Prevention of Depression in At-Risk Adolescents
Longer-term Effects

William R. Beardslee, MD; David A. Brent, MD; V. Robin Weersing, PhD; Gregory N. Clarke, PhD; Giovanna Porta, MS; Steven D. Hollon, PhD; Tracy R. G. Gladstone, PhD; Robert Gallop, PhD; Frances L. Lynch, PhD; Satish Iyengar, PhD; Lynn DeBar, PhD; Judy Garber, PhD

IMPORTANCE Adolescent offspring of depressed parents are at high risk for experiencing depressive disorders themselves.

OBJECTIVE To determine whether the positive effects of a group cognitive-behavioral prevention (CBP) program extended to longer-term (multiyear) follow-up.

DESIGN A 4-site randomized clinical trial with 33 months of follow-up was conducted. Recruitment of participants was from August 2003 through February 2006.

SETTING The study settings included a health maintenance organization, university medical centers, and a community mental health center.

PARTICIPANTS Three hundred sixteen adolescent (aged 13-17 years) offspring of parents with current and/or prior depressive disorders; adolescents had histories of depression, current elevated depressive symptoms, or both but did not currently meet criteria for a depressive disorder.

INTERVENTIONS The CBP program consisted of 8 weekly 90-minute group sessions followed by 6 monthly continuation sessions. Adolescents were randomly assigned to either the CBP program or usual care (UC).

MAIN OUTCOMES AND MEASURES The primary outcome was a probable or definite episode of depression (Depression Symptom Rating score ≥4) for at least 2 weeks through the month 33 follow-up evaluation.

RESULTS Over the 33-month follow-up period, youths in the CBP condition had significantly fewer onsets of depressive episodes compared with those in UC. Parental depression at baseline significantly moderated the intervention effect. When parents were not depressed at intake, CBP was superior to UC (number needed to treat, 6), whereas when parents were actively depressed at baseline, average onset rates between CBP and UC were not significantly different. A 3-way interaction among intervention, baseline parental depression, and site indicated that the impact of parental depression on intervention effectiveness varied across sites.

CONCLUSIONS AND RELEVANCE The CBP program showed significant sustained effects compared with UC in preventing the onset of depressive episodes in at-risk youth over a nearly 3-year period. Important next steps will be to strengthen the CBP intervention to further enhance its preventive effects, improve intervention outcomes when parents are currently depressed, and conduct larger implementation trials to test the broader public health impact of the CBP program for preventing depression in youth.

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT00073671
Depression is a common, chronic, and impairing disorder with first onset often occurring during adolescence1 and affecting close to a quarter of all adults during their lifetime.2 The World Health Organization3 estimates that depression is the third leading cause of global disease, is projected to be the second leading cause by 2020, and will rank first in high-income countries by 2030.4 Thus, depression is a major public health problem that requires the development, implementation, and evaluation of strategies for preventing its onset and recurrence.

In adolescents, depression is associated with impaired social relationships, lower educational attainment, and increased risk of suicide.5 The need for efficacious prevention approaches is widely recognized6-9 and particularly urgent given the low access to and uptake of appropriate treatments among depressed youth.8 Adolescence is a key window for preventive interventions given that the rate of depression significantly increases during this developmental period.9

Meta-analyses of youth depression prevention programs indicate modest effects, even among high-risk samples.10-15 Moreover, most prevention studies have focused on reducing depressive symptoms rather than preventing diagnosed depressive episodes. One notable exception is the work of Clarke and colleagues, who in 2 trials16,17 found significantly fewer episodes of depression in high-risk youth receiving a cognitive-behavioral prevention (CBP) program compared with youth receiving usual community services.

Building on this foundation, we conducted a large (N = 316), multisite randomized clinical trial to examine the effectiveness of the Coping With Depression Course for Adolescents18 modified for prevention. Youth were at high risk because of their parents’ history of depression (ie, selective prevention)19-20 and the youth’s own history of a prior depressive disorder or current depressive symptoms (ie, indicated prevention).21-22 We sought to replicate the original prevention effect, demonstrate generalizability by delivering the program across different samples, settings, and geographic locations, and assess the robustness of the intervention to implementation by different investigative teams, thereby addressing the program’s readiness for more widespread dissemination.

