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Relative Effectiveness of CBT-Components and Sequencing in Indicated Depression Prevention for Adolescents: A Cluster-Randomized Microtrial

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ABSTRACT

Objective: Cognitive Behavioral Therapy (CBT) was dismantled into four modules of three sessions each: cognitive restructuring (Think), behavioral activation (Act), problem solving (Solve) and relaxation (Relax). We investigated the modules' relative effectiveness in indicated depression prevention for adolescents and examined variations in sequencing of these modules.

Method: We performed a pragmatic cluster-randomized microtrial with four parallel conditions: (1) Think-Act-Relax-Solve ($n = 14$ clusters, $n = 81$ participants); (2) Act-Think-Relax-Solve ($n = 13$, $n = 69$); (3) Solve-Act-Think-Relax ($n = 13$, $n = 77$); and (4) Relax-Solve-Act-Think ($n = 12$, $n = 55$). The sample consisted of 282 Dutch adolescents with elevated depressive symptoms ($M_{\text{age}} = 13.8$; 55.7% girls, 92.9% Dutch). In total 52 treatment groups were randomized as a cluster. Assessments were conducted at baseline, after each module and at 6-month follow-up with depressive symptoms as primary outcome.

Results: None of the modules (Think, Act, Solve, Relax) was associated with a significant decrease in depressive symptoms after three sessions and no significant differences in effectiveness were found between the modules. All sequences of modules were associated with a significant decrease in depressive symptoms at post-intervention, except the sequence Relax-Solve-Act-Think. At 6-month follow-up, all sequences showed a significant decrease in depressive symptoms. No significant differences in effectiveness were found between the sequences at post-intervention and 6-month follow-up.

Conclusions: Regardless of the CBT technique provided, one module of three sessions may not be sufficient to reduce depressive symptoms. The sequence in which the CBT components cognitive restructuring, behavioral activation, problem solving and relaxation are offered, does not appear to significantly influence outcomes at post-intervention or 6-month follow-up.

Abbreviations: CDI-2:F: Children's Depression Inventory-2 Full-length version; CDI-2:S: Children's Depression Inventory-2 Short version; STARr: Solve, Think, Act, Relax and repeat.

Depression prevention among adolescents is now more important than ever, given the increasing prevalence. In 2017, the annual prevalence of a major depressive episode among (American) adolescents between 12 and 17 years was 13.2%, a 52% increase since 2005, when the prevalence was 8.7% (Twenge et al., 2019). A further increase in prevalence is expected due to a substantial increase in social and economic risk factors for depression as a consequence of COVID-19 (Holmes et al., 2020). Also, subclinical depression is highly prevalent in this age group, with a literature review showing prevalence rates ranging from 5.3% (annual prevalence) to 29.2% (point prevalence) (Carrellas et al., 2017). Both

clinical and subclinical adolescent depression have been related to diverse adverse consequences (e.g., social/academic problems, comorbid disorders and suicidal ideation) (e.g., Carrellas et al., 2017) and poor prognosis with high recurrence rates into adulthood (e.g., Jonsson et al., 2011), generating substantial costs for the individual and society (Bodden et al., 2018). These findings highlight the importance of detecting and preventing depression in adolescence.

Meta-analyses have shown that indicated prevention programs based on Cognitive Behavioral Therapy (CBT) can reduce the levels of depressive symptoms and the incidence of depressive disorders

among youth (e.g., Horowitz & Garber, 2006; Sregonja et al., 2019). However, the effect sizes are modest. Similarly, modest effects have been found for youth depression treatment programs in meta-analyses – in fact smaller effects than for treatment of other youth mental health problems (Weisz et al., 2017, 2006), and there is evidence that the mean effects of youth depression treatment have actually declined across the decades (Weisz et al., 2019). CBT programs aimed at depression usually consist of a blend of multiple components such as cognitive restructuring, behavioral activation, problem solving and relaxation, with all components having their own goal, content and techniques (e.g., McCarty & Weisz, 2007; Weersing et al., 2009).

Across the decades, both treatment and prevention protocols have developed that are standardized, with rather fixed sequences of sessions and skills, presented in standardized order. More recently, more flexible, modular approaches to treatment have been developed, in which there is no fixed, standardized sequence of components, but the order of components is personalized to fit each young person. An example of this is the Modular Approach to Therapy for Children with Anxiety, Depression, Trauma, or Conduct Problems (MATCH), a transdiagnostic intervention for youth (ages 6–15) which consists of diverse modules based on evidence-based treatments for anxiety, depression, trauma, and conduct problems (from CBT and behavioral parent training) any of which can be provided, and in any order, depending on the perceived needs of the young person (Chorpita & Weisz, 2009). In two RCTs, MATCH outperformed care as usual (CAU) for diverse problems including depression (Chorpita et al., 2017; Weisz et al., 2012). MATCH also outperformed standard evidence-based programs (Weisz et al., 2012), but not at 24-month follow-up (Chorpita et al., 2013). More recently, two RCTs showed no differences in effect between MATCH and CAU (Merry et al., 2020; Weisz et al., 2020). However, across all these RCTs, training clinicians in MATCH was associated with higher levels of adherence to empirically supported treatments, compared to CAU.

Although the findings suggest that MATCH may boost the use of evidence-based practices, including those relevant to depression prevention programs, the RCTs provide no insight into how the specific practices may relate to the outcomes – for example, whether or not the type of component or the sequencing of components has an impact on outcomes. The aim of this study was to investigate the relative effectiveness of four common CBT components (cognitive restructuring, behavioral activation, problem solving and relaxation) and

the relative effectiveness of four different sequences of components in indicated group-administered prevention of depression in adolescents.

To our knowledge, no comprehensive studies have investigated the relative effects of the CBT components, but the relative effectiveness of standalone programs which are related to the components have been investigated in depression prevention and treatment among adolescents. Cognitive Therapy (CT), Behavioral Therapy (BT), and Problem Solving Therapy (PST) have proven to be more effective than waitlist – CT and BT at both post-intervention and follow-up, PST only at post-intervention. CT, BT and PST have generally not differed significantly from one another in their effects. Compared to CBT and Interpersonal Psychotherapy (IPT), CT, BT and PST have proven to be similarly effective – CT and BT at both post-intervention and follow-up, PST only at post-intervention (e.g., Eckshtain et al., 2020; Zhou et al., 2015). Relaxation training (RT) has been found to be more effective than waitlist in treating depressed adolescents, but findings have been contradictory regarding the effect of RT compared to other psychotherapies (e.g., Kahn et al., 1990; Wood et al., 1996). Research on the effect of RT in the context of depression prevention is relatively scarce. In sum, at short term, CT, BT and PST have proven to be equally effective in addressing adolescent depression compared to each other and to CBT and IPT. At long term, both CT and BT were equally effective compared CBT and IPT, while PST was found to be less effective. With regard to RT, no conclusions can be drawn. For a table summarizing these findings on the relative effectiveness of psychotherapies, including their relative effect sizes, we refer to the network meta-analysis by Zhou et al. (2015).

