

Supplementary Appendix

Dismantling, optimising, and personalising internet cognitive behavioural therapy for depression: a systematic review and component network meta-analysis using individual participant data

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1 Search terms

The search strings were developed by combining text and key words for psychotherapy with depression and limiting that to randomized trials. More information about the searches and the full search strings for all databases can be found at the website of the project (www.metapsy.org).

Generic search strings used for PubMed in Jan 1, 2018 and Jan 1, 2019

(Psychotherapy [MH] OR psychotherap*[All Fields] OR cbt[All Fields] OR "behavior therapies"[All Fields] OR "behavior therapy"[All Fields] OR "behavior therapeutic"[All Fields] OR "behavior therapeutical"[All Fields] OR "behavior therapeutics"[All Fields] OR "behavior therapist"[All Fields] OR "behavior therapists"[All Fields] OR "behavior treatment"[All Fields] OR "behavior treatments"[All Fields] OR "behaviors therapies"[All Fields] OR "behaviors therapy"[All Fields] OR "behaviors therapeutics"[All Fields] OR "behaviors therapeutic"[All Fields] OR "behaviors therapeutical"[All Fields] OR "behaviors therapist"[All Fields] OR "behaviors therapists"[All Fields] OR "behaviors treatment"[All Fields] OR "behaviors treatments"[All Fields] OR "behavioral therapies"[All Fields] OR "behavioral therapy"[All Fields] OR "behavioral therapeutics"[All Fields] OR "behavioral therapeutic"[All Fields] OR "behavioral therapeutical"[All Fields] OR "behavioral therapist"[All Fields] OR "behavioral 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"behavioural therapist"[All Fields] OR "behavioural therapists"[All Fields] OR "behavioural treatment"[All Fields] OR "behavioural treatments"[All Fields] OR "cognition therapies"[All Fields] OR "cognition therapie"[All Fields] OR "cognition therapy"[All Fields] OR "cognition therapeutical"[All Fields] OR "cognition therapeutic"[All Fields] OR "cognition therapeutics"[All Fields] OR "cognition therapist"[All Fields] OR "cognition therapists"[All Fields] OR "cognition treatment"[All Fields] OR "cognition treatments"[All Fields] OR psychodynamic[All Fields] OR Psychoanalysis[MH] OR psychoanalysis[All Fields] OR psychoanalytic*[All Fields] OR counselling[All Fields] OR counseling[All Fields] OR Counseling[MH] OR "problem-solving"[All Fields] OR mindfulness[All Fields] OR (acceptance[All Fields] AND commitment[All Fields]) OR "assertiveness training"[All Fields] OR "behavior activation"[All Fields] OR "behaviors activation"[All Fields] OR "behavioral activation"[All Fields] OR "cognitive therapies"[All Fields] OR "cognitive therapy"[All Fields] OR "cognitive therapeutic"[All Fields] OR "cognitive therapeutics"[All Fields] OR "cognitive therapeutical"[All Fields] OR "cognitive therapist"[All Fields] OR "cognitive therapists"[All Fields] OR "cognitive treatment"[All Fields] OR "cognitive treatments"[All Fields] OR "cognitive restructuring"[All Fields] OR ("compassion-focused"[All Fields] OR "compassion-focussed"[All Fields]) AND (therapy[SH] OR therapies[All Fields] OR therapy[All Fields] OR therapie*[All Fields] OR therapis*[All Fields] OR Therapeutics [OR treatment*[All Fields]]) OR ((therapy[SH] OR therapies[All Fields] OR therapy [All Fields] OR therapie*[All Fields] OR therapis*[All Fields] OR Therapeutics[MH] OR treatment*[All Fields]) AND constructivist*[All Fields]) OR "metacognitive therapies"[All Fields] OR "metacognitive therapy"[All Fields] OR "metacognitive therapeutic"[All Fields] OR "metacognitive therapeutics"[All Fields] OR "metacognitive therapeutical"[All Fields] OR "metacognitive therapist"[All Fields] OR "metacognitive therapists"[All Fields] OR "metacognitive treatment"[All Fields] OR "metacognitive treatments"[All Fields] OR "meta-cognitive therapies"[All Fields] OR "meta-cognitive therapy"[All Fields] OR "meta-cognitive therapeutic"[All Fields] OR "meta-cognitive therapeutics"[All Fields] OR "meta-cognitive therapeutical"[All Fields] OR "meta-cognitive therapist"[All Fields] OR "meta-cognitive therapists"[All Fields] OR "meta-cognitive treatment"[All Fields] OR "meta-cognitive treatments"[All Fields] OR "solution-focused therapies"[All Fields] OR "solution-focused therapy"[All Fields] OR "solution-focused therapeutical"[All Fields] OR "solution focused therapies"[All Fields] OR "solution focused therapy"[All Fields] OR "solution focused therapeutic"[All Fields] OR "solution focused therapeutics"[All Fields] OR "solution focused therapeutical"[All Fields] OR "solution-focussed therapies"[All Fields] OR 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therapeutical"[All Fields] OR "self-control therapies"[All Fields] OR "self-control therapy"[All Fields] OR "self-control therapeutics"[All Fields] OR "self-control therapeutical"[All Fields] OR "self-control therapeutic"[All Fields] OR "self-control training"[All Fields] OR "self-control trainings"[All Fields] OR "self control therapies"[All Fields] OR "self control therapy"[All Fields] OR "self control therapeutics"[All Fields] OR "self control therapeutical"[All Fields] OR "self control therapeutic"[All Fields] OR "self control training"[All Fields] OR "self control trainings"[All Fields] AND (Depressive Disorder[MH] OR Depression[MH] OR dysthymi*[All Fields] OR "affective disorder"[All Fields] OR "affective disorders"[All Fields] OR "mood disorder"[All Fields] OR "mood disorders"[All Fields] OR depression*[All Fields] OR depressive*[All Fields] OR "dysthymic disorder"[MeSH Terms]) AND ((randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR randomly [tiab] NOT (animals[mh] NOT (animals[mh] AND humans [mh])))

Generic search strings used for Embase in Jan 1, 2018 and Jan 1, 2019

#1

'psychotherapy'/exp OR 'psychotherapy' OR 'psychotherapies' OR 'psychotherapeutics' OR 'psychotherapeutical' OR 'cognitive therapy'/exp OR 'cognitive behavior therapy'/exp OR 'behavior therapy'/exp OR 'cbt' OR 'cognitive behavioural therapy' OR 'cognitive behavioural therapies' OR 'cognitive behavioral therapy' OR 'cognitive behavioral therapies' OR 'behavior therapy' OR 'behavior therapies' OR 'behaviour therapy' OR 'behaviour therapies' OR 'cognition therapy' OR 'cognitive therapies' OR 'cognitive therapy' OR 'cognitive therapeutic' OR 'cognitive therapeutics' OR 'cognitive therapeutical' OR 'cognitive therapist' OR 'cognitive therapists' OR 'cognitive treatment' OR 'cognitive treatments' OR 'cognitive restructuring' OR 'cognition therapies' OR 'cognition therapie' OR 'cognition therapeutical' OR 'cognition therapeutic' OR 'cognition therapeutics' OR 'cognition therapist' OR 'cognition therapists' OR 'cognition treatment' OR 'cognition treatments' OR 'behavior therapeutic' OR 'behavior therapeutical' OR 'behavior therapeutics' OR 'behavior therapist' OR 'behavior therapists' OR 'behavior treatment' OR 'behavior treatments' OR 'behaviors therapies' OR 'behaviors therapy' OR 'behaviors therapeutics' OR 'behaviors therapeutic' OR 'behaviors therapeutical' OR 'behaviors therapist' OR 'behaviors therapists' OR 'behaviors treatment' OR 'behaviors treatments' OR 'behavioral therapies' OR 'behavioral therapy' OR 'behavioral therapeutics' OR 'behavioral therapeutic' OR 'behavioral therapeutical' OR 'behavioral therapist' OR 'behavioral therapists' OR 'behavioral treatment' OR 'behavioral treatments' OR 'behaviour therapeutic' OR 'behaviour therapeutical' OR 'behaviour therapeutics' OR 'behaviour therapist' OR 'behaviour therapists' OR 'behaviour treatment' OR 'behaviour treatments' OR 'behaviours therapies' OR 'behaviours therapy' OR 'behaviours therapeutics' OR 'behaviours therapeutic' OR 'behaviours therapeutical' OR 'behaviours therapist' OR 'behaviours therapists' OR 'behaviours treatment' OR 'behaviours treatments' OR 'behavioural therapies' OR 'behavioural therapy' OR 'behavioural therapeutics' OR 'behavioural therapeutic' OR 'behavioural therapeutical' OR 'behavioural therapist' OR 'behavioural therapists' OR 'behavioural treatment' OR 'behavioural treatments' OR 'behaviour activation' OR 'behaviors activation' OR 'behavioral activation' OR 'behaviour activation' OR 'behaviours activation' OR 'behavioural activation' OR 'psychoanalytic therapy'/exp OR 'psychodynamic' OR 'psychodynamical' OR 'psychoanalysis' OR 'psychoanalytical' OR 'counselling'/exp OR 'counseling'/exp OR 'counselling' OR 'counseling' OR 'problem-solving' OR 'problem solving' OR 'supportive therapy' OR 'metacognitive therapy' OR 'metacognitive therapies' OR 'metacognitive therapeutic' OR 'metacognitive therapeutics' OR 'metacognitive therapeutical' OR 'metacognitive therapist' OR 'metacognitive therapists' OR 'metacognitive treatment' OR 'metacognitive treatments' OR 'meta-cognitive therapy' OR 'meta-cognitive therapies' OR 'meta-cognitive therapeutic' OR 'meta-cognitive therapeutics' OR 'meta-cognitive therapeutical' OR 'meta-cognitive therapist' OR 'meta-cognitive therapists' OR 'meta-cognitive treatment' OR 'meta-cognitive treatments' OR 'solution-focused therapies' OR 'solution focused therapies' OR 'solution-focussed therapy' OR 'solution focused therapy' OR 'solution-focused therapeutic' OR 'solution focused therapeutic' OR 'solution-focussed therapeutic' OR 'solution focused therapeutic' OR 'solution-focused therapeutics' OR 'solution focused therapeutics' OR 'solution-focussed therapeutics' OR 'solution focused therapeutics' OR 'solution-focused therapeutical' OR 'solution focused therapeutical' OR 'solution-focussed therapeutical' OR 'solution focused therapeutical' OR 'self-control therapies' OR 'self control therapies' OR 'self-control therapy' OR 'self control therapy' OR 'self-control therapeutics' OR 'self control therapeutics' OR 'self-control therapeutical' OR 'self control therapeutical' OR 'self-control therapeutic' OR 'self control therapeutic' OR 'self-control training' OR 'self control training' OR 'self control trainings' OR 'self-control trainings' OR 'mindfulness' OR 'acceptance commitment' OR 'acceptance and commitment' OR 'assertiveness training'

#2

'compassion-focused' OR 'compassion-focussed' OR 'compassion focused' OR 'compassion focussed' OR 'constructivist' OR 'constructivists'

#3

'therapies' OR 'therapy' OR 'therapeutics' OR 'therapist' OR 'treatment' OR 'treatments'

#4

Combine: #2 AND #3

#5: #1 OR #4

#6

'depressive disorder'/exp OR 'depression'/exp OR 'depressive' OR 'major depression'/exp OR 'major depressive disorder'/exp OR 'depression' OR 'depressions' OR 'depressive' OR 'dysthymic disorder'/exp OR 'dysthymic disorder' OR 'dysthymia'/exp OR 'dysthymic' OR 'mood disorder'/exp OR 'affective disorder'/exp OR 'affective disorder' OR 'affective disorders' OR 'mood disorder' OR 'mood disorders'

Combine: #5 AND #6

Limits: RCTs

Generic search strings used for PsycINFO in Jan 1, 2018 and Jan 1, 2019

(DE "Psychotherapy" OR "Psychotherapy" OR "psychotherapies" OR "psychotherapeutic" OR "psychotherapeutical" OR "psychotherapeutics" OR DE "Behavior Therapy" OR DE "Cognitive Behavior Therapy" OR "CBT" OR "behavior therapies" OR "behavior therapy" OR "behavior therapeutic" OR "behavior therapeutical" OR "behavior therapeutics" OR "behavior therapist" OR "behavior therapists" OR "behavior treatment" OR "behavior treatments" OR "behaviors therapies" OR "behaviors therapy" OR "behaviors therapeutics" OR "behaviors therapeutical" OR "behaviors therapist" OR "behaviors therapists" OR "behaviors treatment" OR "behaviors treatments" OR "behavioral therapies" OR "behavioral therapy" OR "behavioral therapeutics" OR "behavioral therapeutical" OR "behavioral therapist" OR "behavioral therapists" OR "behavioral treatment" OR "behavioral treatments" OR "behaviour therapies" OR "behaviour therapy" OR "behaviour therapeutic" OR "behaviour therapeutical" OR "behaviour therapeutics" OR "behaviour therapist" OR "behaviour therapists" OR "behaviour treatment" OR "behaviour treatments" OR "behaviours therapies" OR "behaviours therapy" OR "behaviours therapeutics" OR "behaviours therapeutical" OR "behaviours therapist" OR "behaviours therapists" OR "behaviours treatment" OR "behaviours treatments" OR "behavioural therapies" OR "behavioural therapy" OR "behavioural therapeutics" OR "behavioural therapeutical" OR "behavioural therapist" OR "behavioural therapists" OR "behavioural treatment" OR "behavioural treatments" OR "cognition therapies" OR "cognition therapy" OR "cognition therapeutic" OR "cognition therapeutical" OR "cognition therapist" OR "cognition therapists" OR "cognition treatment" OR "cognition treatments" OR "cognitive therapies" OR "cognitive therapy" OR "cognitive therapeutic" OR "cognitive therapeutics" OR "cognitive therapeutical" OR "cognitive therapist" OR "cognitive therapists" OR "cognitive treatment" OR "cognitive treatments" OR "cognitive restructuring" OR DE "Emotion Focused Therapy" OR DE "Psychoanalysis" OR "psychoanalysis" OR "psychoanalytic" OR "psychoanalytical" OR DE "Psychodynamic Psychotherapy" OR "psychodynamic" OR DE "Psychotherapeutic Counseling" OR "counselling" OR "counseling" OR "problem-solving" OR "problem solving" OR "mindfulness" OR ("acceptance" AND "commitment") OR "assertiveness training" OR "behavior activation" OR "behaviors activation" OR "behavioral activation" OR "behaviour activation" OR "behaviours activation" OR "behavioural activation" OR "metacognitive therapies" OR "metacognitive therapy" OR "metacognitive therapeutic" OR "metacognitive therapeutics" OR "metacognitive therapeutical" OR "metacognitive therapist" OR "metacognitive therapists" OR "metacognitive treatment" OR "metacognitive treatments" OR "meta-cognitive therapies" OR "meta-cognitive therapy" OR "meta-cognitive therapeutic" OR "meta-cognitive therapeutics" OR "meta-cognitive therapeutical" OR "meta-cognitive therapist" OR "meta-cognitive therapists" OR "meta-cognitive treatment" OR "meta-cognitive treatments" OR DE "Solution Focused Therapy" OR "solution-focused therapies" OR "solution-focused therapy" OR "solution-focused therapeutic" OR "solution-focused therapeutics" OR "solution-focused therapeutical" OR "solution-focussed therapies" OR "solution-focussed therapy" OR "solution-focussed therapeutic" OR "solution-focussed therapeutics" OR "solution-focussed therapeutical" OR "solution focused therapies" OR "solution focused therapy" OR "solution focused therapeutic" OR "solution focused therapeutics" OR "solution focused therapeutical" OR "solution focussed therapies" OR "solution focussed therapy" OR "solution focussed therapeutic" OR "solution focussed therapeutics" OR "solution focussed therapeutical" OR "self-control therapies" OR "self-control therapy" OR "self-control therapeutics" OR "self-control therapeutical" OR "self-control therapeutic" OR "self-control training" OR "self-control trainings" OR "self control therapies" OR "self control therapy" OR "self control therapeutics" OR "self control therapeutical" OR "self control therapeutic" OR "self control training" OR "self control trainings" OR ((("compassion-focused" OR "compassion-focussed" OR "compassion focused" OR "compassion focussed") AND ("therapies" OR "therapy" OR "therapeutic" OR "therapist" OR "therapists" OR "therapeut" OR "treatment" OR "treatments"))) OR ("constructivist" AND ("therapies" OR "therapy" OR "therapeutic" OR "therapist" OR "therapists" OR "therapeut" OR "treatment" OR "treatments")))

AND
(DE "Depression (Emotion)" "depressive disorder" OR "depression" OR "depressions" OR "depressive" OR DE "Major Depression" OR "major depression" OR "major depressive disorder" OR DE "Dysthymic Disorder" OR "Dysthymia" OR

" dysthymic disorder" OR DE "Affective Disorders" OR "Affective Disorder" OR "affective disorders" OR "Mood Disorder" OR "Mood disorders")

Limited to: Methodology is ME=(treatment outcome/clinical trial):

Generic search strings used for the Cochrane Library in Jan 1, 2018 and Jan 1, 2019

- #1 MeSH descriptor: [Depressive Disorder] explode all trees :
- #2 "depress*" (Word variations have been searched) :
- #3 #1 or #2 :
- #4 "major depressive disorder" (Word variations have been searched) :
- #5 #3 or #4 :
- #6 MeSH descriptor: [Dysthymic Disorder] explode all trees :
- #7 "dysthymi*" (Word variations have been searched) :
- #8 #6 or #7 :
- #9 #5 or #8 :
- #10 "mood disorder" (Word variations have been searched) :
- #11 "affective disorder" (Word variations have been searched) :
- #12 #10 or #11 :
- #13 #9 or #12 :
- #14 MeSH descriptor: [Psychotherapy] explode all trees :
- #15 "psychotherap*" (Word variations have been searched) :
- #16 "CBT" (Word variations have been searched) :
- #17 "Cognitive Behav* therap*" (Word variations have been searched) :
- #18 #14 or #15 or #16 or #17 :
- #19 "psychodynamic" (Word variations have been searched) :
- #20 MeSH descriptor: [Psychoanalysis] explode all trees :
- #21 "psychoanaly*" (Word variations have been searched) :
- #22 MeSH descriptor: [Counseling] explode all trees :
- #23 "counseling*" (Word variations have been searched) :
- #24 "problem solving" (Word variations have been searched) :
- #25 #18 or #19 or #20 or #21 or #22 or #23 or #24 :
- #26 "acceptance commitment" (Word variations have been searched) :
- #27 "assertiveness training" (Word variations have been searched) :
- #28 "behavior activation" (Word variations have been searched) :
- #29 "mindfulness" (Word variations have been searched) :
- #30 "metacognitive therap*" (Word variations have been searched) :
- #31 "solution focused therap*" (Word variations have been searched) :
- #32 "self control training" (Word variations have been searched):
- #33 #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32
- #34 "Randomized Controlled Trial":ti,ab,kw (Word variations have been searched) :
- #35 #13 and #33 and #34 in Trials:

Update search strings used for PubMed in August 30, 2018

((Internet[tiab] OR web[tiab] OR online[tiab] OR iCBT[tiab] OR i-CBT[tiab] OR eHealth[tiab] OR e-Health[tiab] OR cCBT[tiab] OR c-CBT[tiab] OR computer*[tiab] OR mHealth[tiab] OR m-Health[tiab] OR mobile[tiab] OR telehealth[tiab] OR tele-health[tiab] OR smartphone[tiab] OR "Smartphone"[Mesh] OR "Computers"[Mesh] OR MoodGym[tiab] OR GetOn[tiab] OR Get.On[tiab] OR Deprexis[tiab] OR MoodHacker[tiab] OR "Cancer Coping Online"[tiab] OR A-Chess[tiab] OR "This way up"[tiab] OR "Colour your life"[tiab] OR Diabetergestemd[tiab] OR MoodKit[tiab] OR "Beating the Blues"[tiab] OR FearFighter[tiab] OR "Online Therapy USER"[tiab] OR "Brighten your mood"[tiab] OR Brightenyourmood[tiab] OR Happy@work[tiab] OR Mom-net[tiab] OR WELL.ME[tiab] OR WELLME[tiab] OR "Therapy, Computer-Assisted"[Mesh] OR cyber*[tiab] OR SPARX[tiab] OR Kokoro*[tiab] OR "Act and Feel"[tiab] OR "Doe en Voel"[tiab] OR "Be a mom"[tiab] OR "Blues Before Birth"[tiab] OR "Kleur je Leven"[tiab] OR CONEMO[tiab] OR dbg.nl[tiab] OR Dcombat[tiab] OR e-couch[tiab] OR ecouch[tiab] OR BackCare-

D[tiab] OR feelbetter.org[tiab] OR GAF-ID[tiab] OR “guided act and feel”[tiab] OR “happy at work”[tiab] OR help4mood[tiab] OR helpID[tiab] OR iFightDepression[tiab] OR imbPST[tiab] OR “living to the full”[tiab] OR “master your mood”[tiab] OR “Grip op je dip”[tiab] OR MindReSolve[tiab] OR mom-net[tiab] OR MoodHelper[tiab] OR MoodHwb[tiab] OR HwbHwyliau[tiab] OR MoodManager[tiab] OR MumMoodBooster[tiab] OR myCompass[tiab] OR Netmums[tiab] OR Push-D[tiab] OR “Sadness Program”[tiab] OR “Smiling is fun”[tiab] OR “Space from Depression”[tiab] OR “Yo puedo sentirme bien”[tiab] OR “Taking Control”[tiab] OR “Alles Onder Controle”[tiab] OR “Tech Mother Care”[tiab] OR “Good Life Compass”[tiab] OR “Think Clearly About Depression”[tiab] OR Thrive[tiab] OR “Todac Todac”[tiab] OR “Tap Tap”[tiab] OR TreadWill[tiab] OR “Worry Less”[tiab] OR “Minder Zorgen”[tiab] OR Depressionhjalpen[tiab] OR Depressionhjälpen[tiab]) AND (depress*[ti] OR "Depression"[Mesh] OR "Depressive Disorder/therapy"[Mesh]) AND (CBT[tiab] OR iCBT[tiab] OR i-CBT[tiab] OR psychotherap*[tiab] OR (cognitive[tiab] AND behavio*[tiab]) OR therap*[tiab] OR "Behavior Therapy"[Mesh] OR intervention*[tiab]) AND (random*[tiab] OR pilot[tiab] OR "Randomized Controlled Trial" [Publication Type])) NOT (meta-analys*[ti] OR metaanalys*[ti] OR review*[ti] OR review[pt] OR Cochrane Database Syst Rev[ta])

Update search strings used for the Cochrane Library in August 30, 2018

(Internet OR web OR online OR iCBT OR i-CBT OR eHealth OR e-Health OR cCBT OR c-CBT OR computer* OR mHealth OR m-Health OR mobile OR telehealth OR tele-health OR smartphone OR cyber*):TI NOT INREVIEW

OR

(MoodGym OR GetOn OR Get.On OR Deprexis OR MoodHacker OR "Cancer Coping Online" OR A-Chess OR "This way up" OR "Colour your life" OR Diabetergestemd OR MoodKit OR "Beating the Blues" OR FearFighter OR "Online Therapy USER" OR "Brighten your mood" OR Brightenyourmood OR Happy@work OR Mom-net OR WELL.ME OR WELLME OR SPARX OR Kokoro* OR "Act and Feel" OR "Be a mom" OR "Blues before Birth" OR "Brighten your mood" OR "Kleur je leven" OR CONEMO OR dbg.nl OR diabetergestemd.nl OR Dcombat OR e-Couch OR ecouch OR BackCare-D OR FeelBetter.org OR GAF-ID OR "Guided act and feel" OR "Happy at work" OR Help4mood OR HelpID OR iFightDepression OR imbPST OR "Living life to the full" OR "master your mood" OR MindReSolve OR Mom-net OR MoodHelper OR MoodHwb OR HwbHwyliau OR MoodManager OR MumMoodBooster OR myCompass OR Netmums OR Push-D OR "Sadness Program" OR "Smiling is fun" OR "Space from depression" OR "Yo pseudo sentirme bien" OR "Taking Control" OR "Alles Onder Controle" OR "Tech Mother Care" OR "Good Life Compass" OR "Think Clearly About depression" OR Thrive OR "Todac Todac" OR "Tap Tap" OR TreadWill OR "Worry Less" OR "Minder Zorgen" OR Depressionhjalpen OR Depressionhjälpen):TI,AB NOT INREVIEW

AND

depress*:TI NOT INREVIEW

AND

(CBT OR iCBT OR i-CBT OR psychotherap* OR (cognitive AND behavio*) OR therap* OR intervention*):TI,KY NOT INREVIEW

2 Description of the statistical models

2.1 Pairwise meta-analyses

We performed pairwise meta-analyses of studies grouped by comparison. For AD studies we used published estimates of relative effects. For IPD studies, to adjust for missing outcomes, we used a multi-level multiple imputation method to create 10 datasets using the jomo package in R (Quartagno, 2019), i.e. taking into account the clustering of patients in studies. We estimated relative treatment effects in each multiply imputed dataset and combined estimates using Rubin's rules (Rubin, 1987).

- Quartagno M, Grund S, Carpenter J. jomo: A flexible package for two-level joint modelling multiple imputation. R Journal 2019; 11(2): 205-28.
- Rubin DB. Multiple Imputation for Nonresponse in Surveys. New York: John Wiley & Sons; 1987.

2.2 Aggregate data component NMA

We used a component NMA (cNMA) model first proposed by Welton et al. in the following paper:

- N.J. Welton, D.M. Caldwell, E. Adamopoulos, K. Vedhara Mixed treatment comparison meta-analysis of complex interventions: psychological interventions in coronary heart disease, Am J Epidemiol, 169 (2009), pp. 1158-1165

Below we provide a brief description of the model. Assume that study i compares treatment X (comprising component c_1 and c_2) and treatment Z (comprising component c_3 and c_4). Also assume that the estimated relative effect (mean difference) is y_i (at the aggregate level), and the corresponding variance is s_i^2 . Then the model is written as follows:

$$\begin{aligned} y_i &\sim N(\delta_i, s_i^2) \\ \delta_i &\sim \text{Normal}(d_Y - d_X, \tau^2) \\ d_X &= d_1 + d_2 \\ d_Z &= d_3 + d_4 \end{aligned}$$

Where τ is the standard deviation of the random effects in the network, assumed common for all treatment comparisons. Thus, a study that compares $c_1 + c_2 + c_3$ versus c_3 estimates the combined effect of c_1 and c_2 .

