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Evidence-Base Update of Psychosocial Treatments for Child and Adolescent Depression

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Abstract

Depression in youth is prevalent and disabling and tends to presage a chronic and recurrent course of illness and impairment in adulthood. Clinical trial research in youth depression has a 30 year history, and evidence-based treatment reviews appeared in 1998 and 2008. The current review of 42 randomized controlled trials (RCTs) updates these reviews to include RCTs published between 2008 and 2014 ($N = 14$) and re-evaluates previously reviewed literature. Given the growing maturity of the field, this review utilized a stringent set of methodological criteria for trial inclusion, most notable for excluding trials based in sub-clinical samples of youth that had been included in previous reviews ($N = 12$) and including well-designed RCTs with null and negative findings ($N = 8$). Findings from the current review suggest that evidence for child treatments is notably weaker than for adolescent interventions, with no child treatments achieving *well-established* status and the evidentiary basis of treatments downgraded from previous reports. Cognitive behavioral therapy (CBT) for clinically depressed children appears to be *possibly efficacious*, with mixed findings across trials. For depressed adolescents, both CBT and Interpersonal Psychotherapy (IPT) are *well-established* interventions, with evidence of efficacy in multiple trials by independent investigative teams. This positive conclusion is tempered by the small size of the IPT literature ($N = 6$) and concern that CBT effects may be attenuated in clinically complicated samples and when compared against active control conditions. In conclusion, data on predictors, moderators, and mediators are examined and priorities for future research discussed.

Worldwide, depression is one of the most prevalent mental health conditions and is the third leading cause of disability, surpassed only by diarrhoeal diseases and respiratory infections, in global burden of disease (Smith, 2014). Depression is associated with impaired family, peer, and romantic relationships, lower educational attainment and socioeconomic status, and increased risk of early mortality from suicide (Hammen, Brennan, & Keenan-Miller, 2008; Weissman et al., 1999). Despite these lifespan sequelae, depression can rightly be considered a disorder of youth. Most adults with depressive illness recall their first episode as occurring in the teenage years, and prospective studies of youth suggest that first onset may be typical in early adolescence (Lewinsohn, Clarke, Seeley, & Rohde, 1994;

Merikangas et al., 2003). Prior to adolescence, rates of depressive disorders are substantially lower (Bufferd, Dougherty, Carlson, Rose, & Klein, 2012; Harrington, 2002); with the onset of puberty, prevalence of disorder doubles, and a significant gender imbalance emerges that persists until late adulthood (Merikangas, Nakamura, & Kessler, 2009). Furthermore, adolescent onset confers an especially high risk for chronic recurrence and poor functioning throughout the lifespan (Avenevoli, Knight, Kessler, & Merikangas, 2008; Zisook et al., 2007). Taken together, these characteristics of depressive illness make clear the need for early, effective intervention to treat depression in youth.

Treatment research in youth depression dates back to the late 1980s (e.g., Reynolds & Coats, 1986), as adult measures of depression symptoms were developmentally adapted to accurately assess and verify the existence of clinically-impairing disorders in children and adolescents (e.g., Kovacs, 1981). Early randomized trials in youth depression treatment relied heavily upon these self-reports of symptoms (a) to define samples of high-symptom youth in need of intervention and (b) as the primary method of outcome assessment. Diagnostic assessment, use of multiple reporters, blinded independent ratings, and measures of clinically significant change and remission entered the youth treatment literature over time, with “conventional” clinical trial designs not appearing until late 1990s (e.g., Brent et al., 1997). The treatments tested in these studies also represent developmental adaptations of adult depression treatment models, drawing primarily from cognitive and behavioral therapy techniques (CBT; Beck, 1967, 1976; Beck, Rush, Shaw, & Emery, 1979; Lewinsohn, 1974; Lewinsohn, Hoberman, Teri, & Hautzinger, 1985) and, more recently, the strategies of Interpersonal Psychotherapy (IPT; Weissman, Markowitz, & Klerman, 2000, 2007) for depression.

The first evidence-based treatment (EBT) review in the area of youth depression was published by Kaslow and Thompson as part of the original 1998 special series in the *Journal of Clinical Child Psychology.* At that time, 14 studies were identified that focused on the treatment of symptoms of depression in children and adolescents and met basic methodological criteria. Of these, the vast majority focused on behavioral or cognitive-behavioral interventions. One non-randomized, open trial probed the promise of *Interpersonal Psychotherapy for Adolescents* (IPT-A; Mufson et al., 1994) with depression, and one randomized trial of CBT for adolescent depression included family therapy and supportive therapy as control arms (Brent et al., 1997). Across this literature, the authors concluded that interventions for depressed youths generally outperformed control conditions (typically waitlists) and that effects did not seem to vary by group versus individual modality or by the involvement of parents in treatment. In evaluating the evidence for treatments, the authors focused in on specific manualized protocols (e.g., *Adolescent Coping with Depression* [CWD-A]; Lewinsohn, Clarke, Hops, & Andrews, 1990), rather than assessing the value of broader theoretical orientations (e.g., CBT). With this perspective, they determined that no treatments met criteria for *well-established* interventions and two treatment programs were *probably efficacious* (*Self Control Therapy*, Stark, Reynolds, & Kaslow, 1987; *Adolescent Coping with Depression*, Lewinsohn et al., 1990).

The youth depression literature was reviewed again in 2008 by David-Ferdon and Kaslow, and, in the intervening decade, 28 additional trials had been published (10 in child samples

and 18 with depressed adolescents). As in the 1998 review, the vast majority of studies tested the effects of CBT, although randomized trials of IPT also entered the literature. Methodological differences became increasingly apparent between RCTs in child versus adolescent samples. Studies of adolescents were far more likely to include diagnostic evaluations (12 studies) and recruit from help-seeking, clinical populations, rather than screening children in school for high symptoms. Adolescent studies were also more likely to be of higher overall quality, with 10 of 18 being coded as "Type 1" -- the highest level of methodological sophistication according to their review criteria (see Nathan & Gorman, 2002). In contrast, none of the child studies passed this threshold due to a range of design flaws (e.g., small sample size, problems with randomization, unclear inclusion/exclusion criteria, lack of standardized assessment). The authors organized their EBT evaluation at the level of the specific program, and then moved outward from this level of analysis to evaluate the evidence in support of broader modalities and theoretical orientations. When adopting this broader perspective, they concluded that CBT as an overall theoretical approach was *well-established*, with child group and child + parent group being *well-established* modalities within CBT. Looking across trials, sufficient evidence also existed to classify child behavior therapy as *probably efficacious* as a stand-alone (not CBT package) intervention (Kahn, Kehle, Jenson, & Clark, 1990; King & Kirschenbaum, 1990; Stark et al., 1987). Other orientations and modalities had been tested in youth at the time of the 2008 review, but data were not available to identify any other treatments as more than experimental in nature, even when evidence was summed across trials. David-Ferdon and Kaslow (2008) further concluded that the adolescent literature also supported the designation of CBT as a *well-established* theoretical approach, with 14 valid studies indicating support for CBT across variations in demographic (e.g., Rosselló & Bernal, 1999) and clinical (e.g., with substantial comorbidity; Rohde, Clarke, Mace, Jorgensen, & Seeley, 2004) characteristics, across stringent comparisons (e.g., compared to alternate treatment; Brent et al., 1997), and by multiple independent investigative teams. IPT, too, reached the level of *well-established*, with a strong, though smaller, evidence base of four randomized trials by two independent investigative teams testing three specific IPT programs (IPT-A, Mufson, Weissman, Moreau, & Garfinkel, 1999; Mufson, et al., 2004; IPT-AST, Young, Mufson, & Davies, 2006a; culturally-adapted IPT, Rosselló & Bernal, 1999).

The growing evidence-base for psychosocial interventions for youth depression, as documented in these EBT reviews, has unfolded against a backdrop of more troubling trends in the depression treatment literature. Several meta-analyses on depression treatment effects have been published in this same time frame, and these analyses have documented a substantial decline in effect sizes over time. Initially, effect sizes for the treatment of adolescent depression were amongst the largest in the literature (Reinecke, Ryan, & DuBois, 1998; Lewinsohn & Clarke, 1999), but more recent analyses of youth depression (Weisz, McCarty, & Valeri, 2006) and adult depression (Johnson & Friborg, 2015) treatments have suggested effects may be quite modest and among the least impressive for evidence-based interventions for psychological disorders (Weisz et al., in press). In youths, this dramatic difference in the size of effects may be due in part to the growing maturity of the depression literature, with more recent studies including active control conditions (e.g., supportive therapy; Brent et al., 1997) and more clinically complicated samples (e.g., treatment of

depression and comorbid conduct disorder; Rohde et al., 2004) than in early reports. These hypotheses dovetail with findings from the largest adolescent depression trial to date, the Treatment of Adolescents with Depression Study (TADS, 2004). The TADS trial targeted adolescents with persistent and impairing major depression and compared CBT as a stand-alone intervention to antidepressant medication (fluoxetine), the combination of CBT and medication, and a placebo sugar pill. Contrary to investigator hypotheses, in this sample (clinically severe) and with this design (placebo control), stand-alone CBT fared very poorly, failing to separate from placebo in many analyses and posting a response rate substantially lower than previous CBT trials. Unique characteristics of the TADS treatment manual and design may have contributed to this poor showing for CBT (see Weersing, Rozenman, & Gonzalez, 2009), and combination treatment performed very well, providing some conceptual support for the value of psychosocial intervention. However, the TADS results provided a shock to the field. Interestingly, the literature on antidepressant medications in youth has followed a similar trajectory of promise and concern, with recent re-analyses undercutting the clinical value and safety profile of agents (Le Noury et al., 2015), meta-analyses highlighting the poorer response to medication in more clinically severe samples, and indications that the size of treatment effects may be significantly impacted by methodological factors (e.g., number of study sites, response rates in control conditions; Bridge et al., 2007). Taken together, these findings suggest growing uncertainty on whether intervention effects for depression are truly reliable and if our treatments are effective in samples of clinically-impaired, depressed youth.

In this context, in the current review, we sought to provide a comprehensive EBT update for psychosocial treatments for child and adolescent depression, paying close attention to the clinical severity of samples, the strength of control conditions, and patterns of null and negative findings in addition to positive effects. Our specific aims were threefold; first, we aimed to provide a detailed review of published trials since the last EBT report in 2008, in order to deliver a snapshot of current findings in youth depression research. Second, we re-evaluated the entire youth depression treatment literature, including studies from previous reviews, to weigh the cumulative evidence for different approaches and revise the status of treatments using updated methodological criteria and standards for evidence. As with both previous reviews, we considered treatment for depressed children and adolescents separately, and we included studies of youths with clinically elevated symptoms of depression, even if these studies were classified as prevention (versus treatment) by the original authors. In our analysis, we assessed the cumulative evidence for broader treatment approaches, rather than evaluating the effects of each specific *brand-name* program manual within every orientation. This perspective viewed specific manualized programs as operationalizations of broader theoretical systems (for rationale, see Southam-Gerow & Prinstein, 2014). Third, we commented on notable findings in the youth depression field in terms of predictors, moderators, and mediators of effects. This final commentary was designed to be a spur for further research and treatment development.

METHOD

Inclusion criteria and search process

Our review was guided by the methods described by Southam-Gerow and Prinstein (2014) for the current special series of *Evidence-Based Updates*. Table 1 summarizes these criteria and notes three ways in which the current review criteria deviate. Namely, (a) we did not screen out low sample studies but instead highlighted in text times when small samples may have influenced results, and we utilized small sample correction for effect sizes calculated for the review of new studies (M.5); (b) we required all studies to be randomized, thus eliminating options 3.3, 4.1, and 4.2; and (c) more broadly, we considered the balance of evidence between positive and negative studies when mixed findings were present in the literature (e.g., positive results in one good experiment would not necessarily outweigh a pattern of mixed findings). Treatment quality was critically evaluated to assign one of the following designations: a *well-established* treatment, or Level 1 treatment, is one that has been shown to be superior to a placebo or another active treatment condition by at least two independent research teams. A Level 2 treatment, or *probably efficacious* treatment, is one that has been shown to be superior to a waitlist control group or active condition in at least two trials, but may lack independent replication by different research teams. A *possibly efficacious* treatment, or Level 3 treatment, is one that has been shown to be superior to a control group in at least one RCT. Given our requirement that all included studies have a randomized design, a Level 4 treatment, or *experimental* treatment, would be unlikely to occur as a function of positive effects hampered solely by a weaker design. Rather *experimental* interventions in our pool would be those with a equivocal record of support across RCTs (some positive but also a large number of negative or null findings). Last, *treatments of questionable efficacy*, or Level 5, are those that have not been shown to have any beneficial effect, when tested in a reasonable RCT design. Note that our classification of treatments is focused on immediate post-intervention outcomes. The durability of effects over follow-up is commented on separately at the end of the *Status of Treatments* section.

Included in the scope of this review are randomized controlled trials (RCT) of psychosocial treatments for depression in children and adolescents. Trials testing medication alone were excluded from this review; however, studies testing combination psychosocial-pharmacotherapy treatments were included. A literature search was conducted to identify (a) new treatment trials published since the 2008 EBT review (January 2007 – December 2014) and (b) secondary analyses from included trial reports (e.g., re-analyses to test mediation or moderation). Search terms were taken from the 2008 EBT review to maintain a consistent literature pool. The search terms were separated into (a) subject and (b) treatment categories that were then searched in combination in the PsycINFO and PubMed databases: (a) *adolescent depression, teen depression, bereaved youth, suicidal youth;* (b) *depression intervention, depression treatment* (David-Ferdon & Kaslow, 2008). In addition, authors who previously had published randomized or open trials for youth depression were searched by name in the PubMed database (Asarnow, Bernal, Brent, Chu, Clarke, Curry, Ehrenreich-May, Fristad, Lejuez, March, McCauley, Mufson, Richardson, Rohde, Rosselló, Shirk, Stark, Stice, Weisz, Young) to identify new RCTs and follow-up reports to their prior work.

