



# What do 30 years of randomized trials tell us about how psychotherapy improves youth depression? A systematic review of candidate mediators

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## Abstract

Psychotherapy for youth depression is only modestly efficacious. Investigating treatment mediators may guide improvement. Among 46 randomized trials of cognitive behavioral therapy and interpersonal psychotherapy with depressed youths, 74% measured candidate mediators (CMs), but only 17% analyzed CMs as mediators. Although four significant CMs emerged, findings were sparse, conflicting, and clouded by methodological issues. We see enormous untapped opportunity in the ample data collected but not yet analyzed using recommended methods. We propose exploiting existing data using mediation meta-analysis, broadening the range of CMs and the rigor of assessments, making measurement longitudinal and idiographic to clarify temporal precedence of CMs over outcomes and detect individual differences, and markedly altering journal and funder policies to promote change process and mechanism research.

## KEYWORDS

change mechanisms, change processes, children and adolescents, depression, evidence-based psychotherapies, mediators

## 1 | INTRODUCTION

Over the past several decades, researchers have made remarkable progress in learning what psychotherapies work

for which disorders in children and adolescents (herein, “youth”). These evidence-based psychotherapies (EBPs)—psychotherapies that have demonstrated efficacy in scientifically credible studies—have been identified and catalogued

in books (Weisz & Kazdin, 2017), journal special issues or sections (Southam-Gerow & Prinstein, 2014), and websites (e.g., <https://effectivechildtherapy.org/>). Among these, EBPs are cognitive behavioral therapy (CBT) and interpersonal psychotherapy (IPT) for youth depression (David-Ferdon & Kaslow, 2008; Weersing, Jeffreys, Do, Schwartz, & Bolano, 2016). CBT and IPT are among frontline interventions recommended for moderate-to-severe youth depression (Birmaher & Brent, 2007; National Institute for Clinical Excellence, 2015; Zhou et al., 2015).

Despite the emergence of EBPs for youth depression, there is still much room for improvement. The most comprehensive meta-analysis of youth psychotherapies to date (Weisz, Kuppens, et al., 2017) revealed that psychotherapies for youth depression produce on average only small–medium between-group treatment effects ( $g = 0.29$ )—significantly smaller than treatment effects for youth anxiety ( $g = 0.61$ ) and conduct problems ( $g = 0.46$ ). A recent meta-analysis (Eckshtain et al., 2020) estimated similarly modest mean effects of CBT for youth depression across 34 RCTs ( $g = 0.31$  and  $0.45$ , respectively, for CBT without and with additional treatment); although the mean effects of IPT were larger ( $g = 0.78$ ), this effect size was computed from only 5 RCTs. Furthermore, the mean effect size of therapies targeting depression has *decreased* over the past few decades of published RCTs (Weisz et al., 2019). These weak and declining effects highlight the need for increased research efforts to guide treatment development for youth depression.

## 1.1 | Studying change processes and mechanisms

Researchers have called for such efforts to be guided by deeper understanding of the change processes and mechanisms through which treatments produce desired change (Doss, 2004; Kraemer, Wilson, Fairburn, & Agras, 2002). In fact, investigating how treatments work has been championed by Kazdin and Nock (2003, p. 1,117) as “probably the best short-term and long-term investment for improving clinical practice and patient care.” According to Doss (2004), such investigations may entail examining three related constructs that ultimately lead to improved symptom or functional outcomes: (a) *Therapy change processes* refer to what the therapist does during sessions, such as therapist use of behavioral activation strategies or cognitive reframing techniques; (b) *client change processes* refer to what the client does during or as a result of sessions, such as client engagement in pleasant activities assigned as therapy homework or their ability to identify and modify negative thoughts in session; and (c) *change mechanisms* refer to changes in client characteristics and skills outside

### Public Health Significance

- We reviewed candidate mediators that may explain how psychotherapies for youth depression work and found that they were often measured but rarely tested in research trials.
- Although several significant mediators were found in a sample of largely cognitive behavioral therapy trials, these findings are inconclusive given the limited strength of the evidence.
- We propose changing scientific practices and policies to fully examine existing data and to collect and analyze new data on candidate mediators using methods that maximize information value.

of sessions, such as client everyday engagement in pleasant activities or their overall level of negative cognition or cognitive reframing skill usage. We used these three terms as defined by Doss (2004) in the present review, along with *therapy–client change process* to refer to therapeutic alliance because it results from the actions and experiences of both therapist and the client.