Some studies have investigated the association of specific components with the overall effect of CBT on adolescent depression (Kennard et al., 2009; Oud et al., 2019). The TORDIA-study revealed that chronically depressed adolescents receiving CBT including problem solving and social skills training were respectively 2.3 and 2.6 times as likely to have a positive response as participants who received CBT without these components (Kennard et al., 2009). Yet, the impact of the components on the treatment effect might have been confounded by dose (number of sessions) and sequence effects, as the components were not randomly assigned but selected based on participants' clinical needs. A meta-regression by Oud et al. (2019) showed that CBT protocols containing a combination of the components cognitive restructuring (specifically challenging thoughts) and behavioral activation were more effective than CBT protocols without these components in

preventing and treating depression among youth, but only in the long term. In sum, little is known about the (relative) effectiveness of distinct CBT components, but there is preliminary evidence that some (combinations of) components are positively associated with overall effectiveness of CBT.

Also, adolescents report that they prefer specific strategies for coping with their depressive symptoms. Structured interviews with 105 adolescents aged 11 to 13 years, with varying depression symptomatology, revealed that the CBT-components behavioral activation, social support seeking and problem solving were most frequently used and also most commonly perceived as effective. Cognitive strategies and relaxation were less frequently used, with relaxation being the least habitual and perceived as least effective (Ng et al., 2016).

To our knowledge, no studies have investigated the sequence of components provided in relation to the effectiveness of CBT in adolescent depression. In current protocols, behavioral activation is often introduced at the start, directly followed by or combined with cognitive restructuring (Weersing et al., 2015), but the modular program MATCH suggests that beginning with problem solving is most optimal (Chorpita & Weisz, 2009). It is unclear whether the position of components is relevant to the effect of CBT. It might be that one intervention component is a primer for effective engagement in another intervention component, through an interaction of the components' supposed mechanisms of change (see Zettle & Hayes, 1987). This could create a "ripple effect," whereby the working mechanism of one component could affect the working mechanism of other components. For example, cognitive restructuring could be a primer for behavioral activation, because being able to identify and change negative and unrealistic beliefs into helpful and more realistic thoughts (cognitive change), may increase motivation to engage in positive activities that evoke positive reinforcement (behavioral change). To support this idea, cognitive theories suggest that cognitive change will lead to behavioral change (Beck et al., 1979). However, the opposite might be plausible too, as engaging in positive activities and consequently gaining positive reinforcement, may increase willingness to change negative thoughts (Dimidjian et al., 2011; Lewinsohn, 1974). Alternatively, mastering simple, effective procedures for solving nagging problems could boost confidence and motivation to engage in other treatment components. Based on current CBT protocols, theory and close consultation with mental health professionals, we selected four sequences of modules for the current study; three of these reflected the most common patterns in CBT protocols and professionals' recommendations (starting with cognitive restructuring, behavioral activation or

problem solving) and one was less often recommended, but offered practical advantages in its simplicity and likely appeal to young people (starting with relaxation).

The current experimental study was aimed at dismantling the relative effectiveness of four common CBT components (cognitive restructuring, behavioral activation, problem solving and relaxation) in indicated group-administered prevention of depression among adolescents, and of four different sequences of these components. Given the preliminary evidence for the positive contribution of the components problem solving and a combination of cognitive restructuring and behavioral activation to the overall effect of CBT (Kennard et al., 2009; Oud et al., 2019), evidence on adolescents' strategy preferences (Ng et al. 2016), the usual sequencing of components (Kennard et al., 2009; Weersing et al., 2015), and expected priming functions of some components (aka ripple effect), we hypothesized that all components and sequences of components would reduce adolescents' depressive symptoms, but that relaxation and a sequence of components starting with relaxation would be least effective.

Methods

Trial Design

We used a pragmatic non-blinded multisite cluster-randomized prevention microtrial with four parallel conditions. A microtrial is a randomized experiment investigating the effect of brief and focused environmental manipulations, such as isolated program components (Howe et al., 2010). The manipulations were four modules based on the CBT components cognitive restructuring (module Think), behavioral activation (module Act), problem solving (module Solve) and relaxation (module Relax). In each condition all four modules were provided, but the sequencing of modules differed per condition:

- condition 1: Think-Act-Relax-Solve;
- condition 2: Act-Think-Relax-Solve;
- condition 3: Solve-Act-Think-Relax;
- condition 4: Relax-Solve-Act-Think.

Assessments were conducted at baseline, after the first module (intermediate assessment 1), the second module (intermediate assessment 2), the third module (intermediate assessment 3), the last module (post-intervention) and at 6-month follow-up. Incentives were provided for each completed assessment and after completing all assessments. Approval for this study was provided by an independent medical ethics committee

of the University Medical Center Utrecht (NL59152.041.16). The study is registered in the Dutch Trial Register (Trial NL5584/NTR6176; www.trialregister.nl/trial/5584) and has been reported in accordance with the CONSORT 2010 statement for parallel group randomized trials (Schulz et al., 2010) and the extension to cluster-randomized trials (Campbell et al., 2012).

Participants and Procedure

Adolescents were recruited via 11 secondary schools located in the urbanized center of the Netherlands between 2017 and 2019. A total of 8,603 adolescents in secondary education (from pre-vocational to pre-university education) were screened on depressive symptoms using the full-length Children's Depression Inventory-2 (CDI-2:F; Bodden. et al., 2016; Kovacs, 2011). Inclusion criteria were ages between 10 and 20, sufficient knowledge of the Dutch language and elevated depressive symptoms (percentile score >75 on CDI-2). Exclusion criteria were absence of adolescents' consent (and parental consent for adolescents aged younger than 16), receiving treatment for mood- or anxiety problems, or presence of acute suicidal ideation (expressed as a score of 2 ("I want to end my life") on item 8 of the CDI-2:F (Bodden. et al., 2016) followed by a total score of ≥ 12 based on the suicide items of the Questionnaire assessing Suicide and Self Injury (VOZZ; Huisman et al., 2015) and a high risk determination in a clinical interview by a licensed psychologist). In case of acute suicidal ideation (concrete plans and intentions), participants were referred to a general practitioner for a referral to mental health care.

Of the adolescents that were screened, 2,009 adolescents met the inclusion criteria and were approached for participation. Of those, 52 (2.6%) adolescents were identified with suicidal ideation (by CDI-2:F and VOZZ), of which 50 were excluded because of acute suicidal ideation (confirmed in a clinical interview), or no interest in participation. The remaining two participated. In total 1,669 adolescents and/or their parents declined to participate or could not be contacted. Among this group, most frequently mentioned reasons for nonparticipation were: depressive symptoms were not recognized or were attributed to external circumstances such as school problems, exam week, menstruation, a stressful life event or overlap with other problems such as Autism Spectrum Disorders, Attention Deficit Hyperactivity Disorder, physical illness or side effects of medication use (35.2%); no motivation or interest in participation due to fear of stigmatization, difficulties with the group format of the training and/or that the training was provided at school or having other priorities (9.2%); and recent or

current treatment or preferring other help (10.3%). There was also a group of adolescents and/or parents that could not be contacted via e-mail and/or phone (25.7%) or provided no reason for declining participation (19.6%).

In total, 290 adolescents were willing to participate of which 285 adolescents (and their parents) provided informed consent. Three of them had to be excluded because they were already in treatment. The remaining 282 adolescents (age range 11–18) were stratified by gender (boys and girls) and age (11–13, 14–15 and 16–18 years) per school. Treatment groups were formed of approximately five students ($M = 5.42$, $SD = 1.41$) from the same school. These treatment groups (52 in total) were randomized as a cluster to one of the four conditions via computer-generated block randomization (block size four). Participants were masked to their treatment allocation up to the introductory meeting. The four conditions consisted of respectively 14, 13, 13 and 12 clusters and 81, 69, 77 and 55 participants. See [Figure 1](#) for the participants' flow through the study. With $n = 282$, our study was powered to detect a clinically relevant effect of $d \geq 0.33$ as statistically significant (at $\alpha \leq 0.05$, 2-tailed) with a power of $(1-\beta) \geq 0.80$ when the primary outcome (depressive symptoms) is evaluated in a baseline adjusted analysis of variance while also taking into account the nesting in the data owing to the cluster randomized trial (StataCorp, 2015).

