Cognitive Behavioral Therapy in Primary Care for Youth Declining Antidepressants: A Randomized Trial

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abstract

BACKGROUND AND OBJECTIVE: Health care providers have few alternatives for youth depression other than antidepressants. We examined whether brief cognitive behavioral therapy (CBT) is a viable alternative in primary care.

METHODS: A total of 212 adolescents aged 12 to 18 with major depression who had recently declined or quickly discontinued new antidepressant treatment were randomized to self-selected treatment as usual (TAU) control condition or TAU plus brief individual CBT. Blinded evaluators followed youth for 2 years. The primary outcome was time to major depression diagnostic recovery.

RESULTS: CBT was superior to the control condition on the primary outcome of time to diagnostic recovery from major depression, with number needed to treat from 4 to 10 across follow-up. A similar CBT advantage was found for time to depression diagnosis response, with number needed to treat of 5 to 50 across time points. We observed a significant advantage for CBT on many secondary outcomes over the first year of follow-up but not the second year. Cohen's *d* effect sizes for significant continuous measures ranged from 0.28 to 0.44, in the small to medium effect range. Most TAU health care services did not differ across conditions, except for psychiatric hospitalizations, which occurred at a significantly higher rate in the control condition through the first year of follow-up.

CONCLUSIONS: Observed results were consistent with recent meta-analyses of CBT for youth depression. The initial year of CBT superiority imparted an important clinical benefit and may reduce the risk of future recurrent depression episodes.

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Dr Clarke conceptualized and designed the study, obtained funding, directed the conduct of the study, and drafted the initial manuscript; Drs DeBar and Pearson assisted with the conduct of the study, and reviewed and revised the initial manuscript; Dr Lynch assisted with conceptualizing and designing the study, obtaining funding, and reviewed and revised the initial manuscript; Dr Gullion conceptualized the initial analysis plan, and reviewed and revised the manuscript; Drs Leo and Dickerson updated and carried out the analyses, conducted data management and quality audits, and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

This trial has been registered at www.ClinicalTrials.gov (identifier NCT00523081).

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WHAT'S KNOWN ON THIS SUBJECT: Depressed youth and families are often reluctant to try antidepressants (ADs), resulting in significant undertreatment. Unfortunately, primary care providers have few alternatives to offer for youth depression other than ADs. Brief cognitive behavioral therapy is a potentially effective alternative.

WHAT THIS STUDY ADDS: This study shows that brief, primary care cognitive behavioral therapy can be effective for depressed youth who decline or discontinue ADs, with benefits that endure for 1 year or longer, and possible reductions in high-intensity services (eg, psychiatric hospitalizations).

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Adolescent depression is often initially identified in primary care, and is increasingly treated there,¹⁻⁴ typically with antidepressant (AD) medications.^{5,6} However, a 2004 warning from the Food and Drug Administration regarding AD-associated suicidality contributed to reduced prescription of ADs over many years, with no corresponding increase in psychotherapy rates.⁷⁻¹⁰ Among depressed youth in primary care, as many as 50% decline pharmacotherapy.⁵ Of those who do initiate ADs, as many as half fail to maintain adherence or duration sufficient to realize the expected benefit.⁷

This mismatch between ADs typically available in primary care, and frequent rejection and/or premature discontinuation of ADs, suggests that many depressed youth may be under/untreated. This is especially concerning given difficulties referring to specialty mental health.^{3,11,12} Consistent with youth and parent preferences for nonpharmacologic treatments such as psychotherapy,¹³⁻¹⁵ we examined whether a viable alternative could be effectively delivered in primary care: brief cognitive behavioral therapy (CBT). Although primary care CBT has been tested with depressed adolescents in several previous trials,^{13,16,17} none specifically examined the effects of CBT in patients unreceptive to pharmacotherapy.

METHODS

Participants

From September 2006 to June 2010 we enrolled 212 depressed adolescents between 12 and 18 years old. All study procedures were approved by the local institutional review board. Participants were 68.4% girls (145/212), 16.0% Hispanic

(34/212), 11.8% racial minority status (25/212), and were an average of 14.6 years old (SD 1.7). Parents had an average socioeconomic status level of 40.8 (12.2), and family income averaged \$64 073 (SD \$27 528). There were no significant differences across study conditions on these factors.

Recruitment, Enrollment

Potential participants ($n = 2387$) were identified by reviewing the health maintenance organization (HMO) electronic medical record for depression diagnoses and a recent AD prescription that was unfilled, or was initially dispensed but not refilled. We sought primary care provider permission to mail study brochures; 455 (19.1%) declined, often for incompatible clinical issues or absence of youth depression. Assenting youth and consenting parents were administered a brief telephone screen ($n = 635$), followed by a full baseline assessment for screen-positive youth ($n = 357$).

Qualifying Criteria

Youth had to have a *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision*¹⁸ diagnosis of major depression obtained via the Children's Schedule for Affective Disorders and Schizophrenia (KSADS).¹⁹ All youth had to have recently declined ADs or discontinued prematurely (<30 days' adherence). Exclusion criteria included the following: current AD use, bipolar disorder or any psychotic diagnosis, or mental retardation or autism spectrum disorder. All other comorbid psychiatric diagnoses were permitted. One youth was excluded due to imminent suicide

risk. Non-CBT psychotherapy once monthly or less was permitted. Three youth were excluded for having received ≥ 8 sessions of CBT.