Earlier research often assessed change processes as predictors of outcome and change mechanisms as a type of outcome alongside symptom severity and adaptive functioning; subsequently, mediation analysis became the recommended method for assessing candidate processes and mechanisms (Crits-Christoph, Connolly Gibson, & Mukherjee, 2013; Doss, 2004; Kraemer et al., 2002; Weersing & Weisz, 2002). Mediation tests, in the context of RCTs, demonstrate whether the treatment changed the process or mechanism relative to the control condition, whether the process or mechanism was in turn associated with outcome, and whether the relationship between the process or mechanism and outcome accounts for the treatment–outcome relationship. Furthermore, mediation methods have advanced considerably from Baron and Kenny’s (1986) causal steps approach to approaches with higher power, fewer assumptions, and broader applicability to a range of study designs and situations. These improved approaches include significance testing of the conjoint mediational pathway (i.e., the indirect effect) rather than testing one path at a time and using bootstrapping rather than normal distributions to generate confidence intervals of the indirect effect (Hayes, 2009). The conflation of mediators, a statistical construct, with the substantive concepts of change processes and mechanisms, prompted multiple criteria to be proposed for change processes or mechanisms, including comparison of plausible candidate processes and mechanisms, frequent assessments to establish temporal precedence of change processes and mechanisms over outcomes, and

experimental manipulation to demonstrate causal relationships (Kazdin, 2007).

## 1.2 | Systematic and meta-analytic reviews of change processes and mechanisms

Undoubtedly, resource-intensive research programs will be needed to satisfy the abovementioned criteria for even a single change process or mechanism; such programs should therefore be guided strategically by extant research. Yet, the current literature poses considerable challenges to researchers looking for this guidance. Existing reviews commonly do not report systematic search and screening procedures (e.g., Webb, Auerbach, & DeRubeis, 2012), thus leaving it unclear whether all relevant portions of the evidence base have been included; those that do often focus on one type of change process or mechanism such as the therapeutic alliance (e.g., McLeod, 2011), thus limiting comparisons among different candidate processes or mechanisms.

We are aware of only three systematic or meta-analytic reviews of change processes or mechanisms of therapies for youth depression. Weersing and Weisz (2002) conducted a systematic review of RCTs testing EBPs targeting various youth problems. They reported that 12 RCTs of CBT and one RCT of CBT and IPT for youth depression assessed candidate mechanisms (e.g., cognitive distortions, self-concept, social adjustment, pleasant activities) and 11 of these found that the EBP changed the candidate mechanism compared to controls, but only two RCTs assessed whether the candidate mechanism predicted outcome and only one RCT tested the candidate mechanism as a mediator. Weersing et al. (2016) conducted a more updated but narrower systematic review that included only change mechanisms tested as mediators in RCTs where all participants met diagnosis for a depressive disorder or met clinical cutoffs on standardized symptom measures or were identified by a mental health provider as experiencing clinical depression. They located five RCTs of CBT (and none of IPT) that reported formal mediation tests, but findings were mixed for cognitive ( $n = 5$ ) and behavioral ( $n = 2$ ) candidate mechanisms, and the motivational ( $n = 1$ ) candidate mechanism was a significant mediator for a CBT plus SSRI combination treatment, compared to placebo. Finally, Chu and Harrison's (2007) meta-analysis of 14 RCTs demonstrated that CBT had significant larger-than-medium effects on symptom outcomes ( $d = 0.60$ ), small-to-medium effects on cognitive candidate mechanisms ( $d = 0.35$ ), and nonsignificant effects on behavioral ( $d = 0.01$ ) and coping ( $d = 0.05$ ) candidate mechanisms. They noted only three RCTs that examined treatment mediators.

To summarize, a growing body of RCT literature published up to the mid-2000s indicated that CBT changed cognitive

mechanisms in the expected direction for depressed youth. However, effects on behavioral and coping mechanisms were equivocal. Moreover, only a minority of RCTs published up until 2014, all testing CBT, tested candidate mechanisms as mediators; they produced inconsistent results and failed to establish temporal precedence. Candidate processes other than therapeutic relationship variables have been omitted from systematic and meta-analytic reviews of EBPs for youth depression. In the past decade, which candidate processes and mechanisms have continued to be assessed, for which EBPs, and how frequently, regardless of whether they were tested as mediators? Have researchers been using the newer, improved mediation tests? How can all these data be harnessed and integrated to draw meaningful conclusions about how EBPs for youth depression work?

## 1.3 | The present systematic review

To address these questions, we conducted a systematic review of candidate change processes and mechanisms in RCTs of EBPs for youth depression. Similar to previous work (Weersing & Weisz, 2002), we focused on EBPs because they have a solid foundation of evidence supporting their efficacy; thus, a logical next step would be to further our understanding of how they work to maximize their effects. We considered EBPs to be CBT and IPT—designated as “well-established” or “probably efficacious” therapies for child or adolescent depression in the latest evidence base update endorsed by the Society of Clinical Child and Adolescent Psychology (Weersing et al., 2016). We updated the three prior systematic and meta-analytic reviews by Chu and Harrison (2007), Weersing and Weisz (2002), and Weersing et al. (2016) to include RCTs published through 2016 and expanded the scope to include all possible change processes and mechanisms—even those not theoretically emphasized in CBT and IPT—regardless of whether they were subjected to mediation testing. For brevity, we refer to these candidate change processes and mechanisms as candidate mediators (CMs). Our rationale for broad inclusion of possible CMs stems from findings that EBPs can have effects on CMs not theoretically emphasized or targeted by that EBP; if relationships found between treatment, CM, and outcome are specific to that CM, then that CM is more likely to have causal effects on outcomes (Kazdin & Nock, 2003). Our aims were (a) to document which CMs were measured in RCTs of psychotherapy for youth depression, what proportion of RCTs measured CMs, and when they were measured; and (b) to examine which CMs were tested as mediators by RCT investigators, what proportion of RCTs that measured CMs subjected them to mediation testing, how mediation testing was conducted, and what results were reported.