The parameters d_c show the benefit (or harm) of adding component c to the treatment.

In essence, this model assumes that for any given component c , the relative effects of $(c + X)$ vs. X are the same for any combination of components X (not including c). For example, this model assumes that the following studies are estimating the same relative effects: $c_1 + c_2$ versus c_2 ; $c_1 + c_3$ versus c_3 ; $c_1 + c_2 + c_3$ versus $c_2 + c_3$; etc. According to the additive model, all these studies are estimating the effect of adding c_1 to a treatment not including c_1 .

Likewise, studies comparing $c_1 + c_2$ versus c_3 are estimating the same effects, according to this model, as studies comparing $c_1 + c_2 + c_4$ versus $c_3 + c_4$. Thus, this model assumes that adding

the same component in both treatments of a comparison (any comparison) will not change the relative treatment effects.

Thus, if $d_c < 0$ (assuming that a smaller outcome is preferable), the model suggests that component c is beneficial and should always included in a treatment.

We call these d_c parameters incremental mean differences (iMD_c). For multi-arm trials we need to use multivariate distributions, as in the usual NMA model.

For the case of a binary outcome we use instead the binomial likelihood to model the probability of an event in each arm, and then we assume:

$$\text{logit}(p_i) = \begin{cases} \mu_i & \text{for intervention } X \\ \mu_i + \delta_i & \text{for intervention } Z \end{cases}$$

$$\delta_i \sim \text{Normal}(d_Z - d_X, \tau^2)$$

$$d_X = d_1 + d_2$$

$$d_Z = d_3 + d_4$$

The parameters d_c are now incremental log-odds ratios, and their exponents are the incremental odds ratio (iOR_c).

As in the case of pairwise analyses, we estimated relative treatment effects in each multiply imputed dataset of each study, and combined estimates using Rubin's rules before fitting the NMA model.

2.3 IPD component NMA

The model is set in a Bayesian setting and has two parts in the likelihood. One that corresponds to AD studies, and one that corresponds to IPD studies. The AD part is exactly as described in the previous section. The IPD part is described below:

Let us assume that study i compares two interventions X and Z , where X comprises components c_1 and c_2 and Z comprises components c_3 and c_4 . Let us assume that patient j in this study received treatment $treat_{ij}$ and had an observed outcome y_{ij} . Let us also assume that for this patient we have a set of patient-level covariates in the form of a vector \mathbf{x}_{ij} (standardized using the overall mean and standard deviation of each covariate across the whole dataset). The model can now be written as follows:

$$y_{ij} \sim N(\delta_{ij}, s^2)$$

$$\delta_{ij} = \begin{cases} u_j + \boldsymbol{\beta}\mathbf{x}_{ij} + \boldsymbol{\gamma}^{(c_1)}\mathbf{x}_{ij} + \boldsymbol{\gamma}^{(c_2)}\mathbf{x}_{ij} & , \text{ if } treat_{ij} = X = (c_1 + c_2) \\ u_j + \boldsymbol{\beta}\mathbf{x}_{ij} + \boldsymbol{\gamma}^{(c_3)}\mathbf{x}_{ij} + \boldsymbol{\gamma}^{(c_4)}\mathbf{x}_{ij} + \delta_j & , \text{ if } treat_{ij} = Z = (c_3 + c_4) \end{cases}$$

In this expression $\boldsymbol{\beta}$ is the vector of regression coefficients associated to the prognostic ability of \mathbf{x} . s^2 is the variance of y_{ij} . $\boldsymbol{\gamma}^{(c_x)}$ is the vector of regression coefficients for effect modification (component-covariate interaction), for component X . Parameter δ_j estimates the relative treatment effects at $\mathbf{x} = \mathbf{0}$. We assume that $\delta_j \sim N(d_3 + d_4 - d_2 - d_1, \tau^2)$, where τ denotes the

random effects standard deviation in the network. Note that β and γ are assumed to be fixed across studies, and that only δ has random effects. For multi-arm studies we use multivariate distributions. Aiming for a better generalizability of our findings, we use a Bayesian LASSO prior for the γ . This has the effect of shrinking the coefficients towards zero, thus avoiding issues related to overfitting.

- Seo M, White IR, Furukawa TA, Imai H, Valgimigli M, Egger M, Zwahlen M, Efthimiou O. Comparing methods for estimating patient-specific treatment effects in individual patient data meta-analysis. *Stat Med*. 2020 Dec 27. doi: 10.1002/sim.8859. Epub ahead of print. PMID: 33368415.

Parameters d_c are jointly estimated using the AD and IPD studies. For a dichotomous outcome we use a Bernoulli distribution.

The model described in this section is one-stage, i.e. all studies are analysed in a single step using the imputed datasets (see below).

2.4 Fitting details and software code used for fitting the models

Multiple imputations were performed using the jomo package in R

- Quartagno, M., Grund, S. & Carpenter, J. (2019). jomo: A flexible package for two-level joint modelling multiple imputation. *R Journal* 11, 205-228.

Imputation was performed while accounting for clustering of patients in the studies. For all Aggregate data analyses (models described in sections 2.1 and 2.2 of this appendix) we estimated treatment effects in each imputed dataset, and we then combined the 10 estimates using Rubin's rules.

For all Frequentist regular NMAs we used the netmeta command, in package netmeta in R. For all Frequentist AD cNMAs we used the discomb command in the netmeta package in R.

For the Bayesian cNMA combining AD and IPD studies (model described in Section 2.3) we fitted the model in each imputed dataset separately (i.e. including all AD and multiply-imputed IPD studies), using two independent chains with 1000 iterations after 500 burn-in. We assessed convergence for the analysis of each dataset by checking the mixing of the chains. The posterior estimates from the multiply-imputed datasets were combined to obtain a final posterior distribution of all parameters, as described here:

- Zhou, X. & Reiter, J. P. (2010). A note on Bayesian inference after multiple imputation. *The American Statistician* 64, 159-163.

All analyses were performed using the rjags package in R

- Plummer, M. (2018). rjags: Bayesian graphical models using MCMC. R package v. 4-8.

We used the following code in rjags for the continuous outcome.

```
model {
##### IPD studies #####
prec.pat<- 1/(sigma*sigma)
sigma~dnorm(0,0.1)I(0,)
for(i in 1:Npatients){y.ipd[i]~dnorm(muIPD[i],prec.pat)
muIPD[i]<- phi.IPD[studyIPD[i],armIPD[i]]+
```

beta.baseline*baseline[i]+beta.age*age[i]+beta.gender*gender[i]+beta.relat*relat[i]+

gamma.base[1]*cIPD_1[studyIPD[i],armIPD[i]]*baseline[i]+
gamma.base[3]*cIPD_3[studyIPD[i],armIPD[i]]*baseline[i]+
gamma.base[4]*cIPD_4[studyIPD[i],armIPD[i]]*baseline[i]+
gamma.base[5]*cIPD_5[studyIPD[i],armIPD[i]]*baseline[i]+
gamma.base[6]*cIPD_6[studyIPD[i],armIPD[i]]*baseline[i]+
gamma.base[7]*cIPD_7[studyIPD[i],armIPD[i]]*baseline[i]+
gamma.base[8]*cIPD_8[studyIPD[i],armIPD[i]]*baseline[i]+
gamma.base[9]*cIPD_9[studyIPD[i],armIPD[i]]*baseline[i]+
gamma.base[10]*cIPD_10[studyIPD[i],armIPD[i]]*baseline[i]+
gamma.base[11]*cIPD_11[studyIPD[i],armIPD[i]]*baseline[i]+
gamma.base[12]*cIPD_12[studyIPD[i],armIPD[i]]*baseline[i]+
gamma.base[13]*cIPD_13[studyIPD[i],armIPD[i]]*baseline[i]+
gamma.base[14]*cIPD_14[studyIPD[i],armIPD[i]]*baseline[i]+
gamma.base[15]*cIPD_15[studyIPD[i],armIPD[i]]*baseline[i]+
gamma.base[16]*cIPD_16[studyIPD[i],armIPD[i]]*baseline[i]+
gamma.base[17]*cIPD_17[studyIPD[i],armIPD[i]]*baseline[i]+

gamma.age[1]*cIPD_1[studyIPD[i],armIPD[i]]*age[i]+
gamma.age[3]*cIPD_3[studyIPD[i],armIPD[i]]*age[i]+
gamma.age[4]*cIPD_4[studyIPD[i],armIPD[i]]*age[i]+
gamma.age[5]*cIPD_5[studyIPD[i],armIPD[i]]*age[i]+
gamma.age[6]*cIPD_6[studyIPD[i],armIPD[i]]*age[i]+
gamma.age[7]*cIPD_7[studyIPD[i],armIPD[i]]*age[i]+
gamma.age[8]*cIPD_8[studyIPD[i],armIPD[i]]*age[i]+
gamma.age[9]*cIPD_9[studyIPD[i],armIPD[i]]*age[i]+
gamma.age[10]*cIPD_10[studyIPD[i],armIPD[i]]*age[i]+
gamma.age[11]*cIPD_11[studyIPD[i],armIPD[i]]*age[i]+
gamma.age[12]*cIPD_12[studyIPD[i],armIPD[i]]*age[i]+
gamma.age[13]*cIPD_13[studyIPD[i],armIPD[i]]*age[i]+
gamma.age[14]*cIPD_14[studyIPD[i],armIPD[i]]*age[i]+
gamma.age[15]*cIPD_15[studyIPD[i],armIPD[i]]*age[i]+
gamma.age[16]*cIPD_16[studyIPD[i],armIPD[i]]*age[i]+
gamma.age[17]*cIPD_17[studyIPD[i],armIPD[i]]*age[i]+

gamma.gender[1]*cIPD_1[studyIPD[i],armIPD[i]]*gender[i]+
gamma.gender[3]*cIPD_3[studyIPD[i],armIPD[i]]*gender[i]+
gamma.gender[4]*cIPD_4[studyIPD[i],armIPD[i]]*gender[i]+
gamma.gender[5]*cIPD_5[studyIPD[i],armIPD[i]]*gender[i]+
gamma.gender[6]*cIPD_6[studyIPD[i],armIPD[i]]*gender[i]+
gamma.gender[7]*cIPD_7[studyIPD[i],armIPD[i]]*gender[i]+
gamma.gender[8]*cIPD_8[studyIPD[i],armIPD[i]]*gender[i]+
gamma.gender[9]*cIPD_9[studyIPD[i],armIPD[i]]*gender[i]+
gamma.gender[10]*cIPD_10[studyIPD[i],armIPD[i]]*gender[i]+
gamma.gender[11]*cIPD_11[studyIPD[i],armIPD[i]]*gender[i]+
gamma.gender[12]*cIPD_12[studyIPD[i],armIPD[i]]*gender[i]+
gamma.gender[13]*cIPD_13[studyIPD[i],armIPD[i]]*gender[i]+
gamma.gender[14]*cIPD_14[studyIPD[i],armIPD[i]]*gender[i]+
gamma.gender[15]*cIPD_15[studyIPD[i],armIPD[i]]*gender[i]+
gamma.gender[16]*cIPD_16[studyIPD[i],armIPD[i]]*gender[i]+
gamma.gender[17]*cIPD_17[studyIPD[i],armIPD[i]]*gender[i]+

gamma.relat[1]*cIPD_1[studyIPD[i],armIPD[i]]*relat[i]+
gamma.relat[3]*cIPD_3[studyIPD[i],armIPD[i]]*relat[i]+
gamma.relat[4]*cIPD_4[studyIPD[i],armIPD[i]]*relat[i]+
gamma.relat[5]*cIPD_5[studyIPD[i],armIPD[i]]*relat[i]+
gamma.relat[6]*cIPD_6[studyIPD[i],armIPD[i]]*relat[i]+
gamma.relat[7]*cIPD_7[studyIPD[i],armIPD[i]]*relat[i]+
gamma.relat[8]*cIPD_8[studyIPD[i],armIPD[i]]*relat[i]+
gamma.relat[9]*cIPD_9[studyIPD[i],armIPD[i]]*relat[i]+
gamma.relat[10]*cIPD_10[studyIPD[i],armIPD[i]]*relat[i]+
gamma.relat[11]*cIPD_11[studyIPD[i],armIPD[i]]*relat[i]+
gamma.relat[12]*cIPD_12[studyIPD[i],armIPD[i]]*relat[i]+
gamma.relat[13]*cIPD_13[studyIPD[i],armIPD[i]]*relat[i]+
gamma.relat[14]*cIPD_14[studyIPD[i],armIPD[i]]*relat[i]+
gamma.relat[15]*cIPD_15[studyIPD[i],armIPD[i]]*relat[i]+
gamma.relat[16]*cIPD_16[studyIPD[i],armIPD[i]]*relat[i]+

```

gamma.relat[17]*cIPD_17[studyIPD[i],armIPD[i]]*relat[i]
}

for(i in 1:Ns.IPD) {
w1[i,1]<- 0
deltal[i,1]<- 0
for (k in 1:naIPD[i]) { phi.IPD[i,k]<-uIPD[i]+deltal[i,k]}
for (k in 2:naIPD[i]) {
deltal[i,k] ~ dnorm(md1[i,k],precd1[i,k])
md1[i,k] <- mean1[i,k] + sw1[i,k]
precd1[i,k] <- 2*prect*(k-1)/k
w1[i,k] <- (deltal[i,k] - mean1[i,k] )
sw1[i,k] <-sum(w1[i,1:(k-1)])/(k-1)

##consistency equations
mean1[i,k] <-AIPD[i,k]-BIPD[i]
AIPD[i,k]<-
d[1]*(1-equals(cIPD_1[i,k],0)) +
d[3]*(1-equals(cIPD_3[i,k],0)) + d[4]*(1-equals(cIPD_4[i,k],0)) +
d[5]*(1-equals(cIPD_5[i,k],0)) + d[6]*(1-equals(cIPD_6[i,k],0)) +
d[7]*(1-equals(cIPD_7[i,k],0)) + d[8]*(1-equals(cIPD_8[i,k],0)) +
d[9]*(1-equals(cIPD_9[i,k],0)) + d[10]*(1-equals(cIPD_10[i,k],0))+
d[11]*(1-equals(cIPD_11[i,k],0)) + d[12]*(1-equals(cIPD_12[i,k],0))+
d[13]*(1-equals(cIPD_13[i,k],0)) + d[14]*(1-equals(cIPD_14[i,k],0))+
d[15]*(1-equals(cIPD_15[i,k],0)) + d[16]*(1-equals(cIPD_16[i,k],0))+
d[17]*(1-equals(cIPD_17[i,k],0))
}
BIPD[i]<-
d[1]*(1-equals(cIPD_1[i,1],0)) +
d[3]*(1-equals(cIPD_3[i,1],0)) + d[4]*(1-equals(cIPD_4[i,1],0)) +
d[5]*(1-equals(cIPD_5[i,1],0)) + d[6]*(1-equals(cIPD_6[i,1],0)) +
d[7]*(1-equals(cIPD_7[i,1],0)) + d[8]*(1-equals(cIPD_8[i,1],0)) +
d[9]*(1-equals(cIPD_9[i,1],0)) + d[10]*(1-equals(cIPD_10[i,1],0)) +
d[11]*(1-equals(cIPD_11[i,1],0))+ d[12]*(1-equals(cIPD_12[i,1],0))+
d[13]*(1-equals(cIPD_13[i,1],0)) + d[14]*(1-equals(cIPD_14[i,1],0))+
d[15]*(1-equals(cIPD_15[i,1],0)) +d[16]*(1-equals(cIPD_16[i,1],0))+
d[17]*(1-equals(cIPD_17[i,1],0))
}

#### AD studies #####
for(i in 1:Ns) {
w[i,1]<- 0
delta[i,1]<- 0

for (k in 1:na[i]) {
se[i,k]<-sd[i,k]/sqrt(n[i,k])
prec[i,k]<- (1/(se[i,k]*se[i,k]))
y[i,k]~dnorm(phi[i,k],prec[i,k])
phi[i,k]<-u[i]+delta[i,k]
}

for (k in 2:na[i]) {
delta[i,k] ~ dnorm(md[i,k],precd[i,k])
md[i,k] <- mean[i,k] + sw[i,k]
precd[i,k] <- 2*prect*(k-1)/k
w[i,k] <- (delta[i,k] - mean[i,k] )
sw[i,k] <-sum(w[i,1:(k-1)])/(k-1)

##consistency equations
mean[i,k] <-A1[i,k]-B1[i]
A1[i,k]<-
d[1]*(1-equals(c1[i,k],0)) +
d[3]*(1-equals(c3[i,k],0)) + d[4]*(1-equals(c4[i,k],0)) +
d[5]*(1-equals(c5[i,k],0)) + d[6]*(1-equals(c6[i,k],0)) +
d[7]*(1-equals(c7[i,k],0)) + d[8]*(1-equals(c8[i,k],0)) +
d[9]*(1-equals(c9[i,k],0)) + d[10]*(1-equals(c10[i,k],0))+
d[11]*(1-equals(c11[i,k],0)) + d[12]*(1-equals(c12[i,k],0))+

```

```

d[13]*(1-equals(c13[i,k],0)) + d[14]*(1-equals(c14[i,k],0))+
d[15]*(1-equals(c15[i,k],0)) + d[16]*(1-equals(c16[i,k],0))+
d[17]*(1-equals(c17[i,k],0))
}
B1[i]<-
d[1]*(1-equals(c1[i,1],0)) +
d[3]*(1-equals(c3[i,1],0)) + d[4]*(1-equals(c4[i,1],0)) +
d[5]*(1-equals(c5[i,1],0)) + d[6]*(1-equals(c6[i,1],0)) +
d[7]*(1-equals(c7[i,1],0)) + d[8]*(1-equals(c8[i,1],0)) +
d[9]*(1-equals(c9[i,1],0)) + d[10]*(1-equals(c10[i,1],0)) +
d[11]*(1-equals(c11[i,1],0))+ d[12]*(1-equals(c12[i,1],0))+
d[13]*(1-equals(c13[i,1],0))+ d[14]*(1-equals(c14[i,1],0))+
d[15]*(1-equals(c15[i,1],0)) +d[16]*(1-equals(c16[i,1],0))+
d[17]*(1-equals(c17[i,1],0))
}
##prior distribution for baseline arm of study i
for (i in 1:Ns) { u[i] ~ dnorm(0,.001) }
for (i in 1:Ns.IPD) { uIPD[i] ~ dnorm(0,.001) }

##prior distribution for heterogeneity
tau ~ dnorm(0,0.1)I(0,)
prect<- 1/tau.sq
tau.sq<- pow(tau,2)

##prior distribution for basic parameters
for(k in 1:Nc) {d[k] ~ dnorm(0,.001)}

## prior distribution for penalization of gamma
lambda ~ dgamma(1, 0.1)
for(k in 1:Nc){
gamma.base[k] ~ ddexp(0, lambda)
gamma.age[k] ~ ddexp(0, lambda)
gamma.gender[k] ~ ddexp(0, lambda)
gamma.relat[k] ~ ddexp(0, lambda)
}
beta.baseline~dnorm(0,1)
beta.age~dnorm(0,1)
beta.relat~dnorm(0,1)
beta.gender~dnorm(0,1)

```

2.5 Assumption of MAR

The analyses described above assumed outcomes were missing at random (MAR) ³⁷. Following the protocol, for studies with large dropout rates in one or more of their arms (i.e. dropout \geq 50%) we explored the impact of missing outcomes being not at random (MNAR). If we deemed that different models led to results that were clinically very different (i.e. having substantially different clinical implications), these studies were removed from analysis of depression severity.

2.6 Component NMA model with interactions among components

The primary cNMA model assumes additivity of the component effects. If this assumption does not hold, the model will be biased. This will be the case when components interact with each other, either synergistically or antagonistically.

Conversely, a full interaction model (i.e one that assumes interaction terms between any two components, but also three-way interactions etc) could not be estimated in practice. This would correspond to performing a network meta-analysis on the network plot shown in section 12.1 of

this appendix, where each combination is a distinct node. This network cannot be estimated because it is disconnected – but even if it was connected the analysis would be problematic due to low power, and due to the fact that it would not take into account the possible similarities between the different combinations. Assuming additivity enables us to analyse the data, but, as noted, the model may be biased if there are in truth component interactions.

A middle-ground solution between the full interaction model and the additive model would be to assume two-way interactions between the different components in the network. Given that there are 17 components (including drug therapy) there would be a total of $17 \times 16 / 2 = 136$ parameters to estimate. This is also problematic, given the low number of studies. Instead, we could build a model including a single interaction term; but we would then need to choose among these 136 models.

To address this issue, we used a sensitivity analysis, where the main idea is to include all 136 two-way interactions in the model, and use a Bayesian variable selection method to select the most prominent ones. This method has the effect of shrinking to zero all interactions for which there was no evidence, while keeping in the model interactions for which there was substantial evidence in the data.

To do this, we modify the model of Section 2.2 as follows:

$$y_i \sim N(\delta_i, s_i^2)$$

$$\delta_i \sim \text{Normal}(d_Z - d_X, \tau^2)$$

$$d_X = d_1 + d_2 + d_{1*2}$$

$$d_Z = d_3 + d_4 + d_{3*4}$$

We then assume a Bayesian LASSO prior on all interaction terms, i.e. we assume the following prior distribution for the interaction between components p and q :

$$\pi(d_{p*q}) = \frac{\lambda}{2} e^{-\lambda |d_{p,q}|}$$

The parameter λ determines the amount of shrinkage performed to the interaction terms. For fitting purposes, we can treat λ as a random parameter and assign an informative hyperprior, $\lambda^{-1} \sim U(0,5)$.

3 Changes from the protocol

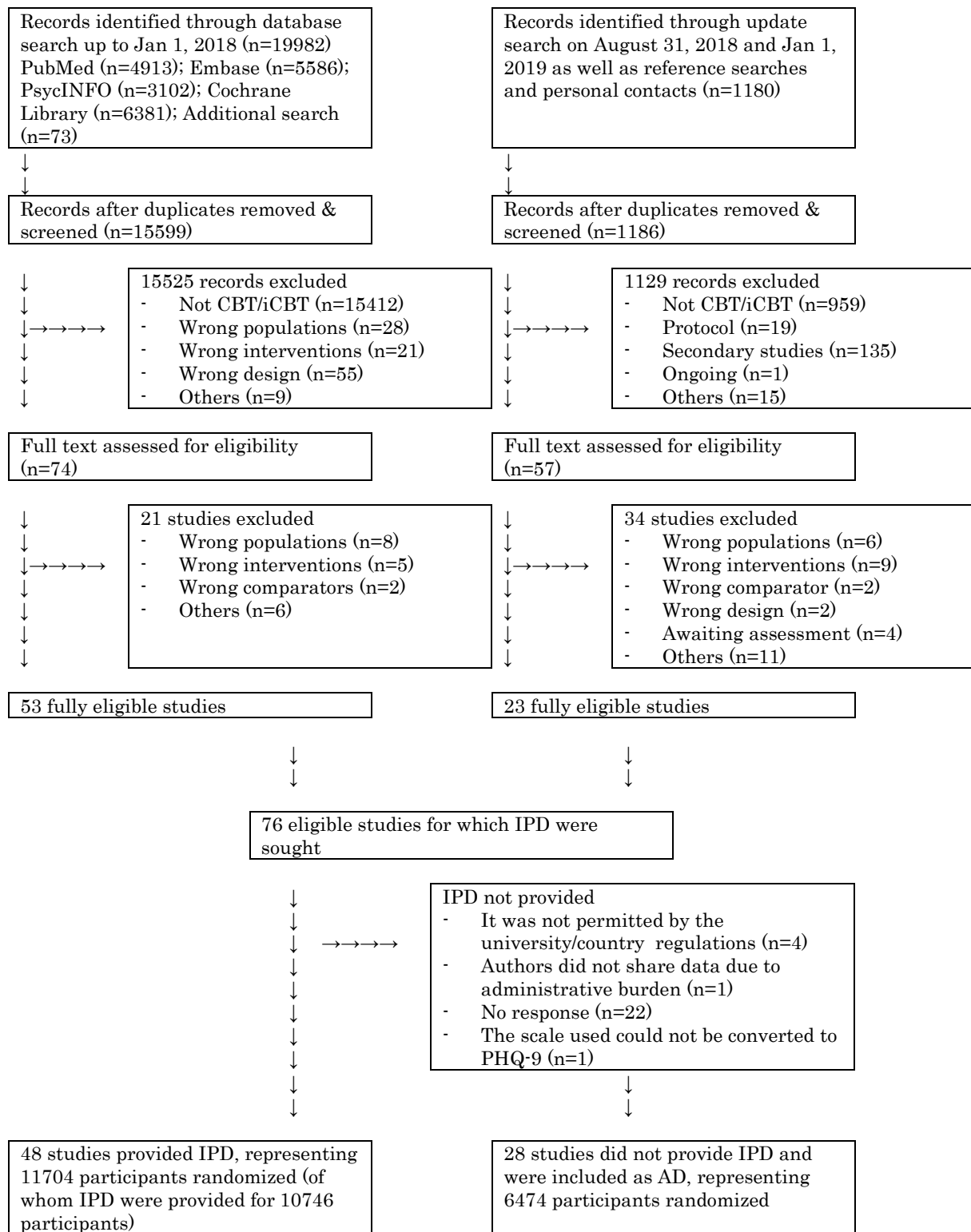
Given the nature of the available data, we were obliged to implement the following changes to the protocol.

1. For the IPD cNMA model, instead of taking an initial step to identify possible covariates that interact with each component, we included all available covariates in the model (see description of the model in Section 12 of this appendix). The reason was that only a few covariates were available in most of the studies, i.e. age, baseline severity, gender and relationship status.
2. For the secondary outcome of dropout from treatment, in the protocol we had specified: *“For the secondary outcome ‘dropout from the treatment’, we will use a different modelling approach. This is because, by definition, for the inactive control conditions, treatment dropout is not observed. This implies that in studies with inactive controls, we cannot infer about relative effects. Such studies are expected to represent the vast majority of all eligible studies. Thus, for the analysis of this outcome, we will synthesise absolute treatment effects. We will model the probability of dropout for each active treatment, using a generalised linear model with a binomial likelihood”*. However, our search found 15 studies that compared active treatments in terms of dropout for treatment. Given this relatively large number of studies, we decided to synthesize relative effects via a component NMA for this outcome, similarly to the primary outcome.
3. The secondary outcome of dropout from the end-of-treatment assessment for any reason was examined but, due to the word limits, is reported in the Appendix only. See Appendix 15.

