Prevention of Depression in At-Risk Adolescents: A Randomized Controlled Trial

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Prevention of Depression in At-Risk Adolescents
A Randomized Controlled Trial

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Context Adolescent offspring of depressed parents are at markedly increased risk of developing depressive disorders. Although some smaller targeted prevention trials have found that depression risk can be reduced, these results have yet to be replicated and extended to large-scale, at-risk populations in different settings.

Objective To determine the effects of a group cognitive behavioral (CB) prevention program compared with usual care in preventing the onset of depression.

Design, Setting, and Participants A multicenter randomized controlled trial conducted in 4 US cities in which 316 adolescent (aged 13-17 years) offspring of parents with current or prior depressive disorders were recruited from August 2003 through February 2006. Adolescents had a past history of depression, current elevated but subdiagnostic depressive symptoms, or both. Assessments were conducted at baseline, after the 8-week intervention, and after the 6-month continuation phase.

Intervention Adolescents were randomly assigned to the CB prevention program consisting of 8 weekly, 90-minute group sessions followed by 6 monthly continuation sessions or assigned to receive usual care alone.

Main Outcome Measure Rate and hazard ratio (HR) of a probable or definite depressive episode (ie, depressive symptom rating score of ≥4) for at least 2 weeks as diagnosed by clinical interviewers.

Results Through the postcontinuation session follow-up, the rate and HR of incident depressive episodes were lower for those in the CB prevention program than for those in usual care (21.4% vs 32.7%; HR, 0.63; 95% confidence interval [CI], 0.40-0.98). Adolescents in the CB prevention program also showed significantly greater improvement in self-reported depressive symptoms than those in usual care (coefficient, −1.1; $z = -2.2$; $P = .03$). Current parental depression at baseline moderated intervention effects (HR, 5.98; 95% CI, 2.29-15.58; $P = .001$). Among adolescents whose parents were not depressed at baseline, the CB prevention program was more effective in preventing onset of depression than usual care (11.7% vs 40.5%; HR, 0.24; 95% CI, 0.11-0.50), whereas for adolescents with a currently depressed parent, the CB prevention program was not more effective than usual care in preventing incident depression (31.2% vs 24.3%; HR, 1.43; 95% CI, 0.76-2.67).

Conclusion The CB prevention program had a significant prevention effect through the 9-month follow-up period based on both clinical diagnoses and self-reported depressive symptoms, but this effect was not evident for adolescents with a currently depressed parent.

Trial Registration clinicaltrials.gov Identifier: NCT00073671

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DEPRESSION IS A COMMON AND episodic condition that is associated with difficulties in relationships, impaired school and work performance, and increased risk for substance abuse and suicide.[1] Adolescent-onset depression is strongly associated with chronic and recurrent depression in adulthood,[2,3] which is a leading cause of morbidity and mortality.[4] Despite substantial progress in the treatment of adolescent depression (ie, acute response and remission rates are about 60% and 30%, respectively),[5] only about 25% of depressed youth receive treatment[6] and at least 20% develop recurrent, persistent, and chronic depression that is very difficult to treat.[5,7] The serious developmental consequences of adolescent depression and the associated treatment challenges once it has developed underscore the need for programs aimed at prevention.[8]

One of the most potent and clinically salient risk factors for the development of depression in youth is parental depression.[9] Offspring of de-

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pressed parents are at a 2- to 3-fold increased risk of developing depressive disorders.[10] Additionally, youth history of a prior depressive episode[11] or subsyndromal symptoms of depression also substantially increase risk of subsequent episodes.[2] Meta-analyses[12,13] have shown that depression can be reduced in selective and indicated samples of adolescents who are at risk for the onset of depression due to these factors. Notably, Clarke and colleagues[14,15] found that a group cognitive behavioral (CB) prevention program was superior to usual care for the prevention of depression in adolescent offspring of parents with a history of depression.

The current study was the logical next step in the development and testing of this CB prevention program. According to the Institute of Medicine,[16(p370)] a large field trial in settings other than where the intervention was initially developed is needed "to assess the generality of the efficacy of the program with different personnel, participants, settings, cultures, and conditions." The primary aim of this study was to examine the effectiveness of this CB program for preventing depression in at-risk adolescents when implemented by other investigators and clinicians across diverse geographic locations. We hypothesized that participants in the CB prevention program would have a significantly lower prospective incidence of episodes of depressive disorders (primary outcome) and show a more favorable trajectory on continuous measures of depressive symptoms than would adolescents in the usual care condition. In addition, guided by previous studies,[17,18] we examined whether baseline qualifying criteria (ie, current parental depression, current adolescent depressive symptoms, and adolescent history of a mood disorder) moderated the effect of the intervention on depressive outcomes.