## 2 | METHOD

### 2.1 | Inclusion and exclusion criteria

RCTs had to meet the following inclusion criteria: (a) randomly assigned individuals to treatment conditions; (b) tested CBT or IPT either as a standalone treatment or in combination with another therapy (e.g., CBT plus separate parent group intervention); (c) employed a control condition consisting of waitlist/no treatment, attention or pill placebo, nondirective supportive therapy, case management, or usual care; (d) sampled participants who were selected or referred due to diagnosis of depressive disorder or elevated symptoms of depression; (e) sampled children or adolescents with a mean age between 4 and 18 years; (f) assessed at least one continuous outcome measure of depression symptoms and one continuous CM measure; and (h) outcome papers were published in English language peer-reviewed journals.

We excluded treatment conditions involving an EBP combined with medication because it is unclear how EBPs may interact with medication to improve symptoms and because it was unlikely that we would find a large number of studies assessing the same combination of EBP plus medication. Also excluded were RCTs that only compared an EBP to another psychotherapy with a specific theoretical rationale, or to a specific medication, as there would not be a clear control condition. Mediation analyses are best conducted, and their results interpreted, in the context of a treatment group–control group comparison. In addition, we excluded RCTs that selected youths on the basis of exhibiting *either* depression symptoms *or* some other problem (e.g., anxiety, negative thinking) as the data from those studies may go beyond what is found with depressed youth.

### 2.2 | Literature search and retrieval

RCTs meeting the above criteria were drawn from a comprehensive meta-analytic database of RCTs testing psychological therapies for youth depression, anxiety, conduct problems, and attention-deficit hyperactivity disorder (ADHD), with outcome papers published from 1963 through 2016. Literature searches were conducted using a set of 21 psychotherapy-related terms (e.g., psychotherapy, counseling) in PsycINFO, and the MeSH indexing system in PubMed, with search limits for clinical or outcome assessment, child and adolescent age group, human subjects, and published in English (see Weisz et al., 2019 for details). The abstracts retrieved were reviewed by one research assistant, and if determined to report a potentially eligible RCT, two research assistants reviewed the full-text article independently, resolving discrepancies through discussion or consultation with a third research assistant.

Because the database was focused on post-treatment and follow-up outcomes, information on CMs reported in secondary analysis papers might have been missed. Thus, we undertook additional literature searches for the present review. For each included RCT, we used PsycINFO and PubMed to search for records of articles that cited the outcome paper(s) or those that were authored or co-authored by the first or second author of the outcome paper(s) from the year the earliest outcome paper was published. Abstracts were screened to decide whether to retrieve the full-text article, which were in turn reviewed to determine if they reported methods or data from any included RCT. We also followed reference trails of included RCTs and of reviews of youth depression EBPs, change processes, and change mechanisms. Finally, we contacted the authors of the included RCTs and the National Institute of Mental Health (NIMH) data repositories to request information. We also retrieved dissertations or theses from the university libraries, Proquest Dissertations and Theses electronic database, or directly from the authors. A flowchart detailing the inclusion and exclusion of RCTs and related articles are detailed in Appendix 1.

### 2.3 | Coding of study characteristics and candidate mediators

Studies were coded for characteristics of participants, treatment/control conditions, and outcome measures. Coders were eight postdoctoral fellows and graduate students in psychology who each independently coded 20 to 30 RCTs to establish intercoder reliability before coding the remainder individually. Coder disagreements for the reliability sample were resolved by discussion and consultation with one another. Target problem ( $k = 0.89$ ) and the treatment and control condition codes ( $k = 0.83$ ) were used to select RCTs that targeted depression and that tested CBT or IPT against an appropriate control condition for inclusion into the present review. We also coded mean participant age (ICC = 0.99), youngest age (ICC = 1.00), oldest age (ICC = 0.99), percent male/female (ICC = 0.95), percent participants who are Caucasian (ICC = 0.87), African-American (ICC = 1.00), Latino (ICC = 0.86), Asian (ICC = 0.70), Native American (ICC = 0.57), and of other (ICC = 0.73) and unknown race/ethnicity (ICC = 0.84), geographical location ( $k = 0.88$ ), recruited versus clinically referred/treatment-seeking versus court-mandated/incarcerated ( $k = 0.66$ ), and diagnosis of depressive disorder required ( $k = 0.79$ ).

