Prevention of Depression in At-Risk Adolescents: Predictors and Moderators of Acute Effects

V. Robin Weersing, PhD, Wael Shamseddeen, MD, Judy Garber, PhD, Steven D. Hollon, PhD, Gregory N. Clarke, PhD, William R. Beardslee, MD, Tracy R. Gladstone, PhD, Frances L. Lynch, PhD, Giovanna Porta, MS, Satish Iyengar, PhD, David A. Brent, MD

Objective: To assess predictors and moderators of a cognitive-behavioral prevention (CBP) program for adolescent offspring of parents with depression.

Method: This 4-site randomized trial evaluated CBP compared to usual community care (UC) in 310 adolescents with familial (parental depression) and individual (youth history of depression or current subsyndromal symptoms) risk for depression. As previously reported by Garber and colleagues, a significant prevention effect favored CBP through 9 months; however, outcomes of CBP and UC did not significantly differ when parents were depressed at baseline. The current study expanded on these analyses and examined a range of demographic, clinical, and contextual characteristics of families as predictors and moderators and used recursive partitioning to construct a classification tree to organize clinical response subgroups.

Results: Depression onset was predicted by lower functioning (hazard ratio [HR] = 0.95, 95% CI = 0.92–0.98) and higher hopelessness (HR = 1.06, 95% CI = 1.01–1.11) in adolescents. The superior effect of CBP was diminished when parents were currently depressed at baseline (HR = 6.38, 95% CI = 2.38–17.1) or had a history of hypomania (HR = 67.5, 95% CI = 10.9–417.1), or when adolescents reported higher depressive symptoms (HR = 1.04, 95% CI = 1.00–1.08), higher anxiety (HR = 1.05, 95% CI = 1.01–1.08), higher hopelessness (HR = 1.10, 95% CI = 1.01–1.20), or lower functioning (HR = 0.94, 95% CI = 0.89–1.00) at baseline. Onset rates varied significantly by clinical response cluster (0%–57%).

Conclusion: Depression in adolescents can be prevented, but programs may produce superior effects when timed at moments of relative wellness in high-risk families. Future programs may be enhanced by targeting modifiable negative clinical indicators of response.

Clinical trial registration information: Prevention of Depression in At-Risk Adolescents; http://clinicaltrials.gov/; NCT00073671

Key words: depression, prevention, adolescents, cognitive-behavioral therapy

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Depression is a highly prevalent, disabling, and recurrent disorder. Nearly a quarter of the population will experience clinically impairing depression,[1] with half of onsets occurring in adolescence,[2] conferring a high risk of chronic recurrence throughout the lifespan.[3] Worldwide, depression has the third highest burden of disease of any ailment, and within higher-income countries, depression is the leading cause of disability.[4,5] Efficacious interventions for depression have been developed, but meta-analytic evidence on treatment effects in youth and adults suggest that effect sizes are not large and that recent, more methodologically rigorous trials may produce smaller effects than historical estimates.[6,7] Furthermore, both early-onset and chronic course of depression have been associated with poorer treatment response.[8] These sobering statistics have led to calls to designate the prevention of depression in adolescence a pressing public health priority and to encourage the dissemination of programs capable of serving a broad swath of those at risk.[9]

Evidence of the effectiveness of depression prevention has been mixed, with meta-analyses suggesting modest effects for universal prevention efforts but more promising outcomes for programs targeting high-risk youth.[10] In this context, we launched the Prevention of Depression (POD)[11] study, a multi-site randomized trial targeting adolescents at both familial and individual risk for depression. The POD trial built on the foundational cognitive-behavioral prevention program (CBP) of Clarke *et al.*,[12,13] who demonstrated significant prevention of depressive episodes with CBP compared to usual community care (UC) for adolescent offspring of parents with depression. The POD study extended this work 3 ways: (a) into a multisite context to test the generalizability of effects; (b) through refining the Clarke *et al.* CBP protocol to a smaller core of weekly sessions and a period of monthly booster sessions; and (c) by enriching the risk profile of the sample by requiring both familial history and individual risk (current high symptoms or history of a depressive disorder). Acute outcomes of POD were quite positive. CBP significantly separated from UC control in preventing onsets of depression, replicating the Clarke *et al.* findings across the larger, multisite sample,[13] and the size of this effect was clinically comparable to the acute efficacy of antidepressant medication.

The depression prevention literature has continued to grow, with additional evidence accumulating for specific CB interventions such as the Penn Resiliency Program,[14] and

recent findings suggesting that there may be value in approaches drawing from Interpersonal Psychotherapy for Depression.[15,16] Across this literature, the POD results represent the strongest depression prevention effects to date, but these encouraging findings are qualified by 2 factors. First, overall onset rates were high, even within CBP (21% onset rate). Second, the positive effects of CBP were significantly moderated by whether parents were in a depressive episode at the time that the adolescents commenced participation in the intervention. When parents were not depressed at baseline, CBP was particularly efficacious, strongly separating from the UC control condition (12% versus 41% onset rate). Conversely, when parents were actively depressed at baseline, the benefit of CBP was erased, and outcome in CBP and UC did not differ significantly (31% versus 24% onset rate).

