ORIGINAL ARTICLE

# A Randomized Trial of a Group Cognitive Intervention for Preventing Depression in Adolescent Offspring of Depressed Parents

*Gregory N. Clarke, PhD; Mark Hornbrook, PhD; Frances Lynch, PhD; Michael Polen, MS; John Gale, MD; William Beardslee, MD; Elizabeth O'Connor, PhD; John Seeley, MS*

**Background:** Adolescent offspring of depressed parents are at high risk for development of depression. Cognitive restructuring therapy holds promise for preventing progression to depressive episodes.

**Methods:** A randomized, controlled trial was conducted to prevent depressive episodes in at-risk offspring (aged 13-18 years) of adults treated for depression in a health maintenance organization (HMO). Potential adult cases were found by reviewing the HMO pharmacy records for dispensation of antidepressant medication and the mental health appointment system. Medical charts were reviewed for a depression diagnosis. Recruitment letters signed by treating physicians were mailed to adults. Eligible offspring had subdiagnostic depressive symptoms insufficient to meet full *DSM-III-R* criteria for affective disorder and/or a past mood disorder. These youth were randomized to usual HMO care (n=49) or usual care plus a 15-session group cognitive therapy prevention program (n=45).

**Results:** We detected significant treatment-by-time (program) effects for the Center for Epidemiological Studies Depression Scale ($P$=.005) and the Global Assessment of Functioning scores ($P$=.04). Survival analysis of incident major depressive episodes during a median 15-month follow-up found a significant advantage ($P$=.003) for the experimental condition (9.3% cumulative major depression incidence) compared with the usual-care control condition (28.8%).

**Conclusion:** A brief, group cognitive therapy prevention program can reduce the risk for depression in the adolescent offspring of parents with a history of depression.

*Arch Gen Psychiatry. 2001;58:1127-1134*

*From the Kaiser Permanente Center for Health Research, Portland, Ore (Drs Clarke, Hornbrook, Lynch, Gale, and O'Connor and Mr Polen); the Judge Baker Children's Center, Children's Hospital Boston, Boston, Mass (Dr Beardslee); and the Oregon Research Institute, Eugene, Ore (Mr Seeley).*

DEPRESSION IS common among adolescents, with a point prevalence estimated at 3% to 8%.[1] By 18 years of age, as many as 25% of adolescents have had at least 1 depressive episode.[2] Most adults with recurrent depression have their initial depressive episodes as teenagers,[3] suggesting that adolescence is an important developmental period in which to intervene.

Research on the treatment of youth depression supports the efficacy of medication[4] and psychotherapy.[5-7] Emerging evidence also exists that psychosocial interventions may prevent depression.[8-10] Recently, intervention research has focused on groups at high risk for affective disorder, including children and adolescents with a depressed parent, in whom depression is up to 6 times more likely to develop than in other children.[11,12] Most offspring studies were noninterventional, limited to investigations of relative risk and longitudinal course.[12] Recently, however, Beardslee and colleagues[8] conducted a trial of a family-based, cognitive intervention for offspring of depressed parents. They found positive effects on functional outcomes of parent and child, but did not report effects for depression diagnoses.

Another frequently studied risk group includes individuals who do not meet full criteria for a *DSM* affective episode, but who report significant "subsyndromal" depressive symptoms. "Full-blown" depression is more likely to develop in these individuals with subsyndromal symptoms,[13-15] who have been the subject of several targeted prevention interventions.[9,10]

This report presents the results from a new prevention trial conducted with the subsyndromal adolescent offspring of parents treated for depression. This study was similar to the investigation by Beardslee et al[8] in that both trials attempted to treat or prevent depression in the at-risk offspring, and both used manual-based, psycho-educational interventions. However, Beardslee et al[8] used an individual,

## SUBJECTS AND METHODS

### SUBJECTS AND RECRUITMENT

The sampling frame included approximately 410 000 members enrolled in the Kaiser Permanente Northwest health maintenance organization (HMO), centered around Portland, Ore. The study research center is located within the HMO but is self-governed. The Human Subjects Committee for the HMO approved all study procedures.

To refresh the available pool of depressed parents and youth, case finding was conducted in 6 separate cohorts across a 2-year recruitment period (September 1994 through October 1996). Each cohort began by identifying those adults aged 30 to 65 years who had been HMO members for at least 6 months, had covered dependents aged 13 to 18 years, and lived reasonably close to the study center.

To generate the initial pool of depressed adults, we searched the HMO computerized pharmacy database for adults who had received at least 2 dispensations of an antidepressant medication within the past 12 months. Nearly all HMO member prescriptions are filled at HMO pharmacies.[16] Across all cohorts, this step identified 4706 potentially depressed parents. We also searched the mental health appointment database, identifying 1316 adults with at least 2 mental health visits in the past 12 months. Approximately 17% of adults (n=1003) were identified using both methods, resulting in a nonoverlapping total of 5954 potentially depressed adults.

Medical chart reviews determined that 3935 of these adults (66.1%) had a depression diagnosis and/or symptoms recorded in association with the medication prescription or the mental health visits. Each parent's physician mailed introductory letters to those adults they judged appropriate for the study (n=2995). A postpaid refusal postcard was returned by 458 adults (15.3%). Study staff attempted to telephone the remaining adults for a brief screening of study criteria. The adolescent offspring of 2083 contacted adults were also asked about their interest in participating. Interested families were invited for an intake evaluation; a written consent was signed by the parent(s) and the adolescent. Up to 2 qualifying siblings from each family could participate. Interviews were scheduled with 744 families (966 youth) and completed with 481 parents (64.7%) and 551 adolescents (57.0%). This assessment confirmed the parent diagnosis of depression and assessed adolescent psychiatric diagnoses, symptoms, and psychosocial functioning.