The following two sensitivity analyses were added post-hoc, in response to the reviewers’ comments.

4. A sensitivity analysis excluding arms which taught more than four CBT components. See Appendix 15.
5. We also examined a model that assumed two-way interactions between the components. See Appendix 16.

4 PRISMA flowchart



Studies were classified as “awaiting assesement” when enough details could not be obtained in the reports or through contacts with the authors whether the study was definitely eligible or ineligible.

5 List of the included studies, excluded studies (with reasons) and studies awaiting assessment

5.1 References for the included studies

* indicate studies for which individual participant data were available.

Andersson2005*

- Andersson, G., Bergström, J., Holländare, F., Carlbring, P. E. R., Kaldø, V., & Ekselius, L. (2005). Internet-based self-help for depression: randomised controlled trial. *The British Journal of Psychiatry*, 187(5), 456-461
- Communication with Andersson: while it was not possible to ask people to stay online for longer periods [and] we did recommend printing, it would be a mistake to name our ICBT approach something else.

Arean2016

- Arean, P. A., Hallgren, K. A., Jordan, J. T., Gazzaley, A., Atkins, D. C., Heagerty, P. J., & Anguera, J. A. (2016). The use and effectiveness of mobile apps for depression: results from a fully remote clinical trial. *Journal of medical Internet research*, 18(12).
- Communication with Anguera: the trial was fully randomized, and the main study arms were really the individuals who had iPads, the others were experimental arms.

Beevers2017

- C. G., Pearson, R., Hoffman, J. S., Foulser, A. A., Shumake, J., & Meyer, B. (2017). Effectiveness of an internet intervention (Deprexis) for depression in a United States adult sample: A parallel-group pragmatic randomized controlled trial. *Journal of consulting and clinical psychology*, 85(4), 367.

Berger2011*

- Berger, T., Hämmerli, K., Gubser, N., Andersson, G., & Caspar, F. (2011). Internet-based treatment of depression: a randomized controlled trial comparing guided with unguided self-help. *Cognitive behaviour therapy*, 40(4), 251-266.

Birney2016

- Birney, A. J., Gunn, R., Russell, J. K., & Ary, D. V. (2016). MoodHacker mobile web app with email for adults to self-manage mild-to-moderate depression: randomized controlled trial. *JMIR mHealth and uHealth*, 4(1).

Boele2018*

- Boele, F. W., Klein, M., Verdonck-de Leeuw, I. M., Cuijpers, P., Heimans, J. J., Snijders, T. J., ... & Reijneveld, J. C. (2018). Internet-based guided self-help for glioma patients with depressive symptoms: a randomized controlled trial. *Journal of neuro-oncology*, 137(1), 191-203.
- Communication with Boele: there was no face-to-face element.

Boeschoten2017

- Boeschoten, R. E., Dekker, J., Uitdehaag, B. M., Beekman, A. T., Hoogendoorn, A. W., Collette, E. H., ... & van Oppen, P. (2017). Internet-based treatment for depression in multiple sclerosis: A randomized controlled trial. *Multiple Sclerosis Journal*, 23(8), 1112-1122.
- Communication with Boeschoten for additional details about subgroups with or without text messages

Buntrock2015*

- Buntrock, C., Ebert, D., Lehr, D., Riper, H., Smit, F., Cuijpers, P., & Berking, M. (2015). Effectiveness of a web-based cognitive behavioural intervention for subthreshold depression: pragmatic randomised controlled trial. *Psychotherapy and psychosomatics*, 84(6), 348-358.
- Communication with Cuijpers: GET.ON belong to the therapeutic guidance category.

Burton2016

- Burton, C., Szentagotai Tatar, A., McKinstry, B., Matheson, C., Matu, S., Moldovan, R., ... & Serrano Blanco, A. (2016). Pilot randomised controlled trial of Help4Mood, an embodied virtual agent-based system to support treatment of depression. *Journal of telemedicine and telecare*, 22(6), 348-355.

Carlbring2013*

- Carlbring, P., Hägglund, M., Luthström, A., Dahlin, M., Kadowaki, Å., Vernmark, K., & Andersson, G. (2013). Internet-based behavioral activation and acceptance-based treatment for depression: a randomized controlled trial. *Journal of Affective Disorders*, 148(2-3), 331-337.

Choi2012*

- Choi, I., Zou, J., Titov, N., Dear, B. F., Li, S., Johnston, L., ... & Hunt, C. (2012). Culturally attuned Internet treatment for depression amongst Chinese Australians: a randomised controlled trial. *Journal of affective disorders*, 136(3), 459-468.
- Communication with Andrews: This was similar to Perini study except for the use of forums for the fear of compromised confidentiality.

Christensen2004*

- Christensen, H., Griffiths, K. M., & Jorm, A. F. (2004). Delivering interventions for depression by using the internet: randomised controlled trial. *Bmj*, 328(7434), 265.

Cooper2011

- Cooper, C. L., Hind, D., Parry, G. D., Isaac, C. L., Dimairo, M., O'Cathain, A., ... & Thake, A. (2011). Computerised cognitive behavioural therapy for the treatment of depression in people with multiple sclerosis: external pilot trial. *Trials*, 12(1), 259.
- Communication with Cooper: participants were randomised to either cCBT or TAU and all those randomised to cCBT accessed the software at home.

Dahne2018*

- Dahne, J., Lejuez, C.W., Diaz, V.A., Player, M.S., Kustanowitz, J., Felton, J.W., Carpenter, M.J. (2019). Pilot randomized trial of a self-help behavioral activation mobile application for utilization in primary care. *Behavior Therapy*, <https://doi.org/10.1016/j.beth.2018.12.003>.

Day2013

- Day, V., McGrath, P. J., & Wojtowicz, M. (2013). Internet-based guided self-help for university students with anxiety, depression and stress: a randomized controlled clinical trial. *Behaviour research and therapy*, 51(7), 344-351.

deGraaf2009*

- De Graaf, L. E., Gerhards, S. A. H., Arntz, A., Riper, H., Metsemakers, J. F. M., Evers, S. M. A. A., ... & Huibers, M. J. H. (2009). Clinical effectiveness of online computerised

cognitive-behavioural therapy without support for depression in primary care: randomised trial. *The British Journal of Psychiatry*, 195(1), 73-80.

- Communication with Cuijpers: “Colour Your Life” belong to the therapeutic guidance category.

Ebert2014*

- Ebert, D. D., Lehr, D., Baumeister, H., Boß, L., Riper, H., Cuijpers, P., ... & Berking, M. (2014). GET. ON Mood Enhancer: efficacy of Internet-based guided self-help compared to psychoeducation for depression: an investigator-blinded randomised controlled trial. *Trials*, 15(1), 39.

Ebert2017

- Ebert, D. D., Lehr, D., Boß, L., Riper, H., Cuijpers, P., Andersson, G., ... & Berking, M. (2014). Efficacy of an internet-based problem-solving training for teachers: results of a randomized controlled trial. *Scandinavian journal of work, environment & health*, 582-596.
- Communication with Cuijpers: “Alles Onder Controle” belong to the therapeutic guidance category.

Ebert2018*

- Ebert, D. D., Buntrock, C., Lehr, D., Smit, F., Riper, H., Baumeister, H., ... & Berking, M. (2018). Effectiveness of web- and mobile-based treatment of subthreshold depression with adherence-focused guidance: a single-blind randomized controlled trial. *Behavior therapy*, 49(1), 71-83.
- Communication with Cuijpers: “GET.ON” belongs to the therapeutic guidance category.

Farrer2011*

- Farrer, L., Christensen, H., Griffiths, K. M., & Mackinnon, A. (2011). Internet-based CBT for depression with and without telephone tracking in a national helpline: randomised controlled trial. *PloS one*, 6(11), e28099.
- Communication with Farrer : No compulsory homework for participants in the MoodGYM.. Some modules did contain suggested exercises that a participant could complete if they wanted to.

Forand2018*

- Forand, N. R., Barnett, J. G., Strunk, D. R., Hindiyeh, M. U., Feinberg, J. E., & Keefe, J. R. (2018). Efficacy of guided iCBT for depression and mediation of change by cognitive skill acquisition. *Behavior therapy*, 49(2), 295-307.

Forsell2017*

- Forsell, E., Bendix, M., Holländare, F., von Schultz, B. S., Nasiell, J., Blomdahl-Wetterholm, M., ... & Jokinen, J. (2017). Internet delivered cognitive behavior therapy for antenatal depression: a randomised controlled trial. *Journal of affective disorders*, 221, 56-64.

Geraedts2014*

- Geraedts, A. S., Kleiboer, A. M., Wiezer, N. M., van Mechelen, W., & Cuijpers, P. (2014). Short-term effects of a web-based guided self-help intervention for employees with depressive symptoms: randomized controlled trial. *Journal of medical Internet research*, 16(5).

Gilbody2015*

- Gilbody, S., Littlewood, E., Hewitt, C., Brierley, G., Tharmanathan, P., Araya, R., ... & Kessler, D. (2015). Computerised cognitive behaviour therapy (cCBT) as treatment for depression in primary care (REEACT trial): large scale pragmatic randomised controlled trial. *Bmj*, 351, h5627.

Gilbody2017*

- Gilbody, S., Brabyn, S., Lovell, K., Kessler, D., Devlin, T., Smith, L., ... & Knowles, S. (2017). Telephone-supported computerised cognitive-behavioural therapy: REEACT-2 large-scale pragmatic randomised controlled trial. *The British journal of psychiatry*, 210(5), 362-367.
- Brabyn S, Araya R, Barkham M, Bower P, Cooper C, Duarte A, Kessler D, Knowles S, Lovell K, Littlewood E, Mattock R, Palmer S, Pervin J, Richards D, Tallon D, White D, Walker S, Worthy G & Gilbody S (2016) The second Randomised Evaluation of the Effectiveness, cost-effectiveness and Acceptability of Computerised Therapy (REEACT-2) trial: does the provision of telephone support enhance the effectiveness of computer-delivered cognitive behaviour therapy? A randomised controlled trial. *Health Technology Assessment*, 20, 1-64.

Glozier2013

- Glozier, N., Christensen, H., Naismith, S., Cockayne, N., Donkin, L., Neal, B., ... & Hickie, I. (2013). Internet-delivered cognitive behavioural therapy for adults with mild to moderate depression and high cardiovascular disease risks: a randomised attention-controlled trial. *PloS one*, 8(3), e59139.

Griffiths2012

- Griffiths, K. M., Mackinnon, A. J., Crisp, D. A., Christensen, H., Bennett, K., & Farrer, L. (2012). The effectiveness of an online support group for members of the community with depression: a randomised controlled trial. *PloS one*, 7(12), e53244.

Hadjistavropoulos2017*

- Hadjistavropoulos HD, Schneider LH, Edmonds M, Karin E, Nugent MN, Dirkse D, Dear BF, Titov N. (2017). Randomized controlled trial of internet-delivered cognitive behaviour therapy comparing standard weekly versus optional weekly therapist support. *J Anxiety Disord*, 52, 15-24.
- Communication with Hadjistavropoulos: participants were strongly encouraged to complete the assignments, and the therapists always asked patients how they were doing with their homework, while emailing their therapist about the homework was optional.

Hur2018

- Hur, J. W., Kim, B., Park, D., & Choi, S. W. (2018). A Scenario-Based Cognitive Behavioral Therapy Mobile App to Reduce Dysfunctional Beliefs in Individuals with Depression: A Randomized Controlled Trial. *Telemedicine and e-Health*.

Johansson2012*

- Johansson, R., Sjöberg, E., Sjögren, M., Johnsson, E., Carlbring, P., Andersson, T., ... & Andersson, G. (2012). Tailored vs. standardized internet-based cognitive behavior therapy for depression and comorbid symptoms: a randomized controlled trial. *PloS one*, 7(5), e36905.
- Communication with Andersson: the program was interactive and had features such as quiz.

Kenter2016*

- Kenter, R. M. F., Cuijpers, P., Beekman, A., & van Straten, A. (2016). Effectiveness of a web-based guided self-help intervention for outpatients with a depressive disorder: short-term results from a randomized controlled trial. *Journal of medical Internet research*, 18(3).

Kivi2014*

- Kivi, M., Eriksson, M. C., Hange, D., Petersson, E. L., Vernmark, K., Johansson, B., & Björkelund, C. (2014). Internet-based therapy for mild to moderate depression in Swedish primary care: short term results from the PRIM-NET randomized controlled trial. *Cognitive behaviour therapy*, 43(4), 289-298.
- Communication with Carlbing: Therapeutic guidance related to the treatment content may be provided on a scheduled basis or as-needed basis. Provision of technical support only was not counted towards this component.

Kleiboer2015*

- Kleiboer, A., Donker, T., Seekles, W., van Straten, A., Riper, H., & Cuijpers, P. (2015). A randomized controlled trial on the role of support in Internet-based problem solving therapy for depression and anxiety. *Behaviour research and therapy*, 72, 63-71.
- Communication with Cuijpers: "Alles Onder Controle" belong to the therapeutic guidance category.

Klein2016*

- Klein, J. P., Berger, T., Schröder, J., Späth, C., Meyer, B., Caspar, F., ... & Hautzinger, M. (2016). Effects of a psychological internet intervention in the treatment of mild to moderate depressive symptoms: results of the EVIDENT study, a randomized controlled trial. *Psychotherapy and psychosomatics*, 85(4), 218-228.

Lambert2018

- Lambert, J. D., Greaves, C. J., Farrand, P., Price, L., Haase, A. M., & Taylor, A. H. (2018). Web-based intervention using behavioral activation and physical activity for adults with depression (The eMotion study): Pilot randomized controlled trial. *Journal of medical Internet research*, 20(7).

Lappalainen2015

- Lappalainen, P., Langrial, S., Oinas-Kukkonen, H., Tolvanen, A., & Lappalainen, R. (2015). Web-based acceptance and commitment therapy for depressive symptoms with minimal support: a randomized controlled trial. *Behavior modification*, 39(6), 805-834.

Lintvedt2013*

- Lintvedt, O. K., Griffiths, K. M., Sørensen, K., Østvik, A. R., Wang, C. E., Eisemann, M., & Waterloo, K. (2013). Evaluating the effectiveness and efficacy of unguided internet-based self-help intervention for the prevention of depression: a randomized controlled trial. *Clinical psychology & psychotherapy*, 20(1), 10-27.

Löbner 2018

- Löbner, M., Pabst, A., Stein, J., Dorow, M., Matschinger, H., Luppä, M., ... & Riedel-Heller, S. G. (2018). Computerized cognitive behavior therapy for patients with mild to moderately severe depression in primary care: a pragmatic cluster randomized controlled trial (@ktiv). *Journal of affective disorders*.

Ludgren2016*

- Lundgren, J. G., Dahlström, Ö., Andersson, G., Jaarsma, T., Köhler, A. K., & Johansson, P. (2016). The effect of guided web-based cognitive behavioral therapy on patients with depressive symptoms and heart failure: a pilot randomized controlled trial. *Journal of medical Internet research*, 18(8).

Ly2014*

- Ly, K. H., Trüschel, A., Jarl, L., Magnusson, S., Windahl, T., Johansson, R., ... & Andersson, G. (2014). Behavioural activation versus mindfulness-based guided self-help treatment administered through a smartphone application: a randomised controlled trial. *BMJ open*, 4(1), e003440.

Mantani2017*

- Mantani, A., Kato, T., Furukawa, T. A., Horikoshi, M., Imai, H., Hiroe, T., ... & Kawanishi, N. (2017). Smartphone cognitive behavioral therapy as an adjunct to pharmacotherapy for refractory depression: randomized controlled trial. *Journal of medical Internet research*, 19(11).

Meyer2015*

- Meyer, B., Bierbrodt, J., Schröder, J., Berger, T., Beevers, C. G., Weiss, M., ... & Hautzinger, M. (2015). Effects of an internet intervention (Deprexis) on severe depression symptoms: randomized controlled trial. *Internet Interventions*, 2(1), 48-59.

Milgrom2016*

- Milgrom, J., Danaher, B. G., Gemmill, A. W., Holt, C., Holt, C. J., Seeley, J. R., ... & Ericksen, J. (2016). Internet cognitive behavioral therapy for women with postnatal depression: a randomized controlled trial of MumMoodBooster. *Journal of medical Internet research*, 18(3).

Mohr2013*

- Mohr, D. C., Duffecy, J., Ho, J., Kwasny, M., Cai, X., Burns, M. N., & Begale, M. (2013). A randomized controlled trial evaluating a manualized TeleCoaching protocol for improving adherence to a web-based intervention for the treatment of depression. *PloS one*, 8(8), e70086.

Montero-Marin2016*

- Montero-Marín, J., Araya, R., Pérez-Yus, M. C., Mayoral, F., Gili, M., Botella, C., ... & Nogueira-Arjona, R. (2016). An internet-based intervention for depression in primary Care in Spain: a randomized controlled trial. *Journal of medical Internet research*, 18(8).

Morthland2011

- Morthland, M. P. (2011). *Technology assisted intervention for improving mood: a portable computer-assisted therapy program for treating depression in older adults* (Doctoral dissertation, University of Alabama Libraries).

Newby2017

- Newby, J., Robins, L., Wilhelm, K., Smith, J., Fletcher, T., Gillis, I., ... & Andrews, G. (2017). Web-based cognitive behavior therapy for depression in people with diabetes mellitus: a randomized controlled trial. *Journal of medical Internet research*, 19(5).
- Communication with Andrews: The study used a technician to ascertain the capabilities of participants to operate the system during lesson 1 & 2, and allowed clinician advice, on demand nonetheless, in the reminder of the intervention.

Nobis2015*

- Nobis, S., Lehr, D., Ebert, D. D., Baumeister, H., Snoek, F., Riper, H., & Berking, M. (2015). Efficacy of a web-based intervention with mobile phone support in treating depressive symptoms in adults with type 1 and type 2 diabetes: a randomized controlled trial. *Diabetes Care*, dc141728.
- Communication with Cuijpers: “GET.ON” belong to the therapeutic guidance category.

Nyström2017

- Nyström, M. B., Stenling, A., Sjöström, E., Neely, G., Lindner, P., Hassmén, P., ... & Carlbring, P. (2017). Behavioral activation versus physical activity via the internet: A randomized controlled trial. *Journal of affective disorders*, 215, 85-93.
- Communication with Carlbring: homework must be finished in order to proceed to the next module. There were no automated email prompts, but humans sent the messages once a week. If the patient followed the treatment the patient would send his/her homework to the human therapist and that person would then respond. If the patient did not complete the homework within that week a reminder was sent by the therapist. Therapeutic guidance related to the treatment content may be provided on a scheduled basis or as-needed basis. Provision of technical support only was not counted towards this component.

O'Moore2018*

- O'Moore, K. A., Newby, J. M., Andrews, G., Hunter, D. J., Bennell, K., Smith, J., & Williams, A. D. (2018). Internet Cognitive–Behavioral Therapy for Depression in Older Adults With Knee Osteoarthritis: A Randomized Controlled Trial. *Arthritis care & research*, 70(1), 61-70.
- Communication with Andrews and Williams: The study used a technician to ascertain the capabilities of participants to operate the system during lesson 1 & 2, and allowed clinician advice, on demand nonetheless, from the start of the intervention.

Perini2009*

- Perini, S., Titov, N., & Andrews, G. (2009). Clinician-assisted Internet-based treatment is effective for depression: randomized controlled trial. *Australian and New Zealand journal of psychiatry*, 43(6), 571-578.
- Communication with Andrews: therapists intervened as they would if they had brief access to the real person with lesson by lesson encouragement and clinical advice averaging 60 minutes per person over the 6 lessons. a moderated forum was set up to offer clinical advice.

Phillips2014*

- Phillips, R., Schneider, J., Molosankwe, I., Leese, M., Foroushani, P. S., Grime, P., ... & Thornicroft, G. (2014). Randomized controlled trial of computerized cognitive behavioural therapy for depressive symptoms: effectiveness and costs of a workplace intervention. *Psychological medicine*, 44(4), 741-752.

Pots2016*

- Pots, W. T., Fledderus, M., Meulenbeek, P. A., Peter, M., Schreurs, K. M., & Bohlmeijer, E. T. (2016). Acceptance and commitment therapy as a web-based intervention for depressive symptoms: randomised controlled trial. *The British Journal of Psychiatry*, 208(1), 69-77.

Pugh2016*

- Pugh, N. E., Hadjistavropoulos, H. D., & Dirkse, D. (2016). A randomised controlled trial of therapist-assisted, Internet-delivered cognitive behavior therapy for women with maternal depression. *PLoS One*, *11*(3), e0149186.

Richards2015*

- Richards, D., Timulak, L., O'Brien, E., Hayes, C., Vigano, N., Sharry, J., & Doherty, G. (2015). A randomized controlled trial of an internet-delivered treatment: its potential as a low-intensity community intervention for adults with symptoms of depression. *Behaviour Research and Therapy*, *75*, 20-31.

Roepke2015

- Roepke, A. M., Jaffee, S. R., Riffle, O. M., McGonigal, J., Broome, R., & Maxwell, B. (2015). Randomized controlled trial of SuperBetter, a smartphone-based/internet-based self-help tool to reduce depressive symptoms. *Games for health journal*, *4*(3), 235-246.

Rollman2018

- Rollman, B. L., Belnap, B. H., Abebe, K. Z., Spring, M. B., Rotondi, A. J., Rothenberger, S. D., & Karp, J. F. (2018). Effectiveness of online collaborative care for treating mood and anxiety disorders in primary care: a randomized clinical trial. *JAMA psychiatry*, *75*(1), 56-64.

Rosso2017*

- Rosso, I. M., Killgore, W. D., Olson, E. A., Webb, C. A., Fukunaga, R., Auerbach, R. P., ... & Rauch, S. L. (2017). Internet-based cognitive behavior therapy for major depressive disorder: A randomized controlled trial. *Depression and anxiety*, *34*(3), 236-245.
- <https://clinicaltrials.gov/ct2/show/NCT01598922>

Santucci2014

- Santucci, L. C., McHugh, R. K., Elkins, R. M., Schechter, B., Ross, M. S., Landa, C. E., ... & Barlow, D. H. (2014). Pilot implementation of computerized cognitive behavioral therapy in a university health setting. *Administration and Policy in Mental Health and Mental Health Services Research*, *41*(4), 514-521.

Sheeber2012*

- Sheeber, L. B., Seeley, J. R., Feil, E. G., Davis, B., Sorensen, E., Kosty, D. B., & Lewinsohn, P. M. (2012). Development and pilot evaluation of an Internet-facilitated cognitive-behavioral intervention for maternal depression. *Journal of Consulting and Clinical Psychology*, *80*(5), 739.

Smith2017*

- Smith, J., Newby, J. M., Burston, N., Murphy, M. J., Michael, S., Mackenzie, A., ... & Williams, A. D. (2017). Help from home for depression: A randomised controlled trial comparing internet-delivered cognitive behaviour therapy with bibliotherapy for depression. *Internet Interventions*, *9*, 25-37.
- Communication with Andrews: For the intervention arm, first technician support was offered and clinician advice was on demand but only 19% of the participants availed themselves.

Spek2007*

- Spek, V., Nyklíček, I., Smits, N., Cuijpers, P. I. M., Riper, H., Keyzer, J., & Pop, V. (2007). Internet-based cognitive behavioural therapy for subthreshold depression in

people over 50 years old: a randomized controlled clinical trial. *Psychological medicine*, 37(12), 1797-1806.

- Cuijpers: “Colour Your Life” belongs to the therapeutic guidance category.
- Communication with Spek: there was no training or any face to face meetings for interpersonal skills nor relaxation in the intervention

Terides2018

- Terides, M. D., Dear, B. F., Fogliati, V. J., Gandy, M., Karin, E., Jones, M. P., & Titov, N. (2018). Increased skills usage statistically mediates symptom reduction in self-guided internet-delivered cognitive-behavioural therapy for depression and anxiety: a randomised controlled trial. *Cognitive behaviour therapy*, 47(1), 43-61.
- Communication with Titov on Wellbeing Course: No provision of guidelines on sleep restriction. Homework completion was not required, even though many patients discussed homework activities with their therapists on a weekly basis. Automated emails were sent for notification of new contents, progress reinforcement, reminders, and support messages.

Titov2010

- Titov, N., Andrews, G., Davies, M., McIntyre, K., Robinson, E., & Solley, K. (2010). Internet treatment for depression: a randomized controlled trial comparing clinician vs. technician assistance. *PloS one*, 5(6), e10939.
- Communication with Andrews: we sought to compare best clinician support/advice with scripted encouragement from a technician.

Titov2011

- Titov, N., Dear, B. F., Schwenke, G., Andrews, G., Johnston, L., Craske, M. G., & McEvoy, P. (2011). Transdiagnostic internet treatment for anxiety and depression: a randomised controlled trial. *Behaviour research and therapy*, 49(8), 441-452.
- Communication with Titov on Wellbeing Course: No provision of guidelines on sleep restriction. Homework completion was not required, even though many patients discussed homework activities with their therapists on a weekly basis. Automated emails were sent for notification of new contents, progress reinforcement, reminders, and support messages.

Titov2013

- Titov, N., Dear, B. F., Johnston, L., Lorian, C., Zou, J., Wootton, B., ... & Rapee, R. M. (2013). Improving adherence and clinical outcomes in self-guided internet treatment for anxiety and depression: randomised controlled trial. *PLoS One*, 8(7), e62873.
- Communication with Titov on Wellbeing Course: No provision of guidelines on sleep restriction. Homework completion was not required, even though many patients discussed homework activities with their therapists on a weekly basis. Automated emails were sent for notification of new contents, progress reinforcement, reminders, and support messages.

Titov2015

- Titov, N., Dear, B. F., Staples, L. G., Terides, M. D., Karin, E., Sheehan, J., ... & McEvoy, P. M. (2015). Disorder-specific versus transdiagnostic and clinician-guided versus self-guided treatment for major depressive disorder and comorbid anxiety disorders: a randomized controlled trial. *Journal of Anxiety Disorders*, 35, 88-102.

Tulbure2018

- Tulbure, B. T., Andersson, G., Sălăgean, N., Pearce, M., & Koenig, H. G. (2018). Religious versus conventional internet-based cognitive behavioral therapy for depression. *Journal of religion and health*, 57(5), 1634-1648.

