THE LANCET
Psychiatry

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Zhou X, Teng T, Zhang Y, et al. Comparative efficacy and acceptability of antidepressants, psychotherapies, and their combination for acute treatment of children and adolescents with depressive disorder: a systematic review and network meta-analysis. *Lancet Psychiatry* 2020; **7:** 581–601.

Comparative efficacy and acceptability of antidepressants, psychotherapies, and their combination for the acute treatment of children and adolescents with depressive disorder: a systematic review and network meta-analysis

Xinyu Zhou, Teng Teng, Yuqing Zhang, Cinzia Del Giovane, Toshi A. Furukawa, John R. Weisz, Xuemei Li, Pim Cuijpers, David Coghill, Yajie Xiang, Sarah E. Hetrick, Stefan Leucht, Mengchang Qin, Jürgen Barth, Arun V. Ravindran, Lining Yang, John F. Curry, Li Fan, Susan G. Silva, Andrea Cipriani, Peng Xie

Supplementary appendix to the manuscript

Contents of supplementary appendix

APPENDIX 1

Search strategy and results

Search Strategy and Results

Number of citations by each database and trial register searched*

Databases and Trial registers	**Citations**
Databases:	
Pubmed	1199
Cochrane	4402
Web of Science	3884
Embase	1450
CINAHL	668
PsycINFO	2214
LILACS	417
ProQuest Dissertations	462
Total (databases)	**14696**
Trial registers:	
USA (ClinicalTrials.gov)	1495
World Health Organization (ICTRP)	1009
USA Food and Drug Administration (FDA)	1878
Australian (ANZCTR)	681
China (ChiCTR)	74
Japan (IMIN-CTR)	80
Netherlands (Trial Register)	23
UN (ISRCTN)	430
Total (trial registers)	**5670**

Full search strategy for each database

PubMed

#1 Search (depress*[Title/Abstract] OR dysthymi*[Title/Abstract] OR mood disorder*[Title/Abstract] OR affective disorder*[Title/Abstract])

#2 Search ((("Depressive Disorder"[Mesh]) OR "Dysthymic Disorder"[Mesh]) OR "Mood Disorders"[Mesh]) OR "Affective Disorders, Psychotic"[Mesh]

#3 #1 or #2

#4 Search (adolesc*[Title/Abstract] OR child*[Title/Abstract] OR boy*[Title/Abstract] OR girl*[Title/Abstract] OR juvenil*[Title/Abstract] OR minors[Title/Abstract] OR paediatri*[Title/Abstract] OR pediatri*[Title/Abstract] OR pubescen*[Title/Abstract] OR school*[Title/Abstract] OR student*[Title/Abstract] OR teen*[Title/Abstract] OR young[Title/Abstract] OR youth*[Title/Abstract] OR preschool[Title/Abstract] OR pre-school[Title/Abstract])

#5 Search "Child"[Majr] OR "Adolescent"[Majr]

#6 #4 or #5

#7 Search (antidepressant*[Title/Abstract] OR selective serotonin reuptake inhibitor*[Title/Abstract] OR SSRI[Title/Abstract] OR SSRIs[Title/Abstract] OR fluoxetine[Title/Abstract] OR fluvoxamine[Title/Abstract] OR paroxetine[Title/Abstract] OR sertraline[Title/Abstract] OR citalopram[Title/Abstract] OR escitalopram[Title/Abstract] OR vortioxetine[Title/Abstract] OR serotonin norepinephrine reuptake inhibitor*[Title/Abstract] OR SNRI[Title/Abstract] OR SNRIs[Title/Abstract] OR duloxetine[Title/Abstract] OR venlafaxine[Title/Abstract] OR desvenlafaxine[Title/Abstract] OR milnacipran[Title/Abstract] OR levomilnacipran[Title/Abstract] OR mirtazapine[Title/Abstract] OR mianserin[Title/Abstract] OR nefazodone[Title/Abstract] OR trazodone[Title/Abstract] OR vilazodone[Title/Abstract] OR bupropion[Title/Abstract] OR reboxetine[Title/Abstract] OR agomelatine[Title/Abstract] OR noradrenergic and specific serotonergic antidepressant*[Title/Abstract] OR NaSSA[Title/Abstract] OR NaSSAs[Title/Abstract] OR mirtazapine[Title/Abstract] OR TCA[Title/Abstract] OR TCAs[Title/Abstract] OR tricyclic[Title/Abstract] OR amersergide[Title/Abstract] OR amineptine[Title/Abstract] OR amitriptyline[Title/Abstract] OR amoxapine[Title/Abstract] OR butriptyline[Title/Abstract] OR chlorpoxiten[Title/Abstract] OR clomipramine[Title/Abstract] OR clorimipramine[Title/Abstract] OR demexiptiline[Title/Abstract] OR desipramine[Title/Abstract] OR dibenzipin[Title/Abstract] OR dothiepin[Title/Abstract] OR doxepin[Title/Abstract] OR imipramine[Title/Abstract] OR lofepramine[Title/Abstract] OR melitracen[Title/Abstract] OR metapramine[Title/Abstract] OR nortriptyline[Title/Abstract] OR noxiptiline[Title/Abstract] OR opipramol[Title/Abstract] OR protriptyline[Title/Abstract] OR quinupramine[Title/Abstract] OR tianeptine[Title/Abstract] OR trimipramine[Title/Abstract])

#8 Search "Antidepressive Agents"[Mesh]

#9 #7 OR #8

#10 Search (psychother*[Title/Abstract] OR psychological[Title/Abstract] OR cogniti*[Title/Abstract] OR behavio*[Title/Abstract] OR CBT[Title/Abstract] OR family therap*[Title/Abstract] OR interpersonal[Title/Abstract] OR relaxation[Title/Abstract] OR bibliotherap*[Title/Abstract] OR play therap*[Title/Abstract] OR physical reinforcement[Title/Abstract] OR reinforced practice[Title/Abstract] OR exposure[Title/Abstract] OR consultation[Title/Abstract] OR biofeedback[Title/Abstract] OR social skill[Title/Abstract] OR client centered[Title/Abstract] OR counsel*[Title/Abstract] OR exercise[Title/Abstract] OR psychoeducation*[Title/Abstract] OR supportive[Title/Abstract] OR mental health[Title/Abstract] OR activity scheduling[Title/Abstract] OR art[Title/Abstract] OR dance[Title/Abstract] OR dialectic*[Title/Abstract] OR emotion focus*[Title/Abstract] OR focus-oriented[Title/Abstract] OR humanistic[Title/Abstract] OR integrative[Title/Abstract] OR integrated[Title/Abstract] OR metacognitive[Title/Abstract] OR meta-cognitive[Title/Abstract] OR nondirective[Title/Abstract] OR non-directive[Title/Abstract] OR problem solving[Title/Abstract] OR psychodynamic[Title/Abstract] OR rational emotive[Title/Abstract] OR self control*[Title/Abstract] OR self talk[Title/Abstract] OR self help[Title/Abstract] OR stress management[Title/Abstract] OR mind training[Title/Abstract] OR functional analys*[Title/Abstract] OR psychoanaly*[Title/Abstract] OR psychodrama[Title/Abstract] OR role play*[Title/Abstract] OR mindfulness*[Title/Abstract])

#11 Search "Psychotherapy"[Mesh]

#12 #10 OR #11

#13 #9 OR #12

#14 #9 AND #12

#15 #3 AND #6 AND #13 [Publication date from 2014/01/01 to 2018/06/30]

#16 #3 AND #6 AND #14 [Publication date from 1800/01/01 to 2014/01/01]

#17 #15 OR #16

Cochrane

#1 depress* or dysthymi* or "mood disorder*" or "affective disorder*":ti or depress* or dysthymi* or "mood disorder*" or "affective disorder*":ab

#2 MeSH descriptor: [Depressive Disorder] explode all trees

#3 MeSH descriptor: [Dysthymic Disorder] explode all trees

#4 MeSH descriptor: [Mood Disorders] explode all trees

#5 #1 or #2 or #3 or #4

#6 adolesc* or child* or boy* or girl* or juvenil* or minors or paediatri* or pediatri* or pubescen* or school* or student* or teen* or young or youth* or preschool or pre-school:ti or adolesc* or child* or boy* or girl* or juvenil* or minors or paediatri* or pediatri* or pubescen* or school* or student* or teen* or young or youth* or preschool or pre-school:ab

#7 MeSH descriptor: [Child] explode all trees

#8 MeSH descriptor: [Adolescent] explode all trees

#9 #6 or #7 or #8

#10 antidepressant* or "selective serotonin reuptake inhibitor*" or SSRI or SSRIs or fluoxetine or fluvoxamine or paroxetine or sertraline or citalopram or escitalopram or vortioxetine or "serotonin norepinephrine reuptake inhibitor*" or SNRI or SNRIs or duloxetine or venlafaxine or desvenlafaxine or milnacipran or levomilnacipran or mirtazapine or mianserin or nefazodone or trazodone or vilazodone or bupropion or reboxetine or agomelatine or "noradrenergic and specific serotonergic antidepressant*" or NaSSA or NaSSAs or mirtazapine or TCA or TCAs or tricyclic or amersergide or amineptine or amitriptyline or amoxapine or butriptyline or chlorpoxiten or clomipramine or clorimipramine or demexiptiline or desipramine or dibenzipin or dothiepin or doxepin or imipramine or lofepramine or melitracen or metapramine or nortriptyline or noxiptiline or opipramol or protriptyline or quinupramine or tianeptine or trimipramine:ti or antidepressant* or "selective serotonin reuptake inhibitor*" or SSRI or SSRIs or fluoxetine or fluvoxamine or paroxetine or sertraline or citalopram or escitalopram or vortioxetine or "serotonin norepinephrine reuptake inhibitor*" or SNRI or SNRIs or duloxetine or venlafaxine or desvenlafaxine or milnacipran or levomilnacipran or mirtazapine or mianserin or nefazodone or trazodone or vilazodone or bupropion or reboxetine or agomelatine or "noradrenergic and specific serotonergic antidepressant*" or NaSSA or NaSSAs or mirtazapine or TCA or TCAs or tricyclic or amersergide or amineptine or amitriptyline or amoxapine or butriptyline or chlorpoxiten or clomipramine or clorimipramine or demexiptiline or desipramine or dibenzipin or dothiepin or doxepin or imipramine or lofepramine or melitracen or metapramine or nortriptyline or noxiptiline or opipramol or protriptyline or quinupramine or tianeptine or trimipramine:ab

#11 MeSH descriptor: [Antidepressive Agents] explode all trees

#12 #10 or #11

#13 psychother* or psychological or cogniti* or behavio* or CBT or "family therap*" or interpersonal or relaxation or bibliotherap* or "play therap*" or "physical reinforcement" or "reinforced practice" or exposure or consultation or biofeedback or "social skill" or "client centered" or counsel* or exercise or psychoeducation* or supportive or "mental health" or "activity scheduling" or art or dance or dialectic*

or "emotion focus*" or "focus-oriented" or humanistic or integrative or integrated or metacognitive or meta-cognitive or nondirective or non-directive or "problem solving" or psychodynamic or "rational emotive" or "self control*" or "self talk" or "self help" or "stress management" or "mind training" or "functional analys*" or psychoanaly* or psychodrama or "role play*" or mindfulness*:ti or psychother* or psychological or cogniti* or behavio* or CBT or "family therap*" or interpersonal or relaxation or bibliotherap* or "play therap*" or "physical reinforcement" or "reinforced practice" or exposure or consultation or biofeedback or "social skill" or "client centered" or counsel* or exercise or psychoeducation* or supportive or "mental health" or "activity scheduling" or art or dance or dialectic* or "emotion focus*" or "focus-oriented" or humanistic or integrative or integrated or metacognitive or meta-cognitive or nondirective or non-directive or "problem solving" or psychodynamic or "rational emotive" or "self control*" or "self talk" or "self help" or "stress management" or "mind training" or "functional analys*" or psychoanaly* or psychodrama or "role play*" or mindfulness*:ab

#14 acceptance* or commitment*:ti or acceptance* or commitment*:ab

#15 *therap*:ti or *therap*:ab

#16 #14 and #15

#17 MeSH descriptor: [Psychotherapy] explode all trees

#18 #13 or #16 or #17

#19 #12 or #18

#20 #12 and #18

#21 #5 and #9 and #19 [Publication year from 2014 to 2018]

#22 #5 and #9 and #20 [Publication year from 1800 to 2013]

#23 #21 or #22

Web of science

#1 TS=(depress* or dysthymi* or “mood disorder*” or “affective disorder*”)

#2 TS=(adolesc* OR child* OR boy* OR girl* OR juvenil* OR minors OR paediatri* OR pediatri* OR pubescen* OR school* OR student* OR teen* OR young OR youth* OR preschool OR pre-school)

#3 TS=(antidepressant* or “selective serotonin reuptake inhibitor*” or SSRI or SSRIs or fluoxetine or fluvoxamine or paroxetine or sertraline or citalopram or escitalopram or vortioxetineor “serotonin norepinephrine reuptake inhibitor*” or SNRI or SNRIs or duloxetine or venlafaxine or desvenlafaxine or milnacipran or levomilnacipran or mirtazapine or mianserin or nefazodone or trazodone or

vilazodone or bupropion or reboxetine or agomelatine or “noradrenergic and specific serotonergic antidepressant*” or NaSSA or NaSSAs or mirtazapine or TCA or TCAs or tricyclic or amersergide or amineptine or amitriptyline or amoxapine or butriptyline or chlorpoxiten or clomipramine or clorimipramine or demexiptiline or desipramine or dibenzipin or dothiepin or doxepin or imipramine or lofepramine or melitracen or metapramine or nortriptyline or noxiptiline or opipramol or protriptyline or quinupramine or tianeptine or trimipramine)

#4 TS=(*therap* and (acceptance* or commitment*))

#5 TS=(psychother* or psychological or cogniti* or behavio* or CBT or “family therap*” or interpersonal or relaxation or bibliotherap* or “play therap*” or “physical reinforcement” or “reinforced practice” or exposure or consultation or biofeedback or “social skill” or “client centered” or counsel* or exercise or psychoeducation* or supportive or “mental health” or “activity scheduling” or art or dance or dialectic* or “emotion focus*” or “focus-oriented” or humanistic or integrative or integrated or metacognitive or meta-cognitive or nondirective or non-directive or “problem solving” or psychodynamic or “rational emotive” or “self control*” or “self talk” or “self help” or “stress management” or “mind training” or “functional analys*” or psychoanaly* or psychodrama or “role play*” or mindfulness*)

#6 #5 OR #4

#7 TS=(random* or allocate* or assign* or cross over* or crossover* or controlled)

#8 #6 OR #3

#9 #6 AND #3

#10 #8 AND #7 AND #2 AND #1 [Publication date from 2014 to 2018]

#11 #9 AND #7 AND #2 AND #1 [Publication date from 1992 to 2013]

#12 #10 OR #11

Embase

#1 depress*:ab,ti OR dysthymi*:ab,ti OR 'mood disorder*':ab,ti OR 'affective disorder*':ab,ti

#2 'depression'/exp OR 'dysthymia'/exp OR 'mood disorder'/exp

#3 #1 OR #2

#4 adolesc*:ab,ti OR child*:ab,ti OR boy*:ab,ti OR girl*:ab,ti OR juvenil*:ab,ti OR minors:ab,ti OR paediatri*:ab,ti OR pediatri*:ab,ti OR pubescen*:ab,ti OR school*:ab,ti OR student*:ab,ti OR teen*:ab,ti OR young:ab,ti OR youth*:ab,ti OR preschool:ab,ti OR 'preschool':ab,ti

#5 'child'/mj OR 'adolescent'/mj

#6 #4 OR #5

#7 antidepressant*:ab,ti OR 'selective serotonin reuptake inhibitor*':ab,ti OR ssri:ab,ti OR ssris:ab,ti OR fluoxetine:ab,ti OR fluvoxamine:ab,ti OR paroxetine:ab,ti OR sertraline:ab,ti OR citalopram:ab,ti OR escitalopram:ab,ti OR vortioxetine:ab,tiOR 'serotonin norepinephrine reuptake inhibitor*':ab,ti OR snri:ab,ti OR snris:ab,ti OR duloxetine:ab,ti OR venlafaxine:ab,ti OR desvenlafaxine:ab,ti OR milnacipran:ab,ti OR levomilnacipran:ab,ti OR mianserin:ab,ti OR nefazodone:ab,ti OR trazodone:ab,ti OR vilazodone:ab,ti OR bupropion:ab,ti OR reboxetine:ab,ti OR agomelatine:ab,ti OR 'noradrenergic and specific serotonergic antidepressant*':ab,ti OR nassa:ab,ti OR nassas:ab,ti OR mirtazapine:ab,ti OR tca:ab,ti OR tcas:ab,ti OR tricyclic:ab,ti OR amersergide:ab,ti OR amineptine:ab,ti OR amitriptyline:ab,ti OR amoxapine:ab,ti OR butriptyline:ab,ti OR chlorpoxiten:ab,ti OR clomipramine:ab,ti OR clorimipramine:ab,ti OR demexiptiline:ab,ti OR desipramine:ab,ti OR dibenzipin:ab,ti OR dothiepin:ab,ti OR doxepin:ab,ti OR imipramine:ab,ti OR lofepramine:ab,ti OR melitracen:ab,ti OR metapramine:ab,ti OR nortriptyline:ab,ti OR noxiptiline:ab,ti OR opipramol:ab,ti OR protriptyline:ab,ti OR quinupramine:ab,ti OR tianeptine:ab,ti OR trimipramine:ab,ti

#8 'antidepressant agent'/exp

#9 #7 OR #8

#10 psychother*:ab,ti OR psychological:ab,ti OR cogniti*:ab,ti OR behavio*:ab,ti OR cbt:ab,ti OR 'family therap*':ab,ti OR interpersonal:ab,ti OR relaxation:ab,ti OR bibliotherap*:ab,ti OR 'play therap*':ab,ti OR 'physical reinforcement':ab,ti OR 'reinforced practice':ab,ti OR exposure:ab,ti OR consultation:ab,ti OR biofeedback:ab,ti OR 'social skill':ab,ti OR 'client centered':ab,ti OR counsel*:ab,ti OR exercise:ab,ti OR psychoeducation*:ab,ti OR supportive:ab,ti OR 'mental health':ab,ti OR 'activity scheduling':ab,ti OR art:ab,ti OR dance:ab,ti OR dialectic*:ab,ti OR 'emotion focus*':ab,ti OR 'focus-oriented':ab,ti OR humanistic:ab,ti OR integrative:ab,ti OR integrated:ab,ti OR metacognitive:ab,ti OR 'meta cognitive':ab,ti OR nondirective:ab,ti OR 'non directive':ab,ti OR 'problem solving':ab,ti OR psychodynamic:ab,ti OR 'rational emotive':ab,ti OR 'self control*':ab,ti OR 'self talk':ab,ti OR 'self help':ab,ti OR 'stress management':ab,ti OR 'mind training':ab,ti OR 'functional analys*':ab,ti OR psychoanaly*:ab,ti OR psychodrama:ab,ti OR 'role play*':ab,ti OR mindfulness*:ab,ti

#11 therap*:ab,ti AND (acceptance*:ab,ti OR commitment*:ab,ti)

#12 'psychotherapy'/exp

#13 #10 OR #11 OR #12

#14 #9 OR #13

#15 #9 AND #13

#16 #3 and #6 and #14 [Publication year from 2014 to 2018]

#17 #3 and #6 and #15 [Publication year from 1966 to 2013]

#18 #16 or #17

CINAHL

S1 TI (depress* or dysthymi* or “mood disorder*” or “affective disorder*”) OR AB (depress* or dysthymi* or “mood disorder*” or “affective disorder*”)

S2 (MH "Affective Disorders+") OR (MH "Depression+") OR (MH "Dysthymic Disorder")

S3 S1 OR S2

S4 TI (adolesc* OR child* OR boy* OR girl* OR juvenil* OR minors OR paediatri* OR pediatri* OR pubescen* OR school* OR student* OR teen* OR young OR youth* OR preschool OR pre-school) OR AB (adolesc* OR child* OR boy* OR girl* OR juvenil* OR minors OR paediatri* OR pediatri* OR pubescen* OR school* OR student* OR teen* OR young OR youth* OR preschool OR pre-school)

S5 (MH "Child") OR (MH "Adolescence")

S6 S4 OR S5

S7 TI (antidepressant* or “selective serotonin reuptake inhibitor*” or SSRI or SSRIs or fluoxetine or fluvoxamine or paroxetine or sertraline or citalopram or escitalopram orvortioxetine or “serotonin norepinephrine reuptake inhibitor*” or SNRI or SNRIs or duloxetine or venlafaxine or desvenlafaxine or milnacipran or levomilnacipran or mirtazapine or mianserin or nefazodone or trazodone or vilazodone or bupropion or reboxetine or agomelatine or “noradrenergic and specific serotonergic antidepressant*” or NaSSA or NaSSAs or mirtazapine or TCA or TCAs or tricyclic or amersergide or amineptine or amitriptyline or amoxapine or butriptyline or chlorpoxiten or clomipramine or clorimipramine or demexiptiline or desipramine or dibenzipin or dothiepin or doxepin or imipramine or lofepramine or melitracen or metapramine or nortriptyline or noxiptiline or opipramol or protriptyline or quinupramine or tianeptine or trimipramine) OR AB (antidepressant* or “selective serotonin reuptake inhibitor*” or SSRI or SSRIs or fluoxetine or fluvoxamine or paroxetine or sertraline or citalopram or escitalopram or “serotonin norepinephrine reuptake inhibitor*” or SNRI or SNRIs or duloxetine or venlafaxine or desvenlafaxine or milnacipran or levomilnacipran or mirtazapine or mianserin or nefazodone or trazodone or vilazodone or bupropion or reboxetine or agomelatine or “noradrenergic and specific serotonergic antidepressant*” or NaSSA or NaSSAs or mirtazapine or TCA or TCAs or tricyclic or amersergide or amineptine or amitriptyline or amoxapine or butriptyline or chlorpoxiten or clomipramine or clorimipramine or demexiptiline or desipramine or dibenzipin or dothiepin or doxepin or imipramine or lofepramine or melitracen or metapramine or nortriptyline or

noxiptiline or opipramol or protriptyline or quinupramine or tianeptine or trimipramine)

S8 (MH "Antidepressive Agents+")

S9 S7 OR S8

S10 TI (psychother* or psychological or cogniti* or behavio* or CBT or “family therap*” or interpersonal or relaxation or bibliotherap* or “play therap*” or “physical reinforcement” or “reinforced practice” or exposure or consultation or biofeedback or “social skill” or “client centered” or counsel* or exercise or psychoeducation* or supportive or “mental health” or “activity scheduling” or art or dance or dialectic* or “emotion focus*” or “focus-oriented” or humanistic or integrative or integrated or metacognitive or meta-cognitive or nondirective or non-directive or “problem solving” or psychodynamic or “rational emotive” or “self control*” or “self talk” or “self help” or “stress management” or “mind training” or “functional analys*” or psychoanaly* or psychodrama or “role play*” or mindfulness*) OR AB (psychother* or psychological or cogniti* or behavio* or CBT or “family therap*” or interpersonal or relaxation or bibliotherap* or “play therap*” or “physical reinforcement” or “reinforced practice” or exposure or consultation or biofeedback or “social skill” or “client centered” or counsel* or exercise or psychoeducation* or supportive or “mental health” or “activity scheduling” or art or dance or dialectic* or “emotion focus*” or “focus-oriented” or humanistic or integrative or integrated or metacognitive or meta-cognitive or nondirective or non-directive or “problem solving” or psychodynamic or “rational emotive” or “self control*” or “self talk” or “self help” or “stress management” or “mind training” or “functional analys*” or psychoanaly* or psychodrama or “role play*” or mindfulness*)

S11 TI *therap* OR AB *therap*

S12 TI (acceptance* or commitment*) OR AB (acceptance* or commitment*)

S13 S11 AND S12

S14 (MH "Psychotherapy+")

S15 S10 OR S13 OR S14

S16 TI (random* or allocate* or assign* or cross over* or crossover* or controlled) OR AB (random* or allocate* or assign* or cross over* or crossover* or controlled)

S17 (MH "Clinical Trials+")

S18 S16 OR S17

S19 S9 OR S15

S20 S9 AND S15

S21 S3 AND S6 AND S18 AND S19 [Publication date from 2014/01/01 to 2018/06/30]

S22 S3 AND S6 AND S18 AND S20 [Publication date from 1800/01/01 to 2013/12/31]

S23 S21 OR S22

PsycINFO

S1 (depress* or dysthymi* or mood disorder* or affective disorder*) OR AB (depress* or dysthymi* or mood disorder* or affective disorder*).ab

S2 MA major depression OR MA affective disorders OR MA dysthymic disorder

S3 S1 OR S2

S4 (adolesc* or child* or boy* or girl* or juvenil* or minors or paediatri* or pediatri* or pubescen* or school* or student* or teen* or young or youth* or preschool or pre-school) OR AB (adolesc* or child* or boy* or girl* or juvenil* or minors or paediatri* or pediatri* or pubescen* or school* or student* or teen* or young or youth* or preschool or pre-school).ab

S5 MA child psychiatry

S6 MA adolescent psychiatry

S7 S4 OR S5 OR S6

S8 (antidepressant* or selective serotonin reuptake inhibitor* or SSRI or SSRIs or fluoxetine or fluvoxamine or paroxetine or sertraline or citalopram or escitalopram or vortioxetine orserotonin norepinephrine reuptake inhibitor* or SNRI or SNRIs or duloxetine or venlafaxine or desvenlafaxine or milnacipran or levomilnacipran or mirtazapine or mianserin or nefazodone or trazodone or vilazodone or bupropion or reboxetine or agomelatine or (noradrenergic and specific serotonergic antidepressant*) or NaSSA or NaSSAs or mirtazapine or TCA or TCAs or tricyclic or amersergide or amineptine or amitriptyline or amoxapine or butriptyline or chlorpoxiten or clomipramine or clorimipramine or demexiptiline or desipramine or dibenzipin or dothiepin or doxepin or imipramine or lofepramine or melitracen or metapramine or nortriptyline or noxiptiline or opipramol or protriptyline or quinupramine or tianeptine or trimipramine) OR AB (antidepressant* or selective serotonin reuptake inhibitor* or SSRI or SSRIs or fluoxetine or fluvoxamine or paroxetine or sertraline or citalopram or escitalopram or vortioxetine or serotonin norepinephrine reuptake inhibitor* or SNRI or SNRIs or duloxetine or venlafaxine or desvenlafaxine or milnacipran or levomilnacipran or mirtazapine or mianserin or nefazodone or trazodone or vilazodone or bupropion or reboxetine or agomelatine or (noradrenergic and specific serotonergic antidepressant*) or NaSSA or NaSSAs or mirtazapine or TCA or TCAs or tricyclic or amersergide or amineptine or amitriptyline or amoxapine or butriptyline or chlorpoxiten or clomipramine or clorimipramine or demexiptiline or desipramine or dibenzipin or dothiepin or doxepin

or imipramine or lofepramine or melitracen or metapramine or nortriptyline or noxiptiline or opipramol or protriptyline or quinupramine or tianeptine or trimipramine).ab

S9 (psychother* or psychological or cogniti* or behavio* or CBT or family therap* or interpersonal or relaxation or bibliotherap* or play therap* or physical reinforcement or reinforced practice or exposure or consultation or biofeedback or social skill or client centered or counsel* or exercise or psychoeducation* or supportive or mental health or activity scheduling or art or dance or dialectic* or emotion focus* or focus-oriented or humanistic or integrative or integrated or metacognitive or meta-cognitive or nondirective or non-directive or problem solving or psychodynamic or rational emotive or self control* or self talk or self help or stress management or mind training or functional analys* or psychoanaly* or psychodrama or role play* or mindfulness*) OR AB (psychother* or psychological or cogniti* or behavio* or CBT or family therap* or interpersonal or relaxation or bibliotherap* or play therap* or physical reinforcement or reinforced practice or exposure or consultation or biofeedback or social skill or client centered or counsel* or exercise or psychoeducation* or supportive or mental health or activity scheduling or art or dance or dialectic* or emotion focus* or focus-oriented or humanistic or integrative or integrated or metacognitive or meta-cognitive or nondirective or non-directive or problem solving or psychodynamic or rational emotive or self control* or self talk or self help or stress management or mind training or functional analys* or psychoanaly* or psychodrama or role play* or mindfulness*).ab

S10 TI (acceptance* or commitment*) OR AB (acceptance* or commitment*)

S11 TI therap* OR AB therap*

S12 S10 and S11

S13 S9 or S12

S14 exp psychotherapy/

S15 S13 or S14

S16 exp clinical trials/

S17 (random* or allocate* or assign* or cross over* or crossover* or controlled) OR AB (random* or allocate* or assign* or cross over* or crossover* or controlled).ab

S18 S16 or S17

S19 S8 OR S15

S20 S8 and S15

S21 S3 and S7 and S18 and S19 [Publication year from 2014 to 2018]

S22 S3 and S7 and S18 and S20[Publication year from 1969 to 2013]

S23 S21 or S22

LILACS

S1 (depress$ or dysthymi$ or “mood disorder$” or “affective disorder$”) and (adolesc$ OR child$ OR boy$ OR girl$ OR juvenil$ OR minors OR paediatri$ OR pediatri$ OR pubescen$ OR school$ OR student$ OR teen$ OR young OR youth$ OR preschool OR pre-school) [Words] and antidepressant$ or “selective serotonin reuptake inhibitor$” or SSRI or SSRIs or fluoxetine or fluvoxamine or paroxetine or sertraline or citalopram or escitalopram or vortioxetineor “serotonin norepinephrine reuptake inhibitor$” or SNRI or SNRIs or duloxetine or venlafaxine or desvenlafaxine or milnacipran or levomilnacipran or mirtazapine or mianserin or nefazodone or trazodone or vilazodone or bupropion or reboxetine or agomelatine or “noradrenergic and specific serotonergic antidepressant$” or NaSSA or NaSSAs or mirtazapine or TCA or TCAs or tricyclic or amersergide or amineptine or amitriptyline or amoxapine or butriptyline or chlorpoxiten or clomipramine or clorimipramine or demexiptiline or desipramine or dibenzipin or dothiepin or doxepin or imipramine or lofepramine or melitracen or metapramine or nortriptyline or noxiptiline or opipramol or protriptyline or quinupramine or tianeptine or trimipramine or psychother$ or psychological or cogniti$ or behavio$ or CBT or “family therap$” or interpersonal or relaxation or bibliotherap$ or “play therap$” or “physical reinforcement” or “reinforced practice” or exposure or consultation or biofeedback or “social skill” or “client centered” or counsel$ or exercise or psychoeducation$ or supportive or “mental health” or “activity scheduling” or art or dance or dialectic$ or “emotion focus$” or “focus-oriented” or humanistic or integrative or integrated or metacognitive or meta-cognitive or nondirective or non-directive or “problem solving” or psychodynamic or “rational emotive” or “self control$” or “self talk” or “self help” or “stress management” or “mind training” or “functional analys$” or psychoanaly$ or psychodrama or “role play$” or mindfulness$ [Words] and random$ or allocate$ or assign$ or cross over$ or crossover$ or controlled [Words]

ProQuest Dissertations

S1 ti(depress* or dysthymi* or “mood disorder*” or “affective disorder*”) OR ab(depress* or dysthymi* or “mood disorder*” or “affective disorder*”) OR su("Affective Disorders*" or depress* or "Dysthymic Disorder")

S2 ti(adolesc* OR child* OR boy* OR girl* OR juvenil* OR minors OR paediatri* OR pediatri* OR pubescen* OR school* OR student* OR teen* OR young OR youth* OR preschool OR pre-school) OR ab(adolesc* OR child* OR boy* OR girl* OR juvenil* OR minors OR paediatri* OR pediatri* OR pubescen* OR school* OR student* OR teen* OR young OR youth* OR preschool OR pre-school) OR su(Child or Adolescence)

S3 ti(antidepressant* or “selective serotonin reuptake inhibitor*” or SSRI or SSRIs or fluoxetine or fluvoxamine or paroxetine or sertraline or citalopram or escitalopram or vortioxetine or “serotonin

norepinephrine reuptake inhibitor*" or SNRI or SNRIs or duloxetine or venlafaxine or desvenlafaxine or milnacipran or levomilnacipran or mirtazapine or mianserin or nefazodone or trazodone or vilazodone or bupropion or reboxetine or agomelatine or "noradrenergic and specific serotonergic antidepressant*" or NaSSA or NaSSAs or mirtazapine or TCA or TCAs or tricyclic or amersergide or amineptine or amitriptyline or amoxapine or butriptyline or chlorpoxiten or clomipramine or clorimipramine or demexiptiline or desipramine or dibenzipin or dothiepin or doxepin or imipramine or lofepramine or melitracen or metapramine or nortriptyline or noxiptiline or opipramol or protriptyline or quinupramine or tianeptine or trimipramine) OR ab(antidepressant* or "selective serotonin reuptake inhibitor*" or SSRI or SSRIs or fluoxetine or fluvoxamine or paroxetine or sertraline or citalopram or escitalopram or vortioxetine or "serotonin norepinephrine reuptake inhibitor*" or SNRI or SNRIs or duloxetine or venlafaxine or desvenlafaxine or milnacipran or levomilnacipran or mirtazapine or mianserin or nefazodone or trazodone or vilazodone or bupropion or reboxetine or agomelatine or "noradrenergic and specific serotonergic antidepressant*" or NaSSA or NaSSAs or mirtazapine or TCA or TCAs or tricyclic or amersergide or amineptine or amitriptyline or amoxapine or butriptyline or chlorpoxiten or clomipramine or clorimipramine or demexiptiline or desipramine or dibenzipin or dothiepin or doxepin or imipramine or lofepramine or melitracen or metapramine or nortriptyline or noxiptiline or opipramol or protriptyline or quinupramine or tianeptine or trimipramine) OR su("Antidepressive Agents*")

S4 ti(psychother* or psychological or cogniti* or behavio* or CBT or "family therap*" or interpersonal or relaxation or bibliotherap* or "play therap*" or "physical reinforcement" or "reinforced practice" or exposure or consultation or biofeedback or "social skill" or "client centered" or counsel* or exercise or psychoeducation* or supportive or "mental health" or "activity scheduling" or art or dance or dialectic* or "emotion focus*" or "focus-oriented" or humanistic or integrative or integrated or metacognitive or meta-cognitive or nondirective or non-directive or "problem solving" or psychodynamic or "rational emotive" or "self control*" or "self talk" or "self help" or "stress management" or "mind training" or "functional analys*" or psychoanaly* or psychodrama or "role play*" or mindfulness*) OR ab(psychother* or psychological or cogniti* or behavio* or CBT or "family therap*" or interpersonal or relaxation or bibliotherap* or "play therap*" or "physical reinforcement" or "reinforced practice" or exposure or consultation or biofeedback or "social skill" or "client centered" or counsel* or exercise or psychoeducation* or supportive or "mental health" or "activity scheduling" or art or dance or dialectic* or "emotion focus*" or "focus-oriented" or humanistic or integrative or integrated or metacognitive or meta-cognitive or nondirective or non-directive or "problem solving" or psychodynamic or "rational emotive" or "self control*" or "self talk" or "self help" or "stress management" or "mind training" or "functional analys*" or psychoanaly* or psychodrama or "role play*" or mindfulness*)

S5 ti(therap*) OR ab(therap*)

S6 ti(acceptance* OR commitment*) OR ab(acceptance* OR commitment*)

S7 S5 AND S6

S8 S4 OR S7

S9 S3 OR S8

S10 S3 AND S8

S11 ti(random* or allocate* or assign* or cross over* or crossover* or controlled) or ab(random* or allocate* or assign* or cross over* or crossover* or controlled)

S12 S1 AND S2 AND S9 AND S11[Publication date from 2014/01/01 to 2019/01/01]

S13 S1 AND S2 AND S10 AND S11[Publication date from 1962/01/01 to 2013/12/31]

S14 S12 OR S13

APPENDIX 2

The detailed descriptions of these psychotherapies and psychological control conditions

The detailed descriptions of these psychotherapies and psychological control conditions

Interventions	Abbreviation	Description
Psychotherapeutic Intervention:		
Behavioural therapy	BT	BT uses some kind of behavioural training and psychoeducation. BT programmes provide parents and youths information about MDD and interventions; teach youths to monitor their mood, thoughts and behaviours; proposed pleasant activity scheduling and behavioural activation.
Cognitive-behavioural therapy	CBT	CBT is a combination of BT and CT. Additional CBT skill-building techniques are used in many programmes by teaching relaxation techniques to cope with environmental stressors, providing social skills and resolution training and teaching general problem-solving.
Family therapy	FT	FT works with families to nurture change and development. FT tends to view change in terms of the systems of interaction between family members. In the case of youth with MDD, FT aims at helping the family to answer the child's needs for completing age-appropriate developmental tasks to relieve depression.
Interpersonal therapy	IPT	IPT aims at educating patients as to how their depression and the quality of interpersonal relationships affect one another and at addressing interpersonal problems that may be contributing to the depression (eg, grief, disputes, role transitions, social deficits). Compared with its adult version, IPT in youths is shorter, involves parents and adds a liaison role for the therapist

		between schools and families.
Problem-solving therapy	PST	PST focus on the problems participants are currently facing and on helping them find solutions to those problems.
Psychodynamic therapy	DYN	DYN proposed patients to help understand the origin and nature of long standing problems by investigating both conscious and non-conscious thoughts and emotional feelings. DYN uses free associations and interpretation of dreams (or drawing in children), and addresses how personal history and experience may alter the patient/therapist transference. In youth MDD, a particular interest is given to psychological trauma, early parent/child relationships, narcissistic organisation and experiences of loss.
Supportive therapy	SUP	SUP is an unstructured therapy without specific psychological techniques that it helped people to ventilate their experiences and emotions and offering empathy. These therapies are commonly described in the literature as either counselling or supportive therapy
Control conditions:		
Psychological placebo	PBO	PBO is a control condition that was regarded as inactive by the researchers, but was to be the participants.
Treatment as usual	TAU	TAU is not considered to be structured psychotherapy, but may have some treatment effects.
Waitlist	WL	WL is a control condition in which the participants receive no active treatment during the study but are forewarned that they can receive one after the study period is over.