Additional screening and coding were performed to identify and characterize CMs and outcome measures by undergraduate or postbachelor's degree research assistants. Literature from the included RCTs was screened to determine whether any formal tests of mediation were conducted, in which the predictor is treatment condition, the mediator

**TABLE 1** Candidate mediators and the frequency with which they were measured at various time points in the included sample of 34 randomized controlled trials

Mediator Category	Explanation and Examples	Putative Role	Frequency (% RCTs)			
			Overall	Pre	Mid	Post
Negative Cognition	Youth cognitive distortions, dysfunctional attitudes, pessimistic attributional style, external locus of control, negative info-processing bias, hopelessness, rumination, negative self-concept/self-esteem, perfectionism	Change mechanism of CBT	26 (76.5)	26 (76.5)	4 (11.8)	26 (76.5)
Social Engagement	Youth participation in social activities, positive self-presentation, social adjustment, social functioning, interpersonal relationship quality, social support, loneliness, sociometric ratings of liking, prosocial behavior	Change mechanism of CBT and IPT	18 (52.9)	18 (52.9)	4 (11.8)	17 (50.0)
Family Functioning	Family/parent expressed emotion, communication problems, relationship quality, lack of cohesion	Change mechanism of IPT	18 (52.9)	18 (52.9)	4 (11.8)	17 (50.0)
Problem-Solving	Youth skill or effort taken to change external conditions, active or primary control coping, conflict resolution skills, generating solutions, asking others for help to solve a problem, family problem-solving, action stage of change	Change mechanism of CBT and IPT	8 (23.5)	8 (23.5)	3 (8.8)	8 (23.5)
Treatment Expectancy	Extent to which one expects to benefit from treatment or prefers a treatment over another, attitudes toward treatment	Client change process and common factor	8 (23.5)	7 (20.6)	2 (5.9)	1 (2.9)
Reframing	Youth skill or effort in changing thinking to deal with stressors or feelings, secondary control coping, distraction, finding the silver lining, alternative explanations, acceptance, identifying negative thoughts, positive problem orientation, reappraisal	Change mechanism of CBT	6 (17.6)	6 (17.6)	2 (5.9)	5 (14.7)
Avoidance	Youth wishful thinking, denial or avoidance of the problem, precontemplation stage of change.	Change mechanism of CBT	5 (14.7)	5 (14.7)	2 (5.9)	5 (14.7)
Pleasant Activities	Youth activity scheduling, engagement in enjoyable activities in general (though not specifically social activities)	Change mechanism of CBT	5 (14.7)	5 (14.7)	1 (2.9)	5 (14.7)
Motivation to Change	Youth desire to reduce depression or change behavior, contemplation stage of change.	Candidate mechanism and common factor	3 (8.8)	3 (8.8)	1 (2.9)	0
Impulsive Coping	Youth finding solutions to problems in a hurried, unsystematic manner, inadequate outcomes monitoring outcomes	Change mechanism not targeted by depression EBPs	2 (5.9)	2 (5.9)	2 (5.9)	2 (5.9)
Expression of Affect	Youth talking/writing about feelings, communicating it through other creative outlets, not suppressing emotions.	Change mechanism of IPT	2 (5.9)	2 (5.9)	1 (2.9)	2 (5.9)

(Continues)

TABLE 1 (Continued)

Mediator Category	Explanation and Examples	Putative Role	Frequency (% RCTs)				
			Overall	Pre	Mid	Post	FU
Therapeutic Alliance	The collaborative and affective relationship between the therapist and the parent/youth, agreement between therapist and parent/youth about goals, techniques implemented to achieve goals, and the therapist–parent/youth bond	Therapy–client change process and common factor	2 (5.9)	1 (2.9)	1 (2.9)	1 (2.9)	0
Role Engagement	Youth or parent involvement in therapy, treatment compliance, homework completion, knowledge of therapy content.	Client change process and common factor	2 (5.9)	0	1 (2.9)	1 (2.9)	0
Maintenance of Gains	Youth effort to consolidate behavioral change, maintenance stage of change	Change mechanism and common factor	1 (2.9)	1 (2.9)	1 (2.9)	0	0
Alexithymia	Youth difficulty identifying emotions	Change mechanism not targeted by depression EBPs	1 (2.9)	1 (2.9)	0	1 (2.9)	0
Attitudes Toward School	Youth perception of and feelings toward school and teachers, comfort with school-related matters	Change mechanism not targeted by depression EBPs	1 (2.9)	1 (2.9)	0	1 (2.9)	1 (2.9)
Health Behaviors	Youth healthy eating, regular exercise, number of hours of sleep	Change mechanism of CBT	1 (2.9)	1 (2.9)	0	1 (2.9)	1 (2.9)
Executive Functioning	Youth cognitive processes including attentional control, inhibition, working memory, and cognitive flexibility.	Change mechanism not targeted by depression EBPs	1 (2.9)	1 (2.9)	0	1 (2.9)	0
Theory of Mind	Youth perception of mental state of another person	Change mechanism not targeted by depression EBPs	1 (2.9)	1 (2.9)	0	1 (2.9)	0
Perceived Stigma	Youth perception of acceptance by others if they thought the youth had depression	Change mechanism not targeted by depression EBPs	1 (2.9)	1 (2.9)	0	0	0
Therapist CBT Strategies	Therapist adherence to, competence in, or knowledge of a CBT protocol	Therapy change process of CBT	1 (2.9)	0	1 (2.9)	0	0
Therapist Client-Centered Strategies	Therapist adherence to, competence in, or knowledge of a client-centered therapy protocol	Therapy change process of non-EBP	1 (2.9)	0	1 (2.9)	0	0
Therapist Family Systems Strategies	Therapist adherence to, competence in, or knowledge of a family systems therapy protocol	Therapy change process of non-EBP	1 (2.9)	0	1 (2.9)	0	0
Therapist Psychodynamic Strategies	Therapist adherence to, competence in, or knowledge of a psychodynamic therapy protocol.	Therapy change process of non-EBP	1 (2.9)	0	1 (2.9)	0	0