The initial search process produced 4332 abstracts (3941 from search terms, 391 from author searches). These abstracts were screened by two authors (KTGS and CB) to delete duplicates and to confirm appropriate age range (mean age less than 18; M.3) and explicit use of a randomized design with at least two groups (M.1). Studies were then triaged with the full authorship team to confirm adequate measurement of depression for enrollment (M. 3) and as an outcome (M.4). For inclusion in this review, all youths in each study sample were required to evidence "clinically significant depression" defined as either (a) meeting diagnostic criteria for a unipolar mood disorder (Major Depressive Disorder [MDD] and/or Dysthymia) with a standardized diagnostic assessment procedure (e.g., the Kiddie-Schedule for Affective Disorders and Schizophrenia [K-SADS], Kaufman et al., 1997), (b) being identified by a mental health provider as suffering from significant and impairing depressive symptoms (as in Rosselló, Bernal, & Rivera-Medina, 2008), and/or (c) demonstrating clinically elevated levels of depression symptoms according to a standardized youth depression symptom measure. Studies varied considerably on this last criterion, with investigators using a variety of symptom tools and a variety of cut-points to select high-symptom samples. Given that the purpose of the current review was to evaluate the *treatment* effects of depression interventions (versus preventive effects), we defined a minimum clinically significant cut-point for all such measures used in our pool of studies. Our cutoff definitions were based on psychometric reports and published manuals for the Beck Depression Inventory (BDI ≥ 20; Beck, Steer, & Brown, 1996), Children's Depression Rating Scale (CDRS-R ≥ 40; Poznanski & Mokros, 1996), Children's Depression Inventory (CDI ≥ 13; Kovacs, 1992), Center for Epidemiological Studies Depression Scale (CES-D ≥ 16; Rudolph & Lambert, 2007), Hamilton Depression Rating Scale (HAM-D ≥ 8; Cusin, Yang, Yeung, & Fava, 2009), Mood and Feelings Questionnaire (MFQ ≥ 23; Wood, Kroll, Harrington, & Moore, 1995), Patient Health Questionnaire (PHQ-9 ≥ 10; Kroenke, Spitzer, & Williams, 2001), and Reynolds Adolescent Depression Scale (RADS ≥ 77; Reynolds, 1987). For these measures, we strove to identify a comparable level of clinical severity; of course, the various assessment tools differed in their original design (e.g., screening versus diagnosis), format (e.g., youth-report versus clinician-rated), and typical populations and normative samples used for comparison (e.g., clinical populations versus primary care patients). As a result, the level of "clinically significant depression" from sample-to-sample in the included studies may differ in part due to variability in the tools used to define the sample. Throughout our report, we highlight when samples are particularly mild or severe or mild. Inclusion criterion for clinically significant depression was not met if the *mean* of a high-symptom subgroup was in the elevated range of a screening measure or the highest symptom youths in a study sample were selected (e.g., top 20%) without evidence that all such youths were above these minimum clinical cut-off scores. Studies in which a subset of the sample had elevated depressive symptoms (e.g., universal prevention trials) were included, only if the results were segregated such that efficacy of the intervention solely among youths with clinically elevated symptoms could be determined. At post-treatment or follow-up, studies were required to include measurement of depression at least at the symptom level (M.4; i.e., youths could be included on the basis of diagnostic criteria but were not required to have diagnostic outcome assessed at post-treatment or follow-up if depression symptoms were assessed by self-report). This process yielded a total of 14 novel RCTs.

In addition, we re-reviewed the literature included in the 1998 and 2008 EBT reports to apply these new criteria. As a result, a total of 18 studies that had been included in prior reviews were excluded from consideration in the current report. Table 2 identifies each of these excluded papers and the reasons for removal from the youth depression treatment evidence base. The most substantive reason for removal was our exclusion of studies targeting youths with subsyndromal levels of depression symptoms. Some of these investigations were described as treatment studies (e.g., Weisz et al., 1997), whereas others were explicitly focused on prevention and aimed to select youths with mild symptoms but who were not yet exhibiting disorder (e.g., Gillham, Hamilton, et al., 2006). This latter category also included prevention trials that enrolled youth at-risk for depression due to a variety of factors (e.g., family conflict; Jaycox et al., 1994), without evidence that all youths in the sample evidenced clinically elevated symptoms. Finally, our review process also identified eight studies published prior to 2008 that met inclusion criteria for the current report but had been excluded previously. These eight trials demonstrated null or negative findings for intervention at post-treatment; previous EBT definitions emphasized accumulation of positive findings and, thus, these studies were excluded from prior consideration. The 2008 EBT report included six of these eight investigations in the descriptive review of studies and in the outcome tables; they were merely excluded from consideration when categorizing the evidentiary status of treatments (e.g., as *well-established*; Clarke, Debar, et al., 2005; Clarke, Hornbrook, et al., 2002; De Cuyper et al., 2004; Goodyer et al., 2007; Liddle & Spence, 1990; Sanford et al., 2006). We do not re-review these six trials in detail here but do consider their results when evaluating the summary status of treatment in the current report. However, two trials (Vostanis, Feehan, Grattan, & Bickerton, 1996a; Kerfoot, Harrington, Harrington, Rogers, & Verduyn, 2004) were omitted entirely from prior descriptive review and, for completeness, are included in the current report as if they were new trials published within our window. Citations for all primary outcome studies included in the current review are indicated in the reference list with an asterisk (*).

Study classification and coding

For review purposes, studies involving children below the age of 13 were considered “child studies”, while adolescents were defined as being between the ages of 13 and 24, with a mean age of less than 18 years. Studies including both children and adolescents were categorized by the mean age of the participants, with samples with mean ages greater than or equal to 13 categorized as adolescent trials. Treatments were categorized as CBT, behavior therapy, or IPT by the authors’ labeling of the intervention and the description of intervention components. In addition, a small number of trials included family-based interventions. This treatment category was quite varied, ranging from systemic and behavioral family therapy models (e.g., as in Brent et al., 1997) to family psychoeducation (Sanford et al., 2006). Our grouping of studies within this category was modeled on Hogue and colleagues’ (2015) EBT review of substance abuse treatments and emphasized the working with multiple family members in all or nearly all sessions as well as a focus on intrafamilial relationships and processes as mechanisms of change. Interventions that included supplemental sessions with parents that focused on coordinating or supporting treatment efforts focused on the child or adolescent (rather than family processes) were not

included in this category (e.g., Clarke, Rohde, Lewinsohn, Hops, & Seeley, 1999). Treatments were further classified by modality, including individual, group, technology-assisted (both video and computer assisted), and bibliotherapy. Studies were not screened out on the basis of sample size, and the smallest sample in the included literature pool enrolled 10 participants per cell. The randomized trials published after the last review were then integrated with those cited in David-Ferdon and Kaslow's review (2008) to create a complete, updated literature of psychosocial treatments for youth depression.

To supplement our narrative review of new trials, we populated Tables 3 and 4 with summary information on study design and results, including measures of effect size. Effect sizes for the primary dimensional outcome measure of each trial were calculated using Hedges *g* (Hedges & Olkin, 1985) to correct for small sample sizes and were based on the unadjusted means and standard deviations provided by each primary outcome paper (using Biostat *Comprehensive Meta-Analysis Version 2.0*). In the table, we also report response rates for each treatment and control group; if multiple response rates were given by an investigation, we chose the most common metric across studies (i.e., clinical response versus clinical remission). The exact definition of response used for each trial can be found in the tables. To provide a metric of clinically significant change, we calculated number-needed-to-treat (NNT) from these response rates, rounding to whole patients, using 0.5 as the dividing point. The NNT is a metric common in evidence-based medicine that captures the number of treated patients needed, on average, to see a benefit of treatment relative to control (see Guyatt & Rennie [2004], p. 358–360, for discussion and definition of NNT). For comparison purposes, the NNT for antidepressants in adolescent depression has been estimated to be 10 (Bridge et al., 2007), indicating that for every ten adolescents receiving antidepressants, we would expect one case to have achieved remission as a *function* of receiving the active intervention (versus due to natural remission or other such factors). When available, NNT and Hedges *g* were derived from the intent to treat sample. If multiple papers were published on the same root study, effect sizes were only calculated from the primary depression outcome data, ensuring that the effect size reflected the published and accepted data at the post-treatment time point. Note that while Hedges *g* and the NNT are standardized metrics designed to facilitate the comparison of results across studies, the magnitude of these effect sizes should be interpreted within the context of each study design. For example, a small *g* or high NNT may still be impressive in a study with an active control group (versus effect sizes calculated against a waitlist) or when calculated on a more clinically meaningful outcome (e.g., interviewer rated measures versus self-reports for *g*; remission versus response rates for the NNT). Our evaluation of the evidentiary status of treatments, thus, is informed by these descriptive metrics but also weighs other factors, such as the strength of study design and independent replication of effects.

In the following sections, we provide a (a) detailed update of the psychosocial treatment literature published since the last EBT review, (b) evaluation of the evidentiary status of treatments, (c) commentary on the durability of effects of interventions over follow-up, and (d) review of predictor, moderator, and mediator findings drawn from the pool of included RCTs. We conclude with a discussion of the results of the review and priorities of future research in child and adolescent depression treatment.

UPDATE OF THE PSYCHOSOCIAL TREATMENT LITERATURE

Treatment research in youth depression (2008–2014)

Within the psychosocial treatment literature for youth depression, 14 new trials have been published since the last review (see Tables 3 and 4). The vast majority of trials (13 of 14) focused on adolescent samples, with one trial including both children and adolescents (Weisz et al., 2009). Several studies included populations historically underrepresented in the treatment literature, such as racial or ethnic minorities (Diamond et al., 2010; Rosselló et al., 2008; Weisz et al., 2009; Young, Mufson, & Gallop, 2010). The majority of new trials were conceived by authors as treatment trials (8) with a number of indicated prevention trials (6) occurring as well.

The majority of trials tested the effects of CBT (12); two trials tested the effects of IPT, one of which was a head-to-head comparison between CBT and IPT (Rosselló et al., 2008), two trials focused on family therapy. Modality varied by the severity of the sample. The majority of treatment (versus indicated prevention) trials were delivered in individual format (6 of 8). One additional treatment trial compared the efficacy of group and individual formats (Rosselló et al., 2008). In contrast, indicated prevention programs were usually delivered in a group format or a classroom setting (5 of 6 trials).

We next review these 14 new trials, grouped by developmental level (child, adolescent), treatment type (CBT, IPT, family-based), and treatment modality (individual, group, technology-assisted, bibliotherapy). As discussed previously, we also review two studies published prior to 2008 (Vostanis et al., 1996a; Kerfoot et al., 2006) that were omitted from detailed analysis in previous EBT reviews but met inclusion criteria for the current report (results of these trials are also included in Tables 3 and 4).

Review of Clinical Trials in Children

Individual CBT in children—Weisz and colleagues (2009) conducted an effectiveness trial of a CBT-based program in a predominantly child sample (M = 11.8 years). Primary and Secondary Control Enhancement Training (PASCET) is a structured protocol that focuses on teaching children how to improve depressed mood by changing objective conditions in their environment (primary control) and changing themselves to buffer environmental stressors (secondary control; see Table 3). The PASCET program had previously been found to be effective as a group-based CBT intervention for schoolchildren with depressive symptoms in a pilot study included in the 2008 review (Weisz, Thurber, Sweeney, Proffitt, & LeGagnoux, 1997).[1] The 2009 trial utilized a revised version of the PASCET manual, consisting of 10 core individual sessions and 5 optional additional sessions, with the flexibility of going beyond these 15 sessions as needed. Weisz et al. tested the transportability of this protocol among a sample of community therapists by randomizing them to one of two conditions: 1) brief training on PASCET in conjunction with supervision, or 2) usual care (UC). Therapists treated a sample (N = 57) of diverse youths (67% racial minority) who met criteria for a *DSM-IV* depressive diagnosis, many of

[1]Note that this initial efficacy trial was excluded from the current review of *Status of Treatments*, given the CDI cutoff for sample inclusion was 11 (below the CDI clinical cutoff of 13).

whom had multiple comorbid diagnoses. In this context, the percentage of youths who no longer met criteria for a depressive disorder post-treatment did not significantly differ between groups following intervention (see Table 3; *NNT* = −25); however, the *time* to response was significantly shorter for youths receiving PASCET (24 weeks) as compared to youths receiving UC (39 weeks).

In addition to this new trial, one study of individual CBT with children excluded from the prior review met inclusion criteria for our purposes. Vostanis et al. (1996a) examined the effect of a brief (9 session) cognitive behavioral treatment administered in a clinic setting. Sessions were designed to be administered biweekly; however, frequency of sessions was flexible, allowing a maximum of 6 months for delivery of all 9 sessions. The effect of brief CBT was compared with non-directive supportive therapy (NST) in which clinicians met with the child to review current problems and social activities, without providing interpretations or suggestions. Youths ages 8 to 17 (*M* = 12.7 years, *N* = 57) meeting criteria for a depressive disorder were recruited from outpatient clinic settings. High rates of recovery from depressive disorder were noted at post-treatment among youths randomized to receive CBT (87%) and NST (75%) with no significant difference between groups (*NNT* = 8). High rates of response across groups were maintained at 9-month and 2-year follow-up. Given the high rates of response in both groups at post-treatment and over follow-up (see Table 3), the authors also suggested that non-specific therapeutic elements may have been important for both groups. Alternately, the length of the intervention window (6 months) introduces the possibility of natural remission of depressive episodes in both groups, a possibility enhanced by the low number of sessions attended (an average of 6 sessions [range 2–9] were attended over an average of 3.5 months [range 1–5]).

Review of Clinical Trials in Adolescents

Individual CBT in adolescents—Five new clinical trials were published testing the effects of individual CBT for adolescents. Additionally, we review one trial of individual CBT omitted from past reviews that met criteria for inclusion in this report.

Szigethy and colleagues (2014) examined the efficacy of the PASCET program in adolescents with depression and inflammatory bowel disease (IBD). Participants in this study were 217 youths ranging in age from 9 to 17 years (*M* = 14.3 years) with IBD, in addition to a diagnosed depressive disorder (see Table 4). Participants were randomized to receive 12 weeks of either CBT (PASCET-PI) or NST. PASCET-PI consisted of 9 modules that targeted depressive symptoms, particularly as they occur in the context of IBD (e.g., relaxation skills also were taught to help manage pain). At post-treatment, participants in both conditions had lower depression symptom scores as compared to baseline, but did not significantly differ from each other (*NNT* = 16). Similarly, rates of treatment response and remission did not significantly differ by condition.

Brent et al. (2008) examined the efficacy of adjunctive CBT in a sample of treatment-resistant, depressed adolescents who had failed to respond to an adequate trial of a selective serotonin reuptake inhibitor (SSRI; age 12–18; *N* = 334). Adolescents were randomized to one of four conditions: switch to Venlafaxine, switch to another SSRI, switch to Venlafaxine and CBT, or switch to another SSRI and CBT. Significant differences were not detected

between switch to SSRI or Venlafaxine and, subsequently, cells were collapsed to (a) medication switch alone and (b) medication switch with CBT. Youths randomized to medication switch with CBT had significantly greater improvements and higher response (54.8%) compared to youths randomized to medication switch alone (40.5%; *NNT* = 7). Though the absolute response rate was slightly lower than typical for CBT for adolescent depression (see Table 4 for comparison), given the severity of depression in the sample, it is broadly consistent with the literature. Differences between combination therapy and medication switch alone diminished over time, with no significant difference in rate of remission at 3, 9, or 15 months post-treatment (Emslie et al., 2010; Vitiello et al., 2011).