APPENDIX 3

Hierarchy of depression symptom severity measurement scales

Hierarchy of depression symptom severity measurement scales

Hierarchy	Depression symptom severity measurement scales	Abbreviation	Included trials
1	Children's Depression Rating Scale	CDRS	30
2	Hamilton Depression Rating Scale	HAMD	16
3	Montgomery Asberg Depression Rating Scale	MADRS	3
4	Beck Depression Inventory	BDI	6
5	Children's Depression Inventory	CDI	8
6	Schedule for Affective Disorders and Schizophrenia for School Aged Children	K-SADS	1
7	Mood and Feeling Questionnaire	MFQ	3
8	Reynolds Adolescent Depression Scale	RADS	1
9	Bellevue Index of Depression	BID	0
10	Child Depression Scale	CDS	0
11	Centre for Epidemiologic Studies Depression Scale	CESD	0
12	Child Assessment Schedule	CAS	0
14	Child Behaviour Checklist-Depression	CBCL-D	0

APPENDIX 4

Network meta-analysis model

NMA model description

1. Random Effects Model for Continuous Data in OpenBUGS

y=a table of the arm-means, sd=a table of the arm sd, n=a table of the arm sample size, t=a table with the names (numbers) of treatments, na=a vector with the number of arms in each study, ref=a number specifying which is the reference treatment

```
model{
for(i in 1:ns){
w[i,1] <- 0
delta[i,t[i,1]]<-0
u[i] ~ dnorm(0,.0001)

for (k in 1:na[i])    {
se[i,t[i,k]]<- sd[i,t[i,k]]/sqrt(n[i,t[i,k]])
var[i,t[i,k]]<- se[i,t[i,k]]*se[i,t[i,k]]
prec[i,t[i,k]]<- 1/var[i,t[i,k]]

#normal likelihood
y[i,t[i,k]] ~ dnorm(phi[i,t[i,k]],prec[i,t[i,k]])
phi[i,t[i,k]]<- (u[i]+delta[i,t[i,k]])*pooled.sd[i]

#calculate the pooled SD
nom1[i,k]<- n[i,t[i,k]]*sd[i,t[i,k]]*sd[i,t[i,k]]    #nominator for the pooled sd
      }

ss[i]<- sum(n[i,1:nt])-nt+na[i]    #total sample size in a study
nom[i]<- sum(nom1[i,1:na[i]])    #nominator for the pooled sd
pooled.sd[i]<- sqrt(nom[i]/(ss[i]-na[i]))    #pooled sd

for (k in 2:na[i]) {
delta[i,t[i,k]] ~ dnorm(md[i,t[i,k]],taud[i,t[i,k]])    # trial-specific SMD distributions
md[i,t[i,k]]<- d[t[i,k]]-d[t[i,1]]+sw[i,k]    # mean of SMD distributions
taud[i,t[i,k]]<- tau*2*(k-1)/k    #precision of SMDdistributions
w[i,k] <- (delta[i,t[i,k]]-d[t[i,k]]+d[t[i,1]])    #adjustment, multi-arm RCTs
sw[i,k] <- sum(w[i,1:k-1])/(k-1) }    # cumulative adjustment for multi-arm trials
      }

d[ref]<-0
for (k in 2:nt) {d[k] ~ dnorm(0,.0001) }
SD~dunif(0,1)    #vague prior for random effects standard deviation
tau<-1/pow(SD,2)
```

```
# Collection of results#
# pairwise SMDs
# for all comparisons
for (c in 1:(nt-1)) { for (k in (c+1):nt) { SMD[c,k] <- d[c] - d[k] }    #to have negative values
      }

#Fit of the Model#
for(i in 1:ns) {
for(k in 1:na[i]) {
Darm[i,k]<-(y[i,t[i,k]]-phi[i,t[i,k]])*(y[i,t[i,k]]-phi[i,t[i,k]])/var[i,t[i,k]]
      }
D[i]<- sum(Darm[i,1:na[i]])
      }
D.bar<- sum(D[])
}
```

2. Random Effects Model for Dichotomous Data in OpenBUGS

r= a table of the number of events, n=a table of the arm sample size, t=a table with the names (numbers) of treatments, na=a vector with the number of arms in each study, ref=a number specifying which is the reference treatment

```
model {
for(i in 1:ns) {
w[i,1]<- 0
delta[i,t[i,1]]<- 0

#Binomial Likelihood#
for (k in 1:na[i]) {
r[i,t[i,k]] ~ dbin(p[i,t[i,k]],n[i,t[i,k]])
      }
#Parameterization of the model#
logit(p[i,t[i,1]])<- mu[i]
for (k in 2:na[i]) {
logit(p[i,t[i,k]])<- mu[i] + delta[i,t[i,k]]
delta[i,t[i,k]] ~ dnorm(md[i,t[i,k]],taud[i,t[i,k]])
taud[i,t[i,k]]<- tau *2*(k-1)/k
md[i,t[i,k]]<-d[t[i,k]] - d[t[i,1]]    + sw[i,k]
w[i,k]<- (delta[i,t[i,k]]    - d[t[i,k]] + d[t[i,1]])
sw[i,k]<- sum(w[i,1:k-1])/(k-1)
      }
      }

#Priors#
sd ~ dnorm(0,1)I(0,1)
```

```
tau<- 1/pow(sd,2)

for(k in 1:(ref-1)) {
d[k] ~ dnorm(0,.0001)
      }
for(k in (ref+1):nt) {
d[k] ~ dnorm(0,.0001)
      }
for(i in 1:ns) {
mu[i] ~ dnorm(0,.0001)
      }

# Collection of results#
#Estimated & Predicted Odds Ratios#
d[ref]<- 0
for(i in 1:(nt-1)) {
for (j in (i+1):nt) {
OR[i,j]<- exp(d[i] - d[j])
LOR[i,j]<- d[i] - d[j]
      }
      }

#Fit of the Model#

for(i in 1:ns) {
for (k in 1:na[i]) {
Darm[i,k]<- -2*( r[i,t[i,k]] *log(n[i,t[i,k]]*p[i,t[i,k]]/ r[i,t[i,k]])+(n[i,t[i,k]] -
      r[i,t[i,k]])*log((n[i,t[i,k]]-n[i,t[i,k]]* p[i,t[i,k]])/(n[i,t[i,k]]- r[i,t[i,k]])))
      }
D[i]<- sum(Darm[i,1:na[i]])
      }
D.bar<- sum(D[])
}
```

3. Meta-regression with a Continuouse Covarite for Continuous Data in OpenBUGS

y=a table of the arm-means, sd=a table of the arm sd, N=a table of the arm sample size, t=a table with the names (numbers) of treatments, na=a vector with the number of arms in each study, ref=a number specifying which is the reference treatment

```
model{
for(i in 1:ns){
            w[i,1] <-0
             delta[i,1]<-0
             u[i] ~ dnorm(0,.0001)
```

```
            for (k in 1:na[i])    {
            se[i,k]<-sd[i,k]/sqrt(n[i,k])
            var[i,k]<-se[i,k]*se[i,k]
            prec[i,k]<-1/var[i,k]

            #normal likelihood
            y[i,k]~dnorm(phi[i,k],prec[i,k])
            phi[i,k]<-(u[i]+delta[i,k])*pooled.sd[i]+(beta[t[i,k]]-beta[t[i,1]]) * (x[i]-mx)
            #calculate the pooled SD
            nom1[i,k]<-n[i,k]*sd[i,k]*sd[i,k] #nominator for the pooled    sd
                  }

            ss[i]<-sum(n[i,1:na[i]]) #total sample size in a study
            nom[i]<-sum(nom1[i,1:na[i]])#nominator for the pooled    sd
            pooled.sd[i]<-sqrt(nom[i]/(ss[i]-na[i]))# pooled    sd

      for (k in 2:na[i]) {
      delta[i,k] ~ dnorm(md[i,k],taud[i,k])        # trial-specific LOR distributions
            md[i,k] <-    d[t[i,k]] - d[t[i,1]]    + sw[i,k]           # mean of LOR distributions
            taud[i,k] <- tau *2*(k-1)/k                                 #precision of LOR distributions
            w[i,k] <- (delta[i,k]    - d[t[i,k]] + d[t[i,1]])    #adjustment, multi-arm RCTs
            sw[i,k] <-sum(w[i,1:k-1])/(k-1) }                           # cumulative adjustment for multi-arm
trials
                        }

d[ref]<-0
beta[1] <- 0
for (k in 2:nt) {
d[k] ~ dnorm(0,.0001)
beta[k] <- B
}
B ~ dnorm(0,.0001)
SD~dunif(0,1)                        #    vague prior for random effects standard deviation
tau<-1/pow(SD,2)

# Extra code for calculating all odds ratios and log odds ratios, and absolute effects, for covariate
# values in vector z, with length nz (given as data)
for (k in 1:nt){
      for (j in 1:nz) { dz[j,k] <- d[k] + (beta[k]-beta[1])*(mx-z[j]) }    # treatment effect when covariate
= z[j]
   }

# Collection of results###########
```

```
# pairwise SMDs
# for all comparisons
for (c in 1:(nt-1)) {
for (k in (c+1):nt)    {
# when covariate is zero
   SMD[c,k] <- d[c] - d[k]
   SMD.neg[c,k] <- d[k] - d[c]
# at covariate=z[j]
for (j in 1:nz) {
SMDz[j,c,k] <- dz[j,c] - dz[j,k]
SMD.negz[j,c,k] <- dz[j,k] - dz[j,c]
        }
      }
    }

#Fit of the Model#

      for(i in 1:ns) {
            for(k in 1:na[i]) {
                  Darm[i,k]<-(y[i,k]-phi[i,k])*(y[i,k]-phi[i,k])/var[i,k]
            }
            D[i]<- sum(Darm[i,1:na[i]])
      }
      D.bar<- sum(D[])

}
```

4. Meta-regression with a Dichotomous Covarite for Continuous Data in OpenBUGS

y=a table of the arm-means, sd=a table of the arm sd, N=a table of the arm sample size, t=a table with the names (numbers) of treatments, na=a vector with the number of arms in each study, ref=a number specifying which is the reference treatment

```
model{
for(i in 1:ns){
              w[i,1] <-0
              delta[i,1]<-0
              u[i] ~ dnorm(0,.0001)

              for (k in 1:na[i])    {
              se[i,k]<-sd[i,k]/sqrt(n[i,k])
              var[i,k]<-se[i,k]*se[i,k]
              prec[i,k]<-1/var[i,k]
```

```
            #normal likelihood
            y[i,k]~dnorm(phi[i,k],prec[i,k])
            phi[i,k]<-(u[i]+delta[i,k])*pooled.sd[i]+(beta[t[i,k]]-beta[t[i,1]]) * x[i]
            #calculate the pooled SD
            nom1[i,k]<-n[i,k]*sd[i,k]*sd[i,k] #nominator for the pooled    sd
                  }

            ss[i]<-sum(n[i,1:na[i]]) #total sample size in a study
            nom[i]<-sum(nom1[i,1:na[i]])#nominator for the pooled    sd
            pooled.sd[i]<-sqrt(nom[i]/(ss[i]-na[i]))# pooled    sd

      for (k in 2:na[i]) {
      delta[i,k] ~ dnorm(md[i,k],taud[i,k])        # trial-specific LOR distributions
            md[i,k] <-    d[t[i,k]] - d[t[i,1]]    + sw[i,k]           # mean of LOR distributions
            taud[i,k] <- tau *2*(k-1)/k                                  #precision of LOR distributions
            w[i,k] <- (delta[i,k]    - d[t[i,k]] + d[t[i,1]])    #adjustment, multi-arm RCTs
            sw[i,k] <-sum(w[i,1:k-1])/(k-1) }                            # cumulative adjustment for multi-arm
trials
                        }

d[ref]<-0
beta[1] <- 0
for (k in 2:nt) {
d[k] ~ dnorm(0,.0001)
beta[k] <- B
}
B ~ dnorm(0,.0001)
SD~dunif(0,1)                        #    vague prior for random effects standard deviation
tau<-1/pow(SD,2)

# Extra code for calculating all odds ratios and log odds ratios, and absolute effects, for covariate
# values in vector z, with length nz (given as data)
for (k in 1:nt){
      for (j in 1:nz) { dz[j,k] <- d[k] + (beta[k]-beta[1])*z[j] }    # treatment effect when covariate = z[j]
   }

# Collection of results###########

# pairwise SMDs
# for all comparisons
for (c in 1:(nt-1)) {
for (k in (c+1):nt)    {
# when covariate is zero
   SMD[c,k] <- d[c] - d[k]
```

```
   SMD.neg[c,k] <- d[k] - d[c]
# at covariate=z[j]
for (j in 1:nz) {
SMDz[j,c,k] <- dz[j,c] - dz[j,k]
SMD.negz[j,c,k] <- dz[j,k] - dz[j,c]
        }
      }
    }

#Fit of the Model#

      for(i in 1:ns) {
            for(k in 1:na[i]) {
                  Darm[i,k]<-(y[i,k]-phi[i,k])*(y[i,k]-phi[i,k])/var[i,k]
            }
            D[i]<- sum(Darm[i,1:na[i]])
      }
      D.bar<- sum(D[])

}
```

5. Meta-regression with a Continuouse Covarite for Dichotomous Data in OpenBUGS

r= a table of the number of events, n=a table of the arm sample size, t=a table with the names (numbers) of treatments, na=a vector with the number of arms in each study, ref=a number specifying which is the reference treatment

```
model {
      for(i in 1:ns) {
      w[i,1]<- 0
          delta[i,1]<- 0

#Binomial Likelihood#

            for (k in 1:na[i]) {
            r[i,k] ~ dbin(p[i,k],n[i,k])
            }

#Parameterization of the model#

            logit(p[i,1])<- mu[i]

            for (k in 2:na[i]) {
      logit(p[i,k])<- mu[i] + delta[i,k]+(beta[t[i,k]]-beta[t[i,1]]) * (x[i]-mx)
                  delta[i,k] ~ dnorm(md[i,k],taud[i,k])
```

```
                taud[i,k]<- tau *2*(k-1)/k
            md[i,k]<-    d[t[i,k]] - d[t[i,1]]    + sw[i,k]
            w[i,k]<- (delta[i,k]    - d[t[i,k]] + d[t[i,1]])
            sw[i,k]<- sum(w[i,1:k-1])/(k-1)
           }
      }

#Priors#

      sd ~ dnorm(0,1)I(0,1)
      tau<- 1/pow(sd,2)
      B ~ dnorm(0,.0001)

      for(k in 2:nt) {
            d[k] ~ dnorm(0,.0001)
                  beta[k] <-B
      }
      for(i in 1:ns) {
            mu[i] ~ dnorm(0,.0001)
      }

#Estimated & Predicted Odds Ratios#

      d[ref]<- 0
beta[1] <- 0

for (k in 1:nt){
      for (j in 1:nz) { dz[j,k] <- d[k] + (beta[k]-beta[1])*(mx-z[j]) }    # treatment effect when covariate
= z[j]
   }
# pairwise ORs and LORs for all possible pair-wise comparisons
for (c in 1:(nt-1)) {
      for (k in (c+1):nt)    {
# when covariate is zero
            OR[c,k] <- exp(d[c] - d[k])
            LOR[c,k] <- (d[c]-d[k])
# at covariate=z[j]
            for (j in 1:nz) {
                  ORz[j,c,k] <- exp(dz[j,c] - dz[j,k])
                  LORz[j,c,k] <- (dz[j,c]-dz[j,k])
               }
        }
  }
#Fit of the Model#
```

```
    for(i in 1:ns) {
        for (k in 1:na[i]) {
            Darm[i,k]<- -2*( r[i,k] *log(n[i,k]*p[i,k]/ r[i,k])+(n[i,k] - r[i,k])*log((n[i,k]-n[i,k]*
p[i,k])/(n[i,k]- r[i,k])))
        }
        D[i]<- sum(Darm[i,1:na[i]])
    }
    D.bar<- sum(D[])
}
```

6. Meta-regression with a Dichotomous Covarite for Dichotomous Data in OpenBUGS

r= a table of the number of events, n=a table of the arm sample size, t=a table with the names (numbers) of treatments, na=a vector with the number of arms in each study, ref=a number specifying which is the reference treatment

```
model {
    for(i in 1:ns) {
    w[i,1]<- 0
        delta[i,1]<- 0

#Binomial Likelihood#

        for (k in 1:na[i]) {
        r[i,k] ~ dbin(p[i,k],n[i,k])
        }

#Parameterization of the model#

        logit(p[i,1])<- mu[i]

        for (k in 2:na[i]) {
    logit(p[i,k])<- mu[i] + delta[i,k]+(beta[t[i,k]]-beta[t[i,1]]) * x[i]
            delta[i,k] ~ dnorm(md[i,k],taud[i,k])
            taud[i,k]<- tau *2*(k-1)/k
         md[i,k]<-    d[t[i,k]] - d[t[i,1]]    + sw[i,k]
         w[i,k]<- (delta[i,k]    - d[t[i,k]] + d[t[i,1]])
         sw[i,k]<- sum(w[i,1:k-1])/(k-1)
        }
    }

#Priors#

    sd ~ dnorm(0,1)I(0,1)
```

```
        tau<- 1/pow(sd,2)
        B ~ dnorm(0,.0001)

        for(k in 2:nt) {
                d[k] ~ dnorm(0,.0001)
                        beta[k] <-B
        }
        for(i in 1:ns) {
                mu[i] ~ dnorm(0,.0001)
        }

#Estimated & Predicted Odds Ratios#

        d[ref]<- 0
beta[1] <- 0

for (k in 1:nt){
        for (j in 1:nz) { dz[j,k] <- d[k] + (beta[k]-beta[1])*z[j] }    # treatment effect when covariate = z[j]
   }
# pairwise ORs and LORs for all possible pair-wise comparisons
for (c in 1:(nt-1)) {
        for (k in (c+1):nt)    {
# when covariate is zero
                OR[c,k] <- exp(d[c] - d[k])
                LOR[c,k] <- (d[c]-d[k])
# at covariate=z[j]
                for (j in 1:nz) {
                        ORz[j,c,k] <- exp(dz[j,c] - dz[j,k])
                        LORz[j,c,k] <- (dz[j,c]-dz[j,k])
                   }
         }
  }
#Fit of the Model#

        for(i in 1:ns) {
                for (k in 1:na[i]) {
                        Darm[i,k]<- -2*( r[i,k] *log(n[i,k]*p[i,k]/ r[i,k])+(n[i,k] - r[i,k])*log((n[i,k]-n[i,k]*
p[i,k])/(n[i,k]- r[i,k])))
                }
                D[i]<- sum(Darm[i,1:na[i]])
        }
        D.bar<- sum(D[])
}
```

APPENDIX 5

Published protocol and changes made to the protocol

The protocol has been registered in PROSPERO (No.CRD42015020841) and published in BMJ Open – available at https://bmjopen.bmj.com/content/7/8/e016608.full.pdf+html

Here below changes and clarifications to the published protocol:

1. In order to obtain more comprehensive data, we added some text words in search strategy. For example, the additional words inclue 'desvenlafaxine', 'mianserin', 'levomilnacipran', 'trazodone', 'vilazodone' and 'vortioxetine'. We also searched additional international trial registers, including Australian New Zealand Clinical Trials Registry (ANZCTR), Chinese Clinical Trial Register (ChiCTR), UMIN Clinical Trials Registry in Japan (UMIN-CTR), the International Standard Randomised Controlled Trial Number (ISRCTN), and the Netherlands Trial Register.

2. We had planed to assess the remission rate (measured by the proportion of patients who achieved the criteria of below the specific threshold scores in depressive symptom scales), tolerability (adverse-event discontinuation measured by the proportion of patients who withdrew for any adverse events), and global functional improvement (estimated by overall change scores on global assessment of functioning scales) as secondary outcomes. However, we found there were not enough available data for network analysis after data extraction. Thus, we didn't perform those three outcomes.

3. We have adjusted some analyses for sensitivity analyses, subgroup and meta-regressions according to the characteristics of trials. First, we added meta-regeression analyses with risk of bias, publication year, comorbidity and type of sponsor for primary outcomes, and rating scale for efficacy. Second, we added sensitivity analyses of omitting non-blind trials, unpublished trials and trials with sample size ≤ 20 for primary outcomes, and omitting trials with inconsistent of treatment duration and selected time-point for efficacy. However, we didn't perform sensitivity analyses of omitting high risk of bias trials and omitting patients with comorbidity trials for primary outcomes due to no available data, and we also didn't perform sensitivity analyse of omitting trials with imputed data for acceptability due to the same reason. Third, we conducted all the continuous covariate for meta-regressions if possible to ensure the integrity of data. We didn't perform any subgroup analysis due to the limitation of study numbers.

4. We used the Confidence In Network Meta-Analysis (CINeMA) approach to evaluate the credibility of each outcome rather than GRADE framework.

APPENDIX 6

References for included trials

1. Kye 1996

- Kye CH, Waterman GS, Ryan ND, et al. A randomized, controlled trial of amitriptyline in the acutetreatment of adolescent major depression. *J Am Acad Child Adolesc Psychiatry* 1996; **35:** 1139-44.

2. Von Knorring 2006

- Von Knorring AL, Olsson GI, Thomsen PH, Lemming OM, Hultén A. A randomized, double-blind, placebo-controlled study of citalopram in adolescents with major depressive disorder. *J Clin Psychopharmacol* 2006; **26:** 311-5.

3. Wagner 2004

- Wagner KD, Robb AS, Findling RL, Jin J, Gutierrez MM, Heydorn WE. A randomized, placebo-controlled trial of citalopram for the treatment of major depression in children andadolescents. *Am J Psychiatry* 2004; **161:** 1079-83.

4. Braconnier 2003

- Braconnier A, Le Coent R, Cohen D, DEROXADO Study Group. Paroxetine versus clomipramine inadolescents with severe major depression: a double-blind, randomized, multicenter trial. *JAm Acad Child Adolesc Psychiatry* 2003; **42:** 22-9.

5. Klein 1998

- Klein RG, Mannuzza S, Koplewicz HS, et al. Adolescent depression: controlled desipraminetreatment and atypical features. *Depress Anxiety* 1998; **7:** 15-31.

6. Kutcher 1994

- Kutcher S, Boulos C, Ward B, et al. Response to desipramine treatment in adolescent depression: afixed-dose, placebo-controlled trial. *J Am Acad Child Adolesc Psychiatry* 1994; **33:** 686-94.

7. Atkinson2018

- Atkinson S, Lubaczewski S, Ramaker S, et al. DesvenlafaxineVersus Placebo in the Treatment of Children and Adolescents with Major Depressive Disorder.*J Child Adolesc Psychopharmacol* 2018; **28:** 55-65.

8. Weihs 2018

- Weihs KL, Murphy W, Abbas R, et al.Desvenlafaxine versus placebo in a fluoxetine-referenced study of children and adolescents with major depressive disorder. *J Child Adolesc Psychopharmacol* 2018; **28:** 36-46.

9. Emslie 2014

- Emslie GJ, Prakash A, Zhang Q, Pangallo BA, Bangs ME, March JS. A double-blind efficacy andsafety study of duloxetine fixed doses in children and adolescents with major depressivedisorder. *J Child Adolesc Psychopharmacol* 2014; **24:** 170-9.

10. Atkinson 2014

- Atkinson SD, Prakash A, Zhang Q, et al. A double-blind efficacy and safety study of duloxetineflexible dosing in children and adolescents with major depressive disorder. *J Child Adolesc Psychopharmacol* 2014; **24:** 180-9.

11. Emslie 2009

- Emslie GJ, Ventura D, Korotzer A, Tourkodimitris S. Escitalopram in the treatment of adolescentdepression: a randomized placebo-controlled multisite trial. *J Am Acad Child Adolesc Psychiatry* 2009; **48:** 721-9.

12. Wagner 2006

- Wagner KD, Jonas J, Findling RL, Ventura D, Saikali K. A double-blind, randomized, placebo-controlled trial of escitalopram in thetreatment of pediatric depression. *J Am Acad Child Adolesc Psychiatry* 2006; **45:** 280-8.

13. Attari 2006

- Attari A, Moghaddam FY, Hasanzadeh A, Soltani M, Mahmoodi M. Comparison of efficacy offluoxetine with nortriptyline in treatment of major depression in children and adolescents: Adouble-blind study.*Journal of Research in Medical Sciences* 2006; **11:** 24-30.

14. Almeida-Montes 2005

- Almeida-MontesLG, Friederichsen A. Treatment of major depressive disorder with fluoxetine inchildren and adolescents. A double-blind, placebo-controlled study. *Psiquiatria Biologica* 2005; **12:** 198-205.

15. Eli Lilly 1986

- B1Y-MC-HCCJ. Fluoxetine: fluoxetine versus placebo in adolescent depressed patients. 17November 2004. http://art45-paediatric-studies-docs.ema.europa.eu/GROUP%20F/Fluoxetine/fluoxetine%20B1Y-MC-HCCJ%20Clinical%20Study%20Summary.pdf (accessed October 9, 2019)

16. Emslie 1997

- Emslie GJ, Rush AJ, Weinberg WA, et al. A double-blind, randomized, placebo-controlled trial offluoxetine in children and adolescents with depression. *Arch Gen Psychiatry* 1997; **54:** 1031-7.

17. Emslie 2002a

- Emslie GJ, Heiligenstein JH, Wagner KD, et al. Fluoxetine for acute treatment of depression inchildren and adolescents: a placebo-controlled, randomized clinical trial. *J Am Acad ChildAdolesc Psychiatry* 2002; **41:** 1205-15.

18. Findling 2009

- Findling RL, Pagano ME, McNamara NK, et al. The short-term safety and efficacy of fluoxetine indepressed adolescents with alcohol and cannabis use disorders: a pilot randomizedplacebo-controlled trial. *Child Adolesc Psychiatry Ment Health* 2009; **3:** 11.

19. Hongfen 2009

- Hongfen C, Weidong J, Guoquan Z, et al. A randomized and double-blind clinical trial ofvenlafaxine hydrochloride sustained release capsules for treating juvenile depression. *EurPsychiatry* 2009; **24:** S502.

20. Puig-Antich 1987

- Puig-Antich J, Perel JM, Lupatkin W, et al. Imipramine in prepubertal major depressive disorders. *Arch Gen Psychiatry*1987; **44:** 81-9.

21. Organon 2002a

- Organon Pharmaceuricals USA Inc. A multicenter, randomized, double-blind, placebo-controlled, efficacy and safety study of Remeron in outpatient children and adolescents with major depressive disorder.

http://www.hma.eu/fileadmin/dateien/Human_Medicines/CMD_h_/Paediatric_Regulation/Assessment_Reports/Article_45_work-sharing/Mirtazapine_2011_06_45PaedAR_Amended.pdf (accessed October 9, 2019).

22. Organon 2002b

- Organon Pharmaceuricals USA Inc. A multicenter, randomized, double-blind, placebo-controlled, efficacy and safety study of Remeron in outpatient children and adolescents with major depressive disorder.

http://www.hma.eu/fileadmin/dateien/Human_Medicines/CMD_h_/Paediatric_Regulation/Assessment_Reports/Article_45_work-sharing/Mirtazapine_2011_06_45PaedAR_Amended.pdf (accessed October 9, 2019).

23. Bristol-Myers Squibb 2002

- Bristol-MyerSquibb. Review and evaluation of clinical data.

https://www.accessdata.fda.gov/drugsatfda_docs/pediatric/020152s032_nefazodone_Serzone_Clinical_BPCA.pdf (accessed October 9, 2019)

24. Emslie 2002b

- Emslie GJ, Heiligenstein JH, Wagner KD, et al. Fluoxetine for acute treatment of depression inchildren and adolescents: a placebo-controlled, randomized clinical trial. *J Am Acad ChildAdolesc Psychiatry* 2002; **41:** 1205-15.

25. Geller 1990

- Geller B, Cooper TB, Graham DL, Marsteller FA, Bryant DM. Double-blind placebo-controlled study of nortriptyline in depressed adolescents using a "fixed plasma level" design. *Psychopharmacol Bull* 1990; **26:** 85-90.

26. Geller 1992

- Geller B, Cooper TB, Graham DL, Fetner HH, Marsteller FA, Wells JM. Pharmacokinetically designed double-blind placebo-controlled study of nortriptyline in 6- to 12-year-olds with major

depressive disorder. *J Am Acad Child Adolesc Psychiatry* 1992; **31:** 34-44.

27. Berard 2006

- Berard R, Fong R, Carpenter DJ, ThomasonC, Wilkinson C. An international, multicenter, placebo-controlled trial of paroxetine in adolescents with major depressive disorder. *J Child Adolesc Psychopharmacol* 2006; **16:** 59-75.

28. Emslie 2006

- Emslie GJ, Wagner KD, Kutcher S, et al. Paroxetine treatment in children and adolescents withmajor depressive disorder: a randomized, multicenter, double-blind, placebo-controlled trial. *J Am Acad Child Adolesc Psychiatry* 2006; **45:** 709-19.

29. GlaxoSmithKline 2009

- Paxil Japanese post marketing paediatric study in depression (double-blind, placebo controlled study) [clinical trial]. ClinicalTrials.gov Identifier: NCT00812812. www.clinicaltrials.gov/ct2/show/study/NCT00812812?term=A+randomised%2C+double-blind%2C+placebo+controlled%2C+parallel+group%2C+flexible+dose+study+to+evaluate+the+efficacy+and+safety+of+Paxil%C2%AE+Tablets+in+children+and+adolescents+with+Major+Depressive+Disorder&rank=1 (accessed October 9, 2019).

30. Noury JL 2015

- Le Noury J, Nardo JM, Healy D, et al. Restoring Study 329: efficacy and harms of paroxetine and imipramine in treatment of major depression in adolescence. *BMJ* 2015; **351:** h4320.

31. Wagner 2003a

- Wagner KD, Ambrosini P, Rynn M, et al. Efficacy of sertraline in the treatment of children andadolescents with major depressive disorder: two randomized controlled trials. *JAMA* 2003; **290:** 1033-41.

32. Wagner 2003b

- Wagner KD, Ambrosini P, Rynn M, et al. Efficacy of sertraline in the treatment of children andadolescents with major depressive disorder: two randomized controlled trials. *JAMA* 2003; **290:** 1033-41.

33. Emslie 2007a

- Emslie GJ, Findling RL, Yeung PP, Kunz NR, Li Y. Venlafaxine ER for the treatment of pediatricsubjects with depression: results of two placebo-controlled trials. *J Am Acad Child Adolesc Psychiatry* 2007; **46:** 479-88.

34. Emslie 2007b

- Emslie GJ, Findling RL, Yeung PP, Kunz NR, Li Y. Venlafaxine ER for the treatment of pediatricsubjects with depression: results of two placebo-controlled trials. *J Am Acad Child Adolesc Psychiatry* 2007; **46:** 479-88.

35. Durgam 2018

- Durgam S, Chen C, Migliore R, Prakash C, Edwards J, Findling RL.A Phase 3, Double-Blind, Randomized, Placebo-Controlled Study of Vilazodone in Adolescents with Major Depressive Disorder. *Paediatr Drugs* 2018; **20:** 353-63.

36. Reed 1994

- Reed MK. Social skills training to reduce depression in adolescents. *Adolescence* 1994; **29:** 293-302.

37. Fine 1991

- Fine S, Forth A, Gilbert M, Haley G. Group therapy for adolescent depressive disorder: a comparison of social skills and therapeutic support. *J Am Acad Child Adolesc Psychiatry* 1991; **30:** 79-85.

38. Charkhandeh 2016

- Charkhandeh M, Talib MA, Hunt CJ. The clinical effectiveness of cognitive behavior therapy and an alternative medicine approach in reducing symptoms of depression in adolescents. *Psychiatry Res* 2016; **239:** 325-30.