To qualify for the study, parents could either be in a current episode of major depression and/or dysthymia, or have had an episode in the past 12 months that touched chronologically on their current course of antidepressant medication and/or psychotherapy. The latter subjects were those who had effectively responded to their depression treatment, were no longer depressed, but were still taking medication or receiving treatment. Parent diagnosis of depression and other disorders was assessed using the Family Schedule for Affective Disorders and Schizophrenia (F-SADS), modeled after the Family History Research Diagnostic Criteria.[17] Parents were asked a series of structured questions probing for the presence or absence of symptoms of psychiatric disorders listed in the *DSM-III-R*.[18] Interviewers assigned appropriate psychiatric diagnoses according to *DSM-III-R* decision rules. The F-SADS demonstrated excellent interrater reliability for lifetime diagnoses in another study (Peter Lewinsohn, PhD, unpublished data, August 1994), with $\kappa=0.92$ for unipolar depression and $\kappa=0.93$ for nonaffective disorders.

Of 551 interviewed youth/parent dyads, 79 were disqualified, usually because the interviewed parent did not meet criteria for major depression or dysthymia (n=70). The remaining 472 youth were classified into 1 of 3 mutually exclusive depression severity groups based on adolescent information gathered during the intake assessment.

A high-severity depression group (n=116; 24.6%), called depressed youth, consisted of adolescents with current *DSM-III-R*[18] diagnoses of major depressive disorder (MDD) and/or dysthymia. A separate randomized treatment trial was conducted with this sample but is not reported herein.

A medium-severity depression group (n=123; 26.1%) was called subsyndromal youth,[13] who reported some subdiagnostic levels of depressive symptoms that were insufficient to meet full criteria for a *DSM-III-R* affective diagnosis, and/or had a Center for Epidemiological Studies–Depression Scale (CES-D)[19] score of greater than 24.[9] These youth are the focus of this report.

A low-severity depression group was identified (n=233; 49.4%), called resilient youth, with no significant depression symptoms and no history of depressive disorder.[20] These youth were not subsequently followed up in this study.

We conducted independent, planned comparisons of baseline data, contrasting the depressed and subsyndromal youth vs the resilient youth, and the depressed vs the subsyndromal youth. Compared with the resilient youth, the depressed and subsyndromal youth were significantly older ($P=.003$), less likely to be enrolled in school ($P=.02$), and more often female ($P<.001$, an expected result given the greater likelihood of depression among female subjects in community samples[2]). Compared with the subsyndromal youth, the depressed youth were older ($P=.003$) and had more special education classes per week ($P=.05$). Compared with the resilient families, the parents of depressed and subsyndromal youth had lower educational levels for the parent in the household with the highest educational attainment level ($P=.05$) and were less likely to be their biological parents ($P=.042$).

### ASSESSMENTS

Unless otherwise noted, all parent and youth instruments were administered at intake (baseline), after treatment, and at follow-up assessments nominally planned for 12 and 24 months after the end of treatment (actual median completion dates were 53 and 107 weeks posttreatment). Assessors had psychology master's degrees and were trained in the use of the diagnostic instruments and received weekly supervision from one of us (G.N.C.) for the duration of the study. Assessors were unaware of the experimental condition of interviewed subjects.

#### Parent Assessment

The Achenbach Child Behavior Checklist (CBCL) consists of several social competence items and 113 youth behavior and emotional problem items that parents rate as

being not true, sometimes or somewhat true, or very or often true.[21,22] The CBCL has good test-retest reliability, and discriminates between clinic-referred and nonreferred children.[23] Scores are reported for an extracted depression subscale created to match *DSM-III-R* criteria for major depression (the CBCL-D[24]) and the standard CBCL externalizing and internalizing symptom subscales.

### Adolescent Assessment

The SADS for School-Age Children, Epidemiological Version (K-SADS-E[25]) was administered to adolescents[26] to obtain *DSM-III-R* diagnoses. Interviewers completed a rigorous program in the use of the K-SADS-E and F-SADS and demonstrated a minimum interrater reliability level[27] of $\kappa = 0.80$ in 2 practice interviews before conducting study assessments. A random 20% of interviews were rerated by a senior diagnostic interviewer. Interrater reliability for the K-SADS-E was excellent for mood disorders ($\kappa = 0.87$ for current diagnoses, $\kappa = 1.00$ for past diagnoses at baseline, and $\kappa = 0.90$ for diagnoses made at follow-up assessments) and good for all other nonaffective disorders ($\kappa = 0.74$, $\kappa = 0.67$, and $\kappa = 0.90$, respectively).

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 adults[28,29] and adolescents.[30,31] Parents and adolescents completed self-rated versions during separate administrations of the CES-D.

Interviewers completed a 14-item "extracted" version of the Hamilton Depression Rating Scale (HAM-D).[32,33] We extrapolated HAM-D item scores from corresponding K-SADS-E depression symptom ratings. Reliability for the extracted HAM-D ranged from $r = 0.87$ to $r = 0.94$ in adults[32]; $\alpha = .83$ for adolescents.[24]

Interviewers rated severity of impairment using the Global Assessment of Functioning scale (GAF). The GAF scores range from 1 to 90 and include behavioral examples that serve as anchor points. Scores below 40 reflect major impairment.

Youth in both conditions were free to continue or initiate use of any other health services. We used computerized HMO data systems to obtain data on extraexperimental health services, including, eg, inpatient and outpatient services, prescriptions, and emergency department visits. Research staff interviewed subjects monthly regarding health care services obtained from non-HMO sources.