(Continues)

TABLE 1 (Continued)

Mediator Category	Explanation and Examples	Putative Role	Frequency (% RCTs)				
			Overall	Pre	Mid	Post	FU
Group Cohesiveness	Youth perception of belonging to the group, acceptance by group members, and attractiveness of the group	Client change process and common factor	1 (2.9)	0	1 (2.9)	0	0
Research Understanding	Youth and parent knowledge of RCT purpose, design, treatment options, consent process, benefits and risks	Change mechanism not targeted by depression EBPs	1 (2.9)	0	1 (2.9)	0	0

Abbreviations: CBT, cognitive behavioral therapy; FU, follow-up assessment; IPT, interpersonal psychotherapy; mid, during treatment assessment; pre, pretreatment assessment; post, post-treatment assessment.

variable is a CM, and the outcome is a depression symptom measure. Four research assistants each screened 20 RCTs for tests of treatment mediation and achieved substantial agreement ( $k = 0.75$ ).

Next, CMs were identified, regardless of whether they were tested as mediators by RCT authors, as were depression symptom outcomes, or if unavailable, internalizing symptom outcomes. To cast a wide net for CMs, coders included all continuous variables measured for both the treatment and control group that could potentially change as a result of treatment (regardless of whether there was change, or whether the variable was measured more than once). We excluded the following variables: (a) participant demographics, side effects or adverse events, service use, economic and time cost measures, and parent or sibling variables that do not pertain to the youth or to their relationship with the youth; (b) outcome measures of overall symptoms, of a target problem other than depression, of general youth functioning, or of treatment satisfaction; (c) percent of participants meeting diagnosis or clinical cutoff for a depressive disorder; (d) time-to-event variables (e.g., length of time to recurrence of disorder); (e) measures administered to only one treatment group, because mediation effects in RCTs are examined for one treatment in relation to the other (Kraemer et al., 2002); and (f) treatment session attendance because this could reflect dose of therapy, youth or parent engagement, or therapists' judgment of the amount of treatment needed if number of sessions was not fixed. Three research assistants coded 2 RCTs for practice and another 12 RCTs for establishing intercoder reliability of variable selection ( $k = 0.69$ ), before individually coding the rest of the sample.

All selected outcomes and CMs were also coded for whether their source was the youths themselves, caregivers, siblings, peers, teachers, therapists, researchers, or life-event data ( $k = 0.89$ ). Coders also indicated whether the outcomes and CMs were measured at pretreatment ( $k = 0.94$ ), during treatment ( $k = 0.88$ ; which we term the "mid-treatment" time point for brevity although the measure could have been given at any time during treatment), at post-treatment ( $k = 0.72$ ), and at follow-up ( $k = 0.73$ ), and number of weeks from pretreatment to each subsequent time point ( $ICC = 0.86-0.98$ ). If multiple mid-treatment time points were available, the one closest to the numerical mid-point of the number of sessions or weeks of treatment was selected.<sup>1</sup> If multiple follow-up time points were available, then coders selected the one closest to six months after post-treatment, which was most common (44%) in the database.

We created 26 mediator categories ( $k = 0.91$ ; see Table 1) with reference to reviews of change processes and mechanisms in therapies for youth depression (Chu & Harrison, 2007) and adult depression (Crits-Christoph et al., 2013), and to chapters describing EBPs for depression among youths (Clarke & DeBar, 2010) and adults (Dimidjian, Martell, Addis, &

Herman-Dunn, 2008). We included an “Other” category to capture plausible change processes and mechanisms that did not fit into existing categories and then decided by consensus whether to combine each one with an existing mediator category or create a new category for it.

### 3 | RESULTS

#### 3.1 | Description of study sample

Among the 46 RCTs that compared an EBP to a control condition for youth depression, 34 RCTs (73.9%), testing a total of 3,868 youth in 39 EBP conditions and 35 eligible control conditions, measured a CM and were included in the present review. The literature searches yielded 128 journal articles and 9 dissertations or theses published from 1986 to 2016 relating to the included RCTs (marked with an asterisk in the Reference section or listed in Appendix 2).