Randomization

We randomized youth 1:1 to either (1) self-selected treatment as usual (TAU) control condition, or (2) TAU plus individual CBT (Table 1). Randomization was stratified on baseline depression severity (Center for Epidemiological Studies-Depression Scale [CES-D] <34 vs ≥ 34), gender, Hispanic ethnicity, and age (12-15 vs 16-18).

Assessments

All instruments were administered at baseline and at 6, 12, 26, 52, 78, and 104 weeks. Figure 1 presents follow-up rates. Assessors were blinded to randomization.

Depression Measures

Assessors administered the KSADS diagnostic interview to generate diagnoses of major depression (MD) and assess suicidal ideation.¹⁹ At each follow-up, the Longitudinal Interval Follow-Up Evaluation²⁰ was used to obtain weekly MD Diagnostic Status Ratings. The primary outcome of depression recovery was defined as ≥ 8 weeks of no or minimal symptoms (Diagnostic Status Rating $\leq 1-2$) and little or no impairment.²¹ Supervisors rerated a random 5% sample of interviews ($n = 64$); diagnostic reliability was high, with MD $\kappa = 0.81$ (92% agreement).

Assessors rated the 17-item Children's Depression Rating Scale-Revised (CDRS-R), a continuous measure of depression symptomatology.²²⁻²⁴ Youth also completed the 20-item CES-D.²⁵

TABLE 1 Outcomes by Randomization Condition and Assessment Week

Measures	CBT + TAU (n=106)		TAU Control (n=106)		<i>P</i>		Effect Size ^a	Mean Difference, Hazard Ratio, or Odds Ratio (95% CI)
	Mean or <i>n</i>	SD or %	Mean or <i>n</i>	SD or %				
Youth measures								
CDRS-R					Spline model			
Baseline	52.10	8.16	53.97	10.58	Through 52	.04 ^b	<i>d</i> = 0.278	−2.25 (−4.45~0.05)
Wk 6	38.43	11.06	41.16	12.27	52 to 104	.36 ^b	<i>d</i> = 0.145	−1.30 (−3.73~1.14)
Wk 12	33.56	10.35	40.67	13.21	—	—	—	—
Wk 26	30.76	10.40	33.78	11.53	—	—	—	—
Wk 52	30.14	11.26	28.24	10.54	—	—	—	—
Wk 78	28.96	10.21	32.34	13.45	—	—	—	—
Wk 104	28.11	9.88	29.17	10.79	—	—	—	—
CDRS-R ≥50% improvement from baseline					Spline model			
Wk 6	35	34.65%	30	30.61%	Through 52	.09 ^b	NNT = 10	1.25 (0.79~1.96)
Wk 12	48	53.33%	35	37.63%	52 to 104	.23 ^b	NNT = 19	1.10 (0.65~1.86)
Wk 26	58	64.44%	50	54.35%	—	—	—	—
Wk 52	59	68.60%	67	77.01%	—	—	—	—
Wk 78	58	71.60%	51	66.23%	—	—	—	—
Wk 104	72	78.26%	64	72.73%	—	—	—	—
CDRS-R <28					Spline model			
Baseline	0	0.0%	0	0.0%	Through 52	.03 ^b	NNT = 16	1.39 (0.88~2.21)
Wk 6	22	21.8%	13	13.3%	52 to 104	.40 ^b	NNT = 20	1.00 (0.62~1.63)
Wk 12	28	31.1%	13	14.0%	—	—	—	—
Wk 26	36	40.0%	31	33.7%	—	—	—	—
Wk 52	43	50.0%	51	58.6%	—	—	—	—
Wk 78	42	51.9%	36	46.8%	—	—	—	—
Wk 104	52	56.5%	48	54.6%	—	—	—	—
MD diagnostic recovery					Survival model			
Baseline	0	0%	0	0%	Through 52	.005	NNT = 10	1.60 (1.15~2.21)
Wk 6	NA	NA	NA	NA	Through 104	.003	NNT = 10	1.59 (1.17~2.17)
Wk 12	31	31.3%	12	12.1%	—	—	—	—
Wk 26	69	69.7%	43	43.4%	—	—	—	—
Wk 52	79	79.8%	68	68.7%	—	—	—	—
Wk 78	86	86.9%	75	75.8%	—	—	—	—
Wk 104	88	88.9%	78	78.8%	—	—	—	—
MD diagnostic response					Survival model			
Baseline	0	0.0%	0	0.0%	Through 52	.03	NNT = 34	1.39 (1.03~1.87)
Wk 6	NA	NA	NA	NA	Through 104	.03	NNT = 50	1.38 (1.03~1.84)
Wk 12	68	68.7%	47	47.5%	—	—	—	—
Wk 26	84	84.9%	73	73.7%	—	—	—	—
Wk 52	90	90.9%	87	87.9%	—	—	—	—
Wk 78	93	93.9%	90	90.9%	—	—	—	—
Wk 104	93	93.9%	91	91.9%	—	—	—	—
CES-D					Spline model			
Baseline	28.34	7.58	27.96	7.74	Through 52	.005 ^c	<i>d</i> = 0.394	−2.88 (−4.87 ~ −0.89)
Wk 12	22.53	6.24	25.25	8.32	52 to 104	.62 ^b	<i>d</i> = 0.055	−0.32 (−1.91~1.27)
Wk 26	21.06	6.48	22.81	7.79	—	—	—	—
Wk 52	22.59	7.00	22.51	7.43	—	—	—	—
Wk 78	20.93	7.03	21.64	8.10	—	—	—	—
Wk 104	21.46	7.44	21.91	6.95	—	—	—	—
CGAS					Spline model			
Baseline	58.38	6.12	57.33	6.88	Through 52	.007 ^c	<i>d</i> = 0.431	4.2 (1.55~6.86)
Wk 6	64.38	8.16	62.12	7.64	52 to 104	.21 ^b	<i>d</i> = 0.016	0.13 (−2.08~2.34)
Wk 12	69.23	8.86	63.91	10.23	—	—	—	—
Wk 26	72.52	9.20	69.63	10.41	—	—	—	—
Wk 52	72.33	9.97	74.10	10.81	—	—	—	—
Wk 78	74.85	10.17	73.83	11.89	—	—	—	—
Wk 104	76.86	11.03	76.45	11.09	—	—	—	—
DAS					Spline model			
Baseline	25.14	7.41	25.08	7.05	Through 52	.003 ^c	<i>d</i> = 0.441	−4.49 (−7.27 ~ −1.72)
Wk 12	22.20	7.37	24.90	7.56	52 to 104	.93 ^b	<i>d</i> = 0.075	−0.51 (−2.33 ~1.32)
Wk 52	22.62	8.10	23.02	7.57	—	—	—	—
Wk 104	21.00	7.64	21.43	7.25	—	—	—	—

