full-text articles excluded (n=5)
Pilot data (n=2)
Other study designs (n=2)
No IPD data available (n=1)
Studies included in IPD meta-analysis (n =06)

QUALITY ASSESSMENT

A) Quality assessment based on the Cochrane Handbook for Systematic Reviews of Interventions.



1) Bias risk assessment in the study of Loo et al. (2010)

Entry	Judgment	Support for judgment
Random sequence generation (selection bias)	Low risk.	Quote: “Subjects were stratified by age and gender and then randomly assigned to active or sham treatment groups
Allocation concealment (selection bias)	Low risk	Comment: allocation concealment confirmed by the authors
Blinding of participants and personnel (performance bias)	Low risk.	Quote: “with (...) subjects blind to treatment group assignment.”; Quote: “The switching on and off of the current was programmed into the stimulator and did not require intervention by the operator. The machine was placed behind the subjects’ heads so that they were unable to see the readout on the front panel of the stimulator..” Personnel blinding confirmed by the authors
Blinding of outcome assessment (detection bias) (patient-reported outcomes)	Low risk.	Quote:" with (...) subjects blind to treatment group assignment."
Blinding of outcome assessment (detection bias) (Mortality)	Low risk.	Quote: "All ratings were conducted by a psychiatrist who was blinded to treatment condition..."
Incomplete outcome data addressed (attrition bias) (Short-term outcomes (2-6 weeks))	Low risk.	Quote: “Intention-to-treat last-observation carried-forward scores were used for the analyses" Comment: measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups.
Incomplete outcome data addressed (attrition bias) (Longer-term outcomes (>6 weeks))	N/A	Comment: work focused in the efficacy of tDCS during the acute phase of the major depressive episode

Selective reporting (reporting bias)	Low risk.	All clinical rating scales and cognitive tasks listed in Methods were reported.

2) Bias risk assessment in the study of Loo et al. (2012)

Entry	Judgment	Support for judgment
Random sequence generation (selection bias)	Low risk.	Quote: “participants were stratified by gender and age and randomly assigned by a computer-generated random sequence”
Allocation concealment (selection bias)	Low risk.	Quote: “The treatment assignment was indicated by a code on study treatment sheets, which were concealed from raters.”
Blinding of participants and personnel (performance bias)	Low risk	Quote: “ ...participants(...) masked to group allocation." Personnel blinding confirmed by the authors.
Blinding of outcome assessment (detection bias) (patient-reported outcomes)	Low risk.	Quote: “"...participants (...) masked to group allocation."
Blinding of outcome assessment (detection bias) (Mortality)	Low risk.	Quote: “"... raters masked to group allocation."
Incomplete outcome data addressed (attrition bias) (Short-term outcomes (2-6 weeks))	Low risk.	Quote:" Intention-to-treat last observation-carried-forward scores were used for the analyses". Comment: measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups.
Incomplete outcome data addressed (attrition bias) (Longer-term outcomes (>6 weeks))	N/A	Comment: work focused in the efficacy of tDCS during the acute phase of the major depressive episode
Selective reporting (reporting bias)	Low risk.	All clinical rating scales and cognitive tasks listed in Methods were reported.

3) Bias risk assessment in the study of Palm et al. (2012)

Entry	Judgment	Support for judgment
Random sequence generation (selection bias)	Low risk.	Quote: “patients were randomized in two groups.”
Allocation concealment (selection bias)	Low risk.	Quote: “...using a PC-generated random number list”. Concealment confirmed by the authors.
Blinding of participants and personnel (performance bias)	Low risk.	Quote: “double blind”; “Two indistinguishable CE-certified programmable constant current DC-Stimulator were used for active and placebo tDCS. ” Personnel blinding confirmed by authors