Richardson et al. (2014) examined the effect of a collaborative care intervention for depressed adolescents (age 13–17; *M* = 15.3 years) based in primary care. Study inclusion criteria required youths to either (a) meet diagnostic criteria for MDD (60%), or (b) have elevated symptom scores at two time points. Eligible youth (*N* = 101) were randomized to either a collaborative care intervention with depression care managers or to UC. For teens in the collaborative care arm, the depression care manager conducted an initial engagement session in which the adolescent chose between brief CBT, medication, or combination treatments. Teen progress in collaborative care was monitored; youths who experienced less than a 50% reduction in symptoms at mid-treatment were given the option of changing or augmenting treatment (adding medication, increasing dose, changing medications, or receiving CBT). Overall, the majority of collaborative care youths elected to receive combination treatment (54%), with 38% of youths receiving CBT alone and a small minority of youths receiving medication alone (4%). At the 12-month assessment, collaborative care had a significantly higher response rate (67.6%) than usual care (38.6%) as defined by a 50% reduction in symptoms, with a clinically impressive effect (*NNT* = 3; see Table 4).

Shirk et al. (2014) examined the efficacy of individually-based CBT when implemented in a sample of depressed adolescents with history of interpersonal trauma. The authors recruited adolescents (age 13–17; *N* = 43) who met criteria for a depressive disorder. Nearly half the sample (46%) also met criteria for comorbid PTSD. Youth were randomized to receive either adapted CBT or usual care. Adapted CBT consisted of 12 sessions delivered weekly in an individual format. The content of treatment consisted of core CBT strategies for depression, including identifying and challenging distorted thoughts and increasing level of activity. Modifications for this sample with trauma history included use of mindfulness exercises throughout the course of treatment and addressing cognitions related to the trauma experience. Youth seen in usual care received weekly treatment from therapists who primarily described their treatment style as eclectic. At the post-treatment assessment, no significant difference in level of depressive symptoms, as measured by the BDI-II, was found between groups (*g* = -.16). Response rates were similar across treatment arms with 50% of youth in the experimental condition and 48% of youth in the control condition no longer meeting criteria for a depressive disorder (*NNT* = 50).

The final trial was a direct comparison of CBT and IPT manuals, both of which had been culturally adapted for Puerto Rican teens (Rosselló et al., 2008). Adolescents (age 12–18; *N* = 112) who met criteria for MDD (66%) or had clinically impairing depressive symptoms (34%) were randomized to one of four treatments: CBT in individual format, CBT in group

format, IPT in individual format, or IPT in group format. The investigators found no statistically significant differences across modality or theoretical orientation (see Table 4). Given the null findings in this trial, it is possible that youths in all conditions improved from baseline as a function of natural remission. However, all four arms had response rates comparable to the CBT and IPT literatures (62% and 57%, respectively; *NNT* = 20), albeit at the lower end of this range of substantial clinical response. Given these absolute response rates, it is also plausible that the interventions were efficacious but similar in impact.

In addition to these recently published trials, we included one trial excluded in the prior review. Kerfoot et al. (2004) examined the effectiveness of training community mental health workers in CBT. Therapists randomized to CBT, versus routine care, attended a 1-week training that covered general information about adolescent depression, general CBT concepts (e.g., goal setting), and specific strategies in this CBT intervention for depression in adolescents (e.g., pleasant activity scheduling, problem solving). The CBT intervention was designed to last 8 sessions over the course of 8 weeks and had been shown to be efficacious in a prior trial (included in prior reviews; Wood, Harrington, & Moore, 1996). Following the initial 2 psychoeducational sessions, the manual allowed for flexible application of CBT strategies. In addition to initial training in this treatment, therapists had access to biweekly supervision. Therapists recruited adolescents with elevated depression symptom scores (see Table 4). At post-treatment, levels of depressive symptoms did not significantly differ between youths receiving CBT compared to those in TAU nor did youth receiving CBT have higher rates of response to treatment (*NNT* = 33). Notably, several outcomes from this trial suggest that youths randomized to the CBT condition may not have received a sufficient dose of this intervention. First, fewer than half of youths in the CBT arm (45%) completed 4 of the 8 CBT sessions. Second, therapists had a low level of attendance to supervision with a mean of 3 supervision sessions attended, and nearly one third of clinicians (8 of 25) attended 1 or fewer supervision sessions. Despite the lack of a significant treatment effect, therapists in the CBT condition reported significantly higher levels of confidence and perceived knowledge in working with depressed adolescents than those in TAU.

Group CBT in adolescents—Six trials testing the effects of group-based CBT have been conducted since the previous review. Three have examined the effects of variants of the *Adolescents Coping with Depression* (CWD-A) manual, a program identified in previous reviews as *probably efficacious*. Two of these three trials were based on the prevention version of this program, the *Coping with Stress* (CWS) variant of the CWD-A manual. Dobson, Hopkins, Fata, Scherrer, and Allan (2010) examined the efficacy of CWS in preventing development of depression and anxiety disorders in adolescents. Youths (age 13–18, *N* = 46) with elevated depressive symptoms who did not meet criteria for a depressive disorder were randomized to either CWS or a group-based attention control condition. Consistent with prior trials of CWS (Clarke et al., 1995), the manual was implemented as a 15-session group-based treatment primarily focused on teaching cognitive restructuring and behavioral activation. The attention control condition matched CWS in format and number of sessions. The content of this control condition focused on general topics relevant to teens (e.g., confidence, role models) without facilitators providing “expert advice.” No significant

difference in depressive symptoms was found between the CWS and control groups at the end of acute treatment or at the 3- or 6-month follow-up assessments. To better understand this result, the authors employed a benchmarking technique in order to compare outcomes in the current study with the original, positive CWS prevention trial (Clarke et al., 1995). In the current study, baseline levels of depression symptoms appeared to be substantially higher than in the original report, but post-intervention scores for CWS and control were lower than in the original study. The authors suggested that this pattern implied that both CWS and control were effective in reducing symptoms of depression, although CWS was not statistically superior at reducing symptoms compared to the attention control condition.

In a test of a manual adapted from CWS, Stice, Rohde, Seeley, and Gau (2008) also examined the effect of CBT in a sample of adolescents (age 14–19, $N = 341$) with clinically elevated depressive symptoms who did not currently meet criteria for a major depressive disorder. Youth were randomized to either CBT or one of three control conditions: group-based non-directive supportive therapy, CBT bibliotherapy, or an assessment only control condition. The authors adapted the CWS manual, creating a group-based, 6-session protocol that continued to focus on behavioral activation and cognitive restructuring. Similarly, the non-directive supportive therapy group met for 6 weekly 1-hour sessions and consisted primarily of sharing feelings and listening. Youth randomized to the CBT bibliotherapy group were given *Feeling Good* (Burns, 1980), a self-help book designed to help address feelings of depression using CBT techniques. At the post-treatment assessment, youth randomized to CWS had significantly fewer depressive symptoms compared with all three control conditions, and the superiority of CBT to assessment only was maintained at 6-month follow-up ($NNT = 16$; see Table 4). At more extended follow-up, the superiority of CBT over control as measured by depressive symptoms was not maintained, with the only significant pairwise comparison being between CBT and assessment only at 1 year post-intervention (see Table 4). However, through the 2-year follow-up period youth randomized to CBT had significantly lower rates of onset of depressive disorder.

The final new test of the CWD-A manual examined the efficacy of the program in conjunction with family-based treatment for youth with comorbid depressive disorder and substance use disorder (SUD; Rohde, Waldron, Turner, Brody, & Jorgensen, 2014). The authors recruited adolescents (age 13–18; $N = 170$) with a current depressive disorder and substance use disorder (non-nicotine SUD). All eligible youth received CBT for depression (CWD-A) and a traditional treatment for substance use disorders, Functional Family Therapy (FFT; Alexander & Parsons, 1986). Youth were randomized to receive either FFT followed by CWD-A, CWD-A followed by FFT, or simultaneously coordinated FFT and CWD-A treatment. CWD-A was implemented as a group-based treatment for depression with some modifications to the treatment manual (e.g., shorter duration of 12 session, use of reward system for participation). FFT was implemented in individual, family-based format including 12 sessions over 10 weeks. At the post-treatment (20 week) assessment, there were no significant differences across treatment sequences, with 47% of youth experiencing a remission of depression (defined as CDRS-R ≤ 28). The post-treatment effects of this trial are difficult to interpret given the lack of an inert control arm and exposure to CBT in each treatment sequence. Notably, across all three intervention sequences youth experienced a significant decrease in depressive symptoms by the mid-point in treatment. This significant

decrease in depressive symptoms by week 10 was shown in both youth who had received CWD-A only within this timeframe, as well as youth who had received FFT only within this time frame. In contrast, an effect of sequencing was found on substance use outcomes. Youth randomized to FFT prior to CWD-A had lower levels of substance use following treatment compared with youth receiving coordinated treatment. Across conditions, youth depressive symptoms continued to improve at the 12-month assessment (60% achieved remission). Due to the exposure to CBT in each treatment arm, a post-treatment effect size and NNT could not be calculated for this study.

Since the last review, one set of investigators examined the effect of a modified version of the Penn Resiliency Program adapted for Dutch youth (Wijnhoven, Creemers, Vermulst, Scholte, & Engels, 2014). The investigators recruited adolescent girls (age 11–15; $N = 102$) with clinically significant depressive symptoms (CDI ≥ 16) from schools in the Netherlands. Eligible youth were randomized to either group-based CBT classes or an assessment only control condition. The CBT condition consisted of 8 classes lasting 50-minutes each. The focus of these classes was to learn the relationship between thoughts and feelings, identify negative thoughts, and challenge distorted cognitions. At the post-treatment assessment, youth receiving CBT had significantly lower levels of depressive symptoms as measured by the CES-D ($g = .59$). A significant effect of treatment was also found at the 6-month follow-up ($g = .71$); however, the difference between groups was not significant at the 1-month follow-up ($g = .38$).

Stallard et al. (2012) examined the effectiveness of a classroom-based depression prevention program. Though implemented as a universal prevention program, the authors presented data on youths with clinically elevated depression at baseline separately. Youths (age 12–16; $N_{total} = 5030$, $n_{high\ risk} = 1064$) were randomized to either CBT, attention control, or usual school provision. The CBT program was implemented in the classroom setting over the course of 9 classes. Content of the CBT program included learning effective coping skills, building emotion-regulation strategies, and challenging distorted thoughts. The attention control condition included the usual school curriculum (e.g., health education) with the addition of two facilitators not trained in the CBT program. No significant differences were found in self-report of depression symptoms between the CBT, attention control, and usual school provision arms 12 months following study initiation. Youth receiving CBT did not have higher rates of response to treatment at the post-treatment assessment ($NNT = -14$).

Finally, as discussed in the previous sections, Rosselló and colleagues (2008) compared the effects of group to individually-based CBT and group to individually-based IPT. As noted above, these four active treatments did not differ significantly; however, response rates for these four treatment arms were similar in magnitude to those found in trials with significant effects of treatment relative to control. Across group and individual formats, CBT had a response rate of 62%.

Technology-assisted CBT in adolescents—Since the prior review, there has been one trial of technology-assisted CBT meeting our entry criteria. Merry and colleagues (2012) examined the effect of the Smart Positive Active Realistic X-factor Thoughts Program (SPARX) in a sample of depressed adolescents. The authors recruited adolescents (age 12–

19) who were seeking treatment for depression (N = 187; a clinically identified sample). Youth in this trial were randomized to either SPARX or TAU. The SPARX Program consists of seven 30-minute modules covering psychoeducation, relaxation, problem solving, pleasant activity scheduling, cognitive restructuring, and social skills training. The effect of SPARX did not differ significantly from TAU on either self-report measures or rates of response (NNT = 21). At 3-months post-treatment, youth randomized to SPARX continued to report mildly lower depressive symptoms that did not differ significantly from TAU.

Individual IPT in adolescents—In addition to these trials of CBT, two new trials of IPT have been conducted within our review window. One of these trials included individually-based IPT in depressed adolescents; as discussed previously, Rosselló and colleagues (2008) examined the efficacy of group and individual CBT and IPT in a sample of adolescents who met criteria for MDD (66%) or had clinically impairing depressive symptoms. The conditions did not statistically differ, but response rates for IPT were comparable to trials finding a significant effect of treatment against less active controls.

Group IPT in adolescents—In addition to the trial by Rosselló and colleagues (2008), one additional trial of group-based IPT has been conducted since the 2008 review. *Interpersonal Psychotherapy-Adolescent Skills Training* (IPT-AST) was tested in adolescents with clinically elevated symptoms of depression but whom did not yet meet criteria for a depressive disorder (N = 57; Young et al., 2010). Youth were randomized to either group-based IPT-AST or school counseling. Compared to youths in counseling, teens in IPT-AST evidenced fewer self-reported symptoms of depression at post-treatment. Effect of IPT-AST on self-report of depressive symptoms diminished over time with a trend towards significance at 6-month follow-up and no significant difference detected between groups at 12- and 18-month follow-up. Youth in IPT-AST had lower rates of onset of depressive disorder at the 6-month follow-up (0% compared with 19.1%; NNT = 5); however, no between group difference was found at the 18-month follow-up (see Table 4).

Family-based treatment for adolescents—In this review period, two new trials of family-based treatment for youth depression have emerged. Diamond and colleagues (2010) probed the efficacy of *Attachment-Based Family Therapy* (ABFT), a manualized program for depression tested originally in a smaller trial included in the 2008 review. In the ABFT model, disruptions in stable family relationships (e.g., from a period of neglect and an out-of-home placement) are thought to influence adolescent depression both directly as a source of stress and indirectly through the impact of these events on adolescent's individual emotion regulation skills and reluctance to use their caregiver as a buffer and support when coping with future stressors. Thus, the goal of ABFT is to strengthen the connection between the teen and their caregiver through relationship building activities and reduce depression as a function of this improved relationship. Efficacy of ABFT was examined in a sample of adolescents (age 12–17; N = 66) with clinically elevated depressive symptoms and significant suicidality (*Suicidal Ideation Questionnaire* > 31; Reynolds, 1988). Youth were randomized to either 12 weeks of ABFT or enhanced UC, which included assistance with referrals and clinical monitoring. Adolescents randomized to ABFT had significantly lower depressive symptoms and superior treatment response (55%) compared with the UC

condition (31%; *NNT* = 4). While the difference between ABFT and control was statistically significant, these response rates for both treatment and control are on the lower end for the depression treatment literature. This is consistent with the severity of the sample in the trial (62% had history of suicide attempt), and the response rate of ABFT was on par with results of the Brent et al. (2008) study of treatment-resistant depression (54.8% adjunctive CBT; see Table 4).

