Supplemental Online Materials

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This supplemental material has been provided by the authors to give readers additional information about their work.

Supplementary Methods. Specifications for transformation methods used for depressive symptom severity scores.

Depression symptom-level scores were transformed to the 17-item Hamilton Depression Rating Scale (HDRS-17) to (1) determine baseline depressive symptomatology in individual trials; (2) assess any potential moderating effects thereof; and (3) allow comparison of lower boundary inclusion criteria in primary studies. Beck Depression Inventory (BDI), Beck Depression Inventory II (BDI-II), Montgomery-Åsberg Depression Rating Scale (MADRS), Hamilton Depression Rating Scale 24 (HDRS-24) and the Patient Health Questionnaire-9 (PHQ-9) total scores were transformed as follows:[1–4]

BDI/BDI-II → HDRS-17:

Conversion tables, source and/or formulae to transform the BDI and BDI-II to HDRS-17 were used from Furukawa et al. (2020).[5]

MADRS → HDRS-17:

Conversion tables, source and/or formulae to transform the MADRS to HDRS-17 were used from Leucht et al. (2018).[6]

HDRS-24 → HDRS-17:

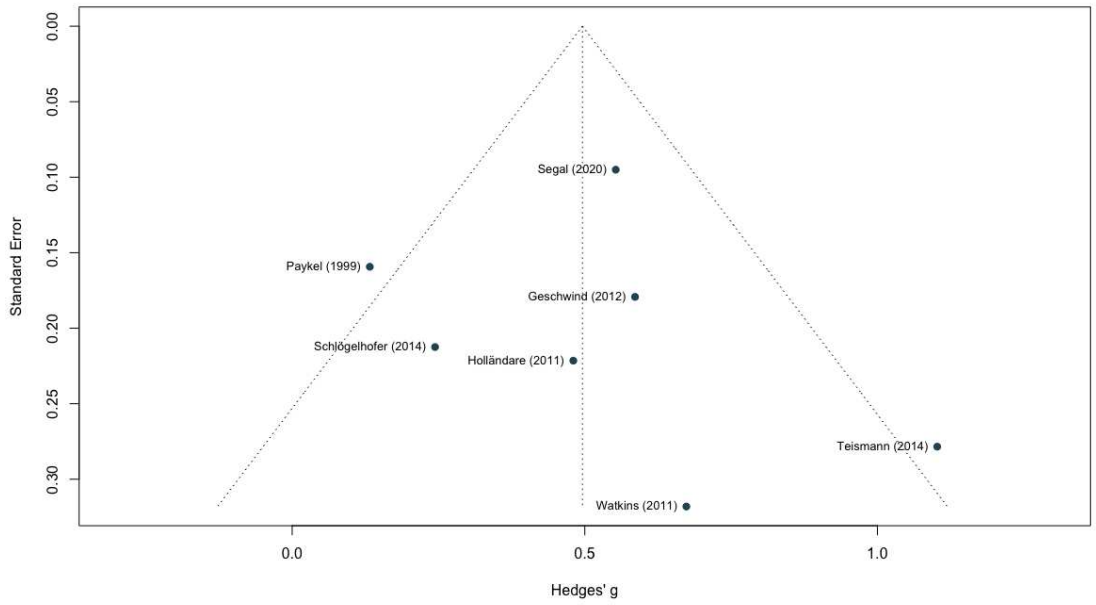
The HDRS-24 was transformed to the HDRS-17 using conversion tables provided online,[3] derived from Rush et al. (2003).[7]

PHQ-9 → HDRS-17:

Conversion tables, sources and/or formulae to transform the PHQ-9 to HDRS-17 were used from Hawley et al. (2020)[4] and Furukawa et al. (2020).[5]

Supplementary Figure 1.

Funnel plot to examine potential small-study effects bias of depressive symptom severity at post-treatment.



Supplementary Figure 2.

Risk-of-Bias assessment per domain for individual studies.

Note. The individual risk-of-bias domains of the RoB2 tool are: D1 = bias arising from the randomization process; D2 = bias due to deviations from intended interventions; D3 = bias due to missing outcome data; D4 = bias in measurement of the outcome; D5 = bias in selection of the reported result.

Supplementary Table 1. Overview of definitions of events in included trials.

Author (Year)	Definition for 'remission'	Definition for 'relapse'
Paykel (1999)[8]	Symptom levels ≤8 on the HDRS and ≤9 on the BDI at 2 successive ratings 4 wk apart.	Met DSM-III-R criteria for MDD for a minimum of 1 mo (2 wk longer than DSM-III-R criteria require). Further, at 2 successive face-to-face assessments at least 1 wk apart meet severity criteria for MDD and score ≥17 on HDRS-17. *Follow-up*: residual symptoms persisted between 2 successive ratings 2 mo apart, reaching ≥13 on HDRS-17 on both occasions and a level of distress or dysfunction for which withholding of additional active treatment was no longer justified.
Holländare (2011)[9]	Score of ≤6 on MADRS-S.	Fulfilling the DSM-IV diagnostic criteria for MDD, based on the SCID-I.
Watkins (2011)[10]	HDRS-17 <8 and BDI-II <9 at termination	Meeting DSM-IV criteria for a new episode of major depression at any point between T1 and T2, based on SCID.
Geschwind (2012)[11]	n/a	n/a
Schlögelhofer (2014)[12]	BDI ≤10 and HDRS-17 ≤7	n/a
Teismann (2014)[13]	BDI-II ≤8.	Reappearance of the clinical syndrome of a MDE for at least 2 wk during year after posttreatment assessment, based on SCID.
Segal (2020)[14]	PHQ-9 <5	PHQ-9 score ≥15

Abbreviations. BDI = Beck Depression Inventory; BDI-II = Beck Depression Inventory - II; HDRS-17 = 17 item Hamilton Depression Rating Scale; MADRS-S = Montgomery Åsberg Depression Rating Scale – Self-rated; MDD = major depressive disorder; MDE = major depressive episode; n/a = not applicable; PHQ-9 = Patient Health Questionnaire-9; SCID = Structured Clinical Interview for the DSM.

Supplementary Table 2. Overview and results of included pharmacotherapy studies.

			Treatment Group		Control Group		
Author (Year)	**Definition Partial Remission of MDD**	**Design**	**Sample (n)**	**Treatment received**	**Sample (n)**	**Treatment received**	**Results**
Kennedy (2003)[15]	Showing partial response (HDRS-17 score 8-15) to 8-14 wk of open-label ADM; initially met DSM-IV criteria for MDE (SCID)	Single-bind RCT comparing two active treatment options	21	*LA*: Lithium carbonate augmentation for 8 wk, while ADM was continued. 600 mg/day was prescribed as a single nighttime dose. Clinicians were permitted to increase lithium dosing by 300 mg/day after 2-4 wk based on clinical response, tolerability, and serum levels. Subjects were seen every 2 wk for routine CM.	23	*CT*: Cognitive therapy for 12 sessions over 8 wk, while ADM was continued. Emphasized acquisition and implementation of a number of core cognitive and behavioral skills. Medication check-up every 4 wk.	Significantly lower symptom severity at 4-week follow-up in LA-treated compared to CT-treated patients (d = 0.32), although neither LA- nor CT-augmentation significantly decreased symptom severity immediately post-treatment. About one-third achieved full remission, although group differences were not significant.
Morgan (2005)[16]	MDD in partial remission (SCID); residual symptoms of 8-14 on HDRS-17; taking ADM for ≥8 wk	Double-blind, placebo controlled RCT (while initially designed as crossover trial)	11	*Estrogen*: Conjugated estrogen (0.625 mg/day) for 6 wk. Participants returned at 2 wk intervals for a new supply of study medication. Participants continued on ADM, prescribed by their primary treating physician.	6	*Placebo*: Matching placebo for 6 wk. Participants returned at 2 wk intervals for new supply of study medication. Participants continued on ADM, prescribed by their primary treating physician.	Women receiving short-term and low-dosage estrogen augmentation showed a significant larger decrease in depressive symptom severity compared to those receiving placebo augmentation (d = 1.48)
Ionescu (2016)[17]	MDD in partial remission (SCID); ≥8 on HDRS-17 (indicating partial response); current treatment with ADM at a stable dose (≥4 wk) and duration (≥3 mo)	Double-blind, placebo controlled, crossover RCT	5	*Iloperidone/placebo order*: Iloperidone of 1–8 mg, orally, once nightly for first 4 wk, followed by one washout wk of single (patient)-blinded placebo and then a further 4 wk of placebo. Dosing regimen was fixed and allowed gradual titration.	8	*Placebo/iloperidone order*: Received placebo for the first 4 wk, followed by one washout week of single-blinded placebo and then iloperidone of 1–8 mg, orally, once nightly for a further 4 wk. Dosing regimen was fixed and allowed gradual titration.	No superior effects on residual depression compared to placebo. Iloperidone did not lead to significant changes compared with placebo over entire study period.

Abbreviations. ADM = antidepressant medication; CM = clinical management; CT = cognitive therapy; DSM = Diagnostic and Statistical Manual of Mental Disorders; HDRS-17 = 17 item Hamilton Depression Rating Scale; LA = lithium augmentation; MDE = major depressive episode; RCT = randomized controlled trial; SCID = Structured Clinical Interview for the DSM; SSRI = selective serotonin reuptake inhibitors; SNRI = serotonin–norepinephrine reuptake inhibitor; wk = weeks.

Supplementary Table 3. GRADE summary of findings table for interventions targeting partial remitted MDD.

		Certainty assessment					No of patients		Effect			
No of studies	**Study design**	**Risk of Bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Treatment Group**	**Control Group**	**Relative (95% CI)**	**Absolute (95% CI)**	**Certainty**	**Importance**
Depressive symptomatology post-treatment.												
7	RCT	serious	not serious	not serious	serious	none	517	507	n/a	Hedge's g 0.50 (0.23-0.76)	⨁⨁◯◯ Low	Crucial
Depressive symptomatology 1-12 months follow-up.												
3	RCT	serious	not serious	not serious	serious	none	352	350	n/a	Hedges' g 0.36 (-0.30 –1.02)	⨁⨁◯◯ Low	Crucial
Depressive symptomatology ≧12 months follow-up.												
3	RCT	serious	not serious	not serious	serious	none	352	350	n/a	Hedges' g 0.02 (-0.09–0.12)	⨁⨁◯◯ Low	Crucial
Relapse rate post-treatment.												
3	RCT	serious	not serious	not serious	extremely serious	none	143	141	OR 0.17 (0.01–4.83)	0 fewer per 1.000 (from 5 to 0 fewer)	⨁◯◯◯ Very low	Crucial
Relapse rate ≧6 months follow-up.												
3	RCT	serious	not serious	not serious	serious	none	352	350	OR 0.46 (0.21–1.03)	0 fewer per 1.000 (from 1 to 0 fewer)	⨁⨁◯◯ Low	Crucial
Remission rate post-treatment.												
5	RCT	serious	not serious	not serious	very serious	none	404	400	OR 2.57 (1.71–3.87)	3 more per 1.000 (from 4 to 2 fewer)	⨁◯◯◯ Very low	Important
Remission rate ≧6 months follow-up.												
3	RCT	serious	not serious	not serious	serious	None	352	350	OR 1.75 (1.21–2.53)	2 more per 1.000 (from 3 to 1 fewer)	⨁⨁◯◯ Low	Important

Abbreviations. OR = Odds Ratio; RCT = Randomized Controlled Trial

Supplementary Appendix 1. PRISMA checklist

Section and Topic	Item #	Checklist item	Location in manuscript where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	pp. 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	pp. 2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	pp. 4-5
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	pp. 4-5
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	pp. 5-6
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	pp. 5
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	pp. 5-6 Supplement
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	pp. 5-6 Supplement
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	pp. 6
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	pp. 5-7
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	pp. 6
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	pp. 7
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	pp. 7
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	pp. 7
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	pp. 7
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	pp. 7
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	pp. 7
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	pp. 7
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	pp. 7-8
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	pp. 7-8
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	pp. 7

Section and Topic	Item #	Checklist item	Location in manuscript where item is reported
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	pp. 8 Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	pp. 8 Supplement
Study characteristics	17	Cite each included study and present its characteristics.	Table 1 pp. 8
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	pp. 12-13 Figure 3 eFigure 2
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	pp. 11-12 Figure 2 Table 2+3
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	pp. 12-13 Figure 1+3 eFigure 2
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	pp. 12-13 Figure 2 Table 2-3
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	pp. 11-12
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	pp. 11-12
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	pp. 12 Figure 3 eFigure 3
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	pp. 13
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	pp. 13-16
	23b	Discuss any limitations of the evidence included in the review.	pp. 13-16
	23c	Discuss any limitations of the review processes used.	pp. 15-16
	23d	Discuss implications of the results for practice, policy, and future research.	pp. 13-16
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	pp. 5
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	pp. 5
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	pp. 17
Competing interests	26	Declare any competing interests of review authors.	pp. 17
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	N/A

Supplementary Appendix 2. Complete search string and terms, per database searched.