Training

We developed an indicated group-administered prevention program in collaboration with certified CBT therapists and experts in the field. For each of the four CBT components a module of three sessions was developed. These modules were based on cognitive and behavioral theories, a taxonomy describing the techniques that diverse CBT components should comprise (Oud et al., 2019), Dutch CBT protocols (e.g., The D(o)epression course; Stikkelbroek et al., 2005) and MATCH (Chorpita & Weisz, 2009). The program was called "STARr-training," an acronym of the first letters of the modules (S from Solve, T from Think, A from Act, R from Relax). The small r means "repeat" referring to the recurring encouragement to practice the lessons learned. The modules' content is described in [Table 1](#).

The program consisted of an introductory meeting (with psychoeducation about depression and CBT) followed by 12 sessions of 45–60 minutes each. It was provided in groups of approximately five adolescents of the same gender and age group, and took place at the participating schools directly after school lessons, one or two times a week (depending on holidays and the schools'

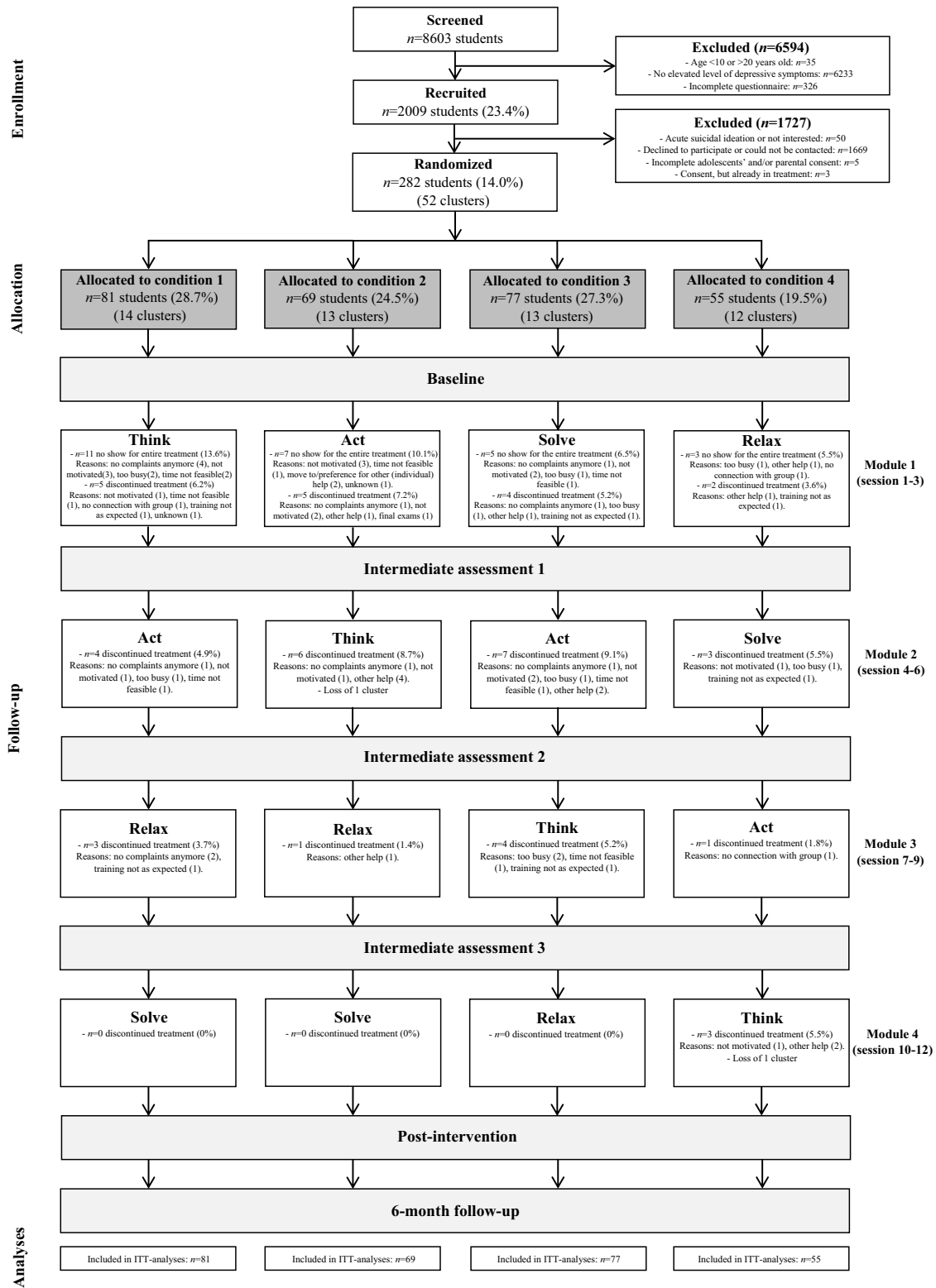


Figure 1. Flow diagram of participants.

preference) ($M = 1.27$, $SD = 0.14$). Trainers were 44 pedagogics/psychology graduates ($M_{age} = 25.84$, $SD = 4.90$; 90.9% female; 93.2% Dutch), who all received

a 2.5-day training and were supervised by a psychologist during the intervention after the first, second and third module. To rate what percentage of the program was

Table 1. Description of the modules of the STARr-training.

Module	Component	Description of module
Solve	Problem solving	<ul style="list-style-type: none"> ● Psychoeducation about problems, coping (avoiding or solving) and consequences. ● Solving problems by: <ol style="list-style-type: none"> 1. defining the problem; 2. setting a goal; 3. generating solutions; 4. evaluating solutions (advantages and disadvantages, effectiveness and feasibility); 5. choosing a solution; 6. making a plan; 7. evaluating the plan and self-reward;
Think	Cognitive restructuring	<ul style="list-style-type: none"> ● Seeking social support as coping ● Psychoeducation about the relationship between thoughts, feelings, behavior and short and long term consequences. ● Challenging negative thoughts and generating positive thoughts by: <ol style="list-style-type: none"> 1. identifying negative thought and scheduling; event, thought, feelings, behavior and consequences; 2. assessing credibility of negative thought; 3. examining evidence for and against negative thought; 4. choosing strongest evidence; 5. generating positive thought and scheduling; 6. assessing credibility of positive thought; 7. reassessing credibility of negative thought.
Act	Behavioral activation	<ul style="list-style-type: none"> ● Psychoeducation about mood fluctuations, and relationship between mood and activities. ● Self-monitoring with daily mood monitors and activity list. ● Examining the link between daily mood and activities in a graph. ● Adapting activity list and goal setting to increase pleasant activities. ● Evaluating the goal.
Relax	Relaxation	<ul style="list-style-type: none"> ● Psychoeducation about stress. ● Four types of relaxation exercises: <ol style="list-style-type: none"> 1. attention/task concentration techniques; 2. breathing techniques; 3. progressive muscle relaxation; 4. guided imagery.

provided as intended, a treatment integrity scale was developed with two categories; content (meeting specific goals) and form (agenda setting and time management). Items were rated on a scale from 0 to 3 (0 = not provided, 1 = minimal, 2 = sufficient and 3 = completely). Per treatment group one or two randomly chosen sessions were videotaped and scored (4 missing because the recordings failed).