As discussed above, one additional trial examined a family focused intervention in addition to group-based CBT for depression (Rohde et al., 2014). The authors in this trial recruited adolescents with comorbid depressive disorder and substance use disorder (age 13–18, *N* = 170). All youth received group-based CWD-A and Functional Family Therapy, a family systems-oriented treatment for youth with substance use disorders (see Hogue et al., 2015). Youth were randomized to receive FFT followed by CWD-A, CWD-A followed by FFT, or coordinated treatment of FFT and CWD-A. Across arms, youth experienced a significant decrease in depression within the first half of treatment, with no significant effect of the sequencing of treatments. Due to the trial design and absence of an inert control condition, it is difficult to interpret these results. Across treatment sequences, the remission rate (47% as defined by CDRS-R ≤ 28) is consistent with other trials in severe or comorbid samples that have demonstrated significant effects favoring intervention relative to control (e.g., Brent et al., 2008; Rohde et al., 2004).

STATUS OF TREATMENTS

In the following section, we evaluate the evidentiary status of psychosocial treatments for depression in youth, guided by the criteria and categories summarized in Table 1. This evaluation is based on the entire published youth depression treatment literature and represents both an update on previous reviews and a reclassification of studies included in previous reports based on current EBT criteria. As discussed previously, this latter process resulted in the exclusion of 18 studies previously included in the depression EBT literature base and the inclusion of eight studies that had previously been omitted (see Table 2) in addition to the 14 new trials published since the last EBT report. In our current evaluation, we focus on the effects of interventions at post-treatment; durability of intervention effects over follow-up is described separately at the end of this section.

Treatments are organized within developmental level (child depression, adolescent depression), and evidence evaluated at the level of treatment type (CBT, behavior therapy [BT], IPT, family-based, other) and then within treatment type by modality (individual, group, technology-assisted, bibliotherapy). Status of treatments is summarized in Tables 5 and 6.

Depression in Children

Cognitive Behavioral Therapy—According to our current review criteria, there are a total of seven randomized trials testing CBT in children with clinically significant depression. One of these studies (Weisz et al., 2009) represents new findings in the literature (published since 2008), and six studies were published in the time windows of prior EBT reviews, including three studies previously excluded from consideration (De Cuyper et al.,

2004; Liddle & Spence, 1990; Vostanis et al., 1996a). In this pool of seven studies, one contained positive findings in favor of CBT over waitlist or psychologically inert controls (Kahn et al., 1990). Four studies had generally positive but more equivocal findings of CBT over a range of comparison conditions (De Cuyper et al., 2004; Nelson, Barnard, & Cain, 2003; Stark et al., 1987; Weisz et al., 2009), and two studies had no significant findings between CBT and control arms (Liddle & Spence, 1990; Vostanis et al., 1996a). In no study was CBT statistically inferior to control. Given this pattern of effects, CBT as a broad intervention approach currently meets criteria as a *possibly efficacious* treatment modality in depressed children. This is a change from the previous classification of CBT as *well-established* due to our inclusion of null findings and exclusion of some studies in subsyndromal samples with positive effects that had been included in previous reviews (see Table 2). In our current pool of studies, CBT has demonstrated positive effects over waitlist in one experiment, but these results have not been clearly replicated by another investigative team. CBT fails to obtain *probably efficacious* or *well-established* status in our estimation, given that the model has not statistically separated from an active control condition or alternate evidence-based intervention for child depression and that the pattern of CBT effects are quite mixed both across (cf. Liddle & Spence, 1990; Weisz et al., 2009) and within investigations (i.e., effects varied substantially across measures; Stark et al., 1987).

Individual CBT for children: Three studies of individual CBT in children met criteria for our review. One had a null finding (Vostanis et al., 1996a; described earlier), and two had equivocal results. Nelson and colleagues (2003) found that youths in individual CBT delivered through two different modalities (videoconferencing versus face-to-face) improved from baseline, with youth in the videoconferencing condition showing significantly accelerated results and greater improvement compared to individual face-to-face CBT (Nelson et al., 2003). Individual face-to-face CBT may have been efficacious in this trial (the absolute response rate was high, with 82% no longer meeting diagnostic criteria), but it is difficult to verify in the absence of a worse performing control condition. In the trial by Weisz and colleagues (2009; described earlier), individual CBT did not outperform UC on depression indices at the end of treatment. However, youth in the CBT condition improved at a faster rate than youth in UC. This mixed pattern of findings suggests that individual CBT in children is best conceived as *experimental* treatment, and additional evidence is needed to demonstrate that the modality can reliably and consistently separate from control. Of note, all three studies of individual CBT for depressed children in this review had active comparison conditions -- supportive therapy (Vostanis et al., 1996), an alternate version of CBT (video CBT; Nelson et al., 2003), or community treatment (Weisz et al., 2009) -- and failure to demonstrate unambiguously positive effects compared to such controls is both far less damning and far less surprising than if individual CBT for children had failed to separate from waitlist.

Group CBT for children: At the time of the 2008 review, the majority of child trials examined group-based CBT, and this form of intervention was deemed *well-established* for the treatment of depression in children. However, of the nine child studies included in 2008, seven failed to meet inclusion criteria for the current review. As can be seen in Table 2, a large proportion of the investigations included in 2008, but screened out of the current

report, focused on the treatment of subsyndromal depression symptoms (below our clinical cutoffs; e.g., Weisz et al., 1997) or on the prevention of depression in children at-risk for disorder, some of whom may have been asymptomatic at baseline (e.g., Jaycox et al., 2004). At the time of our current search, only four studies of group CBT in children appeared to be explicitly focused on the treatment of clinically significant depression. Of these, one study had positive findings in favor of group CBT (Kahn et al., 1990), two studies had a no difference finding between CBT group and control at post-treatment (De Cuyper et al., 2004; Liddle & Spence, 1990), and zero had negative findings. One additional trial had mixed results, with the cognitive-behavioral treatment arm outperforming the comparison group on one index of depression but not others (Stark et al., 1987). Overall, the pattern of results is more promising than that for individual CBT with children, with one clearly positive trial and some additional positive findings within more ambiguous trials. Group-based CBT in children, thus, currently meets criteria as a *possibly efficacious* treatment modality. Again, this designation represents a notable change from previous reviews, in which group-based CBT was listed as *well-established*, due in large part to our exclusion of group-based CBT studies in samples with sub-clinical depression symptoms (see Table 2).

Technology-assisted CBT: One study met criteria for our review that examined the use of technology in delivering CBT to depressed children. Nelson and colleagues (2003) found that CBT delivered through videoconferencing was superior to individual CBT delivered through more traditional face-to-face means. While this one study shows a positive effect of videoconference CBT over another active treatment condition, it is difficult to gauge the effectiveness of traditional face-to-face CBT in this trial. As noted previously, individual CBT for depressed children is not strongly supported in the research literature, and it is possible that the effects of this "active" intervention would not exceed a control condition if a third arm had been included in the design. Conservatively, individual CBT should operate at least as a control for the processes of natural remission; accordingly, CBT delivered through technology is designated as *possibly efficacious* at this time, having demonstrated superior effects to a control condition in a single trial.

Behavior therapy for children—In the 2008 review, behavior therapy was identified as a *probably efficacious* treatment on the basis of three studies (Kahn et al., 1990; King & Kirschenbaum, 1990; Stark et al., 1987). No new trials of behavior therapy meeting our inclusion criteria have been published in our review window, and one of the three trials previously included does not meet the more stringent inclusion criteria for our current report (see Table 2). The two remaining trials (Kahn et al., 1990; Stark et al., 1987) lack specific pairwise comparisons to clearly differentiate the behavioral treatment arms from waitlist (e.g., instead reporting overall treatment effects collapsing across several arms). As such, it is difficult to conclude that independent replication of the behavioral effect has been demonstrated. With the data available in these reports, behavior therapy would clearly meet criteria as a *possibly efficacious* treatment (as classified in Table 5). Also note, the three "behavioral" intervention arms included in these two studies do not share a core set of behavioral techniques but represent a diverse, non-overlapping set of behavioral strategies for reducing stress and treating depression (relaxation training, self-modeling, and behavioral problem solving/effective social activation). It becomes difficult to generalize

across treatment approaches when there is a high level of heterogeneity in treatment manuals within a modality. However, all three programs were based on behavioral principles of symptom change (versus alternate hypothesized mechanisms), supporting the decision to evaluate the evidence for these approaches together as a broader behavioral modality.

Other psychosocial interventions for children—One additional RCT by Trowell and colleagues (2007) met minimum methodological criteria for inclusion in this review. In this study, depressed youths (age 9–15) were randomized to receive either individual psychodynamic therapy or family therapy. Results of the study were equivocal, with both groups demonstrating significant change from baseline but failing to statistically separate at post-treatment in terms of diagnostic recovery and showing a mixed pattern of effects across dimensional measures. At 6-month follow-up, the individual psychodynamic therapy condition showed a marginally superior response rate for Major Depressive Disorder but not for other operationalizations of depression. Furthermore, the study suffered from differential attrition over follow-up, and the effect on MDD varied by how researchers handled missing data. The authors concluded that both treatments were effective, given significant change from baseline status; however, the design cannot rule out natural remission as an alternate explanation of "treatment" effects. As a result, we classified both individual psychodynamic therapy and family therapy as *experimental treatments* on the basis of this single investigation.

Depression in Adolescents

Cognitive Behavioral Therapy—To date, 27 trials of CBT meeting our review entry criteria have been conducted. Of these trials, CBT has significantly separated from comparison conditions in 15 trials; 12 trials found no significant effect of CBT compared with control, and no studies reported CBT performing significantly worse than control. Twelve of the 27 studies were included in the prior reviews, 11 new primary outcome trials have been published since 2007, and four additional studies were included in our review that were screened out of previous reports. Across trials delivering CBT in group and individual formats, CBT meets criteria as a *well-established* treatment. Positive findings for CBT outweigh null reports, findings have been replicated across independent investigative teams, and CBT has outperformed active controls and alternate treatments in many (although not all) studies. Findings are presented in further detail in the following sections, by modality.

Individual CBT for adolescents: Fourteen trials of individual CBT for depression in adolescents met entry criteria for the current review. Included in this evidence base are six trials included in the previous reviews (Asarnow et al., 2005; Brent et al., 1997; Melvin et al., 2006; Rosselló & Bernal, 1999; TADS Team, 2004; Wood et al., 1996), five new trials published since 2007 (Brent et al., 2008; Richardson et al., 2014; Rosselló et al., 2008; Shirk, DePrince, Crisostomo, & Labus, 2014; Szigethy, Bujoreanu, et al., 2014), and three trials published prior to 2008 but not included in previous reviews due to null findings or misclassification as an open trial (Clarke et al., 2005; Goodyer et al., 2007; Kerfoot et al., 2004).

Among trials delivering individually based CBT for depressed adolescents, seven trials found positive effects for CBT compared with control (Asarnow et al., 2005; Brent et al., 2008; Brent, Holder, et al., 1997; Melvin et al., 2006; Richardson et al., 2014; Rosselló & Bernal, 1999; Wood et al., 1996). While one of these investigations compared CBT to a waitlist control (Rosselló & Bernal, 1999), the majority of trials found effects of CBT against more stringent control conditions, including alternative psychosocial treatment (Brent et al., 1997; Wood et al., 1996), medication (CBT versus SSRI, Melvin et al., 2006; CBT + medication switch versus medication switch, Brent et al., 2008), and usual care (Asarnow et al., 2005; Richardson et al., 2014).

While no trial found a significantly negative effect of CBT relative to control, in seven studies CBT did fail to statistically separate from comparison conditions (Clarke et al., 2005; Goodyer et al., 2007; Kerfoot et al., 2004; Rosselló et al., 2008; Shirk et al., 2014; Szigethy et al., 2014; TADS Team, 2004). In general, trials with null findings also tested CBT against stringent controls. Rosselló and colleagues (2008) examined CBT against an alternative evidence-based treatment found to be efficacious in a prior trial (IPT; Rosselló & Bernal, 2009) as well as a similar CBT protocol delivered in a group setting. Clarke and colleagues (2005) examined the effectiveness of CBT with SSRI compared with SSRI alone. Several trials examined the effect of CBT compared with either non-directive supportive therapy or psychosocial TAU (Goodyer et al., 2007; Kerfoot et al., 2004; Shirk et al., 2014; Szigethy et al., 2014). Only one trial failed to find an effect of CBT compared with an attention-placebo control (pill placebo; TADS Team, 2004); however, CBT when used in combination with medication outperformed SSRI alone on some metrics in this study. Furthermore, several trials with null findings examined the effect of CBT in either severe samples or embedded within active clinical practice. For example, Goodyer and colleagues (2007) examined the effect of CBT in a sample of youth with moderate to severe depression also including youth with active suicidality and self-harm, psychosis, and conduct disorder. Similarly, Shirk and colleagues (2014) tested CBT in a sample of adolescents with history of interpersonal trauma and high rates of comorbid PTSD. As described in detail in the review of new studies, the trial by Kerfoot and colleagues (2004) examined the effectiveness of CBT among currently practicing mental health workers with no prior exposure to CBT and who had poor attendance to supervision.

In sum, individual CBT appears to be a reliably efficacious intervention in half of the studies (7 of 14) in a sizeable literature. CBT effects are less reliable in clinically complex samples and when compared against other active interventions, but individual CBT has not proven inferior to alternate treatment under these conditions and has on occasion been significantly superior. Thus, CBT delivered in an individual format to depressed adolescents meets criteria as a *well-established* treatment due to multiple, independently replicated findings supporting superiority of CBT to active controls and alternate treatments (e.g., family therapy, non-directive supportive therapy) and potential equivalence to other well-established interventions (e.g., IPT) in studies by independent investigative teams.

Group CBT for adolescents: There have been 12 studies meeting criteria for the current review in which CBT for adolescent depression was delivered in a group format. Five of these trials were included in the prior review (Clarke et al., 1995; Clarke, Rohde,

Lewinsohn, Hops, & Seeley, 1999; Clarke et al., 2001; Lewinsohn et al., 1990; Rohde et al., 2004) with one trial previously excluded due to null findings (Clarke et al., 2002). Since the prior review, there have been six new trials (Dobson et al., 2010; Stallard et al., 2012; Stice et al., 2008; Rohde et al., 2014; Rosselló et al., 2008; Wijnhoven et al., 2014). Among all trials of group CBT for adolescents, seven have shown positive effects of CBT, and five trials have shown null findings (Clarke et al., 2002; Dobson et al., 2010; Stallard et al., 2012; Rohde et al., 2014; Rosselló et al., 2008). As discussed above, one trial with null findings tested CBT in an individual format against group-based CBT and against group and individually-based IPT (with no inert control group; Rosselló et al., 2008). Similarly, a second trial with null findings tested group-based CBT in combination with family therapy (Rohde et al., 2014). As reported above, no control group was included in this study and three variations in sequencing of these two treatments did not result in statistically significant differences in depressive symptoms. Another trial with null findings was conducted in a particularly difficult-to-treat sample of currently depressed youth with currently depressed parents (Clarke et al., 2002). Both of the other trials with null findings were prevention studies in high symptom samples, with one trial specifically excluding youth meeting criteria for a depressive disorder (Dobson et al., 2010). This trial failed to find an effect of CBT when compared with non-directive supportive treatment; however, when comparing CBT to the control group in a similar depression prevention trial (Clarke et al., 1995) the authors found a significant effect of CBT. The second prevention study failing to find an effect of CBT was conducted by Stallard et al. (2012). Poor rates of response in this trial may in part be related to low dose of intervention (11 sessions administered flexibly in the school curriculum).