## PROCEDURES

Qualifying subsyndromal youth were randomized to conditions using a blocked procedure to ensure that group assignments were never significantly imbalanced. Group assignment was preprinted using a computer program and sealed in sequentially numbered envelopes, which were opened in sequential order by the project coordinator (M.P.). All subjects, regardless of their degree of future participation, were considered part of the study from the point of randomization (an intent-to-treat design). Of 123 qualifying and invited youth, 29 declined to participate before randomization. Of the remaining youth, 45 were randomized to the experimental condition and 49 to the usual-care control condition. The 94 randomized youth did not differ from the 29 declining youth by parent age or sex, youth sex, or youth baseline GAF, HAM-D, or CBCL-D scores. However, randomized youth had higher baseline CES-D scores (mean of 24.4 vs 19.2; $P = .01$) and were roughly a year younger than the nonrandomized youth (mean age of 14.6 vs 15.5 years; $P = .003$).

Compared with the initial pool of potential cases (N = 3374 youth), randomized subsyndromal youth were an average of 5 months older ($P = .04$) and were more likely to be female (60% of subjects [56/94] vs 46% of the initial pool [1558/3375]; $P = .01$).

### Experimental Intervention

The prevention program[34] was an abbreviated version of an adolescent depression treatment program[35] that had been tested in a series of previous controlled outcome investigations.[6,36] The intervention consisted of 15 one-hour sessions for groups of 6 to 10 adolescents, led by a therapist with a master's degree who was trained in the approach. Sessions were conducted at the HMO clinic offices. Adolescents were taught cognitive restructuring techniques[37,38] to identify and challenge irrational unrealistic or overly negative thoughts, with a special focus on beliefs related to having a depressed parent (eg, "I'm doomed to become depressed because my father is depressed, and there's nothing I can do about it."). The prevention program had been tested in a previous randomized trial[9] in which it reduced the risk for future depressive episodes in youth with subdiagnostic depressive symptoms. Youth attended an average of 9.5 treatment sessions (median, 12; range, 0-15) and had completed homework assignments at an average of 46% of the sessions they attended.

We conducted 3 separate parent informational meetings at the beginning, middle, and end of each adolescent group. Parents were informed about the general topics discussed and skills taught in the adolescent groups and the rationale for their use. The parents' own depression was not directly discussed in these parent meetings.

All intervention sessions were audiotaped, and 2 or 3 sessions were randomly selected from each group and rated by a senior supervisor on a 10-item fidelity scale[39] to assess therapist adherence to the study protocol. Mean therapist compliance was 95.9% (SD, 3.9%; range, 90.0%-100.0%) across 15 rated sessions, indicating excellent compliance.

### Usual-Care Control Condition

All youth, whether randomized to receive the experimental cognitive-behavioral treatment intervention or not, were permitted to initiate or continue any nonstudy mental health or other health care services provided by the HMO and/or outside health care providers (including antidepressant medication, of which there was very little). This usual care in the comparison group constituted the control condition. Information regarding the degree and type of usual-care treatment was collected as described above, for examination as a potential covariate of outcome.

Of the 94 randomized participants, 2 did not participate in any of the follow-up interviews. Four, 9, and 16 participants did not participate in the posttreatment and the 12- and 24-month diagnostic interviews, respectively. We found few baseline or treatment interaction

Continued on the next page

differences between participating subjects and those unavailable for follow-up at any follow-up point on any of the key demographic, major affective, or psychopathological measures. None of the few differences were consistent across time, suggesting that there was no systematic bias in dropout. As a further check on bias as a result of attrition, primary outcome analyses were conducted that included only participants who completed all 4 assessments. The pattern of results did not change when the sample was limited in this way, lending further confidence that missing data did not bias results.

### ANALYSIS PLAN

Outcomes for continuous depression and functioning measures were examined using random-effect regression analyses, modeling an unstructured covariance matrix with slope and intercept as random effects.[40,41] We estimated linear and quadratic effects for our data, as this approach was the model that best fit the data. The linear trend indicated the direction and rate of change, whereas the quadratic trend indicated whether the rate of change increased or decreased at some point during the observation period. Significance was reported only for linear trends, as this is relevant for hypothesis testing. Episodes of major depression were the primary outcome and were examined during follow-up using survival analyses[42] and using Pearson $\chi^2$ analyses for cross-sectional comparisons at particular assessment points. All significance tests were 2-tailed, with an $\alpha$ of .05 ($P<.05$).

family-based intervention, provided by psychiatrists or primary care providers, and offered at a similar level of intensity to all youth regardless of depression severity level. In contrast, this study examined the effectiveness of a group cognitive-behavioral treatment program provided by therapists with master's degrees. Furthermore, this investigation categorized offspring into 3 depression severity groups (low, medium, and high severity), and matched the intervention dose to the severity of the presenting depression.

This report presents the overall design of the study (**Figure 1**), and the outcome findings for the group with medium-severity depression, ie, adolescents who presented with subsyndromal depression symptoms but had no active depression episodes. The aim of the randomized trial with these youth was to prevent progression to future episodes of major depression.

## RESULTS

### CHARACTERISTICS OF THE EXPERIMENTAL GROUPS

The 2 experimental conditions did not differ at baseline on rates of current and past psychiatric disorder or on any other key demographic, depression severity, functioning, or other psychosocial measure (**Table 1** and **Table 2**), after correction for multiple comparisons.