Blinding of outcome assessment (detection bias) (patient-reported outcomes)	Low risk.	Quote: “double blind”.
Blinding of outcome assessment (detection bias) (Mortality)	Low risk.	Quote: “rating scales and cognitive tests were administered by experienced raters blind to treatment conditions..."
Incomplete outcome data addressed (attrition bias) (Short-term outcomes (2-6 weeks))	Low risk.	Quote: “Twenty patients completed the study, two dropped out because of personal reasons. The data of all 22 subjects were included in the analysis (last observation carried forward)."
Incomplete outcome data addressed (attrition bias) (Longer-term outcomes (>6 weeks))	N/A	Comment: work focused in the efficacy of tDCS during the acute phase of the major depressive episode
Selective reporting (reporting bias)	Low risk.	All clinical rating scales and cognitive tasks listed in Methods were reported.

4) Bias risk assessment in the study of Blumberger et al. (2012)

Entry	**Judgment**	**Support for judgment**
Random sequence generation (selection bias)	Low risk.	Quote: “subjects were randomly assigned using a computer-generated randomization list”
Allocation concealment (selection bias)	Low risk.	Quote: “...with the information stored on a centralized computer .”
Blinding of participants and personnel (performance bias)	Low risk	Quote: “with (...) subjects blind to treatment group allocation.”; Quote: “Only the treating clinician was aware of subjects’ treatment condition."
Blinding of outcome assessment (detection bias) (patient-reported outcomes)	Low risk.	Quote: “with (...) subjects blind to treatment group allocation.”
Blinding of outcome assessment (detection bias) (Mortality)	Low risk.	Quote:"...with clinical raters (...) blind to treatment group allocation."
Incomplete outcome data addressed (attrition bias) (Short-term outcomes (2-6 weeks))	Low risk.	Quote: “analysis was conducted on an intention to treat basis." Comment: measures of key outcomes were obtained from more than 85% of the subjects initially allocated to groups
Incomplete outcome data addressed (attrition bias) (Longer-term outcomes (>6 weeks))	N/A	Comment: work focused in the efficacy of tDCS during the acute phase of the major depressive episode
Selective reporting (reporting bias)	Low risk	All clinical rating scales and cognitive tasks listed in Methods are reported.

5) Bias risk assessment in the study of Brunoni et al. (2013)

Entry	Judgment	Support for judgment
Random sequence generation (selection bias)	Low risk.	Quote: “A assistant not directly involved in other aspects of the trial performed a 1:1:1:1 permuted block randomization.”
Allocation concealment (selection bias)	Low risk.	Quote: “...the allocation was concealed using a central randomization method.”
Blinding of participants and personnel (performance bias)	Low risk.	Quote: “...patients were blinded to the treatment"; "..., because the nurses were not blinded to the intervention, their interaction with the participants was minimal"
Blinding of outcome assessment (detection bias) (patient-reported outcomes)	Low risk.	Quote: " The raters and patients were blinded to the treatment"
Blinding of outcome assessment (detection bias) (Mortality)	Low risk.	Quote: " The raters and patients were blinded to the treatment"
Incomplete outcome data addressed (attrition bias) (Short-term outcomes (2-6 weeks))	Low risk.	Quote: "Analyses were conducted in the intention-to-treat sample according to last observation carried forward through the time points. Missing data were considered to be at random" Comment: measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups.
Incomplete outcome data addressed (attrition bias) (Longer-term outcomes (>6 weeks))	N/A	Comment: work focused in the efficacy of tDCS during the acute phase of the major depressive episode
Selective reporting (reporting bias)	Low risk.	All clinical rating scales and cognitive tasks listed in Methods were reported.

6) Bias risk assessment in the study of Bennabi et al. (2014).

Entry	Judgment	Support for judgment
Random sequence generation (selection bias)	Low risk	Quote: “subjects were randomly assigned using a computer-generated randomization list”
Allocation concealment (selection bias)	Low risk	Quote: “...with the information stored on a centralized computer to receive either active or sham tDCS."
Blinding of participants and personnel (performance bias)	Low risk	Quote: “Predefined codes assigned to either real or sham stimulation were used to start the stimulator and thus allowed for a double-blind study design."
Blinding of outcome assessment (detection bias) (patient-reported outcomes)	Low risk	Quote: “double blind”.