As reported previously,23 at the 9-month follow-up, adolescents randomized to the CBP condition had significantly fewer episodes of depression (21.4%) compared with those in usual care (UC) (32.7%). Moreover, baseline parental depression significantly moderated the effect; for adolescents whose parents were not depressed at intake, CBP was significantly more effective in preventing subsequent depressive episodes than UC, whereas among youth whose parents were depressed at baseline, the CBP and UC conditions were not significantly different. No significant differences in outcome were found by site.

Few trials have measured and found significant prevention effects on diagnoses of depression, and even fewer have shown sustained effects for reducing episodes over several years.11,12,24 In the current intervention trial, we modified the CBP program by adding 6 monthly continuation sessions explicitly in an effort to extend the duration of the effects beyond those reported by Clarke and colleagues,17 who found that the initial significant effect of CBP vs UC was not sustained beyond 15 months. The primary purpose of the current report was to present the longer-term effects of the CBP program regarding the occurrence of depressive episodes during the interval from baseline through 2 years after the last continuation session. We hypothesized that adolescents in the CBP condition would have a lower hazard of depressive episodes across the 33-month follow-up period compared with youth in UC. Second, given our findings at 9 months,23 we tested whether baseline parental depression continued to moderate the longer-term effects of the CBP program vs UC.

Methods

Sample

The sample was recruited from August 2003 through February 2006 from 4 sites located in Boston, Massachusetts; Nashville, Tennessee; Portland, Oregon; and Pittsburgh, Pennsylvania.23 The institutional review boards of each site approved the study. Parents and adolescents provided written informed consent and assent, respectively. Recruitment sample composition and assessment measures have been described in detail elsewhere.23 The sample included 316 adolescents who had at least 1 parent/caretaker who had had a depressive disorder (ie, major depression or dysthymia) during the past 3 years or had 3 or more depressive episodes or 3 or more years in a depressive episode during the child’s life. At enrollment, 128 (45.4%) of these index parents were in an active depressive episode. Adolescent inclusion criteria were (1) 13 to 17 years old and (2) current subsyndromal depressive symptoms (ie, a score of ≤20 on the Center for Epidemiologic Studies Depression Scale25 [CES-D]) (n = 63; 19.9%) or a history of a depressive disorder26 in remission for at least 2 months (n = 175; 55.4%) or both (n = 78; 24.7%). Thus, for 80.1% of youth, we aimed to prevent episode recurrence.

Exclusion criteria for adolescents were a current DSM-IV mood disorder, currently receiving a therapeutic dose of an antidepressant medication (as defined by Brent et al27), having ever had 8 or more sessions of cognitive behavioral therapy or dialectical behavior therapy, or a diagnosis of bipolar I disorder or schizophrenia in the youth or parents. Three youths were taking subtherapeutic doses of antidepressants at the time of enrollment.

Siblings were allowed to participate and were yoke randomized to ensure assignment to the same condition. There were 33 sets of siblings (1 set of triplets).

Procedures

Adolescents were randomized to either CBP (n = 159) or UC (n = 157) using standard techniques to ensure that the cells were balanced on age, sex, self-identified race and ethnicity, and inclusion criteria. Randomization resulted in a successful balance of these variables between conditions. Information about baseline demographic and clinical characteristics by condition is provided in our earlier report of the short-term (ie, 9-month) outcomes23 and in eTable 1 in Supplement. All par...
Participants were considered part of the study once randomized (ie, an intent-to-treat design).

**Intervention**

The CBP program was a modification of the intervention used by Clarke and colleagues\textsuperscript{16,17,28} and emphasized cognitive restructuring and problem solving. The version used herein consisted of 8 weekly 90-minute (acute) and 6 monthly 90-minute continuation sessions for mixed-sex groups of 3 to 10 adolescents (mean [SD] group size, 6.6 [1.6]). Therapists were at least master’s-level clinicians trained and supervised by experienced PhD clinicians. The interventions were delivered with fidelity across sites.\textsuperscript{23}

Adolescents attended an average of 6.5 acute sessions (median, 8.0; range, 0-8) and an average of 3.8 continuation sessions (median, 5.0; range, 0-6). During the continuation sessions, cognitive and problem-solving strategies were reviewed and other skills (eg, behavioral activation, relaxation, and assertiveness) were introduced or expanded. In weeks 1 and 8, parent meetings were conducted to inform parents about the topics and skills being taught to their children. Parents of 76.4% of the adolescents in CBP attended the first session, and 70.9% attended session 8.

