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**1. Study and participant characteristics**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Study ID | Country | Age (M) | Min. prior episodes | Prior intervention | Intervention Group | Control Group | Weeks Follow-up | IG events/ IG total | CG events/ CG total | Outcome |
| Bockting 2018 | NL | 47 | 2 | ADM | 1) PCT + tapering,  2) PCT + ADM | ADM | 104 | 1) 54/85,  2) 44/104 | 60/100 | SCID |
| Brakelmeier 2014 | DE | 62.5 | 1 | ECT + ADM | CBT +ADM | ADM (+anti-psychotics) | 52 | 6/17 | 12/18 | HAM-D |
| Frank 1990 | USA | 39.5 | 3 | IPT + ADM | 1) IPT  2) IPT + ADM | ADM | 156 | 1) 6/25  2) 16/26 | 6/28 | HRSD |
| Huijbers 2015 | NL | 52 | 3 | ADM | MBCT +AD | ADM | 65 | 12/33 | 13/35 | SCID |
| Jarrett 2013 | USA | 43 | 1 | CT | C-CT | ADM | 104 | 40/86 | 35/86 | SCID |
| Kuyken 2008 | UK | 49 | 3 | ADM | MBCT + tapering | ADM | 65 | 29/61 | 37/62 | SCID |
| Kuyken 2015 | UK | 50 | 3 | ADM | MBCT + tapering | ADM | 104 | 94/212 | 100/212 | SCID |
| Paykel 2005 | UK | 43 | 2 | ADM | CBT + ADM | ADM | 235 | 60/80 | 65/78 | BDI/HAM-D |
| Perlis 2002 | USA | 40 | 3 | ADM | CBT + ADM | ADM | 28 | 4/66 | 5/66 | HAM-D |
| Petersen 2007 | USA | 44 | 3 | ADM | CBT + ADM | ADM | 80 | 4/11 | 4/14 | HAM-D |
| Segal 2010 | CA | 44 | 2 | ADM | MBCT + tapering | ADM | 78 | 10/26 | 13/28 | SCID |

NL = Netherlands, USA = United States of America, CA = Canada, DE = Germany, UK = United Kingdom; CT = Cognitive Therapy, ADM = Antidepressant medication, IPT = Interpersonal Therapy, ECT = Electroconvulsive Therapy, PCT = Preventative Cognitive Therapy, MBCT = Mindfulness Based Cognitive Therapy, CBT = Cognitive Behavioral Therapy, C-CT = Continuation Cognitive Therapy; SCID = Structured Clinical Interview for DSM-IV, BDI = Beck Depression Inventory, HAM-D = Hamilton Depression Rating Scale, HDRS = Hamilton Rating Scale for Depression; NA = Not Applicable (not specified). \* in Brakemeier 2014 both relapse and dropouts were counted as events

**2. Intervention characteristics**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Study** | **Therapy type** | **Brief description** | **Intervention provider** | **Delivery setting** | **Length (weeks)** | **Setting** |
|  |  |  |  |  |  |  |
| Bockting, 2018 | PCT | Identifying dysfunctional attitudes and schemas, teaching patients to challenge schemas, activating positive affect, enhancing specific memories of positive experiences, formulating specific prevention strategies | Trained CBT therapists | Group OR individual | 8 | Multicenter |
|  |  |  |  |  |  |  |
| Brakelmeier 2014 | CBT | *EFFECTiv*, a CBT approach augmented with the situational analysis technique described in the Cognitive Behavioral Analysis System of Psychotherapy. | Psychotherapists | Group setting | 15 | Mental health center (inpatient) |
|  |  |  |  |  |  |  |
| Frank, 1990 | IPT | Interpersonal therapy maintenance without medication, with medication or with placebo | Trained therapist | Face-to-face | 17 | Outpatient Clinic |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
| Huijbers, 2015 | MBCT | Formal meditation exercises (body scan, sitting meditation, walking meditation and mindful movement). Cognitive-behavioral techniques (education, monitoring and scheduling of activities, identification of negative automatic thoughts, and devising a relapse prevention plan). Guided meditation at home | MBCT teacher | Group + home meditation | 8 | University mental health centers |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
| Jarrett, 2013 | CBT | Continuation Cognitive Therapy. Compensatory skills in response to emotional distress, residual, and emerging depressive symptoms. Pre-emptive coping strategies were practiced | Trained therapist | Face-to-face | 32 | University clinic |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
| Kuyken, 2008 | MBCT | MBCT aiming to enable people to learn to become more aware of bodily sensations, thoughts and feelings associated with depressive relapse and to relate constructively to these experiences (e.g., target self-critical thinking and avoidance) | Trained Therapist | Group + Homework Exercises | 8 | Primary care |
|  |  |  |  |  |  |  |
| Kuyken, 2015 | MBCT | Mindfulness practices and CBT skills through sessions & homework. Therapists teach patients to respond adaptively to thoughts, feelings, and experiences that might otherwise have triggered depressive relapse | Trained Therapist & Physician | Group + Homework Exercises | 8 | Primary care |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
| Paykel, 2005, 1999 | CBT | Case formulation and generation of an individualized problem list, cognitive and behavioral strategies to resolve problems. Modification of underlying beliefs and self-management techniques to prevent relapse. Techniques for engagement in CT and schema-focused approaches were permitted | Trained Therapist | NA | 20 | University clinics |
|  |  |  |  |  |  |  |
| Perlis, 2002 | CBT | Manual adapted from Beck. Specifically addressing residual symptoms, enhancing patient coping skills. | Trained Psychotherapist (doctorate level) | Face-to-face | 26 | Outpatient clinic |
|  |  |  |  |  |  |  |
| Petersen, 2007 | CBT | Symptom check, agenda setting, homework review, cognitive and behavioral exercises for specific problem areas, and assignment of new homework | Therapist (doctorate level) | Face-to-face | 80 | General Hospital |
|  |  |  |  |  |  |  |
| Segal, 2010 | MBCT | Mindfulness practices and CBT-based exercises, homework (taped awareness exercises) | Trained Psychologist/Social Worker | Group, Homework Exercises | 8 | Mental health center and community |
|  |  |  |  |  |  |  |