Ünlü 2013*

- Ünlü Ince, B., Cuijpers, P., van 't Hof, E., van Ballegooijen, W., Christensen, H., & Riper, H. (2013). Internet-based, culturally sensitive, problem-solving therapy for Turkish migrants with depression: randomized controlled trial. *Journal of medical Internet research*, 15(10), e227. doi:10.2196/jmir.2853
- Cuijpers: “Alles Onder Controle” belong to the therapeutic guidance category.

vanBastelaar2011*

- Van Bastelaar, K. M., Pouwer, F., Cuijpers, P., Riper, H., & Snoek, F. J. (2011). Web-based depression treatment for type 1 and type 2 diabetic patients: a randomized, controlled trial. *Diabetes Care*, 34(2), 320-325.
- Communication with Cuijpers: “Colour Your Life” belongs to the therapeutic guidance category.

vanLuenen2018*

- van Luenen, S., Garnefski, N., Spinhoven, P., & Kraaij, V. (2018). Guided internet-based intervention for people with HIV and depressive symptoms: a randomised controlled trial in the Netherlands. *The Lancet HIV*, 5(9), e488-e497.

Vernmark2010*

- Vernmark, K., Lenndin, J., Bjärehed, J., Carlsson, M., Karlsson, J., Öberg, J., ... & Andersson, G. (2010). Internet administered guided self-help versus individualized e-mail therapy: A randomized trial of two versions of CBT for major depression. *Behaviour research and therapy*, 48(5), 368-376.

Warmerdam2008*

- Warmerdam, L., van Straten, A., Twisk, J., Riper, H., & Cuijpers, P. (2008). Internet-based treatment for adults with depressive symptoms: randomized controlled trial. *Journal of medical Internet research*, 10(4).
- Communication with Riper: I would classify under ‘human encouragement’ as this is how they were set up, i.e. coaching/motivation instead of therapeutic guidance. The main differences between the two active conditions was the orientation (PST versus CBT) and the CBT intervention had a longer duration than PST. The guidance provided was of a self-help guided nature and not of a therapeutic interaction nature. Main characteristic of the guidance was to support the clients to work with the programme, motivate them and solve technical or other kind of pragmatic questions. In both two brief interventions (5 and 8 sessions), the background of the professionals providing this guidance did not required to be licensed CBT or BA therapists. So human encouragement yes, therapeutic interrelationships not. I know the distinction is not hard core as such but for me it is not based on a therapeutic alliance etc.
- Communication with Cuijpers: “Colour Your Life” belongs to the therapeutic guidance category.

Wilson2018

- Wilson, M., Hewes, C., Barbosa-Leiker, C., Mason, A., Wuestney, K. A., Shuen, J. A., & Wilson, M. P. (2018). Engaging Adults With Chronic Disease in Online Depressive Symptom Self-Management. *Western journal of nursing research*, 40(6), 834-853.
- Communication with Wilson: weekly email, text, or optional phone calls were sent to prompt engagement and resolve questions participants have.

Zagorscak2018*

- Zagorscak, P., Heinrich, M., Sommer, D., Wagner, B., & Knaevelsrud, C. (2018). Benefits of Individualized Feedback in Internet-Based Interventions for Depression: A Randomized Controlled Trial. *Psychotherapy and psychosomatics*, 87(1), 32-45.
- Communication with Heinrich: In the first part of the last module, individuals receive psychoeducation about warning signs and are encouraged to write personal warning signs on a card. They are also encouraged to check how they feel to identify unwanted symptom changes regularly (e.g., write down their activities for one day a week, write a thought-protocol for at least once a month). In the writing task that follows, participants are asked to write a letter to their former selves. On the one hand, they are encouraged to write about how they felt two months ago before they began the intervention, their expectations/fears about participating, changes in their mood while participating, and techniques they found helpful. On the other hand, they are asked to write about personal warning signs that may precede unwanted mood changes and about recently learned strategies they could apply to deal with these unwanted symptoms. Participants are told that this writing assignment is designed to help them (1) visualize successes, and (2) maintain successes that they have achieved.

5.2 List of excluded studies: reasons and references

Study ID	Reason for exclusion
Alavi 2016	Treatment not suitable (not standardized).
Andersson 2013	Comparison not suitable.
Arjadi 2018	Not focusing on adults only.
Beiwinkel 2017	No lower depression threshold nor standardized depression criteria.
Berger 2017	Blended treatment.
Blom 2015	Focusing on the comorbidity between depression and anxiety.
Bolier 2013	Intervention not suitable (random chosen modules).
Bolinski 2018	Not focusing on adults only.
Bowers 1993	Included population was inpatients only.
Buhrman 2015	Treatment was tailored by therapists.
Cartreine 2012	Computerised CBT intervention was provided on a computer on-site, implying not enough interactivity.
Castro 2014	Aborted trial (personal communication).
Christensen 2006	Population was made by spontaneous visitors (no depression threshold nor standardized depression criteria).
Clarke 2002	No lower depression threshold nor standardized depression criteria.
Clarke 2005	No lower depression threshold nor standardized depression criteria.
Clarke 2009	No lower depression threshold nor standardized depression criteria.
Deady 2018	Focusing on mental comorbidity.
Donker 2013	No lower depression threshold nor standardized depression criteria.
Ellis 2011	No lower depression threshold nor standardized depression criteria.
Fischer2015	No lower depression threshold nor standardized depression criteria.
Flanagan 2011	No lower depression threshold nor standardized depression criteria.
Ghosh 2018	Not focusing on adults only.
Grime 2004	Computerised CBT intervention was provided on a computer on-site, implying not enough interactivity.

Hallgren 2015	Interventions not suitable (adapted and modified for patients)
Høifødt 2015	Blended treatment.
Hudson 2017	Blended treatment.
Imamura 2014	Not focusing on depression.
Johansson 2012	Intervention not suitable (psychodynamic).
Kelders 2013	Not randomized.
Kelders 2015	The randomisation procedure was faulty. Also, it involved different components compared to ours; being factorial, in order to make it fit our network several <i>ad hoc</i> assumptions would have been required.
Lappalainen 2014	Comparison not suitable (face to face).
Lokman 2017	Intervention not suitable (not standardized; complaint-directed mini-interventions).
Madsen 2016	Not primary diagnosis of depression.
Messerly-Bürge 2012	The study was aborted due to difficulties with patient recruitment according to personal communication from the first author.
Meyer 2009	No lower depression threshold nor standardized depression criteria.
Mira 2017	No lower depression threshold nor standardized depression criteria.
Moritz 2012	No lower depression threshold nor standardized depression criteria.
Norlund 2018	CBT modules were not compulsory.
O'Mahen 2014	Study included many optional modules and could not be decomposed.
Pittaway 2009	No lower depression threshold nor standardized depression criteria.
Proudfoot 2004	Computerised CBT intervention was provided on a computer on-site, implying not enough interactivity.
Proudfoot 2013	Intervention not suitable (not standardized).
Proudfoot 2017	Intervention not suitable (not standardized).
Richards 2013	Comparison not compatible with network and components assessment.
Ruwaard 2009	Intervention not structured enough, tailored.
Salisbury 2016	Treatment not standardized.

Sandoval 2016	Computerised CBT intervention was provided on a computer on-site, implying not enough interactivity.
Schröder 2014	No lower depression threshold nor standardized depression criteria.
Selmi 1990	Computerised CBT intervention was provided on a computer on-site, implying not enough interactivity.
Sheeber 2017	Motivational interview, not comparing CBT to CBT or CBT to inactive placebo.
Soumet-Leman 2015	Intervention not suitable (cognitive remediation).
Thase 2017	Control group not suitable (standard CBT).
Tomasino 2017	Not randomized.
Topooco 2018	Not focusing on adults only.
Tulbure 2018	Intervention too much focused on the transdiagnostic aspect.
Twomey 2014	No lower depression threshold nor standardized depression criteria.
Van Voorhees 2012	Not randomized.
Williams 2013a	Not randomized.
Williams 2013b	Intervention not suitable (cognitive bias modification + CBT).
Williams 2015	Intervention not suitable (cognitive bias modification + CBT).
Wright 2005	Blended treatment.
Yeung 2017	No lower depression threshold nor standardized depression criteria.

References

Alavi 2016

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5.3 List of studies awaiting assessment & ongoing studies

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6 Evaluation of components for each arm of included studies

The inter-rater reliability of the judgements for components.

Components (abbreviation)	Percentage agreement	Kappa	P _{pos}	P _{neg}
Waiting component (w)	98.0%	0.94	0.99	0.96
Conventional drug treatment (dt)	96.0%	-	0.98	0.00
Non-specific treatment effects (ns)	98.0%	0.93	0.95	0.99
Psychoeducation about depression (pe)	93.3%	0.86	0.91	0.95
Cognitive restructuring (cr)	95.7%	0.91	0.95	0.96
Behavioral activation (ba)	97.9%	0.96	0.97	0.98
Interpersonal skill training (is)	97.4%	0.92	0.98	0.93
Problem-solving (ps)	97.6%	0.94	0.98	0.96
Relaxation (re)	93.3%	0.54	0.96	0.57
Third-wave components (3w)	95.7%	0.48	0.98	0.50
Behavior therapy for insomnia (bi)	92.7%	0.38	0.96	0.40
Relapse prevention (rp)	91.3%	0.82	0.93	0.89
Homework required (hw)	85.4%	0.68	0.89	0.79
Initial face-to-face contact (ff)	84.0%	0.63	0.88	0.75
Automated encouragement to proceed with iCBT (ae)	89.1%	0.76	0.92	0.84
Human encouragement to proceed with iCBT (he)	89.4%	0.78	0.91	0.87
Therapeutic guidance for iCBT (tg)	91.7%	0.55	0.95	0.60

P_{pos}: positive agreement, P_{neg}: negative agreement as per Cicchetti et al (1990)

Cicchetti DV & Feinstein AR (1990) High agreement but low kappa: II. Resolving the paradoxes. Journal of Clinical Epidemiology, 43, 551-558.

Study	Treatment	Details of treatment	Waiting component	Conventional drug treatment	Non-specific treatment effects	Psychoeducation	Cognitive restructuring	Behavioral activation	Interpersonal Skills Training	Problem-solving	Relaxation	Third-wave component	Behavioral therapy for insomnia	Relapse prevention	Homework required	Initial face-to-face contact	Automated encouragement to proceed with CBT	Human encouragement to proceed with CBT	Therapeutic guidance for CBT	Others
Andersson et al, 2005	CBT	iCBT	No	Allowed	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes	No	No	No	Yes	Yes	
	WL	online discussion group	Yes	Allowed	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Arean et al, 2016	PST	iPST	No	Allowed	Yes	No	Unclear	Unclear	Unclear	Yes	No	Unclear	Unclear	Unclear	Unclear	No	Yes	Yes	No	
	APP	Health Tips	No	Allowed	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Beevers et al, 2017	CBT	Deprexis	No	Allowed	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes	No	childhood experiences, positive psychology, dreamwork and emotion-focused interventions
	WL	waitlist	Yes	Allowed	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Berger et al, 2011	CBT	Guided deprexis	No	Allowed	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes	No	
	CBT	Unguided deprexis	No	Allowed	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	No	Yes	No	No	
	WL	Waitlist	Yes	Allowed	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Birney et al, 2016	CBT	MoodHacker (1st version)	No	Unclear	Yes	Yes	Yes	Yes	No	No	No	Yes	No	No	Yes	No	Yes	No	No	positive psychology
	WL	alternative care	Yes	Unclear	Yes	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	
Boele et al, 2017	PST	online guided self-help course founded on PST (Alles onder controle)	No	Allowed	Yes	Yes	No	No	No	Yes	No	No	No	Yes	Yes	No	No	Yes	Yes	glioma-specific adaptation
	WL	waitlist	Yes	Allowed	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Boeschoten et al, 2017	PST	Minder Zorgen ("Worry less") (AOC adapted for MS patients)	No	Allowed	Yes	Yes	No	No	No	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	
	PST	Minder Zorgen ("Worry less") (AOC adapted for MS patients)	No	Allowed	Yes	Yes	No	No	No	Yes	No	No	No	Yes	Yes	Yes	No	Yes	Yes	
	WL	waitlist	Yes	Allowed	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	
Buntrock et al, 2015	BA	Get.ON + TAU	No	Allowed	Yes	Yes	No	Yes	No	Yes	Optional	No	Optional	Yes	Yes	No	Optional	Yes	Yes	
	PE	Psychoeducation	No	Allowed	Yes	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	

Study	Treatment	Details of treatment	Waiting component	Conventional drug treatment	Non-specific treatment effects	Psychoeducation	Cognitive restructuring	Behavioral activation	Interpersonal Skills Training	Problem-solving	Relaxation	Third-wave component	Behavioral therapy for insomnia	Relapse prevention	Homework required	Initial face-to-face contact	Automated encouragement to proceed with CBT	Human encouragement to proceed with CBT	Therapeutic guidance for CBT	Others
Burton et al, 2015	CBT	Help4Mood + TAU	No	Allowed	Yes	No	Yes	Yes	No	No	Yes	No	No	No	No	Yes	No	No	No	
	TAU	TAU	No	Allowed	Yes	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	
Carlbring et al, 2013	3W	Depressionhjälpen	No	Allowed	Yes	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	No	No	Yes	Yes	BA and ACT focused
	WL	waitlist	Yes	Allowed	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Choi et al, 2012	CBT	Chinese iCBT (Sadness adapted)	No	Allowed	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Optional	Yes	Yes	No	Yes	Yes	Yes	
	WL	Waitlist	Yes	Allowed	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Christensen et al, 2004	PE	Bluepages	No	Unclear	Yes	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	
	CBT	Mood GYM	No	Unclear	Yes	Yes	Yes	Yes	No	Yes	Yes	No	No	No	No	No	No	Yes	No	
	APP	Discussion	No	Unclear	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Cooper et al, 2011a	CBT	Beating the Blues	No	Allowed	Yes	Yes	Yes	Yes	No	Yes	No	No	Optional	Yes	No	Yes	No	No	No	
	TAU	TAU	No	Allowed	Yes	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	
Dahne et al, 2018	BA	Moodivate	No	Allowed	Yes	Yes	No	Yes	No	No	No	No	No	No	No	Yes	No	No	No	
	CBT	MoodKit	No	Allowed	Yes	Yes	Yes	Yes	No	No	No	No	No	No	No	Yes	Optional	No	No	Positive psychology
	PE	TAU	No	Allowed	Yes	Yes	No	No	No	No	No	No	No	No	No	Yes	No	No	No	
Day et al, 2013	CBT	intervention	No	Unclear	Yes	Yes	Yes	Yes	Optional	No	Optional	No	No	No	Yes	No	No	Yes	Yes	
	WL	waitlist	Yes	Unclear	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
DeGraaf et al, 2009	CBT	CCBT (Colour your life)	No	Allowed	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	No	No	No	No	
	TAU	TAU	No	Allowed	Yes	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	
	CBT	CCBT+TAU	No	Allowed	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	No	Yes	No	
Ebert et al, 2014a	PE	Online psychoeducation	No	Allowed	Yes	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	
	BA	GET.ON Mood enhancer	No	Allowed	Yes	Yes	No	Yes	No	Yes	Optional	No	Optional	Yes	Yes	No	No	Yes	Yes	
Ebert et al, 2014b	PST	Alles onder controle	No	Allowed	Yes	Yes	No	No	No	Yes	No	No	No	Yes	Yes	No	No	Yes	Yes	rumination
	WL	waitlist	Yes	Allowed	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Ebert et al, 2017	BA	Get.ON + TAU	No	Allowed	Yes	Yes	No	Yes	No	Yes	Optional	No	Optional	Yes	Yes	No	Optional	Yes	Optional	

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	WL	waitlist	Yes	Allowed	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Farrer et al, 2011	CBT	web only (MoodGYM+BluePages)	No	Unclear	Yes	Yes	Yes	Yes	No	Yes	Yes	No	No	No	No	No	No	No	No	
	CBT	web+tracking (MoodGYM + BluePages)	No	Unclear	Yes	Yes	Yes	Yes	No	Yes	Yes	No	No	No	No	No	No	Yes	No	
	PE	tracking only	No	Unclear	Yes	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	
	WL	waitlist	Yes	Unclear	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Forand et al, 2017	CBT	Beating the Blues 2.5	No	Allowed	Yes	Yes	Yes	Yes	No	Yes	No	No	Optional	Yes	No	Yes	No	Yes	No	
	WL	waitlist	Yes	Allowed	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	
Forsell et al, 2017	CBT	iCBT + TAU	No	Allowed	Yes	Yes	Yes	Yes	No	No	No	No	Optional	Yes	Yes	No	No	Yes	Yes	
	WL	TAU	Yes	Allowed	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Geraedts et al, 2014	CBT	Happy@work	No	Allowed	Yes	Yes	Yes	No	No	Yes	No	No	No	Yes	Yes	No	Yes	Yes	Yes	
	NT	Care as Usual	No	Allowed	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Gilbody et al, 2015	CBT	Beating the Blues + TAU	No	Allowed	Yes	Yes	Yes	Yes	No	Yes	No	No	Optional	Yes	No	Yes	No	Yes	No	
	TAU	TAU	No	Allowed	Yes	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	
	CBT	MoodGYM + TAU	No	Allowed	Yes	Yes	Yes	Yes	No	Yes	Yes	No	No	No	No	Yes	No	Yes	No	
Gilbody et al, 2017	CBT	tel support MoodGYM	No	Allowed	Yes	Yes	Yes	Yes	No	Yes	Yes	No	No	No	No	Yes	No	Yes	Yes	
	CBT	min support MoodGYM	No	Allowed	Yes	Yes	Yes	Yes	No	Yes	Yes	No	No	No	No	Yes	No	No	No	
Glozier et al, 2013	CBT	E-couch	No	Unclear	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	No	No	No	Yes	Yes	No	physical activity, interpersonal training program
	APP	HealthWatch	No	Unclear	Yes	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	
Griffiths et al, 2012	APP	WellBeing (ISG)	No	Unclear	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
	CBT	E-couch (ITP)	No	Unclear	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	No	No	No	Yes	Yes	No	physical activity, interpersonal training program
	CBT	ITP+ISG	No	Unclear	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	No	No	No	Yes	Yes	No	physical activity, interpersonal training program
	WL	HealthWatch	Yes	Unclear	Yes	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	

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Hadjistavropoulos et al, 2017	CBT	WellBeing Course - standard support	No	Allowed	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Optional	Yes	Yes	Yes	Yes	Yes	Yes	de-arousal strategies, graded exposure
	CBT	WellBeing Course - optional support	No	Allowed	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Optional	Yes	Yes	Yes	Yes	Optional	Optional	de-arousal strategies, graded exposure
Hur et al, 2018	CT	Todac Todac	No	Unclear	Yes	No	Yes	No	No	No	No	No	No	No	No	No	Yes	No	No	
	APP	mood chart	No	Unclear	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Johansson et al, 2012	CBT	Standardized iCBT	No	Allowed	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes	Yes	No	No	Yes	Yes	
	WL	online discussion group	Yes	Allowed	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Kenter et al, 2016	PST	iPST (Alles Onder Controle)	Yes	Allowed	Yes	No	No	No	No	Yes	No	No	No	Yes	Yes	Yes	No	Yes	Yes	
	WL	unguided self-help book	Yes	Allowed	Yes	Yes	No	No	No	No	No	No	No	No	No	Yes	No	No	No	
Kivi et al, 2014	3W	Depressionshjälp (iCBT)	No	Allowed	Yes	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	Yes	No	Yes	Yes	
	TAU	TAU	No	Allowed	Yes	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	
Kleiboer et al, 2015	PST	iPST without support (Alles Onder Controle)	No	Allowed	Yes	Yes	No	No	No	Yes	No	No	No	Yes	Yes	No	Yes	No	No	Self-examination therapy (SET) type of PST
	PST	iPST with support on request (Alles Onder Controle)	No	Allowed	Yes	Yes	No	No	No	Yes	No	No	No	Yes	Yes	No	Yes	Optional	Optional	Self-examination therapy (SET) type of PST
	PST	iPST with weekly support (Alles Onder Controle)	No	Allowed	Yes	Yes	No	No	No	Yes	No	No	No	Yes	Yes	No	Yes	Yes	Yes	Self-examination therapy (SET) type of PST
	WL	waitlist	Yes	Allowed	Yes	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	
Klein et al, 2016	CBT	Deprexis + CAU (PHQ 10-14)	No	Allowed	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	Partly	Yes	Yes	Yes	
	WL	CAU (PHQ 10-14)	Yes	Allowed	Yes	No	No	No	No	No	No	No	No	No	No	Partly	No	No	No	
	CBT	Deprexis + CAU (PHQ 5-9)	No	Allowed	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	Partly	Yes	No	No	
	WL	CAU (PHQ 5-9)	Yes	Allowed	Yes	No	No	No	No	No	No	No	No	No	No	Partly	No	No	No	
Lambert et al, 2018	BA	eMotion	No	Allowed	Yes	Yes	No	Yes	No	No	No	No	No	No	Yes	No	Yes	Yes	No	physical activity

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	WL	waitlist	Yes	Allowed	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Lappalainen et al, 2015	3W	iACT	No	Allowed	Yes	Yes	No	No	No	No	No	Yes	No	No	Yes	No	Yes	Yes	Yes	
	WL	waitlist	Yes	Allowed	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Lintvedt et al, 2013	CBT	MoodGYM v3+BluePages	No	Unclear	Yes	Yes	Yes	Yes	No	Yes	Yes	No	No	No	No	No	No	No	No	
	WL	waitlist	Yes	Unclear	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Löbner et al, 2018	CBT	MoodGYM v3+TAU	No	Allowed	Yes	Yes	Yes	Yes	No	Yes	Yes	No	No	No	No	Yes	Yes	Yes	No	german adaption
	TAU	TAU	No	Allowed	Yes	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	
Lundgren et al, 2016	BA	iCBT	No	Allowed	Yes	Yes	No	Yes	No	Yes	Optional	No	No	Yes	Yes	Yes	No	Yes	Yes	
	WL	moderated discussion web-forum	Yes	Allowed	Yes	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	
Ly et al, 2014	BA	Behavioural activation	No	Allowed	Yes	Yes	No	Yes	No	No	No	No	No	No	Yes	No	No	Yes	Yes	
	3W	Mindfulness	No	Allowed	Yes	Yes	No	No	No	No	No	Yes	No	No	Yes	No	No	Yes	No	
Mantani et al, 2017	CBT	iCBT (Kokoro) + TAU (switch)	No	Yes	Yes	Yes	Yes	Yes	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes	No	
	WL	TAU (switch)	Yes	Yes	Yes	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	
Meyer et al, 2015	CBT	Deprexis+CAU	No	Allowed	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	No	Yes	No	No	
	WL	CAU	Yes	Allowed	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Milgrom et al, 2016	CBT	MumMoodBooster	No	Not allowed	Yes	Yes	Yes	Yes	Optional	Optional	Yes	No	No	Yes	Yes	No	Yes	Yes	No	
	TAU	TAU	No	Not allowed	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Mohr et al, 2013	CBT	moodManager+TeleCoach	No	Allowed	Yes	Yes	Yes	Yes	Optional	No	Optional	Optional	No	Optional	Yes	No	No	Yes	No	
	CBT	moodManager	No	Allowed	Yes	Yes	Yes	Yes	Optional	No	Optional	Optional	No	Optional	Yes	No	No	No	No	
	WL	waitlist	Yes	Allowed	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Montero-Marín et al, 2016	CBT	low guided Smiling is fun	No	Allowed	Yes	Yes	Yes	Yes	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	positive psychology
	CBT	self Smiling is fun	No	Allowed	Yes	Yes	Yes	Yes	No	No	No	No	No	Yes	Yes	Yes	Yes	No	No	positive psychology
	TAU	TAU	No	Allowed	Yes	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	

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Morthland et al, 2012	CBT	CBT	No	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	No	Yes	No	Yes	No	worry time
	WL	waitlist	Yes	Unclear	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	
Newby et al, 2017	CBT	iCBT	No	Allowed	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Optional	Yes	Yes	Yes	Yes	Yes	Optional	
	WL	Waiting list	Yes	Allowed	Yes	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	
Nobis et al, 2015	BA	GET.ON + TAU	No	Allowed	Yes	Yes	No	Yes	No	Yes	Optional	No	Optional	Yes	Yes	No	Yes	Yes	Yes	
	WL	unguided web psychoeducation + TAU	Yes	Allowed	Yes	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	
Nystrom et al, 2017	APP	PA without rationale	No	Allowed	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	PA without rationale
	APP	PA with rationale	No	Allowed	Yes	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	PA with rationale
	BA	BA Lewinshon	No	Allowed	Yes	Yes	No	Yes	No	No	No	No	No	No	Yes	No	No	Yes	Yes	BA Lewinshon
	BA	BA Martell	No	Allowed	Yes	Yes	No	Yes	No	No	No	No	No	No	Yes	No	No	Yes	Yes	BA Martell
	WL	Control group	Yes	Allowed	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
O'Mahen et al, 2013	BA	Netmums (post-natal IBA)	No	Allowed	Yes	Yes	No	Yes	Yes	No	No	No	No	Yes	No	No	Yes	Optional	Optional	rumination
	WL	Waiting list	Yes	Allowed	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
O'Mahen et al, 2014	BA	NetmumsHWD	No	Allowed	Yes	Yes	No	Yes	Optional	Yes	No	No	Optional	Yes	Yes	Yes	No	Yes	Yes	
	TAU	TAU	No	Allowed	Yes	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	
O'Moore et al, 2017	CBT	iCBT (Sadness) + TAU	No	Allowed	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Optional	Yes	Yes	No	Yes	Yes	Optional	
	TAU	TAU	No	Allowed	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Perini et al, 2009	CBT	Sadness	No	Allowed	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Optional	Yes	Yes	No	No	Yes	Yes	
	WL	waitlist	Yes	Allowed	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Phillips et al, 2014	CBT	Mood GYM	No	Allowed	Yes	Yes	Yes	Yes	No	Yes	Yes	No	No	No	No	No	No	Yes	No	
	PE	online psychoeducation	No	Allowed	Yes	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	
Pots et al, 2016	3W	ACT	No	Not allowed	Yes	Yes	No	No	No	No	No	Yes	No	Yes	Yes	No	Yes	Yes	Yes	
	APP	Expressive writing	No	Not allowed	Yes	Yes	No	No	No	No	No	No	No	Yes	No	No	No	No	No	