**Assessments**

Assessments were conducted at baseline, after the acute intervention (month 2), after the continuation (month 9), and again at 1 year (month 21) and 2 years (month 33) postcontinuation. Independent evaluators unaware of condition assignment conducted the follow-up assessments. Independent evaluators completed extensive training, received ongoing supervision, and demonstrated adequate interrater reliability in practice interviews and on a random subset of participant interviews.\textsuperscript{23}

At baseline, parents were administered the Structured Clinical Interview for DSM-IV Axis I Disorders\textsuperscript{29} to assess their current and past mood diagnoses and the total number and duration of their past depressive episodes; parents also completed the CES-D, a measure of the frequency of depressive symptoms during the prior week. The Schedule for Affective Disorders and Schizophrenia for School-Age Children, Present and Lifetime Version\textsuperscript{30} was administered at baseline to parents and adolescents separately to obtain youths’ current and past DSM-IV diagnoses.\textsuperscript{26} At each follow-up evaluation, parents and adolescents were interviewed about the teen with the Longitudinal Interval Follow-up Evaluation,\textsuperscript{31} which yields information about the onset and offset of diagnosed depressive episodes since the previous assessment and provides a continuous rating of symptoms and impairment scored on a 6-point Depression Symptom Rating scale. The primary outcome of this randomized clinical trial was a probable or definite episode of depression (ie, Depression Symptom Rating score ≥4) for at least 2 weeks. Interrater reliability for this diagnostic variable in this sample was good (κ = 0.92; 95% CI, 0.83 to 1.00).

At each assessment, adolescents also completed the CES-D, and the independent evaluators rated the Children’s Depression Rating Scale–Revised (CDRS-R),\textsuperscript{32} the Children’s Global Assessment Scale, and the Child and Adolescent Services Assessment.\textsuperscript{33,34} which measured adolescents' mental health service use over the follow-up period. Youths in both conditions were permitted to initiate or continue nonstudy mental health services. When acute episodes of depression were identified at a follow-up for youth in either condition (ie, CBP or UC), both parents and youths were informed and clinical referrals were provided.

**Data Analytic Strategy**

Survival analyses were used to assess the impact of CBP on the primary outcome (time to depression onset), and regression models were used to analyze dimensional depression symptom (CES-D and CDRS-R) trajectories over time. For both sets of analyses, a random-effects approach was adopted. Random-effects survival models (ie, gamma frailty models) are designed to account for subject to subject heterogeneity in event times\textsuperscript{35} and often provide a better fit to the data than traditional fixed-effects Cox models when such heterogeneity is significant.\textsuperscript{36,37} Following procedures described by Verbeke and Molenberghs,\textsuperscript{38} we tested the need for random-effects models in our data by comparing the log likelihood between survival models with and without a random gamma frailty effect, adjusting the asymptotic null distribution for the difference of −2 log-likelihood to a mixture of χ²s (ie, by setting the variance of the random effect to zero to account for parameter space restrictions). For all analyses, the gamma frailty random-effect model provided a better fit to the data than a fixed-effects Cox model; accordingly, results of random-effects survival models are presented. To adjust for multiple comparisons, we applied the false discovery rate method\textsuperscript{39} with the Yekutieli multiple-test procedure. The method was carried out with the qvalue package in Stata 11.2.\textsuperscript{39-41} A q-value was calculated, and comparisons were considered significant when q < .05.

Sibling correlations were adjusted for in the mixed-effects models of the CES-D and CDRS-R by including family as a random variable in the models. In the frailty model, we used an approach similar to the group-data method of Bauer and colleagues\textsuperscript{42} where we compared the fit of 2 models, one that included youth with a participating sibling vs a model of youths without a sibling (ie, singletons). No difference in fit was found between these 2 models (1638.4 vs 1638.5 on the corrected Akaike information criterion), indicating no significant effect due to separating the singletons from the siblings. Given the low rate of siblings overall (11.6%), we adopted the more parsimonious analysis that did not specifically model sibling effects.