In sum, given multiple trials finding group based CBT superior to active controls or potentially equivalent to alternate treatments (e.g., IPT) as tested by independent investigative teams, we find group based CBT to be a *well-established* treatment for depressed adolescents.

Technology-assisted CBT: No trials of technology-assisted CBT among depressed adolescents were available at the time of the last review. Subsequently, one trial of technology-assisted CBT meeting our review entry criteria has been conducted (Merry et al., 2012). As discussed previously, the effects of technology-assisted CBT did not significantly differ from the outcomes of TAU consisting of individual psychosocial treatment or medication (Merry et al., 2012). TAU in this investigation may be an active treatment, but it is difficult to gauge the effects of this condition in the absence of a worse performing control group. Accordingly, technology-assisted CBT currently meets criteria as an *experimental* treatment.

Bibliotherapy CBT: Two trials have examined the effect of CBT bibliotherapy as a treatment for adolescent depression. One trial was available at the time of the last review (Ackerson et al., 1998), and one trial including a bibliotherapy condition has been published subsequently (Stice et al., 2008). CBT delivered as bibliotherapy was found to be superior to wait-list control in one trial (Ackerson et al., 1998). In the second trial, CBT bibliotherapy did not separate from assessment-only control at post but effects were present at 6-month

follow-up. Based on post-treatment findings, CBT delivered as bibliotherapy is considered a *possibly efficacious* treatment.

Interpersonal Psychotherapy—A total of six trials of IPT have been conducted in samples of depressed adolescents. Five of these trials had positive findings, with one trial showing no significant difference between CBT and IPT (Rosselló et al., 2008). Summing across evidence from group-based and individual formats, IPT meets criteria as a *well-established* treatment. IPT has consistently separated from active controls, and IPT effects are similar in magnitude to the effects of CBT, another well-established intervention, in head-to-head trials (Rosselló et al., 2008).

Individual IPT for adolescents: Four trials meeting criteria for the current review have examined individually-based IPT in depressed adolescents. Three of these were included in the previous review (Mufson, Dorta, et al., 2004; Mufson, Weissman, et al., 1999; Rosselló, & Bernal, 1999). Among trials of IPT delivered in an individual format, three showed positive effects for IPT (Mufson, Dorta, et al., 2004; Mufson, Weissman, et al., 1999; Rosselló, & Bernal, 1999) across two independent investigative teams. These trials have tested efficacy of IPT against waitlist or clinical monitoring control conditions (Mufson et al., 1999; Rosselló, & Bernal, 1999), as well as efficacy of IPT when delivered by school counselors compared with TAU (Mufson et al., 2004). The only null finding for individual IPT comes from the Roselló study (2008) comparing individual IPT to group IPT and to individual and group CBT. As noted above, response rates for IPT in this trial were consistent with trials finding positive effects of treatment relative to control, albeit within the lower end of this range. Positive effects of individual IPT found by two independent teams suggest this model should be considered a *well-established* treatment.

Group IPT for adolescents: A total of three trials have examined group-based IPT in depressed adolescents, with one trial included in the last review (Young et al., 2006a) and two trials published subsequently (Rosselló et al., 2008; Young et al., 2010). Two of these three trials found positive effects of group IPT compared with school counseling for adolescents with elevated depression symptoms (Young, Mufson, & Davies, 2006a; Young, Mufson, & Gallop, 2010). As described in the review of new studies, the third trial found no statistically significant difference between individual and group versions of IPT and CBT in a sample of youths with clinically diagnosed depression (Rosselló et al., 2008). This latter null finding is somewhat difficult to interpret, given the absence of a worse performing inert, control condition in the design. Response rates for all four intervention arms in this study were within the range of the published literature for CBT and individual IPT, and, thus, the null finding could be construed as evidence of equivalence between group IPT and other *well-established* treatments. Conservatively, group IPT currently meets criteria as *probably efficacious* intervention (see Table 6), having shown positive effects compared to control in two studies by the same investigative team.

Family-based Treatment—Five trials of family-based intervention met entry criteria for the current review, with two new trials published in the review window (Diamond et al., 2010; Rohde et al., 2014). In this pool, two trials found significantly superior effects of

family treatment compared with control (Diamond, Reis, Diamond, Siqueland, & Isaacs, 2002; Diamond et al., 2010); two trials failed to find significant differences between treatment and control (Rohde et al., 2014; Sanford et al., 2006), and one investigation found that family therapy was significantly inferior to CBT and failed to separate from non-directive supportive therapy (Brent et al., 1997).

A major challenge in interpreting the findings for this treatment modality is the diversity of family-based interventions, ranging from adjunctive family psychoeducation (Sanford et al., 2006) to full courses of an established family therapy (Brent et al., 1997; Rohde et al., 2014). Within this sample, only one manual, Attachment-Based Family Therapy (ABFT), was tested in more than one trial (Diamond et al., 2002; Diamond et al., 2010). As discussed in our review of behavioral therapy for child depression, it becomes difficult to generalize across treatment approaches when there is a high level of heterogeneity in treatment manuals within a modality. However, all included interventions were based on family process models of symptom change (versus, for example, being CBT treatments with adjunctive family sessions), supporting the decision to evaluate the evidence for these approaches together as a broader family modality. Taken together, the evidence supporting family-based therapy as a general approach to intervention falls within the criteria of a *possibly efficacious* treatment. Of note, if the current review had taken a manual-by-manual approach to evaluating the status of treatments, the two positive trials of ABFT would suggest the protocol was *probably efficacious* as a specific family therapy model.

DURABILITY OF EFECTS OVER FOLLOW-UP

In our evaluation of the status of treatments, we focused on the effects of interventions at the immediate post-treatment assessment. Here, we comment briefly on the effects of the above interventions over time. Follow-up data reviewed here were restricted to analyses preserving randomization. Analyses in which the control group received the intervention (e.g., Ackerson et al., 1998) or only included a subset of the sample (e.g., youth depressed at the end of acute treatment; Clarke et al., 1999) were not included in this review of follow-up reports.

Within the child depression literature, four original trials included in the current review reported follow-up data (De Cuyper et al., 2004; Kahn et al., 1990, Liddle & Spence, 1990; Trowell et al., 2007; Vostanis et al., 1996; Vostanis, Feehan, & Grattan, 1998). Latency of the final follow-up assessment from post-treatment varied substantially between trials ranging from 1 month (Kahn et al., 1990) to 2 years (Vostanis et al., 1998). Among trials with shorter follow-up windows (< 6 months), outcomes appear to be mixed. Two trials reported positive effects of treatment relative to control (De Cuyper et al., 2004; Kahn et al., 1990), while another showed improvement in all groups across most measures (Liddle & Spence, 1990). Two studies included longer (≥ 6 months) follow-up windows. One found no effect of treatment group relative to control (Vostanis, Feehan, & Grattan, 1998; Vostanis, Feehan, Grattan, & Bickerton, 1996a), while another found improvement in both treatment arms across a 6-month follow-up (Trowell et al., 2007).

In contrast, the majority of trials in adolescents (22 of 34) reported follow-up data. In comparison with studies of childhood depression, trials in adolescent samples tended to report on longer follow-up periods with 12-month (Asarnow, Jaycox, et al., 2009; Clarke et al., 1995; Rohde et al., 2004; Rohde et al., 2014), 18-month (TADS Team, 2009; Vitiello et al., 2011; Young et al., 2010), and 24-month (Birmaher et al., 2000; Clarke, Hornbrook, Lynch, Polen, Gale, Beardslee, et al., 2001; Clarke, Hornbrook, Lynch, Polen, Gale, O'Connor, et al., 2002; Stice et al., 2010) post-treatment assessments not uncommon. Across CBT and IPT intervention studies, most youth randomized to both active treatment and control conditions recovered over time, with few findings of significant differences between groups. Intervention studies that did find significant treatment effects over follow-up tended to have very short assessment windows (maximum of 1 month post; Mufson et al., 2004). However, several indicated prevention trials (Clarke, Hawkins, et al., 1995; Clarke, Hornbrook, et al., 2001; Stice, Rohde, Gau, et al., 2010; Stice, Rohde, Seeley, et al., 2008; Young et al., 2006a; Wijnhoven et al., 2014) found significant effects of intervention on depressive symptoms and episodes for periods as long as 24 months.

Taken together, these results suggest only weak durability of specific *treatment* effects on depression over time, due in large part to continued improvement in depression in control conditions over follow-up (consistent with data on natural remission and the episodic course of untreated depression; Kovacs, 1996). In contrast, prevention studies with high symptom youth have a more promising profile of effects over time. Youths in these investigations are typically selected to have clinically-significant symptoms but not yet meet full diagnostic criteria for disorder, and interventions appear to be more successful in inoculating against negative outcomes over extended follow-up compared to control.

PREDICTORS, MODERATORS, AND MEDIATORS

We next turn from our review of primary outcome papers to examine data on the limits to and mechanisms of treatment response. As per Kraemer and colleagues (2002), *predictors* were coded as baseline characteristics of youths and families that were associated with poor response regardless of condition. Clinically, predictors serve as general prognostic variables. In terms of treatment development, identification of a predictor may highlight a new intervention target, outside the realm of currently investigated interventions. Conversely, *moderators* were identified as baseline variables associated with differential responses to intervention; moderators are useful in making clinical decisions about to whom an intervention should be provided. Moderators also may be useful in treatment development, as they help to identify areas of weakness in the mechanisms of action of specific interventions. We end with a summary and critique of the small literature exploring mediators of treatment response in youth depression. Mediation analyses serve as tests of the causal theories underlying treatment models (e.g., change in negative cognitive style causes change in depressive symptoms within CBT), and results of such analyses may guide efforts to refine and strengthen interventions.

To produce a pool of studies for this section, we reviewed all included primary outcome papers for relevant analyses within the original report and searched for secondary papers from the same datasets by following reference trails, conducting author searches, and

screening abstracts from our original primary outcome search. We limited our consideration to empirical investigations of post-treatment data in which treatment and control conditions were analyzed separately (versus pooled for analysis), and results were provided for primary depression outcomes versus alternative treatment targets (e.g., suicidality). As with the youth depression treatment literature at large, evidence on predictors, moderators, and mediators of treatment effects is largely based on samples of depressed adolescents and drawn from trials testing the effects of CBT. Throughout this section we highlight occasions where findings are demonstrated in child samples or with alternate interventions.

Predictors of Treatment Response

Table 7 summarizes results of predictor analyses from 19 publications representing six independent trials for adolescent depression (Brent, Emslie, et al., 2008; Brent, Holder, et al., 1997; Lewinsohn et al., 1990; Mufson et al., 2004; Rohde et al., 2014; TADS Team, 2004); no child depression study included such analyses. We did not observe systematic variability by specific measures (e.g., the *Dysfunctional Attitudes Scale;* Weissman & Beck, 1978); thus, the table condenses results into broader constructs (e.g., cognitive processes). Results of studies including IPT treatment arms are indicated with bold font and italics; all other results represent findings from CBT trials. Studies of family-based interventions alone have not published predictor analyses, although family therapy was a control arm within Brent et al. (1997) and a treatment component within Rohde et al. (2014). Results are coded as indicating a significant positive association between the predictor and response, a significant negative association between the predictor and response, or a null/non-significant association between a tested predictor and response. Note that within the same study a predictor could be coded into multiple categories, if, for example, results varied by operationalization of depression (e.g., different findings for self-report of symptoms versus diagnostic remission).

Overall, predictor analyses indicate that demographic factors do not seem to play a substantial role in response to treatment. However, this conclusion is qualified by restriction of range issues. Age has only been tested within a sample of adolescents, not across the age range from childhood through adolescence, finding that treatment effects diminish as youths get older (Curry et al., 2006). Similarly, most investigations do not include large numbers of ethnic and racial minority youth, limiting power to detect effects. Comparing *across* trials, there is evidence that EBTs for depression can work well in both non-Hispanic White and diverse samples of children and adolescents (cf. Rosselló & Bernal, 1999; Weisz et al., 1997), but direct tests of this association *within* trials are lacking.

In contrast to the null findings for demographic factors, indices of clinical severity and life stress are more reliably related to outcome. Of these factors, higher levels of depression symptoms, poor global functioning, high levels of suicidality, comorbid anxiety, cognitive distortions, hopelessness, and family conflict most consistently predicted poor response across treatment and control conditions. The remaining factors listed in Table 7 were infrequently tested or yielded highly inconsistent results, making it difficult to confidently draw generalizable inferences. Summary of these mixed results is provided in the table to guide additional research.

Moderators of effects

Are our evidence-based treatments broadly applicable to depressed youth, or do these interventions work more or less well across demographic groups, with different types of depression, and in the presence of comorbid disorders? Table 8 summarizes results of 23 publications reporting moderator analyses from eight independent trials for adolescent depression (Brent, Emslie, et al., 2008; Brent, Holder, et al., 1997; Diamond et al., 2010; Lewinsohn et al., 1990; Mufson et al., 2004; Rohde et al., 2014; TADS Team, 2004; Young et al., 2006a); no child depression study included such analyses. Again, effects did not appear to reliably vary by measure; therefore, categories have been collapsed for simplicity. Results of studies including an IPT treatment arm are indicated with bold and italic formatting, while results from analyses of family-based interventions are labeled with a $^{+}$; all other results represent findings from CBT trials. Moderator results were coded in the table as indicating a significantly enhanced effect for the target treatment in comparison to control, significantly diminished effect for the target treatment relative to control, or a null/non-significant moderating relationships (i.e., treatment and control appear to fare equally well in the presence of the moderator). Note that these results were necessarily study specific, in that relationship between treatment and control was enhanced or diminished relative to the main effect reported within the primary outcome analyses for that particular investigation. Also note that within the same study, a moderator could be coded in multiple categories if: (a) results varied by operationalization of depression (e.g., different findings for self-report of symptoms versus diagnostic remission; Clarke et al., 1992), (b) authors explored the moderating variable at different levels yielding differential effects on treatment (e.g., Gau et al., 2012), or (c) the action of the moderator was dependent on other higher order interactions (e.g., Amaya et al., 2010).