The pooled participant sample had a mean age of 13.9 years ( $SD = 2.2$ ); the participants across all RCTs ranged from 7 to 21 years old. Nearly two-thirds (64.7%) of the samples were primarily adolescents (i.e., mean age  $\geq 13.0$  y). Just under half the youths were male ( $M = 42.0\%$ ,  $SD = 13.2$ ). Caucasian youths made up nearly half the sample ( $M = 42.4\%$ ,  $SD = 37.0$ ), with other youths identifying as Latino ( $M = 17.1\%$ ,  $SD = 29.7$ ), African-American ( $M = 7.6\%$ ,  $SD = 13.1$ ), Asian ( $M = 4.5\%$ ,  $SD = 10.2$ ), Native American ( $M = 0.3\%$ ,  $SD = 1.7$ ), other race/ethnicity ( $M = 11.6\%$ ,  $SD = 21.8$ ), or of unknown race/ethnicity ( $M = 16.4\%$ ,  $SD = 35.5$ ). The majority (73.5%) of RCTs were conducted in North America; the remainder were conducted in Australia or New Zealand (14.7%), Europe (5.9%), and Asia (5.9%). Most (70.6%) participant samples comprised youths who were recruited for the RCT, 23.5% comprised clinically referred or treatment-seeking youths, 2.9% comprised juvenile justice youths, and 2.9% comprised youths recruited through unknown means. One-third (32.4%) of the RCTs required youths to be diagnosed with a depressive disorder, including major depressive disorder, dysthymia, depressive disorder—not otherwise specified, and adjustment disorder with depressed mood from the Diagnostic and Statistical Manual of Mental Disorders (DSM, American Psychiatric Association, 1994), or minor depressive disorder and intermittent depressive disorder from research diagnostic criteria (RDC; Spitzer, Endicott, & Robins, 1978).

Most (82.1%) treatment conditions involved CBT; IPT comprised only 17.9% of treatment conditions. Of the 32 CBT conditions, 59.4% were delivered in group format, 21.9% were delivered individually, 9.4% as bibliotherapy, and 9.4% as computerized programs. The seven IPT conditions were delivered in either group (71.4%) or individual (28.6%) format. The most common control condition was no treatment

or waitlist (40.0%), followed by usual care (31.4%), attention placebo (17.1%), and nondirective supportive therapy (5.7%); pill placebo (2.9%) and case management (2.9%) were each employed in only one control condition. Study characteristics and treatment conditions for each RCT are detailed in Appendix 3.

The remaining 12 RCTs that did not report measuring any CM but otherwise met all other inclusion criteria tested 2,162 youths in 14 EBP conditions and 15 eligible control conditions (see Appendix 4 for list of articles). Comparing to these 12 RCTs, the 34 included RCTs had a significantly larger proportion of Latino participants (4.6% vs. 17.1%). No significant differences were found on other study characteristics (all  $p > .05$ ). Our included study sample thus appears to be somewhat more diverse, but still largely generalizable to the broader evidence base—at least to CBT trials for youth depression, given the small numbers of IPT trials. We note that two IPT trials did not meet inclusion criteria due to not having a control group (Gunlicks-Stoessel, Mufson, Westervelt, Almirall, & Murphy, 2016; Rosselló, Bernal, & Rivera-Medina, 2008).

#### 3.2 | Description of outcomes and candidate mediators

We coded a total of 79 outcome measures and 247 CMs. All 34 RCTs measured at least one outcome at pretreatment and at post-treatment, 67.6% measured at least one outcome at follow-up, and only 20.6% measured at least one outcome during treatment. The relative frequency with which CMs were measured at each time point mirrored those of outcomes: All 34 RCTs measured at least one CM at pretreatment, and 97.1%, 61.8%, and 26.5% measured at least one CM at post-treatment, follow-up, and during treatment, respectively. On average, the mid-treatment, post-treatment, and follow-up measures were given at 5.6 weeks ( $SD = 4.0$ ), 12.1 weeks ( $SD = 7.9$ ), and 35.5 weeks ( $SD = 20.2$ ) after pretreatment. The most common informant was the youth (69.6% outcomes, 78.5% CMs), then the caregiver (17.7% outcomes, 15.8% CMs), researchers (11.4% outcomes, 3.6% CMs), and school staff (1.3% outcomes, 0.8% CMs). A few CMs were completed by therapists (0.8%) and an unreported informant (0.4%).

Table 1 lists descriptions and examples of each mediator category, frequency of measurement at various time points, and whether each category is a putative therapy or client change process or change mechanism. Negative cognition is the most common mediator category, followed by social engagement and family functioning—all were measured in 18 or more RCTs. Moderately common mediator categories, measured by three to eight RCTs, comprise problem-solving, treatment expectancy, reframing, avoidance, pleasant

activities, and motivation to change. Infrequently measured categories include change mechanisms not typically targeted by EBP of depression (e.g., impulsive coping) and change processes, including common factors (e.g., role engagement) and those specific to an EBP (e.g., therapist CBT strategies) or a non-EBP (e.g., client-centered strategies). Mid-treatment assessments—particularly relevant for understanding change processes and mechanisms—although available for most (76.9%) mediator categories, were only conducted by one to four RCTs per category.