To benchmark the clinical significance of the findings, we computed the number needed to treat (NNT), a metric used in evidence-based medicine to indicate the number of persons who would need to receive the intervention to prevent 1 additional onset of the disorder in question.\textsuperscript{43} In our earlier report through 9 months,\textsuperscript{23} we found an NNT of 9 for the main effect of CBP. The current analyses again (1) examined the main effect of the intervention, (2) tested whether baseline parental depression status was a significant moderator, and (3) added site and its interactions to the analytic models.
Results

Sample Characteristics and Retention

Sample Characteristics at Baseline

As is common in multisite trials, differences by site were found on some baseline variables: demographics, chronicity of parental depression, level of adolescent depressive symptoms at intake, and proportion of youth who had a history of a depressive episode (eTable 2 in Supplement). Importantly, however, the CBP and UC conditions did not differ significantly in any baseline demographic or clinical variables across sites (eTable 1 in Supplement). 23

Sample Retention

This report describes findings through 2 years postcontinuation (mean [SD], 156 [24] weeks after baseline; range, 119-279 weeks); given this wide range, we truncated the data at 150 weeks, which corresponds to the median time of the evaluation (mean [SD], 156 [24] weeks after baseline; range, 119-279 weeks); given this wide range, we truncated the data at 150 weeks, which corresponds to the median time of the evaluation. Figure 1 presents the Consolidated Standards of Reporting Trials diagram through this follow-up period. Overall, sample retention to 33 months was high, and there was no differential attrition by condition, either across or within sites (CBP, 137 of 159 [86.2%] vs UC, 131 of 157 [83.4%]; χ² = 0.46; P = .50). Retention rates varied significantly across sites (χ² = 58.21; P < .001; range, 61.5%-100%). Retained and missing participants differed on 3 of 23 variables: retained participants had lower baseline CES-D scores (mean [SD], 18.2 [9.3] vs 21.4 [9.4]; t154 = 2.20; P = .03), a parent with more than a high school education (190 of 237 [80.2%] vs 28 of 45 [62.2%]; χ² = 6.94; P = .008), and higher socioeconomic status as measured by the Hollingshead Index (mean [SD], 46.3 [22.1] vs 42.6 [11.1]; t153 = −2.01; P = .046). When baseline CES-D score, parent education, and socioeconomic status were covaried in the analyses, site differences in attrition rates remained.

Intervention Effects: Time to Depression Onset

Main Effect of CBP vs UC

The overall main effect for the intervention was significant (β = −0.63 [SE = 0.31]; t86.9 = −2.04; P = .04). For the sample as a whole, the onset rate was slower for CBP compared with UC. Over the 33-month follow-up, 36.8% of adolescents in CBP had a depression onset vs 47.7% of youth in the UC condition, corresponding to an NNT of 10 (95% CI, 5 to 2624).

Moderating Effect of Baseline Parental Depression

We next added parental depression to the model and found, similar to the results at 9 months, 23 that baseline parental depression significantly moderated the effect of the intervention on the onset of depression in adolescents across the 33-month interval (β = 1.39 [SE = 0.44]; t58.2 = 3.16; P = .002). Cognitive-behavioral prevention was superior to UC when parents were not currently depressed at intake (β = 1.18 [SE = 0.34]; t56.9 = 3.46; P = .001), whereas when parents were depressed at baseline, average onset rates between CBP and UC did not differ (β = 0.24 [SE = 0.32]; t58.2 = 0.75; P = .45). In families with no current baseline parental depression, on average, 32.1% of youth in CBP experienced an onset of depression compared with 51.9% of youth in UC, corresponding to an NNT of 6 (95% CI, 3 to 23). In families with parental depression at baseline, differences in onset rates between conditions were negligible (CBP, 41.6% vs UC, 43.4%), with an estimated NNT of 54. All results remained unchanged when analyses were rerun excluding the 3 adolescents (2 in CBP and 1 in UC) taking subtherapeutic doses of antidepressants at study enrollment.

