The effects of cognitive-behavior therapy for depression on repetitive negative thinking: A meta-analysis

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Abstract

It is not clear if treatments for depression targeting repetitive negative thinking (RNT: rumination, worry and content-independent perseverative thinking) have a specific effect on RNT resulting in better outcomes than treatments that do not specifically target rumination. We conducted a systematic search of PsycINFO, PubMed, Embase and the Cochrane library for randomized trials in adolescents, adults and older adults comparing CBT treatments for (previous) depression with control groups or with other treatments and reporting outcomes on RNT. Inclusion criteria were met by 36 studies with a total of 3307 participants. At post-test we found a medium-sized effect of any treatment compared to control groups on RNT ($g = 0.48$; 95% CI: 0.37–0.59). Rumination-focused CBT: $g = 0.76$, $< .01$; Cognitive Control Training: $g = 0.62$, $p < .01$; CBT: $g = 0.57$, $p < .01$; Concreteness training: $g = 0.53$, $p < .05$; and Mindfulness-based Cognitive Therapy: $g = 0.42$, $p < .05$ had medium sized and significantly larger effect sizes than other types of treatment (i.e., anti-depressant medication, light therapy, engagement counseling, life review, expressive writing, yoga) ($g = 0.14$) compared to control groups. Effects on RNT at post-test were strongly associated with the effects on depression severity and this association was only significant in RNT-focused CBT. Our results suggest that in particular RNT-focused CBT may have a more pronounced effect on RNT than other types of interventions. Further mediation and mechanistic studies to test the predictive value of reductions in RNT following RNT-focused CBT for subsequent depression outcomes are called for.

Keywords: Meta-analysis; Depression; Rumination; Worry; Repetitive Negative Thinking; Cognitive-Behavior Therapy

Introduction

An influential definition of rumination is provided by response styles theory (RST; Nolen-Hoeksema, 2004). In this view, rumination is characterized by "repetitively focusing on the fact that one is depressed; on one's symptoms of depression; and on the causes, meanings, and consequences of depressive symptoms" (p. 569). This tendency to ruminate about one's feelings and problems is relatively stable over time and expresses itself in perseverating in thinking on problems and associated negative feelings (Moulds, Kandris, Starr, & Wong, 2007; Nolen-Hoeksema, Morrow, & Fredrickson, 1993).

According to RST, rumination is related to the onset, persistence and relapse of depression. People who ruminate about the causes and implications of their symptoms are hypothesized to have a higher chance to become depressed, remain depressed for longer periods of time, and to relapse more quickly. In accordance with this hypothesis, longitudinal research showed that rumination predicts the onset of a subsequent major depressive episode in non-depressed students (Just & Alloy, 1997) and non-depressed community adults (Huffziger, Reinhard, & Kuehner, 2009; Nolen-Hoeksema, 2000), as well as relapse of depression in previously depressed persons (Spinhoven, Drost, de Rooij, van Hemert, & Penninx, 2016), also after taking baseline levels of depression into account. Most likely the association between rumination and depression is reciprocal with rumination predicting subsequent depression and vice versa (Moberly & Watkins, 2008). Still, ruminating about depressive symptoms and problems can be seen as a maladaptive coping response which further exacerbates depressive feelings.

However, the specificity of the relationship of rumination with depression has been questioned. Rumination may greatly overlap with worry. Worry, as a sequence of elaborated verbal thoughts, may be initiated in response to intrusive catastrophic images (Borkovec, Ray, & Stober, 1998). In a similar way, it has been hypothesized that rumination may be

initiated by an intrusive concern over a discrepancy between one's current state and ideal goals in a persistent attempt to resolve unattained goals (Martin & Tesser, 1996). Correlations between measures of rumination and worry are typically high (r = .60–.70) (Calmes & Roberts, 2007). Moreover, trait worry may also be a psychological risk factor for depressive disorders with some studies even finding that patients with generalized anxiety disorder and major depression do not differ in the frequency and intensity of worry (see Olatunji, Wolitzky-Taylor, Sawchuk, & Ciesielski, 2010 for an overview).

Given the high overlap among different measures for worry, rumination and repetitive negative thinking (RNT), a few studies have tried to identify common variance across measures of the construct using structural equation modelling (Arditte, Shaw, & Timpano, 2016; Hur, Heller, Kern, & Berenbaum, 2017; McEvoy & Brans, 2012; Segerstrom, Tsao, Alden, & Craske, 2000; Spinhoven, Drost, van Hemert, & Penninx, 2015). Overall, these studies show that the shared variance of worry, rumination and perseverative thinking scales is very large and that an underlying factor for RNT is associated with severity of depressive and anxiety symptoms (Arditte et al., 2016; Hur et al., 2017; McEvoy & Brans, 2012; Segerstrom et al., 2000; Spinhoven et al., 2015), as well as with individual depressive and anxiety disorders and comorbidity among depressive and among anxiety disorders (Drost, van der Does, van Hemert, Penninx, & Spinhoven, 2014; Spinhoven, van Hemert, & Penninx, 2017; Spinhoven et al., 2015).

In a comprehensive review of RNT across psychological disorders, Ehring and Watkins (2008) concluded that worry and rumination are more similar than different, including the fact that both are repetitive, difficult to control, negative in content, predominantly verbal, and relatively abstract. The only replicated diagnosis-specific differences were reported to be the thought content and temporal orientation, with depressive rumination more likely to be past-oriented and worry more likely to be future-oriented.

Moreover, worry tends to be more strongly associated with anxiety symptoms and rumination more strongly with depressive symptoms (Drost et al., 2012; McLaughlin, Borkovec, & Sibrava, 2007; Nolen-Hoeksema, 1991).

As RNT is involved in the onset, maintenance and relapse of depression, it could be a malleable proximal risk factor open to intervention (Kraemer, Stice, Kazdin, Offord, & Kupfer, 2001). Given the focus of cognitive-behavior therapy (CBT) on identifying and modifying negative thoughts, one would expect that CBT would have been applied to reduce RNT. However, as standard CBT stresses changing dysfunctional cognitions into more adaptive ones using cognitive restructuring and behavioral experiments, changes in RNT have not been regularly assessed in CBT trials. As a result, to date, our knowledge of the effect of CBT on RNT as a process of thinking is quite limited.

Recently, several CBT interventions have been developed that explicitly aim to prevent or reduce psychopathology by specifically targeting RNT (Watkins, 2015). Meta-Cognitive Therapy (MCT) assumes that rumination is initiated by positive metacognitive beliefs about the usefulness of rumination and exacerbated by negative metacognitive beliefs about the negative consequences of rumination (Wells, 2009). Rumination-focused CBT (rf-CBT) conceptualizes rumination as negatively reinforced learned habitual avoidance behavior and clients are coached to identify and control exposure to antecedent cues to rumination and to practice alternative responses to these cues when they do occur. Moreover, they are systematically taught to shift their unconstructive global processing style to a more constructive concrete style (Watkins, 2015). Repeated practice at focusing on the specific details, context, and sequence of events to help dysphoric persons to shift from an abstract and evaluative thinking style to a more helpful and concrete thinking style as a standalone intervention is called Concreteness training (CNT) (Watkins, Baeyens, & Read, 2009).

Mindfulness-based Cognitive Therapy (MBCT) teaches clients experientially to shift their attention to their momentary experiences in a non-judgmental and accepting way. Being mindful to the present is hypothesized to change the habitual patterns of rumination and mood deterioration (Segal, Williams, & Teasdale, 2002).

Moreover, lately, several interventions have been developed based on experimental studies that aim to modify automatic information processes thought to underlie the occurrence of repetitive thoughts and hold promise to treat RNT also in clinical settings. Cognitive Control Training (CCT), Attention Bias Modification (ABM), and Cognitive Bias Modification (CBM) all try to break automatic patterns of selectively processing information. In CCT attentional and working memory processes (e.g. disengagement and updating of information) are trained (De Raedt & Koster, 2010; Siegle, Ghinassi, & Thase, 2007). In ABM attention towards positive relative to negative stimuli is selectively reinforced (Hakamata et al., 2010; Hertel & Mathews, 2011). In CBM clients are taught an automatic bias to positively interpret novel ambiguous information (Hirsch, Meeten, Krahe, & Reeder, 2016; Holmes, Lang, & Shah, 2009). Recent research has begun to examine to what extent these interventions can also help to reduce persistent RNT in depressed persons as a standalone or add-on treatment.

To date, it is unclear if these recently developed treatments targeting RNT are more effective at reducing RNT and thereby enhance treatment outcome in depression compared to standard CBT or other treatment approaches. A recent systematic review (Querstret & Cropley, 2013) concluded that mindfulness-based and cognitive-behavioral interventions may be effective in reducing both rumination and worry and this effect may be due to encouraging clients to change their thinking style or to disengage from their emotional response to rumination and worry. However, this systematic review was based on 15 randomized controlled trials (RCTs) of which only five were relevant to the treatment of depression and

no meta-analysis was performed. A recent meta-analysis examined mediating mechanisms underlying the effect of MBCT on mental health and well-being (Gu, Strauss, Bond, & Cavanagh, 2015) and identified five RCTs that examined RNT as a mechanism of change in MBCT. However, this meta-analysis did not examine the effect of different types of treatment on RNT and was not focused on depression. So, the results of available systematic reviews and meta-analyses do not provide a sufficient answer to the question whether CBT treatments for depression that specifically target RNT have a greater effect on RNT or produce better outcomes than traditional CBT or alternative treatments.