Databases	Results 07-02-2022	Results 27-02-2022	Total
Embase (OvidSP)	4030	388	4418
APA PsycInfo (OvidSP)	644	87	731
MEDLINE (OvidSP)	838	58	896
SCOPUS	1445	125	1570
Total records (with duplicates)	6957	658	7615
Total records (duplicates removed)	**4934**	**512**	**5446**

EMBASE (THROUGH OVIDSP)

Concept #1: Depression

adolescent depression/ OR chronic depression/ OR depression/ OR late life depression/ OR long term depression/ OR major affective disorder/ OR major depression/ OR mood disorder/ OR recurrent brief depression/ OR treatment resistant depression/ OR (affective disorder* OR depress* OR dysthymi*).ti,ab,kw.

Results 07-02-2022: 896 015

Concept #2: Partial/remission

remission/ OR (partial remission OR partial remitted OR residual symptom* OR subclinical* OR (partial* ADJ3 remiss*) OR (partial* ADJ3 recov*) OR (partial* ADJ3 remit*) OR (residual* ADJ3 symptom*) OR (persis* ADJ3 symptom*)).ti,ab,kw.

Results 07-02-2022: 366 689

Concept #3: Intervention

cognitive remediation therapy/ OR cognitive rehabilitation/ OR neurorehabilitation/ OR psychotherapy/ OR schema therapy/ OR group therapy/ OR cognitive therapy/ OR behavior therapy/ OR interpersonal psychotherapy/ OR secondary prevention/ OR mental health service/ OR psychiatric treatment/ OR psychopharmacology/ OR psychotropic agent/ OR neurotransmitter uptake inhibitor/ OR monoamine oxidase inhibitor/ OR benzodiazepine derivative/ OR dibenzazepine derivative/ OR amoxapine/ OR amitriptyline/ OR amfebutamone/ OR buspirone/ OR citalopram/ OR chlormezanone/ OR clomipramine/ OR clorgyline/ OR desipramine/ OR desvenlafaxine/ OR dosulepin/ OR doxepin/ OR fluoxetine/ OR flunitrazepam/ OR fluvoxamine/ OR iprindole/ OR iproniazid/ OR isocarboxazid/ OR maprotiline/ OR meprobamate/ OR moclobemide/ OR nialamide/ OR nomifensine/ OR norfenfluramine/ OR nortriptyline/ OR pargyline/ OR paroxetine/ OR phenelzine/ OR rolipram/ OR selegiline/ OR sertraline/ OR tranylcypromine/ OR trazodone/ OR tryptophan/ OR venlafaxine/ OR viloxazine/ OR vilazodone/ OR protriptyline/ OR repetitive transcranial magnetic stimulation/ OR transcranial magnetic stimulation/ OR electroconvulsive therapy/ OR brain depth stimulation/ OR (transcranial magnetic stimulation OR repetitive transcranial magnetic stimulation OR rTMS OR electroconvulsive therapy OR ECT OR brain depth stimulation OR deep brain stimulation OR DBS OR relapse prevention OR cognitive training OR cognitive remediation OR cognitive rehabilitation OR cognitive stimulation OR cognitive revalidation OR neurocognitive training OR neurocognitive remediation OR neurocognitive rehabilitation OR neurocognitive stimulation OR neurocognitive revalidation OR neurocognitive intervention OR memory training OR memory remediation OR memory rehabilitation OR memory stimulation OR memory

intervention OR attention training OR attention remediation OR attention rehabilitation OR attention stimulation OR attention intervention OR cognitive control training OR cognitive control interventions OR cognitive control intervention OR brain training OR neurorehabilitation OR neuropsychological training OR neuropsychological remediation OR neuropsychological rehabilitation OR neuropsychological stimulation OR neuropsychological revalidation OR neuropsychological intervention OR treatment OR treatments OR therapy OR therapies OR therapeutic OR supportive psychotherapy OR supportive therapy OR supportive intervention OR intervention OR psychotherapy OR cbt OR cognitive therapy OR cognitive restructuring OR activation OR exposure OR acceptance commitment OR act OR behavioural OR behavioral OR meditation OR mindfulness OR mbct OR mbt OR eye movement desensitization reprocessing OR emdr OR schema-focused OR schema focused OR sft OR interpersonal OR ipt OR psychodynamic OR parent intervention OR family therapy OR family intervention OR alternative medicine OR meditation OR drug therapy OR drug therapies OR pharmaco* OR medication* OR psychotropic* OR antidepress* OR agomelatine OR alaproclate OR alprazolam OR amfebutamone OR amoxapine OR amitriptylin* OR benzodiazepin* OR brofaromine OR bromazepam OR bupropion OR buspiron* OR citalopram OR chlorimipramin* OR chlormezanone OR clomipramin* OR clorazepate OR clorgyline OR depreny OR desipramin* OR desvenlafaxine OR diazepam OR dibenzazepin* OR dopamine reuptake OR dopamine uptake OR dosulepin OR dothiepin OR doxepin OR duloxetine OR escitalopram OR femoxetine OR fluoxetine OR flunitrazepam OR fluvoxamine OR imipramin* OR iprindole OR iproniazid* OR ipsapirone OR isocarboxazid* OR levomilnacipran OR lofepramin* OR lorazepam OR loprazolam OR mao OR maprotiline OR medazepam OR meprobamate OR mianserin OR milnacipran OR minaprine OR mirtazapine OR moclobemide OR monoamine oxidase inhibitor* OR nefazodone OR nialamide OR nitrazepam OR nomifensine OR nordazepam OR norepinephrine reuptake OR norepinephrine uptake OR noradrenaline reuptake OR noradrenaline uptake OR norfenfluramine OR nortriptylin* OR opipramol OR oxazepam OR paroxetine OR pertofrane OR phenelzine OR pheniprazine OR pirlindole OR pizotyline OR prazepam OR reboxetine OR rolipram OR selegiline OR serotonin reuptake OR serotonin uptake OR sertraline OR snri* OR ssri* OR tetracyclic* OR tianeptin* OR tranylcypromin* OR trazodone OR tricyclic* OR trimipramine OR tryptophan OR venlafaxine OR viloxazine OR vilazodone OR vortioxetine OR zimeldine OR cognitive remediation therapy OR cognitive rehabilitation OR neurorehabilitation OR psychotherapy OR secondary prevention OR mental health service OR psychiatric treatment OR psychopharmacology OR psychotropic agent OR neurotransmitter uptake inhibitor OR monoamine oxidase inhibitor OR benzodiazepine derivative OR dibenzazepine derivative OR amoxapine OR amitriptyline OR amfebutamone OR buspirone OR citalopram OR chlormezanone OR clomipramine OR clorgyline OR desipramine OR desvenlafaxine OR dosulepin OR doxepin OR fluoxetine OR flunitrazepam OR fluvoxamine OR iprindole OR iproniazid OR isocarboxazid OR maprotiline OR meprobamate OR moclobemide OR nialamide OR nomifensine OR norfenfluramine OR nortriptyline OR pargyline OR paroxetine OR phenelzine OR rolipram OR selegiline OR sertraline OR tranylcypromine OR trazodone OR tryptophan OR venlafaxine OR viloxazine OR vilazodone OR protriptyline).ti,ab,kw.

Results 07-02-2022: 13 294 785

Concept #4: RCT
randomized controlled trial/ OR randomization/ OR clinical trial/ OR (RCT OR (clinical* AND trial) OR (random* AND control*)).ti,ab,kw.

Results 07-02-2022: 2 155 657

Combined:

1 and 2 and 3 and 4

Results 07-02-2022: 6040

Limit 5 to (embase and English language)

Results 07-02-2022: 4030

PSYCINFO (THROUGH OVIDSP)
Concept #1: Depression
adolescent depression/ OR chronic depression/ OR depression/ OR late life depression/ OR long term depression/ OR major affective disorder/ OR major depression/ OR mood disorder/ OR recurrent brief depression/ OR treatment resistant depression/ OR (affective disorder* OR depress* OR dysthymi*).ab,ti,id.

Results 07-02-2022: 349 705

Concept #2: Partial/remission
remission/ OR (partial remission OR partial remitted OR residual symptom* OR subclinical* OR (partial* ADJ3 remiss*) OR (partial* ADJ3 recov*) OR (partial* ADJ3 remit*) OR (residual* ADJ3 symptom*) OR (persis* ADJ3 symptom*)).ab,ti,id.

Results 07-02-2022: 14 856

Concept #3: Intervention
cognitive remediation therapy/ OR cognitive rehabilitation/ OR neurorehabilitation/ OR psychotherapy/ OR schema therapy/ OR group therapy/ OR cognitive therapy/ OR behavior therapy/ OR interpersonal psychotherapy/ OR secondary prevention/ OR mental health service/ OR psychiatric treatment/ OR psychopharmacology/ OR psychotropic agent/ OR neurotransmitter uptake inhibitor/ OR monoamine oxidase inhibitor/ OR benzodiazepine derivative/ OR dibenzazepine derivative/ OR amoxapine/ OR amitriptyline/ OR amfebutamone/ OR buspirone/ OR citalopram/ OR chlormezanone/ OR clomipramine/ OR clorgyline/ OR desipramine/ OR desvenlafaxine/ OR dosulepin/ OR doxepin/ OR fluoxetine/ OR flunitrazepam/ OR fluvoxamine/ OR iprindole/ OR iproniazid/ OR isocarboxazid/ OR maprotiline/ OR meprobamate/ OR moclobemide/ OR nialamide/ OR nomifensine/ OR norfenfluramine/ OR nortriptyline/ OR pargyline/ OR paroxetine/ OR phenelzine/ OR rolipram/ OR selegiline/ OR sertraline/ OR tranylcypromine/ OR trazodone/ OR tryptophan/ OR venlafaxine/ OR viloxazine/ OR vilazodone/ OR protriptyline/ OR repetitive transcranial magnetic stimulation/ OR transcranial magnetic stimulation/ OR electroconvulsive therapy/ OR brain depth stimulation/ OR (transcranial magnetic stimulation OR repetitive transcranial magnetic stimulation OR rTMS OR electroconvulsive therapy OR ECT OR brain depth stimulation OR deep brain stimulation OR DBS OR relapse prevention OR cognitive training OR cognitive remediation OR cognitive rehabilitation OR cognitive stimulation OR cognitive revalidation OR neurocognitive training OR neurocognitive remediation OR neurocognitive rehabilitation OR neurocognitive stimulation OR neurocognitive revalidation OR neurocognitive intervention OR memory training OR memory remediation OR memory rehabilitation OR memory stimulation OR memory intervention OR attention training OR attention remediation OR attention rehabilitation OR attention stimulation OR attention intervention OR cognitive control training OR cognitive control interventions OR cognitive control intervention OR brain training OR neurorehabilitation OR neuropsychological training OR neuropsychological remediation OR neuropsychological rehabilitation OR