METHODS

Sample

The sample consisted of 316 adolescents. Participants self-identified their race and ethnicity, which were assessed to ensure balance in the 2 randomized conditions. Inclusion criteria required that at least 1 parent or caretaker had experienced either a major depressive episode during the past 3 years or 3 or more major depressive episodes or 3 or more cumulative years in a major depressive or dysthymic episode within the youth's lifetime. Adolescents' inclusion criteria required that they be aged 13 to 17 years and have (1) current subsyndromal depressive symptoms operationalized as an entry score of 20 or higher on the Center for Epidemiological Studies Depression Scale (CES-D),[19] (2) a prior episode of a *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition) (*DSM-IV*) depressive disorder, which was required to be in complete remission for at least 2 months, or (3) both. Adolescents were excluded if (1) either they or their biological parent were diagnosed with bipolar I or schizophrenia; (2) they had a current *DSM-IV* mood disorder diagnosis; (3) they currently were taking a therapeutic dose of an antidepressant medication[20]; or (4) they had received more than 8 sessions of CB therapy for depression. More than 1 sibling was allowed to participate; yoked randomization ensured that siblings within a family were assigned to the same condition. Of the 316 participants, 33 were sets of siblings (1 sibling set was triplets).

The study was conducted at 4 sites with 80 participants at Vanderbilt University, Nashville, Tennessee; 80 at the University of Pittsburgh, Pittsburgh, Pennsylvania; 78 at Kaiser Permanente Center for Health Research, Portland, Oregon; and 78 at Judge Baker Children's Center/Children's Hospital, Boston, Massachusetts. Recruitment began August 2003 and ran through February 2006. Participants were recruited from several sources including a health maintenance organization computerized database; a university medical center e-mail listserv; letters to physicians in the community; letters to parents of students in local schools; and newspaper, radio, and television advertisements. Details of the flow of participants are provided in FIGURE 1.

Approval for this study was provided by the institutional review boards of each site. All parents and adolescents provided written informed consent and assent, respectively. Recruitment, outcomes, and adverse events were monitored by a data and safety monitoring board.

Assessments

Parent and youth instruments were administered at baseline, after the acute intervention phase at about month 3 (median, 14.1 weeks), and after the continuation phase at about month 9 (median, 42.1 weeks) after baseline.

Independent evaluators were blinded to experimental condition throughout the study, were excluded from meetings at which condition assignment was discussed, and were not located in offices in which the CB prevention program was delivered in order to avoid inadvertent discovery of condition. In addition, at the beginning of each follow-up assessment, parents and youth were explicitly instructed not to divulge to the independent evaluator their assigned condition.

Index parents were administered the Structured Clinical Interview for *DSM-IV* axis I disorders (SCID-I)[21] to assess current mood disorder diagnoses and the duration and number of prior mood disorder episodes. The Schedule for Affective Disorders and Schizophrenia for School-Age Children, Epidemiological Version (K-SADS-PL)[22] was administered to parents and adolescents to obtain youth diagnoses according to the *DSM-IV*.[23] All independent evaluators completed extensive training and ongoing supervision for the use of these diagnostic tools and demonstrated a minimum interrater reliability level of $\kappa = 0.80$ in 2 practice interviews before conducting study assessments. Most independent evaluators had at least a master's degree in a mental health field; 3 had a bachelor's degree. A random 48 adolescent interviews (15%) were rerated

by a senior diagnostic interviewer with agreement of 96.2% and 85.9% for current and past mood diagnoses, respectively.

At each follow-up evaluation, parents and adolescents were interviewed about the teen with the Longitudinal Interval Follow-up Evaluation (LIFE),[24] which provides a continuous assessment of symptoms and onset and offset of disorders since the last assessment. A score from 1 through 6 on the Depression Symptom Rating (DSR) scale is given for each week of the follow-up period. Scores of 1 to 2 indicate none, 1, or 2 symptoms with no or mild impairment; 3 reflects at least 3 symptoms with mild to moderate impairment; 4 indicates at least 4 symptoms and mild to moderate impairment; and 5 and 6 indicate that the person meets definite criteria for a major depressive episode. The primary outcome measure used in the current study was a probable or definite episode of depression (ie, a DSR score ≥4) for at least 2 weeks. Interrater reliability was high (97.5% agreement; n=32) on DSR ratings across the follow-up period. Interviewers also completed the 17-item Children's Depression Rating Scale–Revised (CDRS-R)[25] based on parent and youth report about the adolescents' depressive symptoms in the past 2 weeks. Interrater reliability calculated on a random 15% of the interviews yielded an intraclass correlation coefficient of 0.74.