Measures

See the protocol paper for all measures that were included in the study (Van den Heuvel et al., 2019). For this paper we used the following instruments.

Primary Outcome

The CDI-2 (Bodden. et al., 2016) was used to measure *depressive symptoms*. At baseline, post-intervention and 6-month follow-up the 28-item version (CDI-2:F) was administered and at intermediate assessment 1, 2 and 3, the 12-item version (CDI-2:S). The total score of the CDI-2:F ranges from 0 to 56 and of the CDI-2:S from 0 to 24. To ensure clinical relevance, we used a cutoff of 14 (CDI-2:F). Because of overlapping items among the versions, a total score of the short version at all other measurement moments was calculated as well. In previous research, psychometric properties of the Dutch CDI-2:F were found to be good (Bodden. et al.,

2016). In this study, Cronbach's alpha varied between .86 and .90 (CDI-2:F). For the CDI-2:S, no psychometric properties are available. In this study, Cronbach's alpha varied between .79 and .84 (CDI-2:S). Pearson correlations between the two versions ranged from .93 to .96 (all $p < .001$).

Secondary Outcome

To measure the presence of a *depressive disorder*, we used the Kiddie-Schedule for Affective Disorders and Schizophrenia, present and lifetime version (K-SADS-PL; Kaufman et al., 1997; Reichart et al., 2000). The K-SADS-PL is a widely used semi-structured diagnostic interview that assesses a wide range of diagnoses (present and lifetime) including their severity according to DSM criteria. We administered the section related to affective disorders. In this study, we only reported the percentage of adolescents who met the criteria for major depressive disorder (MDD) or persistent depressive disorder (PDD) (see Table 3). The interview was conducted by 60 independent pedagogics/psychology master students by telephone at baseline (present and lifetime), post-intervention (present) and 6-month follow-up (present). Interviewers were trained and supervised in the K-SADS, and masked to the participants' allocation. In previous research, interrater agreement and test-retest reliability of the K-SADS were found to be good (Kaufman et al., 1997). In this study, interrater reliability was assessed by rating four randomly

chosen audiotaped interviews per assessor (36 of 240 recordings were missing due to technical problems). Ratings were done by independent assessors. Interrater reliability, calculated at criteria level by means of Cohen's kappa, was substantial (.66). The average total proportion of agreement for criteria was .92 and the average agreement on present and lifetime diagnoses was .89.

Analyses

We hypothesized that the modules Think (first module of condition 1), Act (first module of condition 2) and Solve (first module of condition 3) would be associated with greater reductions in depressive symptoms than the module Relax (first module of condition 4). For the different sequences of modules, we hypothesized that the sequences Think-Act-Relax-Solve (condition 1), Act-Think-Relax-Solve (condition 2) and Solve-Act-Think-Relax (condition 3) would be associated with greater reductions in depressive symptoms and the prevalence of depressive disorder than the sequence Relax-Solve-Act-Think (condition 4). So, for both research questions, we expected differences between condition 1, 2 and 3 compared to condition 4, with the first three conditions outperforming the last one.

As a first step of analyses, baseline demographic and clinical characteristics were calculated and tested for potential confounding in relation to the effects of the different conditions on depressive symptoms and diagnoses. Variables that were unequally distributed across conditions 1, 2 and 3 versus condition 4, and that were associated with the outcome variable, were seen as possible confounders. All subsequent analyses were done controlling for confounders. Also, all analyses were conducted according to the intention-to-treat (ITT) principle (with one exception, see end of this section).

We used multilevel mixed modeling in Stata 16 (StataCorp, 2019), as our data had a hierarchical structure, with repeated measurements (level 1) nested within individuals (level 2) nested within treatment groups (level 3). For individuals and treatments groups, random effects were included. The four conditions were included as fixed effects using dummy variables for condition 1, 2 and 3 with condition 4 as reference category. Time was included as a categorical variable for measurements at intermediate assessment 1 up to 6-month follow-up with baseline as reference category. Condition*Time interactions were modeled to evaluate treatment effects over time. The analyses were conducted with depressive symptoms as a continuous outcome variable and diagnostic status of depressive disorder as a binary outcome

variable (0 = no diagnosis, 1 = diagnosis present). Marginal means were obtained via the linear mixed model and used to graph the development of depressive symptoms and diagnostic status from baseline to 6-month follow-up in all conditions. To examine effects between screening and baseline, we used regression imputed data.

Finally, we investigated the clinical relevance of the results. We calculated the percentage of adolescents scoring above the clinical cutoff of the full CDI-2:F (raw score 14) at baseline, post-intervention and 6-month follow-up using regression imputed data. We also calculated the percentage of adolescents meeting the criteria for MDD or PDD at these time points, using data from adolescents who attended the K-SADS at baseline, post-intervention and 6-month follow-up only ($n = 186, 66\%$) (thus, not ITT).

Results

The sample consisted of 282 adolescents with elevated levels of depressive symptoms. Adolescents were less likely to participate if they had a lower level of depressive symptoms ($OR = 0.95, p < .001, 95\% CI = 0.93-0.97$), were older ($OR = 1.17, p < .001, 95\% CI = 1.08-1.27$), had a low or moderate educational level ($OR = 1.34, p = .028, 95\% CI = 1.03-1.73$) or had a non-Dutch ethnicity ($OR = 2.76, p < .001, 95\% CI = 1.71-4.46$). Participants attended on average 8.18 sessions ($SD = 4.09$, median = 10, mode = 12). Total treatment dropout was 26.2% ($n = 74$). Both treatment attendance and dropout did not differ between conditions. The mean treatment integrity score for content of the program (e.g., meeting goals) was 84.3% ($SD = 13.85$; range 53.3–100%) and for form (e.g., time management) was 91.9% ($SD = 23.57$; range 50–100%). Ratings were done by nine independent research assistants and the first author, with substantial interrater reliability (Cohen's kappa) of .69.

See Table 2 for demographic variables at baseline and Table 3 for descriptive statistics on the clinical measures, for the total sample and per condition. Due to significant baseline differences and associations with the outcome variable, we added ethnicity and baseline stress level (measured with the Perceived Stress Scale-10, see Van den Heuvel et al., 2019) as covariates in all subsequent analyses to adjust for potential confounding. We also controlled for depressive symptoms as measured at screening.

Primary Outcome (Depressive Symptoms)

Development over Time

In Figure 2a and b, the development of depressive symptoms over time for all four conditions is displayed, including the 95% confidence intervals (CI) around the

Table 2. Baseline demographic variables for the total sample and per condition (as observed).