Blinding of outcome assessment (detection bias) (Mortality)	Low risk	Quote: "A trained, licensed neuropsychologist blinded to the patients' treatment group conducted a complete neuropsychological test battery ..."
Incomplete outcome data addressed (attrition bias) (Short-term outcomes (2-6 weeks))	Low risk	Comment: measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups.
Incomplete outcome data addressed (attrition bias) (Longer-term outcomes (>6 weeks))	Low risk	Comment: work focused in the efficacy o tDCS during the acute phase of the major depressive episode
Selective reporting (reporting bias)	Low risk	All clinical rating scales and cognitive tasks listed in Methods were reported.

B) Quality assessment based on the PEDro Scale.

PEDro scale	Palm (2012)	Brunoni (2013)	Loo(2012)	Loo(2010)	Blumberger(2012)	Bennabi (2014)
1 (Eligibility)	Y	Y	Y	Y	Y	Y
2	Y	Y	Y	Y	Y	Y
3	Y	Y	Y	Y	Y	Y
4	Y	Y	Y	Y	Y	y
5	Y	Y	Y	Y	Y	Y
6	Y	Y	y	Y	Y	Y
7	Y	Y	Y	Y	Y	Y
8	Y	Y	Y	Y	Y	Y
9	Y	Y	Y	Y	Y	Y
10	Y	Y	Y	Y	Y	Y
11	Y	Y	Y	Y	Y	Y
PEDro total score	**10**	**10**	**10**	**10**	**10**	**10**

Palm et al. (2012)

A1 - p.243, ¶1, ln.1-6: "Twenty-two in- and outpatients of the Department of Psychiatry at the Ludwig-Maximilians University, Munich, Germany (14 female, mean age 57 years, range 36-79), having a major depressive episode (DSM-IV criteria; based on a clinical interview by an experienced psychiatrist) were recruited."

A2 - p.243, ¶2, ln. 1-4: "Within a placebo-controlled cross-over design, patients were randomized in two groups (active/sham; sham/active) by the principal investigator (F.P.) using a PC-generated random number list."

A3 – confirmed by authors

A4 - p.247, ¶2, ln. 3-5: "Both groups were comparable in terms of demographic measures, clinical characteristics, and cognitive performance at baseline."

A5 - p.242, ¶2, ln. 5-6: "Patients, raters, and operators were blinded to treatment conditions."

A6 - p.246, ¶1, ln. 4-5: "All operators, tDCS trained MD or PhD students, were blind to treatment conditions."

A7 - p.246, ¶2, ln. 1-3: "The (…) rating scales and cognitive tests were administered by experienced raters blind to treatment conditions."

A8 - p.247, ¶3, ln. 2-4: "The data of all 22 subjects were included in the analysis (last observation carried forward [LOCF])."

A9 - p.247, ¶3, ln. 2-4: "The data of all 22 subjects were included in the analysis (last observation carried forward [LOCF])."

A10 - p.247, ¶3, ln. 4-8: "In the Active/Sham group baseline HAMD scores decreased by 16% during active tDCS and by 8% during sham treatment. In the Sham/Active group HAMD scores decreased by 12% during sham tDCS and by 14% during active treatment."

A11 - p.247, Table 2.

Brunoni et al. (2013)

B1 - p.385, ¶1, ln. 1-6:" We included patients with unipolar, nonpsychotic MDD per *DSM-IV* criteria and confirmed by psychiatrists using the Mini-International Neuropsychiatric Interview. Only those with a 17-item Hamilton Depression Rating Scale score greater than 17, with low suicide risk, and aged between 18 and 65 years were included."

B2 - p.384, ¶5, ln. 14-16:" A research assistant not directly involved in other aspects of the trial performed a 1:1:1:1 permuted block randomization…"

B3 - p.384, ¶5, ln. 16-17:"… the allocation was concealed using a central randomization method."