TABLE 1 Continued

Measures	CBT + TAU (n=106)		TAU Control (n=106)		<i>P</i>		Effect Size ^a	Mean Difference, Hazard Ratio, or Odds Ratio (95% CI)
	Mean or <i>n</i>	SD or %	Mean or <i>n</i>	SD or %				
Carskadon Sleep Habits Survey	Spline model							
Baseline	7.86	1.75	8.10	1.95	Through 52	.21 ^c	<i>d</i> = 0.107	0.21 (−0.33~0.75)
Wk 12	8.05	2.02	8.03	2.55	52 to 104	.98 ^b	<i>d</i> = 0.094	−0.14 (−0.55~0.27)
Wk 26	8.32	1.94	8.09	2.52	—	—	—	—
Wk 52	7.84	1.79	8.00	1.87	—	—	—	—
Wk 78	8.20	1.97	8.26	2.23	—	—	—	—
Wk 104	7.92	1.65	8.10	2.51	—	—	—	—
ISI	Spline model							
Baseline	12.80	5.59	12.77	5.60	Through 52	.13 ^c	<i>d</i> = 0.264	−1.57 (−3.19~0.05)
Wk 12	9.98	5.95	12.02	6.24	52 to 104	.31 ^b	<i>d</i> = 0.097	−0.49 (−1.85~0.87)
Wk 26	9.00	6.08	10.25	6.24	—	—	—	—
Wk 52	9.30	6.09	10.25	5.86	—	—	—	—
Wk 78	8.80	6.02	9.54	6.72	—	—	—	—
Wk 104	8.84	5.73	8.72	6.10	—	—	—	—
PEDS-QL total	Spline model							
Baseline	56.30	13.37	57.66	11.37	Through 52	.03 ^c	<i>d</i> = 0.284	3.77 (0.16~7.39)
Wk 6	66.39	15.54	64.39	13.05	52 to 104	.32 ^b	<i>d</i> = 0.020	−0.23 (−3.38~2.93)
Wk 12	66.87	13.63	62.44	13.67	—	—	—	—
Wk 26	70.19	14.64	67.55	14.47	—	—	—	—
Wk 52	68.23	14.57	66.42	12.92	—	—	—	—
Wk 78	70.23	14.10	71.50	14.25	—	—	—	—
Wk 104	70.88	13.45	71.38	13.22	—	—	—	—
PEDS-QL physical	Spline model							
Baseline	65.77	17.07	68.10	15.69	Through 52	.02 ^c	<i>d</i> = 0.265	0.81 (−2.99~4.61)
Wk 6	73.83	16.36	71.37	15.17	52 to 104	.51 ^b	<i>d</i> = 0.058	4.19 (−0.11~8.48)
Wk 12	73.70	14.65	69.03	17.18	—	—	—	—
Wk 26	75.58	15.83	73.12	16.87	—	—	—	—
Wk 52	74.75	15.88	71.86	16.07	—	—	—	—
Wk 78	75.29	16.59	75.78	17.17	—	—	—	—
Wk 104	76.63	15.60	75.62	17.00	—	—	—	—
PEDS-QL psychosocial	Spline model							
Baseline	51.25	14.16	52.09	12.24	Through 52	.08 ^c	<i>d</i> = 0.250	3.53 (−0.31~7.37)
Wk 6	62.36	17.14	60.66	14.38	52 to 104	.32 ^b	<i>d</i> = 0.063	−0.76 (−4.06~2.54)
Wk 12	63.22	15.30	58.94	14.19	—	—	—	—
Wk 26	67.32	15.66	64.60	15.30	—	—	—	—
Wk 52	64.74	15.44	63.51	13.46	—	—	—	—
Wk 78	67.52	15.26	69.16	14.84	—	—	—	—
Wk 104	67.81	14.10	69.12	13.73	—	—	—	—
CRAFFT ≥2	Spline model							
Baseline	26	25.24	24	22.64	Through 52	.25 ^c	NNT = 19	1.02 (0.50~2.10)
Wk 12	14	16.87	16	17.39	52 to 104	.56 ^b	NNT = 16	1.21 (0.56~2.61)
Wk 26	11	13.41	17	18.89	—	—	—	—
Wk 52	16	18.39	17	19.54	—	—	—	—
Wk 78	21	24.71	15	18.29	—	—	—	—
Wk 104	21	22.83	18	19.57	—	—	—	—
PES: Total number of activities	Spline model							
Baseline	16.47	3.58	16.81	3.51	Through 52	.40 ^b	<i>d</i> = 0.101	0.28 (−0.47~1.04)
Wk 12	17.52	3.34	16.79	3.14	52 to 104	.44 ^b	<i>d</i> = 0.098	0.30 (−0.52~1.11)
Wk 52	17.87	3.42	17.64	3.48	—	—	—	—
Wk 104	18.05	3.53	18.12	3.44	—	—	—	—
PES: Average pleasure for activities	Spline model							
Baseline	1.43	.29	1.43	.31	Through 52	.73 ^b	<i>d</i> = 0.171	0.05 (−0.02~0.11)
Wk 12	1.56	.31	1.47	.31	52 to 104	.070 ^b	<i>d</i> = 0.010	<0.01 (−0.07~0.07)
Wk 52	1.56	.32	1.52	.32	—	—	—	—
Wk 104	1.59	.28	1.63	.26	—	—	—	—
Client satisfaction	Spline model							
Baseline	24.52	5.84	25.50	4.12	Through 52	.22 ^c	<i>d</i> = 0.102	0.89 (−1.50~3.29)
Wk 12	26.10	6.15	25.56	3.82	52 to 104	.99 ^b	<i>d</i> = 0.136	−0.93 (−2.78~0.93)
Wk 26	28.13	3.27	25.37	4.81	—	—	—	—
Wk 52	25.65	5.645	25.68	4.69	—	—	—	—