Site Effects and Interactions

We computed an omnibus random-effects survival model that tested main effects and all higher-order interactions for condition (CBP vs UC), baseline parental depression, and site. Table 1 shows the full specification of this model, and Table 2 presents the pooled data and the targeted contrasts based on the full model. Contrasts are considered significant when q < .05. This omnibus model yielded a significant main effect for the intervention, favoring CBP over UC (Figure 2), and an interaction in the targeted contrasts indicating that this effect was conditioned on parental depression at baseline (Figure 3). Significant 2- and 3-way interactions were found between condition and site and among condition, baseline parental depression, and site, respectively.
The intervention condition × site interaction was due to superior effects for CBP at 2 sites, no significant difference between CBP and UC at a third site, and a significant effect for UC at a fourth site. This latter site had a significantly lower overall onset rate across both the CBP and UC conditions as compared with the other 3 sites (31.3% vs 46.1%; \( \chi^2 = 5.35; P = .02 \)). Thus, the effects at this site were being driven by a significantly smaller number of youths with depression onset relative to the other sites; therefore, the findings at this site should be interpreted with caution.

The significant interaction among intervention, baseline parental depression, and site indicated that the relation of

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Abbreviation: ParDep, parental depression at baseline.
* Regression coefficients represent complementary log-hazard coefficient contribution for each effect.
\( ^{b} \) Dummy variables for site. Site 2 is the reference group.
\( ^{c} \) The df for these analyses are 3,309; for all other analyses, the df are 309.

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Abbreviations: CBP, cognitive-behavioral prevention program; ParDep, parental depression at baseline; UC, usual care.
Intervention Effects: Secondary Outcomes

Changes in youths’ depressive symptoms (ie, CES-D and CDRS-R scores) were analyzed using random-effects regression models for continuous data. For the CES-D, the main effect of intervention was not significant, but similar to our short-term results, the interaction of condition × time × baseline parental depression was significant (β = −1.55; 95% CI, −3.00 to −0.09; z = −2.08; P = .04). Paired comparisons indicated that among adolescents whose parents were depressed at baseline, the CES-D score trajectory was significantly worse for youth in UC as compared with those in CBP (β = 1.21; 95% CI, 0.16 to 2.26; z = 2.25; P = .02). Other pairwise comparisons within this interaction were not significant. The condition × time × site interaction was not significant, indicating that the pattern of intervention effects on the CES-D was consistent across sites. For the CDRS-R, the main effect of intervention, the moderating effect of baseline parental depression, and the interaction × time × site interaction were not significant.

Service Use

Adolescents randomized to the CBP program vs UC did not differ significantly in any type of mental health service use from baseline through the 33-month follow-up period (eTable 3 in Supplement). Thus, the significant differences in the longer-term outcomes between adolescents in CBP vs UC likely were not due to differences in treatment during this period. Finally, we found that although some service use categories differed by site, incorporating these service variables into the survival models altered neither the main effect of the intervention nor the moderating effect of baseline parental depression.

Discussion

The current study demonstrated that, on average, the positive effects of the cognitive-behavioral program for preventing depressive episodes in at-risk offspring of depressed parents persisted for nearly 3 years, such that 1 additional onset was prevented for every 10 participants. The recent Institute of Medicine report asserted that long-term effects are essential for establishing the value of prevention. Enduring effects have been rare with regard to preventing diagnosed depressive disorders in youth. The current study demonstrated the durability of the effects of the CBP program for preventing depressive disorders in at least some high-risk adolescents.

The superior effect of CBP over UC in rates of depression onsets remained statistically significant when baseline parental depression was included as a moderator. Similar to the 9-month results, when parents were not depressed at baseline, CBP was significantly better than UC; 1 additional onset was prevented for every 6 adolescents in the CBP condition. When parents were depressed at baseline, however, differences in onset rates between CBP and UC were negligible, with only 1 additional onset prevented for every 54 participants. Thus, the overall effects of the CBP program compared with UC were conditioned on parents’ depression at intake.