B4 - p.386, ¶3, ln. 3-4:" The groups were similar in clinical and demographic characteristics at baseline."

B5 - p.385, ¶4, ln. 5-7:" The raters and patients were blinded to the treatment, and contact between participants was avoided to enhance study blinding."

B6- NO

B7 - p.385, ¶4, ln. 5-7:" The raters and patients were blinded to the treatment, and contact between participants was avoided to enhance study blinding."

B8 - p.386, ¶4, ln. 1-2:" Nine patients dropped out within the first 2weeks and 103 patients (85.8%) completed the entire trial."

B9 - p.385, ¶10, ln. 3-5:" Analyses were conducted in the intention-to-treat sample according to the last observation carried forward through the time points."

B10 - p.386, Table 1.

B11 - p.386, Table 1.

Loo et al. (2012)

C1 - p.53, ¶1, ln. 1-7: "Sixty-four participants with a DSM-IV major depressive episode and with a score of >=20 on the Montgomery–Asberg Depression Rating Scale (MADRS) gave informed written consent and were enrolled as out-patients. Diagnosis was based on a structured assessment using the Mini-International Neuropsychiatric
Interview (MINI) and confirmed in a clinical interview by a study psychiatrist."

C2 - p.53, ¶3, ln.1-3: "Participants were stratified by gender and age and randomly assigned by a computer-generated random sequence to active (n = 33) or sham (n = 31) treatment."

C3 - p.53, ¶3, ln. 6-8: "The treatment assignment was indicated by a code on study treatment sheets, which were concealed from raters.

C4 - p.54, ¶3, ln.1-2: "The only significant difference between the active and sham groups at baseline was higher CORE scores for the active group."

C5 - p.53, ¶3, ln. 9-10: "…with participants and raters masked to group allocation."

C6 – blinding confirmed by authors

C7 -p.53, ¶3, ln. 9-10: "…with participants and raters masked to group allocation."

C8 - p.55, Fig. 1

C9 - p.53, ¶7, ln.4-5: "Intention-to-treat last-observation-carried-forward scores were used for the analyses…"

C10 - p.55, Table 2

C11 - p.55, Table 2

Loo et al. (2010)

D1 - p.2, ¶3, ln. 1-9:" Forty subjects with unipolar DSM-IV major depressive episode of up to 3 yr duration and a score >=20 on the Montgomery–Asberg Depression Rating Scale (MADRS; Montgomery & Asberg, 1979) were enrolled as outpatients. The diagnosis was based on a structured assessment using the MINI (MINI International Neuropsychiatric Interview; Sheehan et al. 1997) and confirmed in a clinical interview by a study psychiatrist…"

D2 - p.2, ¶6, ln. 1-3:" Subjects were stratified by age and gender and then randomly assigned to active or sham treatment groups."

D3 - confirmed by authors

D4 - p.4, ¶4, ln. 1-2:" There were no significant differences between active and sham treatment groups at baseline…"

D5 – blinding of all patients confirmed by authors

D6 – blinding of all therapists confirmed by authors

D7 -p.3, ¶1, ln. 4-6:" All ratings were conducted by a psychiatrist who was blinded to treatment condition…"

D8 - p.3, Fig.1

D9 - p.4, ln. 2-3:" Intention-to-treat last-observation-carried-forward scores were used for the analyses…"

D10 - p.6, Table 2

D11 - p.6, Table 2

Blumberger et al. (2012)

E1 - p.2, ¶5, ln. 5-13:" All subjects had a diagnosis of unipolar Major Depressive Disorder without psychotic features and were experiencing a Major Depressive Episode, as confirmed by the Structured Clinical Interview for the DSM-IV(SCID-IV). Subjects were required to have a score of >=21 on the 17-item Hamilton Rating Scale for Depression (HRSD-17).Subjects were required to meet stage II criteria on the Thase Scale for treatment- resistance (failure to achieve remission or inability to tolerate two trials of an antidepressant from separate classes;"

E2 - p.3, ¶1, ln. 1-4:"… subjects were randomly assigned using a computer-generated randomization list with the information stored on a centralized computer to receive either active or sham tDCS."