Variable	Total (<i>n</i> = 282)	Condition 1: Think-Act- Relax-Solve (<i>n</i> = 81)	Condition 2: Act-Think- Relax-Solve (<i>n</i> = 69)	Condition 3: Solve-Act- Think-Relax (<i>n</i> = 77)	Condition 4: Relax-Solve- Act-Think (<i>n</i> = 55)
	<i>M</i> (<i>SD</i>) <i>n</i> (%)	<i>M</i> (<i>SD</i>) <i>n</i> (%)	<i>M</i> (<i>SD</i>) <i>n</i> (%)	<i>M</i> (<i>SD</i>) <i>n</i> (%)	<i>M</i> (<i>SD</i>) <i>n</i> (%)
Age (years)	13.82 (1.48)	13.88 (1.56)	13.62 (1.45)	13.95 (1.49)	13.78 (1.41)
Gender					
Girls	157 (55.7)	43 (53.1)	40 (58.0)	40 (51.9)	34 (61.8)
Boys	125 (44.3)	38 (46.9)	29 (42.0)	37 (48.1)	21 (38.2)
Ethnicity					
Dutch	262 (92.9)	78 (96.3)	65 (94.2)	71 (92.2)	48 (87.3)
Other	20 (7.1)	3 (3.7)	4 (5.8)	6 (7.8)	7 (12.7)
Education level					
Low	19 (6.7)	0	14 (20.3)	1 (1.3)	4 (7.3)
Moderate	121 (42.9)	28 (34.6)	27 (39.1)	42 (54.5)	24 (43.6)
High	142 (50.4)	53 (65.4)	28 (40.6)	34 (44.2)	27 (49.1)

Low: pre-vocational secondary education (in Dutch: vmbo-basis/kader/gl), moderate: higher general secondary education (in Dutch: vmbo-tl, vmbo-tl/havo, havo), high: pre-university education (in Dutch: havo/vwo, vwo).

Table 3. Depressive symptoms and presence of a depressive disorder at all assessments for the total sample and per condition (as observed).

Variable	Total (<i>n</i> = 282)		Condition 1: Think-Act- Relax-Solve (<i>n</i> = 81)		Condition 2: Act-Think- Relax-Solve (<i>n</i> = 69)		Condition 3: Solve-Act- Think-Relax (<i>n</i> = 77)		Condition 4: Relax-Solve- Act-Think (<i>n</i> = 55)	
	<i>M</i> (<i>SD</i>)	<i>n</i>	<i>M</i> (<i>SD</i>)	<i>n</i>	<i>M</i> (<i>SD</i>)	<i>n</i>	<i>M</i> (<i>SD</i>)	<i>n</i>	<i>M</i> (<i>SD</i>)	<i>n</i>
Depressive symptoms										
<i>CDI-2:Short version</i>										
Screening	8.71 (3.31)	282	8.53 (3.45)	81	8.81 (3.35)	69	8.86 (3.32)	77	8.64 (3.08)	55
Baseline	7.76 (3.84)	260	7.62 (3.80)	74	7.92 (3.51)	62	8.01 (4.05)	73	7.41 (4.04)	51
Intermediate 1	7.69 (3.90)	234	7.56 (3.96)	64	7.61 (3.71)	57	8.11 (4.10)	64	7.41 (3.87)	49
Intermediate 2	7.55 (4.16)	211	6.86 (4.01)	59	7.78 (4.24)	50	8.25 (4.38)	57	7.33 (3.94)	45
Intermediate 3	7.27 (4.39)	187	6.51 (3.84)	51	7.70 (4.78)	47	7.65 (4.22)	48	7.29 (4.80)	41
Post-intervention	6.49 (4.25)	194	5.94 (3.79)	53	6.70 (4.77)	47	6.70 (4.19)	54	6.70 (4.38)	40
6-month follow-up	5.82 (3.98)	161	5.77 (3.70)	53	6.25 (3.92)	36	5.71 (3.99)	42	5.53 (4.65)	30
<i>CDI-2:Full version</i>										
Screening	18.36 (6.48)	282	18.10 (6.78)	81	18.43 (6.40)	69	18.64 (6.74)	77	18.25 (5.89)	55
Baseline	16.45 (7.60)	260	16.61 (7.50)	74	16.65 (7.21)	62	16.59 (8.14)	73	15.76 (7.57)	51
Post-intervention	13.87 (8.63)	194	12.83 (7.54)	53	14.15 (9.18)	47	14.06 (9.27)	54	14.68 (8.63)	40
6-month follow-up	12.37 (8.10)	161	12.47 (7.39)	53	12.83 (8.17)	36	12.52 (8.50)	42	11.40 (8.97)	30
	<i>n</i> (%)		<i>n</i> (%)		<i>n</i> (%)		<i>n</i> (%)		<i>n</i> (%)	
Depressive disorder ^a										
Yes										
Baseline	39 (13.8)		10 (12.3)		7 (10.1)		13 (16.9)		9 (16.3)	
Post-intervention	13 (4.6)		3 (3.7)		1 (1.4)		5 (6.5)		4 (7.3)	
6-month follow-up	7 (2.5)		1 (1.2)		2 (2.9)		4 (5.2)		0 (0)	
No										
Baseline	223 (79.1)		63 (77.8)		58 (84.1)		59 (76.6)		43 (78.2)	
Post-intervention	195 (69.2)		56 (69.1)		50 (72.5)		51 (66.2)		38 (69.1)	
6-month follow-up	185 (65.6)		55 (67.9)		44 (63.8)		47 (61.0)		39 (70.9)	
Missing										
Baseline	20 (7.1)		8 (9.9)		4 (5.8)		5 (6.5)		3 (5.5)	
Post-intervention	74 (26.2)		22 (27.2)		18 (26.1)		21 (27.3)		13 (23.6)	
6-month follow-up	90 (31.9)		25 (30.9)		23 (33.3)		26 (33.8)		16 (29.1)	

Intermediate = Intermediate assessment; ^a This includes MDD or PDD

means, with respectively the CDI-2:S and CDI-2:F as outcome measures. The average number of weeks between screening (not included in Figures) and baseline was 9.81 (*SD* = 3.19), with depressive symptoms (CDI-2:F) decreasing significantly over time, $t(281) = 5.30$, $p < .001$, $d = 0.28$.

Relative Effectiveness of Distinct Modules after Three Sessions

Between baseline and intermediate assessment 1 (Figure 2a), we evaluated the relative effectiveness of the distinct modules Think, Act, Solve versus Relax (after three sessions). None of the modules was