39. Clarke 1999

- Clarke GN, Rohde P, Lewinsohn PM, Hops H, Seeley JR. Cognitive-behavioral treatment of adolescent depression: efficacy of acute group treatment and booster sessions. *J Am Acad Child Adolesc Psychiatry* 1999; **38:** 272-9.

40. Curtis 1992

- CurtisSE. Cognitive-behavioral treatment of adolescent depression. Doctoral dissertation, Utah State University, Logan, 1992.

41. Lewinsohn 1990

- Lewinsohn PM, Clarke GN, Hops H, Andrews J. Cognitive-behavioraltreatment for depressed adolescents. *Behav Ther* 1990; **21:** 385-401.

42. Brent 1997

- Brent DA, Holder D, Kolko D, et al. A clinical psychotherapy trial for adolescent depression comparing cognitive, family, and supportive therapy.*Arch Gen Psychiatry* 1997; **54:** 877-85.

43. Rossello 1999

- Rosselló J, Bernal G. The efficacy of cognitive-behavioral and interpersonal treatments for depression in Puerto Rican adolescents. *J Consult Clin Psychol* 1999; **67:** 734-45.

44. Rohde 2004

- Rohde P, Clarke GN, Mace DE, Jorgensen JS, Seeley JR. An efficacy/effectiveness study of cognitive-behavioral treatment for adolescents with comorbid major depression and conduct disorder. *J Am Acad Child Adolesc Psychiatry* 2004; **43:** 660-8.

45. Goodyer 2017

- Goodyer IM, Reynolds S,Barrett B,et al. Cognitive behavioural therapy and short-term psychoanalytical psychotherapy versus a brief psychosocial intervention in adolescents with unipolar major depressive disorder (IMPACT): a multicentre, pragmatic, observer-blind, randomised controlled superiority trial. *Lancet psychiatry* 2017; **4:** 109-19.

46. Vostanis 1996

- Vostanis P, Feehan C, Grattan E, Bickerton WL. A randomised controlled out-patient trial of cognitive-behavioural treatment for children and adolescents with depression: 9-month follow-up. *J Affect Disord* 1996; **40:** 105-16.

47. Wood 1996

- Wood A, Moore A, Harrington R, Jayson D. Clinical validity of major depression-endogenous subtype in adolescent patients. *Eur Child Adolesc Psychiatry* 1996; **5:** 155-61.

48. Clarke 2002

- Clarke G, Reid E, Eubanks D, et al. Overcoming depression on the Internet (ODIN): a randomized controlled trial of an Internet depression skills intervention program. *J Med Internet Res* 2002; **4:** E14.

49. Kobak 2015

- Kobak KA, Mundt JC, Kennard B. Integrating technology into cognitive behavior therapy for adolescent depression: a pilot study. *Ann Gen Psychiatry* 2015; **14:** 37.

50. Shirk 2014

- Shirk SR, Deprince AP, Crisostomo PS, Labus J. Cognitive behavioral therapy for depressed adolescents exposed to interpersonal trauma: an initial effectiveness trial. *Psychotherapy (Chic)* 2014; **51:** 167-79.

51. Weisz 2009

- Weisz JR, Southam-Gerow MA, Gordis EB, et al.Cognitive-behavioral therapy versus usual clinical care for youth depression: an initial test of transportability to community clinics and clinicians. *J Consult Clin Psychol* 2009; **77:** 383-96.

52. Trowell 2007

- Trowell J, Joffe I, Campbell J,et al. Childhood depression: a place for psychotherapy. An outcome study comparing individual psychodynamic psychotherapy and family therapy. *Eur Child Adolesc Psychiatry* 2007; **16:** 157-67.

53. Diamond 2002

- Diamond GS, Reis BF, Diamond GM, Siqueland L, Isaacs L. Attachment-based family therapy for depressed adolescents: a treatment development study. *J Am Acad Child Adolesc Psychiatry* 2002; **41:** 1190-6.

54. Luby 2012

- Luby J, Lenze S, Tillman R. A novel early intervention for preschool depression: findings from a pilot randomized controlled trial. *J Child Psychol Psychiatry* 2012; **53:** 313-22.

55. Tompson 2017

- Tompson MC, Sugar CA, Langer DA, Asarnow JR.A randomized clinical trial comparing family-focused treatment and individual supportive therapy for depression in childhood and early adolescence. *J Am Acad Child Adolesc Psychiatry* 2017; **56:** 515-23.

56. Israel 2013

- Israel P, Diamond GS. Feasibility of Attachment Based Family Therapy for depressed clinic-referred Norwegian adolescents. *Clin Child Psychol Psychiatry* 2013; **18:** 334-50.

57. Poole 2017

- Poole LA, Knight T, Toumbourou JW, Lubman DI, Bertino MD, Lewis AJ. A Randomized Controlled Trial of the Impact of a Family-Based Adolescent Depression Intervention on both Youth and Parent Mental Health Outcomes. *J Abnorm Child Psychol* 2018; **46:** 169-81.

58. Dietz 2015

- Dietz LJ, Weinberg RJ, Brent DA, Mufson L. Family-based interpersonal psychotherapy for depressed preadolescents: examining efficacy and potential treatment mechanisms. *J Am Acad Child Adolesc Psychiatry* 2015; **54:** 191-9.

59. Mufson 1999

- Mufson L, Weissman MM, Moreau D, Garfinkel R. Efficacy of Interpersonal Psychotherapy for Depressed Adolescents. *Arch Gen Psychiatry* 1999; **56:** 573-9.

60. Mufson 2004b

- Mufson L, Dorta KP, Wickramaratne P, Nomura Y, Olfson M, Weissman MM. A Randomized Effectiveness Trial of Interpersonal Psychotherapy for DepressedAdolescents. *Arch Gen Psychiatry* 2004; **61:** 577-84.

61. Tang 2009

- Tang TC, Jou SH, Ko CH, Huang SY, Yen CF. Randomized study of school-based intensive interpersonal psychotherapy for depressed adolescents with suicidal risk and parasuicide behaviors. *Psychiatry Clin Neurosci* 2009; **63:** 463-70.

62. Eskin 2008

- Eskin M, Ertekin K, Harlak H, Dereboy C. Prevalence of and factors related to depression in high school students. *Turk Psikiyatri Derg* 2008; **19:** 382-9.

63. Cornelius2009

- Cornelius JR, Bukstein OG, Wood DS, Kirisci L, Douaihy A, Clark DB. Double-blind

placebo-controlled trial of fluoxetine in adolescents with comorbid major depression and an alcohol use disorder. *Addict Behav* 2009; **34:** 905-9.

64. March 2004

- March J, Silva S, Petrycki S, et al. Fluoxetine, cognitive-behavioral therapy, and their combination for adolescents with depression: Treatment for Adolescents With Depression Study (TADS) randomized controlled trial. *JAMA* 2004; **292:** 807-20.

65. Goodyer 2008

- Goodyer IM, Dubicka B, Wilkinson P, et al. A randomised controlled trial of cognitive behaviour therapy in adolescents with major depression treated by selective serotonin reuptake inhibitors. The ADAPT trial. *Health Technol Assess* 2008; **12:** iii-iv, ix-60.

66. Riggs 2007

- Riggs PD, Mikulich-Gilbertson SK, Davies RD, Lohman M, Klein C, Stover SK. A randomized controlled trial of fluoxetine and cognitive behavioral therapy in adolescents with major depression, behavior problems, and substance use disorders. *Arch PediatrAdolesc Med* 2007; **161:** 1026-34.

67. Bernstein 2000

- Bernstein LR, Tanner T, Godfrey C, Noll B. Chemistry and pharmacokinetics of gallium maltolate, a compound with high oral gallium bioavailability. *Met Based Drugs* 2000; **7:** 33-47.

68. Melvin 2006

- Melvin GA, Tonge BJ, King NJ, Heyne D, Gordon MS, Klimkeit E. A comparison of cognitive-behavioral therapy, sertraline, and their combination for adolescent depression. *J Am Acad Child Adolesc Psychiatry* 2006; **45:** 1151-61.

69. Deas 2000

- Deas D, Randall CL, Roberts JS, Anton RF. A double-blind, placebo-controlled trial of sertraline in depressed adolescent alcoholics: a pilot study. *Hum Psychopharmacol* 2000; **15:** 461-69.

70. Iftene F 2015

- Iftene F, Predescu E, Stefan S, David D. Rational-emotive and cognitive-behavior therapy (REBT/CBT) versus pharmacotherapy versus REBT/CBT plus pharmacotherapy in the treatment of major depressive disorder in youth; a randomized clinical trial. *Psychiatry Res* 2015; **225:** 687-94.

71. Mandoki 1997

- Mandoki MW, Tapia MR, Tapia MA, Sumner GS, Parker JL. Venlafaxine in the treatment of children and adolescents with major depression. *Psychopharmacol Bull* 1997; **33:** 149-54.

APPENDIX 7

Risk of bias assessment

The details of rating criteria are in the published protocol (Zhou X, et al. BMJ Open 2017; 7:e016608).

Study ID		Sequence generation	Allocation concealment	Blinding of performance and personnel*	Blinding of outcome assessment	Incomplete outcome data	Selective outcome reporting	Other sources of bias	Risk of bias for trial[#]
1.	Kye 1996	Low risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Low risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias
2.	Von Knorring 2006	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	High risk of bias	High risk of bias	Unclear risk of bias	High risk of bias
3.	Wagner 2004	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	High risk of bias	High risk of bias	Unclear risk of bias	High risk of bias
4.	Braconnier 2003	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias
5.	Klein 1998	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias
6.	Kutcher 1994	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Low risk of bias	Unclear risk of bias
7.	Atkinson 2018	Unclear risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias
8.	Weihs 2018	Unclear risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias
9.	Emslie 2014	Low risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias
10.	Atkinson 2014	Low risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias
11.	Emslie 2009	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Low risk of bias	High risk of bias	Low risk of bias	Unclear risk of bias
12.	Wagner 2006	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Low risk of bias	Unclear risk of bias
13.	Attari 2006	Unclear risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias
14.	Almeida-Montes 2005	Low risk of bias	Low risk of bias	Unclear risk of bias	Low risk of bias	High risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias
15.	Eli Lilly 1986	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	Unclear risk of bias
16.	Emslie 1997	Low risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	High risk of bias	Unclear risk of bias	Unclear risk of bias
17.	Emslie 2002a	Low risk of bias	Unclear risk of bias	Low risk of bias	Unclear risk of bias	Unclear risk of bias	High risk of bias	High risk of bias	High risk of bias

18.	Findling 2009	Low risk of bias	Low risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias
19.	Hongfen 2009	Low risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias
20.	Puig-Antich 1987	Low risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias
21.	Organon 2002a	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	High risk of bias	High risk of bias	High risk of bias
22.	Organon 2002b	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	High risk of bias	Unclear risk of bias	Unclear risk of bias
23.	Bristol-Myers Squibb 2002	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias
24.	Emslie 2002b	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias
25.	Geller 1990	Unclear risk of bias	Unclear risk of bias	Low risk of bias	High risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias
26.	Geller 1992	Unclear risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias
27.	Berard 2006	Low risk of bias	Low risk of bias	Low risk of bias	Unclear risk of bias	Unclear risk of bias	Low risk of bias	Unclear risk of bias	Unclear risk of bias
28.	Emslie 2006	Low risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	Unclear risk of bias	Unclear risk of bias
29.	GlaxoSmithKline 2009	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	High risk of bias	Unclear risk of bias	Unclear risk of bias
30.	Noury 2015	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias
31.	Wagner 2003a	Low risk of bias	Unclear risk of bias	Low risk of bias	Unclear risk of bias	Low risk of bias	High risk of bias	High risk of bias	High risk of bias
32.	Wagner 2003b	Low risk of bias	Unclear risk of bias	Low risk of bias	Unclear risk of bias	Low risk of bias	High risk of bias	High risk of bias	High risk of bias
33.	Emslie 2007 †	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Low risk of bias	High risk of bias	High risk of bias	High risk of bias
34.	Durgam 2018	Low risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias
35.	Reed 1994	Unclear risk of bias	Unclear risk of bias	High risk of bias	High risk of bias	Unclear risk of bias	High risk of bias	Low risk of bias	High risk of bias
36.	Fine 1991	Unclear risk of bias	Unclear risk of bias	High risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	High risk of bias
37.	Charkhandeh 2016	Low risk of bias	Unclear risk of bias	High risk of bias	High risk of bias	High risk of bias	Low risk of bias	Low risk of bias	High risk of bias

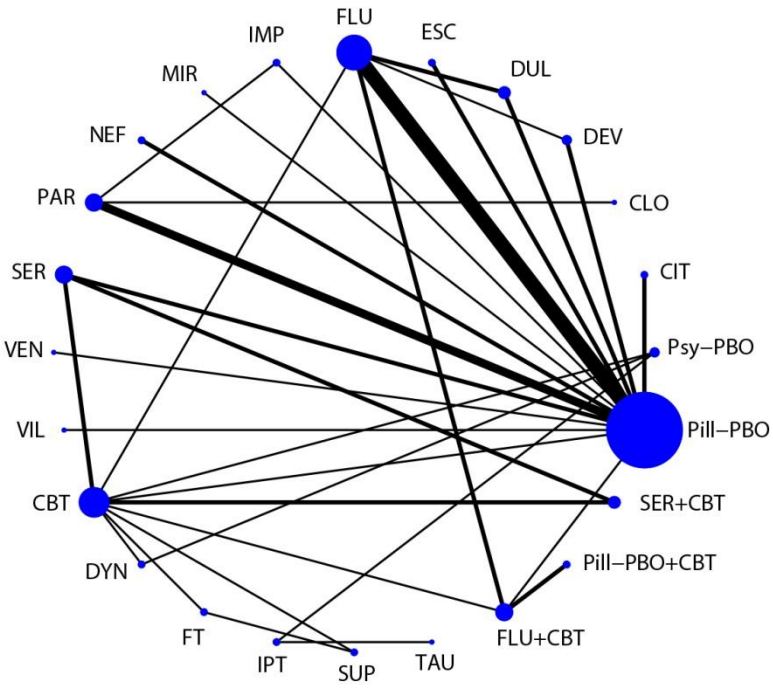
38.	Clarke 1999	Unclear risk of bias	Unclear risk of bias	High risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Unclear risk of bias
39.	Curtis 1992	Unclear risk of bias	Unclear risk of bias	High risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Unclear risk of bias	High risk of bias
40.	Lewinsohn 1990	Unclear risk of bias	Unclear risk of bias	High risk of bias	High risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	High risk of bias
41.	Brent 1997	Low risk of bias	Unclear risk of bias	High risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	High risk of bias
42.	Rossello 1999	Unclear risk of bias	Unclear risk of bias	High risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	High risk of bias
43.	Rohde 2004	Low risk of bias	Unclear risk of bias	High risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	Unclear risk of bias	Unclear risk of bias
44.	Goodyer 2017	Low risk of bias	Unclear risk of bias	High risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	High risk of bias
45.	Vostanis 1996	Unclear risk of bias	Unclear risk of bias	High risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	High risk of bias
46.	Wood 1996	Unclear risk of bias	Unclear risk of bias	High risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	Unclear risk of bias	Unclear risk of bias
47.	Clarke 2002	Unclear risk of bias	Unclear risk of bias	High risk of bias	Unclear risk of bias	High risk of bias	Low risk of bias	Low risk of bias	High risk of bias
48.	Kobak 2015	Unclear risk of bias	Unclear risk of bias	High risk of bias	High risk of bias	Unclear risk of bias	Unclear risk of bias	Low risk of bias	High risk of bias
49.	Shirk 2014	Unclear risk of bias	Unclear risk of bias	High risk of bias	High risk of bias	High risk of bias	High risk of bias	High risk of bias	High risk of bias
50.	Weisz 2009	Low risk of bias	Low risk of bias	High risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Unclear risk of bias	High risk of bias
51.	Trowell 2007	Unclear risk of bias	Unclear risk of bias	High risk of bias	High risk of bias	Unclear risk of bias	Low risk of bias	Unclear risk of bias	High risk of bias
52.	Diamond 2002	Unclear risk of bias	Unclear risk of bias	High risk of bias	Unclear risk of bias	Unclear risk of bias	High risk of bias	Low risk of bias	High risk of bias
53.	Luby 2012	Low risk of bias	Unclear risk of bias	High risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Unclear risk of bias	High risk of bias
54.	Tompson 2017	Low risk of bias	Unclear risk of bias	High risk of bias	Low risk of bias	High risk of bias	Low risk of bias	Unclear risk of bias	High risk of bias
55.	Israel 2013	Low risk of bias	Low risk of bias	High risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Unclear risk of bias
56.	Poole 2018	Low risk of bias	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	High risk of bias	Unclear risk of bias	High risk of bias
57.	Dietz 2015	Unclear risk of bias	Unclear risk of bias	High risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	High risk of bias

58.	**Mufson 1999**	**Low risk of bias**	**Unclear risk of bias**	**High risk of bias**	**Unclear risk of bias**	**Low risk of bias**	**Low risk of bias**	**Unclear risk of bias**	**Unclear risk of bias**
59.	**Mufson 2004**	**Low risk of bias**	**Unclear risk of bias**	**High risk of bias**	**Unclear risk of bias**	**Low risk of bias**	**Low risk of bias**	**Low risk of bias**	**Unclear risk of bias**
60.	**Tang 2009**	**Unclear risk of bias**	**Unclear risk of bias**	**High risk of bias**	**High risk of bias**	**Low risk of bias**	**Low risk of bias**	**High risk of bias**	**High risk of bias**
61.	**Eskin 2008**	**Unclear risk of bias**	**Unclear risk of bias**	**High risk of bias**	**High risk of bias**	**Low risk of bias**	**Low risk of bias**	**Low risk of bias**	**High risk of bias**
62.	**Cornelius 2009**	**Low risk of bias**	**Low risk of bias**	**Low risk of bias**	**Unclear risk of bias**	**Unclear risk of bias**	**Unclear risk of bias**	**High risk of bias**	**Unclear risk of bias**
63.	**March 2004**	**Low risk of bias**	**Low risk of bias**	**Low risk of bias**	**Low risk of bias**	**Low risk of bias**	**High risk of bias**	**Unclear risk of bias**	**Unclear risk of bias**
64.	**Goodyer 2008**	**Low risk of bias**	**Low risk of bias**	**High risk of bias**	**Low risk of bias**	**Low risk of bias**	**Low risk of bias**	**Low risk of bias**	**Unclear risk of bias**
65.	**Riggs 2007**	**High risk of bias**	**Low risk of bias**	**Low risk of bias**	**Low risk of bias**	**Low risk of bias**	**Unclear risk of bias**	**Low risk of bias**	**Unclear risk of bias**
66.	**Bernstein 2000**	**Unclear risk of bias**	**Unclear risk of bias**	**Low risk of bias**	**Low risk of bias**	**Low risk of bias**	**Unclear risk of bias**	**High risk of bias**	**Unclear risk of bias**
67.	**Melvin 2006**	**Low risk of bias**	**Low risk of bias**	**High risk of bias**	**High risk of bias**	**Low risk of bias**	**Low risk of bias**	**Low risk of bias**	**High risk of bias**
68.	**Deas 2000**	**Low risk of bias**	**Low risk of bias**	**Low risk of bias**	**Unclear risk of bias**	**Unclear risk of bias**	**Low risk of bias**	**Unclear risk of bias**	**Unclear risk of bias**
69.	**Iftene 2015**	**Unclear risk of bias**	**Unclear risk of bias**	**Unclear risk of bias**	**Unclear risk of bias**	**Low risk of bias**	**Low risk of bias**	**Low risk of bias**	**Unclear risk of bias**
70.	**Mandoki 1997**	**Unclear risk of bias**	**Unclear risk of bias**	**Low risk of bias**	**Low risk of bias**	**High risk of bias**	**High risk of bias**	**Low risk of bias**	**High risk of bias**

*As it is difficult to use a double-blind design for patients in trials of psychotherapy, we rated all the psychotherapy alone trials with high risk of bias in 'Blinding of performance and personnel'.
#We rated risk of bias for trial follows: high risk study (2 or more items rated as high risk of bias); low risk study (5 or more items rated as low risk and no more than one as high risk); moderate risk study (all remaining situations).

APPENDIX 8

Network plot for secondary outcome



Network of eligible comparisons for suicidality

APPENDIX 9

Results from pairwise meta-analysis for each outcome: numbers, estimates and heterogeneity

a. Summary numbers of studies and patients from pair-wise meta-analysis of direct comparisons

	Mean overall change in symptoms (N / n)*	All-cause discontinuation (N / n)	Suicidality (N / n)
AMIvs.			
Pill-PBO	1/31	1/31	NA
BT vs.			
SUP	1/47	1/66	NA
Psy-PBO	NA	1/18	NA
CBT vs.			
FT	1/64	1/72	1/72
SUP	1/68	1/72	1/72
WL	5/338	5/388	NA
TAU	4/240	3/176	NA
DYN	1/214	1/312	1/312
Psy-PBO	4/418	4/520	1/313
SER	2/109	2/109	2/109
SER+CBT	2/102	2/102	2/102
FLU	1/220	1/220	1/220
FLU+CBT	1/218	1/218	1/218
Pill-PBO	1/223	1/223	1/223
IPT	1/40	1/48	NA
CIT vs.			
Pill-PBO	2/361	2/422	2/422
CLO vs.			
PAR	1/121	1/121	1/121
DES vs.			
Pill-PBO	2/78	2/105	NA
DEV vs.			
Pill-PBO	2/568	2/590	2/590
DUL vs.			

FLU	2/557	2/575	2/575
Pill-PBO	2/552	2/566	2/566
DYN vs.			
Psy-PBO	1/220	1/315	1/315
FT	1/72	1/72	NA
ESC vs.			
Pill-PBO	2/572	2/584	2/584
FLU vs.			
DEV	1/225	1/228	1/228
NOR	1/40	1/40	NA
FLU+CBT	2/415	2/424	2/424
VEN	1/59	1/60	NA
Pill-PBO	9/1288	9/1317	7/1260
FLU+CBT vs.			
Pill-PBO+CBT	2/176	2/176	2/176
Pill-PBO	1/219	1/219	1/219
FT vs.			
SUP	2/178	2/204	1/70
WL	1/32	NA	NA
TAU	2/71	2/84	NA
Psy-PBO	1/43	1/54	NA
IMP vs.			
PAR	1/184	1/188	1/188
Pill-PBO	2/219	2/224	1/182
IMP+CBT vs.			
Pill-PBO+CBT	1/63	1/63	NA
IPT vs.			
Psy-PBO	2/86	2/90	1/48
TAU	2/136	2/137	1/64
WL	1/37	1/46	NA

MIR vs.			
Pill-PBO	2/250	2/259	2/259
NEF vs.			
Pill-PBO	2/468	1/195	2/479
NOR vs.			
Pill-PBO	2/81	1/60	NA
PAR vs.			
Pill-PBO	4/702	4/728	4/728
PST vs.			
WL	1/23	1/24	NA
SER vs.			
Pill-PBO	2/364	2/376	2/376
SER+CBT	2/111	2/111	1/51
SER+CBT vs.			
Pill-PBO+CBT	1/10	1/10	NA
VEN vs.			
Pill-PBO	2/334	2/367	2/367
VEN+CBT vs.			
Pill-PBO+CBT	1/40	1/40	NA
VIL vs.			
Pill-PBO	1/524	1/529	1/529

* N= number of studies; n= number of patients. AMI=Amitriptyline. BT=Behavioural therapy. CBT=Cognitive-behavioural therapy. CIT=Citalopram. CLO=Clomipramine. DYN=Psychodynamic therapy. DES=Desipramine. DEV=Desvenlafaxine. DUL=Duloxetine. ESC=Escitalopram. FT=Family therapy. FLU=Fluoxetine. IPT=Interpersonal therapy. IMP=Imipramine. MIR=Mirtazapine. NA=not available. NEF=Nefazodone. NOR=Nortriptyline. PST=Problem-solving therapy. PAR=Paroxetine. Pill-PBO=Pill placebo. Psy-PBO=Psychological placebo. SUP=Supportive therapy. SER=Sertraline. TAU= Treatment as usual. VEN=Venlafaxine. VIL=Vilazodone. WL= Waitlist.

b. Summary estimates from pair-wise meta-analysis of direct comparisons*

	Mean overall change in symptoms SMD (95% CI)	All-cause discontinuation OR (95% CI)	Suicidality OR (95% CI)
AMIvs.			
Pill-PBO	0.09 (-0.63 to 0.80)	1.67 (0.33 to 8.42)	NA
BT vs.			
SUP	0.47 (-0.12 to 1.05)	1.50 (0.51 to 4.37)	NA
Psy-PBO	NA	1.70 (0.06 to 47.95)	NA
CBT vs.			
FT	**-0.60 (-1.10 to -0.10)**	0.51 (0.17 to 1.51)	1.46 (0.23 to 9.28)
SUP	-0.29 (-0.77 to 0.19)	0.51 (0.17 to 1.51)	0.53 (0.12 to 2.40)
WL	**-0.97 (-1.66 to -0.28)**	0.69 (0.36 to 1.31)	NA
TAU	-0.04 (-0.29 to 0.22)	0.82 (0.25 to 2.68)	NA
DYN	-0.18 (-0.45 to 0.08)	0.69 (0.38 to 1.28)	1.01 (0.06 to 16.34)
Psy-PBO	**-0.28 (-0.48 to -0.09)**	0.90 (0.51 to 1.59)	1.02 (0.06 to 16.45)
SER	-0.03 (-0.71 to 0.65)	0.62 (0.11 to 3.48)	0.11 (0.01 to 2.19)
SER+CBT	-0.22 (-0.61 to 0.17)	0.60 (0.10 to 3.67)	0.36 (0.01 to 9.37)
FLU	**0.67 (0.40 to 0.94)**	1.40 (0.71 to 2.75)	0.52 (0.17 to 1.62)
FLU+CBT	**1.24 (0.95 to 1.53)**	1.69 (0.83 to 3.44)	0.79 (0.24 to 2.68)
Pill-PBO	0.25 (-0.02 to 0.51)	1.07 (0.56 to 2.03)	1.27 (0.33 to 4.87)
IPT	0.50 (-0.13 to 1.13)	0.91 (0.20 to 4.13)	NA
CIT vs.			
Pill-PBO	-0.18 (-0.51 to 0.15)	0.99 (0.65 to 1.51)	1.39 (0.48 to 4.01)
CLO vs.			
PAR	**0.49 (0.13 to 0.85)**	1.52 (0.72 to 3.20)	0.82 (0.29 to 2.38)
DES vs.			
Pill-PBO	-0·46 (-1·48 to 0·57)#	2.38 (0.80 to 7.02)	NA
DEV vs.			
Pill-PBO	-0.04(-0.21 to 0.13)	0.89(0.54 to 1.44)	0.79(0.45 to 1.39)
DUL vs.			

FLU	-0.10 (-0.27 to 0.07)	1.51 (0.78 to 1.68)	0.92 (0.56 to 1.51)
Pill-PBO	-0.12 (-0.32 to 0.09)	1.31 (0.71 to 2.40)	0.90 (0.55 to 1.48)
DYN vs.			
Psy-PBO	-0.02 (-0.28 to 0.25)	1.33 (0.73 to 2.42)	1.01 (0.06 to 16.23)
FT	**0.66 (0.19 to 1.13)**	0.14 (0.01 to 2.79)	NA
ESC vs.			
Pill-PBO	**-0.17 (-0.34 to -0.01)**	1.47 (0.96 to 2.24)	0.99 (0.47 to 2.08)
FLU vs.			
DEV	-0.18(-0.44 to 0.09)	0.80(0.37 to 1.76)	1.40(0.57 to 3.46)
NOR	**-4.33 (-5.48 to -3.17)**	0.44 (0.07 to 2.76)	NA
FLU+CBT	0.21 (-0.58 to 1.00)	0.87 (0.39 to 1.93)	1.33 (0.63 to 2.83)
VEN	0.00 (-0.51 to 0.51)	1.00 (0.06 to 16.67)	NA
Pill-PBO	**-0.25 (-0.45 to -0.05)**	0.88 (0.58 to 1.33)	1.56(0.78 to 1.71)
FLU+CBT vs.			
Pill-PBO+CBT	-0.02 (-0.48 to 0.45)	0.66 (0.09 to 4.97)	4.20 (0.46 to 38.71)
Pill-PBO	**-1.08 (-1.36 to -0.79)**	0.63 (0.31 to 1.29)	1.60 (0.44 to 5.85)
FT vs.			
SUP	-0.01(-0.47 to 0.44)	1.69(0.58 to 4.94)	0.36 (0.07 to 2.02)
WL	**-1.10 (-1.85 to -0.36)**	NA	NA
TAU	-0.68 (-1.78 to 0.42)	0.65 (0.23 to 1.85)	NA
Psy-PBO	-0.15 (-0.75 to 0.46)	**0.25 (0.08 to 0.77)**	NA
IMP vs.			
PAR	0.22 (-0.07 to 0.51)	1.80 (0.98 to 3.30)	0.33 (0.10 to 1.07)
Pill-PBO	-0.01 (-0.28 to 0.25)	2.75 (0.87 to 8.75)	1.87 (0.33 to 10.46)
IMP+CBT vs.			
Pill-PBO+CBT	-0.44 (-0.94 to 0.06)	0.75 (0.24 to 2.33)	NA
IPT vs.			
Psy-PBO	**-0.69 (-1.14 to -0.65)**	0.60 (0.02 to 23.86)	0.46 (0.08 to 2.76)
TAU	**-0.84 (-1.19 to -0.48)**	0.61 (0.08 to 4.43)	2.73 (0.11 to 69.60)
WL	**-0.90 (-1.58 to -0.22)**	0.76 (0.18 to 3.28)	NA

MIR vs.			
Pill-PBO	-0.23 (-0.52 to 0.05)	0.91 (0.48 to 1.74)	1.58 (0.06 to 39.29)
NEF vs.			
Pill-PBO	-0.14 (-0.40 to 0.13)	**0.55 (0.30 to 1.00)**	NA
NOR vs.			
Pill-PBO	-0.11 (-0.55 to 0.34)	0.62 (0.16 to 2.45)	NA
PAR vs.			
Pill-PBO	-0.11 (-0.26 to 0.04)	1.28 (0.91 to 1.79)	1.74 (0.46 to 6.62)
PST vs.			
WL	**-1.31 (-2.23 to -0.40)**	0.26 (0.01 to 7.03)	NA
SER vs.			
Pill-PBO	**-0.23 (-0.44 to -0.03)**	1.52 (0.48 to 4.82)	1.92 (0.33 to 11.06)
SER+CBT	-0.20 (-0.61 to 0.21)	0.99 (0.37 to 2.67)	4.36 (0.45 to 42.09)
SER+CBT vs.			
Pill-PBO+CBT	0.40 (-0.86 to 1.65)	7.86 (0.28 to 217.11)	NA
VEN vs.			
Pill-PBO	-0.14 (-0.36to 0.07)	1.26 (0.80 to 1.97)	**17.67 (1.01 to 308.51)**
VEN+CBT vs.			
Pill-PBO+CBT	**0.75 (0.11 to 1.39)**	1.42 (0.27 to 7.34)	NA
VIL vs.			
Pill-PBO	-0.09(-0.27 to 0.09)	0.64(0.393 to 1.06)	2.47(0.29 to 21.32)

Significant results are bolded and underscored. *DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials*1986; **7:** 177–87. #:for Kutcher 1994 we used the followingstandard deviations(7.56 for desipramine and 7.38 for placebo) rather than the standard deviationsused in the Cochrane review by Hazell & Mirzaie, 2013 (4.61 and 4.32, respectively), as reported in the original publication of the trial and confirmed by the study author. AMI=Amitriptyline. BT=Behavioural therapy. CBT=Cognitive-behavioural therapy. CIT=Citalopram. CLO=Clomipramine. DYN=Psychodynamic therapy. DES=Desipramine. DEV=Desvenlafaxine. DUL=Duloxetine. ESC=Escitalopram. FT=Family therapy. FLU=Fluoxetine. IPT=Interpersonal therapy. IMP=Imipramine. MIR=Mirtazapine. NA=not available. NEF=Nefazodone. NOR=Nortriptyline. PST=Problem-solving therapy. PAR=Paroxetine. Pill-PBO=Pill placebo. Psy-PBO=Psychological placebo. SUP=Supportive therapy. SER=Sertraline. TAU= Treatment as usual. VEN=Venlafaxine. VIL=Vilazodone. WL= Waitlist.

c. Heterogeneity test result, I^2 and heterogeneity estimate

Mean overall change in symptoms

	No. of studies	P-value	I^2	τ^2
CBT vs Psy-PBO	4	0.6649	0.0%	0.0000
CBT vs SER*	2	0.0762	68.2%	0.1634
CBT vs SER+CBT	2	0.5714	0.0%	0.0000
CBT vs TAU	4	0.5103	0.0%	0.0000
CBT vs WL*	5	0.0000	86.4%	0.5146
CIT vs Pill-PBO*	2	0.1109	60.7%	0.0345
DES vs Pill-PBO*	2	0.0225	80.8%	0.4720
DEV vs Pill-PBO	2	0.4291	0.0%	0.0000
DUL vs FLU	2	0.6265	0.0%	0.0000
DUL vs Pill-PBO	2	0.2388	27.9%	0.0062
ESC vs Pill-PBO	2	0.6070	0.0%	0.0000
FLU vs FLU+CBT*	2	0.0001	93.9%	0.3032
FLU vs Pill-PBO*	9	0.0043	64.2%	0.0536
FLU+CBT vs Pill-PBO+CBT*	2	0.1503	51.7%	0.0604
FT vs SUP*	2	0.1373	54.7%	0.0605
FT vs TAU*	2	0.0482	74.4%	0.4779
IMP vs Pill-PBO	2	0.6721	0.0%	0.0000
IPT vs Psy-PBO	2	0.8388	0.0%	0.0000
IPT vs TAU	2	0.3203	0.0%	0.0000
MIR vs Pill-PBO	2	0.2810	14.0%	0.0058
NEF vs Pill-PBO	2	0.1659	47.9%	0.0170
NOR vs Pill-PBO	2	0.3214	0.0%	0.0000
PAR vs Pill-PBO	4	0.4844	0.0%	0.0000
SER vs Pill-PBO	2	0.7951	0.0%	0.0000
SER vs SER+CBT	2	0.2765	15.6%	0.0136
VEN vs Pill-PBO	2	0.9094	0.0%	0.0000

*The comparisons between CBT and SER, between CBT and WL, between CIT and Pill-PBO, between DES and Pill-PBO, between FLU and FLU+CBT, between FLU and Pill-PBO, between FLU+CBT and Pill-PBO+CBT, between FT and SUP, and between FT and TAU had higher I^2 values than the other comparisons. CBT=Cognitive-behavioural therapy. CIT=Citalopram. DES=Desipramine. DEV=Desvenlafaxine. DUL=Duloxetine. ESC=Escitalopram. FT=Family therapy. FLU=Fluoxetine. IPT=Interpersonal therapy. IMP=Imipramine. MIR=Mirtazapine. NEF=Nefazodone. NOR=Nortriptyline. PAR=Paroxetine. Pill-PBO=Pill placebo. Psy-PBO=Psychological placebo. SUP=Supportive therapy. SER=Sertraline. TAU= Treatment as usual. VEN=Venlafaxine. WL= Waitlist.