Moreover, it is also not clear whether treatments that specifically target RNT actually produce their effects by reducing RNT. As understanding the mechanisms of therapeutic change can help to improve treatment, assessing possible mediators of change is important. In line with Lorenzo-Luaces and colleagues (Lorenzo-Luaces, German, & DeRubeis, 2015) four conditions need to be met in order to conclude that reducing RNT may be causally related to symptom improvement, and is specifically targeted by an intervention (see Fig. 1): (1) differential efficacy of treatments on symptoms (path c; i.e. do treatments focusing on RNT result in more symptom improvement than treatments emphasizing changes in other domains); (2) differential effects of treatments on mediators (path a; i.e., do treatments focusing on RNT result in lower levels of RNT than other treatments); (3) effects of change in mediators on symptom change (path b; i.e., do changes in RNT result in symptom improvement, irrespective of the treatment that produced them); and (4) cognitive specificity (path d, i.e., does change in RNT following treatments focusing on RNT result in greater symptom reduction than changes in RNT brought about by other treatments). If these conditions are met, it is warranted to infer a causal link between treatment and mediator or between treatment and outcome, but not between mediator and outcome since the mediator may itself not be the actual causal mechanism but rather its correlate (anything “downstream”

from the mechanism itself will pass the statistical test for mediation). Moreover, both the putative mediator and the outcome of interest must be assessed at least three times across the course of treatment in order to rule out reverse causality (MacKinnon, Fairchild, & Fritz, 2007). Multiple assessment is the main change needed in research as assessment on multiple occasions yields information on the timeline of mediators and outcomes and offers the possibility to determine possible bidirectional changes (Kazdin, 2007).

As we did not expect to identify a sufficient number of studies reporting a formal mediation analysis to examine whether post-treatment effects on depression are (partly) due to preceding treatment- induced changes in RNT, as a preliminary step we only analyzed whether certain associations consistent with such a mediation model could be identified. More specifically, in line with the conditions specified by Lorenzo-Luaces et al. (2015), we sought to address the following questions:

(a) What is the effect of any treatment on depression severity and do treatments focusing on RNT result in lower levels of depression?

(b) What is the effect of any treatment on RNT and do treatments focusing on RNT result in lower levels of RNT?

(c) Are treatments effect on RNT associated with treatment effects on depression severity?

(d) Is the association of reductions in RNT with reductions in depression severity greater in treatments focusing on RNT?

To this end we conducted a meta-analysis of treatment studies examining the effect of any (psychological or psychiatric) treatment for depression on RNT (i.e., rumination or worry with a negative thought content and content-independent RNT that is experienced in a negative way) in adolescents and adults. We restricted our analysis to RCTs as RCTs have a more valid study design for causal inference compared with studies using an observational design. Moreover, we included studies investigating both acute treatments for depression as

well as treatments for the prevention of relapse/recurrence in previously depressed persons compared to either control groups or alternative treatments.

Methods

Identification and selection of studies

The following electronic databases were examined in September 2017: PsycINFO, PubMed, Embase and the Cochrane library. We used search terms that were related to depression in combination with either prevention or treatment, as well as content-dependent (i.e., rumination and worry) or content-independent repetitive negative thinking (RNT), and RCTs (see Table 1 of the supplementary material for a detailed description of the PubMed search terms).

We included (a) randomized controlled trials in which (b) an active intervention (c) was compared to a control condition or another intervention (d) in adolescents or adults with previous or current depressive disorder (established through a diagnostic interview) or elevated depressive symptoms (as established through a cut-off on a self-report scale) and (e) in which the effects on content-dependent or content-independent RNT were measured. Moreover, studies (f) not in English, with mixed samples (i.e. samples also including persons with another primary mental disorder than depression) and with 10 or fewer participants per condition were excluded.

All measures targeting RNT as identified in our search were allowed, including the Ruminative Response Scale (RRS; Nolen-Hoeksema & Morrow, 1991) and variations thereof (Response-Styles Questionnaire (RSQ-D; Kuhner, Huffziger, & Nolen-Hoeksema, 2007) and Responses to Depression Questionnaire (RDQ; Park, Goodyer, & Teasdale, 2005)), Rumination on Sadness Scale (RSS; Conway, Csank, Holm, & Blake, 2000),

Rumination/Reflection Questionnaire (RRQ; Trapnell & Campbell, 1999) and Experiences Questionnaire – Rumination (EQ-R; Fresco et al., 2007) for rumination; the Penn State Worry Questionnaire (PSWQ; Meyer, Miller, Metzger, & Borkovec, 1990) for worry and the Repetitive Thinking Questionnaire (RTQ; McEvoy, Mahoney, & Moulds, 2010) and Perseverative Thinking Questionnaire (PTQ; Ehring et al., 2011) for content-independent repetitive negative thinking.

Titles and abstracts from all references identified by the literature search were independently screened by pairs of two authors (PS, CB, NK, MK) against the inclusion criteria. Full-text versions of potential articles were subsequently obtained for more detailed analysis. Also, these full-text versions were independently screening by pairs of two authors (PS, CB, NK, MK). Moreover, additional papers were identified by screening the reference list of the selected papers and relevant meta-analyses. For each study, we not only checked the papers in which the effect on rumination, worry or RNT were reported, but also protocol papers and other primary or secondary results papers if necessary for extracting relevant data for the meta-analysis. When necessary data were missing, the authors of the articles were contacted to request these data. Details regarding methodology and outcome measurements of all included studies were independently extracted into a Microsoft Excel spreadsheet and differences in extraction were resolved by consensus (PS, NK,MK). In extracting these characteristics of the included studies, we followed the coding system for the most important study characteristics as described by Cuijpers, van Straten, Warmerdam, & Andersson (2008) on the basis of previous meta-analyses of the psychological treatment of depression.

Quality assessment

The validity of the included studies was evaluated using four criteria of the 'Risk of bias' assessment tool, developed by the Cochrane Collaboration (*2011*). This tool assesses

possible sources of bias in randomized controlled trials, including the adequate generation of allocation sequence; the concealment of allocation to conditions; the prevention of knowledge of the allocated intervention (masking of outcome assessments by independent raters); and dealing with incomplete outcome data (assessed as positive when analyses were intention-to-treat).

Meta-analysis

For each comparison of an active treatment condition with a control condition or an alternative treatment, we calculated the effect size indicating the difference between the two groups at post-test. We used Hedges' *g* as effect size measure to address small sample sizes, according to the procedures described in Hedges and Olkin (1985).

In the calculation of effect sizes, only those instruments that explicitly measured RNT (rumination, worry or content-independent RNT) were used. If authors reported outcome data for a total scale for RNT (e.g., RRS) as well as for a subscale (e.g., RRS-Brooding), we used the former scores. When more than one independent instrument was used, the mean of the effect sizes was calculated so that each comparison yielded only one effect size (Borenstein, Hedges, Higgins, & Rothstein, 2009). When more than one depression measure was used, we calculated effect sizes for each instrument measuring severity of depressive symptoms and pooled effect sizes within the study before pooling effect sizes across studies.

To calculate the pooled mean effect size, we used the computer program Comprehensive Meta-Analysis (version 3.3.070). Because considerable heterogeneity among studies was expected, a random effects pooling model was used in all analyses. As a test of homogeneity of effect sizes, the I^2-statistic as an indicator of heterogeneity in percentages was calculated. A value of 0% indicates no observed heterogeneity, and larger values indicate increasing heterogeneity, with 25% indicating low, 50% indicating moderate, and 75%

indicating high heterogeneity. We also calculated 95% confidence intervals around I^2 (Ioannidis, Patsopoulos, & Evangelou, 2007), using the non-central chi-squared-based approach within the "heterogi" module for Stata.

In order to examine possible moderators of outcome and potential sources of heterogeneity, we examined the following variables: recruitment (community, clinical versus combined), goal of treatment (acute treatment or prevention of relapse/recurrence), Phase II or Phase III study, treatment format (individual, group, guided self-help), number of sessions (less than 8 vs 8 or more), target group (adults vs others (i.e., adolescents, students, older adults), type of control group (waiting list, care-as-usual, attention/placebo, pill placebo), definition of depression (according to a diagnostic interview versus self-report), and quality (3–4 criteria versus 0–2 criteria). Subgroup analyses were conducted with a mixed effects model (Borenstein et al., 2009), in which studies within subgroups are pooled by means of random effects, while tests for significant differences between subgroups are conducted by means of fixed effects. Meta-regression analyses were performed to test for significant relationships between predictor variable(s) and effect size, as indicated by a Z-value and an associated *p*-value. Publication bias was tested by inspecting the funnel plot on primary outcome measures and by Duval and Tweedie's trim and fill procedure (Duval & Tweedie, 2000), which yields an estimate of the effect size after the publication bias has been taken into account. We also conducted Egger's test for the asymmetry of the funnel plot. These analyses assume that studies with high precision will be plotted near the average, and studies with low precision will be spread evenly on both sides of the average, creating a roughly funnel-shaped distribution and that deviation from this shape can indicate publication bias.

Results

Selection of studies and characteristics of included studies

Pairs of two authors (PS, CB, NK, MK) independently screened titles and abstracts from 2239 references identified by the literature search and screening reference lists of selected papers against the inclusion criteria. In 92.6% of the cases agreement on exclusion on the basis of titles and abstracts was directly reached. Next full-text versions of 248 potentially relevant articles were reviewed and 212 articles were excluded from this review for the following reasons: study protocol (n = 8), not an RCT (n = 7), no measure of rumination/worry/RNT (n = 133), participants inappropriate (no (previous) depressive disorder or elevated depression severity) (n = 53), sample overlapping with other study (n = 5), authors did not send the data despite repeated requests (n = 2), otherwise (n = 4). The remaining 36 articles were included in this review (see Studies included in the review in the Supplementary Material for the full reference list). Fig. 2 presents a flow-chart describing the inclusion process.