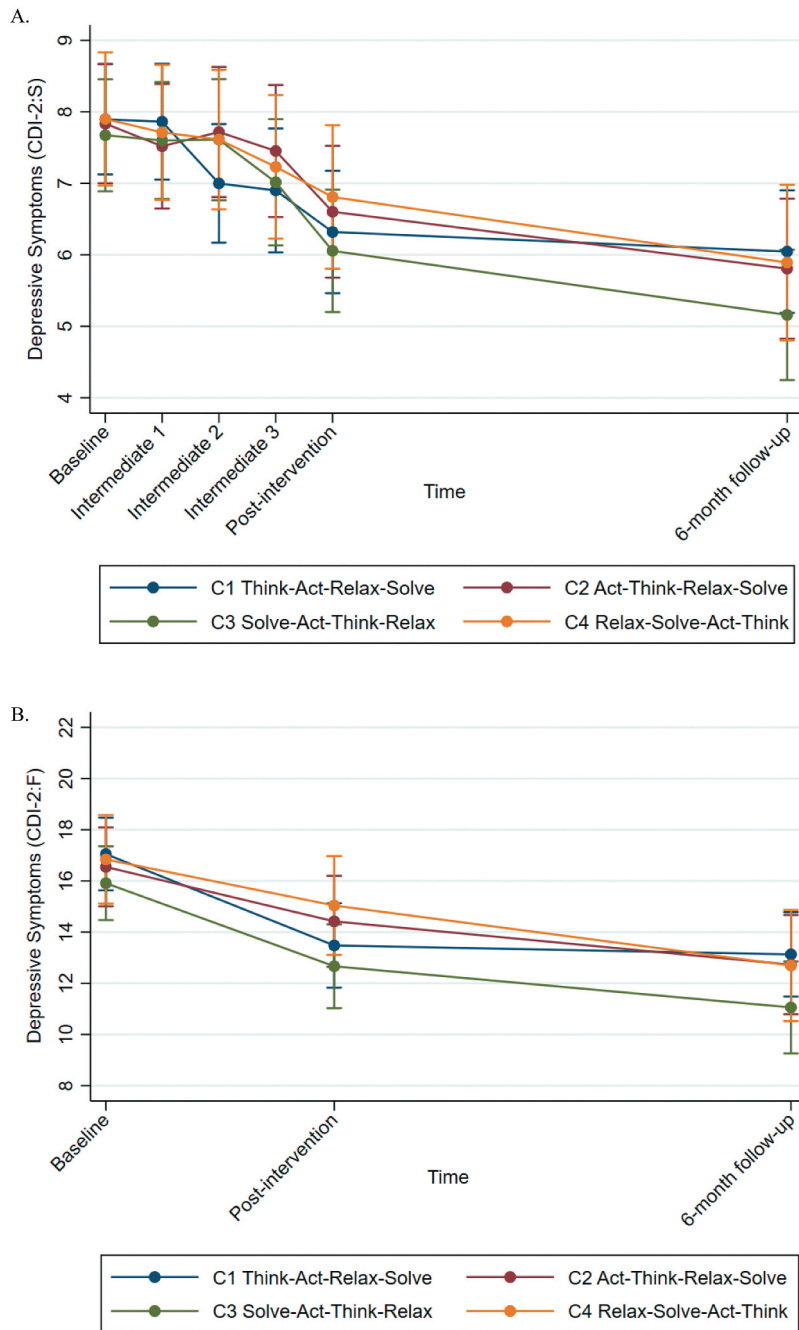


Figure 2. Marginal means for depressive symptoms over time per condition with 95% CI (controlled for ethnicity, stress level at baseline and depressive symptoms at screening) ($N = 282$). a: CDI-2:S, b: CDI-2:F.

associated with a significant decrease in depressive symptoms between baseline and intermediate assessment 1 measured with the CDI-2:S (see Table 4). Also, no significant Condition*Time interaction effects were found, indicating no significant differences between the modules Think, Act and Solve compared to Relax in the effect on depressive symptoms after three sessions.

Relative Effectiveness of Different Sequences of Modules at Post-intervention and 6 Month Follow-up Between baseline and respectively post-intervention and 6-month follow-up (Figure 2a and b), we evaluated the relative effectiveness of the sequences of modules Think-Act-Relax-Solve, Act-Think-Relax-Solve, Solve-Act-Think-Relax versus Relax-Solve-Act-Think directly after training and after 6 months. All

Table 4. Within-group time effects on depressive symptoms relative to baseline, controlling for ethnicity, stress at baseline and depressive symptoms at screening.

	<i>B</i>	<i>p</i>	95% CI		<i>d</i>
			LL	UL	
Condition 1: Think-Act-Relax-Solve					
<i>CDI-2:Short version</i>					
Intermediate assessment 1	-0.11	.764	-0.87	0.64	-0.01
Intermediate assessment 2	-0.90	.023	-1.67	-0.13	-0.24
Intermediate assessment 3	-0.89	.031	-1.70	-0.08	-0.27
Post-intervention	-1.65	<.001	-2.45	-0.85	-0.43
6-month follow-up	-1.87	<.001	-2.67	-1.07	-0.50
<i>CDI-2:Full version</i>					
Post-intervention	-3.69	<.001	-5.48	-1.89	-0.49
6-month follow-up	-3.94	<.001	-5.74	-2.14	-0.54
Condition 2: Act-Think-Relax-Solve					
<i>CDI-2:Short version</i>					
Intermediate assessment 1	-0.40	.336	-1.21	0.41	-0.09
Intermediate assessment 2	-0.12	.786	-0.97	0.73	-0.03
Intermediate assessment 3	-0.28	.525	-1.14	0.58	-0.11
Post-intervention	-1.30	.003	-2.16	-0.44	-0.36
6-month follow-up	-2.05	<.001	-2.97	-1.12	-0.59
<i>CDI-2:Full version</i>					
Post-intervention	-2.24	.024	-4.18	-0.30	-0.30
6-month follow-up	-3.84	<.001	-5.93	-1.75	-0.54
Condition 3: Solve-Act-Think-Relax					
<i>CDI-2:Short version</i>					
Intermediate assessment 1	-0.15	.688	-0.91	0.60	-0.02
Intermediate assessment 2	-0.06	.876	-0.85	0.72	-0.02
Intermediate assessment 3	-0.56	.187	-1.38	0.27	-0.16
Post-intervention	-1.69	<.001	-2.48	-0.89	-0.41
6-month follow-up	-2.53	<.001	-3.39	-1.67	-0.63
<i>CDI-2:Full version</i>					
Post-intervention	-3.36	<.001	-5.15	-1.56	-0.40
6-month follow-up	-4.88	<.001	-6.82	-2.94	-0.60
Condition 4: Relax-Solve-Act-Think					
<i>CDI-2:Short version</i>					
Intermediate assessment 1	-0.27	.544	-1.14	0.60	-0.05
Intermediate assessment 2	-0.29	.531	-1.19	0.62	-0.07
Intermediate assessment 3	-0.57	.235	-1.50	0.37	-0.17
Post-intervention	-1.16	.015	-2.10	-0.23	-0.28
6-month follow-up	-2.03	<.001	-3.05	-1.00	-0.51
<i>CDI-2:Full version</i>					
Post-intervention	-1.92	.075	-4.02	0.19	-0.24
6-month follow-up	-4.17	<.001	-6.50	-1.85	-0.56

different sequences were associated with a significant decrease in depressive symptoms between baseline and respectively post-intervention and 6-month follow-up, measured with the CDI-2:S. Using the CDI-2:F, comparable results were found with one exception. The sequence Relax-Solve-Act-Think (condition 4) was not associated with a significant decrease in depressive symptoms between baseline and post-intervention (see Table 4). No significant Condition*Time interaction effects were found, measured with the CDI-2:S and CDI-2:F, indicating no significant differences between the sequences Think-Act-Relax-Solve, Act-Think-Relax-Solve, Solve-Act-Think-Relax compared to Relax-Solve-Act-Think in the effect on depressive symptoms immediately after training (12 sessions) and after six months.

Relative Effectiveness of Different Sequences of Modules after Six and Nine Sessions

Between baseline and respectively intermediate assessment 2 and 3 (Figure 2a), we explored intermittent effects after six and nine sessions. None of the sequences of modules was associated with a significant decrease in depressive symptoms between baseline and respectively intermediate assessment 2 (after six sessions) and intermediate assessment 3 (after nine sessions) measured with the CDI-2:S, with one exception. The sequence Think-Act-Relax-Solve showed a significant decrease in depressive symptoms between baseline and respectively intermediate assessment 2 and 3 (see Table 4). No significant Condition*Time interaction effects were found, indicating no significant differences between the sequences Think-Act-Relax-Solve, Act-Think-Relax-Solve, Solve-Act-Think-Relax compared to Relax-Solve-Act-Think in the effect on depressive symptoms after six and nine sessions.