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	WL	Waitlist	Yes	Not allowed	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Pugh et al, 2016	CBT	Maternal Depression online	No	Allowed	Yes	Yes	Yes	Yes	No	Yes	Yes	No	No	Yes	Yes	No	No	Yes	Yes	
	WL	waitlist	Yes	Allowed	Yes	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	
Richards et al, 2015	CBT	iCBT	No	Allowed	Yes	Yes	Yes	Yes	No	No	No	No	No	Yes	Unclear	No	No	Yes	No	
	WL	waitlist	Yes	Allowed	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Roepke et al, 2015	CBT	SuperBetter (CBT-PP v)	No	Allowed	Yes	No	Yes	Yes	No	No	No	No	No	No	No	No	No	No	No	positive psychology
	3W	SuperBetter (general v)	No	Allowed	Yes	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	
	WL	waitlist	Yes	Allowed	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Rollman et al, 2018	CBT	Beating the Blues	No	Allowed	Yes	Yes	Yes	Yes	No	Yes	No	No	Optional	Yes	Yes	Yes	No	Yes	Yes	
	CBT	Beating the Blues + ISG	No	Allowed	Yes	Yes	Yes	Yes	No	Yes	No	No	Optional	Yes	Yes	Yes	No	Yes	Yes	
	TAU	usual care	No	Allowed	Yes	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	
Rosso et al, 2017	CBT	Sadness	No	Not allowed	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Optional	Yes	Yes	Yes	Yes	Yes	No	USA adaptation
	WL	Monitored Attention Control	Yes	Not allowed	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	
Santucci et al, 2013	CBT	Beating the Blues + reminder	No	Allowed	Yes	Yes	Yes	Yes	No	Yes	No	No	Optional	Yes	Yes	Yes	No	Yes	No	
	CBT	Beating the Blues no reminder	No	Allowed	Yes	Yes	Yes	Yes	No	Yes	No	No	Optional	Yes	Yes	Yes	No	No	No	
Sheeber et al, 2012	CBT	Mom-Net	No	Unclear	Yes	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes	Yes	No	Yes	Yes	
	WL	delayed intervention with TAU	Yes	Unclear	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	
Smith et al, 2017	CBT	Sadness	No	Allowed	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Optional	Yes	Yes	No	Yes	Yes	Optional	
	WL	waiting list	Yes	Allowed	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Spek et al, 2007	CBT	CYL (internet intervention)	No	Unclear	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes	No	Yes	No	No	No	
	WL	waitlist	Yes	Unclear	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	
Terides et al, 2017	CBT	Wellbeing Course	No	Allowed	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Optional	Yes	Yes	No	Yes	No	No	de-arousal strategies,

Study	Treatment	Details of treatment	Waiting component	Conventional drug treatment	Non-specific treatment effects	Psychoeducation	Cognitive restructuring	Behavioral activation	Interpersonal Skills Training	Problem-solving	Relaxation	Third-wave component	Behavioral therapy for insomnia	Relapse prevention	Homework required	Initial face-to-face contact	Automated encouragement to proceed with CBT	Human encouragement to proceed with CBT	Therapeutic guidance for CBT	Others
																				graded exposure
	WL	waiting list	Yes	Allowed	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Titov et al, 2010	CBT	Sadness technician-assisted	No	Allowed	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Optional	Yes	Yes	No	Yes	Yes	No	
	CBT	Sadness clinician-assisted	No	Allowed	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Optional	Yes	Yes	No	Yes	Yes	Yes	
	WL	waiting list	Yes	Allowed	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Titov et al, 2011	CBT	Wellbeing Program	No	Allowed	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	Yes	de-arousal strategies, graded exposure
	WL	waiting list	Yes	Allowed	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Titov et al, 2013	CBT	Wellbeing Course + automated email	No	Allowed	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Optional	Yes	Yes	No	Yes	No	No	de-arousal strategies, graded exposure
	CBT	Wellbeing Course	No	Allowed	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Optional	Yes	Yes	No	No	No	No	de-arousal strategies, graded exposure
	WL	waiting list	Yes	Allowed	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Titov et al, 2015	CBT	TD-CBT, clinician guided	No	Allowed	Yes	Yes	Yes	Yes	Optional	Optional	Yes	No	Optional	Yes	Yes	No	Yes	Yes	Yes	graded exposure + optional worry time, shifting attention
	CBT	DS-CBT, clinician guided	No	Allowed	Yes	Yes	Yes	Yes	Optional	Optional	No	No	Optional	Yes	Yes	No	Yes	Yes	Yes	
	CBT	TD-CBT, self-guided	No	Allowed	Yes	Yes	Yes	Yes	Optional	Optional	Yes	No	Optional	Yes	Yes	No	Yes	No	No	graded exposure + optional worry time, shifting attention
	CBT	DS-CBT, self-guided	No	Allowed	Yes	Yes	Yes	Yes	Optional	Optional	No	No	Optional	Yes	Yes	No	Yes	No	No	
Tulbure et al, 2017	CBT	conventional CBT	No	Allowed	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Unclear	Yes	No	No	Yes	Yes	
	WL	waitlist	Yes	Allowed	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Unlu et al, 2013	PST	Alles Onder Controle-TR	No	Unclear	Yes	Yes	No	No	No	Yes	No	No	No	Yes	Yes	No	No	Yes	Yes	

Study	Treatment	Details of treatment	Waiting component	Conventional drug treatment	Non-specific treatment effects	Psychoeducation	Cognitive restructuring	Behavioral activation	Interpersonal Skills Training	Problem-solving	Relaxation	Third-wave component	Behavioral therapy for insomnia	Relapse prevention	Homework required	Initial face-to-face contact	Automated encouragement to proceed with CBT	Human encouragement to proceed with CBT	Therapeutic guidance for CBT	Others
	WL	waitlist	Yes	Unclear	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
vanBastelaar et al, 2011	CBT	internet intervention	No	Allowed	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	No	Yes	Yes	Yes	
	WL	waitlist	Yes	Allowed	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
vanLuenen et al, 2018	CBT	iCBT	No	Allowed	Yes	Yes	Yes	Yes	No	No	Yes	No	No	No	Yes	Yes	No	Yes	Yes	HIV content
	WL	waiting list	Yes	Allowed	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	
Vernmark et al, 2010	CBT	self-help treatment	No	Allowed	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes	Yes	Yes	No	Yes	Yes	
	WL	waitlist	Yes	Allowed	No	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	
Warmerdam et al, 2008	PST	Internet-based self-help PST (Alles Onder Controle)	No	Allowed	Yes	Yes	No	No	No	Yes	No	No	No	Yes	Yes	No	Yes	Yes	Yes	
	CBT	Kleur je leven (Coping with depression-derived)	No	Allowed	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	No	Yes	Yes	Yes	
	WL	waitlist	Yes	Allowed	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Wilson et al, 2017	CT	Think Clearly About Depression	No	Allowed	Yes	Yes	Yes	No	No	No	No	No	No	No	No	No	No	Yes	No	
	APP	Control	No	Allowed	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	
Zagorscak et al, 2018	CBT	iCBT - contact on demand	No	Allowed	Yes	Yes	Yes	Yes	No	No	No	No	No	No	Yes	No	Yes	Optional	No	
	CBT	iCBT - individual counseling	No	Allowed	Yes	Yes	Yes	Yes	No	No	No	No	No	No	Yes	No	Yes	Yes	Yes	

7 Characteristics of included studies

Study			Population								Interventions			Baseline depression severity	
Study	IPD	Country	Diagnostic criteria	Scale used for inclusion	Threshold score used	Recruitment	No randomised	Mean age	Women (%)	Drug therapy (%)	Treatment	Duration (wks)	No of sessions	Scale used	Baseline, mean (SD)
Andersson et al, 2005	Available	Sweden	*	MADRS	15	Community	57	36.4	78	35	CBT	10	5	BDI	20.5 (6.7)
							60	36.3	72	35	WL	10	0	BDI	20.9 (8.5)
Areal et al, 2016	Unavailable	USA	*	PHQ-9	5	Community	211	33.4	77	20.6	PST	4	*	PHQ-9	13.5 (5.1)
							206	33.6	84	18.6	APP	4	*	PHQ-9	13.6 (4.9)
Beevers et al, 2017	Unavailable	USA	*	QIDS	10	Community	285	31.2	73.6	39.6	CBT	8	10	QIDS-SR	15.1 (3.78)
							91	34.1	76.9	48.3	WL	8	*	QIDS-SR	15.4 (3.9)
Berger et al, 2011	Available	Switzerland, Germany	DSM-IV	BDI-II	13	Community	25	38.2	68	32	CBT	10	10	BDI	28.8 (8.2)
							25	38.6	72	20	CBT	10	10	BDI	29.8 (8.6)
							26	39.6	69.2	23.1	WL	10	0	BDI	29.8 (8.6)
Birney et al, 2016	Unavailable	USA	*	PHQ-9	10	Community	150	40.6	74.6	*	CBT	6	*	PHQ-9	13.2 (4.3)
							150	40.7	78.7	*	WL	6	*	PHQ-9	13.6 (3.8)
Boele et al, 2017	Available	Netherlands	*	CES-D	12	Secondary	45	43.58	57.8	17.8	PST	5	6	CES-D	21.96 (5.9)
							44	46.43	59.1	13.6	WL	5	*	CES-D	24.98 (6.9)
Boeschoten et al, 2017	Unavailable	Netherlands	*	BDI-II	20	Secondary	40	48.4	83.5	11.8	PST	10	5	BDI-II	27.9 (6.2)
							45	48.4	83.5	11.8	PST	10	5	BDI-II	28.42 (7.0)
							86	49.4	76.7	14	WL	10	*	BDI-II	27.2 (6.6)
Buntrock et al, 2015	Available	Germany	*	CES-D	16	Community	202	45.71	73.8	24.8	BA	6	6	CES-D	26.25 (7.85)
							204	44.38	74	21.6	PE	6	*	CES-D	26.42 (7.99)
Burton et al, 2015	Unavailable	Romania, Spain, UK	*	BDI-II	10	Primary	13	35.3	76.9	61.5	CBT	4	*	BDI-II	19.6 (8.1)
							14	42	57.1	35.7	TAU	4	*	BDI-II	21.8 (6.8)
Carlbring et al, 2013	Available	Sweden	DSM-IV	MADRS-S	15	Community	40	43.6	77.5	10	3W	8	7	BDI-II	26.32 (5.97)
							40	45.3	87.5	17.5	WL	8	*	BDI-II	25.13 (5.19)
Choi et al, 2012	Available	Australia	DSM-IV	PHQ-9	19	Community	32	40.6	88	*	CBT	8	6	BDI	25.76 (8.53)
							31	37.8	73	*	WL	8	0	BDI	20.83 (7.58)

Christensen et al, 2004	Available	Australia (Canberra)	*	Kessler	22	Community	165	37.25	69	*	PE	6	*	CES-D	21.1 (10.4)
							182	35.85	75	*	CBT	6	5	CES-D	21.8 (10.5)
							178	36.29	70	*	APP	6	0	CES-D	21.6 (11.1)
Cooper et al, 2011a	Unavailable	UK	*	BDI	14	Secondary	12	48	92	58.3	CBT	8	8	BDI	21 (4)
							12	42	58	50	TAU	8	*	BDI	23 (5.2)
Dahne et al, 2018	Available	USA	*	PHQ-8	11	Primary	24	44.67	83.3	37.5	BA	8	1	BDI-II	28.08 (7.83)
							19	43	78.9	36.8	CBT	8	1	BDI-II	28.63 (11.3)
							9	43.11	84.6	33.3	PE	8	*	BDI-II	32.33 (13.03)
Day et al, 2013	Unavailable	Canada	*	DASS-21	10	Community	33	24.12	84.9	*	CBT	6	5	DASS-21	20.06 (11.2)
							33	22.97	93.9	*	WL	6	*	DASS-21	19.88 (10.4)
DeGraaf et al, 2009	Available	Netherlands (south)	*	BDI-II	16	Community	100	44.3	52	0	CBT	9	9	BDI	28.2 (7.7)
							103	45.1	55.3	0	TAU	9	4.5	BDI	27.9 (7.5)
							100	45.2	63	0	CBT	9	13.5	BDI	27.4 (8.2)
Ebert et al, 2014a	Available	Germany	DSM-V	CES-D	16	Community	*	*	*	18.2	PE	*	*	HDRS 24	* (*)
							*	*	*	21.5	BA	4.5	6	HDRS 24	* (*)
Ebert et al, 2014b	Unavailable	Germany	*	CES-D	16	Community	75	46.4	83.3	*	PST	5	5	CES-D	22.76 (9.24)
							75	47.8	84	*	WL	5	*	CES-D	22.81 (9.15)
Ebert et al, 2017	Available	Germany	*	CES-D	16	Community	102	44.66	80.4	*	BA	6	6	CES-D	26.67 (6.5)
							102	43.75	80.4	*	WL	6	*	CES-D	27.73 (7.5)
Farrer et al, 2011	Available	Australia	*	Kessler	22	Community	38	37.5	86	*	CBT	6	6	CES-D	35 (10.8)
							45	41.7	82	*	CBT	6	6	CES-D	34.9 (10.1)
							37	43.4	78	*	PE	6	0	CES-D	37.6 (10.7)
							35	43.7	80	*	WL	6	0	CES-D	38.6 (8.8)
Forand et al, 2017	Available	USA	*	PHQ-9	8	Community	60	33.3	75.6	44.1	CBT	8	8	PHQ-9	16.55 (3.99)
							30	32.4	76.7	26.7	WL	8	*	PHQ-9	18.22 (4.84)
Forsell et al, 2017	Available	Sweden	DSM-IV	MADRS-S	15	Community	22	31.2	100	5	CBT	10	10	MADRS	24.2 (5.2)
							20	30.8	100	5	WL	10	*	MADRS	24.4 (5.9)
Geraedts et al, 2014	Available	Netherlands	*	CES-D	16	International companies	116	43	66.4	6% altogether	CBT	6	6	CES-D	25.7 (7.5)
							115	43.8	58.3	6% altogether	NT	6	0	CES-D	26.1 (7)
Gilbody et al, 2015	Available	England	ICD-10	PHQ-9	10	Primary	210	39.61	68	*	CBT	8	8	PHQ-9	16.78 (4.21)

							239	40.52	68	*	TAU	*	*	PHQ-9	16.32 (4.52)
							242	39.43	65	*	CBT	6	6	PHQ-9	16.87 (3.99)
Gilbody et al, 2017	Available	UK	*	PHQ-9	10	Primary	187	41	66.8	38.5	CBT	6	6	PHQ-9	16.8 (3.9)
							182	40.3	62.1	39	CBT	6	6	PHQ-9	16.4 (4.1)
Glozier et al, 2013	Unavailable	Australia	*	Kessler	16	Community	280	57.5	61.8	*	CBT	12	12	PHQ-9	12 (3.4)
							282	58.4	61	*	APP	12	*	PHQ-9	11.8 (3.4)
Griffiths et al, 2012	Unavailable	Australia	*	Kessler	23	Community	123	44.4	61	*	APP	12	*	CES-D	26.2 (11.55)
							121	41.2	75.7	*	CBT	12	12	CES-D	24.3 (10.18)
							117	45.3	72.6	*	CBT	12	12	CES-D	24.4 (10.44)
							117	44.7	60.8	*	WL	12	12	CES-D	25.93 (11.43)
Hadjistavropoulos et al, 2017	Available	Canada	*	PHQ-9	6	Community	92	38.19	82.4	64.8	CBT	8	5	PHQ-9	11.85 (6.07)
							88	38.4	74.7	54.2	CBT	8	5	PHQ-9	10.52 (5.79)
Hur et al, 2018	Unavailable	South Korea	DSM-V	*	*	Community	24	24.76	*	*	CT	3	1	BDI	22.65 (7.94)
							24	22.65	*	*	APP	3	*	BDI	25.59 (7.93)
Johansson et al, 2012	Available	Sweden	DSM-IV	MADRS-S	15	community	40	43.7	70	30	CBT	10	8	BDI-II	25.3 (8)
							42	44.8	69	40.5	WL	10	*	BDI-II	26.24 (7.9)
Kenter et al, 2016	Available	Netherlands	DSM-IV	*	*	Primary	136	38.6	57.4	21.3	PST	8	5	CES-D	37 (11.6)
							133	37.4	50.4	28.6	WL	8	*	CES-D	35.2 (12.2)
Kivi et al, 2014	Available	Sweden	DSM-IV	*	*	Primary	45	36.6 together	66 together	24.44	3W	12	7	BDI-II	25.5 (7.87)
							47	36.6 together	66 together	23.40	TAU	12	*	BDI-II	26.09 (9.39)
Kleiboer et al, 2015	Available	Netherlands	*	CES-D	16	Community	107	42.8	65	*	PST	5	5	CES-D	27.2 (6.9)
							108	44.4	64	*	PST	5	5	CES-D	26.5 (6.9)
							106	42.9	68	*	PST	5	5	CES-D	27.2 (6.7)
							106	45.6	63	*	WL	5	*	CES-D	27 (6.4)
Klein et al, 2016	Available	Germany	*	PHQ-9	5	Community	509	42.8	68.8	*	CBT	12	10	PHQ-9	10.23 (2.41)
							504	42.9	68.5	*	WL	12	*	PHQ-9	10.34 (2.4)
							509	42.8	68.8	*	CBT	12	10	PHQ-9	10.23 (2.41)
							504	42.9	68.5	*	WL	12	*	PHQ-9	10.34 (2.4)
Lambert et al, 2018	Unavailable	UK	*	PHQ-8	10	Community	32	39.3	81	56	BA	8	13	PHQ-8	14.4 (3.4)
							30	36.9	87	60	WL	8	*	PHQ-8	14.8 (2.9)
Lappalainen et al, 2015	Unavailable	Finland	DSM-IV	*	*	Community	19	50.32	68.4	15.8	3W	6	6	BDI-II	22.11 (7.79)

							20	53.4	75	25	WL	6	*	BDI-II	20.65 (6.8)
Lintvedt et al, 2013	Available	Norway	*	Kessler	20	Community	81	28.8	67.9	*	CBT	8	5	CES-D	22.1 (10)
							82	27.5	85.4	*	WL	8	*	CES-D	19.5 (10)
Löbner et al, 2018	Unavailable	Germany	ICD-10	PHQ-9	5	Primary	320	40.2	69	52	CBT	6	5	BDI-II	23.6 (11)
							327	47.5	67.9	59	TAU	6	*	BDI-II	20.4 (11.5)
Lundgren et al, 2016	Available	Sweden	*	PHQ-9	5	Secondary	25	63.6	40	12	BA	9	7	PHQ-9	10.8 (5.7)
							25	62.3	42	24	WL	9	*	PHQ-9	10.6 (5)
Ly et al, 2014	Available	Sweden	DSM-IV	PHQ-9	5	Community	40	36.6	70	30	BA	8	1	BDI-II	23.5 (7.85)
							41	35.6	70.7	34.1	3W	8	1	BDI-II	24.68 (9.47)
Mantani et al, 2017	Available	Japan	DSM-V	BDI-II	10	Secondary	60	40.2	57	100	CBT	8	8	PHQ-9	13.5 (5.5)
							57	41.6	50	100	WL	8	*	PHQ-9	12.9 (5.3)
Meyer et al, 2015	Available	Germany	*	PHQ-9	15	Community	78	44	74.4	50	CBT	12	10	PHQ-9	16.62 (3.44)
							85	40	75.3	52.9	WL	12	*	PHQ-9	17.2 (3.86)
Milgrom et al, 2016	Available	Australia	DSM-IV	EPDS	11	Community	21	31.7	100	5	CBT	12	6	BDI-II	25.3 (6.4)
							22	31.5	100	19	TAU	12	*	BDI-II	26.3 (8.6)
Mohr et al, 2013	Available	USA	DSM-IV	QIDS	11	Primary	34	47.6	73.5	35.3	CBT	12	7	PHQ-9	15.71 (4.8)
							35	48.9	71.4	34.3	CBT	12	7	PHQ-9	15.51 (4.9)
							33	48.49	69.7	33.3	WL	6	*	PHQ-9	15.36 (4.8)
Montero-Marin et al, 2016	Available	Spain	*	BDI-II	14	Primary	96	43.19	79.2	91.7	CBT	12	10	BDI-II	22.36 (4.91)
							98	42.57	73.5	85.7	CBT	12	10	BDI-II	22.33 (4.85)
							102	43.04	74.5	89.2	TAU	12	*	BDI-II	22.18 (5.25)
Morthland et al, 2012	Unavailable	USA	*	GDS-30	10	Community	17	63.82	47.1	*	CBT	4	11	HAM-D 17	15.97 (7.6)
							17	61.53	41.1	*	WL	4	*	HAM-D 17	15.53 (8.43)
Newby et al, 2017	Unavailable	Australia	DSM-IV	PHQ-9	5	Community	49	43.5	81	32	CBT	10	6	PHQ-9	15.95 (5.25)
							57	49.3	63	50	WL	10	*	PHQ-9	14.29 (5.25)
Nobis et al, 2015	Available	Germany	*	CES-D	23	Community	130	50	64	*	BA	8	6	CES-D	32.17 (6.95)
							130	51	63	*	WL	8	*	CES-D	31.53 (7.51)
Nystrom et al, 2017	Unavailable	Sweden	DSM-IV	MADRS	15	Community	70	*	*	*	APP	12	8	PHQ-9	12.99 (5.11)
							65	*	*	*	APP	12	8	PHQ-9	12.68 (4.7)
							71	*	*	*	BA	12	8	PHQ-9	12.77 (3.99)
							51	*	*	*	BA	12	8	PHQ-9	13.31 (4.65)

							55	*	*	*	WL	12	*	PHQ-9	12.01 (5.08)
O'Mahen et al, 2013	Unavailable	UK	*	EPDS	13	Community	462	32.3	100	*	BA	15	11	EPDS	19.46 (3.81)
							448	32.2	100	*	WL	15	*	EPDS	19.44 (3.8)
O'Moore et al, 2017	Available	Australia	DSM-IV	*	*	Secondary	49	63.16	86.4	45.5	CBT	10	6	PHQ-9	13.95 (4.78)
							28	59.68	68	32	TAU	10	*	PHQ-9	12.75 (4.8)
Perini et al, 2009	Available	Australia	DSM-IV	PHQ-9	6	Community	29	49.28	85.2	40.7	CBT	8	6	PHQ-9	13.78 (4.53)
							19	49.3	66.7	66.7	WL	8	*	PHQ-9	14.72 (3.91)
Phillips et al, 2014	Available	UK	*	PHQ-9	10	Community	318	42.2	55	97	CBT	5	5	PHQ-9	14.6 (5.4)
							319	42.7	48	98	PE	5	*	PHQ-9	14.6 (5.6)
Pots et al, 2016	Available	Netherlands	*	CES-D	10	Community	82	45.15	92.7	0	3W	12	9	CES-D	26.7 (8.02)
							67	46.73	59.7	0	APP	12	9	CES-D	27.07 (9.17)
							87	48.54	72.4	0	WL	24	0	CES-D	26.51 (8.16)
Pugh et al, 2016	Available	Canada	*	EPDS	10	Community	25	NA	100	38	CBT	7	7	EPDS	14.92 (4.32)
							25	NA	100	22	WL	7	*	EPDS	15.13 (4.06)
Richards et al, 2015	Available	Ireland	*	BDI-II	14	Community	133	40.63	74	19.8	CBT	8	7	BDI-II	20.9 (3.83)
							129	39.05	71.7	21.7	WL	8	*	BDI-II	20.84 (4.17)
Roepke et al, 2015	Unavailable	USA	*	CES-D	16	Community	93	42.28	61.29	37.63	CBT	4	1	CES-D	34.48 (9.24)
							97	37.99	74.23	49.49	3W	4	1	CES-D	33.07 (8.81)
							93	40.27	76.34	44.09	WL	*	*	CES-D	32.62 (10.15)
Rollman et al, 2018	Unavailable	USA	*	PHQ-9	10	Primary	301	43	78.1	66.4	CBT	24	8	PHQ-9	13.2 (5.3)
							302	42.6	81.1	68.2	CBT	24	8	PHQ-9	13.4 (4.7)
							101	41.7	81.2	65.3	TAU	24	*	PHQ-9	13.1 (4.9)
Rosso et al, 2017	Available	USA	DSM-IV	PHQ-9	10	Community	37	29.2	62.2	*	CBT	10	6	PHQ-9	13.92 (3.89)
							40	28.8	75	*	WL	10	*	PHQ-9	15.58 (3.97)
Santucci et al, 2013	Unavailable	USA	*	PHQ-9	5	Community	21	*	*	*	CBT	8	8	PHQ-9	*(*)
							23	*	*	*	CBT	8	8	PHQ-9	*(*)
Sheeber et al, 2012	Available	USA	*	CES-D	21	Community	35	31.1	100	*	CBT	14	8	BDI	26.2 (9.8)
							35	30.9	100	*	WL	14	*	BDI	25.4 (9)
Smith et al, 2017	Available	Australia	DSM-IV	PHQ-9	5	Community	61	42.5	85.2	44.4	CBT	12	6	PHQ-9	16.39 (5.03)
							68	37.59	74.6	47.5	WL	12	*	PHQ-9	16.07 (5.03)
Spek et al, 2007	Available	Netherlands	*	EDS	12	Community	102	55	67.6	*	CBT	8	8	BDI-II	19.17 (7.21)
							100	55	59	*	WL	10	*	BDI-II	18.13 (8.1)