The included studies contained a total of 3307 participants (see Table 1). Mean age across study conditions was 42.2 years and the mean proportion of female participants across study conditions was 73.2%. Active treatment conditions contained 1965 participants, while control conditions contained 1342 participants. In 15 of the 36 studies participants were recruited from the community, in 13 from clinical samples, and in 8 combined from the community and clinical samples. 28 studies were aimed at adults, 3 at adolescents, 2 at college students, 1 at older adults, and 2 at mixed samples (students/adults and adults/older adults). In 30 studies a diagnostic interview was used to establish the presence of a depressive disorder (current or past), while the remaining 6 studies used a cut-off on a self-report scale to establish presence of clinically relevant depressive symptoms. In 26 studies rumination was measured with the RRS of the RSQ, in 2 with variants thereof (RDQ and RSQ-D), in 4 with the RSS, and in 1 with the EQ-R or RRQ. In the 25 studies using the RRS, 2 used only

the brooding subscale of the RRS (Treynor, Gonzalez, & Nolen-Hoeksema, 2003), while another 5 reported RRS as well as brooding scores. In 5 studies worry was measured with the PSWQ. In 2 studies RNT was measured with the RTQ and in one with the PTQ. Of the 36 studies, 25 examined treatment(s) to alleviate depression or acute depressive symptoms, 10 examined treatment(s) to prevent relapse/recurrence of a depressive episode, and one examined a sample with acutely depressed and euthymic remitted persons. A total of 12 of the 36 studies were conducted in the US (of which one also in Puerto Rico), 17 in Europe (including the UK), and 7 in other countries. A total of 49 treatment conditions were examined across the 36 studies, of which 10 were MBCT, 4 CNT (Concreteness training), 3 rf- CBT (i.e., rumination-focused CBT), 5 cognitive control /bias training (working memory based CCT, ABM, CBM), 10 CBT (i.e. behavioral activation, problem solving therapy, coping with depression course, competitive memory training, complaint-directed mini-interventions), 12 other types of treatment (i.e., antidepressant medication (ADM), light therapy, engagement counseling, life review, expressive writing, yoga), and 5 combined treatments (i.e., CBT plus Light Therapy or SSRI, CCT plus Behavioral Activation or transcranial Direct Current Stimulation (tDCS), CBM plus internet CBT). Of the 33 control conditions, 15 were waiting list/no treatment, 8 were care-as-usual, 8 were attention-control, and 2 were pill-placebo. In 16 of the 49 treatment conditions an individual treatment format was used, 16 used a group format, 15 used guided self-help, 1 used unguided self-help, and 1 used a blended treatment. The number of therapy sessions (excluding unguided self-help, ADM and light therapy conditions) ranged from 4 to 46 with most having 8 to 12 sessions (30 out of 43 conditions). 13 studies reported group data at follow-up for both the active treatment and control condition or another active treatment condition. Follow-up duration ranged from 1 month to 24 months.

Quality assessment

The quality assessment of the included studies with the risk of bias tool showed that one third of the studies did have a low risk of bias (Table 1). 29 of the 36 included studies reported an adequate sequence generation by an independent person, 27 studies reported that the randomization sequence was adequately concealed, 31 studies reported blinding of outcome assessors or used only self-report outcome measures, and in 21 studies used intention- to-treat analyses. 13 studies met all four of the quality criteria, 14 met 3 criteria; and the remaining 9 studies had a lower quality (1 or 2 of the four quality assessment criteria).

The effects of active treatment on depression severity (path c)

The overall effect of active treatment on depression severity relative to control conditions at post-test was medium in magnitude (g = 0.57; 95% CI: 0.46–0.69), with low to moderate heterogeneity (I^2 = 46; 95% CI: 13-63) (see Fig. 1 of the supplementary material for the forest plot). Next, we recoded overall class of treatment as: traditional CBT, RNT-focused treatments (i.e., CNT, rf-CBT, MBCT, or CCT) and other treatments (i.e., ADM, light therapy, engagement counseling, life review, expressive writing, yoga). A subsequent meta-regression analysis indicated no significant differences in the effect of RNT-focused treatments and traditional CBT on depression severity compared to other treatments as reference category (Q (2) = 2.14, p = .34).

The effects of active treatment versus control groups on RNT (path a)

Overall effect of active treatment versus control groups

The overall effect of active treatment on RNT compared with control conditions at post-test was g = 0.48 (95% CI: 0.37–0.59), with moderate heterogeneity (I^2=47; 95% CI: 17-64). The

results of these analyses are presented in Table 2, and the forest plot is given in Fig. 3. There were two outliers with a negative effect size, i.e. studies in which the 95% confidence interval of the effect size did not overlap with the pooled effect size (Jermann et al., 2013; Mogoase, Brailean, & Davind, 2013), although both individual studies reported a non-significant positive effect of treatment on rumination. As this seemed to be due to an uneven distribution of rumination scores across conditions at baseline, we performed a sensitivity analysis using CMA to calculate standard differences in means for all studies based on the means and standard deviation at pre- and post-test in each condition and assuming a conservative value of 0.50 for the correlation between time-points (Balk, Earley, Patel, Trikalinos, & Dahabreh, 2012). Rerunning the analyses with these adapted g values, the resulting pooled effect size remained comparable (g = 0.44; 95% CI: 0.37-0.52), but heterogeneity became low (I^2 = 6; 95% CI: 0-38) (see Fig. 2 of the supplementary material). Moreover, calculating the overall effect of active treatment on RNT excluding these two outliers yielded comparable results (g = 0.51; 95% CI: 0.40-0.61; I^2 = 39; 95% CI: 0-59). In all further analyses, we used Hedges' g effect scores not adapted for outliers to get a conservative estimate.

When the effects were limited to rumination measurements (g = 0.49; 95% CI = 0.37-0.62; I^2=46), and worry (g = 0.42; 95% CI = 0.25 – 0.59; I^2 = 53), the effects were comparable. The effect on rumination as measured in 25 of the 31 comparisons by the RRS or variants of this scale was also comparable to the overall effect on rumination (g = 0.54; 95% CI = 0.39-0.69; I^2 = 48; 95% CI: 7-66). The effects on content-independent repetitive negative thinking were larger (g = 0.77; 95% CI = 0.37 – 1.16; I^2 =0), but based on only 2 comparisons.

In these analyses, we included six studies in which more than one active treatment was compared with the same control group and two studies in which more than one control

group was used. This implies that multiple comparisons from these studies were included in the same analysis, and these were not independent from each other, which may have resulted in an artificial reduction of heterogeneity and may have affected the pooled effect size. We tested for this possibility with sensitivity analyses in which we included only one effect size per study. First, only the comparison with the largest effect size from these studies was included, followed by another analysis in which only the smallest effect size was included. As can be seen in Table 2, the resulting effect sizes as well as the levels of heterogeneity were comparable with the overall analyses.

Moreover, some evidence for publication bias was found. Egger's test was significant, $t(35) = 2.40$, $p = .02$. After adjustment for publication bias according to Duval and Tweedie's trim and fill procedure, the overall effect size was reduced from 0.48 to 0.38 (95% CI: 0.31–0.45; number of imputed studies: 8) (see Fig. 3 of the supplementary material for the funnel plot).

The effects of treatment on RNT were maintained at follow-up (Table 2). Ten comparisons between treatment and a control group led to a significant $g = 0.40$ (95% CI: 0.17–0.63), with moderate heterogeneity ($I^2 = 50$). This result was robust when considering only one ES per study ($g = 0.41$ (95%CI = 0.13 - 0.70; $I^2 = 58$) for the highest effect size per study and $g = 0.34$ (95% CI = 0.07 – 0.62; $I^2 = 52$) for the lowest effect size per study.

In order to examine possible moderators of outcome and potential sources of heterogeneity, a series of subgroup analyses was performed. There was a significant difference for type of study (Phase II versus Phase III), $Q(1) = 5.843$, $p = .02$, with Phase II studies ($g = 0.66$; 95%CI = 0.47 - 0.86; $I^2 = 39$) showing a lager effect size than Phase III studies ($g = 0.38$; 95%CI = 0.26 - 0.50; $I^2 = 41$) (see Fig. 4 of the supplementary material for the forest plot). No indications were found that the effect sizes differed significantly among

the following subgroups of studies: recruitment, goal of treatment, treatment format, number of sessions, target group, type of control group, definition of depression and study quality.

Effects of different classes and types of treatments versus control groups

In comparing traditional CBT, RNT-focused treatments and other treatments, we excluded the study by Williams and colleagues as it used a combination of CBM and iCBT (Williams, Blackwell, Mackenzie, Holmes, & Andrews, 2013). Subgroup analysis revealed a significant effect for class of treatment, $Q(2) = 19.158$, $p < .001$, with only CBT ($g = 0.63$) and RNT-focused treatments ($g = 0.53$), but not other treatments ($g = 0.14$) having an effect size significantly different from zero. A post hoc analysis contrasting traditional CBT with RNT-focused treatments revealed no significant differences in effect on RNT ($Q(1) = 0.580$, $p = 0.446$).

A subsequent meta-regression of the effect of individual types of treatment (i.e., traditional CBT, CNT, rf-CBT, MBCT and CCT) on RNT compared to other types of treatment as reference category revealed significant differences between treatment types ($Q(5) = 14.39$, $p < .01$): rf-CBT: $g = 0.76$, $< .01$; CCT: $g = 0.62$, $p < .01$; CBT: $g = 0.57$, $p < .01$; CNT: $g = 0.53$, $p < .05$; and MBCT: $g = 0.42$, $p < .05$ (see Figure 4). Type of treatment remained a significant predictor also after adding risk of bias as covariate to the meta-regression, $Q(5)=12.29$, $p = .03$. Given the small number of follow-up studies, we could only examine short-term differential effects of type of treatment.

Possible differential effects of treatments as examined within one single study

In addition to the analyses above, in which different active treatments are compared to control conditions across studies, as a sensitivity analysis we also examined the effect of different active treatments compared to each other as studied within one single study (such as

MBCT compared to CBT in the study of Manicavasagar, Perich and Parker (2012)). This analysis could only be performed in 7 comparisons. The differential effect size was negligible, g = 0.10 (95% CI = 0.06 – 0.27). Heterogeneity was low: $I^2 = 0$. The results of this analysis are presented in Table 2 and Fig. 5 of the supplementary material.