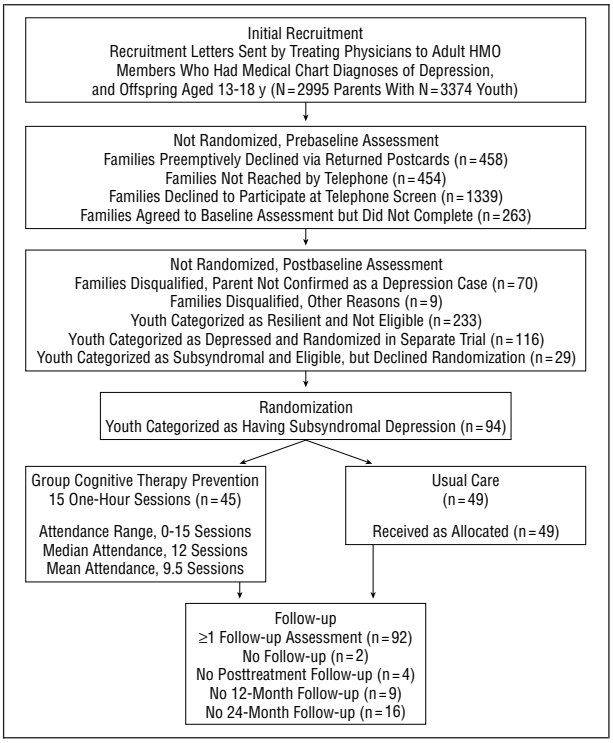


**Figure 1.** Study flowchart. HMO indicates health maintenance organization. Depression categories are described in the "Subjects and Recruitment" subsection of the "Subjects and Methods" section.

**Table 1. Comparison of Experimental Conditions by Baseline Demographics, Psychopathology, and Psychosocial Constructs***

| | Control Group (n = 47) | Treatment Group (n = 40) | *P* Value |
|---|---|---|---|
| Youth demographics | | | |
| Age, y | 14.7 (1.5) | 14.4 (1.4) | .23 |
| No. (%) female | 32 (65) | 24 (53) | .24 |
| No. (%) nonwhite | 2 (4) | 8 (18) | .03 |
| Parent demographics | | | |
| Age, y | 40.6 (5.1) | 42.4 (5.4) | .09 |
| No. (%) female | 38 (78) | 37 (82) | .57 |
| No. (%) nonwhite | 1 (2) | 4 (8.9) | .14 |
| No. (%) married | 40 (82) | 30 (66.7) | .10 |
| No. (%) college graduate | 12 (24) | 16 (35.6) | .24 |
| No. (%) employed | 41 (84) | 37 (82.2) | .85 |
| Psychopathology scores† | | | |
| CES-D | 23.8 (10.3) | 25.2 (8.7) | .48 |
| HAM-D | 3.1 (3.2) | 3.2 (3.4) | .96 |
| No. of K-SADS diagnoses | 0.5 (0.8) | 0.4 (0.8) | .40 |
| GAF | 75.0 (8.7) | 73.3 (9.4) | .36 |
| CBCL-depression | 6.8 (4.1) | 8.8 (5.3) | .04 |
| CBCL-internalizing | 14.8 (8.5) | 17.8 (10.7) | .14 |
| CBCL-externalizing | 12.4 (8.0) | 14.4 (11.1) | .30 |

*Unless otherwise indicated, data are given as mean (SD).
†CES-D indicates Center for Epidemiological Studies–Depression Scale[19]; HAM-D, Hamilton Depression Rating Scale[32,33]; K-SADS, Schedule for Affective Disorders and Schizophrenia for School-Age Children[26]; GAF, Global Assessment of Functioning; and CBCL, Achenbach Child Behavior Checklist.[21,22]

### DEPRESSION OUTCOMES

Three continuous depression measures (the CES-D, the CBCL-D, and the HAM-D) were examined for in-

**Table 2. Prevalence of Current and Past Psychiatric Disorder for Subsyndromal Youth at the Baseline Assessment***

| | No. (%) of Youth | | | |
|---|---|---|---|---|
| | Control Group (n = 49) | | Experimental Group (n = 45) | |
| Diagnosis | Past | Current | Past | Current |
| No diagnoses | 9 (18.4) | 32 (65.3) | 9 (20.0) | 34 (75.6) |
| Affective disorders | | | | |
| Major depression | 33 (67.3) | 0 | 30 (66.7) | 0 |
| Dysthymia | 0 | 0 | 3 (6.7) | 0 |
| Bipolar NOS | 0 | 0 | 1 (2.2) | 0 |
| Anxiety disorders | | | | |
| Phobias | 2 (4.1) | 7 (14.3) | 0 | 2 (4.4) |
| Anxiety without phobia, PTSD | 0 | 6 (12.2) | 1 (2.2) | 4 (8.9) |
| Separation anxiety | 3 (6.1) | 1 (2.0) | 4 (8.9) | 0 |
| Panic disorder | 2 (4.1) | 1 (2.0) | 1 (2.2) | 1 (2.2) |
| Disruptive behavior | | | | |
| ADHD | 2 (4.1) | 2 (4.1) | 2 (4.4) | 6 (13.3) |
| Conduct disorder | 1 (2.0) | 1 (2.0) | 1 (2.2) | 2 (4.4) |
| Oppositional defiant | 2 (4.1) | 2 (4.1) | 0 | 1 (2.2) |
| Substance abuse | | | | |
| Alcohol | 0 | 0 | 0 | 1 (2.2) |
| Marijuana dependence | 1 (2.0) | 0 | 0 | 0 |
| Adjustment disorders | | | | |
| Bereavement | 2 (4.1) | 2 (4.1) | 1 (2.2) | 0 |
| Adjustment disorder | 4 (8.2) | 1 (2.0) | 0 | 0 |
| Eating disorders | | | | |
| Eating disorder | 0 | 0 | 1 (2.2) | 0 |
| Eating disorder NOS | 0 | 2 (4.1) | 1 (2.2) | 0 |
| Psychotic disorder NOS | 0 | 2 (4.1) | 0 | 2 (4.4) |

*NOS indicates not otherwise specified; PTSD, posttraumatic stress disorder; and ADHD, attention-deficit/hyperactivity disorder.

tervention effects using random-effects regression analysis. Linear and quadratic trends of each dependent variable were examined across the entire study period for treatment × time (main program effect) and for number of intervention sessions × time (experimental subjects only). There were significant main program effects (group × time) favoring the experimental condition for the CES-D ($P$=.005; parameter estimate for the linear effect, –0.15; 95% confidence interval [CI], –0.27 to –0.04) and the HAM-D ($P$=.05; parameter estimate for the linear effect, –0.04; 95% CI, –0.08 to 0.00), but not the CBCL-D (**Table 3**).