neuropsychological stimulation OR neuropsychological revalidation OR neuropsychological intervention OR treatment OR treatments OR therapy OR therapies OR therapeutic OR supportive psychotherapy OR supportive therapy OR supportive intervention OR intervention OR psychotherapy OR cbt OR cognitive therapy OR cognitive restructuring OR activation OR exposure OR acceptance commitment OR act OR behavioural OR behavioral OR meditation OR mindfulness OR mbct OR mbt OR eye movement desensitization reprocessing OR emdr OR schema-focused OR schema focused OR sft OR interpersonal OR ipt OR psychodynamic OR parent intervention OR family therapy OR family intervention OR alternative medicine OR meditation OR drug therapy OR drug therapies OR pharmaco* OR medication* OR psychotropic* OR antidepress* OR agomelatine OR alaproclate OR alprazolam OR amfebutamone OR amoxapine OR amitriptylin* OR benzodiazepin* OR brofaromine OR bromazepam OR bupropion OR buspiron* OR citalopram OR chlorimipramin* OR chlormezanone OR clomipramin* OR clorazepate OR clorgyline OR depreny OR desipramin* OR desvenlafaxine OR diazepam OR dibenzazepin* OR dopamine reuptake OR dopamine uptake OR dosulepin OR dothiepin OR doxepin OR duloxetine OR escitalopram OR femoxetine OR fluoxetine OR flunitrazepam OR fluvoxamine OR imipramin* OR iprindole OR iproniazid* OR ipsapirone OR isocarboxazid* OR levomilnacipran OR lofepramin* OR lorazepam OR loprazolam OR mao OR maprotiline OR medazepam OR meprobamate OR mianserin OR milnacipran OR minaprine OR mirtazapine OR moclobemide OR monoamine oxidase inhibitor* OR nefazodone OR nialamide OR nitrazepam OR nomifensine OR nordazepam OR norepinephrine reuptake OR norepinephrine uptake OR noradrenaline reuptake OR noradrenaline uptake OR norfenfluramine OR nortriptylin* OR opipramol OR oxazepam OR paroxetine OR pertofrane OR phenelzine OR pheniprazine OR pirlindole OR pizotyline OR prazepam OR reboxetine OR rolipram OR selegiline OR serotonin reuptake OR serotonin uptake OR sertraline OR snri* OR ssri* OR tetracyclic* OR tianeptin* OR tranylcypromin* OR trazodone OR tricyclic* OR trimipramine OR tryptophan OR venlafaxine OR viloxazine OR vilazodone OR vortioxetine OR zimeldine OR cognitive remediation therapy OR cognitive rehabilitation OR neurorehabilitation OR psychotherapy OR secondary prevention OR mental health service OR psychiatric treatment OR psychopharmacology OR psychotropic agent OR neurotransmitter uptake inhibitor OR monoamine oxidase inhibitor OR benzodiazepine derivative OR dibenzazepine derivative OR amoxapine OR amitriptyline OR amfebutamone OR buspirone OR citalopram OR chlormezanone OR clomipramine OR clorgyline OR desipramine OR desvenlafaxine OR dosulepin OR doxepin OR fluoxetine OR flunitrazepam OR fluvoxamine OR iprindole OR iproniazid OR isocarboxazid OR maprotiline OR meprobamate OR moclobemide OR nialamide OR nomifensine OR norfenfluramine OR nortriptyline OR pargyline OR paroxetine OR phenelzine OR rolipram OR selegiline OR sertraline OR tranylcypromine OR trazodone OR tryptophan OR venlafaxine OR viloxazine OR vilazodone OR protriptyline).ab,ti,id.

Results 07-02-2022: 1 712 126

Concept #4: RCT
randomized controlled trial/ OR randomization/ OR clinical trial/ OR (RCT OR (clinical* AND trial) OR (random* AND control*)).ab,ti,id

Results 07-02-2022: 130 816

#5.
1 and 2 and 3 and 4

Results 07-02-2022: 699

Limit 5 to (peer reviewed journal and english language)

Results 07-02-2022: 644

MEDLINE (THROUGH OVIDSP)

Concept #1: Depression

Dysthymic Disorder/ OR Depression/ OR Depressive Disorder/ OR Depressive Disorder, Major/ OR Depressive disorder, treatment-resistant/ OR Mood Disorders/ OR (affective disorder* OR depress* OR dysthymi*).ti,ab,kf.

Results 07-02-2022: 572 561

Concept #2: Partial/remission

Remission, spontaneous/ OR (partial remission OR partial remitted OR residual symptom* OR subclinical* OR (partial* ADJ3 remiss*) OR (partial* ADJ3 recov*) OR (partial* ADJ3 remit*) OR (residual* ADJ3 symptom*) OR (persis* ADJ3 symptom*)).ti,ab,kf.

Results 07-02-2022: 101 944

Concept #3: Intervention

amitriptyline/ OR amoxapine/ OR anger management therapy/ OR antidepressive agents, second-generation/ OR antidepressive agents, tricyclic/ OR antidepressive agents/ OR applied behavior analysis/ OR aversive therapy/ OR behavior therapy/ OR biofeedback, psychology/ OR bupropion/ OR chlormezanone/ OR citalopram/ OR clomipramine/ OR clorgyline/ OR cognitive behavioral therapy/ OR Cognitive Remediation/ OR cognitive remediation/ OR cognitive restructuring/ OR desensitization, psychologic/ OR desipramine/ OR desvenlafaxine succinate/ OR dialectical behavior therapy/ OR dothiepin/ OR doxepin/ OR emotion-focused therapy/ OR escitalopram/ OR eye movement desensitization reprocessing/ OR feedback, sensory/ OR flunitrazepam/ OR fluoxetine/ OR fluvoxamine/ OR implosive therapy/ OR interpersonal psychotherapy/ OR iprindole/ OR iproniazid/ OR isocarboxazid/ OR Lithium Carbonate/ OR Lithium Chloride/ OR Lithium/ OR maprotiline/ OR meditation/ OR mental health services/ OR meprobamate/ OR mindfulness/ OR moclobemide/ OR monoamine oxidase inhibitors/ OR neurofeedback/ OR nialamide/ OR nomifensine/ OR norfenfluramine/ OR nortriptyline/ OR pargyline/ OR paroxetine/ OR phenelzine/ OR protriptyline/ OR psychopharmacology/ OR psychosocial intervention/ OR psychotherapy, brief/ OR psychotherapy, group/ OR psychotherapy, multiple/ OR psychotherapy, psychodynamic/ OR psychotherapy/ OR psychotropic drugs/ OR relaxation therapy/ OR rolipram/ OR schema therapy/ OR secondary prevention/ OR selegiline/ OR serotonin uptake inhibitors/ OR sertraline/ OR sleep phase chronotherapy/ OR tranylcypromine/ OR trazodone/ OR tryptophan/ OR venlafaxine hydrochloride/ OR vilazodone hydrochloride/ OR viloxazine/ OR virtual reality exposure therapy/ OR repetitive transcranial magnetic stimulation/ OR transcranial magnetic stimulation/ OR electroconvulsive therapy/ OR brain depth stimulation/ OR (transcranial magnetic stimulation OR repetitive transcranial magnetic stimulation OR rTMS OR electroconvulsive therapy OR ECT OR brain depth stimulation OR deep brain stimulation OR DBS OR acceptance commitment OR act OR activation OR agomelatine OR alaproclate OR alprazolam OR alternative medicine OR amfebutamone OR amitriptylin* OR amitriptyline OR amoxapine OR anger management therapy OR antidepress* OR antidepressive agents, second-generation OR antidepressive agents, tricyclic OR applied behavior analysis OR attention intervention OR attention rehabilitation OR attention remediation OR attention stimulation OR attention training OR aversive therapy OR behavior therapy OR behavioral OR behaviour therapy OR behavioural OR benzodiazepin* OR benzodiazepine derivative OR biofeedback, psychology

OR brain training OR brofaromine OR bromazepam OR bupropion OR buspiron* OR cbt OR chlorimipramin* OR chlormezanone OR citalopram OR clomipramin* OR clomipramine OR clorazepate OR clorgyline OR cognitive behavioral therapy OR cognitive behavioural therapy OR cognitive control intervention* OR cognitive control training OR cognitive rehabilitation OR cognitive remediation OR cognitive remediation therapy OR cognitive restructuring OR cognitive revalidation OR cognitive stimulation OR cognitive therapy OR cognitive training OR depreny OR desensitization, psychologic OR desipramin* OR desvenlafaxine OR desvenlafaxine succinate OR dialectical behavior therapy OR diazepam OR dibenzazepin* OR dibenzazepine derivative OR dopamine reuptake OR dopamine uptake OR dosulepin OR dothiepin OR doxepin OR drug therap* OR duloxetine OR emdr OR emotion-focused therapy OR escitalopram OR exposure OR eye movement desensitization reprocessing OR family intervention OR family therapy OR feedback, sensory OR femoxetine OR flunitrazepam OR fluoxetine OR fluvoxamine OR imipramin* OR implosive therapy OR interpersonal OR interpersonal psychotherapy OR intervention OR iprindole OR iproniazid* OR ipsapirone OR ipt OR isocarboxazid* OR levomilnacipran OR Lithium OR Lithium Carbonate OR Lithium Chloride OR lofepramin* OR loprazolam OR lorazepam OR mao OR maprotiline OR mbct OR mbt OR medazepam OR medication* OR meditation OR memory intervention OR memory rehabilitation OR memory remediation OR memory stimulation OR memory training OR mental health service* OR meprobamate OR mianserin OR milnacipran OR minaprine OR mindfulness OR mirtazapine OR moclobemide OR monoamine oxidase inhibitor* OR nefazodone OR neurocognitive intervention OR neurocognitive rehabilitation OR neurocognitive remediation OR neurocognitive revalidation OR neurocognitive stimulation OR neurocognitive training OR neurofeedback OR neuropsychological intervention OR neuropsychological rehabilitation OR neuropsychological remediation OR neuropsychological revalidation OR neuropsychological stimulation OR neuropsychological training OR neurorehabilitation OR neurotransmitter uptake inhibitor OR nialamide OR nitrazepam OR nomifensine OR noradrenaline reuptake OR noradrenaline uptake OR nordazepam OR norepinephrine reuptake OR norepinephrine uptake OR norfenfluramine OR nortriptylin* OR opipramol OR oxazepam OR parent intervention OR pargyline OR paroxetine OR pertofrane OR pharmaco* OR phenelzine OR pheniprazine OR pirlindole OR pizotyline OR prazepam OR protriptyline OR psychiatric treatment OR psychodynamic OR psychopharmacology OR psychosocial intervention OR psychotherapy OR psychotherapy, brief OR psychotherapy, multiple OR psychotherapy, psychodynamic OR psychotropic agent OR psychotropic drugs OR psychotropic* OR reboxetine OR relapse prevention OR relaxation therapy OR rolipram OR schema focused OR schema therapy OR schema-focused OR secondary prevention OR selegiline OR serotonin reuptake OR serotonin uptake OR serotonin uptake inhibitors OR sertraline OR sft OR sleep phase chronotherapy OR snri* OR ssri* OR supportive intervention OR supportive psychotherapy OR supportive therapy OR tetracyclic* OR therap* OR therapeutic OR tianeptin* OR tranylcypromin* OR trazodone OR treatment* OR tricyclic* OR trimipramine OR tryptophan OR venlafaxine OR venlafaxine hydrochloride OR vilazodone OR vilazodone hydrochloride OR viloxazine OR virtual reality exposure therapy OR vortioxetine OR zimeldine).ti,ab,kf

Results 07-02-2022: 9 800 885

Concept #4: RCT
randomized controlled trial/ OR Random Allocation/ OR clinical trial/ OR (RCT OR (clinical* AND trial) OR (random* AND control*)).ti,ab,kf

Results 07-02-2022: 1 459 704
#5
1 and 2 and 3 and 4

Results 07-02-2022: 869

Limit 5 to English language

Results 07-02-2022: 838

SCOPUS
Concept #1: Depression
TITLE-ABS(“mood disorder” OR “affective disorder*” OR “depress*” OR “dysthymi*”) OR AUTHKEY(“mood disorder” OR “affective disorder*” OR “depress*” OR “dysthymi*”)

Results 07-02-2022: 771 603

Concept #2: Partial/remission
TITLE-ABS(“Remission” OR “partial remission” OR “partial remitted” OR “residual symptom*” OR “subclinical*” OR (partial* W/3 remiss*) OR (partial* ADJ3 recov*) OR (partial* W/3 remit*) OR (residual* W/3 symptom*) OR (persis* W/3 symptom*)) OR AUTHKEY(“Remission” OR “partial remission” OR “partial remitted” OR “residual symptom*” OR “subclinical*” OR (partial* W/3 remiss*) OR (partial* ADJ3 recov*) OR (partial* W/3 remit*) OR (residual* W/3 symptom*) OR (persis* W/3 symptom*))