Possible additional effects of combined versus single treatments

The possible effect on RNT of adding an extra treatment component to a single treatment of depression (such as CBM to iCBT in the study of Williams et al., 2015) could be examined in 6 comparisons. The differential effect size was small to moderate, g = 0.42, but not significantly different from zero: 95% CI = - 0.10 – 0.94. Study heterogeneity was high: $I^2 = 75$. The only individual study from this meta-analysis reporting a significant effect showed that adding CBT to SSRI medication in the context of active clinical care caused a greater reduction in mood-related ruminative response style in depressed adolescents (Wilkinson & Goodyer, 2008). The results of this analysis are presented in Table 3 and Fig. 6 of the supplementary material.

Association between effects on RNT and effects on depression (path b)

In order to examine whether the effects of treatment on RNT were concurrently associated with the effects on depression, we conducted a meta-regression analysis with the post-treatment effects on depression as dependent variable and the post-treatment effects on RNT as predictor. As shown in Figure 5, there was a significant association between the effects on RNT and those on depression (slope: 0.72; 95% CI: 0.46–0.99; $p < 0.001$).

Moderation of the association of effect on RNT with effect on depression by type of treatment (path d)

In order to assess the presumed cognitive specificity of classes of treatment specifically targeting RNT, we assessed the association of the effects on RNT and those on depression for each class of treatment separately: RNT-focused treatments (slope: 0.89; 95% CI: 0.52–1.26; $p < 0.001$); traditional CBT (slope: 0.63; 95% CI: -0.02–1.28; $p = .06$); other treatment (slope: -.02; 95% CI: -1.28 – 1.24; $p = .97$).

Discussion

The primary aim of this systematic review and meta-analysis was to examine whether treatments for depression targeting repetitive negative thinking (RNT: rumination, worry and content-independent perseverative thinking) have a specific effect on RNT resulting in better outcomes than treatments that do not specifically target rumination. All types of treatment investigated resulted in a comparable and moderate effect on depression. CBT targeting RNT did have a moderate effect on RNT that was comparable to that produced by more traditional CBT interventions, and both types of interventions were more effective in reducing RNT than other types of treatments (i.e., ADM, light therapy, engagement counseling, life review, expressive writing, yoga), which had only a small effect on RNT. Moreover, effects on RNT at post-test were strongly associated with the effects on depression severity at post-test and this association was only significant in RNT-focused CBT. These correlational results are in line with the supposition that in particular RNT-focused CBT may exert its effect on depression by targeting RNT. Below we will discuss these results into more detail with respect to the criteria laid out by Lorenzo-Luaces and colleagues (2015).

First, we examined whether the studies included in this meta-analysis were effective in reducing depression compared to control conditions (Path c in Fig.1). In concordance with the results of previous meta-analyses on the effects of psychological and pharmacological

treatments for depression (Cuijpers, van Straten, Andersson, & van Oppen, 2008; Cuijpers, van Straten, van Oppen, & Andersson, 2008), we found a medium effect of treatment on depression severity irrespective of type of treatment. A main goal of the present meta-analysis was to study the possible differential effect of treatments on RNT in depression, which has not been addressed before in a meta-analysis (Path b in Fig. 1). Irrespective of type of treatment we found a small effect of treatment on RNT at post-treatment and at follow-up. Adjustment for publication bias attenuated the overall effect to a small extent and study heterogeneity was moderate.

Interestingly, the effect on RNT did not seem to be critically affected by the type of RNT measured. This challenges the presupposition that changes in depressive symptoms are associated with changes in rumination because of criteria contamination between the measures of depressive symptoms and rumination or the particular outcome measure used (which in most of the studies was the RRS). The results are more consistent with a transdiagnostic view of RNT in which the shared variance of rumination, worry and perseverative thinking is considered to be of greater importance than the instantiation of RNT in disorder-specific cognitive content (Watkins, 2008), such as rumination in depression (Spinhoven et al., 2015) or worry in anxiety (Spinhoven, van Hemert, & Penninx, 2017). In line, in the few studies that measured content-independent RNT, effect sizes were larger than in studies measuring rumination. Moreover, a post-hoc analysis of five studies in our meta-analysis reporting both RRS rumination and brooding scores (presumably less confounded with depressed item content (Treynor, Gonzalez, & Nolen-Hoeksema, 2003)) showed a larger effect size for brooding than for rumination of only 0.11, while scores on both scales were highly associated (intercept = 0.00; slope = 1.00, $p < .001$).

The effect on RNT however proved to be higher in Phase II RCT's designed to show sufficient preliminary efficacy of a new treatment compared to Phase III RCT's

primarily designed to demonstrate efficacy/effectiveness more definitively against a control treatment or condition in a larger trial. Of note is that each of the Phase II studies involved RNT-focused CBT treatments (CNT:5; ABM:2; CCT:2; rf-CBT:2; MBCT=1) of which many are primarily derived from laboratory-based studies. Their first testing in mostly community settings appears to be very promising, but more studies in clinical samples are needed to investigate to what extent these positive effects will generalize to Phase III studies.

The effects of traditional and RNT-focused CBT treatments (i.e., CNT, rf-CBT, CCT, MBCT) on depression were medium and significantly larger than the small effect of other types of treatments (i.e., a heterogeneous group of diverse treatments as ADM, light therapy, engagement counseling, life review, expressive writing, and yoga). These results did not support the notion that treatments specifically focusing on RNT would show superior effects compared to traditional CBT treatments. Apparently, all forms of CBT are effective in reducing RNT. However, it has to be acknowledged that almost no studies directly compared treatments with or without focus on RNT. The fact that diverse CBT treatments such as behavioral activation, problem solving therapy, coping with depression course, and competitive memory training also effectively reduce RNT may be due to different factors. These treatment packages may also include interventions to target RNT and even interventions that do not explicitly target RNT may nonetheless induce changes in RNT (cp. Hofmann, 2008)). For example, initiating activities that are positively reinforced via behavioral activation may break the vicious circle of RNT and mood deterioration and competitive memory training may yield the same result via developing a more positive self-image. Moreover, the finding of similar effects on RNT does not automatically imply that these are the result of similar mechanism, as reductions in RNT may be a mechanism of

change in treatments targeting RNT, but an epiphenomenon of therapeutic improvement in other forms of treatment.

The superiority of CBT treatments compared to non-CBT treatments was not confirmed by our sensitivity analysis of the effects of different types of treatment as compared within one single study (e.g., directly comparing the effect of MBCT on RNT with that of maintenance antidepressant medication (mADM) (Bieling et al., 2012)). Also, a combined treatment in which an additional intervention was added to treatment did not produce better results than a single treatment (e.g. adding CCT to behavioral activation (Moshier & Otto, 2017)). However, these results are based on a limited amount of studies. There is a dearth of studies that directly compare CBT treatments with or without a direct focus on RNT, directly compare different CBT treatments with mADM and examine when and how CBT interventions specifically targeting RNT provide a useful adjunct to treatment for depression.

As a next step, we performed several analyses to examine whether changes in RNT are related to changes in depression severity (Path c in Fig. 1). A meta-regression analysis showed a significant linear relationship of treatment effects on RNT with treatment effects on depression severity. Interestingly, this relationship had the same large effect size as the association between the effects of CBT on dysfunctional thinking and those on depression as found in a recent meta-analysis (Cristea et al., 2015). Although this strong relationship is consistent with the idea that reductions in RNT mediate the effect of treatment on depression, this conclusion is premature for the following reasons. The strong association of the effect on rumination with the effect on depression could also indicate that reductions in RNT represent an epiphenomenon or consequence of reductions in depression severity (reverse causality). One of the great values of meta-analyses is that it helps to identify gaps in the existing literature. Strikingly, only five of the included 36 studies conducted a formal mediation

analysis to examine whether post-treatment effects are (partly) due to treatment- induced changes in RNT (Lamers, Bohlmeijer, Korte, & Westerhof, 2015; Shahar, Britton, Sbarra, Figueredo, & Bootzin, 2010; van Aalderen et al., 2012; Warmerdam, van Straten, Jongsma, Twisk, & Cuijpers, 2010; Watkins et al., 2011). However, four of these studies had only pre- and post-treatment measurements so that temporal precedence of early changes in the mediator in relation to subsequent changes in outcome could not be established (Kazdin, 2007). The only study that examined the mediating role of RNT in the form of worry with three measurement moments reported that reductions in worry mediated concurrent pre- to post-treatment reductions in depressive symptoms, but that early changes in worry during the first five weeks of treatment were not significantly related to subsequent changes in depression severity during the last three weeks of treatment (when most of the therapeutic change has already occurred) (Warmerdam et al., 2010). However, in a recent study of internet CBT for mixed anxiety and depression (a study therefore not included in the present meta-analysis) by Newby and colleagues (Newby, Mewton, Williams, & Andrews, 2014) changes in positive beliefs and RNT between pre- and mid-treatment mediated subsequent changes in depression severity. This study illustrates the importance of repeated measures of symptoms and proposed mediators, especially early in treatment, to ensure that the predictive value of changes in the mediator for subsequent changes in outcome can be tested and reverse causality can be ruled out (Kazdin, 2007; Kraemer, Wilson, Fairburn, & Agras, 2002).

Finally, we examined the cognitive specificity hypothesis stating that changes in RNT following treatments focusing on RNT will result in greater symptom reduction than changes in RNT brought about by other treatments (Path d in Fig. 1). Interestingly, the association of reductions in RNT with reductions in depression seems mainly driven by RNT-focused CBT studies explicitly focusing on reducing RNT. In traditional CBT treatments, the association was less pronounced and only borderline significant, while in other treatments the association

was null. Although these results have to be interpreted with caution given the small number of studies, they are consistent with the hypothesis that targeting RNT could be a working mechanism in treatments focusing on RNT. These results are consistent with the habit model of rumination (Watkins & Nolen-Hoeksema, 2014), according to which the amount of rumination can be reduced either through changing the underlying habit by learning new responses to the triggers of the habit (such as depressed mood) or by temporarily reducing the expression of the habit by temporarily removing its triggers (i.e., by alleviating low mood). Possibly, CBT and in particular RNT-focused treatments thereby change the underlying habit fostering treatment gains and making individuals less vulnerable to relapse or recurrence because RNT will be less likely reactivated once stress or low mood occurs again. Because of the small number of studies with follow-up data, we were not able to examine whether post-treatment changes in RNT following different forms of CBT predict maintenance of treatment gains or prevent relapse and recurrence. As prior CBT has been shown to have a prophylactic effect on depression compared to medication withdrawal (Cuijpers et al., 2008), the predictive value of reducing RNT for long-term results deserves more attention. Reduction of RNT following CBT -in particular with an emphasis on targeting RNT- may drive further symptom improvement, while reductions in RNT following other types of treatment (such as ADM) may primarily represent an epiphenomenon of therapeutic improvement with less prognostic significance.