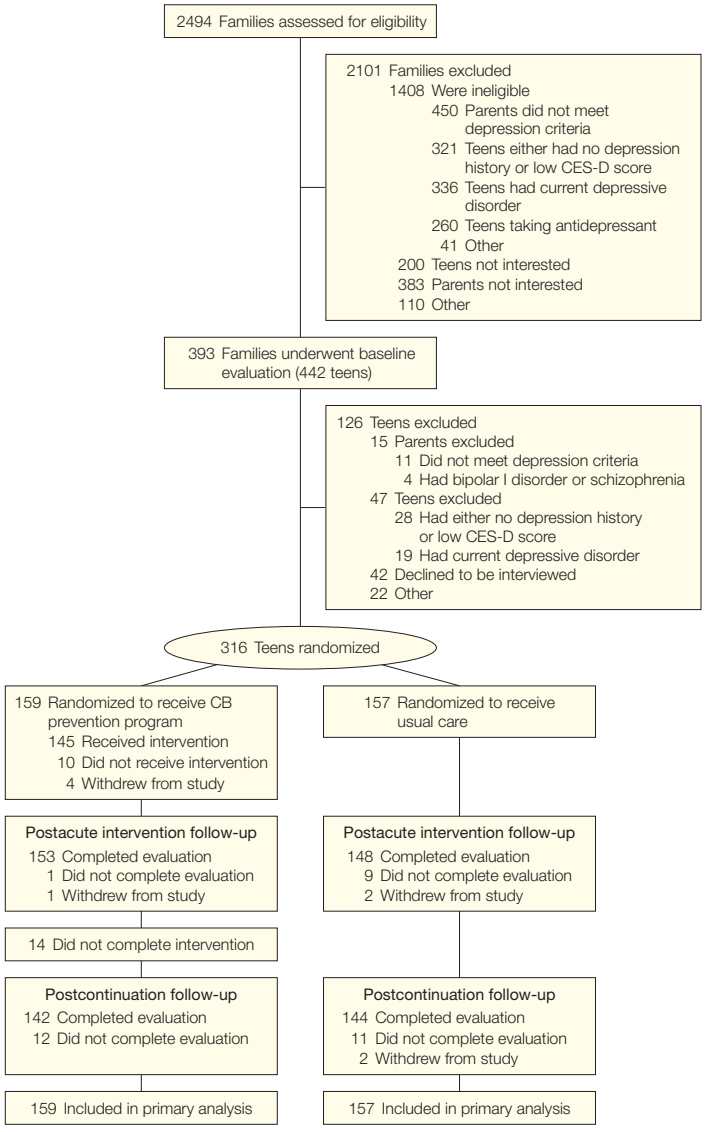
The CES-D[19] is a self-report measure of the frequency of 20 depressive symptoms during the past week. It has good psychometric properties when used with adolescents.[26] Internal consistency of the CES-D for youth report in this sample was $\alpha = .89$. Adolescents were considered to have current subthreshold depressive symptoms based on a CES-D score of 20 or more at telephone screen or baseline interview.[27] Youth were excluded if they met *DSM-IV* criteria for a current mood disorder.

The Child and Adolescent Services Assessment (CASA)[28] measured mental health service use during the 3 months before baseline and through the follow-up period. The CASA has acceptable reliability and validity.[29]

Procedures

Adolescents were randomized using the Begg and Iglewicz[30] modification of the Efron[31] biased coin toss to ensure that the 2 cells were balanced on age, sex, race/ethnicity, and inclusion criteria (ie, history of depressive episode, high CES-D score). Randomization successfully balanced these variables between intervention conditions both within and across sites. All participants, regardless of their degree of future participation, were considered part of the study from the point of randomization (an intent-to-treat design). Participants were randomized centrally at the Pittsburgh site by a computer program. Of the 442 adolescents screened to be eligible for a baseline assessment, 159 were randomized to the CB prevention program and 157 to usual care (Figure 1).

Figure 1. Study Flow of Participants From Screening to Analysis



CES-D indicates Center for Epidemiological Studies Depression Scale.

Intervention

The prevention program used in the current study was a modification of the intervention tested in prior single-site randomized controlled trials conducted in Oregon.[14,15] The preventive intervention consisted of 8 weekly 90-minute (acute) and 6 monthly (continuation) sessions for mixed-sex groups of 3 to 10 adolescents (mean [SD] group size, 6.6 [1.6]). Each group was led by a therapist with at least a master's degree in a mental health field, who was trained and supervised by an experienced clinician. In the CB prevention program, adolescents were taught cognitive restructuring techniques to identify and challenge unrealistic and overly negative thoughts[32] and were taught problem-solving skills.[33] Participants attended an average of 6.5 acute sessions (median, 8.0; range, 0-8 sessions) and an average of 3.8 continuation sessions (median, 5.0; range, 0-6 sessions). During the continuation sessions, cognitive and problem-solving strategies were reviewed and new skills (eg, behavioral activation, relaxation, assertiveness) were introduced. Parent meetings also were conducted at weeks 1 and 8 of the acute adolescent sessions to inform parents about the general topics and skills taught to the adolescents and to provide the rationale for their use. Parents of 76.4% of the 159 adolescents attended the first information session and 70.9% attended the second session.

All intervention sessions were digitally audiorecorded. An early and a late session were randomly selected from each group (total of 12.5% of all sessions; n=18) and rated by a senior supervisor using a 9-item fidelity scale.[34] Therapist compliance rating scores ranged from 88.1% to 95.8%.