TABLE 1 Continued

Measures	CBT + TAU (n=106)		TAU Control (n=106)		<i>P</i>		Effect Size ^a	Mean Difference, Hazard Ratio, or Odds Ratio (95% CI)
	Mean or <i>n</i>	SD or %	Mean or <i>n</i>	SD or %				
Wk 78	25.67	6.12	27.90	3.65	—	—	—	—
Wk 104	26.57	5.48	27.58	4.77	—	—	—	—
TCC					Spline model			
Wk 12	8.76	3.12	7.40	3.18	Through 52	.01 ^b	<i>d</i> = 0.299	0.78 (0.07~1.49)
Wk 26	8.57	3.05	8.04	3.08	52 to 104	.65 ^b	<i>d</i> = 0.101	−0.25 (−0.94~0.43)
Wk 52	8.93	2.77	9.21	2.57	—	—	—	—
Wk 78	8.95	4.31	9.04	3.08	—	—	—	—
Wk 104	8.87	3.02	9.36	3.15	—	—	—	—
KSAD suicidal behavior					Spline model			
Baseline	24	22.5%	28	26.4%	Through 52	.27 ^b	NNT = 37	1.03 (0.47~2.27)
Wk 12	2	2.3%	10	1.9%	52 to 104	.51 ^b	NNT = 11	1.21 (0.32~3.78)
Wk 26	1	1.2%	2	2.3%	—	—	—	—
Wk 52	5	5.8%	2	2.4%	—	—	—	—
Wk 78	2	2.5%	3	3.8%	—	—	—	—
Wk 104	1	1.1%	1	1.1%	—	—	—	—
Parent Report about Child					Spline model			
CBCL depression score					Through 52	.35 ^c	<i>d</i> = 0.073	−0.38 (−1.82~1.05)
Baseline	10.63	4.40	10.43	5.32	52 to 104	.80 ^b	<i>d</i> = 0.061	−0.27 (−1.48~0.94)
Wk 12	7.97	4.38	7.57	4.64	—	—	—	—
Wk 26	7.29	4.32	7.85	4.84	—	—	—	—
Wk 52	6.92	4.57	6.70	4.25	—	—	—	—
Wk 78	7.14	4.75	7.62	4.74	—	—	—	—
Wk 104	7.39	5.48	7.30	5.19	—	—	—	—
CBCL internalizing					Spline model			
Baseline	19.65	8.46	19.94	9.56	Through 52	.67 ^c	<i>d</i> = 0.056	−0.54 (−3.14~2.07)
Wk 12	15.25	8.61	14.57	8.15	52 to 104	.90 ^b	<i>d</i> = 0.062	−0.51 (−2.73~1.71)
Wk 26	13.75	7.13	14.69	8.80	—	—	—	—
Wk 52	13.33	8.28	13.39	8.14	—	—	—	—
Wk 78	13.58	8.32	13.91	8.34	—	—	—	—
Wk 104	13.14	10.29	13.23	9.09	—	—	—	—
CBCL externalizing					Spline model			
Baseline	13.87	8.93	15.67	1.53	Through 52	.96 ^c	<i>d</i> = 0.180	−1.70 (−4.29~0.88)
Wk 12	11.22	7.33	13.23	8.87	52 to 104	.49 ^b	<i>d</i> = 0.094	−0.80 (−3.14~1.53)
Wk 26	11.60	7.00	12.30	9.01	—	—	—	—
Wk 52	10.19	7.41	11.66	9.65	—	—	—	—
Wk 78	10.46	7.87	10.57	7.76	—	—	—	—
Wk 104	10.10	8.58	9.77	8.17	—	—	—	—
PEDS-QL total					Spline model			
Baseline	70.64	11.16	70.65	12.46	Through 52	.73 ^c	<i>d</i> = 0.040	0.55 (−3.21~4.31)
Wk 6	72.49	12.17	72.56	14.66	52 to 104	.15 ^b	<i>d</i> = 0.086	1.05 (−2.27~4.36)
Wk 12	73.33	12.57	73.72	15.26	—	—	—	—
Wk 26	74.24	12.20	73.77	15.32	—	—	—	—
Wk 52	75.40	14.57	76.94	12.43	—	—	—	—
Wk 78	77.30	11.75	76.29	14.39	—	—	—	—
Wk 104	77.03	13.22	75.52	16.17	—	—	—	—
PEDS-QL physical					Spline model			
Baseline	80.74	13.62	81.22	12.41	Through 52	.25 ^c	<i>d</i> = 0.117	1.91 (−2.51~6.32)
Wk 6	79.75	14.79	80.10	15.94	52 to 104	.15 ^b	<i>d</i> = 0.137	1.96 (−1.93~5.85)
Wk 12	78.02	16.13	78.40	18.24	—	—	—	—
Wk 26	80.97	14.10	77.75	17.82	—	—	—	—
Wk 52	80.64	15.77	81.68	15.26	—	—	—	—
Wk 78	83.57	13.01	80.06	19.48	—	—	—	—
Wk 104	82.61	15.92	80.15	19.31	—	—	—	—
PEDS-QL psychosocial					Spline model			
Baseline	65.25	13.06	64.91	15.02	Through 52	.89 ^c	<i>d</i> = 0.013	−0.19 (−4.28~3.91)
Wk 6	68.59	13.69	68.53	15.59	52 to 104	.24 ^b	<i>d</i> = 0.044	0.58 (−2.99~4.15)
Wk 12	70.73	13.00	71.17	15.58	—	—	—	—
Wk 26	70.67	13.66	71.64	16.27	—	—	—	—
Wk 52	72.60	15.80	74.45	14.11	—	—	—	—
Wk 78	73.95	14.12	74.27	14.11	—	—	—	—
Wk 104	74.04	14.43	72.92	17.67	—	—	—	—