Simple analyses of covariance predicting each of the outcomes at each time point, adjusted for baseline scores, indicated that CES-D main effects were principally noted across baseline to posttreatment ($P$=.008) and posttreatment to first annual follow-up diagnostic interviews ($P$=.006). The HAM-D scores were not significantly different at any of the cross-sectional times.

Another significant main program effect favoring the experimental condition ($P$=.04) was found for the total number of suicide items summed from the depression section of the K-SADS-E interview.

Survival analysis of incident major depressive episodes (**Figure 2** and **Table 4**) indicated a significant advantage ($P$=.003) for the experimental condition (9.3% cumulative major depression estimated incidence) compared with the usual-care control condition (28.8%) at the 12-month follow-up. Because the 12-month follow-up actually occurred a median of 14 months after randomization, when adjusted for a true-year period these rates were actually 8.0% and 24.7%, respectively. The hazard ratio of depression at 12-month follow-up was 5.64 (95% CI, 1.56-20.39) when adjusted for sex, age, CES-D score, and depression history (the latter 2 were the criteria for inclusion in the subsyndromal group).

This significant preventive effect persisted but at a diminished level at the 18- and 24-month follow-ups (Table 4), suggesting that the preventive effects of the experimental program had faded over time.

Because many participants were censored at the 24-month follow-up, the median survival time is difficult to interpret. To derive a more meaningful comparison, we computed the mean time to onset for the youth in both groups in whom an episode of mood disorder developed and who had available 24-month data; we compared them by condition. The 9 experimental youth in whom a mood diagnosis developed had a mean time to onset of 14.0 months (SD, 6.5 months) and a median of 16.0 months. The 12 control youth in whom a mood diagnosis developed had a mean time to onset of 6.3 months (SD, 5.8 months), with a median of 4.0 months. This represented a significant delay in onset for the experimental youth ($t_{19}$, 2.90; $P$=.009).

Intervention participants reported an average of 33 fewer depressed days in the year after intake than did control participants (11 vs 44 days). Because so many participants did not have a depression episode in the year after the baseline assessment, and therefore had 0 de-

**Table 3. Random Effects Regression Outcome Results***

| Measure, Treatment | Mean (SD) RER | | | | Treatment by Time, Significance† | |
|---|---|---|---|---|---|---|
| | Baseline | Posttreatment | 12-Month Follow-up | 24-Month Follow-up | *P* Value | F |
| CES-D | | | | | | |
| Intervention | 25.2 (8.7) | 17.8 (8.7) | 15.1 (10.0) | 19.5 (9.8) | .005 | 7.42 |
| Usual care | 23.8 (10.3) | 22.5 (11.3) | 21.5 (13.6) | 19.9 (10.4) | | |
| HAM-D | | | | | | |
| Intervention | 3.2 (3.4) | 1.8 (2.1) | 1.5 (2.7) | 2.2 (2.9) | .05 | 3.82 |
| Usual care | 3.1 (3.2) | 2.9 (4.6) | 2.6 (4.9) | 2.6 (4.8) | | |
| K-SADS-E suicide symptom total | | | | | | |
| Intervention | 0.34 (1.14) | 0.14 (0.54) | 0.08 (0.35) | 0.20 (0.68) | .04 | 4.34 |
| Usual care | 0.17 (0.72) | 0.20 (0.72) | 0.44 (1.05) | 0.13 (0.47) | | |
| No. other current diagnoses | | | | | | |
| Intervention | 0.4 (0.8) | 0.2 (0.4) | 0.1 (0.4) | 0.4 (0.8) | .21 | 1.59 |
| Usual care | 0.5 (0.8) | 0.3 (0.9) | 0.4 (0.8) | 0.3 (0.6) | | |
| CBCL-depression | | | | | | |
| Intervention | 8.8 (5.3) | 7.8 (5.5) | 7.2 (5.7) | 8.0 (6.5) | .62 | 0.24 |
| Usual care | 6.8 (4.1) | 6.4 (3.5) | 5.4 (3.9) | 3.9 (2.9) | | |
| CBCL-internalizing | | | | | | |
| Intervention | 17.8 (10.7) | 14.7 (10.3) | 14.2 (11.4) | 14.9 (12.4) | .93 | 0.01 |
| Usual care | 14.8 (8.5) | 12.9 (7.0) | 10.5 (7.3) | 8.7 (5.4) | | |
| CBCL-externalizing | | | | | | |
| Intervention | 14.4 (11.1) | 12.7 (9.8) | 10.6 (9.6) | 12.2 (11.6) | .69 | 0.16 |
| Usual care | 12.4 (8.0) | 12.7 (9.6) | 9.6 (6.5) | 7.6 (5.6) | | |
| GAF | | | | | | |
| Intervention | 73.3 (9.4) | 77.8 (12.5) | 81.6 (8.7) | 78.8 (11.0) | .04 | 4.20 |
| Usual care | 75.0 (8.7) | 78.2 (9.6) | 79.3 (12.8) | 79.9 (9.9) | | |

*RER indicates random effects regression. Abbreviations are described in the second footnote to Table 1. n = 94.
†Indicates program effect. F indicates type III F statistic for fixed effect of treatment by time.