Usual Care

All enrolled youth, regardless of randomization condition, were permitted to initiate or continue nonstudy mental health or other health care services. Service use was documented using the CASA.[28]

Retention and Missing Data

At follow-up, 301 participants (95.2%) completed the postacute evaluations and 286 (90.5%), the postcontinuation evaluations. No significant differences were found on any demographic, entry characteristics, or depression measures between retained participants and those who did not complete follow-up. Consistent with an intent-to-treat design and standard survival analysis procedures,[35] all participants were entered into the survival analyses and censored at the point of their last available data onward. In the random regression analyses, every randomized case was included. Thus, the baseline information of all 316 participants accounted for the estimation of the baseline intercepts. No data were missing for the variables used to predict outcome (ie, intervention, site, baseline parental depression, adolescent's history of depression at baseline, and baseline CES-D). At the postacute assessment, CES-D values were missing for 26 participants (8.2%) and CDRS-R values were missing for 19 participants (6.0%). At the postcontinuation evaluation,CES-D values were missing for for 38 participants (12.0%) and CDRS-R values were missing for 30 participants (9.5%).

Data Analysis Plan

The primary outcome was onset of a depressive episode (ie, DSR of ≥4 for at least 2 weeks). Kaplan-Meier curves and Cox regression were used to test the main effect of the intervention and potential effects of site or family membership (ie, sibling pairs). The effects of intervention on the secondary outcomes of self-reported (CES-D) and clinician-rated (CDRS-R) depressive symptoms were assessed with mixed models. Scores from baseline and follow-up assessments were used to construct symptom slopes for these analyses.

Each model included a fixed effect for the intervention, a random time effect, and an interaction term that respectively estimated the average condition (CB prevention program vs usual care) specific intercepts, the rate of change over time (slope), and the specific rate for each group. Logarithmic transformation of time was conducted and an unstructured covariance matrix was used. As with the survival analyses, additional random-effects models were conducted to examine the effects of site and family grouping. To adjust for sibling correlation, family was used as a random variable in the mixed models and for clustering in the Cox regression models. Power was calculated for study design using Power Analysis and Sample Size (PASS) version 2000 software and tables,[36,37] which estimated that the study could detect a 12% difference in incidence rate of depression, with 80% power, $P=.05$, controlling for up to 6 covariates.

We also tested moderating effects of entry characteristics (ie, current parental depression, youth symptom severity, youth history of mood disorder) for both dichotomous and continuous outcomes by examining interactions between the baseline variable and time (for survival analyses) or time by condition (for random-effects regressions) in the presence of relevant main effects. All significance tests were 2-tailed. The Bonferroni correction was applied when multiple post hoc comparisons were conducted within a family of tests (eg, unpacking interactions).

RESULTS

Demographic and Clinical Characteristics

Participants' mean (SD) age was 14.8 (1.4) years (range, 13-17 years) at study onset. Overall, 58.5% of participants were female and 24.7% were self-identified members of an ethnic/racial minority group. Participants did not differ significantly by study intervention condition on any demographic or clinical characteristic at entry (TABLE 1).

Clinical Outcome

Incident Depression (Primary Outcome). The rate and hazard ratio (HR) for incident depression were lower for those in the CB prevention pro-

gram than for those in usual care through the postcontinuation follow-up (21.4% vs 32.7%, risk difference, –11.3%, 95% confidence interval [CI], –21.10 to –1.39; χ^2_1=4.90; *P*=.03; HR, 0.63; 95% CI, 0.40 to 0.98; FIGURE 2). There was a significant main effect for site, indicating mean differences in depression rates across sites, but there was no site × intervention interaction; that is, the effects of the intervention on incident depression did not vary significantly by site.

Change in Depressive Symptoms. There was a significant intervention × time interaction on the CES-D (coefficient, –1.10; *z*=–2.22; *P*=.03) indicating that self-reported depressive symptoms declined at a significantly greater rate for youth in the CB prevention program than for those in usual care (TABLE 2, Model 1). Site and the site × time interaction were significant, indicating that sites differed in overall mean levels of adolescents' depression symptoms (χ^2_3=48.54; *P*<.001) and in mean rate of improvement over time (χ^2_3=23.95; *P*<.001). However, the intervention-×-time-×-site interaction was not significant (χ^2_3=5.47; *P*=.14) indicating that the effect of the intervention on symptom change was robust and consistent across site differences in adolescents' symptom levels. On the CDRS-R, there was a significant main effect for time (*z*=–6.14; *P*<.001) but not for condition, and the interaction of condition by time × site was not significant. TABLE 3 presents the means and standard deviations on these measures at the 3 time points.