Terides et al, 2017	Unavailable	Australia	*	PHQ-9	5	Community	68	46.31	88	43	CBT	8	5	PHQ-9	10.82 (5.24)
							80	43.24	75	35	WL	8	*	PHQ-9	10.19 (5.2)
Titov et al, 2010	Unavailable	Australia	DSM-IV	PHQ-9	10	Community	47	44	63.4	63.4	CBT	8	6	PHQ-9	14.2 (4.2)
							49	40	86.9	46.5	CBT	8	6	PHQ-9	14.15 (4.39)
							45	46	70	55	WL	8	*	PHQ-9	13.35 (4.62)
Titov et al, 2011	Unavailable	Australia	DSM-IV	*	*	Community	18	*	*	*	CBT	10	8	PHQ-9	14.39 (4.27)
							20	*	*	*	WL	10	*	PHQ-9	13.35 (6.25)
Titov et al, 2013	Unavailable	Australia	*	PHQ-9	10	Community	109	40.31	77	45	CBT	8	5	PHQ-9	11.71 (4.72)
							110	40.71	73.6	28.3	CBT	8	5	PHQ-9	10.99 (4.92)
							55	44.45	66.7	47.1	WL	8	*	PHQ-9	10.53 (4.63)
Titov et al, 2015	Unavailable	Australia	*	PHQ-9	5	Community	*	*	*	*	CBT	8	5	PHQ-9	*(*)
							*	*	*	*	CBT	8	5	PHQ-9	*(*)
							*	*	*	*	CBT	8	5	PHQ-9	*(*)
							*	*	*	*	CBT	8	5	PHQ-9	*(*)
Tulbure et al, 2017	Unavailable	Romania	DSM-IV	BDI-II	14	Community	34	29.21	88.2	*	CBT	9	9	BDI-II	34.47 (8.56)
							26	35.65	73.1	*	WL	9	*	BDI-II	31.88 (7.11)
Unlu et al, 2013	Available	Netherlands	*	CES-D	16	Community	49	34.9	65	*	PST	5	5	CES-D	29.6 (9.2)
							47	35.6	57	*	WL	5	*	CES-D	30.1 (10.1)
vanBastelaar et al, 2011	Available	Netherlands	*	CES-D	16	Community	125	48	66	11	CBT	8	8	CES-D	29 (7)
							130	51	56	11	WL	8	*	CES-D	28 (7)
vanLuenen et al, 2018	Available	Netherlands	*	PHQ-9	5	Secondary	97	45.53	12	12	CBT	8	8	PHQ-9	11.74 (2.49)
							91	47.12	11	11	WL	8	*	PHQ-9	11.11 (2.37)
Vemmark et al, 2010	Available	Sweden	DSM-IV	MADRS-S	15	Community	29	37.2	79.3	10.3	CBT	8	7	BDI	22.2 (6.3)
							29	32.7	55.2	24.1	WL	8	*	BDI	21.8 (6.6)
Warmerdam et al, 2008	Available	Netherlands	*	CES-D	16	Community	88	45.1	64.8	34.1	PST	5	5	CES-D	31.9 (9.3)
							88	45.7	69.3	37	CBT	8	8	CES-D	31.2 (9.3)
							87	44.1	79.3	34.5	WL	*	*	CES-D	32.1 (9.3)
Wilson et al, 2017	Unavailable	USA	*	PHQ-9	10	Community	27	45.7	91	*	CT	8	14	PHQ-8	22.18 (4.87)
							26	47.5	80	*	APP	8	*	PHQ-8	22.2 (3.38)
Zagorscak et al, 2018	Available	Germany	ICD-10	BDI-II	14	Primary	534	45.8	66.3	31.3	CBT	6	7	PHQ-9	11.7 (3.5)
							555	45.7	64.9	32.3	CBT	6	7	PHQ-9	11.9 (3.4)

8 Risk of bias of included studies

The inter-rater reliability of the assessment of risk of bias

Domains	Patterns			Percentage agreement	Weighted kappa
	Low	Some	High		
	Some				
	High				
Bias arising from the randomization process	47	4	0	97.8%	0.74
	3	4	0		
	0	0	2		
Bias due to deviations from intended interventions	1	2	0	92.1%	0.17
	6	39	8		
	0	3	1		
Bias due to missing outcome data	46	0	4	87.5%	0.54
	0	0	0		
	3	2	5		
Bias in measurement of the outcome	0	1	1	94.8%	0.29
	0	0	0		
	1	0	57		
Bias in selection of the reported result	39	0	0	97.5%	0.84
	5	13	1		
	0	0	2		

	Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result
Andersson2015	+	?	+	-	+
Arean2016	+	+	+	-	?
Beevers2017	+	?	+	-	+
Berger2011	+	?	+	-	+
Birney2016	+	?	+	-	?
Boele2017	-	?	-	-	+
Boeschoten2017	+	?	+	-	+
Buntrock2015	+	?	+	-	+
Burton2015	+	?	-	-	?
Carlbring2013	+	?	+	-	+
Choi2012	+	?	+	-	+
Christensen2004	+	?	+	-	+
Cooper2011a	+	?	-	-	+
Dahne2018	?	?	+	-	+
Day2013	+	?	+	-	?
DeGraaf2009	+	+	+	-	+
Ebert2014a	+	?	+	-	+
Ebert2014b	+	?	+	-	?
Ebert2017	+	+	+	-	+
Farrer2011	+	?	+	-	+
Forand2017	+	?	+	-	+
Forsell2017	+	?	+	-	+
Geraedts2014	+	+	+	-	+
Gilbody2015	+	?	+	-	+
Gilbody2017	+	?	+	-	+
Glozier2013	+	?	+	-	+
Griffiths2012	+	?	+	-	-
Hadjistavropoulos2017	+	?	+	-	+
Hur2018	+	-	-	-	?
Johansson2012	+	?	+	-	+
Kenter2016	+	?	+	-	+
Kivi2014	+	-	+	-	+
Kleiboer2015	+	?	+	-	+
Klein2016	+	?	+	-	+
Lambert2018	+	?	-	-	?
Lappalainen2015	+	?	+	-	?
Lintvedt2013	?	?	+	-	+
Löbner2018	-	?	+	-	?
Lundgren2016	+	?	+	-	+
Ly2014	+	?	+	-	+
Mantani2017	+	?	+	+	+
Meyer2015	+	+	+	-	+
Milgrom2016	+	-	+	-	+
Mohr2013	+	?	+	-	+
Montero-Marin2016	+	-	+	-	+
Morthland2012	+	?	-	+	?
Newby2017	+	?	+	-	+
Nobis2015	+	-	+	-	+
Nystrom2017	+	?	+	-	-
O'Mahen2013	+	?	-	-	?
O'Moore2017	+	?	+	-	+
Perini2009	?	?	+	-	+
Phillips2014	+	?	+	-	+
Pots2016	+	?	+	-	+
Pugh2016	+	-	+	-	+
Richards2015	+	?	-	-	+
Roepke2015	+	?	-	-	?
Rollman2018	+	+	+	-	-
Rosso2017	?	?	+	-	+
Santucci2013	?	?	-	-	?
Sheeber2012	+	?	+	-	+
Smith2017	+	?	+	-	+
Spek2007	+	?	+	-	+
Terides2017	+	?	+	-	?
Titov2010	+	?	?	-	?
Titov2011	+	?	?	-	?
Titov2013	+	?	?	-	?
Titov2015	+	?	+	-	?
Tulbure2017	?	?	-	-	?
Unlu2013	?	?	+	-	+
vanBastelaar2011	+	?	+	-	+
vanLuenen2018	+	?	+	-	+
Vernmark2010	+	?	+	-	+
Warmerdam2008	+	?	+	-	+
Wilson2017	?	-	+	-	?
Zagorscak2018	+	?	+	-	+

 Low risk
 Some conc
 High risk

9 Studies with high dropout

One of the studies (Richards 2015) had an extreme imbalance in the dropout among arms (0% vs. 50%). Following the protocol, only for this study, we performed sensitivity analyses using different assumptions regarding the missingness mechanism (See Appendix 2.5). We fit a series of missing completely at random (MCAR), missing at random (MAR) and missing not at random (MNAR) models. For MNAR, we assumed that missingness was related to unobserved outcomes. We explored scenarios where patients dropped out because of treatment inefficacy (i.e. when they do not gain any benefit from treatment), and other scenarios where they dropped out due to response (i.e. when they feel better, and thus decide to stop treatment). The MAR and MNAR analyses were adjusted for baseline, gender, and age.

MCAR analysis gave an estimate of -1.0 (95% CrI -2.7 to 0.7), favoring CBT vs. WL.

MAR analysis gave an estimate of -1.1 (95% CrI -2.8 to 0.6), favoring CBT vs. WL.

We used the following Bayesian model to implement the MNAR analyses.

```
model {  
  A~dnorm(0,0.01)  
  B~dnorm(0,0.01)  
  C~dnorm(0,0.01)  
  D~dnorm(0,0.01)  
  a~dnorm(0,1)  
  b~dnorm(0,100)I(0,)  
  c~dnorm(0,1)  
  d~dnorm(0,1)I(0,)  
  
  for (i in 1:Np){  
    missing[i]~dbern(p.miss[i])  
    logit(p.miss[i])<-a-b*(base[i]-y[i]) +c*age[i]+d*gender[i]### if changed to +b, lower outcome increases probability  
    of dropout  
  
    y[i]~dnorm(mu[i],prec.pat)  
    mu[i]<-A+B*treat[i]+C*age[i]+D*gender[i]  
    prec.pat~dunif(0,1)  
  }  
}
```

A MNAR analysis that assumed that dropout patients were more likely to have good outcomes rather than bad, gave the following estimated treatment effects: -5.0 (95% CrI -7.2 to -3.0). This analysis was based on assuming a prior for b (dnorm(0,100)I(0,)) in the code i.e. the positive part of $N(0,0.01)$ such that a unit decrease in the unobserved outcome would increase the log-odds of dropping out by 0.07.

Conversely, a MNAR analysis that assumed that dropout patients were more likely to have bad outcomes rather than good gave the following results: +0.1 (95% CrI -2.1 to 4.5). This analysis assumed that a unit increase in the unobserved outcome would increase the log-odds of dropping out by 0.07.

Moreover, both MNAR analyses were influenced by the choice of prior distributions. E.g. assuming $b \sim \text{dnorm}(0,10)I(0,)$ instead of $b \sim \text{dnorm}(0,100)I(0,)$ the results of the analysis were +4.8 (95% CrI 1.8 to 7.2).

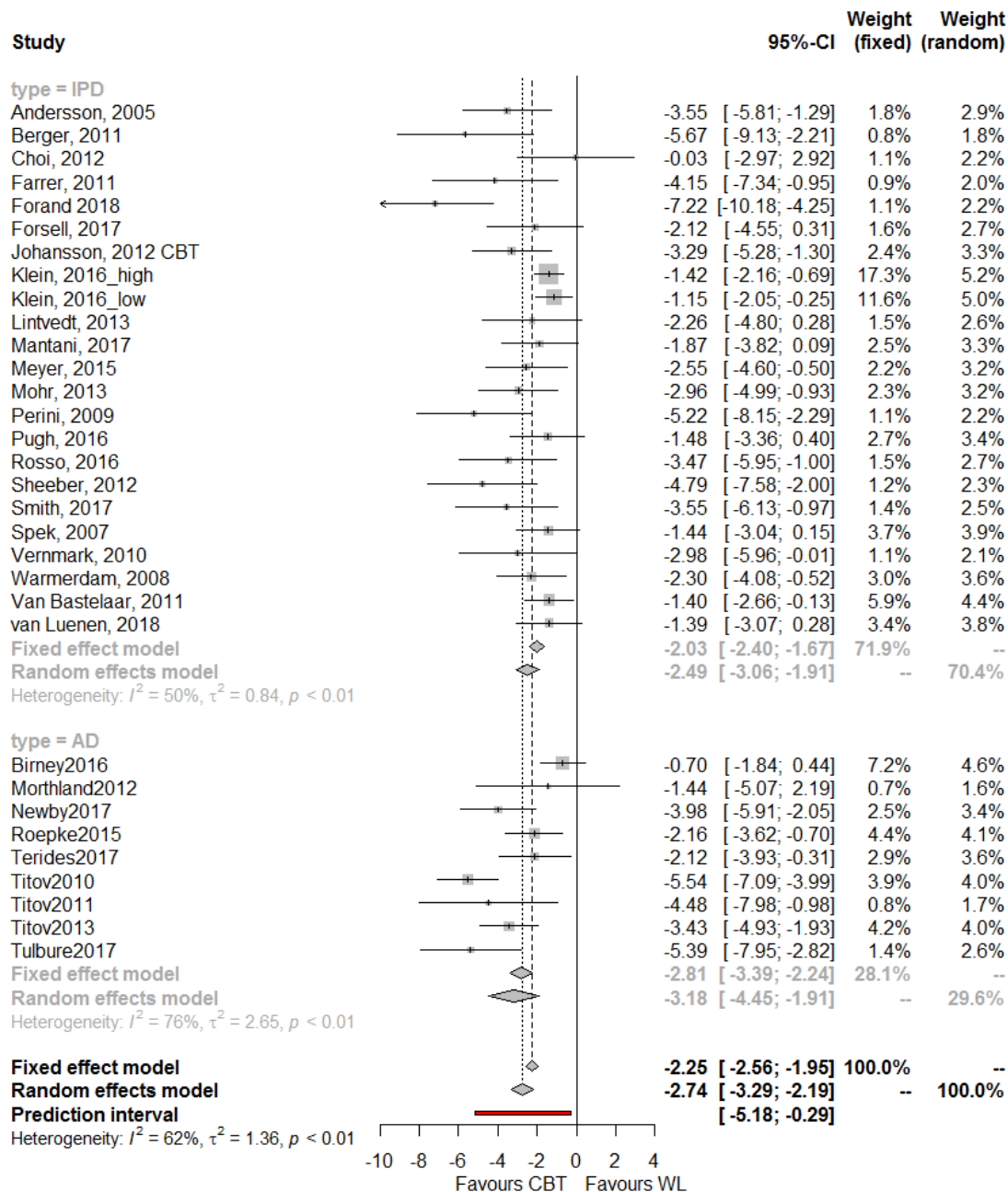
Thus, we see that overall the results from this study with the particularly large dropout are very sensitive to the various assumptions we can make about the unknown missing mechanism, and the estimated relative effects may vary substantially. Based on these results, we decided to exclude Richards 2015 from the analyses of the primary outcome.

10 Pairwise meta-analyses for depression severity

As detailed in Sections 2.1 and 2.4 of this appendix, we performed 10 multiple imputations for each study with IPD. We estimated treatment effects in each of such studies using Rubin's rules, and then we combined these study-level results with the study-level results from studies where IPD were not available and only published results could be used.

10.1 CBT vs WL

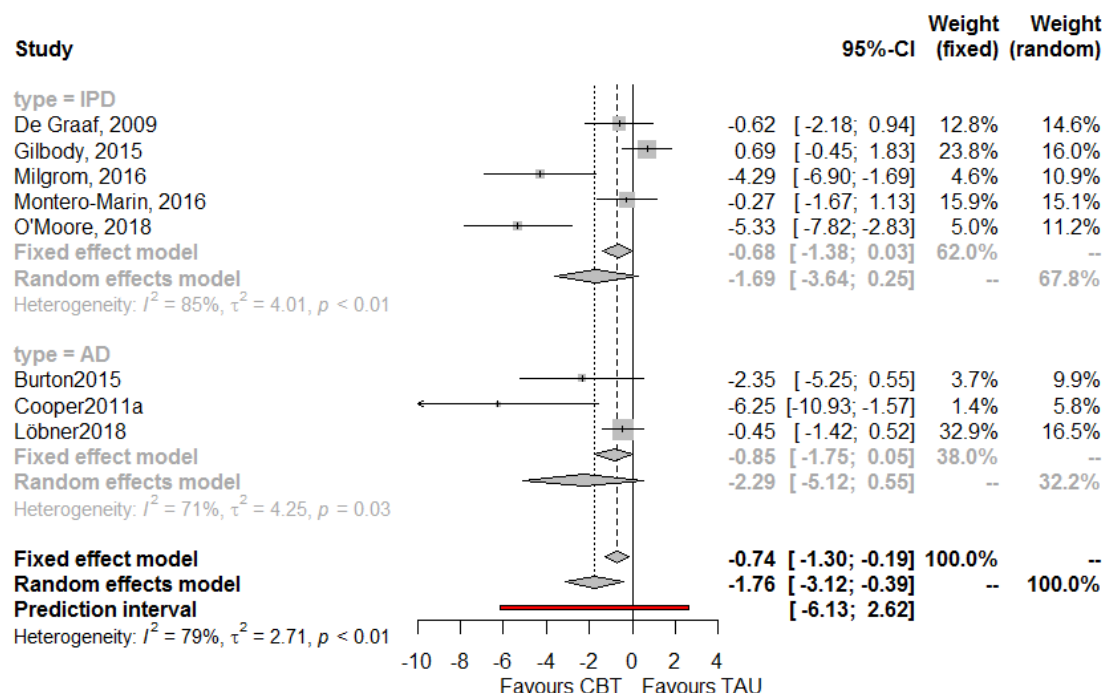
A total of 32 studies performed this comparison. Below we show the forest plot, by type of data each study provided (IPD or AD).



Test for subgroup differences (random effects model):
Q d.f. p-value

Between groups 0.97 1 0.3256

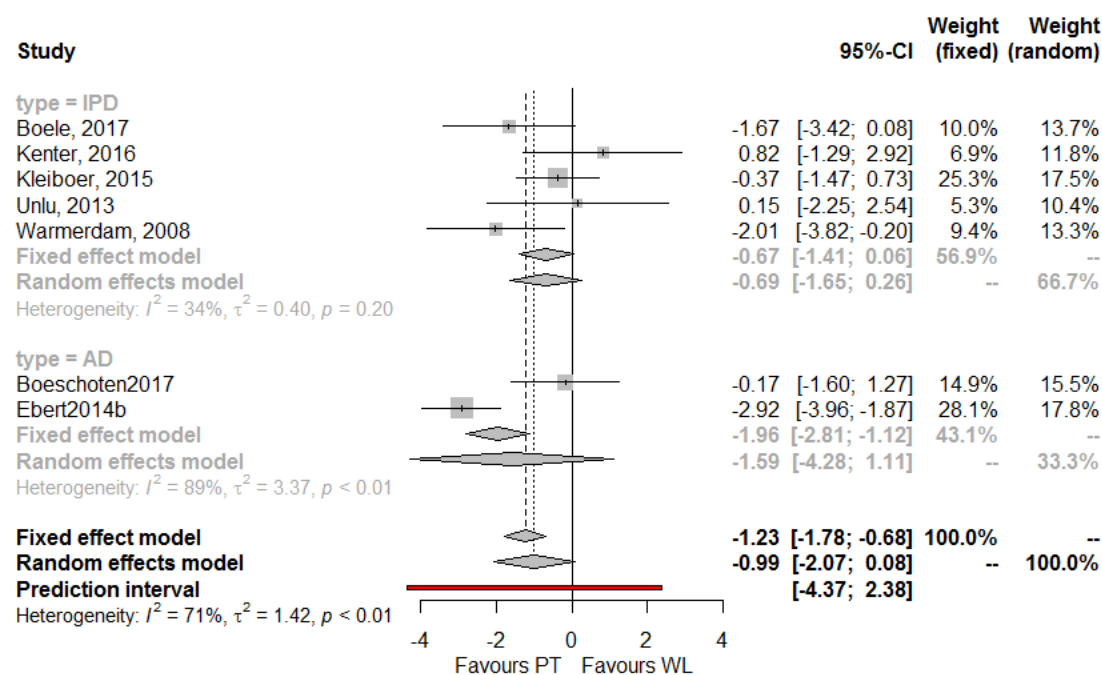
10.2 BT vs TAU



Test for subgroup differences (random effects model):

Q d.f. p-value
Between groups 0.11 1 0.7357

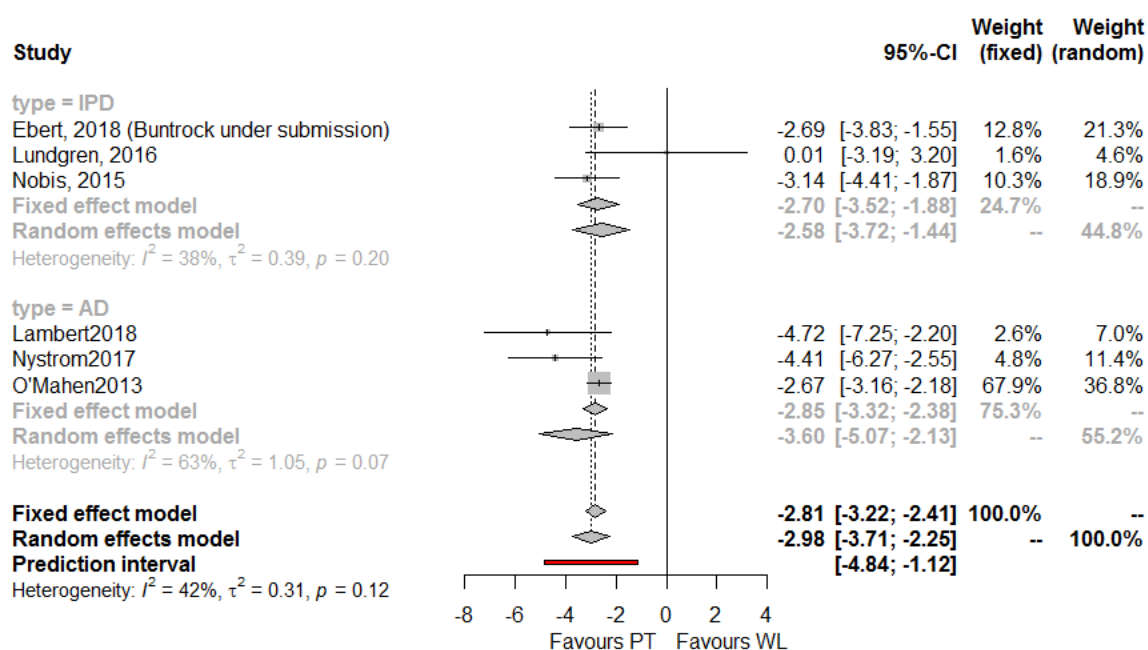
10.3 PST vs WL



Test for subgroup differences (random effects model):

Between groups Q d.f. p-value
 0.38 1 0.5393

10.4 BA vs WL



11 NMA of treatments for depression severity

11.1 Assessment of transitivity

Below we give the mean age, baseline severity and gender for studies grouped by comparison. There is one comparison that stands out, i.e. CT vs APP. This is informed by two AD studies only, both of which have very high baseline. CT is not present in any other study. High baseline is expected to be associated with larger effects. Thus, we expect CT to be shown to be particularly effective in the NMA, but this will be an overestimation.

	studlab	comp	age	baseline	gender
66	Pots, 2016- ACT	3W - APP	45	11.6	94
56	Ly, 2014	3W - BA	35	13.4	72
17	Roepke2015	3W - CBT	40	14.7	71
50	Kivi, 2014	3W - TAU	36	14.2	66
9	Lappalainen2015	3W - WL	52	11.4	72
18	Roepke2015	3W - WL	40	14.7	71
30	Carlbring, 2013	3W - WL	44	14.0	75
67	Pots, 2016- ACT	3W - WL	45	11.6	94
13	Nystrom2017	APP - BA	NaN	12.6	NaN
6	Glozier2013	APP - CBT	58	11.9	61
32	Christensen, 2004	APP - CBT	37	11.1	69
7	Hur2018	APP - CT	24	17.1	NaN
25	Wilson2017	APP - CT	47	25.0	86
33	Christensen, 2004	APP - PE	37	11.1	69
14	Nystrom2017	APP - WL	NaN	12.6	NaN
68	Pots, 2016- ACT	APP - WL	45	11.6	94
35	Dahne, 2018	BA - CBT	45	14.9	83
29	Buntrock, 2015	BA - PE	46	11.5	75
36	Dahne, 2018	BA - PE	45	14.9	83
39	Ebert, 2014	BA - PE	47	10.4	27
8	Lambert2018	BA - WL	38	16.4	84
15	Nystrom2017	BA - WL	NaN	12.6	NaN
16	O'Mahen2013	BA - WL	32	13.2	100
40	Ebert, 2018 (Buntrock under submission)	BA - WL	45	11.3	80
55	Lundgren, 2016	BA - WL	61	12.9	50
62	Nobis, 2015	BA - WL	50	14.1	64
46	Geraedts, 2014	CBT - NT	43	10.8	66
34	Christensen, 2004	CBT - PE	37	11.1	69
37	Dahne, 2018	CBT - PE	45	14.9	83
41	Farrer, 2011	CBT - PE	40	15.5	84
65	Philips, 2014	CBT - PE	42	14.8	57
79	Warmerdam, 2008	CBT - PST	46	13.6	69
3	Burton2015	CBT - TAU	39	11.1	67
4	Cooper2011a	CBT - TAU	45	15.8	75
10	Löbner2018	CBT - TAU	44	11.8	68
38	De Graaf, 2009	CBT - TAU	45	18.4	57
47	Gilbody, 2015	CBT - TAU	NaN	16.8	66
59	Milgrom, 2016	CBT - TAU	32	11.3	100
61	Montero-Marin, 2016	CBT - TAU	43	11.9	24
63	O'Moore, 2018	CBT - TAU	63	14.1	86
1	Birney2016	CBT - WL	41	13.4	77
11	Morthland2012	CBT - WL	63	11.8	44
12	Newby2017	CBT - WL	46	15.1	72
19	Roepke2015	CBT - WL	40	14.7	71
20	Terides2017	CBT - WL	45	10.5	82
21	Titov2010	CBT - WL	43	13.9	73
22	Titov2011	CBT - WL	NaN	13.9	NaN
23	Titov2013	CBT - WL	42	11.1	72
24	Tulbure2017	CBT - WL	32	17.6	81
26	Andersson, 2005	CBT - WL	36	14.8	77
27	Berger, 2011	CBT - WL	38	19.0	70
31	Choi, 2012	CBT - WL	41	12.9	88
42	Farrer, 2011	CBT - WL	40	15.5	84
44	Forand 2018	CBT - WL	33	16.6	74
45	Forsell, 2017	CBT - WL	31	11.0	100
48	Johansson, 2012	CBT - WL	45	13.7	72
52	Klein, 2016_high	CBT - WL	43	11.8	73
53	Klein, 2016_low	CBT - WL	43	7.6	61
54	Lintvedt, 2013	CBT - WL	29	10.5	68
57	Mantani, 2017	CBT - WL	39	13.7	58
58	Meyer, 2015	CBT - WL	44	16.6	74
60	Mohr, 2013	CBT - WL	48	15.6	72
64	Perini, 2009	CBT - WL	49	14.2	85
69	Pugh, 2016	CBT - WL	31	10.5	100
70	Richards, 2015	CBT - WL	41	11.1	74

71	Rosso, 2016	CBT - WL	29	14.0	61
72	Sheeber, 2012	CBT - WL	31	13.8	100
73	Smith, 2017	CBT - WL	43	16.7	87
74	Spek, 2007	CBT - WL	55	10.4	68
76	Van Bastelaar, 2011	CBT - WL	48	12.2	66
77	van Luenen, 2018	CBT - WL	45	12.0	13
78	Vernmark, 2010	CBT - WL	37	15.3	79
80	Warmerdam, 2008	CBT - WL	46	13.6	69
43	Farrer, 2011	PE - WL	40	15.5	84
2	Boeschoten2017	PST - WL	49	14.9	81
5	Ebert2014b	PST - WL	47	9.2	84
28	Boele, 2017	PST - WL	43	9.6	60
49	Kenter, 2016	PST - WL	39	16.9	59
51	Kleiboer, 2015	PST - WL	43	11.0	65
75	Unlu, 2013	PST - WL	33	13.2	62
81	Warmerdam, 2008	PST - WL	46	13.6	69

N.B. The percentage for gender here refers to the percentage male among the analysed sample, excluding those with baseline PHQ-9 scores <5 or those missing both baseline and endpoint PHQ-9 scores for studies with IPD. For studies with AD only we used the numbers as originally reported in the publications. They therefore may be slightly different from the figures reported in the Appendix 7.