The results of this meta-analysis have to be interpreted in the context of some limitations. First, the number of studies was relatively small. However, as the only available meta-analysis on treatments used to reduce RNT (Querstret & Cropley, 2013) only included 15 RCTs for various disorders, the present study including 36 RCTs in depression disorder gives a more comprehensive overview and may also help to pinpoint areas in which more research is urgently needed. By not only reporting Hedges'g but also 95% CI's, we tried to

show the degree of uncertainty about the effect sizes found. Given the relative small number of studies also the results of our subgroup and meta-regression analyses to examine possible sources of heterogeneity should be considered with caution. Even if predictors are found to be significant in meta-regression analyses they can only provide indirect evidence and the findings can easily be explained by third variables that were not measured. On the other hand, the failure to find a statistically significant p-value could mean that the effect (if any) is quite small, but could also mean that the analysis had poor power to detect even a large effect. For example, the number of studies could have been too small to detect a significant effect for type of control conditions with smaller effects for comparisons to active control conditions like CAU in contrast to larger effects for comparisons to passive control conditions like a waiting list.

Second, as RNT does not represent a primary endpoint in RCTs of depression, journal titles or abstract may have been incomplete in referring to secondary RNT measurements and consequently relevant studies may have been missed. Third, due to practical reasons we only included studies that were published in English and grey literature and unpublished studies were not included in this meta-analysis. Fourth, our literature search was restricted to a limited set of databases (PsycINFO, PubMed, Embase and the Cochrane library). Although we tried to address this limitation by examining the reference list of previous meta-analyses and articles included in the present meta-analysis, this may have resulted in unintentionally missing relevant papers that would have met our inclusion criteria. Fifth, we performed many subgroup and meta-regression analyses to explore possible reasons for study heterogeneity and association between variables of interest. Because the results of these analyses are purely observational, causal inferences are unwarranted, because subgroups may also have differed in other important ways and correlations do not imply causality. Finally, study quality as assessed with our risk of bias scale was not optimal with only one third of the studies having

low risk of bias. However, we did not find differences in results between lower and higher quality studies.

Moreover, there are several problems associated with the measurement and conceptualization of RNT inherent in the studies we reviewed. All studies relied on self-report measures of RNT and self-report measures may conflate change in RNT with symptom change. In addition, response bias may confound self-report RNT measurements, especially after treatments that aim to alter RNT. Future studies using multi-modal assessments are needed (e.g., using experimental tasks to measure deficits in the inhibition of irrelevant emotional stimuli in working memory (Joormann, Dkane, & Gotlib, 2006) or negative thought intrusions during a baseline period of focused breathing (Ruscio, Seitchik, Gentes, Jones, & Hallion, 2011)) to cross-validate findings based on self-report. In addition, most measures of rumination only assess its frequency, but not its intensity, duration, controllability, automaticity, repetitiveness, or levels of interference with daily tasks. These variables all have been discussed as theoretically important in understanding rumination and are likely to be clinically significant (see Watkins, 2008).

Moreover, there is a growing interest in possible dimensions underlying repetitive thinking. The extent to which persons engage in repetitive thinking may fail to capture important qualitative differences that could be related to the differential effects of repetitive thinking on mental and physical health (Watkins, 2008). For example, it may prove important to differentiate between reflection and brooding components of rumination, because they have quite different relations to depression (Treynor et al., 2003). Similarly, worry has been differentiated in constructive worry facilitating goal-pursuit and threat reduction and unconstructive worry hindering goal-pursuit and sustaining threat awareness (McNeill & Dunlop, 2016). Several studies have identified two dimensions characterizing repetitive thinking: valence and purpose (Segerstrom et al., 2016). Results of the present meta-analysis

suggest that existing measures of RNT may primarily tap unconstructive repetitive thinking, although measures included in this meta-analysis are clearly insufficient to differentiate between constructive and unconstructive repetitive thinking. Including dimensional assessments of repetitive thinking in future studies could help to address more refined questions about to whether the amount of repetitive thinking or the valence and purpose of repetitive thinking are most important in explaining why and how symptom reduction is achieved.

Despite these limitations, the strength of our study is that it is the first to systematically review the effect of treatment on RNT in depressive disorder, across treatment types (e.g., CBT, MBCT and other treatment approaches), treatment goals (treatment of depression and relapse prevention), delivery formats (e.g., face-to-face individual and group, as well as computerized treatments) and age groups (adolescents, adults, and older adults). Our results suggest that CBT (both generic and rumination focused) may have a more pronounced effect on RNT than other types of interventions and that the effect on RNT is strongly associated with the effect depression. The quality of RCTs was subpar, and heterogeneity was moderate. Further high quality RCTs are warranted to examine the sources of this heterogeneity to identify the most effective treatment components and to further our understanding of RNT as a possible mechanism of sustainable change.

Supplementary data to this article can be found online at http://

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Contributors

Professors Spinhoven and Bockting designed the study. Dr. Kennis helped to develop the search strategy and conducted the literature searches. Prof. Spinhoven and Bockting, Dr. Kennis and Drs. Klein independently screened the titles, abstracts, and full-texts for eligibility for inclusion into the meta-analysis. Prof. Spinhoven and Dr. Klein independently coded the risk of bias of all RCTs and independently extracted the data from manuscripts. Prof. Spinhoven conducted the data analysis with the help of prof. Cuijpers. All authors contributed to and have approved the final version of the manuscript.

Conflict of interest

All authors declare that they have no conflicts of interest.

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Figure legends

Fig. 1. Association between different treatments, reductions in RNT and improvement of depression severity

Fig. 2. Flowchart for inclusion of studies

Fig. 3. Forrest plot of the effect sizes indicating the difference between active treatment and control groups on RNT

Fig. 4. Regression of the effect of treatment on RNT on type of treatment (Hedges' g)

Fig. 5. Regression of the effect of treatment on depression on the effect on RNT (Hedges' g)