Entry Criteria as Moderators

Current Parental Depression. Current parental depression at baseline significantly moderated the effect of the CB prevention program on incident depression (HR, 5.98; 95% CI, 2.29-15.58; *P*=.001; TABLE 4 and FIGURE 3). Bonferroni-corrected pairwise comparisons indicated that the CB prevention program was significantly better than usual care in preventing depressive episodes if a parent did *not* have a current depressive episode (11.7% vs 40.5%; HR, 0.24; 95% CI, 0.11-0.50; *P*<.001). When parents were actively depressed at baseline, rates of youth incident depression did not differ significantly between the CB prevention program and usual care (31.2% vs 24.3%; HR, 1.43; 95% CI, 0.76-2.67; *P*=.26). Comparisons within the CB prevention program condition indicated that offspring of currently depressed parents had a significantly higher rate of incident depression than adolescents of currently nondepressed parents (31.2% vs 11.7%; HR, 3.21; 95% CI, 1.50-6.89; *P*=.003). Within the usual care group, rates of incident depression did not differ significantly between offspring of currently depressed vs nondepressed parents (24.3% vs 40.5%; HR, 0.51; 95% CI, 0.30-0.96; unadjusted *P*=.04) after adjusting for multiple comparisons.

A moderating effect of current parental depression was also found for the trajectory of self-reported depression on the CES-D (Table 2, model 2). Paired comparisons indicated that among adolescents with a currently depressed parent, the CES-D trajectory was significantly worse for youth in usual care than for those in the CB prevention program (coefficient, 2.20, *P*<.001). None of the other pairwise comparisons was significant.

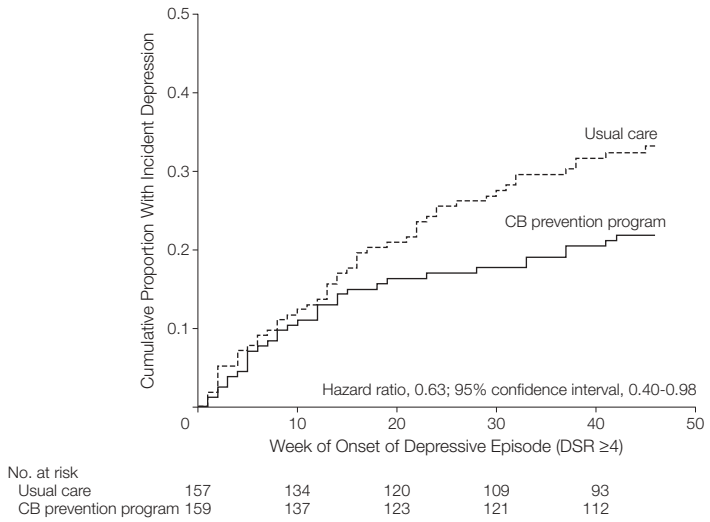
Adolescents' Depressive Symptoms and History of Depression. Table 4 shows that adolescents' entry CES-D scores did not significantly moderate the effect of the intervention on incident depression (χ^2_1=2.70; *P*=.10) or CES-D slopes (*P*=.17). Adolescents' history of depressive episodes also did not significantly interact with intervention to predict depression onsets

Table 1. Baseline Demographic and Clinical Characteristics of Index Parents and Adolescents Randomized to the Cognitive Behavioral Prevention Program or Usual Care

Baseline Characteristics	Cognitive Behavioral Prevention Program	Usual Care	*P* Value
Demographics			
Teens, No.	159	157	
Age, mean (SD), y	14.8 (1.5)	14.8 (1.3)	.66
Female, No. (%)	93 (58.5)	92 (58.6)	.98
White, No. (%)	129 (82.7)	125 (80.6)	.64
Latino or Hispanic ethnicity, No. (%)	10 (6.3)	11 (7.1)	.78
Sibling pairs, No. (%)	19 (24.5)	14 (17.8)	.15
Index parents, No.	139	143	
≥High school education, No. (%)	108 (77.7)	110 (76.9)	.88
Employed full- or part-time, No. (%)	114 (82.0)	117 (81.8)	.97
Socioeconomic status, mean (SD)[a]	46.3 (12.1)	45.2 (11.9)	.39
Parental depression			
CES-D, mean (SD)	19.2 (12.8)	19.5 (11.8)	.84
Current major depressive episode, No. (%)	66 (47.5)	62 (43.4)	.49
No. of major depressive episodes, mean (SD)	4.1 (3.7)	4.1 (4.9)	.94
Lifetime dysthymia, No. (%)	24 (17.3)	21 (14.7)	.55
Age at earliest onset of depressive disorder, mean (SD), y	23.7 (11.5)	24.3 (11.1)	.63
Total duration of depressive disorders, wk	90.5 (100.0)	85.4 (113.6)	.69
Qualifying criteria, No. (%)			
CES-D ≥20	29 (18.2)	34 (21.7)	.65
History of a depressive episode	88 (55.3)	87 (55.4)	
Both	42 (26.4)	36 (22.9)	
CES-D entry qualifying score, mean (SD)	18.5 (9.1)	18.8 (9.6)	.83
Children's Depression Rating Scale–Revised, mean (SD)	28.6 (8.0)	29.1 (8.5)	.52

Abbreviations: CES-D, Center for Epidemiological Studies Depression Scale.
[a] Index of Social Status.[38]

Figure 2. Risk of Incident Depression by Intervention Condition



CB indicates cognitive behavioral.