Such an attenuated effect of the CBP program in the presence of current parental depression is consistent with studies that have shown that cognitive-behavioral interventions for various youth disorders work less well when a parent is actively depressed. Exactly why parental depression at the time of study enrollment was related to differential intervention effects is a matter of conjecture. Perhaps active parental depression directly affected intervention uptake or use, or it represents a marker of some third variable such as shared genetic vulnerability, a more chronic or recurrent course of parental depression, disrupted parenting, or more extensive exposure to stressful life events. The moderator effect of baseline
parental depression also could have been an artifact of differences in sample composition or differential attrition across sites.

If current parental depression somehow suppresses intervention effectiveness, then the CBP program might be best delivered when parents are not acutely depressed. This may mean waiting until the parents’ depression has resolved or actively treating parents’ current depression prior to or concurrently with providing the CBP program to their children. Large-scale randomized clinical trials are needed to test the direct impact of treating parents’ depression on children’s general adjustment and on their response to preventive interventions. If current parental depression is a marker of different causal processes, however, then other steps will be needed to detect and target the mechanisms that underlie youth onsets.

From a public policy perspective, the magnitude of the observed effects was in line with other recommended evidence-based medical interventions. When parents are not currently depressed, only 6 at-risk youth would need to receive CBP to improve on outcomes in UC, which is a noteworthy NNT. Even within this “best” outcome group, however, almost one-third of these adolescents still experienced a depressive episode during the 33-month follow-up period. One reason for such high onset rates might be that the majority of youth in this sample had had a prior depressive episode, that is, they were experiencing recurrent episodes. In the current study, youth were enrolled based on their current symptoms or history of depression in addition to parental depression, whereas most other depression prevention trials have recruited participants on the basis of either child characteristics or familial risk. The relatively high rate of onsets of depressive episodes found even among youth who had received the CBP intervention and whose parents were not currently depressed suggests that a more comprehensive range of services may need to be provided to such at-risk youth and their families.

Another aim of this study was to test the generalizability and robustness of the CBP program when implemented at diverse settings by different investigators to determine the program’s readiness for more widespread dissemination. Results indicated that the relation between the intervention condition and baseline parental depression was not consistent across sites. The clearest evidence of the enduring effect of CBP as compared with UC, regardless of baseline parental depression, was found at the 2 sites with minimal attrition, whereas the findings were more variable and baseline parental depression mattered at the 2 sites with higher attrition. This differential retention rate across sites might partially account for the significant subject-to-subject heterogeneity in survival rates observed herein. If the moderating effect of parental depression is related to attrition or other sample characteristics, then pragmatic steps will be needed to ensure that youth stay involved in the intervention. The fact that site moderated the intervention effect suggests that larger-scale dissemination trials are still needed to understand the full range of setting, provider, and organizational characteristics that impact the effectiveness and ultimate uptake of the program in practice.
The recent Institute of Medicine volume on depression and parenting strongly recommended combining treatments for reducing parents’ symptoms with interventions aimed at improving their parenting. Indeed, prevention programs that enhance parenting skills and the quality of the parent-child relationship have shown positive effects on youth outcomes and lower rates of depression in adolescents and adults in particular. Although the current study found that compared with UC, the CBP program significantly reduced the hazard of depressive episodes, the addition of an intervention that directly targets parents’ behaviors toward their offspring might enhance youths’ outcomes further and for even longer intervals as suggested by the more sustained (ie, 2-7 years) effects found in some prevention programs that have included a parenting component. Sustained effects also might be enhanced by including additional booster sessions as has been found in some treatment studies aimed at preventing relapse or by using a “family checkup” approach as a way to maintain the positive effects of the CBP intervention.

The CBP program used in this study is a relatively straightforward intervention that can be delivered by clinicians with modest training in cognitive-behavioral approaches. From a public health perspective, interventions that are likely to be widely adopted are clear-cut and easily taught and can be implemented in a variety of settings, all of which characterize this CBP intervention. Thus, for offspring of depressed parents, the CBP program is user friendly and effective, particularly when parents are not currently depressed.

Limitations of this study should be noted. First, the current trial focused on the prevention of the onset of new depressive episodes, but not necessarily first episodes, given that 80% of the sample had had prior depression. Second, sites differed in attrition, but we were unable to explain these differences based on the available data. Sites also likely varied on a range of characteristics not assessed in this study, such as regional differences in the availability and acceptability of mental health services. Third, a small subset of adolescents reported taking antidepressants after randomization, but this did not differ between the 2 conditions and therefore cannot explain the significant preventive effect.