TABLE 1 Continued

Measures	CBT + TAU (n=106)		TAU Control (n=106)		<i>P</i>	Effect Size ^a	Mean Difference, Hazard Ratio, or Odds Ratio (95% CI)	
	Mean or <i>n</i>	SD or %	Mean or <i>n</i>	SD or %				
CES-D	Spline model							
Baseline	18.80	6.65	20.55	7.82	Through 52	.97 ^c	<i>d</i> = 0.291	−0.89 (−2.38~0.60)
Wk 12	18.26	6.93	19.05	6.95	52 to 104	.74 ^b	<i>d</i> = 0.384	−0.70 (−2.28~0.88)
Wk 26	17.71	6.56	19.45	6.89	—	—	—	—
Wk 52	17.60	5.62	19.12	7.12	—	—	—	—
Wk 78	17.07	5.78	19.96	7.88	—	—	—	—
Wk 104	16.76	6.82	17.86	6.38	—	—	—	—
TCC	Spline model							
Wk 12	7.66	2.82	6.76	3.02	Through 52	.07 ^b	<i>d</i> = 0.150	0.41 (−0.34~1.16)
Wk 26	7.83	3.02	7.36	3.14	52 to 104	.55 ^b	<i>d</i> = 0.025	−0.07 (−0.79~0.66)
Wk 52	8.70	2.77	8.87	2.84	—	—	—	—
Wk 78	8.26	2.96	8.75	2.93	—	—	—	—
Wk 104	9.18	2.79	8.81	3.18	—	—	—	—

NA, not applicable.

^a Cohen *d* for continuous measures, NNT for dichotomous measures.^b Linear time trend.^c Quadratic time trend.

Other Psychological Outcomes

Youth completed the 7-item self-report Insomnia Severity Index (ISI)²⁶ and 12 items from the Carskadon sleep survey captured insomnia severity and other sleep parameters.²⁷ Youth also completed the 6-item CRAFFT screener for substance use.²⁸ Parents completed the Child Behavior Checklist (CBCL),²⁹ rating youth internalizing and externalizing symptoms, and social competence.

Assessors administered an abbreviated, 10-item Dysfunctional Attitudes Scale (DAS) to assess unrealistic and irrational cognitions.³⁰

Youth completed an abbreviated 12-item Pleasant Events Schedule (PES)³¹ as a measure of behavioral activation.

Assessors administered the Target Complaint Checklist (TCC).³² Each youth and parent identified up to 3 target complaints at baseline (eg, “Having no friends”) and then at each follow-up rated the severity and degree of improvement for all targets.