Results 07-02-2022: 234 339

Concept #3: Intervention
TITLE-ABS(“transcranial magnetic stimulation” OR “repetitive transcranial magnetic stimulation” OR “rTMS” OR “electroconvulsive therapy” OR “ECT” OR “brain depth stimulation” OR “deep brain stimulation” OR “DBS” OR “acceptance commitment” OR “act” OR “activation” OR “agomelatine” OR “alaproclate” OR “alprazolam” OR “alternative medicine” OR “amfebutamone” OR “amitriptylin*” OR “amitriptyline” OR “amoxapine” OR “anger management therapy” OR “antidepress*” OR “antidepressive agents second-generation” OR “antidepressive agents tricyclic” OR “applied behavior analysis” OR “attention intervention” OR “attention rehabilitation” OR “attention remediation” OR “attention stimulation” OR “attention training” OR “aversive therapy” OR “behavior therapy” OR “behavioral” OR “behaviour therapy” OR “behavioural” OR “benzodiazepin*” OR “benzodiazepine derivative” OR “biofeedback psychology” OR “brain training” OR “brofaromine” OR “bromazepam” OR “bupropion” OR “buspiron*” OR “cbt” OR “chlorimipramin*” OR “chlormezanone” OR “citalopram” OR “clomipramin*” OR “clomipramine” OR “clorazepate” OR “clorgyline” OR “cognitive behavioral therapy” OR “cognitive behavioural therapy” OR “cognitive control intervention*” OR “cognitive control training” OR “cognitive rehabilitation” OR “cognitive remediation” OR “cognitive remediation therapy” OR “cognitive restructuring” OR “cognitive revalidation” OR “cognitive stimulation” OR “cognitive therapy” OR “cognitive training” OR “depreny” OR “desensitization psychologic” OR “desipramin*” OR “desvenlafaxine” OR “desvenlafaxine succinate” OR “dialectical behavior therapy” OR “diazepam” OR “dibenzazepin*” OR “dibenzazepine derivative” OR “dopamine reuptake” OR “dopamine uptake” OR “dosulepin” OR “dothiepin” OR “doxepin” OR “drug therap*” OR “duloxetine” OR “emdr” OR “emotion-focused therapy” OR “escitalopram” OR “exposure” OR “eye movement desensitization reprocessing” OR “family intervention” OR “family therapy” OR “feedback sensory” OR “femoxetine” OR “flunitrazepam” OR “fluoxetine” OR “fluvoxamine” OR “imipramin*” OR “implosive therapy” OR “interpersonal” OR “interpersonal psychotherapy” OR “intervention” OR “iprindole” OR “iproniazid*” OR “ipsapirone” OR “ipt” OR “isocarboxazid*” OR “levomilnacipran” OR “Lithium” OR “Lithium

Carbonate" OR "Lithium Chloride" OR "lofepramin*" OR "loprazolam" OR "lorazepam" OR "mao" OR "maprotiline" OR "mbct" OR "mbt" OR "medazepam" OR "medication*" OR "meditation" OR "memory intervention" OR "memory rehabilitation" OR "memory remediation" OR "memory stimulation" OR "memory training" OR "mental health service*" OR "meprobamate" OR "mianserin" OR "milnacipran" OR "minaprine" OR "mindfulness" OR "mirtazapine" OR "moclobemide" OR "monoamine oxidase inhibitor*" OR "nefazodone" OR "neurocognitive intervention" OR "neurocognitive rehabilitation" OR "neurocognitive remediation" OR "neurocognitive revalidation" OR "neurocognitive stimulation" OR "neurocognitive training" OR "neurofeedback" OR "neuropsychological intervention" OR "neuropsychological rehabilitation" OR "neuropsychological remediation" OR "neuropsychological revalidation" OR "neuropsychological stimulation" OR "neuropsychological training" OR "neurorehabilitation" OR "neurotransmitter uptake inhibitor" OR "nialamide" OR "nitrazepam" OR "nomifensine" OR "noradrenaline reuptake" OR "noradrenaline uptake" OR "nordazepam" OR "norepinephrine reuptake" OR "norepinephrine uptake" OR "norfenfluramine" OR "nortriptylin*" OR "opipramol" OR "oxazepam" OR "parent intervention" OR "pargyline" OR "paroxetine" OR "pertofrane" OR "pharmaco*" OR "phenelzine" OR "pheniprazine" OR "pirlindole" OR "pizotyline" OR "prazepam" OR "protriptyline" OR "psychiatric treatment" OR "psychodynamic" OR "psychopharmacology" OR "psychosocial intervention" OR "psychotherapy" OR "psychotherapy brief" OR "psychotherapy multiple" OR "psychotherapy psychodynamic" OR "psychotropic agent" OR "psychotropic drugs" OR "psychotropic*" OR "reboxetine" OR "relapse prevention" OR "relaxation therapy" OR "rolipram" OR "schema focused" OR "schema therapy" OR "schema-focused" OR "secondary prevention" OR "selegiline" OR "serotonin reuptake" OR "serotonin uptake" OR "serotonin uptake inhibitors" OR "sertraline" OR "sft" OR "sleep phase chronotherapy" OR "snri*" OR "ssri*" OR "supportive intervention" OR "supportive psychotherapy" OR "supportive therapy" OR "tetracyclic*" OR "therap*" OR "therapeutic" OR "tianeptin*" OR "tranylcypromin*" OR "trazodone" OR "treatment*" OR "tricyclic*" OR "trimipramine" OR "tryptophan" OR "venlafaxine" OR "venlafaxine hydrochloride" OR "vilazodone" OR "vilazodone hydrochloride" OR "viloxazine" OR "virtual reality exposure therapy" OR "vortioxetine" OR "zimeldine") OR AUTHKEY("transcranial magnetic stimulation" OR "repetitive transcranial magnetic stimulation" OR "rTMS" OR "electroconvulsive therapy" OR "ECT" OR "brain depth stimulation" OR "deep brain stimulation" OR "DBS" OR "acceptance commitment" OR "act" OR "activation" OR "agomelatine" OR "alaproclate" OR "alprazolam" OR "alternative medicine" OR "amfebutamone" OR "amitriptylin*" OR "amitriptyline" OR "amoxapine" OR "anger management therapy" OR "antidepress*" OR "antidepressive agents second-generation" OR "antidepressive agents tricyclic" OR "applied behavior analysis" OR "attention intervention" OR "attention rehabilitation" OR "attention remediation" OR "attention stimulation" OR "attention training" OR "aversive therapy" OR "behavior therapy" OR "behavioral" OR "behaviour therapy" OR "behavioural" OR "benzodiazepin*" OR "benzodiazepine derivative" OR "biofeedback psychology" OR "brain training" OR "brofaromine" OR "bromazepam" OR "bupropion" OR "buspiron*" OR "cbt" OR "chlorimipramin*" OR "chlormezanone" OR "citalopram" OR "clomipramin*" OR "clomipramine" OR "clorazepate" OR "clorgyline" OR "cognitive behavioral therapy" OR "cognitive behavioural therapy" OR "cognitive control intervention*" OR "cognitive control training" OR "cognitive rehabilitation" OR "cognitive remediation" OR "cognitive remediation therapy" OR "cognitive restructuring" OR "cognitive revalidation" OR "cognitive stimulation" OR "cognitive therapy" OR "cognitive training" OR "depreny" OR "desensitization psychologic" OR "desipramin*" OR "desvenlafaxine" OR "desvenlafaxine succinate" OR "dialectical behavior therapy" OR "diazepam" OR "dibenzazepin*" OR "dibenzazepine derivative" OR "dopamine reuptake" OR "dopamine uptake" OR "dosulepin" OR "dothiepin" OR "doxepin" OR "drug therap*" OR "duloxetine" OR "emdr" OR "emotion-focused therapy" OR "escitalopram" OR "exposure" OR "eye movement desensitization reprocessing" OR "family intervention" OR "family therapy" OR "feedback sensory" OR "femoxetine" OR "flunitrazepam" OR "fluoxetine" OR "fluvoxamine" OR "imipramin*" OR

"implosive therapy" OR "interpersonal" OR "interpersonal psychotherapy" OR "intervention" OR "iprindole" OR "iproniazid*" OR "ipsapirone" OR "ipt" OR "isocarboxazid*" OR "levomilnacipran" OR "Lithium" OR "Lithium Carbonate" OR "Lithium Chloride" OR "lofepramin*" OR "loprazolam" OR "lorazepam" OR "mao" OR "maprotiline" OR "mbct" OR "mbt" OR "medazepam" OR "medication*" OR "meditation" OR "memory intervention" OR "memory rehabilitation" OR "memory remediation" OR "memory stimulation" OR "memory training" OR "mental health service*" OR "meprobamate" OR "mianserin" OR "milnacipran" OR "minaprine" OR "mindfulness" OR "mirtazapine" OR "moclobemide" OR "monoamine oxidase inhibitor*" OR "nefazodone" OR "neurocognitive intervention" OR "neurocognitive rehabilitation" OR "neurocognitive remediation" OR "neurocognitive revalidation" OR "neurocognitive stimulation" OR "neurocognitive training" OR "neurofeedback" OR "neuropsychological intervention" OR "neuropsychological rehabilitation" OR "neuropsychological remediation" OR "neuropsychological revalidation" OR "neuropsychological stimulation" OR "neuropsychological training" OR "neurorehabilitation" OR "neurotransmitter uptake inhibitor" OR "nialamide" OR "nitrazepam" OR "nomifensine" OR "noradrenaline reuptake" OR "noradrenaline uptake" OR "nordazepam" OR "norepinephrine reuptake" OR "norepinephrine uptake" OR "norfenfluramine" OR "nortriptylin*" OR "opipramol" OR "oxazepam" OR "parent intervention" OR "pargyline" OR "paroxetine" OR "pertofrane" OR "pharmaco*" OR "phenelzine" OR "pheniprazine" OR "pirlindole" OR "pizotyline" OR "prazepam" OR "protriptyline" OR "psychiatric treatment" OR "psychodynamic" OR "psychopharmacology" OR "psychosocial intervention" OR "psychotherapy" OR "psychotherapy brief" OR "psychotherapy multiple" OR "psychotherapy psychodynamic" OR "psychotropic agent" OR "psychotropic drugs" OR "psychotropic*" OR "reboxetine" OR "relapse prevention" OR "relaxation therapy" OR "rolipram" OR "schema focused" OR "schema therapy" OR "schema-focused" OR "secondary prevention" OR "selegiline" OR "serotonin reuptake" OR "serotonin uptake" OR "serotonin uptake inhibitors" OR "sertraline" OR "sft" OR "sleep phase chronotherapy" OR "snri*" OR "ssri*" OR "supportive intervention" OR "supportive psychotherapy" OR "supportive therapy" OR "tetracyclic*" OR "therap*" OR "therapeutic" OR "tianeptin*" OR "tranylcypromin*" OR "trazodone" OR "treatment*" OR "tricyclic*" OR "trimipramine" OR "tryptophan" OR "venlafaxine" OR "venlafaxine hydrochloride" OR "vilazodone" OR "vilazodone hydrochloride" OR "viloxazine" OR "virtual reality exposure therapy" OR "vortioxetine" OR "zimeldine")

Results 07-02-2022: 15 069 462

Concept #4: RCT
TITLE-ABS(randomized controlled trial OR randomization OR randomization OR clinical trial OR RCT OR (clinical* AND trial) OR (random* AND control*)) OR AUTHKEY(randomized controlled trial OR randomization OR randomization OR clinical trial OR RCT OR (clinical* AND trial) OR (random* AND control*))

Results 07-02-2022: 346 477

Combined:
#1 AND #2 AND #3 AND #4
Results 07-02-2022: 1823

DOCTYPE(ar) AND LANGUAGE(english)
INDEX(medline)

Results 07-02-2022: 1445

Supplementary Appendix 3. Included and excluded full-text articles and studies based on full-text assessment.

Studies included in quantitative analysis (*k* = 14).

Study 1 'Paykel et al. (1999)' (k= 3).

- Paykel, E. S., Scott, J., Teasdale, J. D., Johnson, A. L., Garland, A., Moore, R., ... & Pope, M. (1999). Prevention of relapse in residual depression by cognitive therapy: a controlled trial. Archives of General Psychiatry, 56(9), 829-835.
- Scott, J., Teasdale, J. D., Paykel, E. S., Johnson, A. L., Abbott, R., Hayhurst, H., ... & Garland, A. (2000). Effects of cognitive therapy on psychological symptoms and social functioning in residual depression. The British journal of psychiatry, 177(5), 440-446.
- Paykel, E. S., Scott, J., Cornwall, P. L., Abbott, R., Crane, C., Pope, M., & Johnson, A. L. (2005). Duration of relapse prevention after cognitive therapy in residual depression: follow-up of controlled trial. Psychological Medicine, 35(1), 59-68.

Study 2 'Holländare et al. (2011)' (k = 2).

- Holländare, F., Johnsson, S., Randestad, M., Tillfors, M., Carlbring, P., Andersson, G., & Engström, I. (2011). Randomized trial of Internet-based relapse prevention for partially remitted depression. Acta Psychiatrica Scandinavica, 124(4), 285-294.
- Holländare, F., Anthony, S. A., Randestad, M., Tillfors, M., Carlbring, P., Andersson, G., & Engström, I. (2013). Two-year outcome of internet-based relapse prevention for partially remitted depression. Behaviour Research and Therapy, 51(11), 719-722.