All-cause discontinuation

	No. of studies	P-value	I^2	τ^2
CBT vs Psy-PBO	4	0.9891	0.0%	0.0000
CBT vs SER	2	0.1713	46.6%	0.7735
CBT vs SER+CBT	2	0.1612	49.0%	0.8830
CBT vs TAU	2	0.2536	23.3%	0.1745
CBT vs WL	4	0.9355	0.0%	0.0000
CIT vs Pill-PBO	2	0.6071	0.0%	0.0000
DES vs Pill-PBO	2	0.2480	25.1%	0.1567
DEV vs Pill-PBO	2	0.2966	8.2%	0.0110
DUL vs FLU	2	0.8322	0.0%	0.0000
DULvs Pill-PBO*	2	0.1379	54.6%	0.1074
ESC vs Pill-PBO	2	0.6838	0.0%	0.0000
FLU vs FLU+CBT	2	0.2012	38.8%	0.1340
FLU vs Pill-PBO*	9	0.0337	52.0%	0.1899
FLU+CBT vs Pill-PBO+CBT	2	0.1614	49.0%	1.2537
FT vs SUP*	2	0.1495	51.9%	0.3107
FT vs TAU	2	0.3327	0.0%	0.0000
IMP vs Pill-PBO	2	0.2649	19.5%	0.2957
IPT vs Psy-PBO*	2	0.0259	79.8%	5.7112
IPT vs TAU	2	0.2091	36.6%	0.8647
MIR vs Pill-PBO	2	0.5374	0.0%	0.0000
PAR vs Pill-PBO	4	0.7785	0.0%	0.0000
SER vs Pill-PBO*	2	0.0279	79.3%	0.5501
SER vs SER+CBT	2	0.9408	0.0%	0.0000

*The comparisons between DUL and Pill-PBO, between FLU and Pill-PBO, between FT and SUP, between IPT and Psy-PBO, and between SER and Pill-PBO had higher I^2 values than the other comparisons. CBT=Cognitive-behavioural therapy. CIT=Citalopram. CLO=Clomipramine. DES=Desipramine. DEV=Desvenlafaxine. DUL=Duloxetine. ESC=Escitalopram. FT=Family therapy. FLU=Fluoxetine. IPT=Interpersonal therapy. IMP=Imipramine. MIR=Mirtazapine. PAR=Paroxetine. Pill-PBO=Pill placebo. Psy-PBO=Psychological placebo. SUP= Supportive therapy. SER=Sertraline. TAU= Treatment as usual. WL= Waitlist.

Suicidality

	No. of studies	P-value	I^2	τ^2
CIT vs Pill-PBO	2	0.3090	3.4%	0.0325
DEV vs Pill-PBO	2	0.4284	0.0%	0.0000
DUL vs FLU	2	0.8295	0.0%	0.0000
DUL vs Pill-PBO	2	0.9188	0.0%	0.0000
ESC vs Pill-PBO	2	0.4711	0.0%	0.0000
FLU vs FLU+CBT	2	0.7432	0.0%	0.0000
FLU vs Pill-PBO	7	0.8037	0.0%	0.0000
PAR vs Pill-PBO	4	0.1532	43.1%	0.7880
SER vs Pill-PBO	2	0.2947	8.9%	0.1630

No comparison had higher I^2 value. CBT=Cognitive-behavioural therapy. CIT=Citalopram. DEV=Desvenlafaxine. DUL=Duloxetine. ESC=Escitalopram. FLU=Fluoxetine. PAR=Paroxetine. Pill-PBO=Pill placebo. SER=Sertraline.

APPENDIX 10

Network meta-analysis of suicidality

CBT																				
0·70 (0·11 to 2·23)	**CIT**																			
0·71 (0·07 to 2·87)	1·46 (0·14 to 6·07)	**CLO**																		
1·10 (0·25 to 2·93)	2·23 (0·50 to 6·79)	2·82 (0·41 to 10·04)	**DEV**																	
0·87 (0·21 to 2·31)	1·76 (0·42 to 5·18)	2·26 (0·32 to 7·92)	0·88 (0·35 to 1·87)	**DUL**																
11·62 (0·02 to 62·03)	29·35 (0·03 to 181·3)	46·06 (0·03 to 226·2)	0·05 (0·02 to 83·06)	0·07 (0·02 to 117·62)	**DYN**															
0·87 (0·16 to 2·67)	1·74 (0·32 to 5·73)	2·25 (0·27 to 8·66)	0·87 (0·25 to 2·18)	1·08 (0·32 to 2·58)	12·48 (0·01 to 40·56)	**ESC**														
0·72 (0·20 to 1·73)	1·49 (0·38 to 4·21)	1·89 (0·29 to 6·39)	0·74 (0·33 to 1·41)	0·89 (0·48 to 1·51)	11·18 (0·01 to 33·87)	1·04 (0·35 to 2·46)	**FLU**													
0·88 (0·21 to 2·36)	1·88 (0·35 to 6·20)	2·36 (0·29 to 8·71)	0·93 (0·28 to 2·30)	1·13 (0·38 to 2·62)	16·26 (0·01 to 40·52)	1·31 (0·32 to 3·74)	1·28 (0·50 to 2·64)	**FLU+CBT**												
2·75 (0·21 to 12·02)	8·05 (0·25 to 41·04)	8·96 (0·22 to 49·68)	3·57 (0·17 to 18·98)	4·39 (0·21 to 22·8)	43·41 (0·01 to 144·3)	4·98 (0·20 to 26·75)	1·26 (0·26 to 25·43)	1·03 (0·21 to 23·1)	**FT**											
1·41 (0·16 to 5·44)	2·83 (0·30 to 11·67)	3·15 (0·35 to 12·85)	1·41 (0·22 to 5·04)	1·74 (0·28 to 5·68)	21·24 (0·01 to 76·63)	2·00 (0·27 to 7·27)	2·00 (0·34 to 6·42)	1·88 (0·24 to 7·67)	1·64 (0·04 to 8·54)	**IMP**										
40·48 (0·02 to 207·3)	113·80 (0·04 to 515·1)	156·30 (0·03 to 692·9)	60·16 (0·02 to 279)	72·83 (0·03 to 355·9)	33·4 (0·03 to 173·6)	88·53 (0·03 to 396·1)	81·88 (0·03 to 382·6)	69·03 (0·02 to 334·3)	43·5 (0·01 to 246·9)	0·04 (0·02 to 362·84	**IPT**									
1·60 (0·02 to 8·74)	3·22 (0·03 to 17·46)	3·91 (0·04 to 25·01)	1·58 (0·02 to 8·46)	1·92 (0·02 to 10·02)	29·61 (0·00 to 72·01)	2·19 (0·02 to 11·46)	2·18 (0·03 to 11·13)	1·97 (0·02 to 10·20)	1·91 (0·01 to 12·31)	1·88 (0·02 to 11·12)	28·35 (0·00 to 49·66)	**MIR**								
2·81 (0·09 to 15·50)	5·75 (0·17 to 33·14)	7·55 (0·14 to 41·80)	2·87 (0·11 to 14·34)	3·45 (0·14 to 17·04)	55·59 (0·01 to 112·4)	4·05 (0·14 to 19·95)	3·94 (0·17 to 19·44)	3·65 (0·13 to 20·46)	3·13 (0·02 to 22·56)	3·23 (0·08 to 17·79)	58·09 (0·00 to 109·7)	28·99 (0·07 to 152·6)	**NEF**							
0·48 (0·09 to 1·42)	0·98 (0·17 to 3·24)	1·00 (0·24 to 2·76)	0·48 (0·13 to 1·21)	0·60 (0·16 to 1·49)	8·13 (0·00 to 25·47)	0·68 (0·15 to 1·95)	0·68 (0·21 to 1·59)	0·63 (0·14 to 1·80)	0·54 (0·02 to 2·91)	0·51 (0·11 to 1·45)	9·77 (0·00 to 21·37)	5·79 (0·04 to 20·04)	0·74 (0·02 to 4·42)	**PAR**						
0·61 (0·23 to 1·95)	1·18 (0·46 to 4·43)	1·18 (0·35 to 6·85)	0·74 (0·41 to 1·49)	0·93 (0·55 to 1·71)	0·05 (0·01 to 40·14)	0·94 (0·44 to 2·55)	1·11 (0·74 to 1·75)	0·88 (0·41 to 2·35)	0·23 (0·05 to 4·31)	0·59 (0·19 to 3·07)	0·01 (0·00 to 36·14)	0·53 (0·10 to 40·83)	0·29 (0·06 to 6·31)	1·71 (0·81 to 5·05)	**Pill-PBO**					
7·78 (0·29 to 45·30)	16·55 (0·56 to 100·7)	19·45 (0·52 to 126·8)	8·14 (0·34 to 45·63)	9·90 (0·45 to 55·03)	173·00 (0·03 to 289·2)	11·50 (0·41 to 64·32)	11·22 (0·56 to 58·67)	8·98 (0·61 to 43·66)	7·39 (0·09 to 46·01)	9·56 (0·24 to 58·01)	194·8 (0·01 to 262·6)	91·44 (0·20 to 286·6)	12·28 (0·11 to 84·86)	20·45 (0·85 to 124·1)	9·81 (0·50 to 54·81)	**Pill-PBO+CBT**				
11·31 (0·01 to 46·11)	32·76 (0·02 to 139·3)	43·48 (0·02 to 183·7)	17·39 (0·01 to 75·69)	20·89 (0·01 to 98·84)	8·64 (0·01 to 40·05)	26·59 (0·01 to 102·7)	23·54 (0·01 to 108)	19·09 (0·01 to 93·37)	11·31 (0·00 to 63·92)	18·46 (0·01 to 93·58)	0·64 (0·04 to 2·59)	50·90 (0·01 to 253·9)	38·22 (0·01 to 103)	44·35 (0·02 to 190·7)	21·15 (0·01 to 95·40)	8·85 (0·00 to 37·70)	**Psy-PBO**			
0·33 (0·05 to 1·03)	0·75 (0·08 to 3·14)	0·93 (0·07 to 3·87)	0·37 (0·06 to 1·25)	0·45 (0·07 to 1·42)	4·67 (0·00 to 14·92)	0·52 (0·07 to 1·81)	0·52 (0·09 to 1·60)	0·48 (0·06 to 1·60)	0·38 (0·01 to 2·03)	0·46 (0·03 to 1·93)	4·66 (0·00 to 10·27)	4·00 (0·03 to 17·61)	0·58 (0·01 to 3·58)	0·97 (0·12 to 3·59)	0·45 (0·08 to 1·33)	0·20 (0·00 to 1·00)	8·93 (0·00 to 22·43)	**SER**		
1·35 (0·09 to 6·77)	3·22 (0·14 to 16·85)	4·07 (0·13 to 22·43)	1·58 (0·10 to 7·39)	1·97 (0·12 to 9·14)	18·70 (0·01 to 64·51)	2·20 (0·11 to 10·64)	2·25 (0·16 to 10·31)	2·06 (0·11 to 10·23)	1·59 (0·03 to 11·82)	1·96 (0·06 to 10·53)	24·11 (0·00 to 46·38)	21·30 (0·05 to 71·25)	2·41 (0·03 to 14·93)	4·12 (0·21 to 20·41)	1·92 (0·14 to 8·81)	0·85 (0·01 to 5·42)	45·94 (0·01 to 89·73)	4·78 (0·54 to 22·34)	**SER+CBT**	
0·70 (0·09 to 2·48)	1·99 (0·10 to 10·31)	2·44 (0·10 to 12·53)	0·97 (0·07 to 4·41)	1·18 (0·09 to 5·32)	10·56 (0·01 to 45·41)	1·39 (0·08 to 6·71)	1·33 (0·11 to 5·90)	1·18 (0·09 to 5·28)	0·51 (0·04 to 1·96)	1·20 (0·05 to 6·62)	13·78 (0·00 to 42·03)	32·45 (0·03 to 42·98)	1·52 (0·02 to 9·82)	2·49 (0·15 to 12·17)	1·18 (0·10 to 5·16)	0·47 (0·01 to 2·75)	26·57 (0·01 to 76·84)	1·02 (0·20 to 21·34)	0·24 (0·04 to 9·51)	**SUP**
276·9 (0·02 to 1163)	736·3 (0·04 to 3352)	1154 (0·04 to 3572)	406·9 (0·02 to 1687)	569 (0·03 to 2057)	218 (0·03 to 1146)	680·9 (0·03 to 2227)	616·7 (0·03 to 2314)	511·7 (0·03 to 2049)	309·8 (0·01 to 1372)	490·8 (0·02 to 1979)	8·58 (0·14 to 54·07)	1228 (0·03 to 4941)	648·6 (0·01 to 2201)	1403 (0·06 to 3919)	537·4 (0·03 to 2073)	259·8 (0·00 to 870·7)	30·92 (0·19 to 183·7)	1650 (0·10 to 6481)	774·9 (0·03 to 2517)	684·5 (0·03 to 3304)	**TAU**
0·10 (0·00 to 0·50)	**0·20 (0·00 to 0·99)**	0·25 (0·00 to 1·30)	**0·10 (0·00 to 0·45)**	**0·12 (0·00 to 0·54)**	1·67 (0·00 to 4·82)	**0·14 (0·00 to 0·68)**	**0·14 (0·00 to 0·60)**	**0·13 (0·00 to 0·59)**	**0·12 (0·00 to 0·78)**	**0·12 (0·00 to 0·64)**	3·13 (0·00 to 4·13)	0·78 (0·00 to 4·15)	0·17 (0·00 to 1·03)	0·25 (0·01 to 1·22)	**0·12 (0·00 to 0·52)**	**0·05 (0·00 to 0·32)**	4·15 (0·00 to 7·68)	0·43 (0·01 to 2·42)	0·22 (0·00 to 1·39)	0·30 (0·00 to 1·88)	1·92 (0·00 to 4·41)	**VEN**
0·42 (0·01 to 2·08)	0·82 (0·01 to 4·07)	1·08 (0·01 to 5·95)	0·42 (0·01 to 1·93)	0·52 (0·01 to 2·31)	7·79 (0·00 to 22·49)	0·60 (0·01 to 2·83)	0·59 (0·01 to 2·64)	0·56 (0·01 to 2·78)	0·47 (0·00 to 2·78)	0·51 (0·01 to 2·79)	14·21 (0·00 to 15·70)	5·72 (0·00 to 23·74)	0·72 (0·00 to 4·63)	1·10 (0·02 to 5·60)	0·51 (0·01 to 2·22)	0·22 (0·00 to 1·32)	26·05 (0·00 to 28·83)	1·96 (0·02 to 10·73)	0·99 (0·00 to 5·65)	1·24 (0·01 to 7·19)	7·37 (0·00 to 14·66)	29·30 (0·10 to 178·0)	**VIL**

Treatment Suicidality (OR [95% CrI])

Interventions are reported in alphabetical order. Comparisons between treatments should be read from left to right, and the estimate is in the cell in common between the column-defining treatment and the row-defining treatment. For suicidality, an odds ratio (OR) below 1 favors the column -defining treatment.

APPENDIX 11

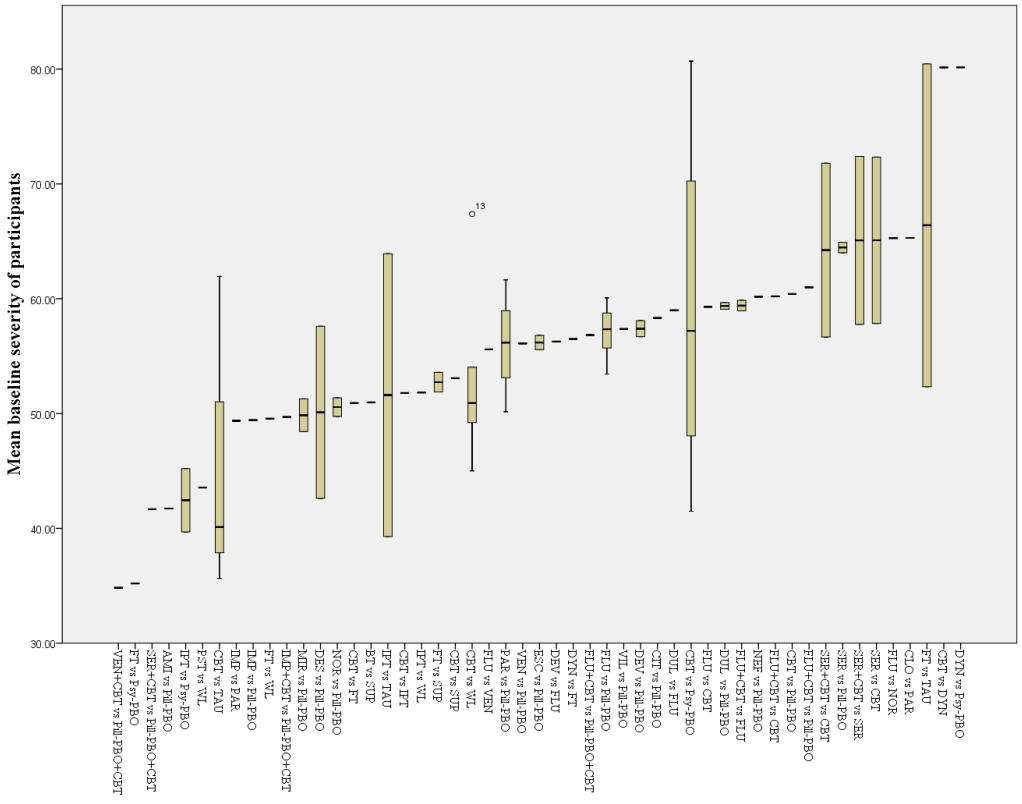
Number of patients with suicidality according to treatments

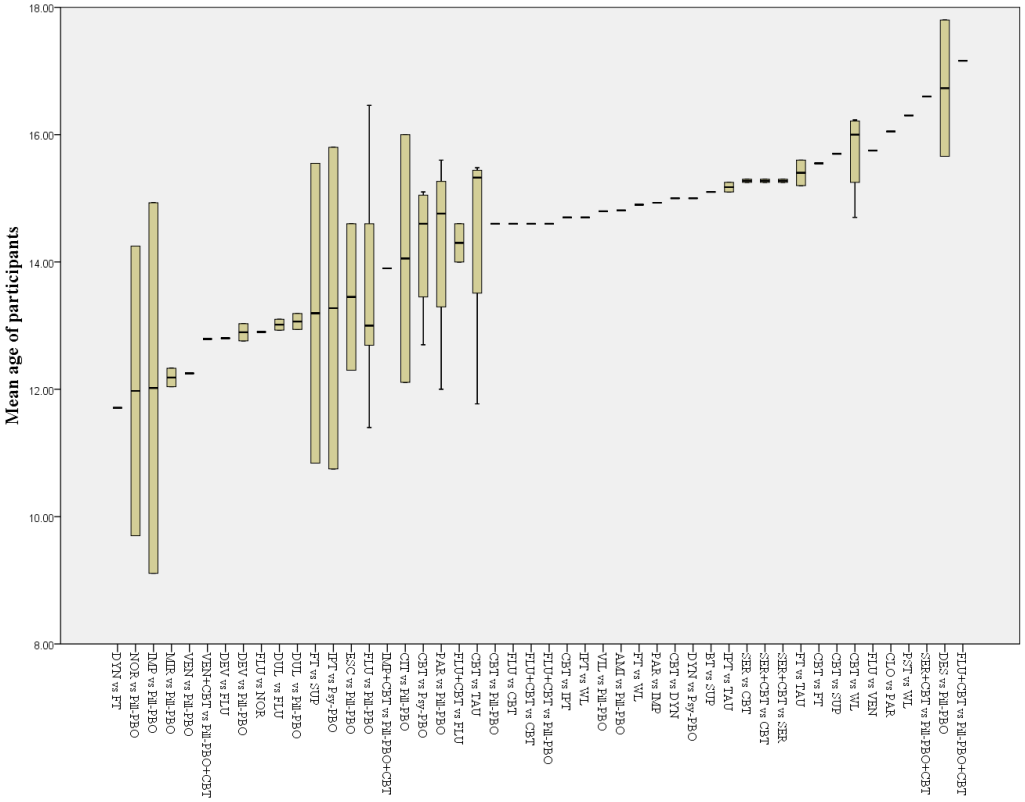
Comparisons	Number of trials	Events/total (%)		Comparisons	Number of trials	Events/total (%)	
		Group 1	Group 2			Group 1	Group 2
CBT vs DYN	1	1/155 (1%)	1/157 (1%)	FLU vs Pill-PBO	7	62/634 (10%)	53/626 (8%)
CBT vs Psy-PBO	1	1/155 (1%)	1/158 (1%)	FLU vs FLU+CBT	2	17/212 (8%)	13/212 (6%)
CBT vs Pill-PBO	1	5/111 (5%)	4/112 (4%)	FLU+CBT vs Pill-PBO	1	6/107 (6%)	4/112 (4%)
CBT vs FLU+CBT	1	5/111 (5%)	6/107 (6%)	FLU+CBT vs Pill-PBO+CBT	2	4/87 (5%)	1/89 (1%)
CBT vs FT	1	3/37 (8%)	2/35 (6%)	FT vs SUP	1	2/35 (6%)	5/35 (14%)
CBT vs SUP	1	3/37 (8%)	5/35 (14%)	IMP vs PAR	1	4/95 (4%)	11/93 (12%)
CBT vs SER+CBT	2	0/50 (0%)	1/52 (2%)	IMP vs Pill-PBO	1	4/95 (4%)	2/87 (2%)
CIT vs Pill-PBO	2	10/217 (5%)	7/205 (3%)	IPT vs Psy-PBO	1	2/24 (8%)	4/24 (17%)
CLO vs PAR	1	7/58 (12%)	9/63 (14%)	IPT vs TAU	1	1/34 (3%)	0/30 (0%)
DEV vs FLU	1	9/115 (8%)	12/113 (11%)	NEF vs Pill-PBO	2	0/289 (0%)	0/190 (0%)
DEV vs Pill-PBO	2	32/358 (9%)	24/232 (10%)	PAR vs Pill-PBO	4	19/413 (5%)	8/315 (3%)
DUL vs FLU	2	44/341 (13%)	33/234 (14%)	SER vs CBT	2	4/59 (7%)	0/50 (0%)
DUL vs Pill-PBO	2	44/341 (13%)	32/225 (14%)	SER vs Pill-PBO	2	5/189 (3%)	2/187 (1%)
DYN vs Psy-PBO	1	1/157 (1%)	1/158 (1%)	SER vs SER+CBT	2	4/59 (7%)	1/52 (2%)
ESC vs Pill-PBO	2	15/290 (5%)	15/294 (5%)	VEN vs Pill-PBO	2	8/184 (4%)	0/183 (0%)
FLU vs CBT	1	9/109 (8%)	5/111 (5%)	VIL vs Pill-PBO	1	5/355 (1%)	1/174 (1%)
MIR vs Pill-PBO	2	1/170 (1%)	0/89 (0%)				

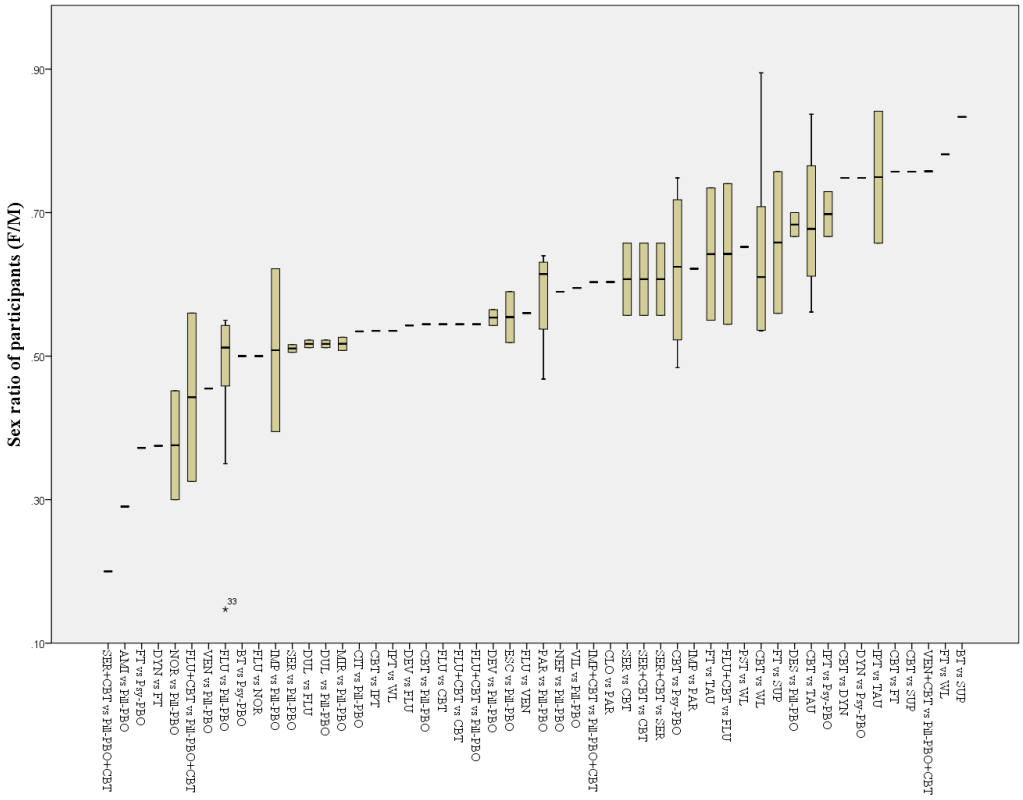
CBT=Cognitive-behavioural therapy. CIT=Citalopram. CLO=Clomipramine. DYN=Psychodynamic therapy. DES=Desipramine. DUL=Duloxetine. ESC=Escitalopram. FT=Family therapy. FLU=Fluoxetine. IMP=Imipramine. MIR=Mirtazapine. NA=not available. NEF=Nefazodone. PAR=Paroxetine. Pill-PBO=Pill placebo. Psy-PBO=Psychological placebo. SUP=Supportive therapy. SER=Sertraline. TAU=Treatment as usual. VEN=Venlafaxine. VIL=Vilazodone.

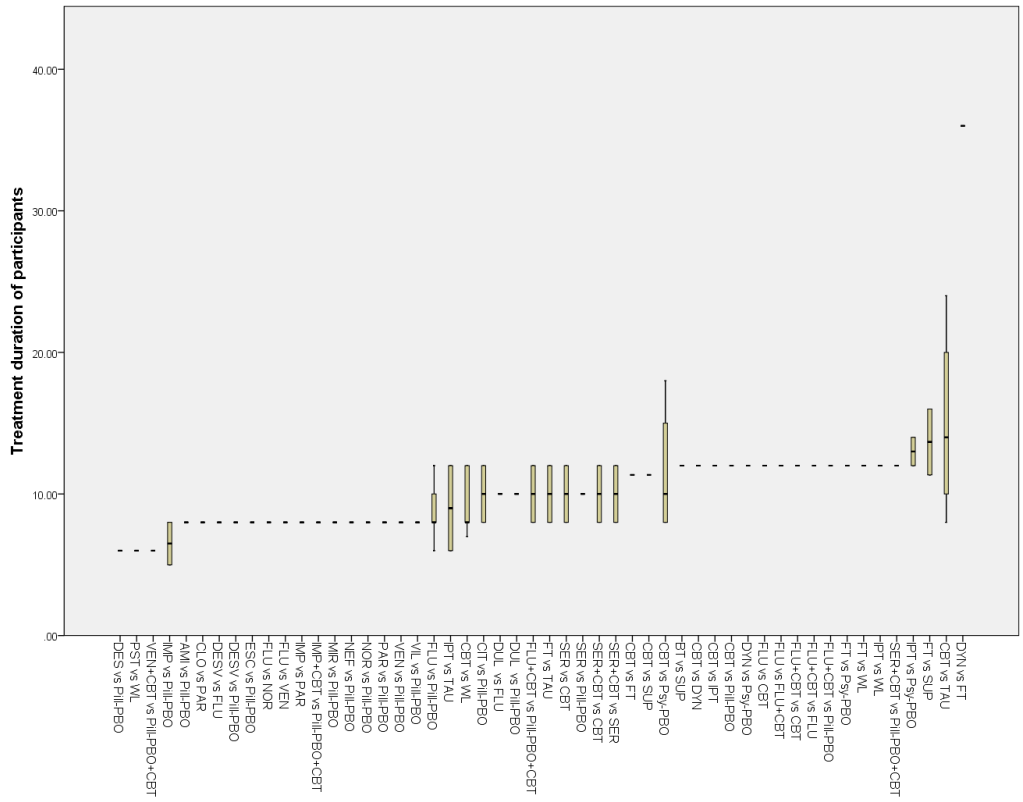
APPENDIX 12

Assessment of transitivity


Mean baseline severity of participants
80.00
70.00
60.00
50.00
40.00
30.00
13
VEN+CBT vs FM-PBO+CBT
FT vs Psy-PBO
SER+CBT vs FM-PBO+CBT
AMI vs FM-PBO
IPT vs Psy-PBO
EST vs WL
CBT vs TAU
DMP vs PAR
DMP vs FM-PBO
FT vs WL
DMP+CBT vs FM-PBO+CBT
DMP vs FM-PBO
DES vs FM-PBO
NOR vs FM-PBO
CBT vs FT
BT vs SUP
IPT vs TAU
CBT vs IPT
IPT vs WL
FT vs SUP
CBT vs SUP
CBT vs WL
FLU vs VEN
PAR vs FM-PBO
VEN vs FM-PBO
ESC vs FM-PBO
DEV vs FLU
DYN vs FT
FLU+CBT vs FM-PBO+CBT
FLU vs FM-PBO
VIL vs FM-PBO
DEV vs FM-PBO
DUL vs FLU
CIT vs FM-PBO
CBT vs Psy-PBO
FLU vs CBT
DUL vs FM-PBO
FLU+CBT vs FLU
NEE vs FM-PBO
FLU+CBT vs CBT
CBT vs FM-PBO
FLU+CBT vs FM-PBO
SER+CBT vs CBT
SER vs FM-PBO
SER+CBT vs SER
SER vs CBT
FLU vs NOR
CLO vs PAR
FT vs TAU
CBT vs DYN
DYN vs Psy-PBO


Mean age of participants
18.00
16.00
14.00
12.00
10.00
8.00
DYN vs FT
NOR vs FM-PBO
DMP vs FM-PBO
MDR vs FM-PBO
VEN vs FM-PBO
VEN+CBT vs FM-PBO+CBT
DEV vs FLU
DEV vs FM-PBO
FLU vs NOR
DUL vs FLU
DUL vs FM-PBO
FT vs SUP
IPT vs Psy-PBO
ESC vs FM-PBO
FLU vs FM-PBO
DMP+CBT vs FM-PBO+CBT
CIT vs FM-PBO
CBT vs Psy-PBO
PAR vs FM-PBO
FLU+CBT vs FLU
CBT vs TAU
CBT vs FM-PBO
FLU vs CBT
FLU+CBT vs CBT
FLU+CBT vs FM-PBO
CBT vs IPT
IPT vs WL
VIL vs FM-PBO
AMI vs FM-PBO
FT vs WL
PAR vs IMP
CBT vs DYN
DYN vs Psy-PBO
BT vs SUP
IPT vs TAU
SER vs CBT
SER+CBT vs CBT
SER+CBT vs SER
FT vs TAU
CBT vs FT
CBT vs SUP
CBT vs WL
FLU vs VEN
CLO vs PAR
EST vs WL
SER+CBT vs FM-PBO+CBT
DES vs FM-PBO
FLU+CBT vs FM-PBO+CBT


Sex ratio of participants (F/M)
.90
.70
.50
.30
.10
33
SER+CBT vs FM-PBO+CBT
AMI vs FM-PBO
FT vs Psy-PBO
DYN vs FT
NOR vs FM-PBO
FLU+CBT vs FM-PBO+CBT
VEN vs FM-PBO
FLU vs FM-PBO
BT vs Psy-PBO
FLU vs NOR
DAP vs FM-PBO
SER vs FM-PBO
DUL vs FLU
DUL vs FM-PBO
MAR vs FM-PBO
CIT vs FM-PBO
CBT vs IPT
IPT vs WL
DEV vs FLU
CBT vs FM-PBO
FLU vs CBT
FLU+CBT vs CBT
FLU+CBT vs FM-PBO
DEV vs FM-PBO
ESC vs FM-PBO
FLU vs VEN
PAR vs FM-PBO
NEF vs FM-PBO
VIL vs FM-PBO
IMP+CBT vs FM-PBO+CBT
CLO vs PAR
SER vs CBT
SER+CBT vs CBT
SER+CBT vs SER
CBT vs Psy-PBO
DAP vs PAR
FT vs TAU
FLU+CBT vs FLU
PST vs WL
CBT vs WL
FT vs SUP
DES vs FM-PBO
CBT vs TAU
IPT vs Psy-PBO
CBT vs DYN
DYN vs Psy-PBO
IPT vs TAU
CBT vs FT
CBT vs SUP
VEN+CBT vs FM-PBO+CBT
FT vs WL
BT vs SUP


Treatment duration of participants
40.00
30.00
20.00
10.00
.00
DES vs Pill-PBO
PST vs WL
VEN+CBT vs Pill-PBO+CBT
IMP vs Pill-PBO
AMI vs Pill-PBO
CLO vs PAR
DESV vs FLU
DESV vs Pill-PBO
ESC vs Pill-PBO
FLU vs NOR
FLU vs VEN
IMP vs PAR
IMP+CBT vs Pill-PBO+CBT
MIR vs Pill-PBO
NEF vs Pill-PBO
NOR vs Pill-PBO
PAR vs Pill-PBO
VEN vs Pill-PBO
VIL vs Pill-PBO
FLU vs Pill-PBO
IPT vs TAU
CBT vs WL
CIT vs Pill-PBO
DUL vs FLU
DUL vs Pill-PBO
FLU+CBT vs Pill-PBO+CBT
FT vs TAU
SER vs CBT
SER vs Pill-PBO
SER+CBT vs CBT
SER+CBT vs SER
CBT vs FT
CBT vs SUP
CBT vs Psy-PBO
BT vs SUP
CBT vs DYN
CBT vs IPT
CBT vs Pill-PBO
DYN vs Psy-PBO
FLU vs CBT
FLU vs FLU+CBT
FLU+CBT vs CBT
FLU+CBT vs FLU
FLU+CBT vs Pill-PBO
FT vs Psy-PBO
FT vs WL
IPT vs WL
SER+CBT vs Pill-PBO+CBT
IPT vs Psy-PBO
FT vs SUP
CBT vs TAU
DYN vs FT

APPENDIX 13

Assessment of incoherence for each outcome: global, local and from the node-splitting model

a. The summary of results for incoherence

Outcome	Number of study	Number of inconsistent loops out of total	Percentage of the inconsistent loops	Number of inconsistent comparisons out of total	Percentage of the inconsistent comparisons
Mean overall change in symptoms	71	6/25	24.0%	4/51	7.8%
All-cause discontinuation	66	1/24	4.2%	4/51	7.8%
Suicidality	34	0/11	0.0%	0/31	0.0%

b. Evaluation of the global incoherence

For evaluating the global incoherence, we present the mean posterior deviance (D), the number of data points and the Deviance Information Criterion (DIC) of the NMA model. The mean posterior deviance should approximate the number of data points for models with good fit to the data. The DIC is a Bayesian model evaluation criterion that measures model fit adjusted with complexity of the model; smaller DIC values correspond to more preferable models.

