Behaviour Research and Therapy 100 (2018) 1–6

Contents lists available at ScienceDirect

Behaviour Research and Therapy

journal homepage: www.elsevier.com/locate/brat

Major depression prevention effects for a cognitive-behavioral adolescent indicated prevention group intervention across four trials

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ARTICLE INFO

Keywords:
Major depression
Prevention
Adolescents
Cognitive-behavioral
Group intervention
Bibliotherapy

ABSTRACT

Major depressive disorder (MDD) in young people is a leading cause of disability but most depressed youth are not treated, emphasizing the need for effective prevention. Our goal is to synthesize MDD onset prevention effects for the *Blues Program*, a brief cognitive-behavioral (CB) indicated prevention group, by merging data from four trials (three of which included CB bibliotherapy) and conducting an individual patient data (IPD) meta-analysis. Data were available from 766 high school/college students (*M* age = 16.4, *SD* = 2.3; 60% female, 64% White). CB group resulted in significantly lower MDD incidence rates relative to brochure control that persisted to 6-month follow-up; CB group also was associated with a lower 2-year MDD incidence rate relative to bibliotherapy but heterogeneity across trials was detected. Contrasts between bibliotherapy and brochure control were nonsignificant. For significant contrasts, the number needed to treat (NNT) by CB group to prevent one MDD onset relative to brochure or bibliotherapy ranged from 10 to 21. A brief CB group depression prevention intervention for at-risk adolescent is achieving meaningful effects compared to both active and minimal controls but outcomes need to be improved, perhaps by better screening or augmentations to produce more persistent intervention effects.

Major depressive disorder (MDD) in young people is common and highly impairing (e.g., Avenevoli, Swendsen, He, Burstein, & Merikangas, 2015). However, 60–80% of depressed young people do not receive treatment (Cummings & Druss, 2011) and many do not fully benefit from extant treatments (Cuijpers et al., 2014), underscoring the need for effective depression prevention programs. Several depression prevention programs for young people, predominantly focused on high school samples, have been developed, with selective and indicated, but not universal, cognitive-behavioral (CB) prevention programs having the strongest evidence base (e.g., Hetrick, Cox, Witt, Bir, & Merry, 2016; Horowitz & Garber, 2006).

The goal of this report is to synthesize MDD onset prevention effects for the briefest evidence-based group-based CB indicated depression prevention intervention, the *Blues Program* (Stice, Burton, Bearman, & Rohde, 2007) by merging data from the four available randomized controlled trials (RCTs) that collected diagnostic data and conducting an individual patient data (IPD) meta-analysis. IPD meta-analysis is a specific type of review that differs from standard meta-analysis. In standard meta-analysis, summary scores on a topic are extracted from each study; conversely, in IPD meta-analysis the original data for that topic from participants in each of the various studies are obtained, combined, and re-analyzed. By increasing statistical power, IPD meta-analyses should improve the reliability of results regarding both intervention effects and allow for testing the role of participant-level covariates on effects (Thomas, Radji, & Benedetti, 2014). The first study, which was an efficacy trial conducted with 341 high school students with elevated depressive symptoms, found that participants randomized to CB group or CB bibliotherapy showed lower depressive disorder (MDD or minor depression) onset relative to educational brochure controls over 2-year follow-up (Stice, Rohde, Gau, & Wade, 2010). Based on promising results, the second study, which was an effectiveness trial conducted with 378 high school students with elevated depressive symptoms, found that participants randomized to CB group showed lower MDD onset relative to CB bibliotherapy participants over 2-year follow-up, but neither group differed from educational brochure controls (Rohde, Stice, Shaw, & Gau, 2015). Because youth attending college show high rates of MDD, both due to first incidence and recurrence (e.g., Rohde, Lewinsohn, Klein, Seeley, & Gau, 2013), the next two studies examined this population. The third study, an effectiveness trial conducted with 79 college students with elevated depressive symptoms, found no differences in MDD onset between CB group, CB Bibliotherapy, or educational brochure controls by 1-year

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http://dx.doi.org/10.1016/j.brat.2017.10.013
Received 31 May 2017; Received in revised form 24 October 2017; Accepted 30 October 2017
Available online 31 October 2017
0005-7967/

follow-up (Rohde, Stice, Shaw, & Gau, 2014). In the fourth trial, we added dissonance-induction elements and participant-driven cognitive and behavioral change plans to improve the depression prevention effects among college students, based on successful outcomes achieved in eating disorder prevention for interventions using cognitive dissonance and participant-driven change principles (Stice, Rohde, Shaw, & Gau, 2017); this efficacy pilot with 58 college students with elevated depressive symptoms found no significant differences in MDD onset between CB group and educational brochure controls by 3-month follow-up (Rohde, Stice, Shaw, & Gau, 2016). Thus, the trials differed across sample age, recruitment procedures, exact intervention content, and duration of follow-up, but all examined a 6-session CB group-based prevention program designed to prevent MDD onset versus a brochure control condition. Further, three trials included CB-based bibliotherapy as a second active intervention condition, providing the evaluation of a low-cost intervention previously shown to effectively treat and prevent depression (Gregory, Schwer-Canning, Lee, & Wise, 2004).