Study 3 'Watkins et al. (2011)' (k = 1).

- Watkins, E. R., Mullan, E., Wingrove, J., Rimes, K., Steiner, H., Bathurst, N., ... & Scott, J. (2011). Rumination-focused cognitive–behavioural therapy for residual depression: Phase II randomised controlled trial. The British Journal of Psychiatry, 199(4), 317-322.

Study 4 'Geschwind et al. (2012)' (k = 4).

- Geschwind, N., Peeters, F., Huibers, M., van Os, J., & Wichers, M. (2012). Efficacy of mindfulness-based cognitive therapy in relation to prior history of depression: randomised controlled trial. The British Journal of Psychiatry, 201(4), 320-325.
- Batink, T., Peeters, F., Geschwind, N., van Os, J., & Wichers, M. (2013). How does MBCT for depression work? Studying cognitive and affective mediation pathways. PloS one, 8(8), e72778.
- Collip, D., Geschwind, N., Peeters, F., Myin-Germeys, I., van Os, J., & Wichers, M. (2013). Putting a hold on the downward spiral of paranoia in the social world: a randomized controlled trial of mindfulness-based cognitive therapy in individuals with a history of depression. PloS one, 8(6), e66747.
- Forkmann, T., Wichers, M., Geschwind, N., Peeters, F., van Os, J., Mainz, V., & Collip, D. (2014). Effects of mindfulness-based cognitive therapy on self-reported suicidal ideation: results from a randomised controlled trial in patients with residual depressive symptoms. Comprehensive psychiatry, 55(8), 1883-1890.

Study 5 'Schlögelhofer et al. (2014)' (k = 1).

- Schlögelhofer, M., Willinger, U., Wiesegger, G., Eder, H., Priesch, M., Itzlinger, U., ... & Aschauer, H. (2014). Clinical study results from a randomized controlled trial of cognitive behavioural guided self-help in patients with partially remitted depressive disorder. Psychology and Psychotherapy: Theory, Research and Practice, 87(2), 178-190.

Study 6 'Teismann et al. (2014)' (k = 1).

- Teismann, T., Von Brachel, R., Hanning, S., Grillenberger, M., Hebermehl, L., Hornstein, I., & Willutzki, U. (2014). A randomized controlled trial on the effectiveness of a rumination-focused group treatment for residual depression. Psychotherapy Research, 24(1), 80-90.

Study 7 'Segal et al. (2020)' (k = 2).

- Segal, Z. V., Dimidjian, S., Beck, A., Boggs, J. M., Vanderkruik, R., Metcalf, C. A., ... & Levy, J. (2020). Outcomes of online mindfulness-based cognitive therapy for patients with residual depressive symptoms: a randomized clinical trial. JAMA psychiatry, 77(6), 563-573.
- Boggs, J. M., Ritzwoller, D. P., Beck, A., Dimidjian, S., & Segal, Z. V. (2022). Cost-effectiveness of a web-based program for residual depressive symptoms: Mindful Mood Balance. Psychiatric Services, 73(2), 158-164.

Studies only included in qualitative analysis (*k* = 3).

Study 1 'Kennedy et al. (2003)' (k = 1).

- Kennedy, S. H., Segal, Z. V., Cohen, N. L., Levitan, R. D., & Bagby, R. M. (2003). Lithium carbonate versus cognitive therapy as sequential combination treatment strategies in partial responders to antidepressant medication: an exploratory trial. The Journal of clinical psychiatry, 64(4), 10432.

Study 2 'Morgan et al. (2005)' (k = 1).

- Morgan, M. L., Cook, I. A., Rapkin, A. J., & Leuchter, A. F. (2005). Estrogen augmentation of antidepressants in perimenopausal depression: a pilot study. J Clin Psychiatry, 66(6), 774-780.

*Study 3 '*Ionescu *et al. (2016)' (k = 1).*

- Ionescu, D. F., Fava, M., Kim, D. J. H., Baer, L., Shelton, R. C., & Cusin, C. (2016). A placebo-controlled crossover study of iloperidone augmentation for residual anger and irritability in major depressive disorder. Therapeutic Advances in Psychopharmacology, 6(1), 4-12.

Excluded studies.

Reason: Reports not retrieved after repeated requests (*k* = 2).

Study 1 'Žourková et al. (2001)' (k = 1).

- Žourková, A. (2001). Effect of mirtazapine and paroxetine on residual symptoms of depressive disorders and their effect on P450 CYP 2D6 activity.

Study 2 'Rouillon et al. (1994)' (k = 1).

- Rouillon, F., Markabi, S., Febvre, N., Phillips, R., & Vaillant, J. (1994). Controlled study of treatment of residual depression by clomipramine versus placebo. L'encephale, 20(2), 139-145.

Reason: Mixed population. Did not specifically target partial remitted MDD and/or no lower boundary stated (*k* = 28)

Study 1 'van Aalderen et al. (2012)' (k = 2).

- Van Aalderen, J. R., Donders, A. R. T., Giommi, F., Spinhoven, P., Barendregt, H. P., & Speckens, A. E. M. (2012). The efficacy of mindfulness-based cognitive therapy in recurrent depressed patients with and without a current depressive episode: a randomized controlled trial. Psychological medicine, 42(5), 989-1001.

- Cladder-Micus, M. B., van Aalderen, J., Donders, A. R. T., Spijker, J., Vrijsen, J. N., & Speckens, A. E. M. (2018). Cognitive reactivity as outcome and working mechanism of mindfulness-based cognitive therapy for recurrently depressed patients in remission. Cognition and Emotion, 32(2), 371-378.

*Study 2 '*Barnhofer *et al. (2009)' (k = 1).*

- Barnhofer, T., Crane, C., Hargus, E., Amarasinghe, M., Winder, R., & Williams, J. M. G. (2009). Mindfulness-based cognitive therapy as a treatment for chronic depression: A preliminary study. Behaviour research and therapy, 47(5), 366-373.

Study 3 'Biesheuvel-Leliefeld et al. (2017)' (k = 2).

- Biesheuvel-Leliefeld, K. E., Dijkstra-Kersten, S. M., Van Schaik, D. J., Van Marwijk, H. W., Smit, F., Van Der Horst, H. E., & Bockting, C. L. (2017). Effectiveness of supported self-help in recurrent depression: a randomized controlled trial in primary care. Psychotherapy and psychosomatics, 86(4), 220-230.
- Dijkstra-Kersten, S. M., Biesheuvel-Leliefeld, K. E., van der Wouden, J. C., van Schaik, D. J., Bosmans, J. E., van Marwijk, H. W., & van der Horst, H. E. (2019). Supported self-help to prevent relapse or recurrence of depression: Who benefits most?. Journal of Affective Disorders, 257, 180-186.

Study 4 'Britton et al. (2012)' (k = 4).

- Britton, W. B., Shahar, B., Szepsenwol, O., & Jacobs, W. J. (2012). Mindfulness-based cognitive therapy improves emotional reactivity to social stress: results from a randomized controlled trial. Behavior therapy, 43(2), 365-380.
- Shahar, B., Britton, W. B., Sbarra, D. A., Figueredo, A. J., & Bootzin, R. R. (2010). Mechanisms of change in mindfulness-based cognitive therapy for depression: Preliminary evidence from a randomized controlled trial. International Journal of Cognitive Therapy, 3(4), 402-418.
- Britton, W. B., Haynes, P. L., Fridel, K. W., & Bootzin, R. R. (2012). Mindfulness-based cognitive therapy improves polysomnographic and subjective sleep profiles in antidepressant users with sleep complaints. Psychotherapy and psychosomatics, 81(5), 296-304.
- Britton, W. B., Haynes, P. L., Fridel, K. W., & Bootzin, R. R. (2010). Polysomnographic and subjective profiles of sleep continuity before and after mindfulness-based cognitive therapy in partially remitted depression. Psychosomatic Medicine, 72(6), 539-548.

Study 5 'Elices et al. (2017)' (k = 1).

- Elices, M., Soler, J., Feliu-Soler, A., Carmona, C., Tiana, T., Pascual, J. C., ... & Álvarez, E. (2017). Combining emotion regulation and mindfulness skills for preventing depression relapse: a randomized-controlled study. Borderline personality disorder and emotion dysregulation, 4(1), 1-9.

Study 6 'Huijbers et al. (2015)' (k = 1).

- Huijbers, M. J., Spinhoven, P., Spijker, J., Ruhé, H. G., van Schaik, D. J., van Oppen, P., ... & Speckens, A. E. (2015). Adding mindfulness-based cognitive therapy to maintenance antidepressant medication for prevention of relapse/recurrence in major depressive disorder: randomised controlled trial. Journal of Affective Disorders, 187, 54-61.

Study 7 'Huijbers et al. (2016)' (k = 2).

- Huijbers, M. J., Spinhoven, P., Spijker, J., Ruhe, H. G., van Schaik, D. J., van Oppen, P., ... & Speckens, A. E. (2016). Discontinuation of antidepressant medication after mindfulness-based cognitive therapy for recurrent depression: randomised controlled non-inferiority trial. The British Journal of Psychiatry, 208(4), 366-373.
- Huijbers, M. J., Wentink, C., Simons, E., Spijker, J., & Speckens, A. (2020). Discontinuing antidepressant medication after mindfulness-based cognitive therapy: a mixed-methods study exploring predictors and outcomes of different discontinuation trajectories, and its facilitators and barriers. BMJ open, 10(11), e039053.

*Study 8 '*Jacobs *et al. (2016)' (k = 1).*

- Jacobs, R. H., Watkins, E. R., Peters, A. T., Feldhaus, C. G., Barba, A., Carbray, J., & Langenecker, S. A. (2016). Targeting ruminative thinking in adolescents at risk for depressive relapse: rumination-focused cognitive behavior therapy in a pilot randomized controlled trial with resting state fMRI. PloS one, 11(11), e0163952.4

*Study 9 '*Kiermeier *et al. (2012)' (k = 1).*

- Kiermeir, J., Gassner, L. M., Siebörger, A., Wiethoff, K., Ricken, R., Stamm, T., ... & Adli, M. (2012). Euthymic Therapy to Reduce Residual Symptoms of Depression and Strengthen Self-Care A Randomised Controlled Trial. German Journal of Psychiatry, 15(1).

Study 10 'Kocsis et al. (1996)' (k = 1).

- Kocsis, J. H., Friedman, R. A., Markowitz, J. C., Leon, A. C., Miller, N. L., Gniwesch, L., & Parides, M. (1996). Maintenance therapy for chronic depression: a controlled clinical trial of desipramine. Archives of General Psychiatry, 53(9), 769-774.

*Study 11 '*Kuyken *et al. (2008)' (k = 1).*

- Kuyken, W., Byford, S., Taylor, R. S., Watkins, E., Holden, E., White, K., ... & Teasdale, J. D. (2008). Mindfulness-based cognitive therapy to prevent relapse in recurrent depression. Journal of consulting and clinical psychology, 76(6), 966.

*Study 12 '*Kuyken *et al. (2015)' (k = 1).*

- Kuyken, W., Hayes, R., Barrett, B., Byng, R., Dalgleish, T., Kessler, D., ... & Byford, S. (2015). Effectiveness and cost-effectiveness of mindfulness-based cognitive therapy compared with maintenance antidepressant treatment in the prevention of depressive relapse or recurrence (PREVENT): a randomised controlled trial. The Lancet, 386(9988), 63-73.

*Study 13 '*Lecrubier *et al. (1997)' (k = 1).*

- Lecrubier, Y., Boyer, P., Turjanski, S., Rein, W., & Amisulpride Study Group. (1997). Amisulpride versus imipramine and placebo in dysthymia and major depression. Journal of affective disorders, 43(2), 95-103.

*Study 14 '*Listunova *et al. (2020)' (k = 2).*

- Listunova, L., Kienzle, J., Bartolovic, M., Jaehn, A., Grützner, T. M., Wolf, R. C., ... & Roesch-Ely, D. (2020). Cognitive remediation therapy for partially remitted unipolar depression: A single-blind randomized controlled trial. Journal of Affective Disorders, 276, 316-326.

- Listunova, L., Bartolovic, M., Kienzle, J., Jaehn, A., Grützner, T. M., Wolf, R. C., ... & Roesch-Ely, D. (2020). Predictors of cognitive remediation therapy improvement in (partially) remitted unipolar depression. Journal of Affective Disorders, 264, 40-49.