Model assumption	D	# of data points	DIC
Mean overall change in symptoms [Test of global incoherence: P<0.0001]			
Consistency	156.20	151	664.00
Inconsistency	156.30	151	655.90
All-cause discontinuation [Test of global incoherence: P =0.5531]			
Consistency	147.90	143	773.20
Inconsistency	149.80	143	782.30
Suicidality [Test of global incoherence: P =0.5941]			
Consistency	74.92	76	354.70
Inconsistency	76.88	76	358.70

c. Evaluation of the local incoherence

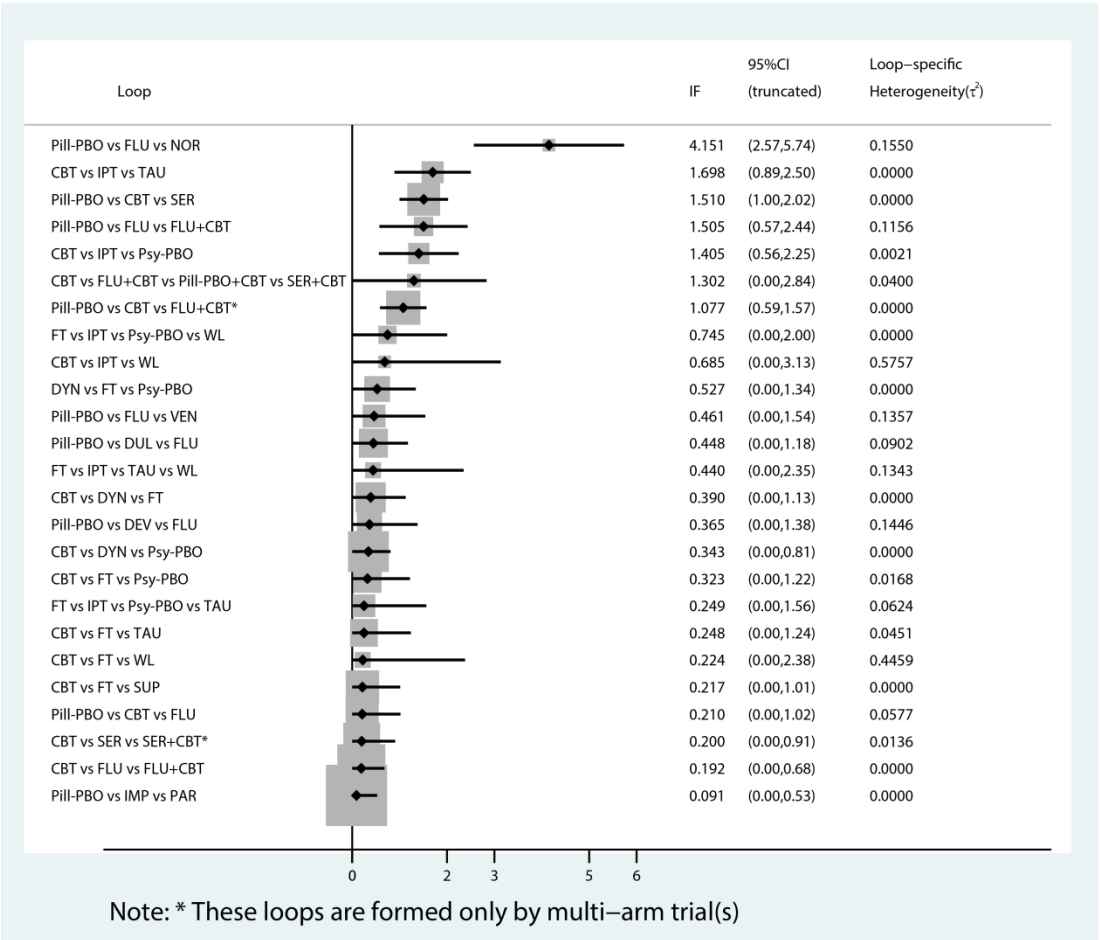
Tests of local incoherence revealed that the percentages for inconsistent loops were to be expected according to empirical data with the methods of Veroniki et al (Int J Epidemiol 2013; 42:332-45).

Mean overall change in symptoms

Loop	IF	z-value	P-value	95%CI	τ^2
Pill-PBO vs FLU vs NOR	4.151	5.131	0.0000	(2.57,5.74)	0.1550
CBT vs IPT vs TAU	1.698	4.130	0.0000	(0.89,2.50)	0.0000
Pill-PBO vs CBT vs SER	1.510	5.764	0.0000	(1.00,2.02)	0.0000
Pill-PBO vs FLU vs FLU+CBT	1.505	3.168	0.0015	(0.57,2.44)	0.1156
CBT vs IPT vs Psy-PBO	1.405	3.266	0.0011	(0.56,2.25)	0.0021
CBT vs FLU+CBT vs Pill-PBO+CBT vs SER+CBT	1.302	1.663	0.0963	(0.00,2.84)	0.0400
Pill-PBO vs CBT vs FLU+CBT*	1.077	4.296	0.0000	(0.59,1.57)	0.0000
FT vs IPT vs Psy-PBO vs WL	0.745	1.160	0.2461	(0.00,2.00)	0.0000
CBT vs IPT vs WL	0.685	0.549	0.5833	(0.00,3.13)	0.5757
DYN vs FT vs Psy-PBO	0.527	1.269	0.2046	(0.00,1.34)	0.0000

Pill-PBO vs FLU vs VEN	0.461	0.836	0.4033	(0.00,1.54)	0.1357
Pill-PBO vs DUL vs FLU	0.448	1.203	0.2288	(0.00,1.18)	0.0902
FT vs IPT vs TAU vs WL	0.440	0.451	0.6518	(0.00,2.35)	0.1343
CBT vs DYN vs FT	0.390	1.035	0.3006	(0.00,1.13)	0.0000
Pill-PBO vs DEV vs FLU	0.365	0.705	0.4810	(0.00,1.38)	0.1446
CBT vs DYN vs Psy-PBO	0.343	1.438	0.1505	(0.00,0.81)	0.0000
CBT vs FT vs Psy-PBO	0.323	0.704	0.4812	(0.00,1.22)	0.0168
FT vs IPT vs Psy-PBO vs TAU	0.249	0.371	0.7104	(0.00,1.56)	0.0624
CBT vs FT vs TAU	0.248	0.492	0.6226	(0.00,1.24)	0.0451
CBT vs FT vs WL	0.224	0.203	0.8390	(0.00,2.38)	0.4459
CBT vs FT vs SUP	0.217	0.533	0.5943	(0.00,1.01)	0.0000
Pill-PBO vs CBT vs FLU	0.210	0.509	0.6107	(0.00,1.02)	0.0577
CBT vs SER vs SER+CBT*	0.200	0.555	0.5790	(0.00,0.91)	0.0136
CBT vs FLU vs FLU+CBT	0.192	0.770	0.4416	(0.00,0.68)	0.0000
Pill-PBO vs IMP vs PAR	0.091	0.407	0.6838	(0.00,0.53)	0.0000

*These loops are formed only by multi-arm trials.
AMI=Amitriptyline. BT=Behavioural therapy. CBT=Cognitive-behavioural therapy. CIT=Citalopram. CLO=Clomipramine. DYN=Psychodynamic therapy. DES=Desipramine. DEV=Desvenlafaxine. DUL=Duloxetine. ESC=Escitalopram. FT=Family therapy. FLU=Fluoxetine. IPT=Interpersonal therapy. IMP=Imipramine. MIR=Mirtazapine. NEF=Nefazodone. NOR=Nortriptyline. PST=Problem-solving therapy. PAR=Paroxetine. Pill-PBO=Pill placebo. Psy-PBO=Psychological placebo. SUP= Supportive therapy. SER=Sertraline. TAU=Treatment as usual. VEN=Venlafaxine. VIL=Vilazodone. WL=Waitlist.

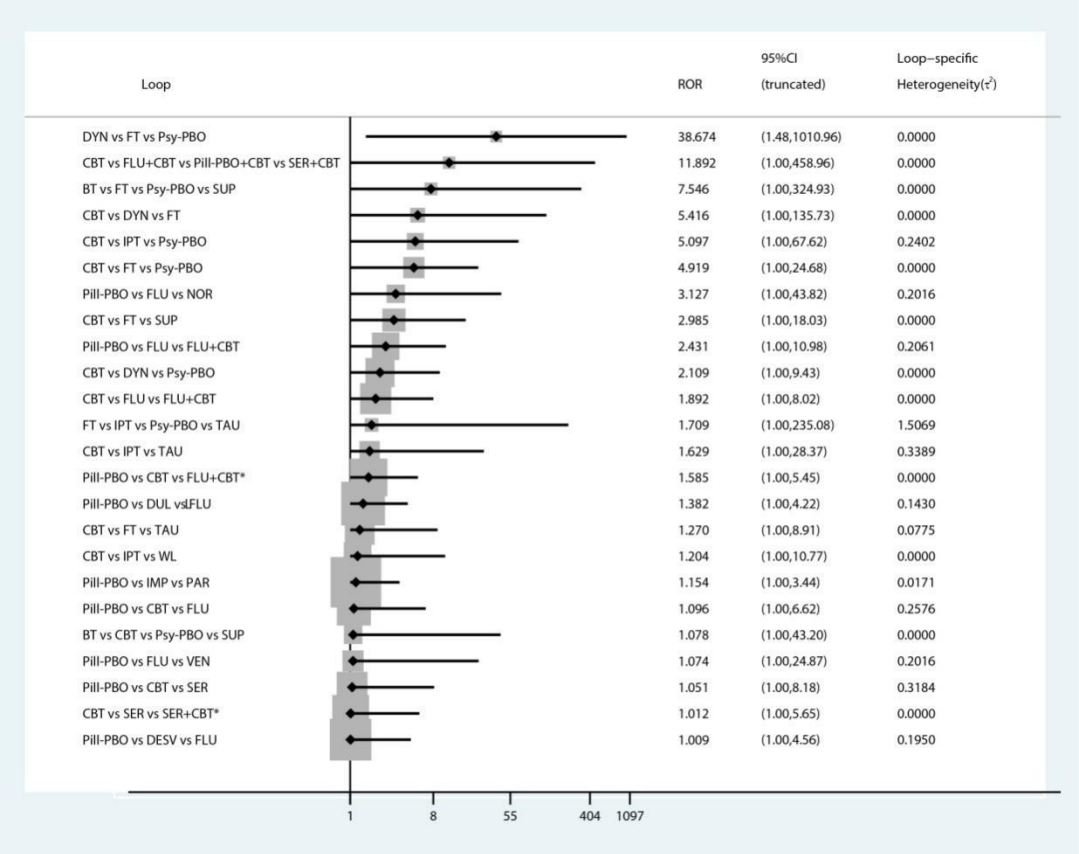


*These loops are formed only by multi-arm trials.

All-cause discontinuation

Loop	RoR	z-value	P-value	95%CI	τ^2
DYN vs FT vs Psy-PBO	38.674	2.195	0.0282	(1.48,1010.9)	0.0000
CBT vs FLU+CBT vs Pill-PBO+CBT vs SER+CBT	11.892	1.328	0.1841	(1.00,458.96)	0.0000
BT vs FT vs Psy-PBO vs SUP	7.546	1.053	0.2924	(1.00,324.93)	0.0000
CBT vs DYN vs FT	5.416	1.028	0.3040	(1.00,135.73)	0.0000
CBT vs IPT vs Psy-PBO	5.097	1.235	0.2169	(1.00,67.62)	0.2402
CBT vs FT vs Psy-PBO	4.919	1.936	0.0529	(1.00,24.68)	0.0000
Pill-PBO vs FLU vs NOR	3.127	0.846	0.3974	(1.00,43.82)	0.2016
CBT vs FT vs SUP	2.985	1.192	0.2333	(1.00,18.03)	0.0000
Pill-PBO vs FLU vs FLU+CBT	2.431	1.154	0.2485	(1.00,10.98)	0.2061
CBT vs DYN vs Psy-PBO	2.109	0.976	0.3289	(1.00,9.43)	0.0000
CBT vs FLU vs FLU+CBT	1.892	0.865	0.3869	(1.00,8.02)	0.0000
FT vs IPT vs Psy-PBO vs TAU	1.709	0.213	0.8310	(1.00,235.08)	1.5069
CBT vs IPT vs TAU	1.629	0.335	0.7380	(1.00,28.37)	0.3389
Pill-PBO vs CBT vs FLU+CBT*	1.585	0.731	0.4646	(1.00,5.45)	0.0000
Pill-PBO vs DUL vs FLU	1.382	0.568	0.5702	(1.00,4.22)	0.1430
CBT vs FT vs TAU	1.270	0.240	0.8102	(1.00,8.91)	0.0775
CBT vs IPT vs WL	1.204	0.166	0.8683	(1.00,10.77)	0.0000
Pill-PBO vs IMP vs PAR	1.154	0.257	0.7973	(1.00,3.44)	0.0171
Pill-PBO vs CBT vs FLU	1.096	0.100	0.9205	(1.00,6.62)	0.2576
BT vs CBT vs Psy-PBO vs SUP	1.078	0.040	0.9683	(1.00,43.20)	0.0000
Pill-PBO vs FLU vs VEN	1.074	0.044	0.9646	(1.00,24.87)	0.2016
Pill-PBO vs CBT vs SER	1.051	0.047	0.9624	(1.00,8.18)	0.3184
CBT vs SER vs SER+CBT*	1.012	0.014	0.9888	(1.00,5.65)	0.0000
Pill-PBO vs DEV vs FLU	1.009	0.012	0.9907	(1.00,4.56)	0.1950

*These loops are formed only by multi-arm trials.

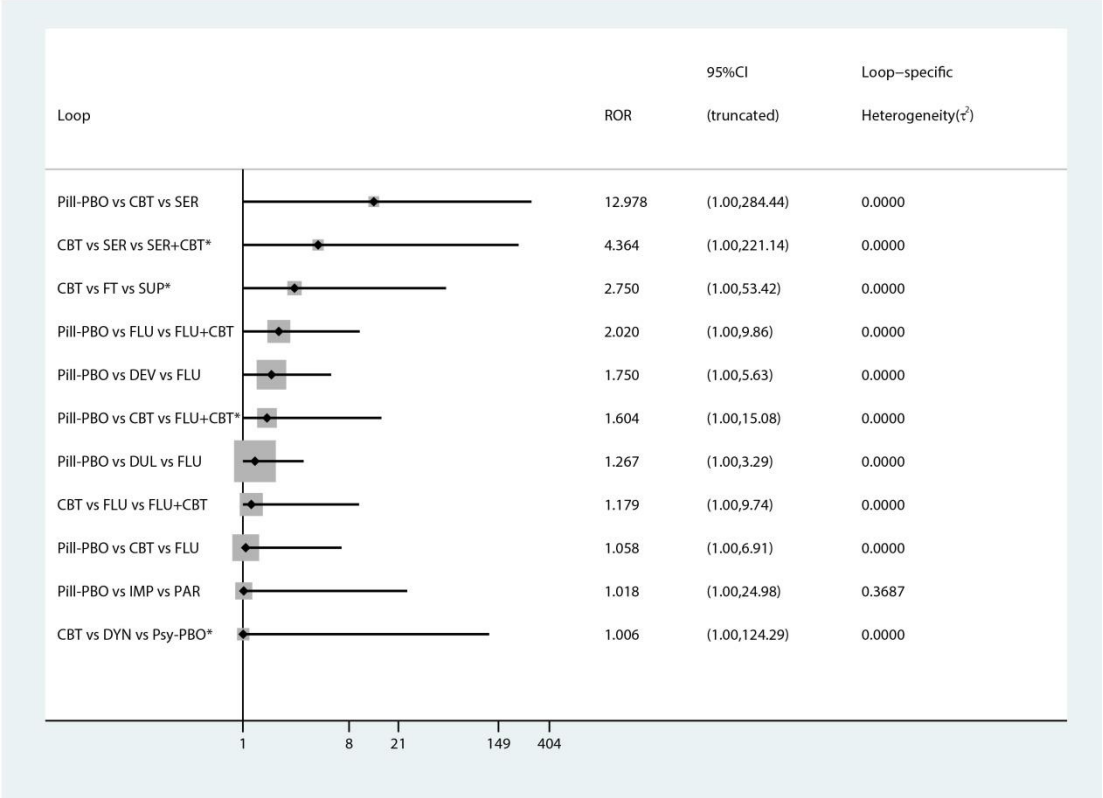


*These loops are formed only by multi-arm trials.

Suicidality

Loop	RoR	z-value	P-value	95%CI	τ^2
Pill-PBO vs CBT vs SER	12.978	1.627	0.1037	(1.00,284.44)	0.0000
CBT vs SER vs SER+CBT*	4.364	0.736	0.4620	(1.00,221.14)	0.0000
CBT vs FT vs SUP*	2.750	0.668	0.5039	(1.00,53.42)	0.0000
Pill-PBO vs FLU vs FLU+CBT	2.020	0.869	0.3846	(1.00,9.86)	0.0000
Pill-PBO vs DEV vs FLU	1.750	0.938	0.3482	(1.00,5.63)	0.0000
Pill-PBO vs CBT vs FLU+CBT*	1.604	0.413	0.6795	(1.00,15.08)	0.0000
Pill-PBO vs DUL vs FLU	1.267	0.487	0.6261	(1.00,3.29)	0.0000
CBT vs FLU vs FLU+CBT	1.179	0.153	0.8785	(1.00,9.74)	0.0000
Pill-PBO vs CBT vs FLU	1.058	0.059	0.9528	(1.00,6.91)	0.0000
Pill-PBO vs IMP vs PAR	1.018	0.011	0.9914	(1.00,24.98)	0.3687
CBT vs DYN vs Psy-PBO*	1.006	0.003	0.9979	(1.00,124.29)	0.0000

*These loops are formed only by multi-arm trials.



*These loops are formed only by multi-arm trials.

d. Evaluation of the incoherence by node-splitting model

Tests of incoherence by node-splitting method fitted the node-splitting model of Dias et al (Stat Med 2010; 29:932-44). The results reported the estimated direct and indirect treatment effects and their difference; the P-value for the difference is the test of incoherence.

Mean overall change in symptoms

Comparisons	Direct		Indirect		Difference			τ^2
	SMD	SE	SMD	SE	SMD	SE	P-value	
SER vs Pill-PBO	-0.23	0.24	0.29	0.39	-0.52	0.46	0.2606	0.3043
VEN vs Pill-PBO	-0.14	0.25	-0.40	0.43	0.26	0.49	0.5970	0.3160
VIL vs Pill-PBO	…	…	…	…	…	…	…	…
Pill-PBO vs AMI	…	…	…	…	…	…	…	…
SUP vs BT*	-0.46	0.43	0.36	632.08	-0.82	632.08	0.9990	0.3096
Pill-PBO vs CBT	-0.25	0.35	-0.04	0.32	-0.21	0.47	0.6603	0.3188
DYNvs CBT	0.18	0.34	0.58	0.39	-0.40	0.52	0.4388	0.3122
FTvs CBT	0.56	0.39	-0.26	0.23	0.81	0.45	0.0724	0.2970
FLU vs CBT	-0.69	0.34	-0.37	0.34	-0.32	0.48	0.5046	0.3152
FLU+CBT vs CBT	-1.29	0.30	0.07	0.41	-1.35	0.51	0.0077	0.2597
IPT vs CBT	-0.52	0.45	-0.44	0.24	-0.08	0.51	0.8710	0.3155
Psy-PBO vs CBT	0.30	0.19	0.19	0.33	0.11	0.38	0.7691	0.3160
SUP vs CBT	0.30	0.40	-0.18	0.43	0.47	0.58	0.4167	0.3141
SER vs CBT	0.01	0.29	-0.64	0.37	0.65	0.47	0.1692	0.3021
SER+CBTvs CBT	0.22	0.29	-0.86	0.65	1.08	0.71	0.1311	0.3000
TAU vs CBT	0.01	0.20	0.58	0.29	-0.57	0.35	0.1085	0.3052
WL vs CBT	0.93	0.19	0.85	0.48	0.08	0.52	0.8739	0.3151
Pill-PBO vs CIT	…	…	…	…	…	…	…	…
PAR vs CLO*	-0.49	0.36	-0.31	626.39	-0.18	626.39	0.9998	0.3096
FT vs DYN	-0.65	0.39	-0.21	0.36	-0.45	0.54	0.4039	0.3107
Psy-PBO vs DYN	0.02	0.34	-0.22	0.42	0.24	0.54	0.6606	0.3165
Pill-PBO vs DES	…	…	…	…	…	…	…	…
Pill-PBO vsDEV*	0.03	0.24	0.53	0.65	-0.50	0.69	0.4701	0.3159
FLU vs DEV	-0.18	0.35	-0.41	0.33	0.23	0.48	0.6300	0.3183
Pill-PBO vs DUL*	0.11	0.22	1.09	0.47	-0.98	0.52	0.0601	0.2908
FLU vs DUL*	0.10	0.22	-0.88	0.47	0.98	0.52	0.0601	0.2908
Pill-PBO vs ESC	…	…	…	…	…	…	…	…
Psy-PBO vs FT	0.14	0.44	0.40	0.26	-0.25	0.51	0.6243	0.3150
SUP vs FT*	0.00	0.26	1.34	0.82	-1.34	0.87	0.1231	0.3030
TAUvs FT	0.54	0.34	0.05	0.29	0.49	0.45	0.2706	0.3127
WL vs FT	1.07	0.49	0.95	0.29	0.13	0.57	0.8242	0.3144
Pill-PBO vs FLU*	0.24	0.12	1.26	0.30	-1.02	0.33	0.0019	0.2882
FLU+CBT vs FLU	-0.20	0.24	-0.68	0.52	0.48	0.57	0.4057	0.3054
NOR vs FLU	4.22	0.64	0.17	0.30	4.06	0.71	0.0000	0.2449
VEN vs FLU	0.00	0.41	0.26	0.28	-0.26	0.49	0.5970	0.3160
Pill-PBOvs FLU+CBT	1.03	0.33	0.38	0.30	0.66	0.44	0.1354	0.2960
Pill-PBO+CBT vs FLU+CBT	0.00	0.27	0.61	0.80	-0.61	0.85	0.4744	0.3124

Psy-PBO vs IPT	0.68	0.32	0.79	0.31	-0.12	0.45	0.7931	0.3150
TAU vs IPT	0.82	0.28	0.45	0.32	0.37	0.43	0.3876	0.3106
WL vs IPT	0.87	0.46	1.62	0.31	-0.76	0.55	0.1701	0.3046
Pill-PBO vs IMP*	0.04	0.28	-0.17	0.74	0.21	0.79	0.7861	0.3180
PAR vs IMP	-0.21	0.35	0.00	0.46	-0.21	0.58	0.7138	0.3164
Pill-PBO+CBT vs IMP+CBT*	0.44	0.40	-1.20	633.10	1.64	633.10	0.9979	0.3096
Pill-PBO vs MIR	…	…	…	…	…	…	…	…
Pill-PBO vs NEF	…	…	…	…	…	…	…	…
Pill-PBO vs NOR	0.12	0.29	-3.93	0.65	4.06	0.71	0.0000	0.2449
WL vs PST*	1.26	0.56	1.96	634.71	-0.70	634.71	0.9991	0.3096
Pill-PBO vs PAR*	0.14	0.18	0.50	1.09	-0.36	1.11	0.7460	0.3157
SER+CBT vs Pill-PBO+CBT	0.35	0.71	0.96	0.46	-0.61	0.85	0.4744	0.3124
VEN+CBT vs Pill-PBO+CBT*	0.73	0.45	1.21	621.07	-0.48	621.07	0.9994	0.3097
SER+CBT vs SER	0.20	0.29	0.62	0.69	-0.42	0.74	0.5733	0.3100

*All the evidence about these contrasts comes from the trials which directly compare them.
AMI=Amitriptyline. BT=Behavioural therapy. CBT=Cognitive-behavioural therapy. CIT=Citalopram. CLO=Clomipramine. DYN=Psychodynamic therapy. DES=Desipramine. DEV=Desvenlafaxine. DUL=Duloxetine. ESC=Escitalopram. FT=Family therapy. FLU=Fluoxetine. IPT=Interpersonal therapy. IMP=Imipramine. MIR=Mirtazapine. NEF=Nefazodone. NOR=Nortriptyline. PST=Problem-solving therapy. PAR=Paroxetine. Pill-PBO=Pill placebo. Psy-PBO=Psychological placebo. SUP= Supportive therapy. SER=Sertraline. TAU=Treatment as usual. VEN=Venlafaxine. VIL=Vilazodone. WL=Waitlist.

All-cause discontinuation

Comparisons	Direct		Indirect		Difference			τ^2
	LogOR	SE	LogOR	SE	LogOR	SE	P-value	
SER vs Pill-PBO	0.44	0.33	0.56	0.71	-0.12	0.79	0.8823	0.2833
VEN vs Pill-PBO	0.23	0.36	-0.24	1.47	0.47	1.52	0.7565	0.2724
VIL vs Pill-PBO	…	…	…	…	…	…	…	…
Pill-PBO vs AMI	…	…	…	…	…	…	…	…
Psy-PBO vs BT	-0.53	1.73	0.28	0.81	-0.80	1.91	0.6733	0.2727
SUPvs BT	-0.41	0.61	-1.21	1.81	0.80	1.91	0.6733	0.2727
Pill-PBO vs CBT	-0.07	0.43	-0.34	0.53	0.28	0.69	0.6861	0.2849
DYNvs CBT	0.38	0.41	0.89	1.00	-0.50	1.08	0.6420	0.2641
FT vs CBT	0.63	0.62	-0.14	0.48	0.77	0.77	0.3199	0.2657
FLU vs CBT	-0.33	0.45	-0.53	0.55	0.20	0.72	0.7831	0.2839
FLU+CBT vs CBT	-0.51	0.45	0.04	0.87	-0.54	0.99	0.5804	0.2770
IPT vs CBT	0.10	0.82	-0.44	0.55	0.54	0.99	0.5861	0.2714
Psy-PBO vs CBT	0.11	0.33	1.60	0.58	-1.49	0.67	0.0250	0.2048
SUP vs CBT	0.67	0.60	-1.30	0.72	1.97	0.94	0.0360	0.2179
SER vs CBT	0.28	0.62	0.29	0.51	-0.01	0.80	0.9936	0.2819
SER+CBT vs CBT	0.26	0.64	0.83	1.16	-0.57	1.36	0.6766	0.2772
TAU vs CBT	0.22	0.54	0.44	0.58	-0.22	0.80	0.7813	0.2790
WL vs CBT*	0.37	0.36	-0.84	1.83	1.21	1.87	0.5173	0.2697
Pill-PBOvs CIT	…	…	…	…	…	…	…	…
PAR vs CLO*	-0.42	0.47	0.54	1274.4	-0.96	1274.4	0.9994	0.2693

				7		7		
FT vs DYN	1.97	1.55	-0.56	0.51	2.54	1.63	0.1206	0.2659
Psy-PBO vs DYN	-0.29	0.38	1.87	0.96	-2.15	1.04	0.0379	0.2239
Pill-PBO vs DES	…	…	…	…	…	…	…	…
Pill-PBO vs DEV*	0.10	0.32	0.24	0.94	-0.14	1.00	0.8847	0.2870
FLU vs DEV	-0.23	0.49	-0.04	0.43	-0.19	0.66	0.7745	0.2888
Pill-PBO vs DUL*	-0.25	0.26	0.83	0.59	-1.08	0.66	0.1007	0.2153
FLU vs DUL*	-0.13	0.25	-1.21	0.59	1.08	0.66	0.1007	0.2153
Pill-PBO vs ESC	…	…	…	…	…	…	…	…
Psy-PBO vs FT	1.40	0.62	-0.35	0.50	1.74	0.80	0.0295	0.2242
SUP vs FT	-0.51	0.41	1.82	1.22	-2.33	1.29	0.0715	0.2357
TAU vs FT	0.45	0.58	-0.16	0.63	0.62	0.86	0.4697	0.2785
Pill-PBO vs FLU*	0.18	0.17	0.96	0.59	-0.78	0.61	0.2025	0.2678
FLU+CBT vs FLU	0.13	0.38	-0.46	0.80	0.58	0.88	0.5069	0.2925
NORvs FLU	0.81	0.97	-0.27	0.77	1.08	1.24	0.3850	0.2730
VEN vs FLU	0.00	1.46	0.47	0.39	-0.47	1.52	0.7565	0.2724
Pill-PBO vs FLU+CBT	0.45	0.46	-0.07	0.51	0.52	0.67	0.4410	0.2810
Pill-PBO+CBT vs FLU+CBT	0.02	0.53	-1.43	1.83	1.44	1.90	0.4480	0.2739
Psy-PBO vs IPT	1.36	0.70	0.29	0.63	1.08	0.94	0.2525	0.2552
TAU vs IPT	0.31	0.75	0.82	0.67	-0.51	1.01	0.6133	0.2702
WL vs IPT	0.29	0.79	0.83	0.70	-0.54	1.06	0.6088	0.2730
Pill-PBO vs IMP*	-0.91	0.42	-0.93	0.94	0.02	1.05	0.9870	0.2922
PAR vs IMP	-0.58	0.43	-0.87	0.86	0.29	0.97	0.7641	0.2916
Pill-PBO+CBT vs IMP+CBT*	0.29	0.64	-0.61	1441.12	0.90	1441.12	0.9995	0.2693
Pill-PBO vs MIR	…	…	…	…	…	…	…	…
Pill-PBO vs NEF	…	…	…	…	…	…	…	…
Pill-PBO vs NOR	0.49	0.76	-0.59	0.99	1.08	1.24	0.3850	0.2730
WL vs PST*	1.45	1.71	1.28	2329.82	0.17	2329.82	0.9999	0.2693
Pill-PBO vs PAR*	-0.25	0.23	-3.64	3.18	3.39	3.19	0.2877	0.2688
SER+CBT vs Pill-PBO+CBT	2.06	1.72	0.62	0.82	1.44	1.90	0.4480	0.2739
VEN+CBT vs Pill-PBO+CBT*	0.35	0.88	0.58	1658.11	-0.23	1658.11	0.9999	0.2693
SER+CBT vs SER	0.03	0.54	0.57	1.25	-0.53	1.36	0.6937	0.2842

*All the evidence about these contrasts comes from the trials which directly compare them.

Suicidality

Comparisons	Direct		Indirect		Difference			τ^2
	LogOR	SE	LogOR	SE	LogOR	SE	P-value	
SER vs Pill-PBO	0.62	0.84	1.13	1.30	-0.52	1.55	0.7395	0.0000
VEN vs Pill-PBO	…	…	…	…	…	…	…	…
VIL vs Pill-PBO	…	…	…	…	…	…	…	…
Pill-PBO vs CBT	-0.23	0.68	1.18	0.83	-1.41	1.11	0.2027	0.0000
DYN vs CBT*	-0.01	1.42	1.69	1683.81	-1.70	1683.81	0.9992	0.0000

FT vs CBT*	-0.38	0.95	0.04	2088.69	-0.41	2088.69	0.9998	0.0000
FLU vs CBT	0.69	0.57	-0.11	0.86	0.80	0.97	0.4091	0.0000
FLU+CBT vs CBT	0.24	0.62	0.45	1.16	-0.22	1.31	0.8679	0.0000
Psy-PBO vs CBT*	-0.02	1.42	0.85	845.51	-0.87	845.51	0.9992	0.0000
SUP vs CBT*	0.64	0.77	1.14	2219.92	-0.50	2219.92	0.9998	0.0000
SER vs CBT*	1.41	1.18	0.90	1.00	0.52	1.55	0.7395	0.0000
SER+CBT vs CBT*	0.44	1.27	-0.59	2.60	1.03	3.10	0.7395	0.0000
Pill-PBO vs CIT	…	…	…	…	…	…	…	…
PAR vs CLO*	0.19	0.54	1.49	1884.09	-1.29	1884.09	0.9995	0.0000
Psy-PBO vs DYN*	-0.01	1.42	1.74	1679.09	-1.74	1679.09	0.9992	0.0000
Pill-PBO vs DEV*	0.23	0.29	0.60	0.90	-0.37	0.95	0.6976	0.0000
FLU vs DEV	0.36	0.46	0.40	0.40	-0.03	0.61	0.9553	0.0000
Pill-PBO vs DUL*	0.10	0.25	-0.44	0.72	0.54	0.78	0.4872	0.0000
FLU vs DUL*	0.08	0.25	0.62	0.72	-0.54	0.78	0.4872	0.0000
Pill-PBO vs ESC	…	…	…	…	…	…	…	…
SUP vs FT	…	…	…	…	…	…	…	…
Pill-PBO vs FLU*	-0.14	0.20	0.32	0.83	-0.46	0.86	0.5906	0.0000
FLU+CBT vs FLU*	-0.29	0.38	1.11	1.18	-1.39	1.22	0.2531	0.0000
Pill-PBO vs FLU+CBT	-0.40	0.66	0.36	0.53	-0.76	0.86	0.3773	0.0000
Pill-PBO+CBT vs FLU+CBT*	-1.11	0.99	-0.05	2734.00	-1.06	2734.00	0.9997	0.0000
Psy-PBO vs IPT*	0.79	0.92	-0.67	1340.99	1.46	1340.99	0.9991	0.0000
TAU vs IPT*	-1.00	1.65	2.02	3696.37	-3.02	3696.37	0.9993	0.0000
Pill-PBO vs IMP*	-0.62	0.88	2.67	1.66	-3.29	2.01	0.1011	0.0000
PAR vs IMP*	1.12	0.60	-2.18	2.00	3.29	2.01	0.1011	0.0000
Pill-PBO vs MIR	…	…	…	…	…	…	…	…
Pill-PBO vs NEF	…	…	…	…	…	…	…	…
Pill-PBO vs PAR*	-0.74	0.49	-0.09	931.63	-0.65	931.63	0.9994	0.0000
SER+CBT vs SER*	-0.97	0.88	0.06	3.04	-1.03	3.10	0.7395	0.0000

*All the evidence about these contrasts comes from the trials which directly compare them.