In the current report, we sought to unpack these findings and to identify demographic, clinical, and contextual predictors and moderators of acute response to CBP and to define clusters of responders and nonresponders to the intervention. Given the breadth of this inquiry, we adopted a model-building approach, with a planned series of univariate tests leading to more complex multivariate models. We hypothesized that parental depression at baseline would emerge as a significant moderator of acute effects, even within this multivariate context.

METHOD

Participants

Participant characteristics and sampling procedures have been described in detail elsewhere[13] and are summarized here. The current sample consisted of 310 adolescents (aged 13–17 years) who were children of parents with depression. In addition to parental history of depression, adolescents were at risk for depression by the presence of the following: current subsyndromal depressive symptoms (i.e., Center for Epidemiological Studies–Depression Scale [CES-D] >20; n = 62 [20%]); prior history of a *DSM-IV* depressive disorder (n = 170; 55%); or both (n = 78; 25%). Exclusion criteria were lifetime bipolar I disorder or schizophrenia in parents or youth, a current *DSM-IV* mood disorder in the adolescent, or current use of antidepressant medication for youth depression. Children of nonbiological target parents were excluded from the current analyses (n = 6). In 2-parent households in which both parents endorsed a history of depression, a primary target parent was selected for assessment based on family preference. More than 1 sibling was allowed to participate; siblings were yoke randomized to the same intervention condition. There were 32 sets of siblings, including 1 set of triplets.

The sample was recruited August 2003 through February 2006 evenly across 4 sites (Boston, MA; Nashville, TN; Pittsburgh, PA; Portland, OR). Sample retention did not differ across study arms or across sites (mean = 90.5% retained).[13] No significant differences were found on demographic, entry characteristics, or depression measures between retained participants and those who did not complete the follow-up.

Procedures

Design. Adolescents were randomized to CBP or UC using Begg and Iglewicz's[17] modification of Efron's[18] biased coin toss to balance cells on age, sex, race/ethnicity, and inclusion criteria. Randomization was successful, and intervention groups did not significantly differ on baseline parent, adolescent, or family characteristics, within or across sites. The study used an intent-to-treat design, and all participants were considered part of the study from the point of randomization.

Intervention Conditions. The Cognitive Behavioral Prevention (CBP) program was delivered to small groups of adolescents in 8 weekly and 6 monthly (booster) sessions of 90 minutes each. Groups were led by a trained clinician with a master's or doctoral degree, and clinicians demonstrated high adherence (88% of content delivered). The principal focus of the program was on teaching cognitive restructuring skills for unrealistic and overly negative

TABLE 1 Parent Characteristics as Predictors of Outcome Across Cognitive-Behavioral Prevention (CBP) and Usual Community Care (UC)

Candidate Predictor	n	HR (95% CI)	*p* Value
Parent demographic characteristics			
Sex	301	0.92 (0.46–1.82)	.80
Minority status	298	1.30 (0.70–2.50)	.44
Hispanic background	298	1.00 (0.40–2.80)	.94
Age	300	1.03 (0.99–1.07)	.15
Marital status	301	0.74 (0.48–1.15)	.18
Socioeconomic status	300	1.00 (0.98–1.02)	.67
Education beyond high school	301	0.88 (0.53–1.48)	.64
Employed	300	0.88 (0.53–1.48)	.64
Features of parental depression			
CESD at baseline	298	1.02 (0.99–1.03)	.08
Current parental depression at baseline	301	1.14 (0.74–1.77)	.55
Age of onset of first MDD	292	0.99 (0.98–1.01)	.79
Lifetime duration of MDD episodes	286	1.00 (0.99–1.00)	.42
Lifetime duration of MDD and dysthymia	295	1.00 (0.99–1.00)	.21
Lifetime number of MDD episodes	289	1.01 (0.97–1.04)	.68
Comorbidity at baseline			
Anxiety	295	0.98 (0.58–1.66)	.94
Substance abuse	295	3.29 (0.91–11.80)	.07
Substance dependence	295	2.18 (0.55–8.66)	.27
Suicidal behavior	295	0.50 (0.07–3.50)	.49
Comorbidity by history			
Hypomania	295	2.71 (0.68–10.80)	.16
Anxiety	295	1.08 (0.68–1.71)	.74
Substance abuse	295	0.96 (0.49–1.90)	.92
Substance dependence	295	0.72 (0.28–1.80)	.49
Suicidal behavior	294	0.86 (0.49–1.53)	.61
Suicide attempt	294	0.85 (0.42–1.71)	.65

Note: CESD = Center for Epidemiological Scale Depression; HR = hazard ratio; MDD = major depressive disorder.