*Study 15 '*Madhoo *et al. (2014)' (k = 1).*

- Madhoo, M., Keefe, R. S., Roth, R. M., Sambunaris, A., Wu, J., Trivedi, M. H., ... & Lasser, R. (2014). Lisdexamfetamine dimesylate augmentation in adults with persistent executive dysfunction after partial or full remission of major depressive disorder. Neuropsychopharmacology, 39(6), 1388-1398.

*Study 16 '*Morokuma *et al. (2013)' (k = 1).*

- Morokuma, I., Shimodera, S., Fujita, H., Hashizume, H., Kamimura, N., Kawamura, A., ... & Inoue, S. (2013). Psychoeducation for major depressive disorders: A randomised controlled trial. Psychiatry Research, 210(1), 134-139.

*Study 17 '*Nierenberg *et al. (2019)' (k = 1).*

- Nierenberg, A. A., Loft, H., & Olsen, C. K. (2019). Treatment effects on residual cognitive symptoms among partially or fully remitted patients with major depressive disorder: A randomized, double-blinded, exploratory study with vortioxetine. Journal of Affective Disorders, 250, 35-42.

Study 18 'Shallcross et al. (2015)' (k = 1).

- Shallcross, A. J., Gross, J. J., Visvanathan, P. D., Kumar, N., Palfrey, A., Ford, B. Q., ... & Mauss, I. B. (2015). Relapse prevention in major depressive disorder: Mindfulness-based cognitive therapy versus an active control condition. Journal of Consulting and Clinical Psychology, 83(5), 964.

*Study 19 '*Smeraldi *et al. (1998)' (k = 1).*

- Smeraldi, E. (1998). Amisulpride versus fluoxetine in patients with dysthymia or major depression in partial remission: a double-blind, comparative study. Journal of affective disorders, 48(1), 47-56.

*Study 20 '*Wang *et al. (2017)' (k = 1).*

- Wang, H. N., Wang, X. X., Zhang, R. G., Wang, Y., Cai, M., Zhang, Y. H., ... & Zhang, Z. J. (2017). Clustered repetitive transcranial magnetic stimulation for the prevention of depressive relapse/recurrence: a randomized controlled trial. Translational psychiatry, 7(12), 1-9.

Study 21 'Watanabe et al. (2011)' (k = 1).

- Watanabe, N., Furukawa, T. A., Shimodera, S., Morokuma, I., Katsuki, F., Fujita, H., ... & Perlis, M. L. (2011). Brief behavioral therapy for refractory insomnia in residual depression: an assessor-blind, randomized controlled trial. The Journal of clinical psychiatry, 72(12), 2128.

Reason: Wrong patient population - Full remission/severity too low (*k* = 22).

- Bockting, C. L., Schene, A. H., Spinhoven, P., Koeter, M. W., Wouters, L. F., Huyser, J., & Kamphuis, J. H. (2005). Preventing relapse/recurrence in recurrent depression with cognitive therapy: a randomized controlled trial. Journal of consulting and clinical psychology, 73(4), 647.

- Bockting, C. L., Klein, N. S., Elgersma, H. J., van Rijsbergen, G. D., Slofstra, C., Ormel, J., ... & Burger, H. (2018). Effectiveness of preventive cognitive therapy while tapering antidepressants versus maintenance antidepressant treatment versus their combination in prevention of depressive relapse or recurrence (DRD study): a three-group, multicentre, randomised controlled trial. The Lancet Psychiatry, 5(5), 401-410.
- Bondolfi, G., Jermann, F., Van der Linden, M., Gex-Fabry, M., Bizzini, L., Rouget, B. W., ... & Bertschy, G. (2010). Depression relapse prophylaxis with Mindfulness-Based Cognitive Therapy: replication and extension in the Swiss health care system. Journal of affective disorders, 122(3), 224-231.
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- de Jonge, M., Bockting, C. L., Kikkert, M. J., van Dijk, M. K., van Schaik, D. J., Peen, J., ... & Dekker, J. J. (2019). Preventive cognitive therapy versus care as usual in cognitive behavioral therapy responders: A randomized controlled trial. Journal of Consulting and Clinical Psychology, 87(6), 521.
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Reason: Wrong population – Other reasons (*k* = 14)

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Reason: Wrong population – Too severe/current MDE (*k* = 11).

- Altamura, A. C., Dell'Osso, B., Buoli, M., Bosi, M., & Mundo, E. (2008). Short-term intravenous citalopram augmentation in partial/nonresponders with major depression: a randomized placebo-controlled study. International clinical psychopharmacology, 23(4), 198-202.
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Reason: Wrong population – No previous MDD (required) (*k* = 10).

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Reason: Wrong study design (*k* = 8).

- Dimidjian, S., Beck, A., Felder, J. N., Boggs, J. M., Gallop, R., & Segal, Z. V. (2014). Web-based mindfulness-based cognitive therapy for reducing residual depressive symptoms: an open trial and quasi-experimental comparison to propensity score matched controls. Behaviour Research and Therapy, 63, 83-89.
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Reason: No comparable measure of depression severity as inclusion criterium available (*k* = 6)
Study 1 'Fava et al. (1994)' (k = 3).

- Fava, G. A., Grandi, S., Zielezny, M., Canestrari, R., & Morphy, M. A. (1994). Cognitive behavioral treatment of residual symptoms in primary major depressive disorder. The American journal of psychiatry.
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Study 2 'Katon et al. (1999)' (k = 3)

- Simon, G. E., Katon, W. J., VonKorff, M., Unützer, J., Lin, E. H., Walker, E. A., ... & Ludman, E. (2001). Cost-effectiveness of a collaborative care program for primary care patients with persistent depression. American Journal of Psychiatry, 158(10), 1638-1644.
- Katon, W., Russo, J., Von Korff, M., Lin, E., Simon, G., Bush, T., ... & Walker, E. (2002). Long-term effects of a collaborative care intervention in persistently depressed primary care patients. Journal of general internal medicine, 17(10), 741-748.
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Reason: Study protocol paper (*k* = 1).

- Bolinski, F., Kleiboer, A., Karyotaki, E., Bosmans, J. E., Zarski, A. C., Weisel, K. K., ... & Riper, H. (2018). Effectiveness of a transdiagnostic individually tailored Internet-based and mobile-supported intervention for the indicated prevention of depression and anxiety (ICare Prevent) in Dutch college students: study protocol for a randomised controlled trial. Trials, 19(1), 1-13.

Reason: Other reasons (*k* = 1).

- Home-based programme significantly reduces depressive symptoms and improves health status in chronically ill older adults with minor depression or dysthymia. (2004). Evidence-Based Healthcare and Public Health, 8(5), 257â€“258. doi:10.1016/j.ehbc.2004.08.035

Supplementary Appendix 4. Overview of risk of bias judgement and supportive descriptions, based on the RoB-2 tool.

Study: Paykel (1999)[8]		
Domain 1: Randomization Process		
Signaling Question	**Response**	**Description**
1.1. Was the allocation sequence random?	Y	"...were then randomized. Assignments in consecutively numbered sealed envelopes were prepared by the trial statistician (A.L.J.)..."
1.2. Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	PY	
1.3. Did baseline differences between intervention groups suggest a problem with the randomization process?	N	Two treatment groups are of comparable sizes. Baseline characteristics and the variables used for stratification are similar in both groups. No imbalances apparent or incompatible with chance.
Authors risk-of-bias judgement of domain:	**LOW**	
Domain 2: Deviations from intended interventions		
Signaling Question	**Response**	**Description**
2.1. Were participants aware of their assigned intervention during the trial?	Y	Awareness of the assigned interventions is inherent to the design of the trial and the intervention examined, given that participants could be allocated to CT +. CM vs. CM only.
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?	PY	"The control group received significantly more clinical management sessions than the CT group."
2.4. If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	PN	"The findings confirmed that the benefits of CT were not due to higher medication doses or compliance."
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	N/A	N/A
2.6. Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	"Analyses were conducted for the 2 relapse criteria combined and for major depression relapse alone and in 2 separate samples: intention to treat, including all subjects randomized in the study (including dropouts), and per protocol…"
2.7. If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	N/A	N/A
Authors risk-of-bias judgement of domain:	**SOME CONCERNS**	
Domain 3: Risk of bias due to missing outcome data		
Signaling Question	**Response**	**Description**
3.1. Were data for this outcome available for all, or nearly all, participants randomized?	N	"Full or fairly complete ratings to relapse or end of study were obtained for all except 6 subjects in the clinical management group and 10 in the CT group." This equates to 10.13% of participants with missing outcome data.
3.2. If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	PN	As far as the reviewers are aware, no analyses were done that correct for bias; no imputations or sensitivity analyses were conducted showing that results can be considered similar without missingness.
3.3. If N/PN to 3.2: Could missingness in the outcome depend on its true value?	Y	"The most common reasons for nonadherence to the protocol (...) were failure to attend (clinical management group = 4, CT group = 10), withdrawal of consent (clinical management group = 2, CT group = 6), development of additional excluded diagnosis (clinical management group = 3, CT group = 1)."
3.4. If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	PY	

		There are differences between the intervention groups in the proportions of missing outcome data and the reasons for missing outcome data differ between the intervention groups, amongst other things. The reasons for missing outcome data or nonadherence provided give some indication that missingness in the outcome depends on its true value.
Authors risk-of-bias judgement of domain:	**HIGH**	
Domain 4: Risk of bias in measurement of the outcome		
Signaling Question	**Response**	**Description**
4.1. Was the method of measuring the outcome inappropriate?	N	"Repeated symptom ratings included the 17-item HDRS,[18] the BDI,[19] and other secondary measures."
4.2. Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	"Subjects were assessed every 4 to 20 weeks and every 8 weeks thereafter by the study psychiatrist and at baseline, 8 weeks, 20 weeks, and 68 weeks by a research assistant. Both were blind to treatment group and patients were requested not to reveal significant details."
4.3. If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?	PN	"Both were blind to treatment group and patients were requested not to reveal significant details." Combination of clinician-rated and self-reported measurements used.
4.4. If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	N/A	N/A
4.5. If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	N/A	
Authors risk-of-bias judgement of domain:	**LOW**	
Domain 5: Risk of bias in selection of the reported result		
Signaling Question	**Response**	**Description**
5.1. Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	No detailed pre-specified intentions available to the review authors. Thus, planned outcome measures and analyses cannot be compared to those presented in the reviewed trials/articles.
Is the numerical result being assessed likely to have been selected, on the basis of the results, from...		
5.2. ...multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	Based on the reports across multiple articles - including those reporting on follow-up data - reviewers are fairly confident that all eligible results are reported. All eligible reported results for the outcome measurement seem correspond to all intended measurement.
5.3. ...multiple eligible analyses of the data?	NI	Analysis intentions are not available or reported in sufficient detail to facilitate the assessment and reach a valid judgement.
Authors risk-of-bias judgement of domain:	**SOME CONCERNS**	
Study: Holländare (2011)[9]		
Domain 1: Randomization Process		
Signaling Question	**Response**	**Description**
1.1. Was the allocation sequence random?	Y	"...were then randomized to Internet-based CBT or a control group by drawing numbers (each corresponding to a person) out of an opaque bowl." No information available/reported regarding allocation sequence concealment; however, it is stated that randomization followed a final decision of inclusion/exclusion at a diagnostic conference.
1.2. Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	PY	

1.3. Did baseline differences between intervention groups suggest a problem with the randomization process?	N	Two treatment groups are of comparable sizes. Baseline characteristics are similar in both groups as follows from Table 1. No imbalances apparent between groups or incompatible with chance.
Authors risk-of-bias judgement of domain:	**LOW**	
Domain 2: Deviations from intended interventions		
Signaling Question	**Response**	**Description**
2.1. Were participants aware of their assigned intervention during the trial?	Y	Awareness of the assigned interventions is inherent to the design of the trial and the intervention examined, given that participants could be allocated to online CBT or the control condition (consisting of low intensity contact only). "Over a 10-week period, participants in the treatment group worked through CBT modules with guidance (via e-mail) from a personal therapist, after which no guidance was received; however, they were offered the remaining modules." "Control group participants had the possibility of e-mail contact with a personal therapist; however, the content of the correspondence was restricted to non-specific support."
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?	NI	No comments in the papers found by reviewers on whether deviations arose because of the trial's context.
2.4. If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	N/A	N/A
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	N/A	N/A
2.6. Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	Mixed models were used to test difference in symptom levels over time, not excluding any subjects but using all available data (when data is missing), which minimizes the risk of biasing the sample. "Mixed models were used to test differences in symptom levels between the groups over time. This method is preferable when some data are missing (48) because it does not exclude any participants from the analysis, but rather uses all available data, which minimizes the risk of biasing the sample."
2.7. If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	N/A	N/A
Authors risk-of-bias judgement of domain:	**SOME CONCERNS**	
Domain 3: Risk of bias due to missing outcome data		
Signaling Question	**Response**	**Description**
3.1. Were data for this outcome available for all, or nearly all, participants randomized?	N	At post-treatment ± 11.5% of data was missing. At 6 mo FU, this increased to ±15.5%
3.2. If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	PY	Yes, a mixed model was used to correct for any potential bias. "Mixed models were used to test differences in symptom levels between the groups over time. This method is preferable when some data are missing (48) because it does not exclude any participants from the analysis, but rather uses all available data, which minimizes the risk of biasing the sample."
3.3. If N/PN to 3.2: Could missingness in the outcome depend on its true value?	N/A	N/A