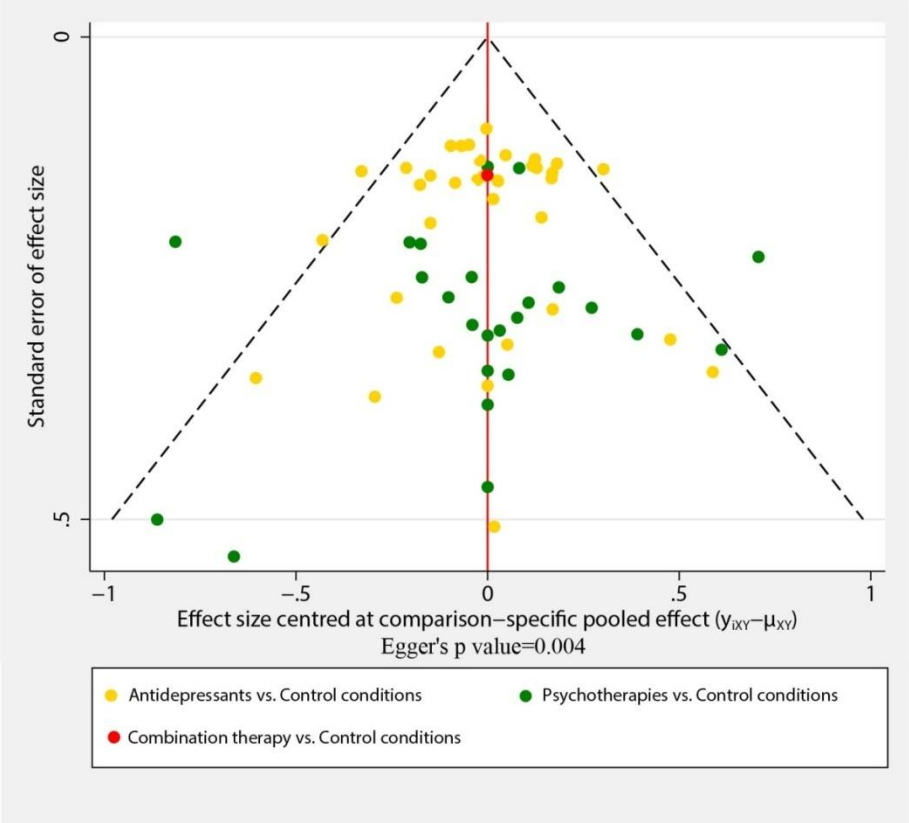
APPENDIX 14

Comparison-adjusted funnel plot for each outcome from the network meta-analysis

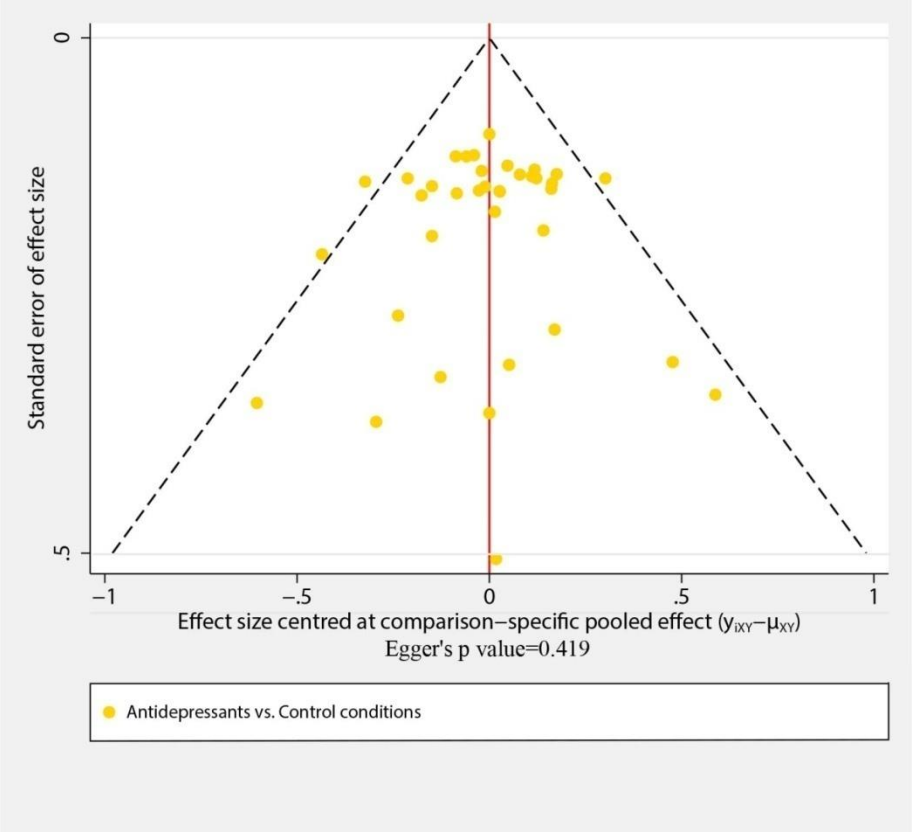
The comparison-adjusted funnel plot was conducted to assess small-study effects within network meta-analysis. All the active treatments vs. control conditions (Pill-PBO, Psy-PBO, TAU, WL) in our network were shown in the comparison-adjusted funnel plot. Then, two subheading comparison-adjusted funnel plots (Antidepressants vs. Control conditions and Psychotherapies vs. Control conditions) showed the node of specific comparisons from the comparison-adjusted funnel plot, respectively. The comparison-adjusted funnel plots of the network meta-analysis were suggestive of obvious publication bias for efficacy outcome, of which mainly resulted from psychotherapy trials, but not for acceptability.

a. Comparison-adjusted funnel plot for mean overall change

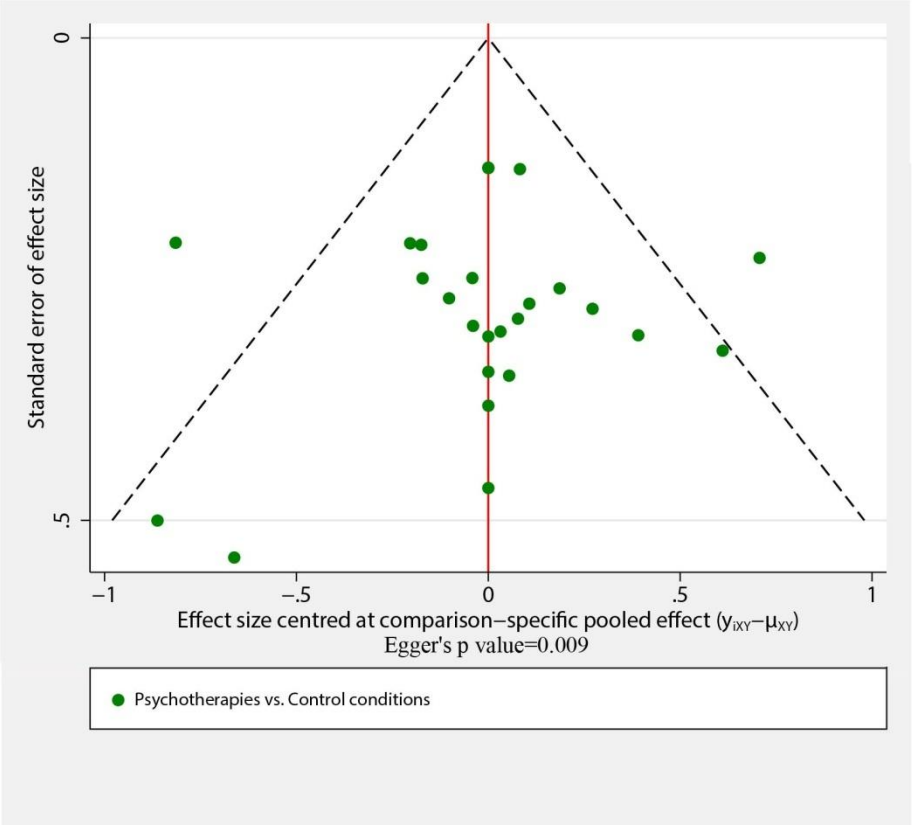
Active treatments vs. Control conditions



(1) Antidepressants vs. Control conditions

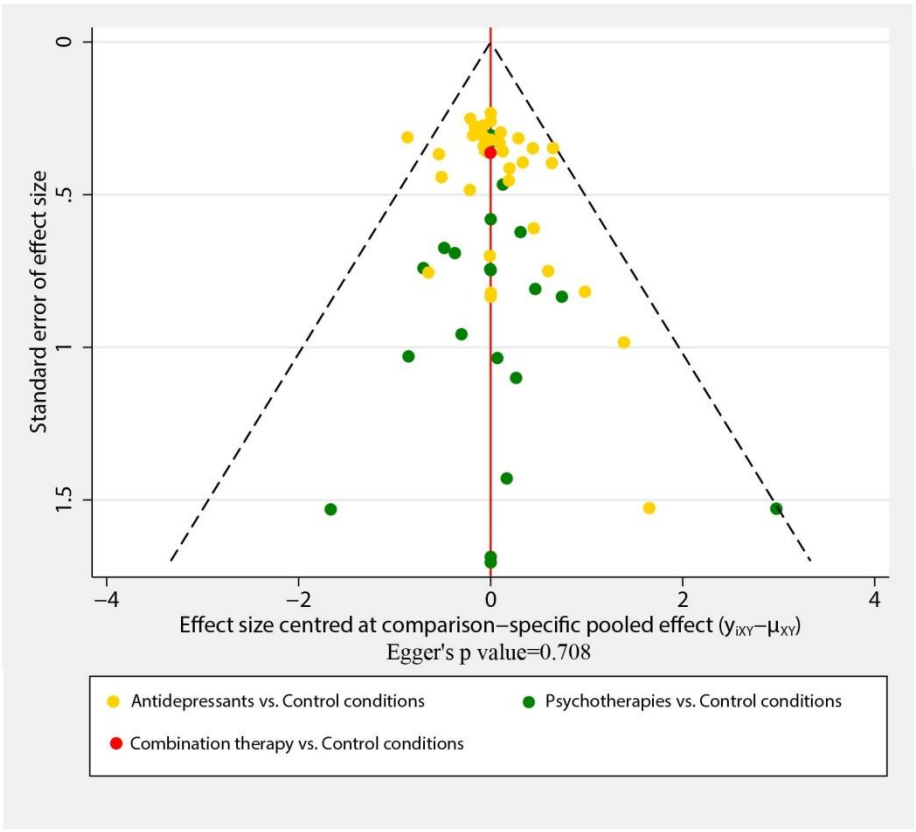


(2) Psychotherapies vs. Control conditions

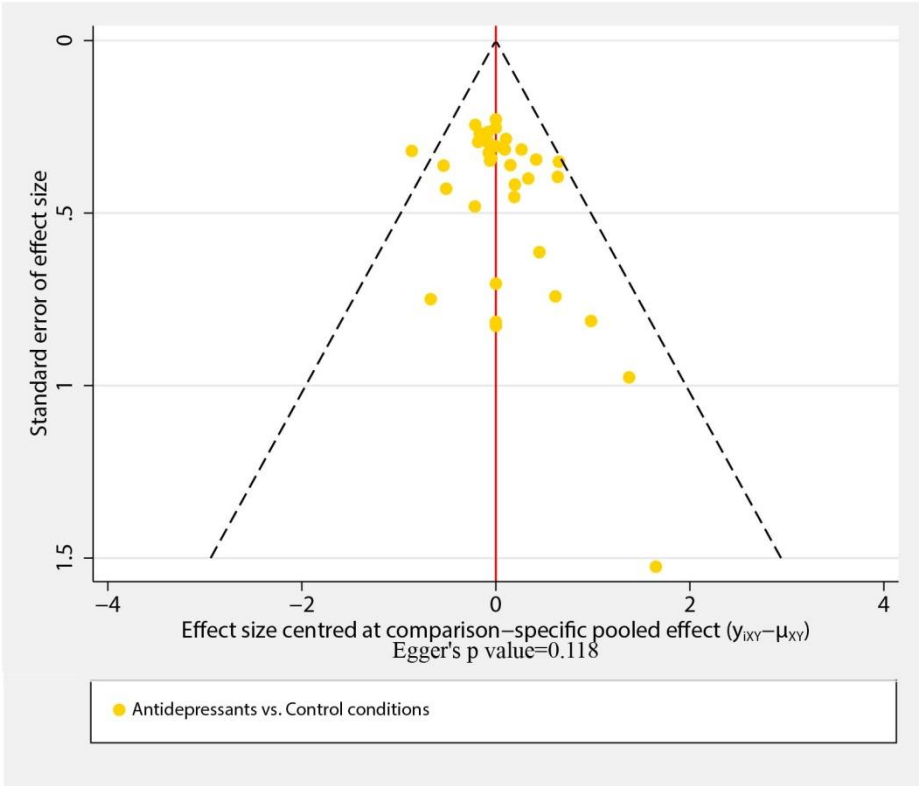


b. Comparison-adjusted funnel plot for all-cause discontinuation

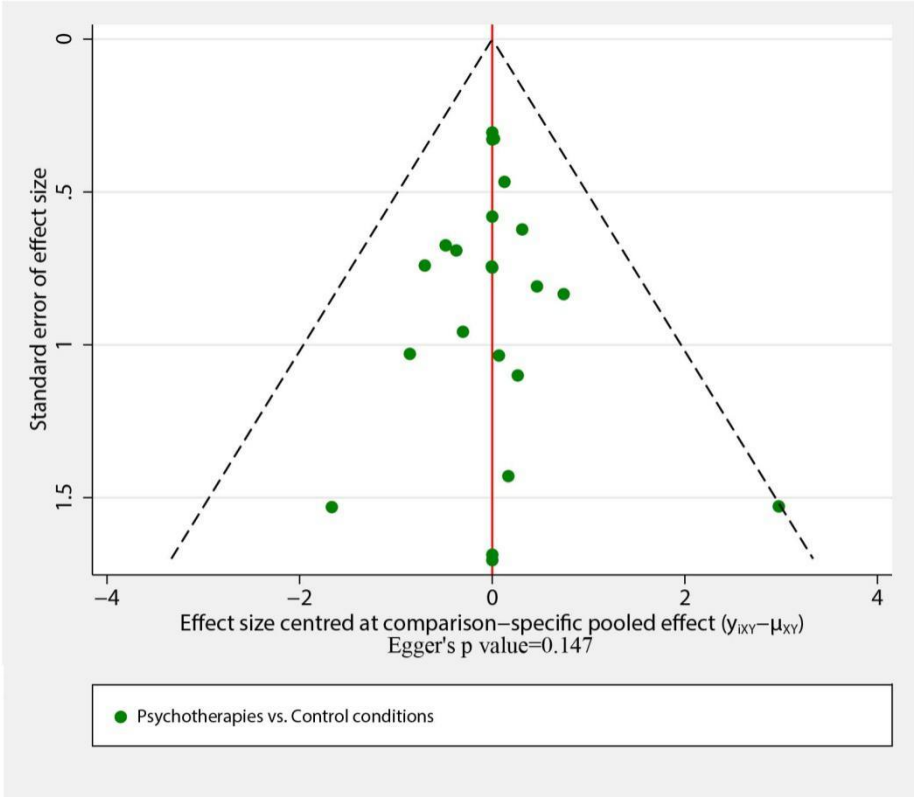
Active treatments vs. Control conditions



(1) Antidepressants vs. Control conditions

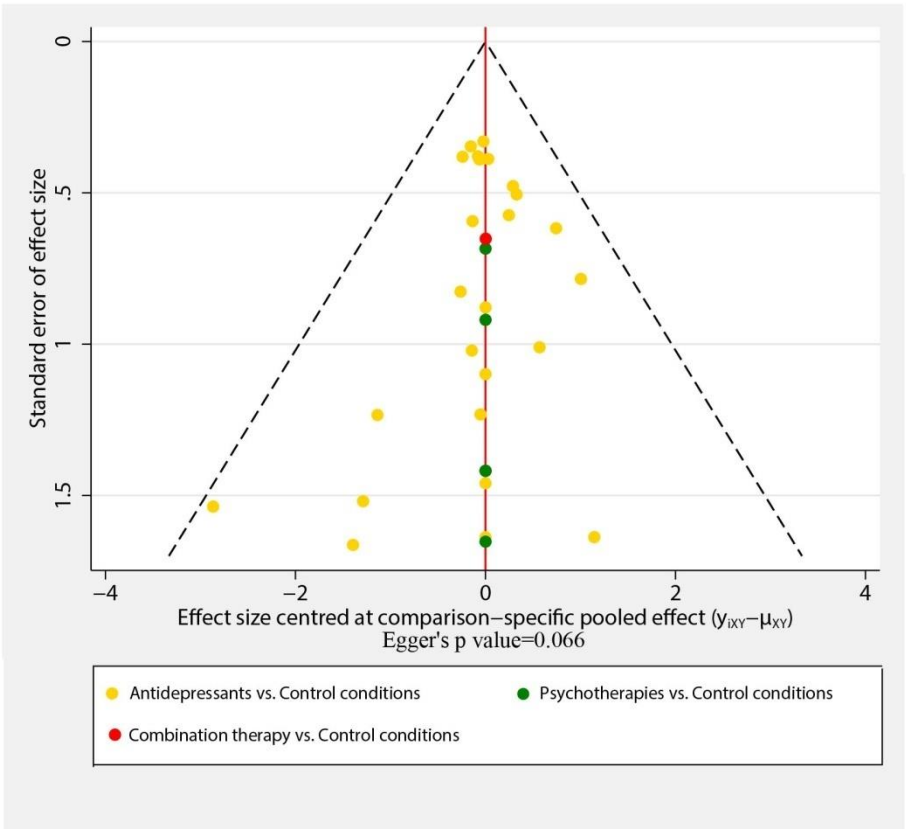


(2) Psychotherapies vs. Control conditions

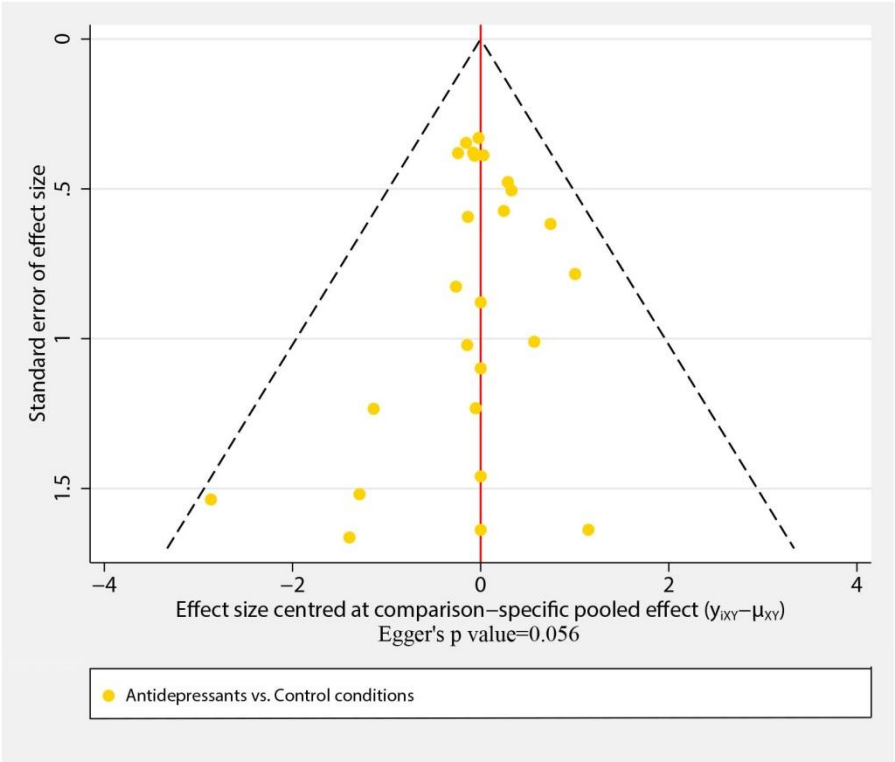


c. Comparison-adjusted funnel plot for suicidality

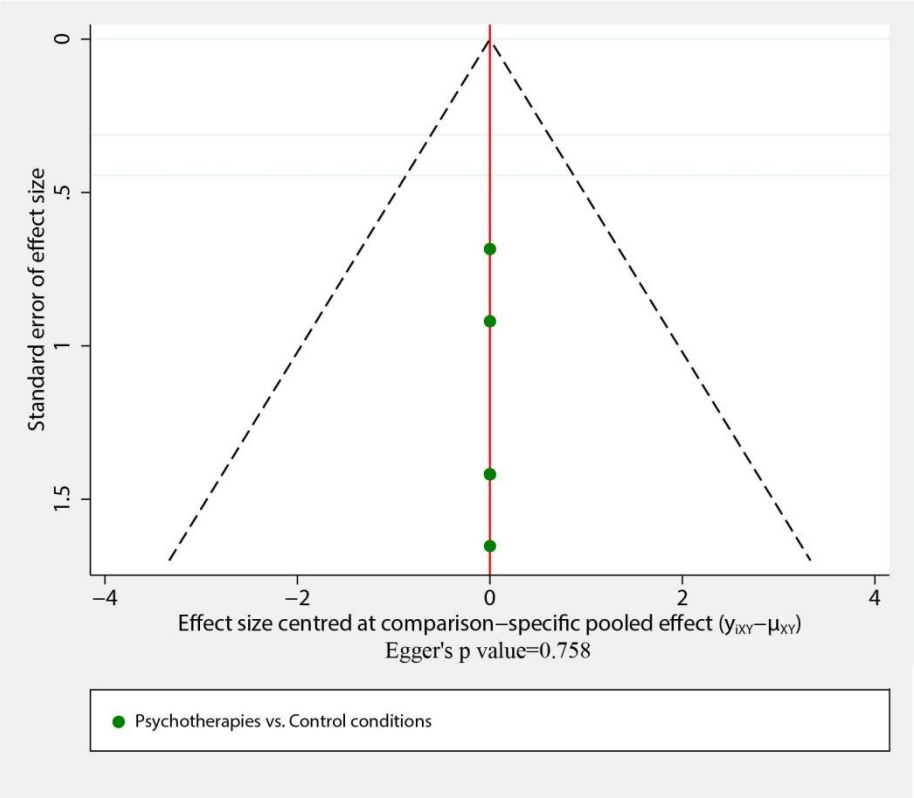
Active treatments vs. Control conditions



(1) Antidepressants vs. Control conditions



(2) Psychotherapies vs. Control conditions



APPENDIX 15

Network meta-regression and sensitivity analyses for each outcome

a. Summary of the network meta-regression and sensitivity analyses

We conducted network meta-regression and sensitivity analyses to estimate the impact of variable for each outcome.

The potential modifiers for network meta-regression we choose are listed below:

Continuous variable	Mean overall change in depressive symptoms	All-caused discontinuation
Sample size of trials	√	√
Sex ratio of participants	√	√
Mean age of participants	√	√
Treatment duration	√	√
Publication year of trials	√	√
Mean baseline severity	√	√
Dichotomous variable	**Mean overall change in depressive symptoms**	**All-caused discontinuation**
Risk of bias rating of trials	√	√
Patients including in the trials with or without comorbidity	√	√
Sponsorship	√	√
Self-rating or other-rating scales*	√	

*We did not perform meta-regression analysis with rating scale for all-caused discontinuation due to the scale just for rating depressive symptoms.

The potential modifiers for sensitivity analyses we choose are listed below:

Sensitivity analyses	Mean overall change in depressive symptoms	All-caused discontinuation
Omitting unpublished trials	√	√
Omitting non-blind trials	√	√
Omitting trials with sample size ≤ 20	√	√
Omitting trials with imputed data*	√	
Omitting trials with inconsistent of treatment duration and selected time-point[#]	√	

*We did not perform sensitivity analysis with omitting trials where missing data have been imputed for all-caused discontinuation due to no available study.

[#]We did not perform sensitivity analysis with omitting trials with inconsistent of treatment duration and selected time-point for all-caused discontinuation due to no available study.

In part b and c, network meta-regression results of primary outcomes for each condition with pill-PBO were listed. In continuous variable, we chose mean publication years, mean baseline severity when meta-regression centring due to normal distribution, and we chose the median of sample size, sex ratio, mean age and treatment duration when meta-regression centring due to abnormal distribution. In dichotomous variable, we defined low or unclear risk of bias as 0 and high risk of bias as 1 in meta-regression analysis.We defined no or not stated manufactory funder as 0 and manufactory funder as 1. We defined other-rating as 0 and self-rating as 1. We defined without comorbidity as 0 and with comorbidity as 1. The beta of meta-regression reflects the changes of SMD or OR when the covariate increase one unit. In part d and e the sensitivity analyses results of of primary outcomes for each condition with pill-PBO were listed.

b. Network meta-regression of each condition for mean overall change in depressive symptoms with Pill-PBO*

Characteristics	All trials	Sample size	Sex ratio	Mean age	Treatment duration	Mean baseline severity[#]	Publication year	Risk of bias	Rating scale	Comorbidity	Sponsorship
AMI	0.08 (-1.11 to 1.27)	0.14 (-1.06 to 1.34)	0.15 (-1.11 to 1.41)	0.09 (-1.14 to 1.30)	0.09 (-1.11 to 1.28)	1.17 (-0.46 to 2.83)	0.12 (-1.09 to 1.32)	0.08 (-1.10 to 1.29)	0.09 (-1.11 to 1.29)	-0.50 (-1.98 to 0.98)	0.09 (-0.70 to 0.88)
BT	0.56 (-0.95 to 2.08)	0.42 (-1.16 to 1.97)	0.56 (-1.03 to 2.15)	0.68 (-1.00 to 2.36)	0.55 (-1.01 to 2.10)	0.35 (-1.26 to 1.96)	0.57 (-0.99 to 2.12)	0.55 (-1.03 to 2.14)	0.55 (-1.00 to 2.11)	0.52 (-1.02 to 2.04)	0.56 (-0.36 to 1.46)
CBT	0.05 (-0.61 to 0.70)	-0.09 (-0.82 to 0.63)	0.06 (-0.64 to 0.75)	0.25 (-0.61 to 1.11)	0.05 (-0.64 to 0.73)	-0.16 (-0.90 to 0.57)	0.06 (-0.61 to 0.73)	0.05 (-0.68 to 0.78)	0.05 (-0.63 to 0.73)	0.02 (-0.66 to 0.68)	0.06 (-0.32 to 0.42)
CIT	-0.18 (-0.89 to 0.55)	-0.24 (-0.97 to 0.49)	-0.35 (-1.42 to 0.72)	-0.18 (-0.92 to 0.57)	-0.18 (-0.91 to 0.55)	-0.46 (-1.52 to 0.59)	-0.18 (-0.90 to 0.55)	-0.19 (-1.11 to 0.72)	-0.23 (-0.98 to 0.52)	-0.35 (-1.12 to 0.41)	-0.35 (-0.78 to 0.08)
CLO	0.33 (-0.83 to 1.48)	0.26(-0.91 to 1.43)	0.34 (-0.86 to 1.55)	0.35 (-0.85 to 1.54)	0.34 (-0.84 to 1.51)	0.31 (-0.89 to 1.50)	0.35 (-0.82 to 1.51)	0.34 (-0.84 to 1.51)	0.33 (-0.83 to 1.50)	0.29 (-0.86 to 1.44)	0.20 (-0.44 to 0.83)
DYN	0.41 (-0.58 to 1.38)	0.26 (-0.77 to 1.29)	0.42 (-0.62 to 1.44)	0.57 (-0.58 to 1.72)	0.40 (-0.60 to 1.41)	0.21 (-0.85 to 1.26)	0.42 (-0.59 to 1.41)	0.40 (-0.64 to 1.44)	0.41 (-0.60 to 1.41)	0.37 (-0.62 to 1.36)	0.38 (-0.15 to 0.89)
DES	-0.43 (-1.26 to 0.39)	-0.40 (-1.22 to 0.42)	-0.50 (-1.42 to 0.41)	-0.45 (-1.30 to 0.39)	-0.41 (-1.26 to 0.43)	-0.02 (-0.94 to 0.93)	-0.39 (-1.23 to 0.44)	-0.43 (-1.26 to 0.40)	-0.43 (-1.25 to 0.40)	-0.74 (-1.67 to 0.20)	-0.43 (-0.95 to 0.10)
DEV	-0.12 (-0.79 to 0.54)	-0.27 (-0.99 to 0.45)	-0.12 (-0.82 to 0.57)	-0.12 (-0.81 to 0.57)	-0.13 (-0.80 to 0.55)	-0.25 (-0.95 to 0.45)	-0.14 (-0.81 to 0.53)	-0.13 (-0.80 to 0.55)	-0.13 (-0.80 to 0.54)	-0.15 (-0.81 to 0.51)	-0.29 (-0.71 to 0.14)
DUL	-0.22 (-0.85 to 0.42)	-0.35 (-1.04 to 0.34)	-0.20 (-0.87 to 0.46)	-0.20 (-0.87 to 0.46)	-0.22 (-0.87 to 0.44)	-0.36 (-1.04 to 0.31)	-0.22 (-0.87 to 0.43)	-0.21 (-0.86 to 0.44)	-0.23 (-0.87 to 0.42)	-0.25 (-0.89 to 0.38)	-0.32 (-0.71 to 0.09)
ESC	-0.17 (-0.88 to 0.54)	-0.27 (-1.01 to 0.47)	-0.17 (-0.91 to 0.57)	-0.16 (-0.90 to 0.57)	-0.17 (-0.89 to 0.55)	-0.23 (-0.97 to 0.51)	-0.17 (-0.89 to 0.54)	-0.17 (-0.89 to 0.55)	-0.17 (-0.89 to 0.55)	-0.17 (-0.88 to 0.54)	-0.36 (-0.78 to 0.06)
FT	-0.03 (-0.87 to 0.79)	-0.18 (-1.07 to 0.71)	-0.03 (-0.91 to 0.85)	0.06 (-0.98 to 1.10)	-0.04 (-0.90 to 0.82)	-0.23 (-1.15 to 0.68)	-0.03 (-0.87 to 0.82)	-0.04 (-0.93 to 0.86)	-0.04 (-0.90 to 0.82)	-0.07 (-0.93 to 0.77)	-0.06 (-0.55 to 0.41)
FLU	**-0.51 (-0.84 to -0.18)**	**-0.60 (-0.98 to -0.23)**	**-0.50 (-0.84 to -0.16)**	**-0.49 (-0.83 to -0.15)**	**-0.51 (-0.84 to -0.18)**	**-0.64 (-1.01 to -0.28)**	**-0.51 (-0.84 to -0.18)**	**-0.51 (-0.87 to -0.16)**	**-0.53 (-0.87 to -0.20)**	**-0.58 (-0.93 to -0.24)**	**-0.50 (-0.78 to -0.20)**

FLU+CBT	**-0.73 (-1.39 to -0.07)**	**-0.88 (-1.61 to -0.15)**	**-0.72 (-1.41 to -0.02)**	-0.69 (-1.40 to 0.02)	**-0.74 (-1.41 to -0.07)**	**-0.95 (-1.67 to -0.25)**	**-0.73 (-1.39 to -0.06)**	**-0.73 (-1.41 to -0.04)**	**-0.75 (-1.41 to -0.08)**	**-0.79 (-1.44 to -0.13)**	**-0.77 (-1.13 to -0.40)**
IPT	-0.38 (-1.24 to 0.47)	-0.53 (-1.45 to 0.39)	-0.37 (-1.28 to 0.53)	-0.21 (-1.25 to 0.82)	-0.38 (-1.28 to 0.51)	-0.58 (-1.52 to 0.36)	-0.37 (-1.25 to 0.51)	-0.38 (-1.30 to 0.54)	-0.38 (-1.27 to 0.50)	-0.42 (-1.29 to 0.45)	-0.37 (-0.90 to 0.16)
IMP	-0.03 (-0.75 to 0.68)	0.01 (-0.71 to 0.73)	0.08 (-0.83 to 0.99)	0.09 (-0.85 to 1.03)	0.04 (-0.87 to 0.95)	0.14 (-0.82 to 1.09)	0.13 (-0.75 to 1.01)	-0.03 (-0.76 to 0.70)	-0.03 (-0.76 to 0.69)	-0.04 (-0.75 to 0.67)	-0.06 (-0.45 to 0.33)
IMP+CBT	-1.08 (-2.48 to 0.32)	-1.22 (-2.67 to 0.23)	-1.06 (-2.52 to 0.40)	-0.76 (-2.34 to 0.83)	-1.09 (-2.52 to 0.34)	-1.08 (-2.64 to 0.47)	-1.08 (-2.49 to 0.34)	-1.08 (-2.53 to 0.37)	-1.10 (-2.52 to 0.32)	-1.14 (-2.54 to 0.26)	**-1.13 (-1.95 to -0.31)**
MIR	-0.23 (-0.97 to 0.51)	-0.26 (-1.00 to 0.48)	-0.23 (-1.00 to 0.54)	-0.23 (-0.99 to 0.54)	-0.23 (-0.98 to 0.51)	-0.10 (-0.87 to 0.67)	-0.23 (-0.98 to 0.51)	-0.24 (-1.06 to 0.58)	-0.23 (-0.98 to 0.52)	-0.45 (-1.26 to 0.35)	-0.45 (-0.94 to 0.03)
NEF	-0.14 (-0.85 to 0.57)	-0.22 (-0.95 to 0.51)	-0.28 (-1.34 to 0.78)	...	-0.14 (-0.86 to 0.59)	-0.19 (-1.25 to 0.87)	-0.14 (-0.86 to 0.58)	-0.14 (-0.87 to 0.59)	-0.14 (-0.86 to 0.58)	-0.33 (-1.10 to 0.43)	-0.33 (-0.76 to 0.10)
NOR	**1.14 (0.46 to 1.81)**	**1.12 (0.46 to 1.80)**	**1.16 (0.46 to 1.86)**	**1.16 (0.46 to 1.85)**	**1.14 (0.46 to 1.82)**	**1.21 (0.51 to 1.90)**	**1.16 (0.48 to 1.84)**	**1.14 (0.46 to 1.82)**	**1.13 (0.46 to 1.80)**	**1.12 (0.44 to 1.78)**	-0.13 (-0.64 to 0.38)
PST	-0.26 (-1.73 to 1.18)	-0.41 (-1.90 to 1.08)	-0.25 (-1.77 to 1.26)	-0.29 (-1.90 to 1.32)	-0.28 (-1.77 to 1.22)	-0.46 (-2.00 to 1.08)	-0.25 (-1.74 to 1.23)	-0.27 (-1.78 to 1.25)	-0.26 (-1.75 to 1.22)	-0.30 (-1.77 to 1.16)	-0.03 (-197.10 to 195.50)
PAR	-0.16 (-0.67 to 0.35)	-0.22 (-0.75 to 0.30)	-0.15 (-0.68 to 0.39)	-0.14 (-0.67 to 0.40)	-0.15 (-0.67 to 0.38)	-0.18 (-0.72 to 0.36)	-0.14 (-0.65 to 0.37)	-0.16 (-0.67 to 0.36)	-0.16 (-0.67 to 0.36)	-0.20 (-0.71 to 0.31)	-0.29 (-0.63 to 0.04)
Pill-PBO+CBT	-0.64 (-1.54 to 0.24)	-0.78 (-1.73 to 0.16)	-0.63 (-1.56 to 0.31)	-0.32 (-1.42 to 0.80)	-0.66 (-1.57 to 0.26)	-0.65 (-1.72 to 0.43)	-0.64 (-1.54 to 0.26)	-0.65 (-1.57 to 0.29)	-0.66 (-1.57 to 0.25)	-0.70 (-1.59 to 0.20)	**-0.69 (-1.22 to -0.17)**
Psy-PBO	0.32 (-0.47 to 1.11)	0.18 (-0.68 to 1.03)	0.33 (-0.51 to 1.16)	0.54 (-0.44 to 1.53)	0.32 (-0.50 to 1.14)	0.12 (-0.75 to 0.99)	0.33 (-0.48 to 1.14)	0.32 (-0.54 to 1.18)	0.33 (-0.49 to 1.14)	0.29 (-0.52 to 1.09)	0.33 (-0.12 to 0.77)
SUP	0.10 (-0.91 to 1.11)	-0.04 (-1.13 to 1.03)	0.11 (-0.97 to 1.18)	0.23 (-0.99 to 1.43)	0.10 (-0.96 to 1.15)	-0.10 (-1.22 to 1.00)	0.11 (-0.93 to 1.15)	0.10 (-0.99 to 1.19)	0.10 (-0.97 to 1.16)	0.07 (-0.97 to 1.09)	0.10 (-0.49 to 0.67)
SER	-0.11 (-0.71 to 0.49)	-0.21 (-0.84 to 0.42)	-0.10 (-0.73 to 0.52)	0.23 (-0.90 to 1.37)	-0.12 (-0.74 to 0.49)	-0.35 (-1.03 to 0.32)	-0.11 (-0.72 to 0.50)	-0.12 (-0.86 to 0.61)	-0.11 (-0.72 to 0.49)	-0.13 (-0.74 to 0.47)	-0.25 (-0.61 to 0.12)
SER+CBT	0.10 (-0.71 to 0.89)	-0.03 (-0.88 to 0.81)	0.10 (-0.74 to 0.93)	0.37 (-0.70 to 1.45)	0.09 (-0.74 to 0.91)	-0.09 (-0.97 to 0.79)	0.10 (-0.71 to 0.92)	0.09 (-0.79 to 0.96)	0.09 (-0.73 to 0.90)	0.06 (-0.74 to 0.87)	0.06 (-0.44 to 0.54)