Table 2. Random-Effects Regression Analyses of Adolescents' Depressive Symptoms on the Center for Epidemiological Studies Depression Scale at Baseline, Postacute, and Postcontinuation Evaluations

Models	Statistical Tests	
	Coefficient (SE)	*z*
1		
Time	–1.00 (0.50)	–2.86[a]
Intervention	–0.79 (1.10)	–0.72
Time × intervention	–1.10 (0.50)	–2.22[b]
2		
Time	–1.60 (0.48)	–3.33[c]
Intervention	–3.18 (1.54)	–2.06[b]
Baseline parental depression	–1.86 (1.54)	–1.21
Time × intervention	–0.10 (0.69)	–0.15
Time × baseline parental depression	1.27 (0.70)	1.82
Intervention × baseline parental depression	4.80 (2.19)	2.19[b]
Time × intervention × baseline parental depression	–2.05 (0.99)	–2.07[b]

[a] $P<.01$.
[b] $P<.05$.
[c] $P<.001$.

Table 3. Scores on the Center for Epidemiological Studies Depression Scale and Children's Depression Rating Scale–Revised at Baseline, Postacute Intervention, and Postcontinuation Evaluations

Measure of Depression	Evaluation Time Points, Mean (SD)		
	Baseline	Postacute Intervention	Postcontinuation
Center for Epidemiological Studies Depression Scale			
Cognitive behavioral prevention program	15.5 (9.4)	12.3 (8.7)	10.9 (8.4)
Usual care	15.8 (10.0)	15.1 (9.8)	13.5 (8.3)
Children's Depression Rating Scale–Revised			
Cognitive behavioral prevention program	28.6 (8.0)	25.1 (7.1)	23.6 (6.3)
Usual care	29.1 (8.5)	27.1 (7.7)	25.0 (7.2)

(Wald $\chi^2_1=0.08$; $P=.77$) or moderate the effect of the intervention on trajectories of depressive symptoms on the CES-D ($P=.11$).

Independent Evaluator Blinding

As a check on allocation concealment, independent evaluators were asked to guess participant group assignment after completion of their interview. The independent evaluators correctly guessed participants' conditions at a rate higher than chance (postacute, 71.7%; $\chi^2_1=58.80$; $P<.001$; postcontinuation, 64.5%; $\chi^2_1=24.60$; $P<.001$). Blinding was most often compromised because participants in the CB prevention program condition disclosed their assignment to the independent evaluator, despite explicit instructions not to do so. However, independent evaluator's guess of condition (CB prevention program vs usual care) was not significantly associated with whether a depression diagnosis was made (postacute, $\chi^2_1=0.38$; $P=.57$; postcontinuation, $\chi^2_1=2.62$; $P=.10$). After controlling for correct guessing, the logistic regression revealed that the effect of intervention was not statistically significant (coefficient, –0.52; $P=.07$; OR, 0.59; 95% CI, 0.34-1.04), although the pattern of effects remained consistent across analyses.

Service Utilization

Adolescents assigned to the CB prevention program vs usual care did not differ significantly in service use in the 3 months before randomization or in nonstudy-service use from baseline through the follow-up period (TABLE 5).

COMMENT

Summary

This 4-site randomized prevention trial demonstrated that the CB prevention program compared with usual care significantly reduced the incidence of depressive episodes and self-reported depressive symptoms in adolescents with high familial and individual risk for depression. This replicates and extends the work of Clarke and colleagues[15] and demonstrates that this CB prevention

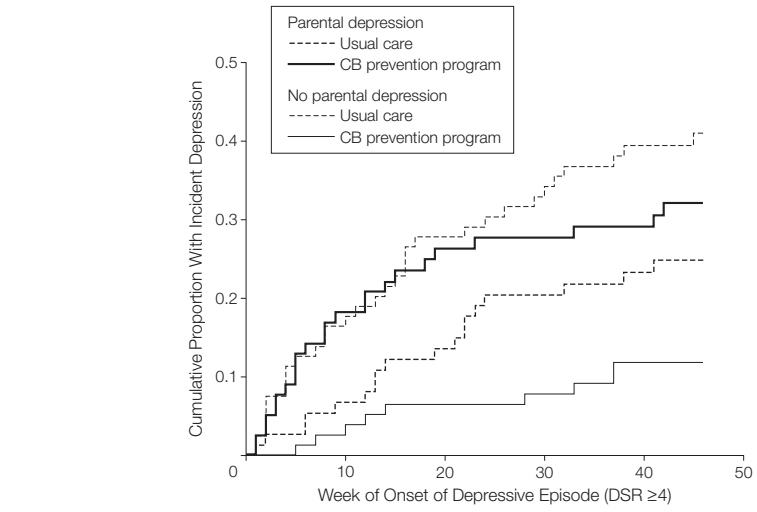
Table 4. Entry Characteristics as Moderators of the Effect of the Cognitive Behavioral Prevention Program on Onset of Depressive Episodes