Clinical Relevance

At post-intervention the marginal means of depressive symptoms (CDI-2:F) of the sequences Think-Act-Relax-Solve and Solve-Act-Think-Relax were below the clinical cutoff of 14, but that was not true for the other sequences. At 6-month follow-up, all sequences showed a clinically relevant effect (see Figure 2b). With regard to the total sample, 74.5% ($n = 210$) scored above the cutoff at screening. At baseline this was 57.5% ($n = 162$), at post-intervention 42.6% ($n = 120$) and at 6-month follow-up 36.9% ($n = 104$), which is a significant reduction relative to baseline for both subsequent time points. The reduction between screening and baseline was also significant (all $p < .01$).

Secondary Outcome (Depressive Disorder)

Development Over Time

Figure 3 shows the pattern of depressive disorders over time for all four conditions, including the 95% CI around the means.

Relative Effectiveness of Different Sequences of Modules at Post-intervention and 6-month Follow-up

Between baseline and post-intervention, we found a significant decrease in rates of depressive disorder only for the sequence Think-Act-Relax-Solve (condition 1). Between baseline and 6-month follow-up, all sequences were associated with a significant decrease in rates of depressive disorder, except the sequence Act-Think-Relax-Solve (condition 2) (see Table 5). No

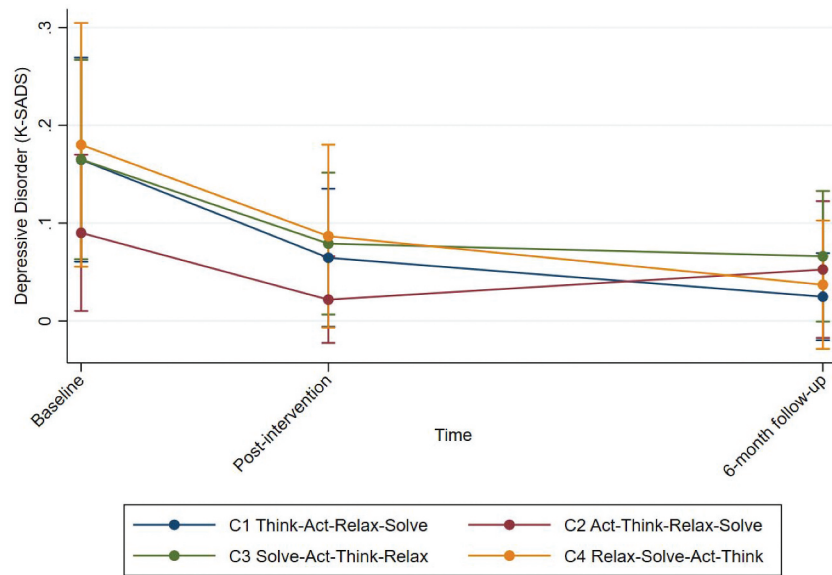


Figure 3. Marginal means for depressive disorder* over time per condition with 95% CI (controlled for ethnicity, stress level at baseline and depressive symptoms at screening) ($N = 282$).

Note. The K-SADS (Table 3) showed that at 6-month follow-up no participant within condition 4 met criteria for a depressive disorder. Although this is a positive result, STATA cannot handle outcome variables without variation and thus automatically excluded condition 4 at that time point. In order to perform the analyses so that they included condition 4, we changed the outcome of a randomly selected participant to 1 (=diagnosis present). This is a conservative solution as it reduces the risk of Type-I-error. Only the adjusted analyses have been reported.*The probability (number between 0–1) of having MDD or PDD based on the K-SADS.

Table 5. Within-group time effects on depressive disorder^a relative to baseline, controlling for ethnicity, stress at baseline and depressive symptoms at screening.

	OR	<i>p</i>	95% CI	
			LL	UL
Condition 1: Think-Act-Relax-Solve				
Post-intervention	0.16	.046	0.03	0.97
6-month follow-up	0.04	.012	0.00	0.48
Condition 2: Act-Think-Relax-Solve				
Post-intervention	0.10	.124	0.01	1.87
6-month follow-up	0.40	.407	0.05	3.49
Condition 3: Solve-Act-Think-Relax				
Post-intervention	0.24	.058	0.05	1.05
6-month follow-up	0.17	.034	0.03	0.87
Condition 4: Relax-Solve-Act-Think				
Post-intervention	0.23	.119	0.04	1.46
6-month follow-up	0.06	.034	0.00	0.81

^aThis includes MDD or PDD

significant Condition*Time interaction effects were found, indicating no significant differences between the sequences Think-Act-Relax-Solve, Act-Think-Relax-Solve, Solve-Act-Think-Relax compared to Relax-Solve-Act-Think in the effect on depressive disorders immediately after training (12 sessions) and after six months.

Clinical Relevance

Of the 186 participants who completed the K-SADS at baseline, post-intervention and 6-month follow-up, respectively, 15.1% ($n = 28$), 4.8% ($n = 9$) and 3.2%

($n = 6$) met diagnostic criteria for MDD or PDD; that is a significant reduction relative to baseline for both subsequent time points (both $p < .01$).

Discussion

In this study, we dismantled CBT into four common components (cognitive restructuring, behavioral activation, problem solving and relaxation) and investigated their relative effectiveness in indicated depression prevention among Dutch adolescents. In addition, the relative effectiveness of four different sequences of these CBT components was examined. Each component was operationalized into a module of three sessions. Results can be summarized as follows. Relative to baseline, none of the *distinct modules* (Think, Act, Solve or Relax) was associated with a significant decrease in the level of depressive symptoms directly measured after three sessions of that module. Also, no significant differences in effect were found between the modules. All *sequences of (four) modules* were associated with a significant decrease in depressive symptoms from baseline to post-intervention (after 12 sessions), except the sequence Relax-Solve-Act-Think which showed no significant reduction with the full CDI-2. At 6-month follow-up, all sequences showed a significant decrease in depressive symptoms relative to baseline. No significant differences were found between

the sequences at both post-intervention and 6-month follow-up. These results suggest that the sequencing of the four CBT components may not be relevant to the overall effectiveness of CBT in indicated depression prevention among adolescents.

Contrary to our first hypothesis, we found that none of the distinct modules was associated with a significant post-intervention reduction in depressive symptoms and that there were no significant differences between the modules. This suggests that regardless of the CBT technique offered, a single module of three sessions, might be not sufficient to reduce depressive symptoms among adolescents. An explanation for this lack of effect could be the small dose provided by only three sessions. More sessions might be needed to reduce the level of depressive symptoms. More sessions might have helped adolescents internalize the techniques more fully, and given them more opportunity to practice the techniques in daily life; that could have been especially helpful with complex modules, such as cognitive restructuring. Length of sessions might also play a role. As the training was given in groups averaging five adolescents, time was required for group interaction, alliance and cohesiveness. Sessions took 45–60 minutes, which might be too short to develop these group processes and also address CBT content. A meta-analysis of 69 depression prevention programs (not only CBT), showed that programs with more than 8 sessions and programs with session lengths of 60–90 minutes had the largest effect sizes among different age groups including adolescents (Jané-Llopis et al., 2003), suggesting the importance of both dose and duration of sessions on the effect. Future research should focus on the effect of dose and session length of each specific module.