TAU	0.28 (-0.52 to 1.06)	0.13 (-0.72 to 0.98)	0.29 (-0.55 to 1.11)	0.44 (-0.53 to 1.43)	0.27 (-0.54 to 1.09)	0.10 (-0.79 to 0.99)	0.28 (-0.52 to 1.09)	0.27 (-0.57 to 1.13)	0.28 (-0.54 to 1.09)	0.24 (-0.56 to 1.04)	0.20 (-0.26 to 0.66)
VEN	-0.25 (-0.87 to 0.36)	-0.31 (-0.94 to 0.31)	-0.24 (-0.88 to 0.40)	-0.24 (-0.88 to 0.39)	-0.25 (-0.87 to 0.37)	-0.34 (-0.98 to 0.30)	-0.25 (-0.87 to 0.37)	-0.26 (-1.06 to 0.52)	-0.26 (-0.88 to 0.36)	-0.42 (-1.08 to 0.24)	-0.35 (-0.80 to 0.11)
VEN+CBT	0.09 (-1.37 to 1.53)	-0.05 (-1.53 to 1.43)	0.10 (-1.40 to 1.62)	0.41 (-1.20 to 2.04)	0.07 (-1.41 to 1.54)	0.08 (-1.52 to 1.66)	0.09 (-1.38 to 1.55)	0.08 (-1.40 to 1.58)	0.07 (-1.40 to 1.54)	0.03 (-1.41 to 1.47)	…
VIL	-0.09 (-1.09 to 0.90)	-0.35 (-1.48 to 0.78)	-0.10 (-1.14 to 0.94)	-0.09 (-1.12 to 0.94)	-0.09 (-1.10 to 0.92)	-0.20 (-1.24 to 0.83)	-0.11 (-1.12 to 0.88)	-0.09 (-1.09 to 0.92)	-0.09 (-1.09 to 0.91)	-0.32 (-1.36 to 0.72)	-0.32 (-0.86 to 0.23)
WL	**0.99 (0.18to 1.79)**	0.85 (-0.01 to 1.70)	**1.00 (0.15 to 1.84)**	0.97 (-0.03 to 1.98)	**0.99 (0.16 to 1.81)**	0.79 (-0.10 to 1.67)	**1.00 (0.18 to 1.81)**	**0.99 (0.12 to 1.85)**	**0.99 (0.17 to 1.81)**	**0.96 (0.14 to 1.76)**	**0.63 (0.12 to 1.13)**
Beta of meta-regression		0.01 (-0.01 to 0.02)	0.35 (-1.34 to 2.05)	0.04 (-0.15 to 0.23)	0.04 (-0.30 to 0.38)	**0.41 (0.01 to 0.84)**	0.02 (-0.04 to 0.07)	0.21 (-8.18 to 8.78)	1.77 (-4.34 to 7.94)	2.73 (-1.44 to 6.86)	2.75 (-0.97 to 6.40)

*Negative effect sizes indicate superiority of the specific intervention against placebo control. #The method for transforming other depressive scales to CDRS-R: Schünemann HJ, Oxman AD, Higgins JPT, Vist GE, Glasziou P, Guyatt GH, et al. Presenting results and "Summary of findings" tables. In: Higgins JPT, Green S, eds. Cochrane handbook for systematic reviews of interventions. Wiley, 2008:335-8. AMI=Amitriptyline. BT=Behavioural therapy. CBT=Cognitive-behavioural therapy. CIT=Citalopram. CLO=Clomipramine. DYN=Psychodynamic therapy. DES=Desipramine. DEV=Desvenlafaxine. DUL=Duloxetine. ESC=Escitalopram. FT=Family therapy. FLU=Fluoxetine. IPT=Interpersonal therapy. IMP=Imipramine.

c. Network meta-regression of each condition for all-cause discontinuation with Pill-PBO*

Characteristics	All trials	Sample size	Sex ratio	Mean age	Treatment duration	Publication year	Mean baseline severity[#]	Risk of bias	Comorbidity	Sponsorship
AMI	1.16 (0.29 to 12.13)	1.14 (0.28 to 12.70)	0.67 (0.15 to 8.91)	1.21 (0.32 to 10.53)	1.16 (0.29 to 12.40)	1.29 (0.32 to 14.71)	1.46 (0.32 to 22.95)	1.17 (0.30 to 11.03)	0.48 (0.11 to 6.85)	1.17 (0.29 to 12.79)
BT	1.20 (0.31 to 9.61)	1.30 (0.35 to 11.58)	1.13 (0.30 to 9.00)	1.44 (0.39 to 11.67)	1.23 (0.30 to 13.14)	1.27 (0.36 to 10.07)	0.78 (0.19 to 7.75)	1.60 (0.46 to 10.43)	1.23 (0.35 to 8.94)	1.18 (0.32 to 10.16)
CBT	1.08 (0.55 to 2.43)	1.14 (0.52 to 3.24)	0.97 (0.48 to 2.28)	1.05 (0.57 to 2.19)	1.31 (0.61 to 3.55)	1.10 (0.56 to 2.48)	0.87 (0.41 to 2.21)	1.32 (0.71 to 2.87)	1.04 (0.55 to 2.28)	1.03 (0.50 to 2.67)
CIT	0.96 (0.52 to 1.97)	1.00 (0.52 to 2.36)	0.94 (0.37 to 3.16)	0.94 (0.57 to 1.65)	1.14 (0.56 to 2.85)	0.95 (0.52 to 2.00)	0.90 (0.36 to 3.06)	1.82 (0.82 to 5.08)	0.40 (0.15 to 1.46)	0.81 (0.35 to 2.54)
CLO	1.75 (0.66 to 6.57)	1.81 (0.65 to 7.84)	1.85 (0.68 to 7.75)	1.68 (0.72 to 5.07)	1.72 (0.63 to 6.90)	1.67 (0.63 to 6.54)	1.59 (0.58 to 6.19)	1.75 (0.70 to 5.83)	1.64 (0.62 to 6.06)	1.55 (0.54 to 7.15)
DYN	1.42 (0.54 to 4.92)	1.47 (0.51 to 6.16)	1.23 (0.44 to 4.64)	1.38 (0.59 to 4.05)	1.70 (0.59 to 7.06)	1.42 (0.52 to 5.04)	1.11 (0.39 to 4.30)	1.81 (0.73 to 5.77)	1.36 (0.53 to 4.57)	1.34 (0.48 to 5.35)
DES	2.21 (0.88 to 7.67)	2.17 (0.86 to 7.85)	**3.23 (1.04 to 17.06)**	**2.86 (1.21 to 9.70)**	1.77 (0.66 to 6.74)	2.38 (0.90 to 8.64)	2.35 (0.93 to 8.40)	2.22 (0.94 to 7.24)	1.34 (0.49 to 5.26)	2.19 (0.88 to 7.70)
DEV	0.85 (0.47 to 1.74)	0.90 (0.41 to 2.61)	0.82 (0.43 to 1.75)	0.71 (0.42 to 1.34)	0.87 (0.47 to 1.84)	0.75 (0.39 to 1.81)	0.76 (0.40 to 1.67)	0.87 (0.51 to 1.68)	0.84 (0.47 to 1.69)	0.74 (0.34 to 2.19)
DUL	1.04 (0.62 to 1.96)	1.11 (0.53 to 3.03)	0.92 (0.51 to 1.87)	0.90 (0.57 to 1.52)	1.19 (0.66 to 2.53)	0.98 (0.57 to 1.98)	0.90 (0.49 to 1.88)	1.12 (0.70 to 1.96)	1.01 (0.60 to 1.88)	0.93 (0.45 to 2.51)
ESC	1.40 (0.77 to 2.86)	1.47 (0.71 to 3.91)	1.38 (0.73 to 2.98)	1.23 (0.74 to 2.25)	1.39 (0.74 to 2.95)	1.35 (0.74 to 2.86)	1.33 (0.71 to 2.82)	1.41 (0.82 to 2.67)	1.39 (0.77 to 2.82)	1.19 (0.51 to 3.71)
FT	1.26 (0.49 to 4.31)	1.34 (0.50 to 5.26)	1.14 (0.44 to 4.02)	1.93 (0.79 to 6.64)	1.51 (0.56 to 6.04)	1.30 (0.51 to 4.41)	0.95 (0.35 to 3.59)	1.56 (0.66 to 4.81)	1.21 (0.49 to 3.96)	1.19 (0.46 to 4.57)
FLU	0.78 (0.56 to 1.15)	0.83 (0.48 to 1.65)	0.67 (0.44 to 1.09)	**0.70 (0.51 to 0.99)**	0.86 (0.58 to 1.37)	0.77 (0.54 to 1.15)	0.67 (0.44 to 1.09)	0.89 (0.63 to 1.29)	0.73 (0.51 to 1.07)	0.72 (0.42 to 1.48)

FLU+CBT	0.75 (0.39 to 1.65)	0.78 (0.34 to 2.30)	0.66 (0.32 to 1.57)	0.70 (0.39 to 1.40)	0.87 (0.41 to 2.30)	0.74 (0.38 to 1.68)	0.62 (0.30 to 1.57)	0.83(0.44 to 1.78)	0.71 (0.37 to 1.58)	0.71 (0.34 to 1.84)
IPT	0.76 (0.28 to 2.88)	0.83 (0.29 to 3.64)	0.69 (0.25 to 2.82)	0.68 (0.26 to 2.25)	0.94 (0.33 to 4.18)	0.78 (0.29 to 3.07)	0.58 (0.21 to 2.44)	0.92 (0.36 to 3.31)	0.73 (0.28 to 2.71)	0.84 (0.30 to 3.76)
IMP	**2.51 (1.26 to 6.24)**	**2.63 (1.24 to 7.63)**	**2.76 (1.31 to 7.37)**	**2.29 (1.27 to 4.83)**	**2.44 (1.19 to 6.37)**	**2.44 (1.20 to 6.40)**	**2.17 (0.99 to 5.81)**	**2.47 (1.31 to 5.61)**	**2.44 (1.24 to 5.94)**	**2.43 (1.18 to 6.63)**
IMP+CBT	0.40 (0.10 to 3.64)	0.40 (0.10 to 4.77)	0.34 (0.08 to 3.66)	0.25 (0.06 to 2.00)	0.45 (0.11 to 5.05)	0.39 (0.10 to 3.90)	0.20 (0.05 to 2.30)	0.44 (0.11 to 3.72)	0.37 (0.09 to 3.61)	0.37 (0.09 to 4.02)
MIR	0.83 (0.40 to 2.08)	0.86 (0.41 to 2.23)	0.75 (0.34 to 1.98)	0.64 (0.32 to 1.55)	0.83 (0.39 to 2.16)	0.86 (0.41 to 2.16)	0.94 (0.42 to 2.63)	1.16 (0.55 to 2.99)	0.35 (0.12 to 1.50)	0.72 (0.29 to 2.59)
NEF	0.49 (0.21 to 1.39)	0.50 (0.21 to 1.60)	0.52 (0.22 to 1.65)	...	0.48 (0.20 to 1.45)	0.50 (0.21 to 1.43)	...	0.50 (0.24 to 1.25)	0.20 (0.07 to 0.93)	0.41 (0.15 to 1.70)
NOR	0.76 (0.28 to 3.41)	0.79 (0.28 to 3.47)	0.55 (0.18 to 2.77)	0.51 (0.18 to 2.20)	0.80 (0.29 to 3.46)	0.82 (0.28 to 3.58)	0.78 (0.28 to 3.36)	0.80 (0.30 to 3.17)	0.74 (0.26 to 3.08)	0.41 (0.11 to 2.96)
PST	0.08 (0.01 to 8.45)	0.07 (0.01 to 10.61)	0.06 (0.01 to 8.45)	0.08 (0.01 to 6.30)	0.04 (0.01 to 11.91)	0.06 (0.01 to 9.67)	0.05 (0.01 to 8.45)	0.10 (0.02 to 10.44)	0.06 (0.01 to 8.93)	...
PAR	1.30 (0.81 to 2.27)	1.36 (0.77 to 2.81)	1.41 (0.85 to 2.62)	1.22 (0.82 to 1.92)	1.30 (0.79 to 2.33)	1.26 (0.78 to 2.28)	1.20 (0.73 to 2.15)	1.30 (0.85 to 2.13)	1.23 (0.76 to 2.10)	1.18 (0.62 to 2.69)
Pill-PBO+CBT	0.68 (0.25 to 2.75)	0.70 (0.23 to 3.60)	0.60 (0.21 to 2.67)	0.43 (0.16 to 1.63)	0.79 (0.27 to 3.73)	0.68 (0.25 to 2.84)	0.35 (0.11 to 1.82)	0.77 (0.29 to 2.81)	0.65 (0.24 to 2.65)	0.65 (0.23 to 3.02)
Psy-PBO	1.66 (0.71 to 5.13)	1.76 (0.70 to 6.54)	1.50 (0.60 to 4.81)	1.25 (0.55 to 3.39)	2.07 (0.81 to 7.48)	1.70 (0.72 to 5.22)	1.32 (0.54 to 4.53)	2.02 (0.91 to 5.85)	1.59 (0.70 to 4.74)	1.63 (0.64 to 5.78)
SUP	0.85 (0.29 to 3.65)	0.92 (0.31 to 4.55)	0.79 (0.27 to 3.41)	1.15 (0.43 to 4.64)	1.00 (0.33 to 5.02)	0.89 (0.32 to 3.81)	0.64 (0.21 to 2.98)	1.09 (0.41 to 4.01)	0.85 (0.31 to 3.43)	0.83 (0.29 to 3.87)
SER	1.61 (0.89 to 3.27)	1.66 (0.86 to 3.84)	1.41 (0.74 to 3.05)	1.52 (0.52 to 7.10)	1.89 (0.96 to 4.51)	1.63 (0.89 to 3.32)	1.14 (0.50 to 3.29)	2.75 (1.31 to 6.88)	1.58 (0.88 to 3.15)	1.41 (0.65 to 3.97)
SER+CBT	1.74 (0.68 to 6.03)	1.82 (0.67 to 7.27)	1.56 (0.60 to 5.72)	1.68 (0.58 to 7.28)	2.11 (0.78 to 8.60)	1.77 (0.69 to 6.23)	1.25 (0.44 to 5.24)	2.51 (0.97 to 9.11)	1.68 (0.65 to 5.85)	1.60 (0.57 to 6.79)

TAU	1.50 (0.60 to 5.45)	1.60 (0.58 to 6.63)	1.36 (0.51 to 4.96)	1.67 (0.70 to 5.53)	1.84 (0.67 to 7.48)	1.55 (0.61 to 5.38)	1.02 (0.36 to 4.43)	1.80 (0.76 to 5.94)	1.45 (0.59 to 4.93)	1.32 (0.51 to 5.43)
VEN	1.12 (0.53 to 2.69)	1.19 (0.48 to 4.15)	0.86 (0.37 to 2.47)	0.89 (0.48 to 1.90)	1.12 (0.52 to 2.89)	1.10 (0.52 to 2.76)	1.05 (0.49 to 2.69)	2.11 (0.89 to 6.28)	0.49 (0.18 to 1.94)	0.97 (0.38 to 3.70)
VEN+CBT	0.65 (0.13 to 12.41)	0.63 (0.13 to 14.74)	0.55 (0.11 to 11.04)	0.44 (0.10 to 6.42)	0.74 (0.16 to 15.95)	0.64 (0.13 to 12.24)	0.34 (0.07 to 7.08)	0.69 (0.15 to 10.71)	0.63 (0.13 to 10.77)	…
VIL	0.59 (0.27 to 1.54)	0.62 (0.21 to 3.38)	0.64 (0.28 to 1.87)	0.61 (0.33 to 1.27)	0.58 (0.26 to 1.63)	0.50 (0.21 to 1.61)	0.54 (0.24 to 1.51)	0.60 (0.30 to 1.41)	0.24 (0.08 to 1.07)	0.50 (0.19 to 1.93)
WL	1.40 (0.58 to 4.54)	1.48 (0.55 to 5.78)	1.27 (0.49 to 4.43)	1.34 (0.57 to 3.85)	1.70 (0.64 to 6.62)	1.43 (0.58 to 4.74)	1.12 (0.43 to 4.07)	1.74 (0.71 to 5.33)	1.35 (0.56 to 4.32)	1.38 (0.53 to 5.07)
Beta of meta-regression		0.00 (-0.01 to 0.01)	-0.53 (-1.46 to 0.38)	-0.11 (-0.23 to 0.02)	-0.09 (-0.28 to 0.09)	0.01 (-0.03 to 0.05)	0.03 (-0.05 to 0.11)	**-0.71 (-1.40 to -0.01)**	0.77 (-0.17 to 1.70)	0.09 (-0.64 to 0.77)

*OR<1 indicate superiority of the specific intervention against placebo control. #The method for transforming other depressive scales to CDRS-R: Schünemann HJ, Oxman AD, Higgins JPT, Vist GE, Glasziou P, Guyatt GH, et al. Presenting results and "Summary of findings" tables. In: Higgins JPT, Green S, eds. Cochrane handbook for systematic reviews of interventions. Wiley, 2008:335-8. AMI=Amitriptyline. BT=Behavioural therapy. CBT=Cognitive-behavioural therapy. CIT=Citalopram. CLO=Clomipramine. DYN=Psychodynamic therapy. DES=Desipramine. DEV=Desvenlafaxine. DUL=Duloxetine. ESC=Escitalopram. FT=Family therapy. FLU=Fluoxetine. IPT=Interpersonal therapy. IMP=Imipramine. MIR=Mirtazapine. NEF=Nefazodone. NOR=Nortriptyline. PST=Problem-solving therapy. PAR=Paroxetine. Pill-PBO=Pill placebo. Psy-PBO=Psychological placebo. SUP= Supportive therapy. SER=Sertraline. TAU=Treatment as usual. VEN=Venlafaxine. VIL=Vilazodone. WL=Waitlist.

d. Sensitivity network meta-analysis for mean overall change in depressive symptoms with Pill-PBO by standard mean difference (95%CrI)*

Characteristics	All trials	Omitting the unpublished trials	Omitting trials with imputed data	Omitting non-blind trials	Omitting trials with inconsistent of treatment duration and selected time-point	Omitting trials with sample size ≤ 20
AMI	0.08 (-1.11 to 1.27)	0.08 (-1.17 to 1.33)	0.08 (-1.17 to 1.34)	0.09 (-1.16 to 1.34)	0.09 (-1.18 to 1.35)	0.09 (-1.09 to 1.27)
BT	0.56 (-0.95 to 2.08)	0.52 (-1.12 to 2.15)	0.69 (-1.04 to 2.40)	…	0.56 (-1.14 to 2.25)	0.70 (-0.84 to 2.23)
CBT	0.05 (-0.61 to 0.70)	0.03 (-0.68 to 0.73)	0.20 (-0.70 to 1.07)	0.33 (-0.62 to 1.28)	0.02 (-0.79 to 0.80)	0.09 (-0.59 to 0.76)
CIT	-0.18 (-0.89 to 0.55)	-0.18 (-0.95 to 0.58)	-0.18 (-0.95 to 0.60)	-0.18 (-0.94 to 0.59)	-0.18 (-0.96 to 0.61)	-0.18 (-0.90 to 0.53)
CLO	0.33 (-0.83 to 1.48)	0.38 (-0.88 to 1.63)	0.33 (-0.91 to 1.56)	0.34 (-0.90 to 1.57)	0.32 (-0.97 to 1.61)	0.33 (-0.81 to 1.49)
DYN	0.41 (-0.58 to 1.38)	0.38 (-0.68 to 1.42)	0.55 (-0.65 to 1.72)	0.51 (-0.85 to 1.87)	0.63 (-0.93 to 2.16)	0.51 (-0.49 to 1.51)
DES	-0.43 (-1.26 to 0.39)	-0.43 (-1.29 to 0.43)	-0.43 (-1.29 to 0.44)	-0.44 (-1.30 to 0.42)	-0.43 (-1.30 to 0.45)	-0.43 (-1.24 to 0.38)
DEV	-0.12 (-0.79 to 0.54)	-0.14 (-0.85 to 0.57)	-0.13 (-0.84 to 0.59)	-0.12 (-0.83 to 0.59)	-0.13 (-0.85 to 0.60)	-0.13 (-0.79 to 0.53)
DUL	-0.22 (-0.85 to 0.42)	-0.24 (-0.93 to 0.45)	-0.21 (-0.90 to 0.47)	-0.21 (-0.89 to 0.47)	-0.21 (-0.91 to 0.48)	-0.22 (-0.85 to 0.42)
ESC	-0.17 (-0.88 to 0.54)	-0.17 (-0.93 to 0.59)	-0.21 (-1.29 to 0.85)	-0.17 (-0.92 to 0.59)	-0.17 (-0.94 to 0.61)	-0.17 (-0.87 to 0.54)
FT	-0.03 (-0.87 to 0.79)	-0.07 (-0.99 to 0.81)	0.11 (-0.96 to 1.14)	0.00 (-1.24 to 1.23)	-0.02 (-1.04 to 0.97)	0.15 (-0.73 to 1.00)
FLU	**-0.51 (-0.84 to -0.18)**	**-0.57 (-0.94 to -0.19)**	**-0.51 (-0.88 to -0.15)**	**-0.50 (-0.85 to -0.15)**	**-0.51 (-0.86 to -0.16)**	**-0.51 (-0.84 to -0.19)**
FLU+CBT	**-0.73 (-1.39 to -0.07)**	**-0.76 (-1.47 to -0.05)**	-0.68 (-1.42 to 0.06)	**-0.74 (-1.50 to 0.00)**	**-0.73 (-1.46 to 0.00)**	**-0.80 (-1.49 to -0.12)**
IPT	-0.38 (-1.24 to 0.47)	-0.42 (-1.34 to 0.50)	-0.23 (-1.31 to 0.82)	-0.20 (-1.41 to 1.01)	-0.40 (-1.42 to 0.60)	-0.37 (-1.25 to 0.50)
IMP	-0.03 (-0.75 to 0.68)	-0.02 (-0.79 to 0.75)	-0.03 (-0.79 to 0.74)	-0.03 (-0.79 to 0.72)	-0.04 (-0.82 to 0.74)	-0.03 (-0.74 to 0.68)
IMP+CBT	-1.08 (-2.48 to 0.32)	-1.11 (-2.60 to 0.39)	-1.00 (-2.53 to 0.52)	-1.19 (-2.79 to 0.40)	-1.21 (-2.86 to 0.46)	-1.24 (-2.73 to 0.24)
MIR	-0.23 (-0.97 to 0.51)	…	-0.24 (-1.02 to 0.56)	-0.23 (-1.01 to 0.55)	-0.23 (-1.03 to 0.56)	-0.23 (-0.97 to 0.50)
NEF	-0.14 (-0.85 to 0.57)	…	…	-0.14 (-0.91 to 0.62)	-0.14 (-0.93 to 0.64)	-0.14 (-0.86 to 0.57)
NOR	**1.14 (0.46 to 1.81)**	**1.12 (0.41 to 1.83)**	**1.14 (0.43 to 1.85)**	**1.14 (0.43 to 1.84)**	**1.14 (0.41 to 1.86)**	**1.14 (0.47 to 1.81)**
PST	-0.26 (-1.73 to 1.18)	-0.38 (-1.95 to 1.18)	-0.12 (-1.77 to 1.51)	…	-0.28 (-1.89 to 1.32)	-0.20 (-1.68 to 1.27)
PAR	-0.16 (-0.67 to 0.35)	-0.11 (-0.72 to 0.50)	-0.16 (-0.70 to 0.39)	-0.15 (-0.70 to 0.38)	-0.17 (-0.81 to 0.48)	-0.16 (-0.67 to 0.35)
Pill-PBO+CBT	-0.64 (-1.54 to 0.24)	-0.67 (-1.62 to 0.28)	-0.56 (-1.55 to 0.44)	-0.76 (-1.86 to 0.34)	-0.77 (-1.93 to 0.41)	-0.81 (-1.83 to 0.20)
Psy-PBO	0.32 (-0.47 to 1.11)	0.30 (-0.57 to 1.14)	0.47 (-0.55 to 1.47)	0.53 (-0.56 to 1.60)	0.30 (-0.69 to 1.26)	0.38 (-0.43 to 1.18)
SUP	0.10 (-0.91 to 1.11)	0.06 (-1.04 to 1.16)	0.24 (-1.00 to 1.45)	0.22 (-1.45 to 1.87)	0.10 (-1.09 to 1.28)	0.24 (-0.81 to 1.27)

SER	-0.11 (-0.71 to 0.49)	-0.12 (-0.77 to 0.52)	0.15 (-1.03 to 1.30)	-0.23 (-0.99 to 0.54)	-0.08 (-0.77 to 0.61)	-0.07 (-0.68 to 0.55)
SER+CBT	0.10 (-0.71 to 0.89)	0.08 (-0.79 to 0.93)	0.28 (-0.82 to 1.35)	...	-0.04 (-1.12 to 1.03)	0.22 (-0.66 to 1.10)
TAU	0.28 (-0.52 to 1.06)	0.25 (-0.61 to 1.10)	0.42 (-0.59 to 1.41)	0.57 (-0.58 to 1.71)	0.26 (-0.69 to 1.19)	0.23 (-0.59 to 1.04)
VEN	-0.25 (-0.87 to 0.36)	-0.14 (-0.91 to 0.62)	-0.26 (-0.91 to 0.39)	-0.25 (-0.90 to 0.40)	-0.26 (-0.93 to 0.41)	-0.25 (-0.86 to 0.36)
VEN+CBT	0.09 (-1.37 to 1.53)	0.06 (-1.47 to 1.60)	0.17 (-1.40 to 1.74)	-0.03 (-1.66 to 1.59)	-0.04 (-1.73 to 1.66)	-0.08 (-1.61 to 1.43)
VIL	-0.09 (-1.09 to 0.90)	-0.09 (-1.16 to 0.98)	-0.09 (-1.15 to 0.98)	-0.09 (-1.15 to 0.97)	-0.09 (-1.18 to 1.00)	-0.09 (-1.07 to 0.90)
WL	**0.99** **(0.18 to 1.79)**	0.88 (-0.01 to 1.75)	**1.14** **(0.11 to 2.14)**	0.81 (-0.51 to 2.12)	**0.97** **(0.00 to 1.89)**	**1.05** **(0.23 to 1.86)**

*Negative effect sizes indicate superiority of the specific intervention against placebo control

e. Sensitivity network meta-analysis for all-cause discontinuation with Pill-PBO by standard mean difference (95%CrI)*

Characteristics	All trials	Omitting the unpublished trials	Omitting non-blind trials	Omitting trials with sample size ≤ 20
AMI	1.16 (0.29 to 12.13)	1.14 (0.28 to 13.09)	1.19 (0.31 to 10.80)	1.17 (0.30 to 12.07)
BT	1.20 (0.31 to 9.61)	1.22 (0.33 to 10.27)	…	1.35 (0.36 to 10.53)
CBT	1.08 (0.55 to 2.43)	1.06 (0.54 to 2.57)	1.10 (0.54 to 2.71)	1.08 (0.56 to 2.36)
CIT	0.96 (0.52 to 1.97)	0.95 (0.50 to 2.05)	0.96 (0.53 to 1.92)	0.96 (0.53 to 1.96)
CLO	1.75 (0.66 to 6.57)	1.70 (0.61 to 7.18)	1.74 (0.69 to 6.27)	1.74 (0.66 to 6.60)
DYN	1.42 (0.54 to 4.92)	1.33 (0.48 to 5.08)	1.49 (0.56 to 5.86)	1.45 (0.55 to 5.10)
DES	2.21 (0.88 to 7.67)	2.15 (0.85 to 7.67)	2.20 (0.90 to 7.39)	2.19 (0.87 to 7.69)
DEV	0.85 (0.47 to 1.74)	0.84 (0.45 to 1.81)	0.86 (0.49 to 1.70)	0.85 (0.47 to 1.74)
DUL	1.04 (0.62 to 1.96)	1.02 (0.58 to 2.02)	1.04 (0.64 to 1.92)	1.05 (0.62 to 1.99)
ESC	1.40 (0.77 to 2.86)	1.39 (0.73 to 3.01)	1.41 (0.79 to 2.77)	1.40 (0.77 to 2.86)
FT	1.26 (0.49 to 4.31)	1.24 (0.49 to 4.58)	0.28 (0.08 to 1.75)	1.40 (0.55 to 5.03)
FLU	0.78 (0.56 to 1.15)	0.75 (0.52 to 1.14)	0.78 (0.57 to 1.15)	0.79 (0.56 to 1.16)
FLU+CBT	0.75 (0.39 to 1.65)	0.72 (0.36 to 1.70)	0.80 (0.42 to 1.83)	0.79 (0.41 to 1.80)
IPT	0.76 (0.28 to 2.88)	0.76 (0.28 to 3.11)	0.33 (0.10 to 2.01)	0.74 (0.29 to 2.73)
IMP	**2.51 (1.26 to 6.24)**	**2.53 (1.22 to 6.83)**	**2.48 (1.27 to 6.01)**	**2.55 (1.28 to 6.37)**
IMP+CBT	0.40 (0.10 to 3.64)	0.37 (0.09 to 3.97)	0.47 (0.11 to 4.75)	0.49 (0.12 to 5.03)
MIR	0.83 (0.40 to 2.08)	…	0.84 (0.42 to 2.06)	0.84 (0.41 to 2.08)
NEF	0.49 (0.21 to 1.39)	…	0.49 (0.22 to 1.34)	0.48 (0.21 to 1.38)
NOR	0.76 (0.28 to 3.41)	0.75 (0.26 to 3.32)	0.76 (0.28 to 3.05)	0.78 (0.28 to 3.22)
PST	0.08 (0.01 to 8.45)	0.02 (0.02 to 9.96)	…	0.04 (0.01 to 8.91)
PAR	1.30 (0.81 to 2.27)	1.30 (0.77 to 2.44)	1.29 (0.82 to 2.19)	1.30 (0.82 to 2.27)
Pill-PBO+CBT	0.68 (0.25 to 2.75)	0.66 (0.23 to 2.89)	0.82 (0.29 to 3.82)	0.83 (0.29 to 3.85)
Psy-PBO	1.66 (0.71 to 5.13)	1.63 (0.67 to 5.38)	1.18 (0.47 to 4.13)	1.71 (0.73 to 5.15)
SUP	0.85 (0.29 to 3.65)	0.86 (0.30 to 3.88)	**0.07 (0.02 to 0.86)**	0.95 (0.33 to 3.96)
SER	1.61 (0.89 to 3.27)	1.58 (0.86 to 3.37)	1.47 (0.78 to 3.13)	1.55 (0.85 to 3.19)
SER+CBT	1.74 (0.68 to 6.03)	1.73 (0.66 to 6.57)	…	1.47 (0.54 to 5.43)

TAU	1.50 (0.60 to 5.45)	1.49 (0.58 to 5.71)	0.50 (0.14 to 3.59)	1.35 (0.53 to 4.67)
VEN	1.12 (0.53 to 2.69)	1.13 (0.50 to 3.17)	1.13 (0.56 to 2.62)	1.13 (0.54 to 2.75)
VEN+CBT	0.65 (0.13 to 12.41)	0.62 (0.13 to 12.76)	0.78 (0.17 to 15.49)	0.80 (0.16 to 16.13)
VIL	0.59 (0.27 to 1.54)	0.57 (0.25 to 1.68)	0.59 (0.29 to 1.48)	0.58 (0.27 to 1.54)
WL	1.40 (0.58 to 4.54)	1.40 (0.55 to 5.19)	1.16 (0.37 to 5.97)	1.41 (0.58 to 4.44)

*OR<1 indicate superiority of the specific intervention against placebo control

APPENDIX 16

Treatment ranking and SUCRA plot for each outcome

Treatment ranking and SUCRA plot for mean overall change in depressive symptoms

Treatment ranking:

Rank	Treatments	SUCRA (%)	Rank	Treatments	SUCRA (%)
1	IMP+CBT	89.1%	17	VIL	51.4%
2	FLU+CBT	87.3%	18	FT	49.5%
3	Pill-PBO+CBT	81.0%	19	IMP	47.8%
4	FLU	79.8%	20	Pill-PBO	43.7%
5	DES	71.0%	21	VEN+CBT	43.2%
6	IPT	70.4%	22	AMI	43.1%
7	VEN	62.0%	23	CBT	42.7%
8	MIR	60.3%	24	SUP	41.5%
9	PST	59.9%	25	SER+CBT	39.9%
10	DUL	59.5%	26	CLO	31.3%
11	CIT	56.9%	27	TAU	28.9%
12	ESC	56.5%	28	Psy-PBO	26.5%
13	PAR	56.2%	29	DYN	24.7%
14	NEF	54.6%	30	BT	24.7%
15	DEV	53.5%	31	WL	5.4%
16	SER	53.4%	32	NOR	4.3%

***** Larger SUCRAs denote more effective interventions.
AMI=Amitriptyline. BT=Behavioural therapy. CBT=Cognitive-behavioural therapy. CIT=Citalopram. CLO=Clomipramine. DYN=Psychodynamic therapy. DES=Desipramine. DEV=Desvenlafaxine. DUL=Duloxetine. ESC=Escitalopram. FT=Family therapy. FLU=Fluoxetine. IPT=Interpersonal therapy. IMP=Imipramine. MIR=Mirtazapine. NEF=Nefazodone. NOR=Nortriptyline. PST=Problem-solving therapy. PAR=Paroxetine. Pill-PBO=Pill placebo. Psy-PBO=Psychological placebo. SUP=Supportive therapy. SER=Sertraline. TAU= Treatment as usual. VEN=Venlafaxine. VIL=Vilazodone. WL= Waitlist.