E3 – confirmed by authors.

E4 - p.3, ¶8, ln. 1-3:" The subjects' baseline clinical and demographic characteristics are summarized in Table1. There were no clinically important differences between groups."

E5 - p.3, ¶1, ln. 7-8:" … with clinical raters and subjects blind to treatment group allocation."

E6 – blinding confirmed by authors.

E7 -p.3, ¶1, ln. 7-8:" … with clinical raters and subjects blind to treatment group allocation."

E8 - p.4, Fig. 1

E9 - p.3, ¶6, ln. 1-2:" … and the analysis was conducted on an intention to treat basis."

E10 - p.5, Table 2

E11 - p.5, Table 2

Bennabi et al. (2014)

F1-p.2, ¶3, ln. 1-8:" Twenty-four patients (18 females, 6 males, mean 61.8 ± 16.3 years) meeting Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria for unipolar depression were recruited from the psychiatric wards of the university hospital of Besançon (France). Patients were required to have a score P25 on the Montgomery

Asberg Depression Rating Scale (MADRS) (Montgomery and Asberg, 1979) and to meat at least stage II treatment resistant criteria (Montgomery and Asberg 1979; Rush et al., 2003)."

F2- p.2, ¶4, ln. 4-7:" Following completion of baseline clinical measures, subjects were randomly assigned using a computer-generated randomization list with the information stored on a centralized computer to receive either active or sham tDCS."

F3- concealment confirmed by authors

F4- p.3, ¶3, ln. 3-11:" Demographic characteristics did not differ across the treatment groups for age ($t21 = 0.09$, $p = 0.93$), gender ($z = 1.33$, $p = 0.09$) or educational level ($t21 = 1.72$, $p = 0.18$). Statistical analyzes revealed no difference at baseline between active and sham stimulations groups in depression severity (HDRS: $t21 = 0.66$, $p = 0.51$; MADRS: $t21 = 1.72$, $p = 0.1$; BDI: $t21 = 0.25$, $p = 0.8$), anxiety level (STAI-A: $t21 = 0.78$, $p = 0.44$: STAI-B: $t21 = 0.25$, $p = 0.81$), psychomotor retardation (SRRS: $t21 = 0.49$, $p = 0.63$) and all cognitive performances (Table 2: $ps > 0.05$)."

F5- p.2, ¶5, ln. 11-13:" Predefined codes assigned to either real or sham stimulation were used to start the stimulator and thus allowed for a double-blind study design."

F6- p.2, ¶5, ln. 11-13:" Predefined codes assigned to either real or sham stimulation were used to start the stimulator and thus allowed for a double-blind study design."

F7- blinding of all assessor confirmed by authors

F8- p.3, ¶3, ln. 12-13:" One patient experienced mania and was subsequently withdrawn from the trial."

F9- confirmed by authors

F10- p.3, ¶2, ln. 1-7:" Concerning our primary outcome (HDRS 21) the mixed model revealed no significant differences between the two groups ($F(2,28) = 0.37$, $p = 0.69$) (Fig. 1a). The score decreased from 40% and 45.6% in active and sham groups respectively. ANCOVA showed no

significant effect of the main factor ‘time’ in both rating scales at T2 (HDRS p = 0.17; MADRS: p = 0.35), T3 (HDRS p = 0.08; MADRS: p = 0.18) or T4 (HDRS p = 0.80; MADRS: p = 0.85).”

F11- p.3, Fig.1.