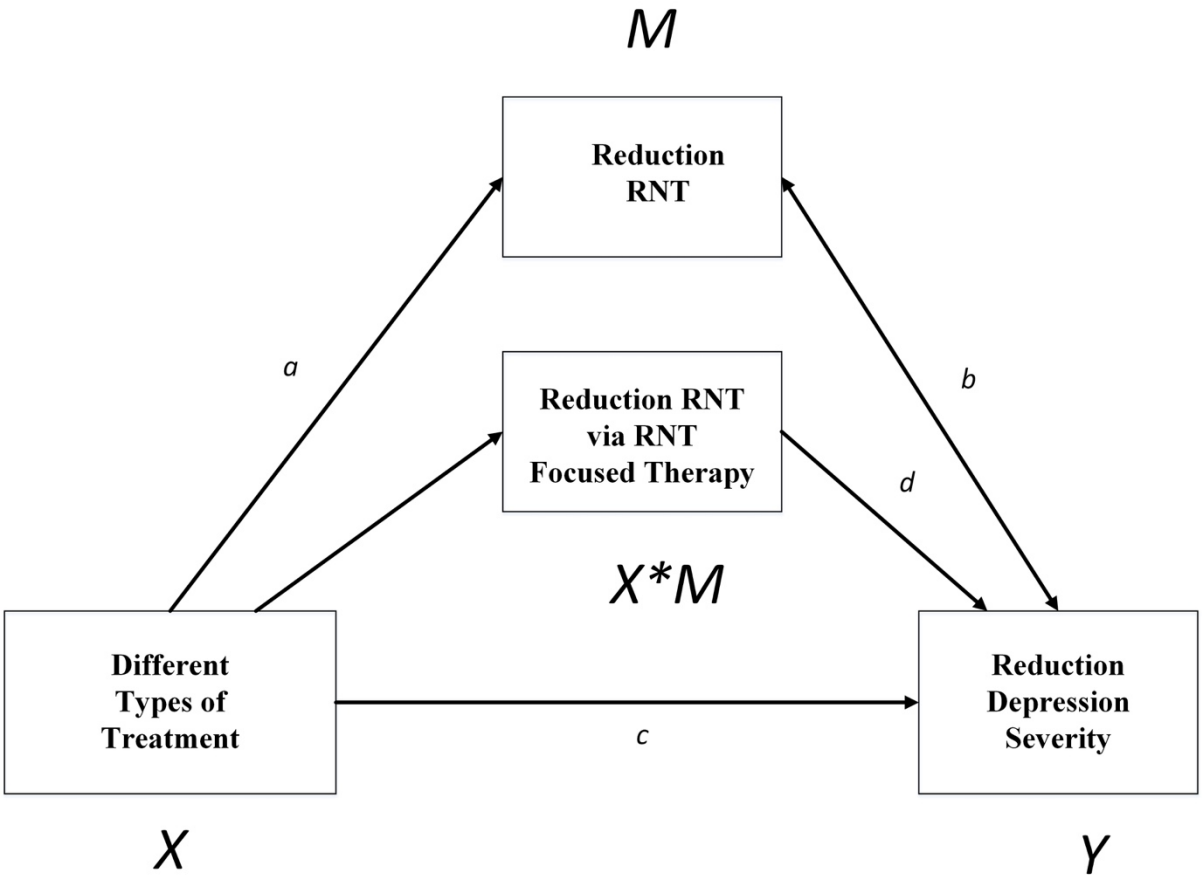
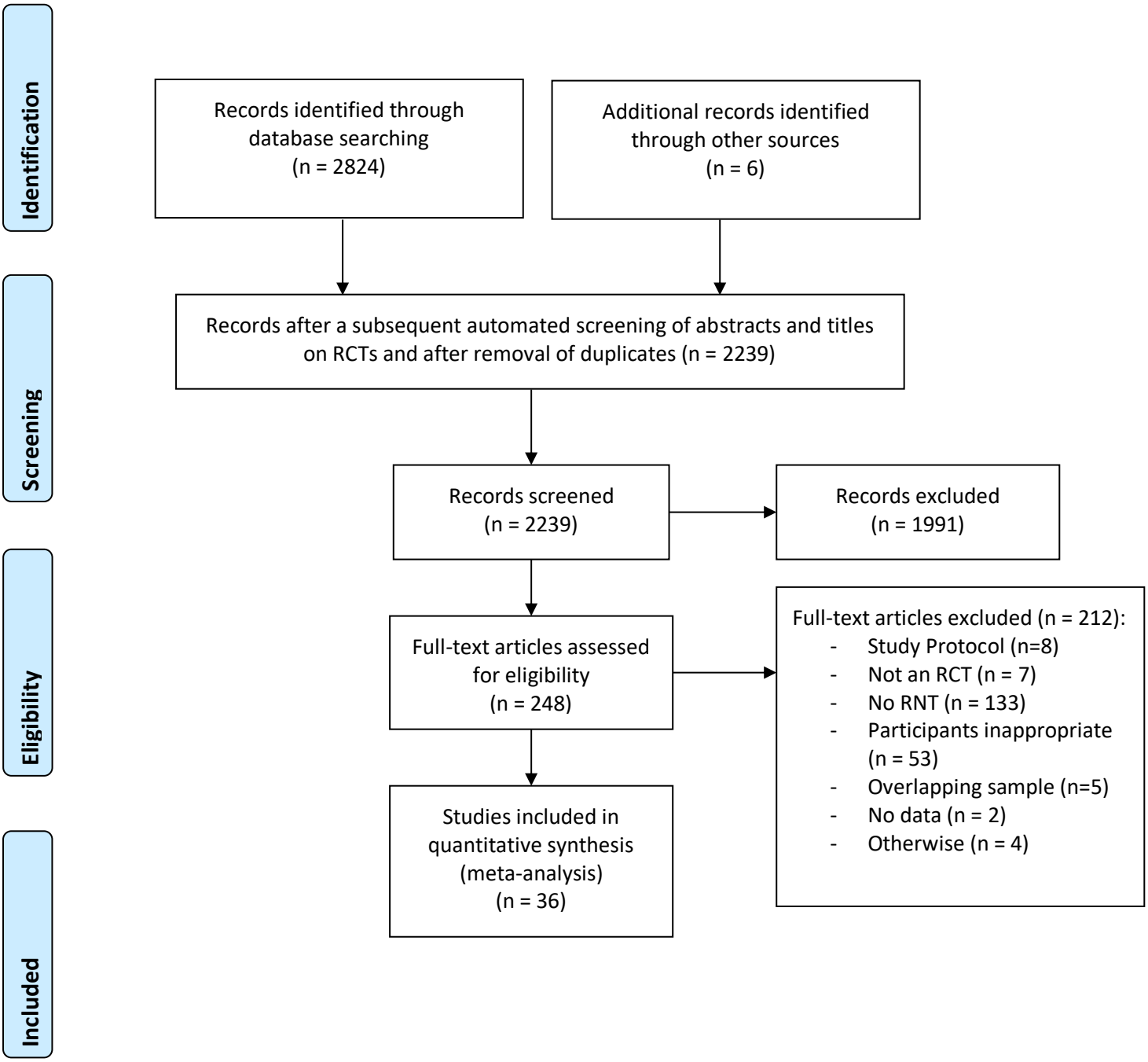
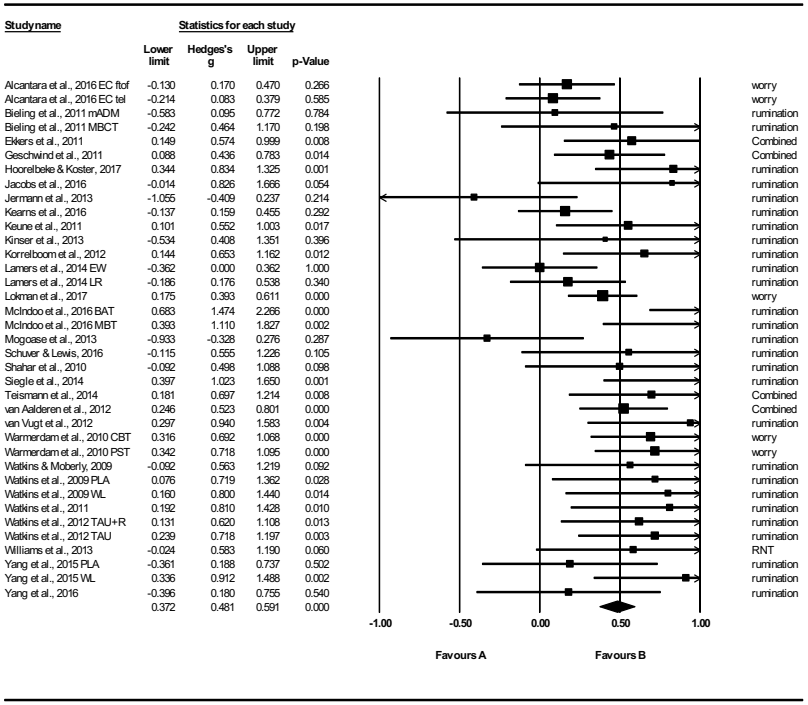
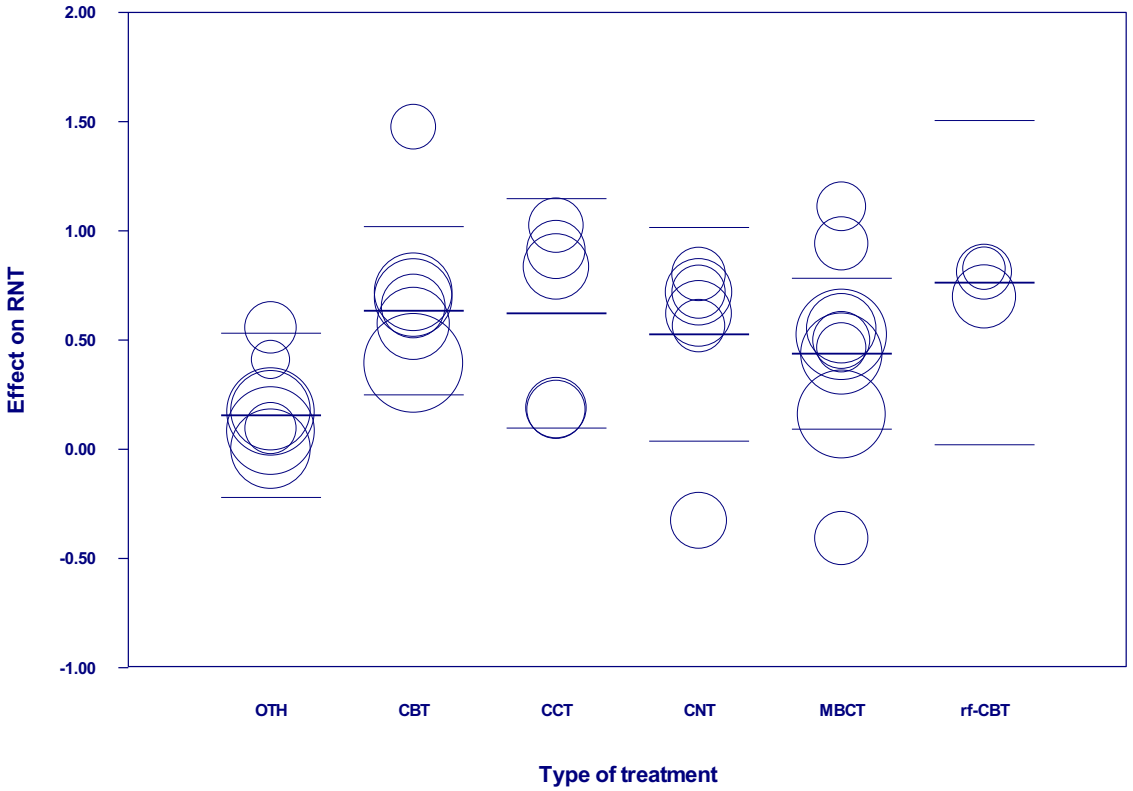

M
Reduction RNT
a
b
Reduction RNT via RNT Focused Therapy
d
X*M
Different Types of Treatment
c
Reduction Depression Severity
X
Y