Moderators of CBT effects—Demographic factors as a whole were not strong moderators of CBT effects, with only a single positive finding suggesting that older age enhanced CBT efficacy (Asarnow, Emslie, et al., 2009). However, developmental level and, to a lesser extent, ethnicity and socioeconomic status suffered from problems with restriction of range, limiting the interpretation of these null effects (as noted previously). CBT also appeared to be generally robust in the face of clinical moderators. The modal moderator result for clinical factors was a null finding (see Table 8, final column); however, two studies found significant group differences in the direction of enhanced effects of CBT for participants with more severe depressive symptoms (Asarnow, Emslie, et al., 2009; cf. Curry et al., 2006). There is some evidence that CBT may separate more strongly from control in the face of comorbidity, with the possible exception of substance abuse. This positive moderation of CBT effects is present even for comorbid anxiety. Anxiety broadly predicted poorer outcome across conditions (see Table 7), but CBT seems to be less strongly impacted by the presence of anxiety, perhaps due to the common pathological processes underlying depression and anxiety and shared elements present in CBT interventions for depression and evidence-based treatments for anxiety (see Garber & Weersing, 2010).

CBT fared less well in the presence of significant life stress. Effects for parental depression are mixed, but, in one key analysis, maternal depression at the time of treatment participation functionally eliminated the superiority of CBT to alternate treatments (NST

and family therapy; Brent et al., 1998). Trauma exposure also may prove to be an important moderator, with positive effects from CBT more likely among youth without abuse histories (Asarnow, Emslie, et al., 2009; Barbe et al., 2004a; Shamseddeen et al., 2011). These findings align with the outcomes of the Shirk et al. (2014) investigation. Although the authors did not explore moderation, they found that the effects of CBT in a sample exposed to interpersonal trauma failed to separate from those of the control group, with an overall low response rate to CBT. Moderator results vary by investigation on the impact of type of trauma on CBT response, but sexual abuse appears to be most consistently related to a diminished CBT response and failure of the intervention to exceed control conditions (Lewis et al., 2010; Shamseddeen et al., 2011). At this time, it is unclear how these moderators operated, with author hypotheses ranging from negative impact on the therapeutic relationship and engagement in the tasks of therapy to impaired executive functioning (secondary to trauma) interfering with the uptake of cognitive interventions.

Moderators of IPT effects—Although sufficient evidence has accumulated to designate IPT as a *well-established* intervention for adolescent depression, little information is available on moderators of IPT effects. Similar to CBT, IPT may be more efficacious in older adolescents; however, generalizability across demographic factors remains largely unknown. Only depression severity and comorbid anxiety have been investigated as clinical moderators (see Table 8), with mixed results across studies. Additional data on the robustness of the model to these factors would seem to be a key step toward promoting the widespread adoption of IPT as a treatment option for depression in adolescents.

Some intriguing data are available on the impact of interpersonal variables in IPT response. As noted in Table 7, poor social functioning and heightened family conflict predicted poor response across both IPT and control; however, these variables also operated as moderators. The positive effect of IPT (relative to TAU within the school setting) was particularly strong for adolescents who reported at baseline higher levels of conflict with their mothers and more difficulties in their peer relationships (Gunlicks-Stoessel et al., 2010), providing indirect support for a compensation model of IPT response.

Moderators of family-based intervention effects—To date, there is no evidence for differential efficacy of family therapy, alone, as a function of moderating variables. Three trials examined demographic factors, symptom severity, lifetime suicidality, cognitive distortions, hopelessness, family conflict, family environment, and history of sexual trauma as potential moderators, but none of these analyses reached statistical significance (Barbe et al., 2004b; Brent et al., 1998; Diamond et al., 2012; Rohde et al., 2014).

Evidence of Mediation

Despite 30 years of clinical trial research in youth depression, we were able to find only six studies meeting our entry criteria (Ackerson, Scogin, McKendree-Smith, & Lyman, 1998; Kolko et al., 2000; Kaufman et al., 2005; Lewis et al., 2009; Jacobs et al., 2009; Stice, Rohde, Seeley, & Gau, 2010) that formally tested whether the processes hypothesized to drive intervention effects statistically mediated the impact of intervention on depression outcomes. All five studies focused on CBT for depressed adolescents and relied on youth

self-report of cognitive (five studies), behavioral (two studies), and motivational (one study) processes, and, more often than not, the design or results of the mediation tests left directionality of effects unclear (i.e., failure to establish temporal precedence of changes). Furthermore, the six studies utilized different CBT treatment protocols that varied in their relative focus on cognitive versus behavioral techniques, involvement of family members, and number of sessions, and the trials had very different inclusion criteria in terms of level of severity and comorbidity.

It is not surprising that this limited pool of studies has not yielded a definitive set of results. Cognitive and behavioral change may be related to change in depression symptoms, but these findings are not consistent across studies or measures of processes. In a trial of cognitive bibliotherapy for teens with mild depression seen in primary care, Ackerson and colleagues (1998) found that change in dysfunctional attitudes (DAS), but not negative automatic thoughts (*Automatic Thoughts Questionnaire* [ATQ]; Hollon & Kendall, 1980), significantly mediated the effects of the intervention on youth-reported depression symptoms only and not for other measures of depression (i.e., interviewer ratings). Conversely, Kaufman et al. (2005) found non-significant results for the DAS but small significant effects on the ATQ in a secondary analysis examining the process and outcome of CBT adapted for youth with depression and comorbid conduct disorder. In this trial, depressed teens involvement in pleasant activities improved in both CBT and the life skills tutoring intervention, and, thus, the mediating role of this behavioral process was not tested.

Stice and colleagues (2010) found stronger support for the mediating role of cognitive and behavioral change in an indicated prevention sample of high symptom adolescents. In this trial, the CB prevention program significantly lowered depression symptom scores compared to supportive therapy and bibliotherapy control conditions. Reduction in depressogenic thinking (ATQ) and increased involvement in pleasant activities statistically mediated CB intervention effects; however, using data from a mid-point assessment, it appeared that changes in depression symptoms temporally preceded change in the putative mediators. Furthermore, the CB condition also significantly impacted mediators that were designed to be theoretically specific to the supportive therapy control, undermining the hypothesis that CB “worked” through cognitive processes.

In the TADS trial, cognitive style (DAS perfectionism subscale) also statistically mediated superior effects of combination treatment over CBT and placebo on interviewer-rated depression symptoms (Jacobs et al., 2009). Although this finding is consistent with a mediating role for cognitive change in CBT effects, this conclusion is weakened by (a) the overall poor effects of CBT alone in TADS on both the outcomes and mediator, and (b) poor evidence of temporal precedence showing cognitive change before symptom outcome. Also within the TADS dataset, Lewis and colleagues (2009) examined changes in motivational factors as potential mediators of depression outcome. In their analysis, changes in “readiness to change” (self-report of action orientation) between baseline and the midpoint of treatment was significantly higher for youths in the COMB (CBT+SSRI) and CBT arms of the study compared to medication alone and placebo, and change in action orientation partially mediated the effects of COMB on depression symptoms at post-treatment. As with the analyses of Jacobs et al (2009), temporal change between action orientation and depression

symptoms was unclear. Further, data were not provided linking analyses across these mediator papers within the same trial.

Kolko and colleagues' (2000) reanalysis of the Brent et al. (1997) comparative trial of cognitive, family, and supportive therapy aimed to test mediation using a different cognitive measure (*Children's Negative Cognitive Errors Questionnaire*; Leitenberg, Yost, & Carroll-Wilson, 1986). However, missing data across measures of mediators and outcome appeared to compromise power, and mediation analyses were cut short by the lack of a primary effect of treatment on depression symptoms (the main trial reported significant effects favoring CBT over alternate treatments). As in Stice et al. (2010), the Kolko paper also showed evidence of nonspecific effects of CBT. While mediation analyses were not completed, CBT did have a specific, superior effect on cognitive style compared to family and supportive therapy, but CBT also significantly impacted marital conflict and parental behavior control, both of which were designed to be theoretically specific to family therapy.

The field still awaits empirical data on the mechanisms of action of IPT and family-based interventions. Many clinical trials of these treatments have included measures of processes, such as interpersonal functioning, that may well function as mediators; however, these measures have only been evaluated as post-treatment outcomes, and statistical tests of mediation have not been conducted. In general, it appears that both IPT and family therapy significantly impact interpersonal and family variables at post-treatment (for review, see Weersing, Rozenman, & Gonzalez, 2009), but it is unclear if these effects are theoretically specific or whether change in these potential processes occurs as a result of change in depressive symptoms.

DISCUSSION

In this report, we sought to update and re-evaluate the empirical status of psychosocial treatments for depression in youth. Our methods were largely similar to past, foundational reviews in 1998 and 2008 with three key differences, namely: (a) adopting theories over manuals as the primary unit of analysis, (b) focusing on treatment of clinically significant depression rather than including a broader sample of depression prevention studies in at-risk and subsyndromal youth, and (c) considering the balance of positive, negative, and null findings when evaluating interventions and classifying their level of support. We applied these criteria when searching for new trials and 14 novel investigations met all entry criteria (also see Table 1). We also re-evaluated studies published during the window of previous EBT reviews, and both excluded a number of investigations reviewed previously (18; see Table 2) and included trials that had been previously omitted (8). As a result, the youth depression evidence base evaluated in this review differed considerably from past reports, varying by 40 primary outcome papers. In line with trends in effect sizes in the depression meta-analyses (see Weisz et al., 2006), results of the current review suggest the evidence base supporting depression treatments in youth is more modest than suggested by past reports. Our conclusions, however, were broadly in keeping with central messages of prior reviews. First, cognitive behavioral therapy continued to be the best-supported treatment model in the evidence base, and, second, evidence supporting treatments for depression in children was weak overall and notably worse than evidence for adolescent interventions.

CBT was clearly the dominant intervention model in the literature. Across individual and group formats, CBT met criteria as a *well-established* intervention for adolescents with depression, and group-based CBT reached *possibly efficacious* status for the treatment of depressed children (no child treatments were rated more highly than this level). This dominance rested largely on the number of CBT trials and replications rather than purely on the strength of individual trial findings. As a case in point, there were 27 CBT trials for depressed teens versus 6 trials of IPT; CBT had a larger absolute number of positive findings replicated across investigative teams, although the positive "hit rate" was higher for the smaller IPT literature (5/6 versus 15/27 for CBT). As a function of this larger primary outcome literature, CBT for adolescent depression also had substantially more evidence on moderators of effects, with data suggesting that the model has been broadly generalizable across demographic factors and robust to comorbidity (see Table 8). Data were less clear on whether CBT was robust to other forms of clinical complexity, and effects were attenuated in analyses probing teen trauma history (Asarnow, Emslie, et al., 2009; Barbe et al., 2004a; Lewis et al., 2010; Shamseddeen et al., 2011), concurrent maternal depression (Brent et al., 1998; cf. Curry et al., 2006), high stressful life events (Gau et al., 2012), and low income (Curry et al., 2006).

These findings dovetail with poor results for CBT in many effectiveness studies when compared to other community interventions. CBT did not perform well when (a) delivered as a training intervention to community mental health workers and compared to their usual services (Kerfoot et al., 2004), (b) implemented in child guidance clinics and compared to usual community care (Weisz et al., 2009), (c) delivered in a health maintenance organization as a brief CBT+SSRI intervention and compared to SSRI alone (Clarke et al., 2005), or (d) embedded in the National Health Service in the United Kingdom as a combined CBT+SSRI model and compared to SSRI alone (Goodyer et al., 2008). The exception to this troubling pattern of dissemination findings is the success of CBT for adolescent depression when delivered as part of a collaborative care model in primary care (Asarnow et al., 2005; Richardson et al., 2014). These primary care designs make it difficult to evaluate the effect of CBT relative to other components of the collaborative care package; however, difficulty in determining mechanisms of treatment action was not unique to primary care studies. Data on mediation processes in CBT was sparse and mixed (at best), and little appears to be known about which cognitive or behavioral processes might be responsible for the effects of the intervention model. Poor understanding of the mechanisms of CBT is problematic theoretically and links to the question of effectiveness. If the core processes of an intervention model are unknown, there is little scientific basis to guide improvements to the treatment when poor effects are observed in practice settings (e.g., community guidance clinics) or in the presence of a significant "real world" moderator (e.g., poverty, trauma exposure). Full discussion of these issues are beyond the scope of the current review but have been commented on extensively by others (e.g., Kazdin & Nock, 2003; Weersing, Rozenman, & Gonzalez, 2009), and research on mechanisms of depression treatment action, including for models other than CBT, remains a critical area for additional research.

Additional research also appears to be sorely needed to shore up the evidence for child depression treatment. As in previous reviews, we found the child literature to be smaller,

methodologically weaker, and reporting notably poorer effects than the adolescent depression research base. Unsurprisingly, the child literature was strongly impacted by the more stringent inclusion criteria for the current review. Of the 18 studies included in prior reports but excluded from our review, 12 focused on children. As a result, no child depression treatment currently met criteria for *well-established* or *probably efficacious*, and the evidence base for individual child CBT became sufficiently thin that the modality was re-classified as *experimental*. This was due in large part to the exclusion of studies conducted in child samples that did not clearly meet criteria for having clinically significant depression (e.g., studies supporting the *Penn Prevention Program*). While these RCTs fell outside the scope of our review of *treatment* for depressed children, results from many of these sub-syndrome studies were promising, and these intervention models exist as a preventive resource and a potential base for future treatment development. However, the evidentiary status of child treatments was also strongly impacted by (a) the *inclusion* of null trials in clinical samples excluded from previous reports and (b) our decision to evaluating the balance of evidence (including mixed findings within trials) when evaluating the status of an intervention.

Given the mixed effects for extant treatments, it also may be worth debating whether child depression research should move forward in a straight path from its current foundation or re-evaluate the models of intervention needed to successfully treat depression in pre-pubertal youth. There are data to suggest that childhood depression may not be of a piece with adolescent and adult mood disorder. At a gross level, total prevalence rates and prevalence by gender vary dramatically between childhood and later developmental periods; there is poorer continuity of childhood depression compared to the strong link between adolescent depression and recurrent mood disorder in adulthood, and genetic investigations have suggested lower heritability for childhood depression and stronger environmental influence (for review see Rutter, Kim-Cohen, & Maughan, 2006). The heightened environmental aspect of childhood depression and younger children's greater dependence on caregivers for assistance with the basic tasks of treatment (such as completing therapy homework) may suggest value in investigating parent-mediated interventions; however, family-based models have not had a strong track record in the literature to date, with the exception of ABFT for teens. Outcomes are not yet available from a recent intriguing study of developmentally-based intervention designed to teach pre-pubertal depressed youth (age 7–12) emotion regulation strategies, using parents as coaches and models for how to cope with environmental stress and disruptions in positive mood, adaptively reduce dysphoria, and return to a more stable mood state (Kovacs et al., 2012). New work adapting IPT for children also may prove fruitful in this regard. Preliminary studies of family-based IPT (FB-IPT) for preadolescents with depression suggest it is well tolerated by families, with high compliance with the tasks of treatment (Dietz, Mufson, Irvine, & Brent, 2008), and a recent trial suggests significant impact on depression outcomes compared to a supportive therapy control (Dietz et al., 2015).