Quality of Life, Functioning

Both youth and parents completed the Pediatric Quality of Life Inventory (PEDS-QL),³³ with additional items to address school and family functioning. Assessors rated youth overall functioning on the Children’s Global Adjustment Scale (CGAS).³⁴

Health Care Services

Assessors obtained youth and parent report of youth health care utilization with the Child and Adolescent Services Assessment (CASA).³⁵ Youth completed the 8-item, self-report Client Satisfaction Questionnaire³⁶ to evaluate satisfaction with TAU depression treatments.

Intervention Conditions

TAU

Youth in both conditions were permitted to continue and/or initiate any nonresearch mental health or general medical treatment (see Table 2). TAU did not mean that all youth received the same type of treatment. Instead, it was self-selected and varied among the options listed in

Table 2. Data regarding HMO services were captured via the electronic medical record. All non-HMO services were assessed with the CASA interview.

CBT-Depression

The acute-phase CBT program consisted of 2, 4-session modules: cognitive therapy (CT) to address unrealistic thinking, and increasing pleasant activities (behavioral activation, or BA). The program had been previously evaluated in individual^{16,37} and group formats.^{38–40} Youth and therapist jointly selected 1 module to begin (Fig 2). Youth could stop after the first module if they were nearly or completely recovered. Partial and nonresponders were encouraged to continue with the second module. Up to 6 elective continuation contacts were permitted. Therapists had at least a master’s degree, and several years’ experience delivering CBT in previous studies.^{16,24,37,41} Biweekly supervision addressed CBT implementation.

CBT Delivery

Figure 1 presents mean and median CBT sessions. Acute sessions were

TABLE 2 TAU Health Care Services by Study Arm

	Cumulative Follow-up Through Year 1, Weeks 1–52			Cumulative Follow-up Through Year 2, Weeks 1–104		
	CBT + TAU, <i>n</i> (%)	TAU, <i>n</i> (%)	<i>P</i>	CBT + TAU, <i>n</i> (%)	TAU, <i>n</i> (%)	<i>P</i>
Outpatient mental health	54 (50.9)	51 (48.1)	.68	72 (67.9)	62 (58.5)	.15
Antidepressants	10 (9.4)	8 (7.6)	.62	25 (23.6)	19 (17.9)	.31
Any other mental health medication	15 (14.2)	12 (11.3)	.54	34 (32.1)	25 (23.6)	.17
Inpatient mental health or alcohol/drug	1 (0.9)	9 (8.5)	.01	5 (4.7)	12 (11.3)	.08
School counseling	19 (17.9)	27 (25.5)	.18	31 (29.3)	38 (35.9)	.31
Juvenile court/probation	0 (0)	3 (2.8)	.08	3 (2.8)	4 (3.8)	.70

nearly all in person. Four youth (4% of 106) did not attend any CBT sessions; 84 (79%) received the minimum threshold dose of ≥ 4

sessions, yielding an overall mean of 6.6 sessions (SD 2.5). Of those attending any sessions, 67 (66% of 102) received 1+ sessions of

CT, 63 (62%) received 1+ sessions of BA, and 46 (45%) received 1+ sessions each of both CT and BA. Eighty youth (76%) received ≥ 1 continuation contact, for an average of 3.4 continuation contacts (SD 1.7).

A random selection of 64 audio-recorded sessions (10%) yielded mean adherence of 85% on the Cognitive Therapy Rating Scale,⁴² and a mean of 96% of session content delivered per the CBT manual.

Analysis Plan

The primary outcome analysis used the intent-to-treat sample. The primary outcome was time to recovery from major depression (assessed via Longitudinal Interval Follow-Up Evaluation/KSADS diagnosis). Secondary outcomes included major depression response; CDRS-R continuous total score; $\geq 50\%$ CDRS-R improvement; depression “caseness” (CDRS-R $<$, ≥ 28); psychosocial function on the CGAS; KSADS suicidal ideation; and change on all other symptom or functioning measures.

To address incomplete follow-up data, we used restricted maximum likelihood methods to estimate the treatment effect using mixed models (SAS PROC MIXED or PROC GLIMMIX; SAS Institute, Inc, Cary, NC). For continuous measures, the effect size was the standardized adjusted mean difference between treatments (Cohen *d*). For binary measures, we used Cox

FIGURE 1 CONSORT diagram.

FIGURE 2
Schematic of brief CBT intervention.

proportional-hazards regression and report effect size in terms of number needed to treat (NNT).⁴³ In analyses of both continuous and binary outcomes, we a priori adjusted for baseline depression severity (CDRS-R <, ≥40).

We based power analyses on a 20% difference in major depression recovery, based on an earlier study of depressed adolescents treated in primary care.¹³ With 2-tailed $\alpha =$

0.05, 80% power would be achieved with 92 participants per condition. To account for attrition, we set the enrollment target to 216; actual enrollment was 212.

RESULTS

Retention, Attrition

Figure 1 lists assessment completion at all assessment points, ranging from 79% to 96%, with 210 (99%) youth having at least 1 postbaseline

assessment. Follow-up rates were not significantly different between study arms.

Primary Depression Outcome

Depression Recovery

Figure 3 presents major depression diagnostic recovery by condition. Significantly better rates of recovery were observed for the CBT condition from baseline to each of study follow-up points, with maximal separation between the curves at 15 to 20 weeks after enrollment. At immediate posttreatment (week 12) the NNT was 6; for time points from weeks 52 through 104 the NNT was 10. TAU youth had an average of 30.0 weeks to recovery (95% confidence interval [CI] 25.3–34.7; median 23 weeks), compared with an average of 22.6 weeks for CBT youth (95% CI 18.7–26.5, median 15 weeks).