PREDICTOR VARIABLES

a) *Demographic variables*: gender (binary) and age (years, continuous);

b) *Depression characteristics*: age of onset (years, continuous); bipolar depression (binary); melancholic depression (binary); atypical depression (binary) and presence of any concomitant anxiety disorder (binary). Treatment-resistant depression (<2 vs. ≥2 adequate failed antidepressant trials); recurrent depression (≤5 vs. >5 previous depressive episodes); chronic depression (≤2 vs. >2 years of length of the current depressive episode) and severe depression (MADRS ≤30 vs. >30 or HDRS ≤24 vs. >24 according to the study primary outcome measure) were also handled as binary.

c) *Treatment of the current depressive episode,* in which the binary variables employed were: ECT (electroconvulsive therapy) and rTMS (repetitive transcranial magnetic stimulation) use in the present episode; and concomitant psychotherapy, SSRI (selective serotonin reuptake inhibitor), TCA (tricyclic antidepressant), SNRI (serotonin-noradrenaline reuptake inhibitor), anticonvulsant drug, lithium, antipsychotic and benzodiazepine use. In addition, simultaneous augmentation with sertraline was included as a predictor variable, considering the factorial design of Brunoni et al. (13).

d) *tDCS treatment:* cathode position (F4 vs. right supraorbital area); session duration (binary, 20 vs. 30 min); current dose (binary, 1 vs. 2mA); number of completed sessions (continuous); number of weeks of stimulation (1, 2 or 3 weeks) and the interaction of this variable with frequency of the sessions (every other day; once a day or twice a day); total charge (in Coulombs, C) and total charge density (in C/m^2)[1]. For

[1] Total Charge (C) = Dose (A) * session duration (sec) * number of sessions; Total Charge Density (C/m^2) = Total Charge / electrode size (m^2)

these two last variables, as they were not normally distributed, they were arranged in three groups according to its percentile distribution. Moreover, only Brunoni et al. used 25 cm^2 (vs. 35 cm^2) electrodes, which lead to "total charge" and "total charge density" stratifying into the same subjects. Therefore, we considered "total charge" and "total charge density" representing a "tDCS dose", further classifying this variable into three levels: (i) <36C or <10285 C/m^2; (ii) 36C or 10285 – 14400 C/m^2 and; (iii) 43.2C or 17280 C/m^2.

Supplementary Table – Univariate analyses of predictors of remission and depression improvement (difference in z-scores) to tDCS.