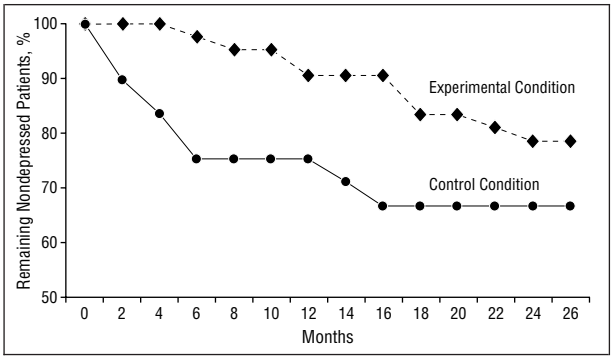


**Figure 2.** Cumulative proportion of youth remaining nondepressed for experimental and control groups during the 2-year follow-up. Treatment conditions are described in the "Procedures" subsection of the "Subjects and Methods" section.

pressed days, between-group differences were tested using Poisson regression. The Wald $\chi^2$ for the difference was 760.62 ($P<.001$).

## NONAFFECTIVE OUTCOMES

There were no significant effects for any of the nonaffective continuous mental health outcome measures, such as the CBCL internalizing and externalizing scales, and the sum of other, nonaffective diagnoses at each assessment point (Table 3).

There were no significant differences in time to the development of a new episode of a nonaffective disorder (Table 4). Although the cumulative estimated incidence of new, nonaffective episodes was higher in the control group than the intervention group at 12 (15.9% vs 4.9%, respectively) and 24 months after treatment (24.3% vs 19.5%, respectively), this difference was never statistically significant.

## FUNCTIONING OUTCOMES

Results of random-effects regression analyses indicated significant program effects for the GAF ($P=.04$), although the GAF scores were not significantly different across conditions at any of the specific follow-up assessment points.

## DOSE-OUTCOME EFFECTS

We examined the relationship between dose (defined here as number of intervention sessions) and each major outcome variable, restricting the sample to just the experimental youth. We were unable to detect significant dose effects for any measures.

# COMMENT

We obtained significant preventive effects in this at-risk group of offspring, across continuous and diagnostic depression outcome variables, suicide symptoms, and functioning. The adjusted risk for development of depres-

**Table 4. Survival Analyses for Affective and Nonaffective Episodes During Follow-up***

| Follow-up Point, mo† | Life-Table Analyses | | Cox Regression Analyses | | Hazards Ratio (95% Confidence Interval) |
|---|---|---|---|---|---|
| | Wilcoxon‡§ | *P* Value | Likelihood Ratio, $\chi^2$‡ | *P* Value | |
| Affective episodes | | | | | |
| 12 | 8.74 | .003 | 9.30 | .002 | 5.64 (1.56-20.39) |
| 18 | 5.17 | .02 | 4.78 | .03 | 2.67 (1.06-6.72) |
| 24 | 3.87 | .05 | 3.32 | .07 | 2.16 (0.92-5.04) |
| Nonaffective episodes | | | | | |
| 12 | 1.64 | .20 | 1.58 | .21 | 2.34 (0.59-9.33) |
| 18 | 0.93 | .33 | 0.78 | .38 | 1.56 (0.58-4.19) |
| 24 | 0.62 | .43 | 0.47 | .49 | 1.39 (0.59-3.63) |

*n = 94. All *P* values are 2-tailed.
†All follow-up points are from the posttreatment assessment, which was an average of 2 months after the baseline interview.
‡*df* = 1.
§n = 92.

sion in the control group was more than 5 times that of the prevention group. Preventive effects were clinically significant[43]; that is, large enough to be considered meaningful in the real world. The 8.0% total annual rate of depression in the experimental group approximated the 6.5% naturalistic total annual incidence rate of depression[44] in a comparably aged community sample,[2] suggesting that depression risk in the prevention group had been reduced to close to the "community-normal" range.

These positive results replicate and extend the findings of an earlier study by our group,[9] in which prospective depressive episodes were prevented in a community sample of at-risk youth with elevated but subdiagnostic depression symptoms. This earlier sample of youth was not identified through having a depressed parent, and the intervention was provided in the schools rather than in an HMO. However, the prevention program was essentially the same in both trials.

Despite these generally positive findings, there were several limitations of this study. By the 2-year follow-up, the conditions were beginning to converge on many measures, suggesting that preventive effects faded over time. Clearly, the effects were more proximal than distal. What can be done to sustain the protective effects of the intervention? Despite previous negative findings regarding continuation treatment,[6] periodic boosters following acute intervention may be warranted to sustain preventive effects.

Another limitation of this program was the multistage case-finding mechanism used to identify potentially depressed parents; this method would be difficult to duplicate in many settings. However, alternatives such as provider and family referrals could be substituted.

Another limitation was that only a small number of subjects were enrolled out of a large initial pool of potential subjects. The enrolled subjects were older and more often female, raising generalization issues. The relatively low randomization rates also raise concern about patient interest in preventive services. However, low participation in a research study (with its associated assessment burden) is not necessarily equivalent to lack of interest in prevention.

Another issue relates to the very heart of outreach and prevention. This study systematically recruited families that were not actively seeking care for the target youth from the HMO. This is a different way of doing business for a large health care system, although well-known exceptions include outreach for vaccinations, well-infant visits, and mammograms. However, outreach and prevention of this type may be particularly fruitful for health care systems with a known, enrolled membership. If proactive mental health care can yield more functional and less distressed members, and if these services cost the same or less than the traditional approach, then health care systems are ahead financially and in terms of member satisfaction.