Secondary Outcomes

Depression Response

We employed Figure 3 survival analyses to examine treatment response, defined as ≥8 weeks below the threshold of 5 or more MD symptoms necessary for full diagnosis, but where full recovery has not yet occurred. CBT condition response was significantly better through each study follow-up point compared with TAU. NNT ranged from 5 at posttreatment to 50 at the final follow-up point (week 102). TAU participants had an average of 18.0 weeks until response (95% CI 14.7–21.3, median 12 weeks), versus an average of 13.3 weeks for CBT youth (95% CI 10.6–15.9, median 9 weeks).

CDRS-R

CDRS-R scores were significantly lower for the CBT arm from baseline to week 52 ($P = .04$, Cohen $d = 0.28$) but in year 2 there was no between-condition difference. A similar pattern was observed for CDRS-R

FIGURE 3
Survival analysis of time until recovery from MD and/or dysthymia (at least 8 weeks of well time).

“depression caseness” ($<, \geq 28$),⁴⁴ with a significant advantage for the CBT condition through week 52 ($P = .03$, NNT = 16), but no difference in weeks 52 to 104. A final CDRS variable, $\geq 50\%$ improvement from baseline score, was not significantly different across conditions through any time period.

CES-D

The CES-D total score was significantly improved for the CBT condition compared with the control condition, from baseline to week 52 ($P = .005$, $d = 0.39$). However, no significant differences were found between conditions from week 52 through week 104.

Substance Use

A CRAFFT^{28,45} cutoff score of ≥ 2 did not differentiate between conditions through either of the 2 time periods.

Insomnia, Sleep Problems

Neither the Carskadon sleep scale nor the ISI significantly differed between conditions in either of the 2 time periods.

Functioning

The CGAS was significantly improved in the CBT arm compared with the TAU control through week 52 ($P = .007$, $d = 0.43$), but no differences were found in the second year.

Quality of Life

CBT youth had improved PEDS-QL quality of life ($P = .03$, $d = 0.28$) and physical subscale scores ($P = .22$, $d = 0.27$) through week 52 compared with control youth, but not in the second year. No effects were found for the psychosocial subscale.

Dysfunctional Thoughts

Through week 52, youth in the CBT condition demonstrated a greater reduction in dysfunctional thoughts on the DAS compared with the TAU control youth ($P = .003$, $d = 0.44$), but this was not observed in the second year.

Suicidal Behavior

There was no statistical difference between CBT and TAU conditions.

Activity Level, Enjoyment

Neither PES subscale was significantly different between conditions across time.

Satisfaction With Treatment

There were no differences across conditions regarding satisfaction with depression treatment in either the first or second year of the study.

TCC

CBT youth reported significantly greater improvement in their self-identified TCC complaints than TAU youth through week 52 ($P = .01$, $d = 0.251$), but there was no difference through the second year.

Parent-Reported Outcomes

None of the parent-report scales (CES-D; PEDS-QL total, physical, or psychosocial subscales; TCC; CBCL depression, Internalizing or Externalizing subscales) were significantly different across conditions over time.

TAU Health Care

Table 2 summarizes self-selected TAU health care services reported by youth and/or parents on the CASA. There were no differences across conditions for outpatient mental health visits, school counseling, juvenile justice contact, use of antidepressants, or any type of mental health medication. Youth in the TAU condition did report significantly higher rates of psychiatric hospitalization through week 52 compared with CBT youth (8.5% vs 0.9%, $P = .01$, odds ratio [95% CI] = 9.7 [1.2–78.3]).

DISCUSSION

This study represents the most recent large trial of CBT for

youth depression. Previous large investigations include the single-site Adolescent Depression Antidepressants and Psychotherapy Trial (ADAPT) ($n = 208$),⁴⁶ and the multisite Treatment of Adolescents with Depression Study (TADS) ($n = 439$) and Treatment Of Resistant Depression In Adolescents trial (TORDIA) ($n = 334$).^{23,24} Across these large trials and many smaller studies, CBT for youth depression has performed inconsistently. In TADS and TORDIA, combined CBT and ADs was superior to monotherapy ADs, suggesting an important adjunctive benefit; however, the ADAPT trial⁴⁶ failed to find a similar benefit for combined treatment. Further, meta-analyses of monotherapy CBT for youth depression have found it to be only moderately effective.^{47–49} For instance, the TADS study monotherapy CBT was significantly less effective than monotherapy AD, and was not superior to a medication placebo control.²³ In contrast, our earlier trial¹⁶ found a general pattern of modest superiority of brief CBT plus TAU ADs over a control condition of TAU ADs without CBT.

In the current trial, brief CBT plus TAU was superior to the TAU control condition on the primary outcome of recovery from major depression (Fig 3), with a posttreatment NNT of 4. Although there are no standards for a clinically meaningful NNT, a review of ADs for adolescent depression found an overall posttreatment NNT of 10.⁵⁰ We found a similar result for depression diagnosis response, with a significant CBT advantage at all follow-up time points and an NNT of 5 at posttreatment.