Although this review explicitly adopted a model-based approach to evaluating interventions, we can imagine a productive move toward greater specificity in the next generation of depression treatment research. We do not envision this as being specific at the level of individual manuals but rather a greater focus on techniques, mechanisms, and processes of

disorder (and subtypes of disorder). The category of CBT includes a dizzying array of specific techniques targeting cognitive and behavioral processes, and CBT manuals may be implemented in such a way as to have very little overlap in the content covered (see Weersing, Rozenman, & Gonzalez, 2009). Conversely, it may well be that putatively distinct models, such as IPT, share active elements with some CBT approaches such as problem-solving and coaching in social skills and assertiveness. Indeed, a component analysis of a multi-technique CBT manual has suggested that emphasis on the more generic skills of problem solving and social skills training may be associated with enhanced positive outcomes, even within the context of other active CBT elements (Kennard et al., 2009). Response rates for "active" interventions for depression in childhood and in adolescence are quite similar, and meta-analytic evidence on treatment effects in youth and adulthood suggest that a ceiling may have been reached with current depression treatments (or that early effects may have been over-estimates; Weisz, McCarty, & Valeri, 2006; Johnsen & Friborg, 2015; Driessen, Hollon, Bockting, Cuijpers, & Turner, 2015). As the field continues to mature, we see value in searching for these change mechanisms within treatments as a path for refining and strengthening the interventions available for child and adolescent depression.

The field would also benefit from additional research on (a) stepping or matching care to the clinical severity and complexity of depressed youths and (b) addressing long-term efficacy of interventions and prevention of relapse. Our analysis of the predictor and moderator literature was promising, but substantially limited by the small number of studies including such analyses. All data understanding variability in response come from studies of adolescents, which may be especially problematic given the pressing need to enhance effects within the child literature (new child treatment targets identified through such analyses would be a boon). Also of note, two of the eight trials providing moderator results were investigations that included medication and CBT+medication combination conditions (TADS, 2004; Brent et al., 2006). Throughout our review, we highlighted the effects of CBT in these studies given the overall focus of this report on psychosocial interventions. However, efficacy data from both trials provide solid support for the combination of CBT and antidepressant medication in the treatment of moderately to severely depressed youths, with the TORDIA trial analyses suggesting adding adjunctive CBT to medication management procedures may be especially valuable at higher levels of clinical severity (Asarnow et al. 2009). It is currently unclear at what threshold of severity would adoption of combination approach be justified versus selection of a *well-established* psychosocial treatment for adolescent depression. Further, the reduced response rates for CBT in the presence of serious comorbidity (e.g., Rohde et al., 2014) may call for enhanced interventions to adequately serve multi-problem youth for whom depression is one of many major, clinically impairing problems. The trial of combined FFT and CBT for teens with comorbid depression and substance abuse, suggested that depression outcomes were not particularly sensitive to the order of intervention components, but substance outcomes and retention may differ significantly depending on not simply the content but the order of interventions. Work by John Weisz and colleagues (Weisz et al., 2012) on modular approaches to treating multi-problem youths with depression, anxiety, and/or conduct problems has raised the intriguing possibility that community therapist may be able to

reliably deliver personalized treatment components, under supervision, and enhance outcomes compared to usual care, although results specific to youths with clinically elevated levels of depression have not been published. At the other end of the severity spectrum, CBT delivered as a component of collaborative care models within primary care was a stand-out in terms of treatment effectiveness (as was IPT in school-based clinics; Mufson et al., 2004). Better data on when, how, where, and to whom to guide specific depression treatments is necessary in order to move toward a public health approach to treatment matching and effective delivery.

It is also unclear what models of intervention would best serve depressed children and adolescents over the long-term. In this report we provided a brief summary of effects of our included trials over follow-up. For treatment (versus prevention) studies, significant differences between active intervention and control faded over follow-up, an unsurprising outcome given the cyclical nature of untreated depressive disorder (see Kovacs, 1996). The cyclical pattern of depression also suggests these youths will experience high rates of relapse and recurrence. While full discussion of this issue is beyond the scope of the current review, long-term, non-experimental follow-ups of treated youth suggest little to no protective effect of successful short-term acute treatments (see Birmaher et al., 2000), a difference between the youth and adult treatment literatures. Findings from the prevention literature are perhaps more promising. Within our pool of prevention studies targeting youth with clinically elevated symptoms (but not yet meeting criteria for disorder), interventions demonstrated significant effects as long as 24 months after baseline. Recent long-term data from the large Prevention of Depression (POD) trial focusing on the offspring of mood disordered parents suggest that CBT may be able to alter the developmental trajectory of at-risk adolescents, with differences in depression episodes and functioning observed six years after program implementation (Brent et al., 2015). Youths in the POD trial were especially likely to benefit when the intervention was given at “moments of wellness” -- when teens were high functioning, more hopeful, less anxious, and less exposed to their own parents’ depression (Weersing et al., 2015; Garber et al., 2015). The majority of youths in the POD trial had experienced previous episodes of depression, suggesting the lessons learned from this prevention study may be highly applicable to work on continuation models of treatment and relapse prevention (e.g., Kennard et al., 2014).

Overall, results of the current review are sobering in many respects, especially for the treatment of depression in children, and are in line with trends in the depression literature toward smaller effect sizes and less consistency in effects. Across all domains, much work remains to be done to develop, test, and implement effective interventions for depressed children and adolescents capable of producing enduring positive outcomes.

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TABLE 1

Review criteria for evidence base updates in *Journal of Clinical Child and Adolescent Psychology*

Methods Criteria

M.1. **Group design**: Study involved a randomized controlled design

M.2. **Independent variable defined**: Treatment manuals or logical equivalent were used for the treatment

M.3. **Population clarified**: Conducted with a population, treated for specified problems, for whom inclusion criteria have been clearly delineated

M.4. **Outcomes assessed**: Reliable and valid outcome assessment measures gauging the problems targeted (at a minimum) were used

M.5. **Analysis adequacy**: Appropriate data analyses were used and sample size was sufficient to detect expected effects *

Evaluation of Treatments

Level 1: Well-Established Treatments

Evidence criteria

1.1 Efficacy demonstrated for the treatment by showing the treatment to be either:

1.1.a. Statistically significantly superior to pill or psychological placebo or to another active treatment

OR

1.1.b. Equivalent (or not significantly different) to an already well-established treatment in experiments *

AND

1.1.c. In at least two (2) independent research settings and by two (2) independent investigatory teams demonstrating efficacy

AND

1.2 **All five (5)** of the ***Methods Criteria***

Level 2: Probably Efficacious Treatments

Evidence criteria

2.1 There must be at least two good experiments showing the treatment is superior (statistically significantly so) to a wait-list control group

OR

2.2 One or more good experiments meeting the Well-Established Treatment level except for criterion 1.1.c. (i.e., Level 2 treatments will not involve independent investigatory teams)

AND

2.3 All five (5) of the ***Methods Criteria***

Level 3: Possibly Efficacious Treatments

Evidence criteria

3.1 At least one good randomized controlled trial showing the treatment to be superior to a wait list or no-treatment control group

AND

3.2 All five (5) of the ***Methods Criteria***

OR

3.3 Two or more clinical studies showing the treatment to be efficacious, with two or more meeting the last four (of five) ***Methods Criteria***, but none being randomized controlled trials *

Level 4: Experimental Treatments

Evidence criteria

4.1 Not yet tested in a randomized controlled trial *

OR

4.2 Tested in 1 or more clinical studies but not sufficient to meet level 3 criteria. *

Level 5: Treatments of Questionable Efficacy

5.1 Tested in good group-design experiments and found to be inferior to other treatment group and/or wait-list control group; i.e., only evidence available from experimental studies suggests the treatment produces no beneficial effect.

Note:

* The current review varied from these criteria in three ways: (a) adjusting for small sample sizes in effect size calculation rather than screening out low sample studies, (b) requiring all included studies to be randomized, thus eliminating criteria 3.3, 4.1, and 4.2, and (c) more broadly, considering the balance of evidence between positive and negative studies when mixed findings were present in the literature (e.g., positive results in one good experiment not outweighing a pattern of mixed findings.

TABLE 2

Trials included in the 1998 or 2008 reviews excluded from the current review

Trial	Developmental Level	Treatment Type	Modality	Reason for Exclusion from the Current Review
Asarnow et al. (2002)	Child	CBT	Group	Sample not restricted to youth with clinically elevated depression (i.e., minimum cut-off on the CDI not met).
Butler et al. (1980)	Child	CBT	Group	Sample not restricted to youth with clinically elevated depressive symptoms (e.g., youth could qualify with low scores on a measure of self-esteem).
Fine et al. (1991)	Adolescent	SS	Group	Trial did not include random assignment.
*Gillham, Hamilton et al. (2006)	Child	CBT	Group	Sample not restricted to youth with clinically elevated depressive symptoms (i.e., youth scoring at or above the 50th percentile on the depression symptom measure).
*Gillham, Reivich et al. (2006)	Child	CBT	Group	Sample not restricted to youth with clinically elevated depressive symptoms.
*Jaycox et al. (1994)	Child	CBT	Group	Sample not restricted to youth with clinically elevated depressive symptoms (e.g., youth could qualify with elevated scores on a measure of family conflict).
*King & Kirschenbaum (1990)	Child	BT	Group	Sample not restricted to youth with clinically elevated depressive symptoms.
Kowalenko et al. (2005)	Adolescent	CBT	Group	Trial was randomized at the school level, and a participating school forced randomization (i.e., insisted on providing the active intervention).
Lewinsohn et al. (1996)	Adolescent	CBT	Group	Outcomes not published in a peer reviewed journal.
Mufson et al. (1994)	Adolescent	IPT	Individual	Trial did not include random assignment.
Muratori et al. (2003)	Child	Psychodynamic	Individual	Sample not restricted to youth with clinically elevated depression (e.g., youth could qualify with elevated anxiety).
*Pfeffer et al. (2002)	Child	BGI	Group	Sample not restricted to youth with clinically elevated depression (e.g., youth included based on suicide of a family member).
Reynolds & Coats (1986)	Adolescent	CBT	Group	Sample not restricted to youth with clinically elevated depression (i.e., minimum cut-off on the BDI and RADS not met).
*Roberts et al. (2003)	Child	CBT	Group	Sample not restricted to youth with clinically elevated depression (e.g., sample defined by highest scoring youth without reporting a clinically elevated cutoff on screening measures).
*Sheffield et al. (2006)	Adolescent	CBT	Group	Sample not restricted to youth with clinically elevated depression (e.g., sample defined by highest scoring youth without reporting a clinically elevated cutoff on screening measures).
Stark et al. (1991)	Child	CBT	Group	Outcomes not published in a peer reviewed journal.
Weisz et al. (1997)	Child	CBT	Group	Sample not restricted to youth with clinically elevated depression (i.e., minimum cut-off on the CDI and CDRS-R not met).
*Yu & Seligman (2002)	Child	CBT	Group	Sample not restricted to youth with clinically elevated depressive symptoms (e.g., youth could qualify with elevated scores on a measure of family conflict).

Note: Prevention studies are designated by an asterisk. BDI = Beck Depression Inventory; BGI = Bereavement Group Intervention; BT = Behavior Therapy; CBT = Cognitive Behavioral Therapy; CDI = Children's Depression Inventory; CDRS-R = Children's Depression Rating Scale-Revised; IPT = Interpersonal Psychotherapy; Reynolds Adolescent Depression Scale = RADS; SS = Social Skills.

TABLE 3

Update of child depression treatment trials

Author(s)	Trial Type and Design	Target Population	Sample Characteristics	Treatment(s)	Assessment Time Point	Effect Size	Defining Response	Response Rate	NNT
CBT (Individual)									
Vostanis et al. (1996a, b); Vostanis et al. (1998)	RCT Completer	Youths from community clinics with diagnosed depressive disorder	*N* = 57 12.7 years old 56.0% female 87.7% Caucasian	CBT (9 sessions) NST	Posttreatment	MFQ = 0.051	Absence of current depression diagnosis	CBT: 87% NST: 75%	8
					9 Months Posttreatment	MFQ = −0.034		CBT: 71.5% NST: 75%	−29
					2 Years Posttreatment	MFQ = −0.351		CBT:74.1% NST: 85%	−9
Weisz et al. (2009)	RCT ITT	Therapists and youths from community clinics; youth with MDD, Dysthymia, and/or Minor Depression	*N* = 57 11.8 years old 56.0% female 33.0% Caucasian	CBT (10–15 sessions, PASCET) TAU	Posttreatment	CDI: 0.063	Absence of current depression diagnosis	PASCET: 73.3% TAU: 77.3%	−25

Note: CBT = Cognitive Behavioral Therapy; CDI = Children's Depression Inventory; ITT = Intent to Treat; MDD = Major Depressive Disorder; MFQ = Mood and Feelings Questionnaire; NNT = Number Needed to Treat; NST = Non-directive Supportive Therapy; PASCET = Primary and Secondary Control Enhancement Training; RCT = Randomized Controlled Trial; TAU = Treatment as Usual.