Entry Characteristics as Moderators	CB Prevention Program		Usual Care		Hazard Ratio	Risk Difference (95% CI), %
	No. of Participants	No. (%) of Participants Who Had an Episode	No. of Participants	No. (%) of Participants Who Had an Episode		
Parental depression						
Current	77	24 (31.2)	74	18 (24.3)	1.43	6.8 (–7.4 to 21.1)
No current	77	9 (11.7)	79	32 (40.5)	0.24[a]	–28.8 (–41.8 to –15.8)
CES-D						
High entry CES-D, ≥20	72	20 (27.8)	69	27 (39.1)	0.72	–11.3 (–26.8 to 4.1)
Low entry CES-D, <20	82	13 (15.9)	84	23 (27.4)	0.53[b]	–11.5 (–23.9 to 0.1)
Depressive episode						
History	125	27 (21.6)	119	40 (33.6)	0.60[c]	–12.0 (–23.0 to –0.1)
No history	29	6 (20.7)	34	10 (29.4)	0.72	–8.7 (–29.9 to 12.5)

Abbreviations: CB, cognitive behavioral; CES-D, Center for Epidemiological Studies Depression Scale; CI, confidence interval.
[a] $P \leq .001$.
[b] $P \leq .10$.
[c] $P \leq .05$.

program can be reliably and effectively delivered in different settings by clinicians outside of the group who originally developed the intervention. The effect size was consistent with those of previously reported, single-site, indicated depression prevention studies[12,13] and was robust across sites with respect to both depressive disorders and symptoms. Most relevant to prevention trials is the reduction in future incident depressive episodes. In this study, episodes were 11% lower in the CB prevention program condition. Borrowing a concept from the evidence-based medicine literature, this risk reduction could be translated into a number needed to prevent of 9; that is, for every 9 adolescents receiving the intervention, we would expect to prevent one from developing a depressive episode. For comparison purposes, the number needed to treat for antidepressants in adolescent depression is 10,[39] suggesting that the preventive effect of the CB program was of a similar magnitude as treatment response to medication. Moreover, the prevention of a disorder may bring even greater benefit to adolescents and to the public than the amelioration of an acute depressive episode after it has produced other negative consequences. Thus, these positive findings support the clinical utility of this CB prevention program as a preventive intervention to reduce or delay the incidence of depression in offspring of depressed parents. Most youth in the current study had a history of depression and thus the CB prevention program prevented recurrence. Therefore, this program may be useful as a continuation or maintenance intervention.

Figure 3. Risk of Incident Depression by Intervention Condition and Baseline Parental Depression



No. at risk					
Parental depression					
Usual care	76	68	63	57	51
CB prevention program	81	62	53	52	48
No parental depression					
Usual care	81	66	57	52	42
CB prevention program	78	75	70	69	64

Pairwise comparisons indicated that the curve for the cognitive behavioral (CB) program plus no parental depression was significantly different from the curves for the CB program plus parental depression (hazard ratio [HR], 3.21; 95% confidence interval [CI], 1.50-6.89; $P = .003$), and for usual care plus no parental depression (HR, 0.24; 95% CI, 0.11-0.50; $P < .001$).

Additionally, we found that if a parent was currently depressed, the CB prevention program was not more efficacious than usual care in preventing

depressive episodes. This is consistent with the original prevention trials of the CB preventive intervention by Clarke and colleagues,[15] as well as several treatment studies of CB therapy for pediatric depression that have shown that when a parent is depressed at the initiation of treatment, CB therapy is not more efficacious than alternative interventions.[17,40] Interestingly, the CB prevention program was robust to the effects of parental depression on adolescents' self-report of depressive symptoms. Among adolescents who had a currently depressed parent, those in usual care showed significantly less reduction in self-reported depressive symptoms than did those in the CB prevention program. Thus, current parental depression was associated with poorer response, although the interaction with condition varied by outcome measure (ie, weekly DSR ratings vs self-reported depressive symptoms assessed at three time points). Overall, these findings are consistent with recent work showing an association between changes in parental depression and changes in youth symptoms.[41] The potential value of combined or sequenced parent and adolescent depression treatment and prevention, respectively, should be explored in future investigations.

Limitations

In this generalizability trial, we chose a comparison condition that is relevant to public health—usual care. The usual care and CB prevention program conditions did not differ in their use of community services; thus, youth in the CB prevention program received up to 14 sessions (ie, the maximum length of the CB prevention program) of additional services than adolescents in usual care. The current study precludes definitive disaggregation of the effects of additional contact and attention from the specific effects of the CB prevention program. Treatment studies in youth, however, have shown that simple dose of general psychotherapy is only weakly related to outcome,[42] and that CB therapy in particular is superior to attention-control or alternative interventions such as nondirective supportive therapy, relaxation therapy, or usual care conditions for depressed adolescents.[43,44]

The primary outcome for this prevention trial was the incidence of depressive episodes; a significant effect, however, was not found on the CDRS-R. Although the CDRS-R is considered to be a sensitive measure of treatment response,[45] it may be a less appropriate index of prevention effects due to the greater range and less elevated scores among some participants at baseline. In addition, because offspring of depressed parents are at risk for a wide range of difficulties in interpersonal, occupational, legal, and physical health as well as depression, these broader outcomes and the longer-term effect of the CB prevention program should be explored in the future.