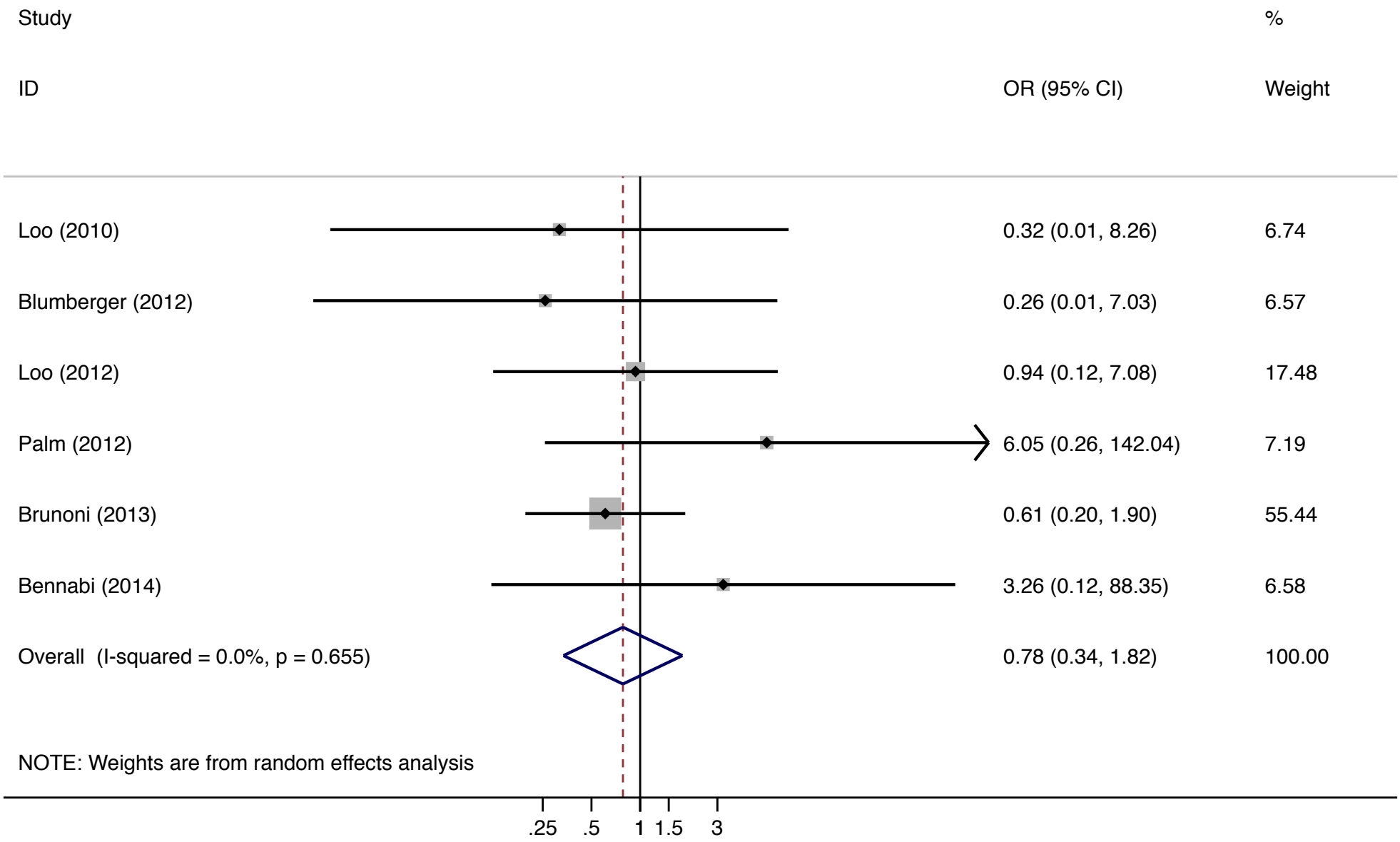
		Remission		Difference in z-scores	
Predictor	Comparison	OR	*p*	β (SE)	*p*
Clinical and demographic variables					
Gender (binary)	Fem vs. Male	0.5 (0.18-1.35)	0.17	-0.34 (0.16)	0.03
Age (continuous)	Continuous	0.99 (0.96-1.02)	0.51	<0.01 (<0.01)	0.91
Age of onset	Continuous	1 (0.96-1.03)	0.96	<0.01 (<0.01)	0.37
Bipolar disorder	No vs. Yes	--	--	0.98 (0.36)	<0.01
Melancholic	No vs. Yes	0.43 (0.17-1.05)	0.06	-0.17 (0.16)	0.29
TRD	<2 v ≥2 trials	0.4 (0.15-1.11)	0.08	-0.42 (0.17)	0.02
MDE duration	<2 v ≥ 2 y	0.28 (0.06 - 1.35)	0.11	-0.33 (0.2)	0.11
Anxiety Disorder	No vs. Yes	0.89 (0.36 - 2.1)	0.78	0.21 (0.16)	0.2
Severe depression	No vs. Yes	1 (0.43 - 2.37)	0.98	0.52 (0.15)	<0.001
ECT use	No vs. Yes	--	--	0.39 (0.36)	0.28
rTMS use	No vs. Yes	--	--	-0.75 (0.56)	0.17
Therapies					
TCA use	No vs. Yes	--	--	-0.16 (0.34)	0.96
SSRI use	No vs. Yes	1.3 (0.23 - 6.8)	0.78	0.4 (0.27)	0.13
SNRI use	No vs. Yes	2.05 (0.38 - 10.9)	0.4	0.15 (0.23)	0.52
AD use	No vs. Yes	1.56 (0.3 - 8.1)	0.59	0.4 (0.22)	0.06
ACV use	No vs. Yes	--	--	0.42 (0.5)	0.41
AP use	No vs. Yes	1.37 (0.19 - 9.7)	0.75	0.33 (0.28)	0.22
BZD use	No vs. Yes	0.6 (0.2 - 2.1)	0.47	-0.24 (0.25)	0.33
Lithium use	No vs. Yes	--	--	0.07 (0.42)	0.86
Sertraline augmentation	No vs. Yes	1.16 (0.41 - 3.3)	0.78	0.46 (0.23)	0.04
Drug free	No vs. Yes	1.33 (0.45 - 3.9)	0.6	-0.32 (0.2)	0.11
TDCS characteristics					
Cathode Position	RSO vs. F3	1.17 (0.1 - 13.6)	0.89	0.28 (0.28)	0.32
Session duration	20m vs. 30m	7.8 (1.2 - 51.5)	0.03	0.11 (0.27)	0.67
Current dose	1mA vs. 2mA	0.96 (0.09 - 10.4)	0.98	0.05 (0.55)	0.93
Number of weeks of stimulation	1 week	Ref			Ref
	2 weeks	0.75 (0.6 - 9.6)	0.83	0.28 (0.28)	0.32
	3 weeks	0.05 (0.01 - 1.31)	0.08	0.16 (0.36)	0.64
N of Sessions	Continuous (5 to 15)	1.05 (0.83 - 1.33)	0.64	0.21 (0.05)	<0.001
TDCS dose	Low	Ref		Ref	
	Medium	0.46 (0.1 - 1.83)	0.27	1.03 (0.46)	0.02
	High	5.5 (1.8 - 16.4)	<0.001	1.7 (0.43)	<0.001