Cumulative probability plots (Random Effects model):

Treatment ranking and SUCRA plot for all-cause discontinuation

Treatment ranking:

Rank	Treatments	SUCRA (%)	Rank	Treatments	SUCRA (%)
1	NEF	84.9%	17	VEN+CBT	49.1%
2	VIL	79.9%	18	VEN	48.5%
3	FLU	75.1%	19	PAR	42.7%
4	IMP+CBT	74.0%	20	FT	40.1%
5	PST	72.8%	21	ESC	37.9%
6	FLU+CBT	72.4%	22	AMI	36.6%
7	Pill-PBO+CBT	67.4%	23	BT	35.3%
8	DEV	66.3%	24	WL	35.0%
9	IPT	65.3%	25	DYN	33.4%
10	MIR	64.7%	26	TAU	31.1%
11	NOR	61.4%	27	SER	30.5%
12	Pill-PBO	61.1%	28	Psy-PBO	26.4%
13	CIT	59.1%	29	CLO	25.8%
14	SUP	57.7%	30	SER+CBT	25.4%
15	DUL	55.3%	31	DES	18.1%
16	CBT	53.1%	32	IMP	13.7%

*****Larger SUCRAs denote less discontinuous interventions.
AMI=Amitriptyline. BT=Behavioural therapy. CBT=Cognitive-behavioural therapy. CIT=Citalopram. CLO=Clomipramine. DYN=Psychodynamic therapy. DES=Desipramine. DEV=Desvenlafaxine. DUL=Duloxetine. ESC=Escitalopram. FT=Family therapy. FLU=Fluoxetine. IPT=Interpersonal therapy. IMP=Imipramine. MIR=Mirtazapine. NEF=Nefazodone. NOR=Nortriptyline. PST=Problem-solving therapy. PAR=Paroxetine. Pill-PBO=Pill placebo. Psy-PBO=Psychological placebo. SUP=Supportive therapy. SER=Sertraline. TAU= Treatment as usual. VEN=Venlafaxine. VIL=Vilazodone. WL= Waitlist.

Cumulative probability plots (Random Effects model):

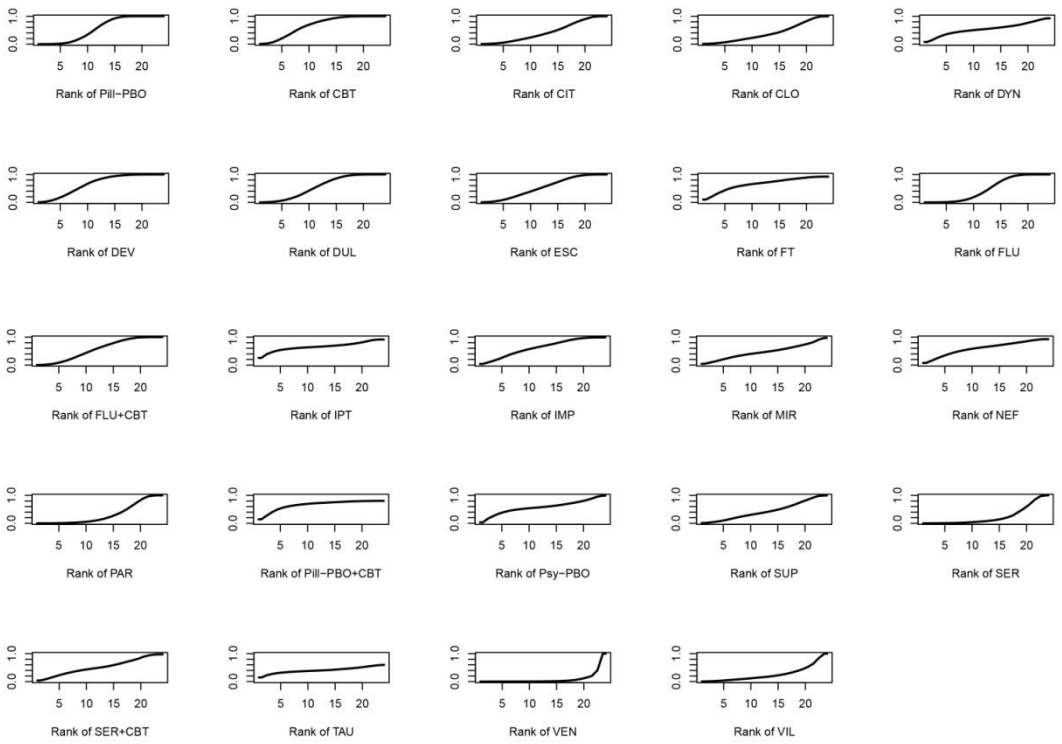
Treatment ranking and SUCRA plot for suicidality

Treatment ranking:

Rank	Treatments	SUCRA (%)	Rank	Treatments	SUCRA (%)
1	Pill-PBO+CBT	82.4%	13	Pill-PBO	51.8%
2	TAU	78.3%	14	SER+CBT	50.6%
3	IPT	70.3%	15	ESC	49.9%
4	FT	69.9%	16	MIR	46.4%
5	CBT	63.9%	17	FLU	44.4%
6	NEF	63.6%	18	SUP	39.8%
7	DEV	62.7%	19	CIT	39.3%
8	IMP	59.5%	20	CLO	36.2%
9	DYN	57.9%	21	PAR	27.3%
10	Psy-PBO	54.7%	22	VIL	21.6%
11	DUL	53.0%	23	SER	19.8%
12	FLU+CBT	52.1%	24	VEN	4.5%

***** Larger SUCRAs denote safer interventions.
CBT=Cognitive-behavioural therapy. CIT=Citalopram. CLO=Clomipramine. DYN=Psychodynamic therapy. DEV=Desvenlafaxine. DUL=Duloxetine. ESC=Escitalopram. FT=Family therapy. FLU=Fluoxetine. IPT=Interpersonal therapy. IMP=Imipramine. MIR=Mirtazapine. NEF=Nefazodone. NOR=Nortriptyline. PAR=Paroxetine. Pill-PBO=Pill placebo. Psy-PBO=Psychological placebo. SUP=Supportive therapy. SER=Sertraline. TAU=Treatment as usualVEN=Venlafaxine. VIL=Vilazodone.

Cumulative probability plots (Random Effects model):



APPENDIX 17

Evaluation of the credibility of each outcome using CINeMA approach

We evaluated the confidence in network estimates for each direct comparison, camparisons with Pill-PBO, and significant comparisons in primary and secondary outcomes according to the following domains: within-study bias, imprecision, heterogeneity, incoherence, indirectness and across-study bias. We used the Confidence In Network Meta-Analysis (CINeMA) software (https://cinema.ispm.unibe.ch/), which is based on the framework developed by Salanti G et al (PLoS One 2014; 9(7): e99682) and refined by Nikolakopoulou et al (bioRxiv 2019; 597047). We assigned 'no concerns', 'some concerns' or 'major concerns' to each network estimate and domain based on the criteria described in the CINeMA documentation and those reported below for each domain. We derived an overall judgment of the confidence that goes from high to very low considering all domains judgments jointly.

(1) Within-study bias: We assigned score 1 to study with low risk of bias, score 2 for moderate risk of bias and 3 for high risk of bias. The risk of bias of each study is reported in **Appendix 7**. We summarised the risk of bias across studies for the comparisons of interest by using the 'average' risk of bias. We assigned 'some concerns' to network estimates when more than 50% of contribution of studies to network estimates was from studies with moderate risk of bias, and "major concerns" when more than 50% of contribution was from studies with high risk of bias and 'no concerns' otherwise. The contribution matrix reporting the contribution of each study to each network estimate and the bar graph presenting the study risk of bias proportional to the percentage contribution are in DOI: 10.17632/kw6nmfn2tb.1. In the bar graph, the bars of each study are coloured according to the study risk of bias (green for low, yellow for unclear and red for high risk of bias).

(2) Imprecision: We judged the imprecision of the network estimates considering whether confidence intervals of network estimates (see **Figure 3** and **Appendix 10**) crossed the values of clinically meaningful difference. We considered a clinically meaningful threshold for SMD to be -0.20 or 0.20, and for OR to be 0.80 or 1.25. The specific criteria used to judge imprecision are reported in the explanatory document within CINeMA. For example, if the upper limit (or the lower limit) of the confidence interval of a network estimate for a continuous outcome was below -0.2 (or above 0.2) we assigned 'no concerns' to the estimate for imprecision.

(3) Heterogeneity: We judged heterogeneity considering the agreement of conclusions based on confidence and prediction intervals output by OpenBUGS (shown at DOI: 10.17632/kw6nmfn2tb.1) as described in the CINeMA documentation. We used the clinically meaningful thresholds defined in Imprecision.For example, if the upper limit (or the lower limit) of both the confidence interval and prediction interval of a network estimate for a continuous outcome were below -0.2 (or above 0.2) we assigned 'no concerns' to the estimate for heterogeneity.

(4) Incoherence: We judged incoherence based on whether the agreement between direct and indirect evidence had an impact on the clinical conclusion and on the p value of the design-by-treatment methods for estimates with only direct or indirect evidence (see **Appendix 13**) as described in Nikolakopoulou et al (bioRxiv 2019;597047).

(5) Indirectness: We assigned score 1 to study with low indirectness, score 2 for moderate indirectness and 3 for high indirectness. We considered two aspects to assign the scores. First, as for the results of meta-regression, we found depressive symptoms in baseline were associated with a larger reduced

depression score. Thus, we assigned score 2 to those studies with lower or higher baseline depressive symptoms (out of the 95% reference interval of baseline depressive symptoms). In particular, we assigned score 2 to study *Goodyer 2017* and *Poole 2018* for higher baseline depressive symptoms, and to study *Mandoki 1997* and *Luby 2012* for lower baseline depressive symptoms. The transforming score of baseline in each study is reported in **Table 1**. Second, the assessment of transitivity (see **Appendix 12**) suggested there were a few comparisons that had relatively low or high values, so we assigned score 2 to studies for which the comparison had extreme value. In particular, we assigned score 2 to this tudy *Charkhandeh 2016* for higher baseline depressive symptoms in CBT vs. WL comparison, to the study *Findling 2009* for lower sex ratio of participants in Flu vs. Pill-PBO comparison, to *Trowell 2007* for higher treatment duration in DYN vs. FT comparison. All the other studies were rated as score 1. We summarised the indirectness across studies for the comparisons of interest by using the 'average' indirectness, similarly to within-study bias. The bar graph presenting the study indirectness proportional to the percentage contribution is reported in DOI: 10.17632/kw6nmfn2tb.1.

(6) Across-study bias: We considered the comprehensiveness of our search strategy and the potential presence of asymmetry by the visual inspection of the comparison-adjusted funnel plots (see **Appendix 14**). We considered our search strategy comprehensive. The comparison-adjusted funnel plots of the network meta-analysis were suggestive of obvious publication bias for efficacy outcome, of which mainly resulted from psychotherapy trials, but not for acceptability and suicide-related outcomes. We assigned 'suspected' to the comparisons with psychotherapies vs. control conditions for efficacy. All the other comparisons of interest for across-study bias were assigned 'undetected'.

a. The confidence in SMD for mean overall change in depressive symptoms for camparisons with Pill-PBO, directed comparisons and significant comparisons by CINeMA approach

Comparison	Within-study bias	Imprecision	Heterogeneity	Incoherence	Indirectness	Across-studies bias	Downgrading	Confidence rating
AMI vs Pill-PBO	Some concerns	Major concerns	No concerns	Major concerns	No concerns	Undetected	-1* within-study bias, -1* imprecision, -1* incoherence	Very low
CBT vs Pill-PBO	Major concerns	Major concerns	No concerns	No concerns	No concerns	Suspected	-2* within-study bias, -2* imprecision, -1* across-studies bias	Very low
CIT vs Pill-PBO	Major concerns	Major concerns	No concerns	Major concerns	No concerns	Undetected	-2* within-study bias, -1* imprecision, -1* incoherence	Very low
DES vs Pill-PBO	Some concerns	Major concerns	No concerns	Major concerns	No concerns	Undetected	-1* within-study bias, -1* imprecision, -1* incoherence	Very low
DEV vs Pill-PBO	No concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* imprecision	Low
DUL vs Pill-PBO	No concerns	Major concerns	No concerns	Some concerns	No concerns	Undetected	-1* imprecision, -1* incoherence	Low
ESC vs Pill-PBO	Some concerns	Major concerns	No concerns	Major concerns	No concerns	Undetected	-1* within-study bias, -1* imprecision, -1* incoherence	Very low
FLU vs Pill-PBO	Some concerns	No concerns	Major concerns	Some concerns	No concerns	Undetected	-1* within-study bias, -1* heterogeneity, -1* incoherence	Very low
FLU+CBT vs Pill-PBO	Some concerns	No concerns	Major concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* heterogeneity	Very low
IMP vs Pill-PBO	No concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* imprecision	Low
MIR vs Pill-PBO	Major concerns	Major concerns	No concerns	Major concerns	No concerns	Undetected	-2* within-study bias, -1* imprecision, -1* incoherence	Very low

NEF vs Pill-PBO	Some concerns	Major concerns	No concerns	Major concerns	No concerns	Undetected	-1* within-study bias, -1* imprecision, -1* incoherence	Very low
NOR vs Pill-PBO	Some concerns	No concerns	Some concerns	Major concerns	No concerns	Undetected	-1* within-study bias, -1* heterogeneity, -1* incoherence	Very low
PAR vs Pill-PBO	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
SER vs Pill-PBO	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
VEN vs Pill-PBO	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
VIL vs Pill-PBO	No concerns	Major concerns	No concerns	Major concerns	No concerns	Undetected	-1* imprecision, -1* incoherence	Low
BT vs Pill-PBO	Major concerns	Major concerns	No concerns	Major concerns	No concerns	Suspected	-2* within-study bias, -1* imprecision, -1* incoherence, -1* across-studies bias	Very low
CLO vs Pill-PBO	No concerns	Major concerns	No concerns	Major concerns	No concerns	Undetected	-1* imprecision, -1* incoherence	Low
DYN vs Pill-PBO	Major concerns	Major concerns	No concerns	Major concerns	No concerns	Suspected	-2* within-study bias, -1* imprecision, -1* incoherence, -1* across-studies bias	Very low
FT vs Pill-PBO	Major concerns	Major concerns	No concerns	Major concerns	No concerns	Suspected	-2* within-study bias, -1* imprecision, -1* incoherence, -1* across-studies bias	Very low
IPT vs Pill-PBO	Major concerns	Major concerns	No concerns	Major concerns	No concerns	Suspected	-2* within-study bias, -1* imprecision, -1* incoherence, -1* across-studies bias	Very low
IMP+CBT vs Pill-PBO	Some concerns	Major concerns	No concerns	Major concerns	No concerns	Undetected	-1* within-study bias, -1* imprecision, -1* incoherence	Very low

PST vs Pill-PBO	Major concerns	Major concerns	No concerns	Major concerns	No concerns	Suspected	-2* within-study bias, -1* imprecision, -1* incoherence, -1* across-studies bias	Very low
Pill-PBO+CBT vs Pill-PBO	Some concerns	Major concerns	No concerns	Major concerns	No concerns	Undetected	-1* within-study bias, -1* imprecision, -1* incoherence	Very low
Psy-PBO vs Pill-PBO	Major concerns	Major concerns	No concerns	Major concerns	No concerns	Undetected	-2* within-study bias, -1* imprecision, -1* incoherence	Very low
SUP vs Pill-PBO	Major concerns	Major concerns	No concerns	Major concerns	No concerns	Suspected	-2* within-study bias, -1* imprecision, -1* incoherence, -1* across-studies bias	Very low
SER+CBT vs Pill-PBO	Major concerns	Major concerns	No concerns	Major concerns	No concerns	Undetected	-2* within-study bias, -1* imprecision, -1* incoherence	Very low
TAU vs Pill-PBO	Major concerns	Major concerns	No concerns	Major concerns	No concerns	Undetected	-2* within-study bias, -1* imprecision, -1* incoherence	Very low
VEN+CBT vs Pill-PBO	Some concerns	Major concerns	No concerns	Major concerns	No concerns	Undetected	-1* within-study bias, -1* imprecision, -1* incoherence	Very low
WL vs Pill-PBO	Major concerns	No concerns	Major concerns	Major concerns	No concerns	Undetected	-2* within-study bias, -1* heterogeneity, -1* incoherence	Very low
BT vs Psy-PBO	Major concerns	Major concerns	No concerns	Major concerns	No concerns	Suspected	-2* within-study bias, -1* imprecision, -1* incoherence, -1* across-studies bias	Very low
BT vs SUP	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
CBT vs DYN	Major concerns	Major concerns	No concerns	No concerns	Some concerns	Undetected	-2* within-study bias, -2* imprecision, -1* indirectness	Very low

CBT vs FT	Major concerns	Major concerns	No concerns	Some concerns	No concerns	Undetected	-2* within-study bias, -1* imprecision, -1* incoherence	Very low
CBT vs FLU	Major concerns	Some concerns	Some concerns	No concerns	No concerns	Undetected	-2* within-study bias, -1* imprecision, -1* heterogeneity	Very low
CBT vs FLU+CBT	Major concerns	No concerns	Major concerns	Major concerns	No concerns	Undetected	-2* within-study bias, -1* heterogeneity, -1* incoherence	Very low
CBT vs IPT	Major concerns	Some concerns	Some concerns	No concerns	No concerns	Undetected	-2* within-study bias, -1* imprecision, -1* heterogeneity	Very low
CBT vs Psy-PBO	Major concerns	Some concerns	Some concerns	No concerns	No concerns	Suspected	-2* within-study bias, -1* imprecision, -1* heterogeneity, -1* across-studies bias	Very low
CBT vs SUP	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
CBT vs SER	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
CBT vs SER+CBT	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
CBT vs TAU	Major concerns	Major concerns	No concerns	No concerns	No concerns	Suspected	-2* within-study bias, -2* imprecision, -1* across-studies bias	Very low
CBT vs WL	Major concerns	No concerns	Some concerns	No concerns	No concerns	Suspected	-2* within-study bias, -1* heterogeneity, -1* across-studies bias	Very low
CLO vs PAR	No concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* imprecision	Low
DYN vs FT	Major concerns	Major concerns	No concerns	No concerns	Some concerns	Undetected	-2* within-study bias, -2* imprecision, -1* indirectness	Very low
DYN vs Psy-PBO	Major concerns	Major concerns	No concerns	No concerns	Some concerns	Suspected	-2* within-study bias, -2* imprecision, -1* indirectness, -1*	Very low

							across-studies bias	
DEV vs FLU	No concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* imprecision	Low
DUL vs FLU	No concerns	Major concerns	No concerns	Some concerns	No concerns	Undetected	-1* imprecision, -1* incoherence	Low
FT vs Psy-PBO	Major concerns	Major concerns	No concerns	No concerns	Some concerns	Suspected	-2* within-study bias, -2* imprecision, -1* indirectness, -1* across-studies bias	Very low
FT vs SUP	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
FT vs TAU	Major concerns	Major concerns	No concerns	No concerns	No concerns	Suspected	-2* within-study bias, -2* imprecision, -1* across-studies bias	Very low
FT vs WL	Major concerns	No concerns	Some concerns	No concerns	No concerns	Suspected	-2* within-study bias, -1* heterogeneity, -1* across-studies bias	Very low
FLU vs FLU+CBT	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
FLU vs NOR	Some concerns	No concerns	No concerns	Major concerns	No concerns	Undetected	-1* within-study bias, -2* incoherence	Very low
FLU vs VEN	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
FLU+CBT vs Pill-PBO+CBT	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
IPT vs Psy-PBO	Major concerns	No concerns	Major concerns	No concerns	No concerns	Suspected	-2* within-study bias, -2* heterogeneity, -1* across-studies bias	Very low
IPT vs TAU	Major concerns	No concerns	Major concerns	No concerns	No concerns	Suspected	-2* within-study bias, -2* heterogeneity, -1* across-studies bias	Very low
IPT vs WL	Major concerns	No concerns	Some concerns	No concerns	No concerns	Suspected	-2* within-study bias, -1* heterogeneity, -1* across-studies bias	Very low
IMP vs PAR	No concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* imprecision	Low

IMP+CBT vs Pill-PBO+CBT	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
PST vs WL	Major concerns	No concerns	Major concerns	No concerns	No concerns	Suspected	-2* within-study bias, -2* heterogeneity, -1* across-studies bias	Very low
Pill-PBO+CBT vs SER+CBT	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
Pill-PBO+CBT vs VEN+CBT	Major concerns	Major concerns	No concerns	No concerns	Some concerns	Undetected	-2* within-study bias, -2* imprecision, -1* indirectness	Very low
SER vs SER+CBT	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
DYN vs FLU+CBT	Major concerns	No concerns	Major concerns	Major concerns	No concerns	Undetected	-2* within-study bias, -1* heterogeneity, -1* incoherence	Very low
FLU vs Psy-PBO	Major concerns	No concerns	Major concerns	Major concerns	No concerns	Undetected	-2* within-study bias, -1* heterogeneity, -1* incoherence	Very low
FLU vs WL	Major concerns	No concerns	No concerns	Major concerns	No concerns	Undetected	-2* within-study bias, -2* incoherence	Very low
FLU+CBT vs Psy-PBO	Major concerns	No concerns	Major concerns	Major concerns	No concerns	Undetected	-2* within-study bias, -1* heterogeneity, -1* incoherence	Very low
FLU+CBT vs TAU	Major concerns	No concerns	Major concerns	Major concerns	No concerns	Undetected	-2* within-study bias, -1* heterogeneity, -1* incoherence	Very low
FLU+CBT vs WL	Major concerns	No concerns	No concerns	Major concerns	No concerns	Undetected	-2* within-study bias, -2* incoherence	Very low

b. The confidence in OR for all-caused discontinuation for camparisons with Pill-PBO, directed comparisons and significant comparisons by CINeMA approach

Comparison	Within-study bias	Imprecision	Heterogeneity	Incoherence	Indirectness	Across-studies bias	Downgrading	Confidence rating
AMI vs Pill-PBO	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
CBT vs Pill-PBO	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
CIT vs Pill-PBO	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
DES vs Pill-PBO	Some concerns	Some concerns	Some concerns	No concerns	No concerns	Undetected	-1* within-study bias, -1* imprecision, -1* heterogeneity	Very low
DEV vs Pill-PBO	No concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* imprecision	Low
DUL vs Pill-PBO	No concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* imprecision	Low
ESC vs Pill-PBO	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
FLU vs Pill-PBO	Some concerns	Some concerns	Some concerns	No concerns	No concerns	Undetected	-1* within-study bias, -1* imprecision, -1* heterogeneity	Very low
FLU+CBT vs Pill-PBO	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
IMP vs Pill-PBO	No concerns	No concerns	Some concerns	No concerns	No concerns	Undetected	-1* heterogeneity	Moderate
MIR vs Pill-PBO	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
NEF vs Pill-PBO	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
NOR vs Pill-PBO	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
PAR vs Pill-PBO	Some concerns	Some concerns	Some concerns	No concerns	No concerns	Undetected	-1* within-study bias, -1* imprecision, -1* heterogeneity	Very low

SER vs Pill-PBO	Major concerns	Some concerns	Some concerns	No concerns	No concerns	Undetected	-2* within-study bias, -1* imprecision, -1* heterogeneity	Very low
VEN vs Pill-PBO	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
VIL vs Pill-PBO	No concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* imprecision	Low
BT vs Pill-PBO	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
CLO vs Pill-PBO	No concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* imprecision	Low
DYN vs Pill-PBO	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
FT vs Pill-PBO	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
IPT vs Pill-PBO	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
IMP+CBT vs Pill-PBO	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
PST vs Pill-PBO	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
Pill-PBO+CBT vs Pill-PBO	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
Psy-PBO vs Pill-PBO	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
SUP vs Pill-PBO	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
SER+CBT vs Pill-PBO	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
TAU vs Pill-PBO	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
VEN+CBT vs Pill-PBO	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
WL vs Pill-PBO	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
BT vs Psy-PBO	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias,	Very low

							-2* imprecision	
BT vs SUP	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
CBT vs DYN	Major concerns	Major concerns	No concerns	No concerns	Some concerns	Undetected	-2* within-study bias, -2* imprecision, -1* indirectness	Very low
CBT vs FT	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
CBT vs FLU	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
CBT vs FLU+CBT	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
CBT vs IPT	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
CBT vs Psy-PBO	Major concerns	Some concerns	No concerns	Major concerns	Some concerns	Undetected	-2* within-study bias, -1* imprecision, -1* incoherence, -1* indirectness	Very low
CBT vs SUP	Major concerns	Major concerns	No concerns	Some concerns	No concerns	Undetected	-2* within-study bias, -1* imprecision, -1* incoherence	Very low
CBT vs SER	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
CBT vs SER+CBT	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
CBT vs TAU	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
CBT vs WL	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
CLO vs PAR	No concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* imprecision	Low
DYN vs FT	Major concerns	Major concerns	No concerns	No concerns	Some concerns	Undetected	-2* within-study bias, -2* imprecision, -1* indirectness	Very low
DYN vs Psy-PBO	Major concerns	Major concerns	No concerns	Some concerns	Some concerns	Undetected	-2* within-study bias,	Very low

							-1* imprecision, -1* incoherence, -1* indirectness	
DEV vs FLU	No concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* imprecision	Low
DUL vs FLU	No concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* imprecision	Low
FT vs Psy-PBO	Major concerns	Major concerns	No concerns	Some concerns	Some concerns	Undetected	-2* within-study bias, -1* imprecision, -1* incoherence, -1* indirectness	Very low
FT vs SUP	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
FT vs TAU	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
FT vs WL	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
FLU vs FLU+CBT	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
FLU vs NOR	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
FLU vs VEN	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
FLU+CBT vs Pill-PBO+CBT	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
IPT vs Psy-PBO	Major concerns	Some concerns	Some concerns	No concerns	No concerns	Undetected	-2* within-study bias, -1* imprecision, -1* heterogeneity	Very low
IPT vs TAU	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
IPT vs WL	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
IMP vs PAR	No concerns	Some concerns	Some concerns	No concerns	No concerns	Undetected	-1* imprecision, -1* heterogeneity	Low
IMP+CBT vs Pill-PBO+CBT	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low

PST vs WL	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
Pill-PBO+CBT vs SER+CBT	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
Pill-PBO+CBT vs VEN+CBT	Major concerns	Major concerns	No concerns	No concerns	Some concerns	Undetected	-2* within-study bias, -2* imprecision, -1* indirectness	Very low
SER vs SER+CBT	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
DES vs FLU	Some concerns	No concerns	Some concerns	No concerns	No concerns	Undetected	-1* within-study bias, -1* heterogeneity	Low
DES vs NEF	Some concerns	No concerns	Some concerns	No concerns	No concerns	Undetected	-1* within-study bias, -1* heterogeneity	Low
DEV vs IMP	Some concerns	No concerns	Some concerns	No concerns	No concerns	Undetected	-1* within-study bias -1* heterogeneity	Low
FLU vs IMP	Some concerns	No concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias	Moderate
FLU vs SER	Some concerns	No concerns	Major concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* heterogeneity	Very low
FLU+CBT vs IMP	Some concerns	No concerns	Some concerns	No concerns	No concerns	Undetected	-1* within-study bias, -1* heterogeneity	Low
IMP vs NEF	Some concerns	No concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias	Moderate
IMP vs VIL	No concerns	No concerns	No concerns	No concerns	No concerns	Undetected	No downgrade	High
NEF vs SER	Some concerns	No concerns	Some concerns	No concerns	No concerns	Undetected	-1* within-study bias, -1* heterogeneity	Low

AMI=Amitriptyline. BT=Behavioural therapy. CBT=Cognitive-behavioural therapy. CIT=Citalopram. CLO=Clomipramine. CrI=credibility interval. DYN=Psychodynamic therapy. DES=Desipramine. DEV=Desvenlafaxine. DUL=Duloxetine. ESC=Escitalopram. FT=Family therapy. FLU=Fluoxetine. IPT=Interpersonal therapy. IMP=Imipramine. MIR=Mirtazapine. NEF=Nefazodone. NOR=Nortriptyline. PST=Problem-solving therapy. PAR=Paroxetine. Pill-PBO=Pill placebo. Psy-PBO=Psychological placebo. SUP= Supportive therapy. SER=Sertraline. SMD=standardised mean difference. TAU=Treatment as usual. VEN=Venlafaxine. VIL=Vilazodone. WL=Waitlist.

c. The confidence in OR for suicidality for camparisons with Pill-PBO, directed comparisons and significant comparisons by CINeMA approach

Comparison	Within-study bias	Imprecision	Heterogeneity	Incoherence	Indirectness	Across-studies bias	Downgrading	Confidence rating
Pill-PBO vs CBT	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
Pill-PBO vs CIT	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
Pill-PBO vs DEV	No concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* imprecision	Low
Pill-PBO vs DUL	No concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* imprecision	Low
Pill-PBO vs ESC	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
Pill-PBO vs FLU	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
Pill-PBO vs FLU+CBT	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
Pill-PBO vs IMP	No concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* imprecision	Low
Pill-PBO vs MIR	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
Pill-PBO vs NEF	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
Pill-PBO vs PAR	Some concerns	Some concerns	Some concerns	No concerns	No concerns	Undetected	-1* within-study bias, -1* imprecision, -1* heterogeneity	Very low
Pill-PBO vs SER	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
Pill-PBO vs VEN	Major concerns	No concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias	Low
Pill-PBO vs VIL	No concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* imprecision	Low
CBT vs DYN	Major concerns	Major concerns	No concerns	No concerns	Some concerns	Undetected	-2* within-study bias, -2* imprecision, -1* indirectness	Very low

CBT vs FT	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
CBT vs FLU	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
CBT vs FLU+CBT	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
CBT vs IPT	Major concerns	Major concerns	No concerns	No concerns	Some concerns	Undetected	-2* within-study bias, -2* imprecision, -1* indirectness	Very low
CBT vs Psy-PBO	Major concerns	Major concerns	No concerns	No concerns	Some concerns	Undetected	-2* within-study bias, -2* imprecision, -1* indirectness	Very low
CBT vs SUP	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
CBT vs SER	Major concerns	Some concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -1* imprecision	Very low
CBT vs SER+CBT	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
CBT vs TAU	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
CLO vs PAR	No concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* imprecision	Low
DYN vs FT	Major concerns	Major concerns	No concerns	No concerns	Some concerns	Undetected	-2* within-study bias, -2* imprecision, -1* indirectness	Very low
DYN vs Psy-PBO	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
DEV vs FLU	No concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* imprecision	Low
DUL vs FLU	No concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* imprecision	Low
FT vs Psy-PBO	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
FT vs SUP	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
FT vs TAU	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low

FLU vs FLU+CBT	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
FLU vs VEN	Some concerns	No concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias	Moderate
FLU+CBT vs Pill-PBO+CBT	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
IPT vs Psy-PBO	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
IPT vs TAU	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
IMP vs PAR	No concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* imprecision	Low
Pill-PBO+CBT vs SER+CBT	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
SER vs SER+CBT	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
Pill-PBO vs CLO	No concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* imprecision	Low
Pill-PBO vs DYN	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
Pill-PBO vs FT	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
Pill-PBO vs IPT	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
Pill-PBO vs Pill-PBO+CBT	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
Pill-PBO vs Psy-PBO	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
Pill-PBO vs SUP	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
Pill-PBO vs SER+CBT	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
Pill-PBO vs TAU	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
CBT vs VEN	Major concerns	No concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias	Low
CIT vs VEN	Major concerns	No concerns	Some concerns	No concerns	No concerns	Undetected	-2* within-study bias,	Very low

							-1* heterogeneity	
ESC vs VEN	Major concerns	No concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias	Low
DEV vs VEN	Some concerns	No concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias	Morderate
DUL vs VEN	Some concerns	No concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias	Morderate
FLU+CBT vs VEN	Some concerns	No concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias	Morderate
FT vs VEN	Major concerns	No concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias	Low
IMP vs VEN	Some concerns	No concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias	Morderate
Pill-PBO+CBT vs VEN	Some concerns	No concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias	Morderate
VIL vs VEN	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
NEF vs VEN	Major concerns	Some concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -1* imprecision	Very low
SER+CBT vs VEN	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
CLO vs VEN	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
PAR vs VEN	Some concerns	Some concerns	Some concerns	No concerns	No concerns	Undetected	-1* within-study bias, -1* imprecision, -1* heterogeneity	Very low
SUP vs VEN	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
SER vs VEN	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
MIR vs VEN	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
DYN vs VEN	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low
TAU vs VEN	Some concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-1* within-study bias, -2* imprecision	Very low
IPT vs VEN	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low

Psy-PBO vs VEN	Major concerns	Major concerns	No concerns	No concerns	No concerns	Undetected	-2* within-study bias, -2* imprecision	Very low

AMI=Amitriptyline. BT=Behavioural therapy. CBT=Cognitive-behavioural therapy. CIT=Citalopram. CLO=Clomipramine. CrI=credibility interval. DYN=Psychodynamic therapy. DES=Desipramine. DEV=Desvenlafaxine. DUL=Duloxetine. ESC=Escitalopram. FT=Family therapy. FLU=Fluoxetine. IPT=Interpersonal therapy. IMP=Imipramine. MIR=Mirtazapine. NEF=Nefazodone. NOR=Nortriptyline. PST=Problem-solving therapy. PAR=Paroxetine. Pill-PBO=Pill placebo. Psy-PBO=Psychological placebo. SUP= Supportive therapy. SER=Sertraline. SMD=standardised mean difference. TAU=Treatment as usual. VEN=Venlafaxine. VIL=Vilazodone. WL=Waitlist.