Although our findings showed that current parental depression moderated depression outcomes, the study was not designed to determine the specific mechanisms (eg, early life adversity, parenting problems, stability of parental symptoms, genes, current shared life stressors) underlying this effect. For example, we cannot determine from these data whether current vs continued parental depression during the trial contributed to this finding. The absence of information about whether parents received treatment during this trial also is a limitation.

Independent evaluators guessed participants' group assignment at a rate higher than chance, primarily because

Table 5. Usual Care Services Received by the Cognitive Behavioral Prevention Program and Usual Care Groups Prior to Baseline and Through the Postcontinuation Evaluation

	3 Months Before Intervention						Follow-up Through Postcontinuation Evaluation					
	Participant Use			Services Use for Users			Participant Use			Services Use for Users		
	No. (%) of Participants			No. of Times Service Used, (Mean) SD			No. (%) of Participants			No. of Times Service Used, (Mean) SD		
Type of Service	Usual Care	CB Prevention Program	*P* Value[a]	Usual Care (n = 157)	CB Prevention Program (n = 159)	*P* Value[b]	Usual Care, No. (%)	CB Prevention Program, No. %	*P* Value[a]	Usual Care (n = 157)	CB Prevention Program (n = 159)	*P* Value[b]
Outpatient mental health visits	15 (9.6)	16.4 (26)	.13	4.60 (5.12)	6.85 (14.34)	.27	46 (29.3)	49 (30.8)	.74	10.46 (16.71)	11.18 (16.97)	.86
Any mental health medication	3 (1.9)	1.9 (3)	.97				11 (7.0)	12 (7.6)	.90			
Antidepressants	1 (0.6)	1.3 (2)	.60				8 (5.1)	9 (5.7)	.84			
Inpatient treatment for mental health or alcohol or drug, d	1 (0.6)	1 (0.6)	.91	1.00 (0.00)	1.00 (0.00)	.98	2 (1.3)	4 (2.5)	.33	11.00 (9.90)	37.75 (62.89)	.77
School counseling visits	14 (8.9)	8 (5)	.61	4.43 (5.35)	3.88 (2.64)	.85	32 (20.4)	27 (17.0)	.36	28.16 (58.80)	16.78 (40.62)	.52
Juvenile court/probation, d	0	0	NA	0.00	0.00	NA	6 (3.8)	3 (1.9)	.35	11.00 (14.44)	7.33 (5.69)	.82

Abbreviations: CB, cognitive behavior; NA, not applicable.
[a] Reported on intervention condition indicator from logistic regression, controlling for age, sex, baseline depression, and history of depression.
[b] Reported on intervention condition indicator from negative binomial regression, controlling for age, sex, baseline depression, and depression history.

CB program participants revealed their group assignment to the independent evaluators. Nevertheless, such guesses, even when correct, were not significantly related to the outcome variable (ie, whether or not a diagnosis was made). Controlling for correct guessing, the intervention effect was no longer statistically significant, and, thus, it is possible that results were biased by independent evaluator knowledge of intervention condition. Conversely, the independent evaluators' guesses might have been the result of participants' actual outcome. To the extent that the observed outcomes determined evaluators' guesses, controlling for guessing may have removed a portion of the true variance in the response and thereby overcorrected for the independent evaluators' guesses. Additionally, collinearity between the correct-guess variable and condition assignment might have obscured intervention effects in the presence of this control factor. Consistent with this hypothesis, change in adolescents' self-reported depressive symptoms, which would be unaffected by independent evaluator bias, also showed a significant intervention effect. Thus, the CES-D results provide convergent and independent evidence of the effectiveness of the CB prevention program.

Finally, although the sample was representative of the communities from which participants were drawn, only 25% of participants were members of an ethnic or racial minority group and no more than 12% were from any one ethnic or racial subgroup. The sample also was predominantly working class to middle class with access to health insurance. Given evidence that CB therapy can be more efficacious for adolescents from homes with higher incomes,[46] it will be important to test the effects of this prevention program with more economically and ethnically diverse samples. Other investigators have shown the value of replicating prevention findings derived from white middle class samples with more ethnically diverse groups.[47,48]

The current study adds to the growing literature on evidence-based prevention programs for families facing adversity.[16] This replication and extension of the single-site prevention study by Clarke and colleagues[15] represents the next step in the NIH Roadmap[49] "translational" progression to move evidence-based interventions from highly controlled, research designs into real-world use. Future steps should include an integration of improved treatment for parental depression, testing of the CB prevention program in a more diverse sample, and a dissemination trial of the tested intervention in settings in which families are most likely to receive services (eg, primary care), with researchers limiting their role to promoting adoption of the program, interventionist training, and evaluation of patient, family, and health system outcomes.

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