11.2 Assessment of inconsistency for the primary outcome

We fit the NMA at the treatment level using the netmeta command in R. Statistical heterogeneity was estimated to be $\tau^2 = 1.2$. The global, design-by-treatment test for inconsistency gave $Q=37.8$, with 17 degrees of freedom, $p\text{-value}=0.003$. The local approach to inconsistency (back-calculation method) gave the following results:

Random effects model:

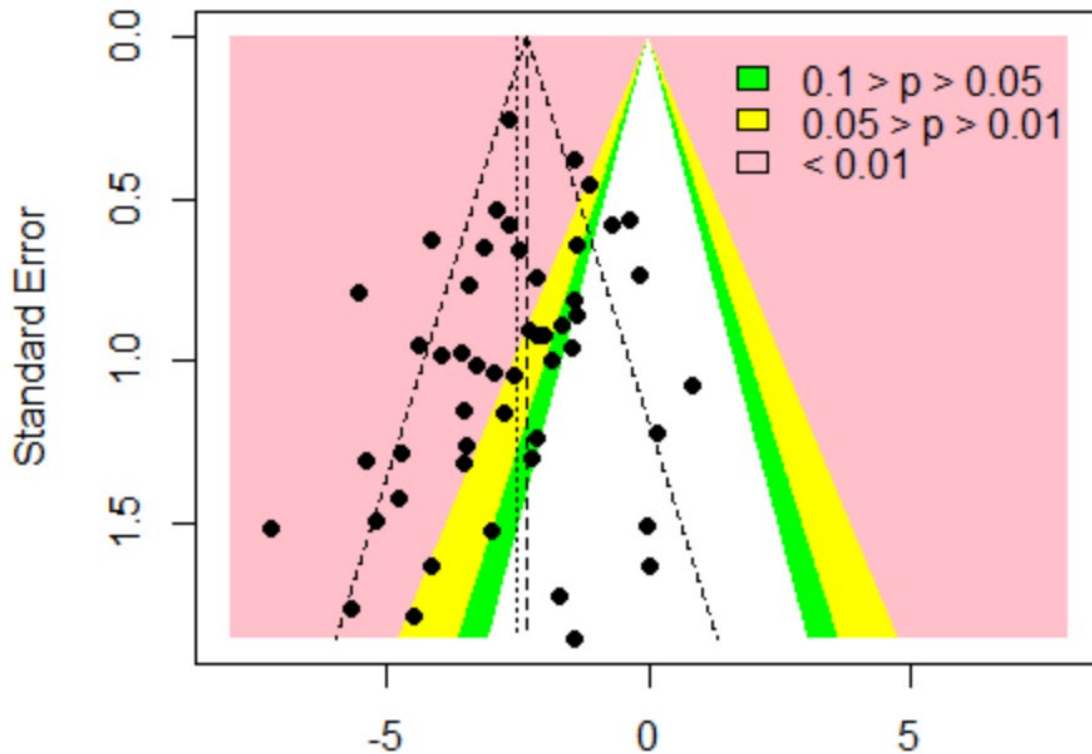
comparison	k	prop	nma	direct	indir.	Diff	z	p-value
3W:APP	1	0.33	-1.9385	-1.7033	-2.0561	0.3528	0.22	0.8250
3W:BA	1	0.19	0.4873	1.5790	0.2322	1.3468	0.77	0.4407
3W:CBT	1	0.21	-0.4292	-1.9900	-0.0175	-1.9725	-1.35	0.1758
3W:CT	0	0	2.2993	.	2.2993	.	.	.
3W:NT	0	0	-1.1502	.	-1.1502	.	.	.
3W:PE	0	0	-1.6112	.	-1.6112	.	.	.
3W:PST	0	0	-1.9494	.	-1.9494	.	.	.
3W:TAU	1	0.18	-1.7631	-0.3404	-2.0754	1.7350	0.90	0.3672
3W:WL	4	0.69	-3.0381	-3.2694	-2.5193	-0.7501	-0.61	0.5438
APP:BA	1	0.32	2.4259	2.0871	2.5826	-0.4955	-0.34	0.7313
APP:CBT	2	0.48	1.5093	1.4466	1.5675	-0.1209	-0.10	0.9191
APP:CT	2	1.00	4.2379	4.2379
APP:NT	0	0	0.7884	.	0.7884	.	.	.
APP:PE	1	0.35	0.3273	2.2149	-0.6843	2.8992	1.84	0.0658
APP:PST	0	0	-0.0109	.	-0.0109	.	.	.
APP:TAU	0	0	0.1754	.	0.1754	.	.	.
APP:WL	2	0.38	-1.0996	-1.4836	-0.8626	-0.6211	-0.51	0.6128
BA:CBT	1	0.04	-0.9165	0.2666	-0.9646	1.2312	0.47	0.6355
BA:CT	0	0	1.8120	.	1.8120	.	.	.
BA:NT	0	0	-1.6375	.	-1.6375	.	.	.
BA:PE	3	0.54	-2.0986	-3.2954	-0.6743	-2.6211	-2.11	0.0345
BA:PST	0	0	-2.4368	.	-2.4368	.	.	.
BA:TAU	0	0	-2.2505	.	-2.2505	.	.	.
BA:WL	6	0.70	-3.5255	-3.0386	-4.6642	1.6257	1.59	0.1123
CBT:CT	0	0	2.7285	.	2.7285	.	.	.
CBT:NT	1	1.00	-0.7210	-0.7210
CBT:PE	4	0.61	-1.1821	-0.7313	-1.8828	1.1515	0.93	0.3542
CBT:PST	1	0.17	-1.5202	-0.2858	-1.7645	1.4788	0.99	0.3212
CBT:TAU	8	0.93	-1.3340	-1.4625	0.2725	-1.7350	-0.90	0.3672
CBT:WL	32	0.90	-2.6089	-2.7163	-1.6714	-1.0448	-1.25	0.2128
CT:NT	0	0	-3.4495	.	-3.4495	.	.	.
CT:PE	0	0	-3.9106	.	-3.9106	.	.	.
CT:PST	0	0	-4.2488	.	-4.2488	.	.	.
CT:TAU	0	0	-4.0625	.	-4.0625	.	.	.
CT:WL	0	0	-5.3375	.	-5.3375	.	.	.
NT:PE	0	0	-0.4611	.	-0.4611	.	.	.
NT:PST	0	0	-0.7993	.	-0.7993	.	.	.
NT:TAU	0	0	-0.6130	.	-0.6130	.	.	.
NT:WL	0	0	-1.8879	.	-1.8879	.	.	.
PE:PST	0	0	-0.3382	.	-0.3382	.	.	.
PE:TAU	0	0	-0.1519	.	-0.1519	.	.	.
PE:WL	1	0.09	-1.4269	-1.6881	-1.4007	-0.2874	-0.13	0.8929

PST:TAU	0	0	0.1863	0.1863				
PST:WL	7	0.95	-1.0887	-1.0074	-2.6628	1.6555	0.71	0.4779
TAU:WL	0	0	-1.2750	-1.2750				

There were one comparisos for which there was strong evidence for inconsistency, out of a total of 18.

11.3 Assessment of publication bias and small study effects

We examined studies that compare an active treatment vs. WL. Below we show the contour-adjusted funnel-plot.



The funnel plot does not appear to be asymmetric. The p-value for Egger's test is 0.13. Overall, there is no evidence of publication bias and/or small study effects.

rp: relapse prevention
 tg: therapeutic guidance for icbt
 w: waiting component

12.2 Two-step component NMA

We performed the component NMA in a Bayesian setting. We used 2 chains, 5000 burn-in period, and 5000 iterations after that. We examined the mixing of the chains to assess convergence.

No covariates were used for this analysis. Note that *dt* was either present or absent in the arms of each RCT. Thus, we could not estimate the effects of *dt*.

Component	Depression severity (iMD in PHQ-9 scores)		
	Median	95% CrI	
<i>w</i> (<i>waiting component</i>)	0.21	-1.05	1.43
<i>ns</i> (<i>non-specific treatment effects</i>)	-1.65	-2.84	-0.46
<i>pe</i> (<i>psychoeducation</i>)	0.05	-0.93	1.02
<i>cr</i> (<i>cognitive restructuring</i>)	0.35	-0.87	1.53
<i>ba</i> (<i>behavioural activation</i>)	-1.95	-3.11	-0.83
<i>is</i> (<i>interpersonal skills training</i>)	-0.55	-1.64	0.56
<i>ps</i> (<i>problem solving</i>)	-0.66	-1.48	0.14
<i>re</i> (<i>relaxation</i>)	1.15	0.05	2.29
<i>3w</i> (<i>third-wave components</i>)	-0.64	-1.75	0.47
<i>bi</i> (<i>behaviour therapy for insomnia</i>)	-2.00	-4.20	0.25
<i>rp</i> (<i>relapse prevention</i>)	0.27	-0.80	1.33
<i>hw</i> (<i>homework required</i>)	0.36	-0.76	1.52
<i>ff</i> (<i>initial face-to-face contact</i>)	0.83	-1.94	3.66
<i>ae</i> (<i>automated encouragement</i>)	-0.27	-1.23	0.70
<i>he</i> (<i>human encouragement</i>)	-0.30	-1.25	0.67
<i>tg</i> (<i>therapeutic guidance</i>)	0.14	-0.85	1.10

iMD: incremental mean difference, CrI: credible interval

Common heterogeneity tau was estimated to be 1.310 (95%CrI: 0.991 to 1.717) in terms of PHQ-9 points.

To help visualize results, we have used a coloring scheme to denote the strength of the evidence for, or against each component. This follows the procedure previously described in the so-called ‘Kilim plot’:

- Seo M, Furukawa TA, Veroniki AA, Pillinger T, Tomlinson A, Salanti G, Cipriani A, Efthimiou O. The Kilim plot: A tool for visualizing network meta-analysis results for multiple outcomes. *Res Synth Methods*. 2021 Jan;12(1):86-95. doi: 10.1002/jrsm.1428. Epub 2020 Jul 16. PMID: 32524754.

More specifically, we calculate a type of Z-score, by dividing the median of the posterior distribution by the corresponding standard deviation for Bayesian analyses, or mean estimate divided by standard error for frequentist analyses. Then we use the following coloring scheme:

Z-score	color
<-3	
[-3,-2]	

[-2, -1]	
[-1,0]	
[0,1]	
[1,2]	
[2,3]	
>3	

Thus, *ba* for example, which has a big negative (i.e. beneficial) estimate, with relatively narrow credible intervals gets a deep green color. Components for which there is large uncertainty, or for which the corresponding estimate is near zero get a white color. Components for which there is evidence of a detrimental effect are colored in red, where the shade is chosen according to the strength of the evidence and the magnitude of the effect.

We repeated the analysis in a Frequentist setting. We fitted the model in R using the `discomb` command in `netmeta`. Results are shown below:

Component	Depression severity (iMD in PHQ-9 scores)		
	Mean	95% CI	
<i>w (waiting component)</i>	0.03	-0.96	1.01
<i>ns (non-specific treatment effects)</i>	-1.56	-2.54	-0.58
<i>pe (psychoeducation)</i>	0.06	-0.72	0.84
<i>cr (cognitive restructuring)</i>	0.54	-0.42	1.50
<i>ba (behavioural activation)</i>	-1.80	-2.7	-0.90
<i>is (interpersonal skills training)</i>	-0.67	-1.6	0.26
<i>ps (problem solving)</i>	-0.42	-1.09	0.26
<i>re (relaxation)</i>	1.14	0.23	2.06
<i>3w (third-wave components)</i>	-0.65	-1.54	0.25
<i>bi (behaviour therapy for insomnia)</i>	-1.82	-3.73	0.1
<i>rp (relapse prevention)</i>	0.24	-0.66	1.14
<i>hw (homework required)</i>	-0.01	-0.95	0.93
<i>ff (initial face-to-face contact)</i>	0.84	-1.62	3.30
<i>ae (automated encouragement)</i>	-0.17	-0.93	0.59
<i>he (human encouragement)</i>	-0.45	-1.28	0.39
<i>tg (therapeutic guidance)</i>	0.34	-0.47	1.14

$$\tau^2 = 0.9$$

Results did not materially differ from the frequentist analysis, although 95% Confidence Intervals were narrower than 95% Credible Intervals, due to the higher estimate for heterogeneity in the Bayesian analysis.

12.3 One-step component NMA

We fitted the one-stage model described in Section 2.3 in all studies, i.e. including both IPD and AD studies. We fitted in each one of the imputed datasets ($m=10$) separately. Each of these imputed datasets includes all AD and IPD studies, with imputations only for the latter. We fit 2 chains, with 1000 iterations each, after 500 burn-in iterations. After fitting the model in each multiply imputed dataset, we combine all MCMC draws from all imputed datasets to approximate the posterior distribution. We use 4 covariates (age, baseline, gender and relationship status). All covariates were standardized for the analysis. We only use the colouring scheme for the main effects of the components.

	Depression severity (iMD in PHQ-9 scores)		
	Median	95% CrI	
age	0.191	-0.089	0.473
baseline depression	2.591	2.322	2.853
gender	-0.034	-0.281	0.176
relationship	-0.122	-0.33	0.119
<i>w (waiting component)</i>	0.415	-0.75	1.534
<i>dt (conventional drug treatment)</i>	-0.238	-61.894	61.998
<i>ns (non-specific treatment effects)</i>	-1.407	-2.515	-0.295
<i>pe (psychoeducation)</i>	0.016	-0.863	0.929
<i>cr (cognitive restructuring)</i>	0.296	-0.871	1.406
<i>ba (behavioural activation)</i>	-1.832	-2.902	-0.8
<i>is (interpersonal skills training)</i>	-0.543	-1.587	0.517
<i>ps (problem solving)</i>	-0.641	-1.412	0.092
<i>re (relaxation)</i>	1.202	0.168	2.274
<i>3w (third-wave components)</i>	-0.528	-1.552	0.492
<i>bi (behaviour therapy for insomnia)</i>	-1.817	-3.922	0.259
<i>rp (relapse prevention)</i>	0.349	-0.685	1.323
<i>hw (homework required)</i>	0.309	-0.689	1.347
<i>ff (initial face-to-face contact)</i>	0.853	-1.797	3.407
<i>ae (automated encouragement)</i>	-0.256	-1.131	0.603
<i>he (human encouragement)</i>	-0.292	-1.173	0.583
<i>tg (therapeutic guidance)</i>	0.007	-0.88	0.889
age*w	0.019	-0.14	0.31
age*dt	0	-0.2	0.207
age*ns	-0.01	-0.196	0.136
age*pe	0	-0.163	0.179
age*cr	-0.006	-0.184	0.152
age*ba	-0.015	-0.205	0.122
age*is	-0.007	-0.209	0.173
age*ps	-0.009	-0.175	0.129
age*re	-0.011	-0.192	0.137
age*3w	-0.013	-0.228	0.14
age*bi	-0.009	-0.234	0.153
age*rp	-0.007	-0.17	0.129
age*hw	0.007	-0.151	0.249
age*ff	-0.039	-0.473	0.122
age*ae	0.001	-0.16	0.18
age*he	-0.023	-0.328	0.135

age*tg	-0.014	-0.277	0.22
baseline depression*w	0.052	-0.075	0.31
baseline depression*dt	0.001	-0.213	0.209
baseline depression*ns	0.01	-0.136	0.241
baseline depression*pe	-0.065	-0.339	0.068
baseline depression*cr	-0.027	-0.24	0.111
baseline depression*ba	-0.063	-0.338	0.072
baseline depression*is	-0.046	-0.335	0.079
baseline depression*ps	0.022	-0.095	0.228
baseline depression*re	0.014	-0.117	0.219
baseline depression*3w	0	-0.18	0.185
baseline depression*bi	0	-0.193	0.198
baseline depression*rp	-0.004	-0.157	0.147
baseline depression*hw	-0.053	-0.287	0.072
baseline depression*ff	0.091	-0.039	0.347
baseline depression*ae	-0.032	-0.243	0.092
baseline depression*he	-0.076	-0.351	0.054
baseline depression*tg	-0.03	-0.243	0.098
gender*w	-0.024	-0.231	0.099
gender*dt	0	-0.206	0.212
gender*ns	0.028	-0.097	0.258
gender*pe	0.001	-0.155	0.152
gender*cr	-0.005	-0.164	0.134
gender*ba	0.002	-0.158	0.151
gender*is	-0.014	-0.215	0.121
gender*ps	0.005	-0.128	0.153
gender*re	0.006	-0.129	0.179
gender*3w	-0.023	-0.265	0.113
gender*bi	0	-0.206	0.185
gender*rp	0.018	-0.107	0.183
gender*hw	0.054	-0.064	0.293
gender*ff	0.01	-0.102	0.17
gender*ae	0.002	-0.152	0.149
gender*he	0.016	-0.113	0.188
gender*tg	0.034	-0.082	0.235
relationship*w	0.001	-0.15	0.153
relationship*dt	-0.001	-0.206	0.21
relationship*ns	-0.015	-0.217	0.117
relationship*pe	-0.009	-0.178	0.126
relationship*cr	-0.008	-0.17	0.121
relationship*ba	-0.018	-0.205	0.104
relationship*is	0.039	-0.084	0.306
relationship*ps	-0.022	-0.202	0.092
relationship*re	0.02	-0.111	0.221
relationship*3w	0.012	-0.135	0.215
relationship*bi	-0.008	-0.248	0.158
relationship*rp	-0.004	-0.151	0.132
relationship*hw	-0.007	-0.165	0.12
relationship*ff	-0.004	-0.148	0.124
relationship*ae	0.01	-0.115	0.177

relationship*he	-0.02	-0.198	0.103
relationship*tg	-0.003	-0.156	0.138

iMD: incremental mean difference, CrI: credible interval

Common heterogeneity tau was estimated to be 1.203 (95%CrI: 0.889 to 1.570) in terms of PHQ-9 points.

13 Component NMA for dropouts from treatment

13.1 Two-step component NMA for dropouts from treatment

We conducted a cNMA of studies comparing active treatments from five trials with AD datasets and 10 trials with IPD datasets. Due to limited sample size, the obtained estimates were rather imprecise. Because of the structure of the network, we were not able to disentangle the effects of some components. Below we show results for the components whose effects we were able to disentangle.

	Dropout from treatment (iOR)		
	Median	95% CrI	
<i>ff (initial face-to-face contact)</i>	0.82	0.24	2.77
<i>ae (automated encouragement)</i>	0.58	0.32	1.16
<i>he (human encouragement)</i>	0.55	0.25	1.23
<i>tg (therapeutic guidance)</i>	1.12	0.49	2.51

iOR: incremental odds ratio

Here we have used the same coloring scheme as mentioned above, but this time the Z-score was calculated on the log odds ratio level.

13.2 One-step component NMA for dropouts from treatment

Due to the limited sample size, we were unable to conduct IPD component NMA of dropout from treatment.

14 Component NMA for dropouts from assessment

14.1 Two-step component NMA for dropouts from assessment

We performed the analysis in a Bayesian setting, as described for the primary outcome. We used 2 chains, 5000 burn-in, 5000 iterations. No imputation was necessary for this analysis, since dropout data was available for all patients. Note that *dt* was either present or absent in the arms of each RCT. Thus, we could not estimate the effects of *dt*.

Component	Dropout from assessment (iOR)		
	Median	95% CrI	
<i>w (waiting component)</i>	0.61	0.30	1.16
<i>ns (non-specific treatment effects)</i>	1.24	0.64	2.30
<i>pe (psychoeducation)</i>	0.78	0.47	1.32
<i>cr (cognitive restructuring)</i>	1.30	0.65	2.57
<i>ba (behavioural activation)</i>	1.05	0.58	1.88
<i>is (interpersonal skills training)</i>	0.47	0.26	0.84
<i>ps (problem solving)</i>	0.79	0.51	1.21
<i>re (relaxation)</i>	1.18	0.65	2.11
<i>3w (third-wave components)</i>	0.95	0.54	1.68
<i>bi (behaviour therapy for insomnia)</i>	1.18	0.32	4.05
<i>rp (relapse prevention)</i>	1.54	0.87	2.70
<i>hw (homework required)</i>	0.79	0.45	1.39
<i>ff (initial face-to-face contact)</i>	1.10	0.21	7.06
<i>ae (automated encouragement)</i>	1.35	0.83	2.18
<i>he (human encouragement)</i>	1.77	1.09	2.84
<i>tg (therapeutic guidance)</i>	0.58	0.35	0.98

iOR: incremental odds ratio, CrI: credible interval

Common heterogeneity tau was estimated to be 0.607 (95%CrI: 0.434 to 0.832) in terms of $\ln(\text{OR})$.

14.2 One-step component NMA for dropouts from assessment

We fit the model in each of the imputed datasets ($m=10$). We fit 2 chains, with 1000 iterations each, after 500 burn-in iterations. We combine all MCMC draws from all imputed datasets to approximate the posterior distribution. We use 4 covariates (age, baseline, gender and relationship status).

	Dropout from assessment (iOR)		
	Median	95% CrI	
age	0.84	0.75	0.94
baseline depression	1.26	1.13	1.43
gender	1.04	0.93	1.17
relationship	0.94	0.84	1.05
<i>w (waiting component)</i>	0.64	0.31	1.28
<i>dt (conventional drug treatment)</i>	1.10	0.00	3.26E+08
<i>ns (non-specific treatment effects)</i>	1.32	0.67	2.61
<i>pe (psychoeducation)</i>	0.76	0.44	1.29

<i>cr (cognitive restructuring)</i>	1.29	0.67	2.50
<i>ba (behavioural activation)</i>	1.07	0.57	2.07
<i>is (interpersonal skills training)</i>	0.49	0.26	0.9
<i>ps (problem solving)</i>	0.80	0.51	1.26
<i>re (relaxation)</i>	1.16	0.64	2.06
<i>3w (third-wave components)</i>	0.96	0.52	1.77
<i>bi (behaviour therapy for insomnia)</i>	1.24	0.35	4.28
<i>rp (relapse prevention)</i>	1.59	0.89	2.84
<i>hw (homework required)</i>	0.77	0.42	1.38
<i>ff (initial face-to-face contact)</i>	1.12	0.18	8.26
<i>ae (automated encouragement)</i>	1.34	0.8	2.17
<i>he (human encouragement)</i>	1.76	1.07	2.86
<i>tg (therapeutic guidance)</i>	0.59	0.35	0.98
age*w	1	0.94	1.08
age*dt	1	0.92	1.09
age*ns	1	0.93	1.08
age*pe	0.99	0.9	1.05
age*cr	0.99	0.9	1.04
age*ba	1	0.93	1.06
age*is	1	0.94	1.08
age*ps	1	0.94	1.07
age*re	0.99	0.92	1.05
age*3w	0.99	0.88	1.05
age*bi	1	0.92	1.09
age*rp	1.03	0.97	1.15
age*hw	1.01	0.96	1.11
age*ff	1	0.95	1.08
age*ae	0.99	0.91	1.05
age*he	1.01	0.95	1.09
age*tg	1	0.95	1.08
baseline depression*w	0.97	0.84	1.03
baseline depression*dt	1	0.92	1.09
baseline depression*ns	1.01	0.95	1.11
baseline depression*pe	1	0.91	1.06
baseline depression*cr	0.99	0.92	1.05
baseline depression*ba	1	0.92	1.06
baseline depression*is	1	0.91	1.06
baseline depression*ps	1	0.93	1.06
baseline depression*re	0.99	0.91	1.04
baseline depression*3w	1	0.93	1.1
baseline depression*bi	1	0.91	1.09
baseline depression*rp	1	0.94	1.06
baseline depression*hw	1	0.93	1.06
baseline depression*ff	1	0.94	1.06
baseline depression*ae	1	0.94	1.08
baseline depression*he	1	0.93	1.06
baseline depression*tg	0.99	0.92	1.05

gender*w	0.98	0.88	1.03
gender*dt	1	0.91	1.09
gender*ns	1.01	0.95	1.11
gender*pe	1.01	0.95	1.09
gender*cr	1.02	0.97	1.12
gender*ba	1.01	0.96	1.11
gender*is	1	0.93	1.06
gender*ps	1	0.94	1.06
gender*re	1	0.95	1.08
gender*3w	1.01	0.94	1.1
gender*bi	1	0.92	1.08
gender*rp	0.97	0.87	1.03
gender*hw	1	0.93	1.06
gender*ff	0.98	0.88	1.02
gender*ae	1.01	0.96	1.1
gender*he	1	0.95	1.08
gender*tg	1.01	0.96	1.09
relationship*w	0.99	0.91	1.05
relationship*dt	1	0.92	1.09
relationship*ns	1.01	0.95	1.1
relationship*pe	1	0.94	1.08
relationship*cr	0.99	0.91	1.04
relationship*ba	1	0.93	1.07
relationship*is	1	0.91	1.06
relationship*ps	1.01	0.96	1.09
relationship*re	0.99	0.9	1.04
relationship*3w	1	0.92	1.07
relationship*bi	1	0.91	1.08
relationship*rp	1	0.95	1.07
relationship*hw	0.99	0.91	1.04
relationship*ff	0.97	0.88	1.02
relationship*ae	1	0.94	1.07
relationship*he	1	0.93	1.05
relationship*tg	0.99	0.9	1.04

iOR: incremental odds ratio, CrI: credible interval

Common heterogeneity tau was estimated to be 0.62 (95%CrI: 0.45 to 0.85) in terms of ln(OR).

15 Sensitivity analyses

We conducted the following four pre-defined sensitivity analyses for the primary outcome:

(i) We examined the impact of studies without formal diagnosis of depression by excluding them from the analyses.