Fig. 2. Flowchart for inclusion of studies




Study name
Statistics for each study
Lower limit
Hedges's g
Upper limit
p-Value
Alcantara et al., 2016 EC ftof -0.130 0.170 0.470 0.266 worry
Alcantara et al., 2016 EC tel -0.214 0.083 0.379 0.585 worry
Bieling et al., 2011 mADM -0.583 0.095 0.772 0.784 rumination
Bieling et al., 2011 MBCT -0.242 0.464 1.170 0.198 rumination
Ekers et al., 2011 0.149 0.574 0.999 0.008 Combined
Geschwind et al., 2011 0.088 0.436 0.783 0.014 Combined
Hoorelbeke & Koster, 2017 0.344 0.834 1.325 0.001 rumination
Jacobs et al., 2016 -0.014 0.826 1.666 0.054 rumination
Jermann et al., 2013 -1.055 -0.409 0.237 0.214 rumination
Kearns et al., 2016 -0.137 0.159 0.455 0.292 rumination
Keune et al., 2011 0.101 0.552 1.003 0.017 rumination
Kinser et al., 2013 -0.534 0.408 1.351 0.396 rumination
Korrelboom et al., 2012 0.144 0.653 1.162 0.012 rumination
Lamers et al., 2014 EW -0.362 0.000 0.362 1.000 rumination
Lamers et al., 2014 LR -0.186 0.176 0.538 0.340 rumination
Lokman et al., 2017 0.175 0.393 0.611 0.000 worry
McIndoo et al., 2016 BAT 0.683 1.474 2.266 0.000 rumination
McIndoo et al., 2016 MBT 0.393 1.110 1.827 0.002 rumination
Mogoase et al., 2013 -0.933 -0.328 0.276 0.287 rumination
Schuer & Lewis, 2016 -0.115 0.555 1.226 0.105 rumination
Shahar et al., 2010 -0.092 0.498 1.088 0.098 rumination
Siegle et al., 2014 0.397 1.023 1.650 0.001 rumination
Teismann et al., 2014 0.181 0.697 1.214 0.008 Combined
van Aalderen et al., 2012 0.246 0.523 0.801 0.000 Combined
van Vugt et al., 2012 0.297 0.940 1.583 0.004 rumination
Warmerdam et al., 2010 CBT 0.316 0.692 1.068 0.000 worry
Warmerdam et al., 2010 PST 0.342 0.718 1.095 0.000 worry
Watkins & Moberly, 2009 -0.092 0.563 1.219 0.092 rumination
Watkins et al., 2009 PLA 0.076 0.719 1.362 0.028 rumination
Watkins et al., 2009 WL 0.160 0.800 1.440 0.014 rumination
Watkins et al., 2011 0.192 0.810 1.428 0.010 rumination
Watkins et al., 2012 TAU+R 0.131 0.620 1.108 0.013 rumination
Watkins et al., 2012 TAU 0.239 0.718 1.197 0.003 rumination
Williams et al., 2013 -0.024 0.583 1.190 0.060 RNT
Yang et al., 2015 PLA -0.361 0.188 0.737 0.502 rumination
Yang et al., 2015 WL 0.336 0.912 1.488 0.002 rumination
Yang et al., 2016 -0.396 0.180 0.755 0.540 rumination
0.372 0.481 0.591 0.000
-1.00
-0.50
0.00
0.50
1.00
Favours A
Favours B


2.00
1.50
1.00
0.50
0.00
-0.50
-1.00
Effect on RNT
OTH
CBT
CCT
CNT
MBCT
rf-CBT
Type of treatment

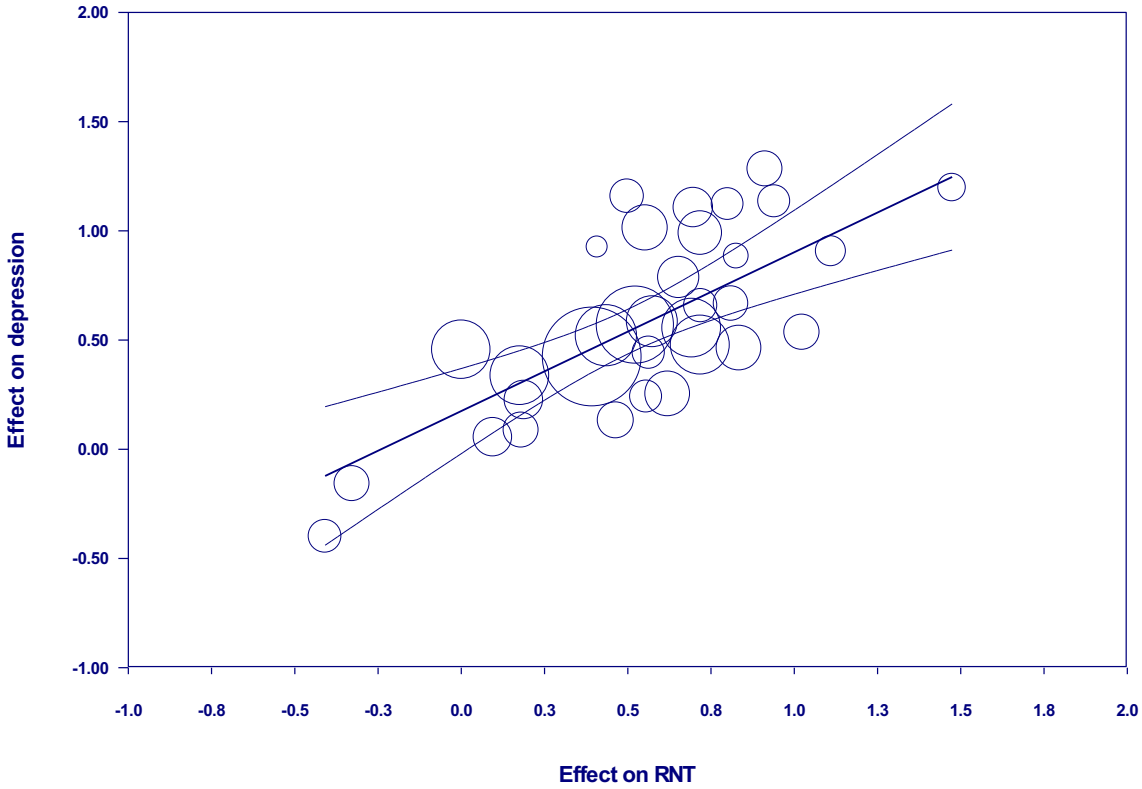

2.00
1.50
1.00
0.50
0.00
-0.50
-1.00
Effect on depression
-1.0
-0.8
-0.5
-0.3
0.0
0.3
0.5
0.8
1.0
1.3
1.5
1.8
2.0
Effect on RNT

Table 1. Selected characteristics of randomized controlled trials examining the effects of different types of treatment on repetitive negative thinking

Authors	Recr[a]	Definition of depression[b]	Target group	Conditions[c]	Aim[d]	Phase II or III[e]	N at baseline	Format[f]	Nse[g]	Quality[h]	Measure of RNT[i]	Country
Alcantara et al. (2016)	Clin	PHQ-9 ≥ 10	Adults	1. Counseling: tel 2. Counseling: f2f 3. CAU	Treat	III	87 84 86	Ind Ind	6-8 6-8	+--+	PSWQ	USA, OTH
Bieling et al. (2012)	Comm + Clin	SCID-I HRSD ≤ 7	Adults	1. MBCT 2. mADM 3. Placebo	Prev	III	26 28 30	Grp Ind	8 + 1 day	-+++	EQ-R	USA
Ekkers et al. (2011)	Clin	Clinical DSM-IV diagnosis GDS ≥ 11	Older adults	1. COMET + CAU 2. CAU	Treat	III	53 40	Grp	7	++++	RRS, RSS	EUR
Evans et al. (2013)	Comm	SCID-I SIGH - SAD	Adults	1. CBT 2. Light therapy 3. Combination	Treat	III	23 24 22	Grp Gsh Grp + Gsh	12	++++	RRS	USA
Geschwind et al. (2011)	Clin	SCID-I HRSD ≥ 7	Adults	1. MBCT 2. WL	Prev	III	64 66	Grp	8	+++-	RSS, PSWQ	EUR
Hoorelbeke & Koster (2017)	Comm	MINI	Adults	1. working memory based CCT 2. Control task	Prev	II	34 34	Gsh	10	++++	RRS	EUR
Jacobs et al. (2016)	Clin	KSADS-PL CDRS-R ≤ 45	Adolescents	1. rf-CBT 2. Assessment	Prev	II	17 16	Ind	8	-+++	RRS	USA
Jerman et al. (2013)	Clin	SCID-I HRSD ≤ 13	Adults	1. MBCT 2. CAU	Prev	III	31 29	Grp	8	-+++	RRQ	EUR
Kearns et al. (2017)	Comm + Clin	CIDI	Adults	1. MBCT + DRAM 2. DRAM	Prev	III	101 102	Grp	8	++++	RRS	AUS
Keune et al. (2011)	Comm	SCID-I	Adults	1. MBCT 2. WLC	Prev	III	40 37	Grp	8	-+++	RSQ-D	EUR
Kinser et al. (2013)	Comm + Clin	MINI PHQ-9 ≥ 10	Adults	1. Yoga 2. Education	Treat	III	15 12	Grp	8	-+-+	RRS	USA
Korrelboom et al. (2012)	Clin	SCID-I	Adults	1. COMET + CAU 2. CAU	Treat	III	31 30	Grp	8	++-+	RSS	EUR
Lamers et al. (2015)	Comm	MINI CES-D ≥ 11	Adults + older adults	1. Life review 2. Expressive writing 3. WLC	Treat	III	58 58 58	Gsh	7	++++	RRS	EUR