CT = Cognitive Therapy, ADM = Antidepressant medication, IPT = Interpersonal Therapy, ECT = Electroconvulsive Therapy, PCT = Preventative Cognitive Therapy, MBCT = Mindfulness Based Cognitive Therapy, CBT = Cognitive Behavioral Therapy, C-CT = Continuation Cognitive Therapy; NA = Not Applicable (not specified).

**3. Risk of Bias – Psychological interventions with and without ADM**

A screenshot of a cell phone

Description automatically generated

**4. Risk of Bias – Individual Study Ratings**

A picture containing food

Description automatically generated

**5. Search strings**

**PubMed**

((((((("depressive disorder"[MeSH Terms] OR "depression"[MeSH Terms] OR depress\*[Title/Abstract] OR affective disorder[Title/Abstract] OR affective disorders[Title/Abstract] OR dysphoria[Title/Abstract] OR dysthymia[Title/Abstract] OR depressed mood[Title/Abstract]) OR mood disorder[Title/Abstract]))) AND (("recurrence"[MeSH Terms]) OR ("recur\*"[Title/Abstract]) OR ("chroni\*"[Title/Abstract]) OR (relaps\*[Title/Abstract]) OR ("remi\*"[Title/Abstract]) OR ("treatment resistant"[Title/Abstract]))) OR (("recurrent depression"[MeSH Terms]) OR ("treatment resistant depression"[Title/Abstract])))) AND ("secondary prevention"[MeSH Terms] OR "prevention"[MeSH] OR "preventive [MeSH Terms]" OR "maintenance"[Title/Abstract]) OR ("continuation"[Title/Abstract]) OR ("prophyla\*"[Title/Abstract]) AND (("randomized controlled trial"[Publication Type] OR controlled clinical trial[Title/Abstract] OR random\*[Title/Abstract] OR prevention and control[Title/Abstract]))

**The Cochrane Library**

ID Search

#1 "depression"

#2 depress\* in Cochrane Reviews (Reviews and Protocols), Other Reviews, Trials, Methods Studies, Technology Assessments and Economic Evaluations

#3 "affective" in Cochrane Reviews (Reviews and Protocols), Other Reviews, Trials, Methods Studies, Technology Assessments and Economic Evaluations

#4 affective disorders in Cochrane Reviews (Reviews and Protocols), Other Reviews, Trials, Methods Studies, Technology Assessments and Economic Evaluations

#5 dysphoria

#6 dysthymia

#7 "mood disorder"

#8 "depressed mood"

#9 "recur\*"

#10 "chroni\*"

#11 "relaps\*"

#12 "remi\*"

#13 "treatment resistant"

#14 "secondary prevention study":ti,ab,kw (Word variations have been searched)

#15 "prevention":ti,ab,kw (Word variations have been searched)

#16 "maintenance":ti,ab,kw (Word variations have been searched)

#17 "prophylaxis":ti,ab,kw (Word variations have been searched)

#18 "continuation":ti,ab,kw (Word variations have been searched)

#19 "randomised control trial":ti,ab,kw (Word variations have been searched)

#20 "randomized controlled trial":ti,ab,kw (Word variations have been searched)

#21 "controlled clinical trial":ti,ab,kw (Word variations have been searched)

#22 "prevention and control":ti,ab,kw

#23 random\*:ti,ab,kw

#24 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8

#25 #9 or #10 or #11 or #12 or #13

#26 #14 or #15 or #16 or #17 or #18

#27 #19 or #20 or #21 or #23

#28 #24 and #25 and #26 and #27 in Cochrane Reviews (Reviews and Protocols), Other Reviews, Trials, Methods Studies, Technology Assessments and Economic Evaluations