Beyond the immediate posttreatment period, CBT's advantage on the primary outcome (MD recovery) and for some secondary outcomes

persisted for the 2-year follow-up period. This enduring effect sets this study apart from most previous youth depression CBT trials. However, CBT's advantage over TAU appears to have occurred mostly in year 1, with some advantages diminishing modestly in year 2. The pattern suggests that adding a maintenance/continuation component might sustain benefit over longer periods.

CBT was not beneficial for nonaffective outcomes such as substance use and sleep problems. This is not surprising, as CBT for depression shares only limited elements with CBT variants addressing other health targets. Broadening the impact of this intervention might require adding other CBT elements, such as exposure and response prevention to address anxiety, or stimulus control and sleep restriction for sleep problems.

The magnitude of effects found in this trial (d 's from 0.08–0.34; NNTs from 5–50) were small to moderate, and are consistent with recent meta-analyses of CBT for depression in youth.^{47–49} However, effects sizes are highly dependent on the potency of the control condition, which in this trial was active TAU, albeit self-selected and highly variable (Table 2). Although this sample declined or discontinued ADs before enrollment, many youth in both conditions initiated ADs or other treatments during follow-up, presumably for unresolved depression but potentially to treat other conditions, such as anxiety. Most categories of post-baseline TAU mental health services were not significantly different across conditions, except for inpatient psychiatric hospitalizations, which occurred at a significantly higher rate in the TAU control arm through week 52. The high cost of these services suggests a possible

advantage for CBT, which we plan to examine in future economic analyses. Detecting CBT effects against this background TAU is challenging. Presumably, in some proportion of youth in both conditions, TAU services imparted a depression benefit that was not “available” for CBT to improve on. The greater the response to TAU (estimated in the control condition), the less variability remains to be impacted by incremental CBT. In this context, the observed small-moderate benefits are a reasonable estimate of real-world benefits when CBT is delivered with good fidelity against a backdrop of usual care.

Is there a genuine clinical benefit to the significant CBT advantage in the first year? First, it is important to recall that not all outcomes showed a loss of significant advantage for CBT in the second year. MD diagnosis recovery and response still favored CBT through the final 24-month follow-up, although the advantage was reduced by this point. Nonetheless, even if there were no advantages in the second year we still believe that the initial year of CBT advantage is an important clinical and developmental benefit. For example, longer-duration depressive episodes increase risk for future depression recurrence.⁵¹ Thus, any intervention that curtails episode duration not only improves short-term outcomes but may also reduce the risk of future recurrent episodes. Furthermore, depressed adolescents often experience social and academic “decoupling” from peer groups during depressive episodes, leading to lower rates of important milestone attainment, such as high school graduation, disadvantages that may persist even after episodes have ended.^{52,53} Thus, any reduction in the duration of depressive episodes may potentially reduce future

recurrence and improve the probability and speed of social and academic reintegration and developmental milestone attainment.

CONCLUSIONS

The conclusions of this study are limited by the low numbers of racial and ethnic minority youth, which hampers our ability to generalize these results to more diverse populations. Nonetheless, this sample was more clinically representative than in many previous CBT trials. All youth had been diagnosed as clinically depressed by their TAU provider before recruitment. Furthermore, CBT was delivered in the context of TAU (Table 2), and all effects were obtained beyond the benefits imparted by TAU.

An important question is whether this sample was comparable to samples in other depression-treatment trials. Consistent with other large recent CBT trials, all youth were required to meet *Diagnostic and Statistical Manual of Mental Disorders* criteria for major depression at baseline. However, depression severity was somewhat lower in this sample (baseline CDRS-R mean = 53.2, SD 9.3) than in other trials such as TADS (mean = 60.0, SD 10.4)⁵⁴ or TORDIA (mean = 59.0, SD 10.0).⁵⁵ That our sample was slightly less

depressed is not surprising, given that these youth were initially identified as depressed in primary care. The enduring CBT benefits observed in this study for major depression recovery may have been partially due to this lower baseline depression level.

One implication for clinical practice is that brief CBT can be delivered in primary care to depressed youth who have initially declined ADs. Also, our results indicate that brief CBT can impart small-to-moderate clinical benefit above and beyond TAU health services, and that this benefit persists for at least 1 year after baseline. These conclusions are contrary to the negative findings regarding CBT from the TADS and ADAPT trials.^{23,46} Along with other positive trials such as TORDIA,²⁴ this study suggests that CBT can be a viable if modest treatment of adolescent depression.

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ABBREVIATIONS

AD:	antidepressant
ADAPT:	Adolescent Depression Antidepressants and Psychotherapy Trial
BA:	behavioral activation
CASA:	Child and Adolescent Services Assessment
CBCL:	Child Behavior Checklist
CBT:	cognitive behavioral therapy
CDRS-R:	Children's Depression Rating Scale-Revised
CES-D:	Center for Epidemiological Studies-Depression Scale
CGAS:	Children's Global Adjustment Scale
CI:	confidence interval
CT:	cognitive therapy
DAS:	Dysfunctional Attitudes Scale
HMO:	health maintenance organization
ISI:	Insomnia Severity Index
KSADS:	Children's Schedule for Affective Disorders and Schizophrenia
MD:	major depression
NNT:	number needed to treat
PEDS-QL:	Pediatric Quality of Life Inventory
PES:	Pleasant Events Schedule
TADS:	Treatment of Adolescents with Depression Study
TAU:	treatment as usual
TCC:	Target Complaint Checklist
TORDIA:	Treatment Of Resistant Depression In Adolescents trial

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