The present report sought to document the magnitude and timing of MDD prevention effects up to 2-years post-intervention for the group-based and bibliotherapy-based CB indicated depression prevention interventions relative to both brochure control and each other, in a one-stage IPD meta-analysis with a binary outcome (Thomas et al., 2014). Given the relatively small number of participants who develop MDD in a single RCT, statistical analyses are often underpowered to detect meaningful differences. Synthesizing data from multiple trials using IPD meta-analysis provides a more sensitive method of examining effects. The greater statistical power provided by IPD meta-analysis also increased our ability to examine whether sex and age moderates MDD onset outcomes, as prior standard meta-analyses have found larger symptom reductions for female and older adolescents receiving depression prevention interventions (Horowitz & Garber, 2006).

1. Method

1.1. Participants and procedures

The current study assembled data from 4 RCTs, resulting in 269 adolescents who received the CB group invention, 229 who received CB bibliotherapy, and 268 who served as brochure controls. An adaptation of the Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS; Puig-Antich & Chambers, 1983) was used to diagnose DSM-IV MDD in all trials; inter-rater agreement for MDD diagnostic is good (κ = 0.73–1.00; Stice et al., 2010). Additional details regarding each trial are provided in the outcome reports.

Trial 1: High School Efficacy Trial. Between 2004 and 2007, 341 high school students were recruited on the basis of elevated scores ($\geq$20) on the Center for Epidemiologic Studies-Depression scale (CES-D; Radloff, 1977). Participants had a baseline mean age of 15.6 years (SD = 1.2) at pretest, were 56% female and 46% European-American. Eligible participants were randomized to 4 conditions: (1) CB group (n = 88), (2) Supportive-expressive group (n = 88), (3) CB bibliotherapy (n = 80), or (4) Brochure control (n = 83). Groups were facilitated by a clinical psychology graduate student with an undergraduate student co-facilitator. Participants were assessed at pretest, posttest, 6-, 12-, and 24-month post-intervention follow-ups. As this was the only study to employ the supportive-expressive group condition, those participants were not included in the present analyses.

Trial 2: High School Effectiveness Trial. Between 2009 and 2011, 378 high school students were recruited based on a streamlined process in which students self-selected on the basis of a modified CES-D. Participants had a baseline mean age of 15.5 years (SD = 1.2), were 68% female and 72% European-American. Eligible participants were randomized to 3 conditions: (1) CB group (n = 126), (2) CB bibliotherapy (n = 128), or (3) Brochure control (n = 124). Groups were facilitated by pairs of trained personnel at each high school. Participants were assessed at pretest, posttest, 6-, 12-, 18-, and 24-month post-intervention follow-ups.

Trial 3: College Effectiveness Pilot. Between 2010 and 2011, 79 first and second-year college students were recruited based on the same streamlined process as in Trial 2. Participants had a baseline age of 19.0 years (SD = 0.9), were 69% female and 81% European-American. Eligible participants were randomized to 3 conditions: (1) CB group (n = 27), (2) CB bibliotherapy (n = 21), or (3) Brochure control (n = 31). Groups were facilitated by pairs of masters-level graduate students in clinical psychology. Participants were assessed at pretest, posttest, 6- and 12-month follow-ups.

Trial 4: College Pilot with Enhanced CB Intervention. Between 2013 and 2014, 58 college students were recruited using the same screening procedure as Trial 1. Participants had a baseline age of 21.8 years (SD = 2.3), were 68% female and 70% European-American. Eligible participants were randomized to 2 conditions: (1) the enhanced CB group (n = 28) or (2) Brochure control (n = 30). Participants were assessed at pretest, posttest, and 3-month follow-up.

1.2. Interventions

CB Group. In all 4 trials, the CB group consisted of 6 weekly 1-h sessions with approximately 5–8 participants focused on building rapport, increasing pleasant activities, cognitive restructuring, and developing response plans for future life stressors. In Trial 4, we added verbal and written dissonance-induction exercises to enhance motivation and participant-driven cognitive and behavioral change plans to enhance efficacy.

CB Bibliotherapy. Bibliotherapy participants were given a copy of *Feeling Good* (Burns, 1980), which provides CB techniques for preventing and reducing negative moods written at a high-school reading level. Research or school staff were encouraged to make two reminder calls encouraging participants to use the book.

Educational Brochure control. Participants were given an NIMH educational brochure describing MDD symptoms and treatment ("Let's Talk About Depression" NIH Pub. 01-4162), as well as referral information, which was provided to participants in all conditions.

1.3. Statistical analysis

We used logistic regressions to compare cumulative MDD incidence (onset) between conditions at posttest and 3-, 6-, 12-, and 24-month follow-up. Datasets were merged and analyzed together, controlling for trial. Mplus 7.1 was used to fit separate logistic regressions at each follow-up. Models were run with permutations in dummy-coded conditions to test all pairwise comparisons between conditions, controlling for trial. Our intention was to model the onset of MDD, which was considered a yes-or-no event. Thus, MDD incidence at one time-point was considered incidence at all subsequent time-points but that does not assume the disorder continued (we did not model the duration of MDD episodes primarily because the follow-up period was too short in 2 of the 4 trials). Each pairwise comparison included all trials with available information. Missing data were taken into account using maximum likelihood estimation (FIML). We tested moderation by sex and age by adding Condition X Sex/Age interaction terms in models. To examine heterogeneity across studies, we examined interactions between intervention effects and trial in fixed effects models (Thomas et al., 2014), which is the most feasible and informative option given the small number of trials.

In merging the data sets, we discovered that six participants had been enrolled who inadvertently met criteria for a current diagnosis of MDD (n = 5) or had incomplete diagnostic information (n = 1) at baseline; these participants were removed from the sample. Table 1 includes descriptive information on individual and combined samples. The pairwise comparison, analyses were balanced in terms of sex, race, parent education.

To supplement our primary analyses examining cumulative MDD