(ii) We examined the impact of studies which recruited patients with depression or another mental disorder (which therefore may have included patients without depression), which focused on patients with depression and a physical disorder, or which involved special populations, by excluding them from the analyses.

(iii) We examined the impact of miscellaneous skills not covered in our classification in Table 1 (e.g. expressive writing, dreamwork) by excluding studies which included such skills.

(iv) We ran a sensitivity analysis including only studies where at least 60% of the participants completed at least 80% of the program, in order to exclude the influence of trials where the completion rate may have been low due to external circumstances that are not inherent to the components themselves.

15.1 Excluding studies without formal diagnosis of major depression

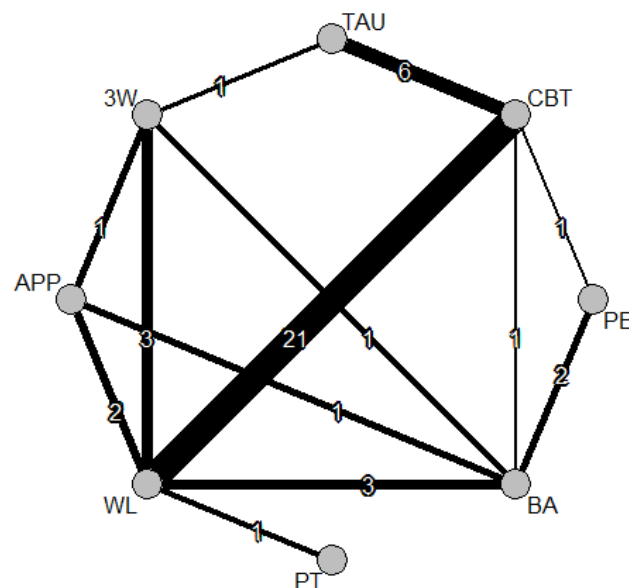
The following studies were included:

AD studies:

Lappalainen2015 Löbner2018 Newby2017 Nystrom2017 Titov2010
Titov2011 Tulbure2017

IPD studies:

Andersson, 2005 Choi, 2012 Dahne, 2018 De Graaf, 2009 Ebert, 2014
Forand 2018 Forsell, 2017 Johansson, 2012 CBT Kenter, 2016 Kivi, 2014
Klein, 2016_high Klein, 2016_low Lundgren, 2016 Mantani, 2017 Meyer, 2015
Milgrom, 2016 Montero-Marín, 2016 Nobis, 2015 O'Moore, 2018 Pots, 2016- ACT
Pugh, 2016 Rosso, 2016 Smith, 2017 Vernmark, 2010 Zagorscak, 2018
Van Bastelaar, 2011 Berger, 2011 Carlbring, 2013 Gilbody, 2015 Ly, 2014
Mohr, 2013 Perini, 2009



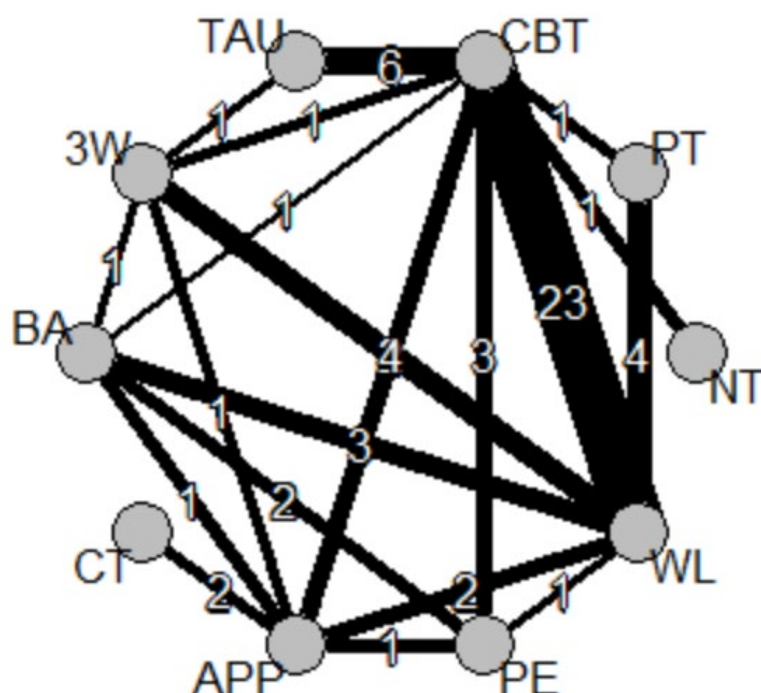
Component	Depression severity (iMD in PHQ-9 scores)		
	Mean	95% CI	
ae (automated encouragement)	-0.753	-2.222	0.697
ba (behavioural activation)	-3.007	-5.145	-0.987
bi (behaviour therapy for insomnia)	-2.311	-5.01	0.473
cr (cognitive restructuring)	0.998	-1.122	3.031
dt (conventional drug treatment)	-0.013	-61.798	62.616
ff (initial face-to-face contact)	1.597	-1.823	5.068
he (human encouragement)	-1.152	-2.832	0.467
hw (homework required)	0.557	-1.078	2.377
is (interpersonal skills training)	-0.591	-2.258	1.105
pe (psychoeducation)	1.236	-0.498	3.025
ns (non-specific treatment effects)	-1.895	-3.595	-0.274
ps (problem solving)	0.031	-1.571	1.656
re (relaxation)	0.976	-0.659	2.57
rp (relapse prevention)	0.192	-1.268	1.625
tg (therapeutic guidance)	1.121	-0.279	2.539
3w (third-wave components)	-0.368	-1.917	1.126
w (waiting component)	0.929	-0.782	2.586

tau 1.42 [0.88, 2.09]

15.2 Excluding studies with patients in special populations

The following studies were included:

Andersson, 2005 Berger, 2011 Buntrock, 2015 Carlbring, 2013 Christensen, 2004
Dahne, 2018 De Graaf, 2009 Farrer, 2011 Geraedts, 2014 Gilbody, 2015
Johansson, 2012 CBT Kenter, 2016 Kivi, 2014 Klein, 2016_high Klein, 2016_low
Lintvedt, 2013 Ly, 2014 Meyer, 2015 Mohr, 2013 Montero-Marin, 2016
Perini, 2009 Pots, 2016- ACT Smith, 2017 Spek, 2007 Vernmark, 2010
Warmerdam, 2008 Birney2016 Boeschoten2017 Burton2015 Cooper2011a
Ebert2014b Glozier2013 Hur2018 Lambert2018 Lappalainen2015
Löbner2018 Morthland2012 Newby2017 Nystrom2017 O'Mahen2013
Roepke2015 Terides2017 Titov2010 Titov2011 Titov2013
Tulbure2017 Wilson2017.



Component	Depression severity (iMD in PHQ-9 scores)		
	Mean	95% CI	
ae (automated encouragement)	0.067	-0.976	1.102
ba (behavioural activation)	-1.996	-3.338	-0.639
bi (behaviour therapy for insomnia)	-2.289	-4.982	0.506
cr (cognitive restructuring)	0.476	-0.968	1.763
dt (conventional drug treatment)	0.341	-61.695	62.13
ff (initial face-to-face contact)	0.781	-2.175	3.764
he (human encouragement)	-0.078	-1.178	1.019
hw (homework required)	0.394	-0.882	1.812
is (interpersonal skills training)	-1.232	-2.663	0.256
pe (psychoeducation)	-0.155	-1.207	0.896
ns (non-specific treatment effects)	-2.176	-3.736	-0.577
ps (problem solving)	-0.86	-1.921	0.184
re (relaxation)	1.543	0.197	2.993
rp (relapse prevention)	0.764	-0.551	2.03
tg (therapeutic guidance)	-0.054	-1.268	1.128
3w (third-wave components)	-0.439	-1.666	0.74
w (waiting component)	0.029	-1.711	1.817

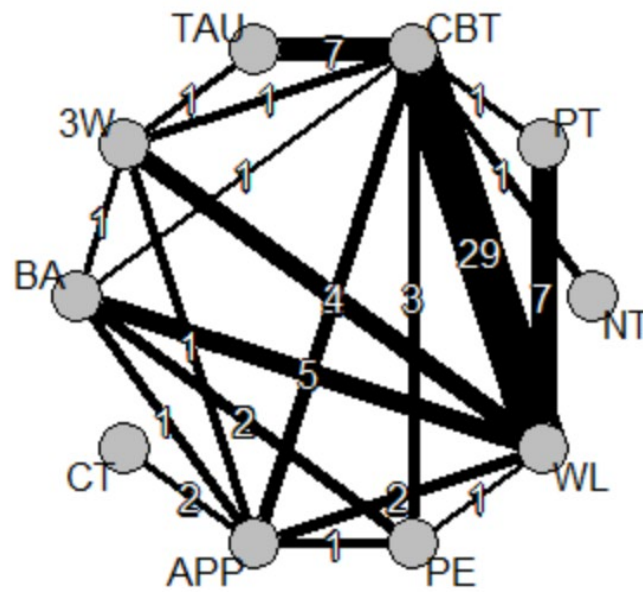
tau 1.24 [0.82, 1.76]

15.3 Excluding arms that used skills not covered in our classifications

The following studies were included:

Andersson, 2005	Berger, 2011	Boele, 2017	Buntrock, 2015	Carlbring, 2013
Choi, 2012	Christensen, 2004	Dahne, 2018	De Graaf, 2009	Farrer, 2011
Forsell, 2017	Geraedts, 2014	Gilbody, 2015	Johansson, 2012	CBT Kenter, 2016
Kivi, 2014	Kleiboer, 2015	Klein, 2016_high	Klein, 2016_low	Lintvedt, 2013

Lundgren, 2016 Ly, 2014 Mantani, 2017 Meyer, 2015 Milgrom, 2016
 Mohr, 2013 Montero-Marin, 2016 Nobis, 2015 Perini, 2009 Pots, 2016- ACT
 Pugh, 2016 Sheeber, 2012 Smith, 2017 Spek, 2007 Unlu, 2013
 Vernmark, 2010 Warmerdam, 2008 van Luenen, 2018 Birney2016 Boeschoten2017
 Burton2015 Cooper2011a Ebert2014b Glozier2013 Hur2018
 Lambert2018 Lappalainen2015 Löbner2018 Morthland2012 Newby2017
 Nystrom2017 O'Mahen2013 Roepke2015 Terides2017 Titov2010
 Titov2011 Titov2013 Tulbure2017 Wilson2017.

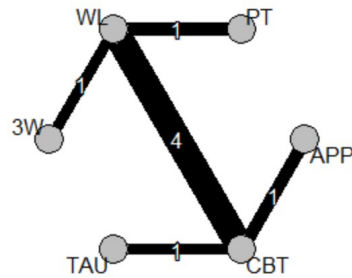


Component	Depression severity (iMD in PHQ-9 scores)		
	Mean	95% CI	
ae (automated encouragement)	-0.344	-1.234	0.539
ba (behavioural activation)	-1.838	-3.022	-0.717
bi (behaviour therapy for insomnia)	-2.172	-4.336	0.042
cr (cognitive restructuring)	0.553	-0.706	1.72
dt (conventional drug treatment)	0.086	-62.235	62.612
ff (initial face-to-face contact)	0.844	-1.995	3.685
he (human encouragement)	-0.442	-1.455	0.565
hw (homework required)	0.264	-0.871	1.447
is (interpersonal skills training)	-0.372	-1.46	0.779
pe (psychoeducation)	0.182	-0.728	1.132
ns (non-specific treatment effects)	-1.636	-2.823	-0.463
ps (problem solving)	-0.3	-1.151	0.543
re (relaxation)	0.625	-0.476	1.759
rp (relapse prevention)	0.169	-0.919	1.236
tg (therapeutic guidance)	0.256	-0.793	1.313
3w (third-wave components)	-0.487	-1.556	0.554
w (waiting component)	0.481	-0.698	1.638

15.4 Limiting to studies with high adherence

The following 8 AD studies had at most 40% dropout:

"Birney2016" "Boeschoten2017" "Burton2015" "Ebert2014b" "Glozier2013"
 "Lappalainen2015"
 "Terides2017" "Titov2010" "Titov2013"

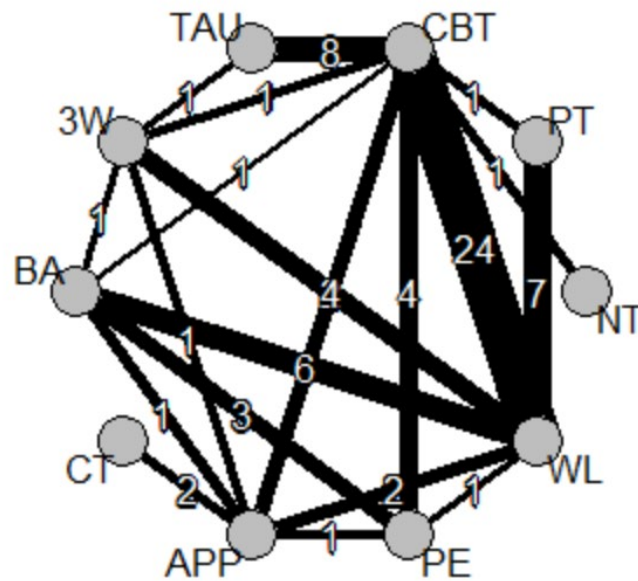


The component NMA could not be conducted.

15.5 Excluding studies teaching more than four CBT skills

The following studies were included:

"Andersson, 2005"	"Boele, 2017"	"Buntrock, 2015"
"Carlbring, 2013"	"Choi, 2012"	"Christensen, 2004"
"Dahne, 2018"	"De Graaf, 2009"	"Ebert, 2014"
"Ebert, 2018 (Buntrock under submission)"	"Farrer, 2011"	"Forand 2018"
"Forsell, 2017"	"Geraedts, 2014"	"Gilbody, 2015"
"Brabyn, 2016"	"Johansson, 2012 CBT"	"Kenter, 2016"
"Kivi, 2014"	"Kleiboer, 2015"	"Lintvedt, 2013"
"Lundgren, 2016"	"Ly, 2014"	"Mantani, 2017"
"Milgrom, 2016"	"Mohr, 2013"	"Montero-Marin, 2016"
"Nobis, 2015"	"O'Moore, 2018"	"Perini, 2009"
"Philips, 2014"	"Pots, 2016- ACT"	"Pugh, 2016"
"Rosso, 2016"	"Sheeber, 2012"	"Smith, 2017"
"Spek, 2007"	"Unlu, 2013"	"Vernmark, 2010"
"Warmerdam, 2008"	"Zagorscak, 2018"	"Van Bastelaar, 2011"
"van Luenen, 2018"	"Birney2016"	"Boeschoten2017"
"Burton2015"	"Cooper2011a"	"Ebert2014b"
"Glozier2013"	"Hur2018"	"Lambert2018"
"Lappalainen2015"	"Löbner2018"	"Newby2017"
"Nystrom2017"	"O'Mahen2013"	"Roepke2015"
"Titov2010"	"Tulbure2017"	"Wilson2017"



Component	Depression severity (iMD in PHQ-9 scores)		
	Mean	95% CI	
ae (automated encouragement)	-0.0296	-0.8789	0.8196
ba (behavioural activation)	-1.7097	-2.6569	-0.7625
bi (behaviour therapy for insomnia)	-1.4205	-3.4591	0.6181
cr (cognitive restructuring)	0.3405	-0.6763	1.3573
dt (conventional drug treatment)			
ff (initial face-to-face contact)	0.9377	-1.6946	3.57
he (human encouragement)	-0.4956	-1.5282	0.5369
hw (homework required)	0.2161	-0.843	1.2753
is (interpersonal skills training)	-0.8342	-1.9173	0.2489
pe (psychoeducation)	-0.123	-0.9829	0.737
ns (non-specific treatment effects)	-1.1184	-2.2779	0.0412
ps (problem solving)	-0.5332	-1.3703	0.3038
re (relaxation)	1.3038	0.3046	2.3031
rp (relapse prevention)	0.4631	-0.5359	1.4621
tg (therapeutic guidance)	0.1149	-0.8259	1.0557
3w (third-wave components)	-0.8723	-1.9634	0.2187
w (waiting component)	0.3298	-0.7511	1.4106

16 Interaction cNMA model

The results from fitting the model presented in Appendix 2.6 are shown below, for the main effects of the components.

Estimated component	cNMA with Bayesian LASSO
<i>w</i> (waiting component)	0.24 [-1.14; 1.56]
<i>dt</i> (conventional drug treatment)	-
<i>ns</i> (non-specific treatment effects)	-1.28 [-2.63; 0.15]
<i>pe</i> (psychoeducation)	-0.21 [-1.62; 0.92]
<i>cr</i> (cognitive restructuring)	0.17 [-1.59; 1.60]
<i>ba</i> (behavioural activation)	-1.75 [-3.17; -0.20]
<i>is</i> (interpersonal skills training)	-0.49 [-2.16; 1.45]
<i>ps</i> (problem solving)	-0.59 [-2.08; 0.99]
<i>re</i> (relaxation)	0.97 [-0.85; 2.56]
<i>3w</i> (third-wave components)	-0.89 [-2.69; 0.50]
<i>bi</i> (behaviour therapy for insomnia)	-1.98 [-4.54; 0.81]
<i>rp</i> (relapse prevention)	0.37 [-1.08; 1.91]
<i>hw</i> (homework required)	0.40 [-1.05; 2.17]
<i>ff</i> (initial face-to-face contact)	0.60 [-2.43; 3.62]
<i>ae</i> (automated encouragement)	-0.44 [-2.25; 0.91]
<i>he</i> (human encouragement)	-0.33 [-1.75; 1.14]
<i>tg</i> (therapeutic guidance)	-0.05 [-2.01; 1.43]
τ (heterogeneity standard deviation)	1.22 [0.83; 1.64]

These results were quite similar to the additive model. The most prominent interactions identified by the model were the following: *ff-ae*; *ff-he*; *ff-pe*; *ff-ps*; *ae-tg*. However, their effects were limited.

As an illustrative example, for the comparison of *ns + cr + ae + ff* versus *w*, the additive model estimated an effect size -0.85 [-4.05; 2.27], while the model with interactions -1.06 [-4.65; 2.27]. Likewise, for the comparison (*ns + cr + ba + ps*) versus (*w*) the additive model gave -3.87 [-5.58; -2.28] and the interaction model -3.74 [-5.74; -1.69].

Thus, we conclude that there is no strong evidence of important interactions in the model, and that the additive model may be sufficient.

17 PRISMA-IPD Checklist

PRISMA-IPD Section/topic	Item No	Checklist item	Reported on page
Title			
Title	1	Identify the report as a systematic review and meta-analysis of individual participant data.	1
Abstract			
Structured summary	2	Provide a structured summary including as applicable:	8
		Background: state research question and main objectives, with information on participants, interventions, comparators and outcomes.	
		Methods: report eligibility criteria; data sources including dates of last bibliographic search or elicitation, noting that IPD were sought; methods of assessing risk of bias.	
		Results: provide number and type of studies and participants identified and number (%) obtained; summary effect estimates for main outcomes (benefits and harms) with confidence intervals and measures of statistical heterogeneity. Describe the direction and size of summary effects in terms meaningful to those who would put findings into practice.	
		Discussion: state main strengths and limitations of the evidence, general interpretation of the results and any important implications.	
		Other: report primary funding source, registration number and registry name for the systematic review and IPD meta-analysis.	
Introduction			
Rationale	3	Describe the rationale for the review in the context of what is already known.	10
Objectives	4	Provide an explicit statement of the questions being addressed with reference, as applicable, to participants, interventions, comparisons, outcomes and study design (PICOS). Include any hypotheses that relate to particular types of participant-level subgroups.	10
Methods			
Protocol and registration	5	Indicate if a protocol exists and where it can be accessed. If available, provide registration information including registration number and registry name. Provide publication details, if applicable.	11
Eligibility criteria	6	Specify inclusion and exclusion criteria including those relating to participants, interventions, comparisons, outcomes, study design and characteristics (e.g. years when conducted, required minimum follow-up). Note whether these were applied at the study or individual level i.e. whether eligible participants were included (and ineligible participants excluded) from a study that included a wider population than specified by the review inclusion criteria. The rationale for criteria should be stated.	14

Identifying studies - information sources	7	Describe all methods of identifying published and unpublished studies including, as applicable: which bibliographic databases were searched with dates of coverage; details of any hand searching including of conference proceedings; use of study registers and agency or company databases; contact with the original research team and experts in the field; open adverts and surveys. Give the date of last search or elicitation.	11
Identifying studies - search	8	Present the full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix 1
Study selection processes	9	State the process for determining which studies were eligible for inclusion.	Appendix 4
Data collection processes	10	Describe how IPD were requested, collected and managed, including any processes for querying and confirming data with investigators. If IPD were not sought from any eligible study, the reason for this should be stated (for each such study).	16
		If applicable, describe how any studies for which IPD were not available were dealt with. This should include whether, how and what aggregate data were sought or extracted from study reports and publications (such as extracting data independently in duplicate) and any processes for obtaining and confirming these data with investigators.	
Data items	11	Describe how the information and variables to be collected were chosen. List and define all study level and participant level data that were sought, including baseline and follow-up information. If applicable, describe methods of standardising or translating variables within the IPD datasets to ensure common scales or measurements across studies.	Protocol paper, pp 5-6
IPD integrity	A1	Describe what aspects of IPD were subject to data checking (such as sequence generation, data consistency and completeness, baseline imbalance) and how this was done.	16
Risk of bias assessment in individual studies.	12	Describe methods used to assess risk of bias in the individual studies and whether this was applied separately for each outcome. If applicable, describe how findings of IPD checking were used to inform the assessment. Report if and how risk of bias assessment was used in any data synthesis.	16
Specification of outcomes and effect measures	13	State all treatment comparisons of interests. State all outcomes addressed and define them in detail. State whether they were pre-specified for the review and, if applicable, whether they were primary/main or secondary/additional outcomes. Give the principal measures of effect (such as risk ratio, hazard ratio, difference in means) used for each outcome.	16-17
Synthesis methods	14	Describe the meta-analysis methods used to synthesise IPD. Specify any statistical methods and models used. Issues should include (but are not restricted to): <ul style="list-style-type: none"> • Use of a one-stage or two-stage approach. • How effect estimates were generated separately within each study and combined across studies (where applicable). • Specification of one-stage models (where applicable) including how clustering of patients within studies was accounted for. 	16-17, Appendix 2

		<ul style="list-style-type: none"> • Use of fixed or random effects models and any other model assumptions, such as proportional hazards. • How (summary) survival curves were generated (where applicable). • Methods for quantifying statistical heterogeneity (such as I^2 and τ^2). • How studies providing IPD and not providing IPD were analysed together (where applicable). • How missing data within the IPD were dealt with (where applicable). 	
Exploration of variation in effects	A2	If applicable, describe any methods used to explore variation in effects by study or participant level characteristics (such as estimation of interactions between effect and covariates). State all participant-level characteristics that were analysed as potential effect modifiers, and whether these were pre-specified.	16-17, Appendix 2
Risk of bias across studies	15	Specify any assessment of risk of bias relating to the accumulated body of evidence, including any pertaining to not obtaining IPD for particular studies, outcomes or other variables.	17
Additional analyses	16	Describe methods of any additional analyses, including sensitivity analyses. State which of these were pre-specified.	17
Results			
Study selection and IPD obtained	17	Give numbers of studies screened, assessed for eligibility, and included in the systematic review with reasons for exclusions at each stage. Indicate the number of studies and participants for which IPD were sought and for which IPD were obtained. For those studies where IPD were not available, give the numbers of studies and participants for which aggregate data were available. Report reasons for non-availability of IPD. Include a flow diagram.	18
Study characteristics	18	For each study, present information on key study and participant characteristics (such as description of interventions, numbers of participants, demographic data, unavailability of outcomes, funding source, and if applicable duration of follow-up). Provide (main) citations for each study. Where applicable, also report similar study characteristics for any studies not providing IPD.	18, Appendices 6-7
IPD integrity	A3	Report any important issues identified in checking IPD or state that there were none.	18
Risk of bias within studies	19	Present data on risk of bias assessments. If applicable, describe whether data checking led to the up-weighting or down-weighting of these assessments. Consider how any potential bias impacts on the robustness of meta-analysis conclusions.	18, Appendix 8
Results of individual studies	20	For each comparison and for each main outcome (benefit or harm), for each individual study report the number of eligible participants for which data were obtained and show simple summary data for each intervention group (including, where applicable, the number of events), effect estimates and confidence intervals. These may be tabulated or included on a forest plot.	Appendices 7, 8

Results of syntheses	21	Present summary effects for each meta-analysis undertaken, including confidence intervals and measures of statistical heterogeneity. State whether the analysis was pre-specified, and report the numbers of studies and participants and, where applicable, the number of events on which it is based.	18-22, Appendixes 11-14
		When exploring variation in effects due to patient or study characteristics, present summary interaction estimates for each characteristic examined, including confidence intervals and measures of statistical heterogeneity. State whether the analysis was pre-specified. State whether any interaction is consistent across trials.	
		Provide a description of the direction and size of effect in terms meaningful to those who would put findings into practice.	
Risk of bias across studies	22	Present results of any assessment of risk of bias relating to the accumulated body of evidence, including any pertaining to the availability and representativeness of available studies, outcomes or other variables.	19, Appendix 11
Additional analyses	23	Give results of any additional analyses (e.g. sensitivity analyses). If applicable, this should also include any analyses that incorporate aggregate data for studies that do not have IPD. If applicable, summarise the main meta-analysis results following the inclusion or exclusion of studies for which IPD were not available.	23, Appendixes 15, 16
Discussion			
Summary of evidence	24	Summarise the main findings, including the strength of evidence for each main outcome.	24
Strengths and limitations	25	Discuss any important strengths and limitations of the evidence including the benefits of access to IPD and any limitations arising from IPD that were not available.	25-26
Conclusions	26	Provide a general interpretation of the findings in the context of other evidence.	26
Implications	A4	Consider relevance to key groups (such as policy makers, service providers and service users). Consider implications for future research.	26
Funding			
Funding	27	Describe sources of funding and other support (such as supply of IPD), and the role in the systematic review of those providing such support.	27

A1 – A3 denote new items that are additional to standard PRISMA items. A4 has been created as a result of re-arranging content of the standard PRISMA statement to suit the way that systematic review IPD meta-analyses are reported.

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