### 3.3 | Mediation assessed by study authors

Although 34 RCTs (73.3%) measured a CM at any time point, only eight (17.4%) statistically analyzed any CM as a mediator. Results were reported in ten articles (see Table 2).

As expected, the three earlier mediation articles (Ackerson, Scogin, McKendree-Smith, & Lyman, 1998; Kolko, Brent, Baugher, Bridge, & Birmaher, 2000; Yu & Seligman, 2002) used Baron and Kenny's (1986) causal steps approach. Two later published mediation articles (Jacobs et al., 2009; Lewis et al., 2009) used another causal steps approach advocated by Kraemer et al. (2002), which builds on the Baron and Kenny approach by adding logical criteria (e.g., mediator should be a postrandomization construct) and a step testing for moderated mediation (i.e., if the mediator variable or the mediator variable  $\times$  treatment condition interaction predicts outcome, then the criterion of the mediator predicting the outcome would be met). Four other articles combined a causal steps approach similar to Baron and Kenny's approach with a significance test of the indirect effect. Specifically, Kaufman, Rohde, Seeley, Clarke, and Stice (2005) determined whether criteria for initial steps were met, if so, they tested whether the difference between the total effect and direct effect (equivalent to the indirect effect) differed from zero. Stice, Rohde, Seeley, and Gau (2010) required change in the mediator variable to predict change in outcome in the intervention condition only, not in the full sample; when initial criteria were met, they tested the difference between the total and direct effects; when the difference was significant, they assessed whether meaningful change in the mediator variable preceded meaningful change in the outcome. Dietz et al. (2014) and Dietz, Weinberg, Brent, and Mufson (2015) tested the significance of the indirect effect when initial steps were met; in their 2014 paper, they used bias-corrected bootstrapping to generate confidence intervals of the indirect effect. Finally, Duong et al. (2016) tested the significance of the indirect effect without requiring initial steps.

The most commonly assessed mediator category was negative cognition. Six RCTs, all testing some form of CBT, assessed 12 measures of negative cognition and found five

to be significant mediators. The findings are mixed not only between studies, but also within studies and within measures. For example, Kaufman, Rohde, Seeley, Clarke, and Stice (2005) and Stice et al. (2010) found that negative automatic thoughts mediated reductions in depression symptoms when comparing group CBT to control, whereas Ackerson et al. (1998) and Stice et al. (2010) found that they did not when comparing CBT bibliotherapy to control. Ackerson et al. (1998) found that dysfunctional attitudes was a mediator for CBT bibliotherapy—though only for one of three depression outcome measures—whereas Kaufman et al. (2005) and Jacobs et al. (2009) found that they were not a mediator for group and individual CBT, respectively.

The next most commonly assessed as mediators were social engagement and family functioning—each assessed by three RCTs. Of the five measures coded under our mediator category of social engagement, only social impairment, based on a subscale of a social functioning measure, was a significant mediator of individual family-based IPT; peer impairment, based on another subscale of the same measure, was not (Dietz et al., 2015). Social skills and loneliness did not mediate the effects of CBT in two RCTs (Kaufman et al., 2005; Stice et al., 2010; although complete testing of loneliness as a mediator of CBT was not reported by Stice et al., 2010). Numerous family functioning measures were found not to be significant mediators in one RCT of family-based IPT (Dietz et al., 2015) and two RCTs of CBT (Kaufman et al., 2005; Kolko et al., 2000).

Problem-solving and pleasant activities were each assessed in two RCTs of CBT. Two out of four measures of problem-solving significantly mediated outcome improvement—with qualifications. The action stage of change, although conceptualized by Lewis et al. (2009) as a motivational construct, was measured by items that closely resemble those in problem-solving measures (e.g., "I am actively working on my problems") and was therefore categorized in the present review as problem-solving. This variable mediated outcomes in omnibus tests involving all four treatment conditions in the Treatment for Adolescents with Depression Study; it is unclear whether mediation would still be significant for pairwise comparisons between CBT only and control. In another study (Dietz et al., 2014), adolescent problem-solving mediated rates of remission for youths whose mothers had mild-to-moderate depression symptoms at pretreatment, but not for youths whose mothers had severe depression. Pleasant activity measures were assessed four times and found to be a significant mediator for group CBT but not for CBT bibliotherapy in one trial (Stice et al., 2010) and not in another CBT trial (Kaufman et al., 2005). Categories examined by one RCT each (e.g., avoidance, motivation to change, therapeutic alliance) were all nonsignificant as mediators. The remaining categories (e.g., reframing, treatment credibility, therapist strategies) were not analyzed as treatment mediators.