However, there is also a cautionary side to outreach. Well-meaning but poorly implemented outreach programs risk being perceived by families as overly intrusive or risk inviting families to participate in unwanted services. Mindful of this, we were cautious in our contacts with parents and did not presume that they or their offspring were depressed. Our telephone scripts acknowledged in advance that many people receive so-called antidepressant medication for many other legitimate uses (eg, insomnia, smoking cessation, neuralgia).

Has this preventive intervention been sufficiently tested to warrant adoption in nonresearch settings? We believe that some additional questions remain to be answered. Another important hurdle would be replication of our findings by an independent group, preferably with a more diverse sample than ours.[45]

Ideally, we would like to know something about the dissemination of this intervention in completely naturalistic settings. How important is fidelity to the intervention? Must the program be delivered essentially as written to achieve similar results?[39] These and related questions could be answered in early naturalistic dissemination efforts, rather than necessitating another randomized trial.

## CONCLUSIONS

Depression risk can be substantially lessened with a brief group program, which in this study's high-risk sample reduced depression symptoms and episode rates to the community-normal range. Future analyses will exam-

ine the impact of this program on use of health care resources and costs.

*Accepted for publication May 2, 2001.*

*This study was supported in part by grant 1R01-MH51318-01A1 from the National Institute of Mental Health, Rockville, Md (Dr Clarke).*

*The authors thank Kimberly Hoagwood, PhD, Lauren Haworth, Steve Berg-Smith, Laura Fenn, Jen Coury, Peter Lewinsohn, PhD, and Lynn DeBar, PhD, for their assistance on this project.*

*Corresponding author and reprints: Gregory N. Clarke, PhD, Kaiser Permanente Center for Health Research, 3800 N Interstate Ave, Portland OR 97227-1098 (e-mail: greg.clarke@kp.org).*