3.4. If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	N/A	
Authors risk-of-bias judgement of domain:	**LOW**	
Domain 4: Risk of bias in measurement of the outcome		
Signaling Question	**Response**	**Description**
4.1. Was the method of measuring the outcome inappropriate?	PN	The SCID-I, MADRS and BDI were used as main outcome measures, which have been shown to have adequate psychometric qualities.
4.2. Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	"During the whole study period, participants in both groups rated their depressive symptoms monthly with MADRS-S, and all such ratings resulted in feedback by means of a graph showing their past and present scores."
4.3. If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?	Y	Yes, all depression severity measures were self-reported. Participants were not blind to treatment allocation.
4.4. If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	Y	Yes, participants are aware of their treatment allocation and assessment of the outcome is measured subjectively, which could have introduced bias in the outcome.
4.5. If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	PY	Knowledge of the intervention could have introduced bias and influenced the outcome assessment; as patients were aware of the intervention, a positive effect could have been expected from the treatment compared to the passive control group.
Authors risk-of-bias judgement of domain:	**HIGH**	
Domain 5: Risk of bias in selection of the reported result		
Signaling Question	**Response**	**Description**
5.1. Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	No detailed pre-specified intentions available to the review authors. Thus, planned outcome measures and analyses cannot be compared to those presented in the reviewed trials/articles.
Is the numerical result being assessed likely to have been selected, on the basis of the results, from...		
5.2. ...multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	Based on the reports across multiple articles - including those reporting on follow-up data - reviewers are fairly confident that all eligible results are reported. All eligible reported results for the outcome measurement seem correspond to all intended measurement.
5.3. ...multiple eligible analyses of the data?	NI	Analysis intentions are not available or reported in sufficient detail to facilitate the assessment and reach a valid judgement.
Authors risk-of-bias judgement of domain:	**SOME CONCERNS**	
Study: Watkins (2011)[18]		
Domain 1: Randomization Process		
Signaling Question	**Response**	**Description**
1.1. Was the allocation sequence random?	Y	"Randomisation was performed by an off-site researcher using computer-generated random numbers, and stratified according to gender and the duration of the index episode of major depression (< v. > 1 year)."
1.2. Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	
1.3. Did baseline differences between intervention groups suggest a problem with the randomization process?	N	Two treatment groups are of comparable sizes. Baseline characteristics and the variables used for stratification are similar in both groups. No imbalances apparent or incompatible with chance. "As no differences in baseline covariates between conditions were noted..." "...prescribed medications were not significantly different across the two groups."
Authors risk-of-bias judgement of domain:	**LOW**	
Domain 2: Deviations from intended interventions		

Signaling Question	**Response**	**Description**
2.1. Were participants aware of their assigned intervention during the trial?	PY	Awareness of the assigned interventions is inherent to the design of the trial and the intervention examined, given that participants could be allocated to RF-CBT or TAU.
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	PY	
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?	PN	"Seven participants in the TAU group (33%) commenced psychological treatment between T1 and T2 and two individuals were lost to follow-up. In the rumination-focused CBT arm, one participant failed to attend any rumination-focused CBT (the individual started a course of CBT from their local service between recruitment and initial contact from the trial therapist), but otherwise rates of adherence to rumination-focused CBT were high, with no one dropping out and participants on average attending 11 out of the 12 sessions offered."
2.4. If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	N/A	N/A
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	N/A	N/A
2.6. Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	"The analysis was performed according to the principle of intention-to-treat (i.e. all participants according to and included in random allocation)."
2.7. If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	N/A	N/A
Authors risk-of-bias judgement of domain:	**LOW**	
Domain 3: Risk of bias due to missing outcome data		
Signaling Question	**Response**	**Description**
3.1. Were data for this outcome available for all, or nearly all, participants randomized?	Y	Only 1 subject dropped out from the RF-CBT and was lost. "In the rumination-focused CBT arm, one participant failed to attend any rumination-focused CBT (the individual started a course of CBT from their local service between recruitment and initial contact from the trial therapist), but otherwise rates of adherence to rumination-focused CBT were high, with no one dropping out and participants on average attending 11 out of the 12 sessions offered." In the TAU condition, 2 patients were lost to follow-up (one subject did not respond to contact and one was posted to Iraq).
3.2. If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	N/A	N/A
3.3. If N/PN to 3.2: Could missingness in the outcome depend on its true value?	N/A	N/A
3.4. If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	N/A	
Authors risk-of-bias judgement of domain:	**LOW**	
Domain 4: Risk of bias in measurement of the outcome		
Signaling Question	**Response**	**Description**
4.1. Was the method of measuring the outcome inappropriate?	PN	HRSD and BDI-II were used, which both have adequate psychometric properties.
4.2. Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	"All participants were assessed by research staff masked to treatment allocation at intake baseline assessment (Time 1 (T1)) and again 6 months later (post-intervention, Time 2 (T2))."

4.3. If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?	PN	"All participants were assessed by research staff masked to treatment allocation…" However, BDI-II, a secondary outcome, was self-reported. Nevertheless, the main outcome (HDRS) was not and assessors were masked to allocation.
4.4. If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	N/A	N/A
4.5. If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	N/A	
Authors risk-of-bias judgement of domain:	**LOW**	
Domain 5: Risk of bias in selection of the reported result		
Signaling Question	**Response**	**Description**
5.1. Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	The study was registered, but only retrospectively. There is no pre-specified analysis protocol available. Thus, planned outcome measures and analyses cannot be compared to those presented in the reviewed trials/articles.
Is the numerical result being assessed likely to have been selected, on the basis of the results, from...		
5.2. ...multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	NI	Intentions are not available or reported in sufficient detail to facilitate the assessment and reach a valid judgement.
5.3. ...multiple eligible analyses of the data?	NI	Intentions are not available or reported in sufficient detail to facilitate the assessment and reach a valid judgement.
Authors risk-of-bias judgement of domain:	**SOME CONCERNS**	
Study: Geschwind (2012)[11]		
Domain 1: Randomization Process		
Signaling Question	**Response**	**Description**
1.1. Was the allocation sequence random?	Y	"Participants were randomised to continue with their usual treatment (if any; waiting list control condition) or to receive 8 weeks of MBCT in addition to their usual treatment (if any). Randomisation was stratified according to number of depressive episodes (one or two v. three or more). An independent researcher not involved in the project generated the randomisation sequence in blocks of five (using the sequence generator on www.random.org), and wrote the randomisation code in sealed numbered envelopes." "After completion of all baseline assessments, the researcher allocated participants to their treatment condition based on the randomization code in the sealed envelope (opened in order of sequence)."
1.2. Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	
1.3. Did baseline differences between intervention groups suggest a problem with the randomization process?	N	"At baseline, there were no differences in sociodemographic and clinical characteristics between the MBCT and the control condition (see Geschwind et al[20])" Two treatment groups are of comparable sizes. Baseline characteristics and the variables used for stratification are similar in both groups. No imbalances apparent or incompatible with chance.
Authors risk-of-bias judgement of domain:	**LOW**	
Domain 2: Deviations from intended interventions		
Signaling Question	**Response**	**Description**
2.1. Were participants aware of their assigned intervention during the trial?	Y	"No masking of treatment condition took place…"

2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	Awareness of the assigned interventions is inherent to the design of the trial and the intervention examined, given that participants could be allocated to the MBCT or control condition. Lack of blinding is expected.
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?	NI	Not sufficiently clear to review authors whether deviations arose because of the trial context/ interventions offered.
2.4. If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	N/A	N/A
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	N/A	N/A
2.6. Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	"We undertook an intention-to-treat analysis." "Primary outcome measures were residual depressive symptoms expressed as total (interviewer-rated) HRSD score. Analyses were repeated using (self-report) IDS total scores to verify whether results using interviewer- and self-rated assessments corresponded with each other."
2.7. If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	N/A	N/A
Authors risk-of-bias judgement of domain:	**SOME CONCERNS**	
Domain 3: Risk of bias due to missing outcome data		
Signaling Question	**Response**	**Description**
3.1. Were data for this outcome available for all, or nearly all, participants randomized?	Y	Yes, in the MBCT group (n = 64), a total of 64 participants completed post intervention measurements. In the control group (n = 66), 66 participants completed the post intervention measurements.
3.2. If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	N/A	N/A
3.3. If N/PN to 3.2: Could missingness in the outcome depend on its true value?	N/A	N/A
3.4. If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	N/A	
Authors risk-of-bias judgement of domain:	**LOW**	
Domain 4: Risk of bias in measurement of the outcome		
Signaling Question	**Response**	**Description**
4.1. Was the method of measuring the outcome inappropriate?	N	"The 17-item HRSD was administered by trained research assistants. The HRSD is a semi-structured interview designed to assess depressive symptoms over the previous week.22 It is one of the most frequently used rating scales in depression research, and sensitivity, internal, interrater and retest reliability estimates for the overall HRSD are good.26 Only the overall score was used for the analyses, and interrater reliability for the total score was high (intraclass correlation coefficient (ICC) = 0.97)." "The IDS24 is a self-rated scale, which includes 30 items rated zero to three."
4.2. Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	No, similar methods of outcome measurements at comparable intervals (i.e. pre-post intervention) were used.
4.3. If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?	PY	"No masking of treatment condition took place (although the therapists were masked to the number of prior major depressive episodes)." "The 17-item HRSD was administered by trained research assistants."

		However, it is unclear whether these assessors were blind to treatment allocation. This cannot be found in the published articles or the study protocol. With regards to the IDS, subjects can be considered the outcome assessors and were thus not blind to treatment allocation.
4.4. If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PY	Yes, it is possible that knowledge of treatment allocation could have influenced the participant reported outcomes (in the case of the IDS) or observer-reported outcomes (using the HDRS). Knowledge of the intervention could have introduced bias and influenced the outcome assessment; as patients were aware of the intervention, a positive effect could understandably have been expected from the treatment compared to the passive control group.
4.5. If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	PY	
Authors risk-of-bias judgement of domain:	**HIGH**	
Domain 5: Risk of bias in selection of the reported result		
Signaling Question	**Response**	**Description**
5.1. Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	PY	Preregistration trial protocol and CONSORT checklist were evaluated. The protocol is sufficiently detailed to avoid the selection of reported results. Data produced were analyzed in accordance with a pre-specified analysis plan and/or study protocol. TRIAL REGISTRATION: MindMaastricht; trial number NTR1084, Netherlands Trial Register; https://trialsearch.who.int/Trial2.aspx?TrialID=NTR1084
Is the numerical result being assessed likely to have been selected, on the basis of the results, from…		
5.2. ...multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	N	All eligible reported results for the outcome measurement seem correspond to all intended measurement.
5.3. ...multiple eligible analyses of the data?	N	All eligible reported results for the outcome measurement seem to correspond to all intended analyses. Additionally, analyses are consistent across several different reports on this trial.
Authors risk-of-bias judgement of domain:	**LOW**	
Study: Schlögelhofer (2014)[12]		
Domain 1: Randomization Process		
Signaling Question	**Response**	**Description**
1.1. Was the allocation sequence random?	Y	"...participants were randomly assigned to either cognitive behavioural guided self-help plus pharmacotherapy ('treatment group') or psychopharmacotherapy alone. Forty-nine participants were randomized into the 'treatment group' and 41 participants into the group with psychopharmacotherapy alone. The randomization process was done using a computer-generated randomization list created by a statistician not involved in the study. The sequence was concealed until interventions were assigned."
1.2. Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	
1.3. Did baseline differences between intervention groups suggest a problem with the randomization process?	PN	"The groups did not differ significantly in mean age (t = 0.409; df = 83; p = 0.683), gender (v2 = 0.6, df = 1; p = 0.454), or employment status (v2 = 0.4; df = 2; p = 0.838). The mean HRSD-17 scores at randomization ('treatment group' mean 12.6; SD 2.7; psychopharmacotherapy group mean 12.5; SD 2.5), as well as the mean BDI scores ('treatment group': 18.8; SD 10.0; psychopharmacotherapy: 17.6; SD 6.7); were in the mild to moderate range for both groups and did not differ significantly (HRSD-17: t = -0.183; df = 88; p = 0.855; BDI: t