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TABLE 4

Update of adolescent depression treatment trials

Author(s)	Trial Type and Design	Target Population	Sample	Treatment(s)	Assessment Time Point	Effect Size	Defining Response	Response Rate	NNT
CBT (Individual)									
Brent et al. (2008); Emslie et al. (2010); Vitiello et al. (2011)	RCT ITT	MDD with failure to respond to 2 months of SSRI treatment	*N* = 334 15.9 years old 70.0% female 82.0% Caucasian 58.0% elevated SI 51.7% comorbid diagnosis	Individual CBT (12 sessions, Modular) + medication change Medication change, alone	Posttreatment	BDI: −0.047 CDRS-R: 0.089	CDRS-R (50% decrease) and CGI-I < 2	Combination: 54.8% Med: 40.5%	7
					3 Months Posttreatment *	Not reported		Combination: 36.7% Med: 41.1%	−23
					9 Months Posttreatment *	Not reported		Combination: 46.8% Med: 53.2%	−16
					15 Months Posttreatment *	Not reported		Combination: 58.9% Med: 63.3%	−23
Kerfoot et al. (2004)	RCT ITT	Therapists and youths from community clinics with MFQ ≥ 23	*N* = 52 13.9 years old 46.0% female	Therapist training in CBT (8 sessions, DTP) TAU	Posttreatment	MFQ = −0.060	Absence of residual depressive symptoms	CBT = 23.0% TAU = 20.0%	33
Merry et al. (2012)	RCT ITT	Treatment-seeking youths with elevated depressive symptoms (PHQ-9 ≥ 10)	*N* = 187 15.6 years old 66.0% female 59.0% New Zealand European	Technology-assisted CBT (7 modules) TAU (7 weeks)	Posttreament	MFQ: 0.318 CDRS-R: 0.109	CDRS-R (30% decrease)	CBT: 59.6% TAU: 54.8%	21
					3 Months Posttreatment	MFQ: 0.195 CDRS-R: 0.043		CBT: 81.9% TAU: 74.2%	13
Richardson et al. (2014)	RCT ITT	Youths meeting criteria for MDD or having elevated depressive symptoms (PHQ ≥ 10 and CDRS-R ≥ 42)	*N* = 101 15.3 years old 72.0% female 69.0% Caucasian	Collaborative care CBT intervention (12 months, CWD) TAU	Posttreatment	CDRS-R: 0.670	CDRS-R (decrease ≥ 50%)	Collaborative Care = 67.6% TAU = 38.6%	3
Shirk et al. (2014)	RCT ITT	Youths exposed to interpersonal trauma with MDD, Dysthymia, and/or Depression – NOS	*N* = 43 15.5 years old 83.7% female 49% Caucasian	CBT (12 sessions, modified) TAU	Posttreatment	BDI-II: −.156	Absence of depression diagnosis	CBT: 50.0% TAU: 48.0%	50

Author(s)	Trial Type and Design	Target Population	Sample	Treatment(s)	Assessment Time Point	Effect Size	Defining Response	Response Rate	NNT
Szigethy et al. (2014)	RCT ITT	Youths with a depressive disorder and IBD	*N* = 217 14.3 years old 51.0% female 89.4% Caucasian	CBT (12 sessions, PASCET) NST (12 sessions)	Posttreatment	CDRS-R: 0.191	CDRS-R ≤ 28	CBT: 53.5% NST: 47.1%	16
CBT (Group)									
Dobson et al. (2010)	RCT Completer	Youths with CES-D ≥ 24 not meeting criteria for MDD or Dysthymia	*N* = 46 15.1 years old 70% female	CBT (15 sessions, CWD) Group Supportive Treatment (15 sessions)	Posttreatment 3 Months 6 Months	CES-D: −0.195 CDI: −0.131 CES-D: −0.212 CDI: −0.132 CES-D: −0.500 CDI: −0.118	Response not defined	N/A	N/A
Rohde et al. (2014)	RCT	Youths with a depressive disorder and substance abuse	*N* = 170 16 years old 22% female 28% Hispanic	Functional Family Therapy followed by CWD (FFT/CWD) CWD followed by FFT (CWD/FFT) Coordinated treatment of FFT and CWD (CT)	Posttreatment 12 Months		CDRS-R ≤ 28	FFT/CWD = 44% CWD/FFT = 45% CT = 52% *** FFT/CWD = 60% CWD/FFT = 54% CT = 65% ***	
Stallard et al. (2012)	RCT ITT	SMFQ ≥ 5	*N* = 1064 14 years old 65% female 80% Caucasian	Classroom CBT (9 sessions, Resourceful Adolescent Program) Classroom Attention Control (9 sessions) Classroom Usual Curriculum (9 sessions)	Posttreatment	SMFQ in CBT: −0.230 SMFQ in Attention: −0.291	SMFQ < 5	CBT: 36.0% Attention: 29.0% Usual Curriculum: 43.0%	−14 −7
Stice et al. (2008, 2010)	RCT ITT	Youths with CES-D ≥ 20 not meeting criteria for a depressive disorder	*N* = 341 15.6 years old 56% female	CBT (6 sessions, CWD) NST (6 sessions)	Posttreatment	***CBT*** BDI: 0.630 K-SADS: 0.491 ***NST*** BDI: 0.199	Onset of MDD		

Author(s)	Trial Type and Design	Target Population	Sample	Treatment(s)	Assessment Time Point	Effect Size	Defining Response	Response Rate	NNT
			46% Caucasian 33% Hispanic	Self-directed reading (*Feeling Good* Handbook) Assessment, only	6 Months	K-SADS: 0.231 ***CBT*** BDI: 0.490 K-SADS: 0.389 ***NST*** BDI: 0.387 K-SADS: 0.324 ***Bibliotherapy*** BDI: 0.139 K-SADS: 0.387		CBT: 93.2% NST: 93.3% Bibliotherapy: 97.5% Assessment, alone: 86.9%	16 16 9
					12 Months	***CBT*** BDI: 0.112 K-SADS: 0.194 ***NST*** BDI: 0.250 K-SADS: 0.219 ***Bibliotherapy*** BDI: 0.187 K-SADS: 0.267			
					24 Months	***CBT*** BDI: 0259 K-SADS: 0.162 ***NST*** BDI: 0.090 K-SADS: 0.174 ***Bibliotherapy*** BDI: 0.111 K-SADS: 0.093		CBT: 86.0% NST: 85.0% Bibliotherapy: 97.0% Assessment, alone: 77.0%	11 13 5
Wijnhoven et al. (2014)	RCT ITT	Youth with current elevated depressive symptoms (16 ≤ CDI ≤ 19)	*N* = 102 11–15 years 100% female 98% Dutch	CBT (8 sessions) Assessment Only	Posttreatment 1 Month Posttreatment 6 Months Posttreatment	CES-D: .590 CES-D: .382 CES-D: .711	Response not defined	N/A	N/A
IPT									
Rosselló, Bernal, & Rivera-Medina (2008)	RCT ITT	Youth with (a) MDD, (b) CDI ≥ 13, or (c) clinically impairing depressive symptoms	*N* = 112 14.5 years old 55.4% female 100% Latino	Group IPT (12 sessions) Individual IPT (12 sessions) Group CBT (12 sessions) Individual CBT (12 sessions)	Posttreatment	CDI: −0.357	CDI < 12	IPT: 57.0% CBT: 62.0%	−20 (IPT) 20 (CBT)

Author(s)	Trial Type and Design	Target Population	Sample	Treatment(s)	Assessment Time Point	Effect Size	Defining Response	Response Rate	NNT
Young, Mufson, & Gallop (2010)	RCT ITT	Adolescents with current elevated depressive symptoms (16 ≤ CES-D ≤ 39) not meeting criteria for a depressive disorder	*N* = 57 14.5 years old 59.7% female 73.7% Hispanic 17.5% non-affective diagnosis	Group IPT-AST (10 sessions) School Counseling	Posttreatment	CES-D: 0.823 ** CDRS-R: 0.830 **	Absence of onset of depressive disorder		
					6 Months Posttreatment	Not reported		IPT-AST: 100% School Counseling: 80.9%	5
					18 Months Posttreatment	Not reported		IPT-AST: 91.7% School Counseling: 81.0%	9
Family therapy									
Diamond et al. (2010)	RCT ITT	Adolescents in primary care with current elevated depressive symptoms (BDI > 20) and suicidality (SIQ-JR > 31)	*N* = 66 15.1 years old 70% African American 47% depressive disorder diagnosis 62% suicide attempt	Individual ABFT (12 weeks) TAU	Posttreatment	BDI: 0.392	BDI ≤ 9	ABFT: 54.8% TAU: 31.0%	4

Note: ABFT = Attachment Based Family Therapy; BDI = Beck Depression Inventory; CBT = Cognitive Behavioral Therapy; CDI = Children's Depression Inventory; CDRS-R = Children's Depression Rating Scale, Revised; CES-D = Center for Epidemiologic Studies Depression Scale; CGI-I = Clinical Global Impression Improvement; CWD = Coping with Depression; DTP = Depression Treatment Program; IBD = Inflammatory Bowel Disease; IPT = Interpersonal Psychotherapy; ITT = Intent to Treat; K-SADS = Schedule for Affective Disorders and Schizophrenia for Children; MDD = Major Depressive Disorder; MFQ = Mood and Feelings Questionnaire; NNT = Number Needed to Treat; NST = Non-directive Supportive Therapy; PASCET = Primary and Secondary Control Enhancement Training; RCT = Randomized Controlled Trial; SI = Suicidal Ideation; SIQ-JR = Suicidal Ideation Questionnaire Junior; SMFQ = Short Mood and Feelings Questionnaire; SSRI = Selective Serotonin Reuptake Inhibitor; TAU = Treatment as Usual.

*Timeframe adjusted from baseline to posttreatment.

**Effect size as reported by the authors, insufficient information reported to be calculated for the current review.

***Effect sizes and NNT could not be calculated as the trial did not include a control arm.

TABLE 5

Evidence-base update for child depression treatment: Summary table

Level 1: Well-established	Level 2: Probably efficacious	Level 3: Possibly efficacious	Level 4: Experimental	Level 5: Not effective
		Overall CBT	Individual CBT	
		Group CBT	Psychodynamic therapy	
		Technology-assisted CBT	Family-based intervention	
		Behavior therapy		

Note: CBT = Cognitive Behavioral Therapy.

TABLE 6

Evidence-base update for adolescent depression treatment: Summary table

Level 1: Well-established	Level 2: Probably efficacious	Level 3: Possibly efficacious	Level 4: Experimental	Level 5: Not effective
Overall CBT	Group IPT	Bibliotherapy CBT	Technology-assisted CBT	
Individual CBT		Family-based interventions		
Group CBT				
Overall IPT				
Individual IPT				

Note: CBT = Cognitive Behavioral Therapy; IPT = Interpersonal Psychotherapy.

TABLE 7

Predictors of post-treatment effects in adolescent depression clinical trials

	Positive response	Negative response	Not statistically significant
Demographic factors			
Sex (female)			1, 7, 8, 9
Developmental level (older/higher)		9	
Ethnicity (minority status)			9
Characteristics of Depression			
Severity of symptoms (high)	9, 17[+]	2, 6, 7	
Global functioning (poor)		2, 9	
Age of onset of first MDE (younger)	7		6
Duration of MDE (shorter)	9		6
Melancholic features (more)		9	
Suicidality (current or lifetime)		2, 4, 9	
Non-suicidal self-harm		2	
Comorbidity			
Total comorbidity (more)	7, 16	9	
Dysthymia			9
Anxiety	16	6, 7, 9, ***19***	***19***
ADHD			13
Disruptive behavior (CD, ODD)			1, 9, 16
Substance use/abuse (high)			16
Cognitive and behavioral processes			
Cognitive distortions		6, 7, 12	7, 9
Hopelessness		2, 6, 9	
Problem solving	5	5	5
Pleasant activities	7		
Interpersonal processes and life stress			
Social functioning (poor)		***11***	***11***
Family conflict (more)		2, 10, ***11***	7, 9, 15
Marital discord			1
Family environment and structure (better)			10
Stressful life events (high)		***19***	
Trauma (none; see text)			3, 18
Other factors			
Treatment expectancy (good outcome)	9		
Readiness to change	14		
Referral source (clinical)		6	

Note: In cases where authors indicated that they planned to test a variable as a predictor but did not report the results, it was presumed that the variable was tested but was not statistically significant. Studies are numbered by first author in alphabetical order. In the body of the table, results

pertaining to IPT are indicated by ***bold italic*** formatting. Moderation results pertaining to family-based interventions are indicated by a $^{+}$: 1. Amaya et al. (2011); 2. Asarnow, Emslie, et al. (2009); 3. Barbe et al. (2004a); 4. Barbe et al. (2004b); 5. Becker-Weidman et al. (2010); 6. Brent et al. (1998); 7. Clarke et al. (1992); 8. Clarke et al. (1999); 9. Curry et al. (2006); 10. Feeny et al. (2009); ***11.*** Gunlicks-Stoessel et al. (2010); 12. Jacobs et al. (2009); 13. Kratochvil et al. (2009); 14. Lewis et al. (2009); 15. Rengasamy et al. (2013); 16. Rohde et al. (2001); 17. Rohde et al. (2014)$^{+}$; 18. Shamseddeen et al. (2011); ***19.*** Young, Mufson, & Davies (2006b).

TABLE 8

Moderators of post-treatment effects in adolescent depression clinical trials

	Effects enhanced	Effects diminished	Not statistically significant
Demographic factors			
Sex (female)	1		1, 7, 13+
Developmental level (older/higher)	2, ***17***		7, 13+
Ethnicity (minority status)		2	7, 13+
SES (income)	7		13+
Characteristics of Depression			
Severity of symptoms (high)	2, 7, ***17***		10*, 20+, ***22****
Global functioning (poor)			7
Duration of MDE (shorter)			7
Melancholic features (more)			7
Suicidality (current or lifetime)			4, 4+, 7
Non-suicidal self-harm		2	
Comorbidity			
Total comorbidity (more)	2		7, 19
Dysthymia			7
Anxiety	2, 6, ***23***		7, 19, ***23***
ADHD	14		2
Disruptive behavior (CD, ODD)	1		7, 19
Substance abuse (high)		10*	19
Cognitive and behavioral processes			
Cognitive distortions	7		6, 12, 13+
Hopelessness		2	6, 7, 13+
Problem solving			5
Pleasant activities			18
Interpersonal processes and life stress			
Social functioning (poor)	***11***		***11***
Perceived Social Support			10*
Family conflict (more)	***11***		7, 9, 13+, 18
Marital discord	1		1
Family environment (better)		9	9, 13+
Stressful life events (high)		10	
Trauma (none; see text)	2, 3, 21	16, 21	3, 8+, 16, 21
Parental depression (present)		6	6, 6+, 7
Other factors			
Treatment expectancy (good outcome)			7
Readiness to change			15

	Effects enhanced	Effects diminished	Not statistically significant
Referral source (clinical)			6, 7

Note: In cases where authors indicated that they planned to test a variable as a moderator but did not report the results, it was presumed that the variable was tested but was not statistically significant. Studies are numbered by first author in alphabetical order. Prevention studies are designated by an asterisk. In the body of the table, moderation results pertaining to CBT alone are presented in plain text; moderation results pertaining to IPT are indicated by ***bold italic*** formatting; moderation results pertaining to family therapy are indicated by a $^{+}$: 1. Amaya et al. (2011); 2. Asarnow, Emslie, et al. (2009); 3. Barbe et al. (2004a); 4. Barbe et al. (2004b)$^{+}$; 5. Becker-Weidman et al. (2010); 6. Brent et al. (1998); 7. Curry et al. (2006); 8. Diamond et al. (2012)$^{+}$; 9. Feeny et al. (2009); 10. Gau et al. (2012)*; ***11.*** Gunlicks-Stoessel et al. (2010); 12. Jacobs et al. (2009); 13. Kolko et al. (2000)$^{+}$; 14. Kratochvil et al. (2009); 15. Lewis et al. (2009); 16. Lewis et al. (2010); ***17.*** Mufson et al. (2004) 18. Rengasamy et al. (2013); 19. Rohde et al. (2001); 20. Rohde et al. (2014)$^{+}$; 21. Shamseddeen et al. (2011); ***22.*** Young, Mufson, & Davies (2006a)*; ***23.*** Young, Mufson, & Davies (2006b).