Contrary to our second hypothesis, we found that all sequences of modules were associated with significant reductions in depressive symptoms at post-intervention (small effect sizes) and 6-month follow-up (medium effect sizes) (except for the sequence Relax-Solve-Act-Think at post-intervention, full CDI-2), and that there were no significant differences between the sequences. This suggests that regardless of the sequencing of components, CBT might reduce depressive symptoms as long as the components are offered. It also suggests that the modules might reasonably be given in any order and thus that flexible, personalizable approaches (such as MATCH; Chorpita & Weisz, 2009) are worth considering and testing in the context of depression prevention. The symptom change seen with the four modules together (called STARr-training) seems comparable to pattern seen in conventional CBT. A recent meta-analysis, that compared protocolled CBT based group depression prevention programs for high risk

adolescents to inactive controls (e.g., waitlist), showed a superior effect for protocolled CBT with small overall effect sizes at post-intervention and 12-month follow-up, but negligible overall effect sizes at 6- and >12-month follow-up (Sregonja et al., 2019). The pattern of change we observed appeared comparable, but cannot be compared directly as we investigated within-group effects and did not compare the sequences to an inactive control. The pattern of change with STARr-training is also comparable to changes seen with OVK 2.0, a Dutch CBT based indicated depression prevention program consisting of 8 sessions (of 60 minutes) and 1 booster session that has recently been found more effective than a psycho-education control at 12-month follow-up (De Jonge-Heesen et al., 2020). Although, we did not include a 12-month follow-up measure, at the other time points the CDI-2 mean scores in our study are comparable to the (imputed) means of the OVK-condition (De Jonge-Heesen et al., 2020). This comparison should be interpreted with caution, as our sample had a broader age range and was more balanced in terms of gender.

Although not significant and robust, there are indications that adolescents receiving the sequence Think-Act-Relax-Solve (Condition 1) responded more rapidly in terms of reduction in depressive symptoms than adolescents receiving one of the other sequences. Cognitive restructuring, the first module of this sequence, is often seen as the basic component of CBT (Beck et al., 1979) and is aimed at cognitive changes to achieve a more helpful way of thinking. In our study, the Think-module might have served as a primer for the Act-module as thinking more positively might increase willingness to engage in activities that evoke positive reinforcement, which in turn might reduce depressive symptoms (“ripple effect”). This is supported by Tang et al. (2005) who conclude that cognitive changes often precede sudden and relatively large decreases in depressive symptoms (“sudden gains”) in the first phase (six sessions) of CBT. Whether this mechanism also applies to our study could be examined in mediation analyses. In addition, the Think-module could have served as additional psycho-education, because in this module the basic principle of CBT (relationship between thoughts, feelings and behavior) is explained. That providing such information might increase effectiveness is suggested by evidence that bibliotherapy has shown beneficial effects in preventing depression among adolescents (Bevan Jones et al., 2018). There are also indications that the short-term (post-intervention) effect of this sequence is larger than the effects of the other sequences (especially Act-Think-Relax-Solve and Relax-Solve-Act-Think). At post-intervention, we found the largest effect sizes for the sequence Think-Act-Relax-Solve with symptom reductions that were not

only significant, but also clinically relevant. In addition, the prevalence of depressive disorders (measured with the K-SADS) decreased significantly at post-intervention in this sequence, but not in the other sequences, which is an important finding given that the K-SADS is a semi-structured interview with good reliability ratings.

As an unintended but positive side-effect, the depressive symptoms significantly decreased between screening and baseline. According to a meta-analysis by Howard et al. (1986), about 15% of patients show measurable improvement before attending the first session of psychotherapy. This spontaneous reduction in symptoms might be explained by natural symptomatic improvement or fluctuations due to the passage of time (Cuijpers et al., 2020). Alternatively, symptoms may have been reduced as a function of contact with the psychologists conducting the research or via stress reduction brought on by knowledge that help is imminent (Boot et al., 2013; Howard et al., 1986).

This study has several strengths. First, this is one of the first studies to investigate the relative effectiveness of four CBT components and four different sequences of these components in indicated depression prevention among adolescents. Second, we used a study design that enabled us to isolate the effects of the components and sequences at multiple time points, both at symptom and diagnosis levels, which are both relevant to prevention. Finally, the large sample made the study well-powered to detect main effects.

The study also has limitations. First, we did not include a control condition. Therefore, we do not know whether (or to what extent) the symptom and diagnosis reduction found can be specifically ascribed to the intervention versus natural symptomatic improvement due to the passage of time. For future research of this type, we would therefore recommend including a control condition. Second, relative to other Dutch and international prevention trials, the participation rate in our study was lower (see Gillham et al., 2012; De Jonge-Heesen et al., 2020; Wijnhoven et al., 2014). Differences might be explained by variability in inclusion criteria (for example, the participation rate in studies with younger adolescents is higher than in studies including (also) older adolescents) and consent procedure for screening (for example, active consent procedures directly at screening generates considerably higher participation rates in the rest of the study than passive consent). Also some programs are part of a regional depression prevention program integrated within the care system. Some people may be more willing to participate in a project that is embedded within the larger system than a stand-alone program that is offered as part of a study. In this study, adolescents were less likely to participate if they had a lower level of depressive

symptoms, were older, had a low or moderate educational level or a non-Dutch ethnicity. Hence, our sample was not representative of the full population of Dutch adolescents in terms of age, ethnicity and school level (CBS Statline, 2020; reference year 2017), limiting generalizability of findings. Future research should explore strategies to increase the participation rate of adolescents aged 16 and older, adolescents with a low educational level and adolescents with a non-Dutch ethnicity in depression prevention trials. Lastly, we did not include long-term follow-ups. As a result, it was difficult to compare the results of our study to other prevention studies, some of which have included a 12-month follow-up (e.g., De Jonge-Heesen et al., 2020). Future research should include longer-term follow-up assessments to help us learn whether the effects of CBT components or of particular sequences “sink in” over time, resulting in effects that emerge only after more than six months have passed.

Implications

The findings suggest that the investigated CBT components for indicated depression prevention among adolescents might be used flexibly regarding the sequencing, without reducing effects. There are some indications that starting with cognitive restructuring may contribute to a faster decrease in depressive symptoms. Although the target group of our study was adolescents with elevated (subclinical) depressive symptoms, it turns out that almost 14% met the criteria for MDD or PDD at baseline. This shows the importance of screening for depressive symptoms in schools, as these adolescents had not sought help themselves. The investigated prevention program STARr can be provided in small groups within secondary schools by trained graduates, providing a low threshold for participation. Generalization of the findings to other indicated prevention programs requires caution, given the diversity of type, dosage and sequencing of CBT modules in conventional protocols.

To gain insight into what works for whom and how, future studies could explore possible moderators and mediators of change of the different CBT components and sequences of components. Future research could also investigate the importance of other aspects of CBT in relation to the effect of CBT, such as dose, frequency, intensity and modality.

Conclusion

CBT is widely used and has proven to be effective in preventing adolescent depression. Our study has shown that the sequence in which the investigated

CBT components cognitive restructuring, behavioral activation, problem solving and relaxation are offered might not be relevant to the outcomes at post-intervention and 6-month follow-up. This indicates that these CBT components might be used and sequenced flexibly without compromising effectiveness. The finding that these CBT components may be offered in various orders without marked differences in outcomes may be seen as encouraging news for those who favor flexible modular prevention approaches for adolescent depression.

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Trial Registration

Dutch Trial Register (NL5584/NTR6176; www.trialregister.nl/trial/5584)

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