## REFERENCES

1. Birmaher B, Ryan ND, Williamson DE, Brent DA, Kaufman J, Dahl RE, Perel J, Nelson B. Childhood and adolescent depression, I: a review of the past 10 years. *J Am Acad Child Adolesc Psychiatry.* 1996;35:1427-1439.
2. Lewinsohn PM, Hops H, Roberts RE, Seeley JR, Andrews JA. Adolescent psychopathology, I: prevalence and incidence of depression and other *DSM-III-R* disorders in high school students [published correction appears in *J Abnorm Psychol.* 1993;102:517]. *J Abnorm Psychol.* 1993;102:133-144.
3. Pine DS, Cohen P, Gurley D, Brook J, Ma Y. The risk for early-adulthood anxiety and depressive disorders in adolescents with anxiety and depressive disorders. *Arch Gen Psychiatry.* 1998;55:56-64.
4. Emslie GJ, Rush AJ, Weinberg WA, Gullion CM, Rintelmann J, Hughes CW. Recurrence of major depressive disorder in hospitalized children and adolescents. *J Am Acad Child Adolesc Psychiatry.* 1997;36:785-792.
5. Brent DA, Holder D, Kolko D, Birmaher B, Baugher M, Roth C, Iyengar S, Johnson BA. A clinical psychotherapy trial for adolescent depression comparing cognitive, family, and supportive therapy. *Arch Gen Psychiatry.* 1997;54:877-885.
6. Clarke GN, Rohde P, Lewinsohn PM, Hops H, Seeley JR. Cognitive-behavioral treatment of adolescent depression: efficacy of acute group treatment and booster sessions. *J Am Acad Child Adolesc Psychiatry.* 1999;38:272-279.
7. Mufson L, Weissman MM, Moreau D, Garfinkel R. Efficacy of interpersonal psychotherapy for depressed adolescents. *Arch Gen Psychiatry.* 1999;56:573-579.
8. Beardslee WR, Salt P, Porterfield K, Rothberg PC, van de Velde, Swatling S, Hoke L, Moilanen DL, Wheelock I. Comparison of preventive interventions for families with parental affective disorder. *J Am Acad Child Adolesc Psychiatry.* 1993; 32:254-263.
9. Clarke GN, Hawkins W, Murphy M, Sheeber LB. Targeted prevention of unipolar depressive disorder in an at-risk sample of high school adolescents: a randomized trial of group cognitive intervention. *J Am Acad Child Adolesc Psychiatry.* 1995;34:312-321.
10. Jaycox LH, Reivich KJ, Gillham J, Seligman ME. Prevention of depressive symptoms in school children. *Behav Res Ther.* 1994;32:801-816.
11. Downey G, Coyne JC. Children of depressed parents: an integrative review. *Psychol Bull.* 1990;108:50-76.
12. Beardslee WR, Versage EM, Gladstone TR. Children of affectively ill parents: a review of the past 10 years. *J Am Acad Child Adolesc Psychiatry.* 1998;37:1134-1141.
13. Roberts RE. Epidemiological issues in measuring preventive effects. In: Munoz RF, ed. *Depression Prevention: Research Directions.* New York, NY: Hemisphere; 1987:45-68.
14. Horwath E, Johnson J, Klerman GL, Weissman MM. Depressive symptoms as relative and attributable risk factors for first-onset major depression. *Arch Gen Psychiatry.* 1992;49:817-823.
15. Weissman MM, Fendrich M, Warner V, Wickramaratne P. Incidence of psychiatric disorder in offspring at high and low risk for depression. *J Am Acad Child Adolesc Psychiatry.* 1992;31:640-648.
16. Freeborn DK, Pope CR. *Promise and Performance in Managed Care: The Prepaid Group Practice Model.* Baltimore, Md: Johns Hopkins University Press; 1994.
17. Zimmerman M, Coryell W, Pfohl B, Stangl D. The reliability of the family history method for psychiatric diagnoses. *Arch Gen Psychiatry.* 1988;45:320-322.
18. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition.* Washington, DC: American Psychiatric Association; 1987.
19. Radloff LS. A CES-D scale: a self-report depression scale for research in the general population. *Appl Psychol Meas.* 1977;1:385-401.
20. Beardslee WR, Podorefsky D. Resilient adolescents whose parents have serious affective and other psychiatric disorders: importance of self-understanding and relationships. *Am J Psychiatry.* 1988;145:63-69.
21. Achenbach TM, Edelbrock CS. The classification of child psychopathology: a review and analysis of empirical efforts. *Psychol Bull.* 1978;85:1275-1301.
22. Achenbach TM. Psychopathology of childhood: research problems and issues. *J Consult Clin Psychol.* 1978;46:759-776.
23. Achenbach TM, Edelbrock C. *Manual for the Child Behavior Checklist.* Burlington: University of Vermont, Dept of Psychology; 1983.
24. Clarke GN, Lewinsohn PM, Hops H, Seeley J. A self- and parent-report measure of adolescent depression: the Child Behavior Checklist Depression scale (CBCL-D). *Behav Assess.* 1992;14:443-463.
25. Orvaschel H, Puig-Antich J. *Schedule for Affective Disorder and Schizophrenia for School-Age Children: Epidemiologic Version: Kiddie SADSE (K-SADS-E) (4th Version).* Pittsburgh, Pa: Western Psychiatric Institute and Clinic; 1986.
26. Cantwell DP, Lewinsohn PM, Rohde P, Seeley JR. Correspondence between adolescent report and parent report of psychiatric diagnostic data. *J Am Acad Child Adolesc Psychiatry.* 1997;36:610-619.
27. Cohen JA. A coefficient of agreement for nominal scales. *Educ Psychol Measures.* 1980;20:37-46.
28. Dohrenwend BP, Shrout PE. Toward the development of a two-stage procedure for case identification and classification in psychiatric epidemiology. In: Simmons R, ed. *Research in Community and Mental Health.* Vol 2. Greenwich, Conn: JAI Press; 1981:295-323.
29. Roberts RE, Vernon SW. The Center for Epidemiologic Studies Depression Scale: its use in a community sample. *Am J Psychiatry.* 1983;140:41-46.
30. Roberts RE, Lewinsohn PM, Seeley JR. Screening for adolescent depression: a comparison of depression scales. *J Am Acad Child Adolesc Psychiatry.* 1991; 30:58-66.
31. Roberts RE, Andrews JA, Lewinsohn PM, Hops H. Assessment of depression in adolescents using the Center for Epidemiological Studies–Depression Scale. *Psychol Assess.* 1990;2:122-128.
32. Endicott J, Cohen J, Nee J, Fleiss J, Sarantakos S. Hamilton Depression Rating Scale: extracted from regular and change versions of the Schedule for Affective Disorders and Schizophrenia. *Arch Gen Psychiatry.* 1981;38:98-103.
33. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry.* 1960; 12:56-62.
34. Clarke GN, Lewinsohn PM. *Instructor's Manual for the Adolescent Coping with Stress Course.* Portland, Ore: Kaiser Permanente Center for Health Research; 1995. Available at: http://www.kpchr.org/acwd/acwd.html. Accessed July 30, 2001.
35. Clarke GN, Lewinsohn PM, Hops H. *Instructor's Manual for the Adolescent Coping With Depression Course.* Portland, Ore: Kaiser Permanente Center for Health Research; 1990. Available at: http://www.kpchr.org/acwd/acwd.html. Accessed July 30, 2001.
36. Lewinsohn PM, Clarke GN, Hops H, Andrews JA. Cognitive-behavioral group treatment of depression in adolescents. *Behav Ther.* 1990;21:385-401.
37. Beck AT, Rush AJ, Shaw BF, Emory G. *Cognitive Therapy of Depression.* New York, NY: Guilford Publications; 1979.
38. Ellis A, Harper RA. *A Guide to Rational Living.* Hollywood, Calif: Wilshire Book; 1961.
39. Clarke GN. Intervention fidelity in adolescent depression prevention and treatment. *J Prev Interv Community.* 1998;17:19-33.
40. Gibbons RD, Hedeker D, Elkin I, Waternaux C, Kraemer HC, Greenhouse JB, Shea MT, Imber SD, Sotsky SM, Watkins JT. Some conceptual and statistical issues in analysis of longitudinal psychiatric data: application to the NIMH Treatment of Depression Collaborative Research Program dataset. *Arch Gen Psychiatry.* 1993; 50:739-750.
41. Nich C, Carroll K. Now you see it, now you don't: a comparison of traditional versus random-effects regression models in the analysis of longitudinal follow-up data from a clinical trial. *J Consult Clin Psychol.* 1997;65:252-261.
42. Singer JD, Willett JB. Modeling the days of our lives: using survival analysis when designing and analyzing longitudinal studies of duration and the timing of events. *Psychol Bull.* 1991;110:268-290.
43. Kendall PC. Clinical significance. *J Consult Clin Psychol.* 1999;67:283-284.
44. Eaton WW, Kramer M, Anthony JC, Dryman A, Shapiro S, Locke BZ. The incidence of specific DIS/*DSM-III* mental disorders: data from the NIMH Epidemiologic Catchment Area Program. *Acta Psychiatr Scand.* 1989;79:163-178.
45. Kaslow NJ, Thompson MP. Applying the criteria for empirically supported treatments to studies of psychosocial interventions for child and adolescent depression. *J Clin Child Psychol.* 1998;27:146-155.