Examination of CBP and related interventions in different settings (eg, primary care and schools) and with other samples (eg, youth with anxiety and different cultural groups) should proceed, albeit with caution, before attempting widespread dissemination. More information is needed about the degree of implementation “scaffolding” that is required to reduce site and program delivery variation. Finally, the contribution of individual and family differences in response to the program should be explored to facilitate the development of more robust and personalized preventive intervention strategies. In summary, the current randomized trial demonstrated an enduring preventive effect of CBP with at-risk youth, particularly when their parents were not in an active depressive episode at the time of intervention initiation. More information is needed regarding what individual and contextual factors enhance or limit the efficacy of this intervention and the mechanisms underlying these differential effects.

Author Contributions: Study concept and design: Beardslee, Brent, Weersing, Clarke, Gladstone, Lynch, Iyengar, DeBar, Garber. Acquisition of data: Beardslee, Brent, Clarke, Gladstone, Lynch, Garber. Analysis and interpretation of data: Beardslee, Brent, Weersing, Clarke, Porta, Holon, Gallop, Lynch, Iyengar, DeBar, Garber. Drafting of the manuscript: Beardslee, Brent, Weersing, Garber. Critical revision of the manuscript for important intellectual content: Beardslee, Brent, Weersing, Clarke, Porta, Holon, Gladstone, Lynch, Iyengar, DeBar, Garber. Statistical analysis: Brent, Weersing, Porta, Gallop, Iyengar. Obtained funding: Beardslee, Brent, Weersing, Clarke, Gladstone, Lynch, Garber. Administrative, technical, or material support: Beardslee, Brent, Weersing, Clarke, Gladstone, Lynch, Garber. Study supervision: Beardslee, Brent, Weersing, Clarke, Porta, Holon, Gladstone, Garber.

Conflict of Interest Disclosures: Dr Brent is a member of the editorial board of UpToDate and receives royalties from the Guilford Press. No other conflicts of interest were reported.

Funding/Support: The project was supported in part by National Institute of Mental Health grants RO1MH064735, RO1 MH64541; RO1 MH64503; and RO1 MH64777 and by National Center for Research Resources grant U1LR024975-01, now National Center for Advancing Translational Sciences grant 2 U1LTR000445-06.

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Additional Contributions: Jamie Zelazny, MPH, RN, and Tim Pitts, MED, University of Pittsburgh; Laurel Duncan, BA, Beth Donaghey, MA, and Liz Ezell, MA, Vanderbilt University; Kevin Rogers, MA, Stephanie Hertert, MED, and Kristina Bookler, BA, Kaiser Permanente, and Phyillis Rothberg, LICSW, Judge Baker Children’s Center/Boston Children’s Hospital, provided assistance with study coordination. Nadine Melhem, PhD, Deena Battista, PhD, and Yuan Brustoloni, MS, University of Pittsburgh School of Medicine, and John Dickerson, MS, Kaiser Permanente, assisted with statistical analyses. Brian McKain, MSN, University of Pittsburgh; Mary Jo Cioiro, PhD, Vanderbilt University; Alison Firemark, MA, Bobbi Jo Yarborough, MA, and Sue Leung, MA, Kaiser Permanente, and Mary Kate Little, LICSW, and Katherine Ginnis, LICSW, Judge Baker Children’s Center/Boston Children’s Hospital, served as study therapists. Sharon Doyle Herzer, RN, MS, Blue Cross/Blue Shield of Tennessee, facilitated access to potential participants. All of these individuals were monetarily compensated for their contributions. Eugene D’Angelo, PhD, Boston Children’s Hospital, provided consultation. C. Hendricks Brown, PhD, and Irwin Sandler, PhD, reviewed and commented on drafts of the manuscript. We thank all of the participating parents and adolescents and independent evaluators. We also thank Don Guthrie, PhD, Joan Asarnow, PhD, Connie Hammen,
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PhD, and Mary Jane Rotheram-Borus, PhD, for serving on the Data Safety and Monitoring Board.

REFERENCES