**EMBASE**

(('treatment resistant depression'/exp OR (('depression'/exp OR 'depression' OR depress\*:ab,ti OR 'affective disorder\*':ab,ti OR 'dysphoria'/exp OR 'dysthymia'/exp OR 'depressed mood':ab,ti OR 'mood disorder'/exp) AND ('recurrent disease'/exp OR 'relapse'/exp OR 'chronic depression'/exp OR remitted OR 'remission'/exp OR 'recur\*':ab,ti OR 'relaps\*':ab,ti OR 'chroni\*':ab,ti))) AND ('secondary prevention'/exp OR 'prevention'/exp OR 'maintenan\*':ab,ti OR 'prophyla\*':ab,ti OR 'continuation':ab,ti) AND ('randomized controlled trial'/exp OR 'controlled clinical trial'/exp OR 'random\*':ti,ab OR 'prevention and control'/exp)) AND ('article'/it OR 'article in press'/it)

**PSYCHINFO**

|  |  |
| --- | --- |
| Participants 1. Depression | major depression/ or depress\*.ti,ab. |
| Participants 2. Mood Disorder | affective disorder.ti,ab. or affective disorders.ti,ab. or dysphoria.ti,ab. or dysthymia.ti,ab. or depressed mood. ti,ab. or mood disorder. ti,ab |
| Participants 3. Remitting/recurring nature | exp Chronic Mental Illness/ or  exp "Relapse (Disorders)"/ or exp "Remission (Disorders)"/ or symptom remission/ or recur$. ti,ab. or chronic. ti,ab. or relaps$. ti,ab. or remi$. ti,ab. |
| OR | OR recurrent depression/ |
| Intervention | or relapse prevention/ or prevention or secondary prevention |
| Intervention 2. Subset of interentions | exp Maintenance Therapy/ or continuation. ti,ab. |
| Randomised | (randomized controlled trial or controlled clinical trial or randomly).mp. or exp clinical trials/ or randomised.mp. or randomized.mp. |

**6. Full reference list of included studies**

1 Segal Z V, Bieling P, Young T, *et al.* Antidepressant monotherapy vs sequential pharmacotherapy and mindfulness-based cognitive therapy, or placebo, for relapse prophylaxis in recurrent depression. *Arch Gen Psychiatry* 2010; **67**: 1256–64.

2 Huijbers MJ, Spinhoven P, Spijker J, *et al.* Adding mindfulness-based cognitive therapy to maintenance antidepressant medication for prevention of relapse/recurrence in major depressive disorder: Randomised controlled trial. *J Affect Disord* 2015; **187**: 54–61.

3 Bockting CLH, Klein NS, Elgersma HJ, *et al.* Effectiveness of preventive cognitive therapy while tapering antidepressants versus maintenance antidepressant treatment versus their combination in prevention of depressive relapse or recurrence (DRD study): a three-group, multicentre, randomised control. *The Lancet Psychiatry* 2018; **0366**: 1–10.

4 Frank E, Kupfer DJ, Perel JM, *et al.* Three-Year Outcomes for Maintenance Therapies in Recurrent Depression. *Arch Gen Psychiatry* 1990; **47**: 1093–9.

5 Brakemeier E-L, Merkl A, Wilbertz G, *et al.* Cognitive-behavioral therapy as continuation treatment to sustain response after electroconvulsive therapy in depression: A randomized controlled trial. Biol. Psychiatry. 2014; **76**: 194–202.

6 Paykel ES, Scott J, Cornwall PL, *et al.* Duration of relapse prevention after cognitive therapy in residual depression: Follow-up of controlled trial. *Psychol Med* 2005; **35**: 59–68.

7 Petersen TJ, Pava JA, Buchin J, *et al.* The role of cognitive-behavioral therapy and fluoxetine in prevention of recurrence of major depressive disorder. *Cognit Ther Res* 2007; **34**: 13–23.

8 Kuyken W, Byford S, Taylor RS, *et al.* Mindfulness-based cognitive therapy to prevent relapse in recurrent depression. *J Consult Clin Psychol* 2008; **76**: 966–78.

9 Kuyken W, Hayes R, Barrett B, *et al.* Effectiveness and cost-effectiveness of mindfulness-based cognitive therapy compared with maintenance antidepressant treatment in the prevention of depressive relapse or recurrence (PREVENT): A randomised controlled trial. Lancet. 2015; **386**: 63–73.

10 Perlis RH, Nierenberg AA, Alpert JE, *et al.* The effects of adding cognitive therapy to fluoxetine dose increase on risk of relapse and residual depressive symptoms in continuation treatment of major depressive disorder. *J Clin Psychopharmacol* 2002; **22**: 474–80.

11 Jarrett RB, Minhajuddin A, Gershenfeld H, Friedman ES, Thase ME. Preventing depressive relapse and recurrence in higher-risk cognitive therapy responders: A randomized trial of continuation phase cognitive therapy, fluoxetine, or matched pill placebo. *JAMA Psychiatry* 2013; **70**: 1152–60.