		= 0.670; df = 88; p = 0.505). Furthermore, groups did not differ in positive or negative stress-coping strategies (positive stress-coping strategies: t = 1.167; df = 86; p = 0.247 and negative stress-coping strategies: t = 0.769; df = 86; p = 0.444) at randomization (Time 2; see Table 1)." Two treatment groups are of comparable sizes. Baseline characteristics as seen in the quoted paragraph and in Table 1 are similar. No imbalances apparent or incompatible with chance.
Authors risk-of-bias judgement of domain:	**LOW**	
Domain 2: Deviations from intended interventions		
Signaling Question	**Response**	**Description**
2.1. Were participants aware of their assigned intervention during the trial?	Y	Awareness of the assigned interventions is inherent to the design of the trial and the intervention examined, given that participants could be allocated to cognitive-behavioral guided self-help plus ADM or ADM only. Lack of blinding is expected.
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?	NI	Not sufficiently clear to review authors whether deviations arose because of the trial context/ interventions offered. Not enough information available to make a valid judgement.
2.4. If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	N/A	N/A
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	N/A	N/A
2.6. Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	Intention-to-treat analyses were used. "An analysis based on the 'intention-to-treat' principle including all randomized participants was performed."
2.7. If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	N/A	N/A
Authors risk-of-bias judgement of domain:	**SOME CONCERNS**	
Domain 3: Risk of bias due to missing outcome data		
Signaling Question	**Response**	**Description**
3.1. Were data for this outcome available for all, or nearly all, participants randomized?	N	Only 38 participants in the intervention group and 35 in the control group had complete data at end of the treatment (T3). Proportionally, this is only 81.11% of all participants randomized in the study.
3.2. If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	PN	As far as the reviewers are aware, no analyses were done that correct for bias; no imputations or sensitivity analyses were conducted showing that results can be considered similar without missingness.
3.3. If N/PN to 3.2: Could missingness in the outcome depend on its true value?	PY	"During the course of the study three participants (all from the treatment group) were admitted to the inpatient unit of the department of Psychiatry and Psychotherapy, Medical University Vienna because of symptom deterioration. Deterioration could not be related specifically to medication or reading the self-help book." No information available with regard to other reasons of drop-out or missingness.
3.4. If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	PY	
Authors risk-of-bias judgement of domain:	**HIGH**	
Domain 4: Risk of bias in measurement of the outcome		
Signaling Question	**Response**	**Description**

4.1. Was the method of measuring the outcome inappropriate?	PN	No, the BDI and HRSD-17 were used as primary outcome measurements, which have adequate psychometric properties.
4.2. Could measurement or ascertainment of the outcome have differed between intervention groups?	N	"All participants were seen at three time points: baseline (Time 1), week 3 (randomization = Time 2), and week 9 (end of treatment = Time 3)."
4.3. If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?	PN	"The three psychiatrists (U.I., H.E., and G.W.) conducting the outcome assessments were blind to participants' treatment assignment." The HDRS-17 was the primary outcome. "Due to the nature of the intervention it was not possible to mask participants and the psychotherapist to the treatment allocation." The BDI was self-reported, but this was considered a secondary outcome. "
4.4. If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	N/A	N/A
4.5. If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	N/A	
Authors risk-of-bias judgement of domain:	**LOW**	
Domain 5: Risk of bias in selection of the reported result		
Signaling Question	**Response**	**Description**
5.1. Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	No detailed pre-specified intentions available to the review authors. Thus, planned outcome measures and analyses cannot be compared to those presented in the reviewed trials/articles.
Is the numerical result being assessed likely to have been selected, on the basis of the results, from...		
5.2. ...multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	NI	Analysis intentions are not available or reported in sufficient detail to facilitate the assessment and reach a valid judgement. There is more than one way to analyze this outcome domain.
5.3. ...multiple eligible analyses of the data?	NI	Analysis intentions are not available or reported in sufficient detail to facilitate the assessment and reach a valid judgement. There is more than one way to analyze this outcome domain.
Authors risk-of-bias judgement of domain:	**SOME CONCERNS**	
Study: Teismann (2014)[13]		
Domain 1: Randomization Process		
Signaling Question	**Response**	**Description**
1.1. Was the allocation sequence random?	PN	"After signing a consent form, the remaining 60 patients were randomly assigned to treatment or to the wait-list according to a predetermined, arbitrary sequence (from one to 64), which was generated before the start of the trial." No further information available on concealment of treatment/group assignment or randomization procedures used.
1.2. Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	NI	
1.3. Did baseline differences between intervention groups suggest a problem with the randomization process?	PN	"There were no significant differences between the groups in any of the assessed characteristics." Two treatment groups are of comparable sizes and no imbalances apparent or incompatible with chance, as can be seen in Table 1.
Authors risk-of-bias judgement of domain:	**SOME CONCERNS**	
Domain 2: Deviations from intended interventions		

Signaling Question	Response	Description
2.1. Were participants aware of their assigned intervention during the trial?	Y	Awareness of the assigned interventions is inherent to the design of the trial and the intervention examined, given that participants could be allocated to CBT-DR or a WL. Lack of blinding is thus expected.
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?	NI	Not entirely clear whether any deviations arose because of the trial context. However, it is mentioned that "Two patients (6.5%) dropped out of treatment before the posttreatment assessment. Two patients (6.9%) dropped out of the wait-list condition…There were no differences in the dropout rates between the two conditions…"
2.4. If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	N/A	N/A
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	N/A	N/A
2.6. Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	"All analyses were intent-to-treat-analysis, with last data carried forward."
2.7. If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	N/A	N/A
Authors risk-of-bias judgement of domain:	**SOME CONCERNS**	
Domain 3: Risk of bias due to missing outcome data		
Signaling Question	**Response**	**Description**
3.1. Were data for this outcome available for all, or nearly all, participants randomized?	Y	"Two patients (6.5%) dropped out of treatment before the posttreatment assessment. Two patients (6.9%) dropped out of the wait-list condition (see Figure 1). There were no differences in the dropout rates between the two conditions…"
3.2. If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	N/A	N/A
3.3. If N/PN to 3.2: Could missingness in the outcome depend on its true value?	N/A	N/A
3.4. If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	N/A	
Authors risk-of-bias judgement of domain:	**LOW**	
Domain 4: Risk of bias in measurement of the outcome		
Signaling Question	**Response**	**Description**
4.1. Was the method of measuring the outcome inappropriate?	PN	BDI-II was used, a self-report measure with adequate validity/reliability and other psychometric qualities.
4.2. Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	"The main assessments were carried out at pretreatment-wait (T1), posttreatment-wait (T2) and at 1-year follow-up (T3)."
4.3. If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?	Y	Outcomes were self-reported, and participants were not masked to allocation given the nature of the study.
4.4. If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PY	Yes, participants are aware of their treatment allocation and assessment of the outcome is measured subjectively, which could have introduced bias in the outcome. Knowledge of the intervention could have introduced bias as a self-reported measure of depression severity was used. This may have influenced the outcome assessment, as patients were aware of the intervention, a positive effect could have been expected from the treatment and
4.5. If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	PY	

		the active intervention was compared to a passive control group.
Authors risk-of-bias judgement of domain:	**HIGH**	
Domain 5: Risk of bias in selection of the reported result		
Signaling Question	**Response**	**Description**
5.1. Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	No detailed pre-specified intentions available to the review authors. Thus, planned outcome measures and analyses cannot be compared to those presented in the reviewed trials/articles.
Is the numerical result being assessed likely to have been selected, on the basis of the results, from...		
5.2. ...multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	NI	Analysis intentions are not available or reported in sufficient detail to facilitate the assessment and reach a valid judgement. There is more than one way to analyze this outcome domain.
5.3. ...multiple eligible analyses of the data?	NI	Analysis intentions are not available or reported in sufficient detail to facilitate the assessment and reach a valid judgement. There is more than one way to analyze this outcome domain.
Authors risk-of-bias judgement of domain:	**SOME CONCERNS**	
Study: Segal (2020)[14]		
Domain 1: Randomization Process		
Signaling Question	**Response**	**Description**
1.1. Was the allocation sequence random?	Y	"Participants were randomized with an allocation ratio of 1:1 using the Research Electronic Data Capture randomization module with a file created by a random number generator in SAS, version 9.4 (SAS Institute Inc). Study staff were blinded to the contents of the randomization file."
1.2. Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	PY	
1.3. Did baseline differences between intervention groups suggest a problem with the randomization process?	PN	No apparent baseline differences or substantial imbalances that could be considered incompatible with chance.
Authors risk-of-bias judgement of domain:	**LOW**	
Domain 2: Deviations from intended interventions		
Signaling Question	**Response**	**Description**
2.1. Were participants aware of their assigned intervention during the trial?	Y	Awareness of the assigned interventions is inherent to the design of the trial and the intervention examined, given that participants could be allocated to MMB as an add-on treatment or CAU. Lack of blinding is thus expected. "The MMB treatment was developed to provide the core components of the in-person mindfulness-based cognitive therapy program23 in an online, 8-session, self-administered platform. During the intervention phase, participants were supported by a coach who provided motivational and technical support." "…single-blind randomized clinical trial…" "Study staff were blinded to the contents of the randomization file."
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	PY	
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?	PN	
2.4. If Y/PY to 2.3: Were these deviations likely to have affected the outcome?	N/A	N/A
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?	N/A	N/A

2.6. Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	Intent-to-treat analyses were used. "All analyses were conducted with the intent-to-treat sample."
2.7. If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?	N/A	N/A
Authors risk-of-bias judgement of domain:	**LOW**	
Domain 3: Risk of bias due to missing outcome data		
Signaling Question	**Response**	**Description**
3.1. Were data for this outcome available for all, or nearly all, participants randomized?	PN	From Figure 1 it can be inferred that 164 subjects had data available at the end of the 12-wk intervention period in the MMB-group, compared to 198 in the CAU group. "Among the 460 patients recruited for the trial, 389 (85%) had completed a PHQ-9 during the follow-up period and were included in the main analysis (UDC, N=210; MMB+UDC, N=179)."
3.2. If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	PY	"As a sensitivity analysis for missing measures..., we implemented a Markov Chain Monte Carlo Imputation method through PROC MI of SAS, version 9.4 (SAS Institute)."
3.3. If N/PN to 3.2: Could missingness in the outcome depend on its true value?	N/A	N/A
3.4. If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	N/A	
Authors risk-of-bias judgement of domain:	**LOW**	
Domain 4: Risk of bias in measurement of the outcome		
Signaling Question	**Response**	**Description**
4.1. Was the method of measuring the outcome inappropriate?	N	PHQ-9 was used as the main outcome in the study, which has adequate psychometric properties.
4.2. Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	All participants completed the PHQ-9 on a monthly basis, regardless of treatment allocation.
4.3. If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?	PY	The PHQ-9 was used, which is a self-report measure and participants were aware of treatment allocation given the nature of the study/interventions offered (MMB vs. CAU).
4.4. If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PY	Yes, participants are aware of their treatment allocation and assessment of the outcome is measured subjectively, which could have introduced bias in the outcome. While knowledge of the intervention could have introduced bias and influenced the outcome assessment, there is no apparent reason to believe that it did.
4.5. If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	PN	
Authors risk-of-bias judgement of domain:	**SOME CONCERNS**	
Domain 5: Risk of bias in selection of the reported result		
Signaling Question	**Response**	**Description**
5.1. Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	PY	Data produced were analyzed in accordance with a pre-specified analysis plan and/or study protocol. TRIAL REGISTRATION: ClinicalTrials.gov identifier: NCT02190968
Is the numerical result being assessed likely to have been selected, on the basis of the results, from...		
5.2. ...multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	All eligible reported results for the outcome measurement seem correspond to all intended measurement.
5.3. ...multiple eligible analyses of the data?	PN	All eligible reported results for the outcome measurement seem to correspond to all intended analyses. Additionally, analyses are consistent across several different reports on this trial.

Authors risk-of-bias judgement of domain:	**LOW**

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