Lokman et al. (2017)	Comm	14 ≤ IDS-SR ≤ 38	Adults	1. CDMI 2. WLC	Treat	III	329	Ugsh	na	++++	PSWQ	EUR
Manicavasagar et al. (2012)	Comm + Clin	CIDI	Adults	1. CBT 2. MBCT	Treat	III	39 30	Grp	8	-+++	RRS	AUS
McIndoo et al. (2016)	Comm	ADIS-IV BDI ≥ 14	Students	1. MBT 2. BAT 3. WLC	Treat	II	20 16 14	Ind Ind	4 4	+++-	RRS	USA
Moshier & Otto (2017)	Comm + Clin	SCID-I	Adults	1. CCT + BAT 2. Control + BAT	Treat	II	21 13	Ind Ind	4 4	++-+	RRS	USA
Mogoase et al. (2013)	Comm	BDI ≥ 12	Students	1. CNT 2. WLC	Treat	II	21 21	Gsh	7	--++	RRS	EUR
Schmaling et al. (2002)	Clin	PRIME-MD HAM-D ≥ 10	Adults	1. PST 2. Paroxetine 3. Placebo	Treat	III	35 27 30	Ind Ind	6	-+++	RRS	USA
Schuver & Lewis (2016)	Comm	SCID-I	Adults	1. Yoga 2. Walking	Treat	III	20 23	Gsh	8	-+++	RRS	USA
Shahar et al. (2010)	Comm	SCID-I HRSD ≤ 20	Adults	1. MBCT 2. WLC	Prev	III	26 19	Grp	8	--++	RRS-br	USA
Siegle et al. (2014)	Clin	SCID-I	Adults	1. CCT 2. CAU	Treat	II	27 26	Gsh	6	---+	RRS	USA
Teismann et al. (2014)	Comm + Clin	SCID-I	Adults	1. rf-CBT 2. WLC	Prev	III	31 29	Grp	11	++-+	RRS-br PTQ	EUR
van Aalderen et al. (2012)	Comm + Clin	MINI / SCID-I	Adults	1. MBCT 2. CAU	Treat/ Prev	III	102 103	Grp	8 + 1 day	+++-	RSS, PSWQ	EUR
van Vught et al. (2012)	Comm	SCID-I	Adults	1. MBCT 2. WLC	Prev	III	29 23	Grp	8	-+++	RRS	EUR
Vanderhasselt et al. (2015)	Comm + Clin	MINI	Adults	1. CCT + tDCS 2. CCT + sham tDCS	Treat	II	19 14	Ind	10	--++	RRS	EUR
Warmerdam et al. (2010)	Comm	CES-D ≥ 16	Adults	1. CBT 2. PST 3. WLC	Treat	III	88 88 87	Gsh Gsh	9 5	++++	PSWQ	EUR
Watkins & Moberly (2009)	Comm	BDI-II ≥ 14	Adults + Students	1. CNT + Relaxation 2. Relaxation	Treat	II	19 20	Gsh	8	---+	RRS	EUR
Watkins et al. (2009)	Comm	BDI-II > 14	Adults	1. CNT 2. Bogus CNT 3. WLC	Treat	II	70	Gsh	8	+---	RRS	EUR
Watkins et al. (2011)	Clin	Clinical DSM-IV diagnosis	Adults	1. rf-CBT 2. CAU	Prev	II	21 21	Ind	12	++++	RRS	EUR

		HRSD ≥ 8 BDI-II ≥ 9										
Watkins et al. (2012)	Clin	SCID-I	Adults	1. CNT + CAU 2. Relaxation + CAU 3. CAU	Treat	II	40 39 42	Gsh	46	++++	RRS	EUR
Wilkinson & Goodyer (2008)	Clin	K-SADS-PL	Adolescents	1. CBT + SSRI 2. SSRI	Treat	III	15 11	Ind Ind	19 19	-+--	RDQ	EUR
Williams et al. (2013)	Clin	MINI	Adults	1. CBM + iCBT 2. WLC	Treat	II	35 28	Gsh	13	++++	RTQ	AUS
Williams et al. (2015)	Clin	MINI	Adults	1. CBM + iCBT 2. Control + iCBT	Treat	II	60 61	Gsh	13	++++	RTQ	AUS
Yang et al. (2015)	Comm	SCID-I BDI-II ≥ 14	Adults	1. ABM 2. Placebo assessment 3. Assessment only	Treat	II	27 27 23	Ind	8	++++	RRS	OTH
Yang et al. (2016)	Comm[j]	K-SADS CES-D ≥ 20	Adolescents	1. ABM 2. Active control placebo	Treat	II	23 22	Ind	16	++++	RRS	OTH

Note. [a] Recr, recruitment; Comm, community recruitment; Clin, recruitment from clinical population.

[b] PHQ-9, Patient Health Questionnaire-9; SCID-I, Structured Clinical Interview for DSM III/IV; HRSD, Hamilton Rating Scale for Depression; GDS, Geriatric Depression Scale; SIGH-SAD, Structured Interview Guide for the Hamilton Rating Scale for Depression–Seasonal Affective Disorder Version; MINI, Mini International Neuropsychiatric Interview; K-SADS-PL, Kiddie – Schedule for Affective Disorders and Schizophrenia-Present and Lifetime Version; CDRS-R, Children's Depression Rating Scale-Revised; CIDI, Composite International Diagnostic Interview; CES-D, Center for Epidemiological Studies-Depression scale; IDS-SR, Inventory of Depressive Symptomatology Self-Report; ADIS-IV, Anxiety Disorders Interview Schedule-IV; BDI, Beck Depression Inventory; PRIME-MD, Primary Care Evaluation of Mental Disorders; HAM-D, Hamilton Rating Scale for Depression.

[c] tel, by telephone; f2f, face-to-face; CAU, care-as-usual; MBCT, Mindfulness-Based Cognitive Therapy; mADM, maintenance Antidepressant Medication; COMET, Competitive Memory Training; CBT, Cognitive Behavior Therapy, WLC, waiting list control; CCT, Cognitive Control Training; rf-CBT, rumination-focused CBT; DRAM, depression relapse active monitoring; MBT, Mindfulness-based Therapy; BAT, Behavioral Activation Therapy; CNT, Concreteness Training; tDCS, Transcranial Direct Current Stimulation; PST, Problem Solving Therapy; CDMI = Complaint-Directed Mini-Interventions; SSRI, Selective Serotonin Reuptake Inhibitor; iCBT, internet CBT;CBM, Cognitive Bias Modification; ABM, Attention Bias Modification.

[d] Treat, treatment for acute depression; Prev, treatment for relapse prevention.

[e] Phase II/III, Phase II RCT's to show sufficient preliminary efficacy of a new treatment vs Phase III RCT's to demonstrate efficacy/effectiveness more definitively against a control treatment in a larger trial

[f] Grp, group; Ind, individual; Gsh, guided self-help; Ugsh, unguided self-help.

[g] Nse, number of sessions

[h] adequate generation of allocation sequence; concealment of allocation to conditions; masking of outcome assessments by independent raters; and dealing with incomplete outcome data.

[i] PSWQ, Penn State Worry Questionnaire; EQ-R, Experiences Questionnaire-Rumination; RRS, Ruminative Response Scale; RSS, Rumination on Sadness Scale; RRQ, Rumination/Reflection Questionnaire, RSQ-D, Response-Styles Questionnaire; PTQ, Perseverative Thinking Questionnaire; RDQ, Responses to Depression Questionnaire; RTQ, Repetitive Thinking Questionnaire.

[j] Using a 2-stage case-finding procedure

Table 2. The effects of treatment for depression on repetitive negative thinking compared to control groups, post-test and follow-up: Hedges' g.

		c	g	95% CI	I^2	95% CI	p[a]
Post-test							
Hedges' g		37	0.48	0.37-0.59	47	17~64	
Standard differences in mean (g)		37	0.44	0.37-0.52	6	0~38	
One effect size per study (highest g)		30	0.52	0.40-0.63	41	0~61	
One effect size per study (lowest g)		30	0.45	0.33-0.56	42	1~62	
Specific measures							
Rumination only	Q = 45.977 (24)	31	0.49	0.37-0.62	46	9~64	.67[b]
Rumination (RRS only)		25	0.54	0.39-0.69	48	7~66	
Worry only		7	0.42	0.25-0.59	53	0~78	
RNT only		2	0.77	0.37-1.16	0	[c]	
Subgroup analyses							
Recruitment	Community	19	0.53	0.36-0.70	53	10~71	.51
	Clinical	12	0.47	0.27-0.67	53	0~74	
	Combination	6	0.38	0.20-0.57	7	0~64	
Goal	Acute treatment	25	0.47	0.34-0.61	52	16~69	.97
	Prevention relapse	11	0.50	0.29-0.71	45	0~71	
Format	Individual	10	0.51	0.22-0.79	64	10~80	.81
	Group	12	0.45	0.30-0.61	27	0~62	
	Guided self-help	14	0.53	0.34-0.72	51	0~72	
	Unguided self-help	1	0.39	0.17-0.61	0	[c]	
Target group	Adults	30	0.48	0.37-0.59	41	0~61	.82
	Other	7	0.53	0.17-0.88	69	4~84	

Number sessions	Less than 8	10	0.42	0.15-0.70	72	39~84	.30
	8 or more	25	0.54	0.43-0.64	10	0~45	
Control group	Waiting list	18	0.52	0.35-0.68	57	17~73	.94
	Care-as-usual	9	0.44	0.20-0.67	64	4~81	
	Attention/control	6	0.46	0.22-0.70	0	0~64	
	Pill placebo	4	0.53	0.19-0.86	5	0~70	
Definition depression	Diagnosis	28	0.51	0.38-0.64	43	1~63	.37
	Cut-off self-report	9	0.33	0.03-0.59	59	0~79	
Quality	3-4 criteria	28	0.51	0.39-0.63	44	2~63	.39
	0-2 criteria	9	0.38	0.12-0.64	53	0~76	
Phase II/III study	Phase II	16	0.66	0.47-0.86	39	0~65	.02
	Phase III	21	0.38	0.26-0.50	41	0~64	
Class of treatment	RNT-focused CBT	23	0.53	0.39-0.68	42	0~64	<.001
	Traditional CBT	6	0.63	0.42-0.85	42	0~76	
	Other	7	0.14	-0.01-0.29	0	0~58	
Type of treatment	CBT	6	0.63	0.42-0.85	42	0~76	<.001
	CNT	6	0.52	0.20-0.85	47	0~77	
	rf-CBT	3	0.76	0.40-1.12	0	0~73	
	MBCT	9	0.44	0.22-0.67	51	0~75	
	CCT	5	0.62	0.27-0.98	50	0~80	
	Other	7	0.14	-0.01-0.29	0	0~58	
Follow-up							
All studies		11	0.40	0.17-0.63	50	0~73	
One effect size per study (highest)		8	0.41	0.13-0.70	58	0~79	
One effect size per study (lowest)		8	0.34	0.07-0.62	52	0~77	

c = number of comparisons; [a] = The p-value in this column indicates whether the effect sizes in subgroup differ significantly from each other. [b] = Based on subgroup analysis excluding 3 studies with multiple RNT measurements; [c] = The 95% CI around I2 cannot be calculated when the number of studies is smaller than 3. RNT = Repetitive Negative Thinking; CBT = Cognitive-Behavioral Treatment; CNT = Concreteness training; rf-CBT = rumination focused - CBT; MBCT = Mindfulness-Based Cognitive Therapy; CCT = Cognitive Control Training.