OR, odds ratio; CI, confidence interval; SE, standard error; TRD, treatment-resistant depression; MDE, major depressive episode; ECT, electroconvulsive therapy; rTMS, repetitive transcranial magnetic stimulation; TCA, tricyclic antidepressants; SSRI, selective serotonin reuptake inhibitors; SNRI, serotonin-noradrenaline reuptake inhibitors; AD, antidepressant; tDCS, transcranial direct current stimulation; Ref, reference. Number of sessions and number of weeks of stimulation are different variables because there were studies performing tDCS sessions once daily, twice daily or in alternated days. Please refer to the main text for details.

Supplementary Table – Multivariate analyses of predictors of depression improvement to tDCS.

Variable	Difference in z-scores		
	β	SE	p
Model 1. Bipolar disorder, TRD, severe depression, sertraline augmentation and number of sessions.			
Bipolar Disorder	0.77	0.3	0.01
TRD	-0.51	0.14	<0.001
Severe Depression	0.55	0.13	<0.001
Sertraline augmentation	0.45	0.19	0.03
N of sessions	0.21	0.04	<0.001
Wald = 88.1 (p<0.001)			
Model 2. Bipolar disorder, TRD, severe depression, sertraline augmentation and tDCS dose.			
Bipolar Disorder	0.81	0.3	0.02
TRD	-0.48	0.14	0.001
Severe Depression	0.51	0.13	0.02
Sertraline augmentation	0.48	0.19	0.01
TDCS "dose"	0.78	0.18	<0.001
Wald = 85.9 (p<0.001)			

TRD, treatment-resistant depression.


Study
ID
OR (95% CI)
%
Weight
Loo (2010)
0.32 (0.01, 8.26)
6.74
Blumberger (2012)
0.26 (0.01, 7.03)
6.57
Loo (2012)
0.94 (0.12, 7.08)
17.48
Palm (2012)
6.05 (0.26, 142.04)
7.19
Brunoni (2013)
0.61 (0.20, 1.90)
55.44
Bennabi (2014)
3.26 (0.12, 88.35)
6.58
Overall (I-squared = 0.0%, p = 0.655)
0.78 (0.34, 1.82)
100.00
NOTE: Weights are from random effects analysis
.25
.5
1
1.5
3

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	N/A
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	4
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	4/5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5/6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	5
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	7/8

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	7
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	9/10
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Fig1
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10/11
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	11
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	11/12
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	12/15
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	16/17
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	18
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	N/A

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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