TABLE 2 Randomized controlled trials that tested treatment mediators and summary of findings

Outcome Paper	Treatment Conditions	Treatment Effect?	Mediation Paper	Candidate Mediator	Significant Mediator?	Finding (treatment effects described reflect comparison to control)
<i>Negative cognition</i>						
Ackerson et al. (1998)	CBT bibliotherapy versus Waitlist	Yes	Ackerson et al. (1998)	1. ATQ 2. DAS	No Yes	CBT did not reduce negative thoughts CBT reduced dysfunctional attitudes, which mediated decrease in depression symptoms measured by the CDI but not CBCL-D or HRSD
Brent et al. (1997)	CBT individual versus Nondirective supportive therapy	Yes	Kolko et al. (2000)	1. Children's Negative Cognitive Error Questionnaire 2. Beck Hopelessness Scale	No No	CBT reduced cognitive distortions, but authors did not continue mediation test as treatment effect was NS in mediation paper CBT did not reduce hopelessness
Rohde, Clarke, Mace, Jorgensen, and Seeley (2004)	CBT group versus Case management	Yes	Kaufman et al. (2005)	1. ATQ 2. DAS (brief)	Yes No	CBT reduced negative thoughts, which mediated decrease in depression symptoms CBT did not reduce dysfunctional attitudes
Stice, Rohde, Seeley, and Gau (2008)	1. CBT group versus No treatment 2. CBT bibliotherapy versus No treatment	Yes No	Stice et al. (2010) Stice et al. (2010)	ATQ (brief) ATQ (brief)	Yes No	CBT reduced negative thoughts, which mediated decrease in depression symptoms, but change in negative thoughts did not precede change in outcome for most participants CBT did not reduce negative thoughts, but reduced negative thoughts predicted decreases in depression symptoms
TADS Team (2004)	CBT individual versus Pill placebo	No	Jacobs et al. (2009)	DAS Perfectionism scale	No	CBT did not decrease perfectionism, treatment effect across four treatment conditions decreased when perfectionism change scores were added to model, but effect size of CBT was not different with change scores added
Yu and Seligman (2002)	CBT group versus Waitlist	Yes	Yu and Seligman (2002)	1. CASQ—Negative scale 2. CASQ—Positive scale 3. Difference between CASQ Positive and Negative scale scores	Yes No Yes	CBT reduced negative explanatory style, which mediated decrease in depression symptoms CBT did not increase positive explanatory style CBT reduced negative explanatory style relative to positive explanatory style, which mediated decrease in depression symptoms
<i>Social Engagement</i>						

(Continues)

TABLE 2 (Continued)

Outcome Paper	Treatment Conditions	Treatment Effect?	Mediation Paper	Candidate Mediator	Significant Mediator?	Finding (treatment effects described reflect comparison to control)
Dietz et al. (2015)	IPT individual family-based versus Nondirective supportive therapy	Yes	Dietz et al. (2015)	1. SAS-SR—Peer Impairment scale 2. SAS-SR—Social Impairment scale	No Yes	IPT reduced peer impairment, which was associated with decrease in depression symptoms, but mediation was NS IPT reduced social impairment, which mediated decrease in depression symptoms
Rohde et al. (2004)	CBT group versus Case management	Yes	Kaufman et al. (2005)	PES—Social Skills scale	No	CBT did not improve social skills
Stice et al. (2008)	1. CBT group versus No treatment 2. CBT bibliotherapy versus No treatment	Yes No	Stice et al. (2010) Stice et al. (2010)	Loneliness Scale (brief) Loneliness Scale (brief)	No No	CBT reduced loneliness but authors did not continue mediation test CBT did not reduce loneliness
<i>Family Functioning</i>						
Brent et al. (1997)	CBT individual versus Nondirective supportive therapy	Yes	Kolko et al. (2000)	1. FAD—Affective Involvement, Affective Responsiveness, Behavioral Control, Communication, General Functioning, and Roles scales (parent-report) 2. FAD—Affective Involvement, Affective Responsiveness, Behavioral Control, Communication, General Functioning, and Roles scales (youth-report) 3. ACQ (parent-report) 4. ACQ (youth-report) 5. CBQ (parent-report) 6. CBQ (youth-report) 7. FICS—Dyadic Conflict scale	No No No No No No No	CBT reduced parent-reported family dysfunction on FAD General Functioning and Behavioral Control scales, but not on any other scale; authors did not continue to test for mediation as treatment effect was NS in mediation paper CBT did not reduce youth-reported family dysfunction on any FAD scale CBT did not reduce parent-reported family relationship problems CBT did not reduce youth-reported family relationship problems CBT did not reduce parent-reported family conflict CBT did not reduce youth-reported family conflict CBT did not reduce observed family conflict

(Continues)

TABLE 2 (Continued)

Outcome Paper	Treatment Conditions	Treatment Effect?	Mediation Paper	Candidate Mediator	Significant Mediator?	Finding (treatment effects described reflect comparison to control)
Dietz et al. (2015)	IPT individual family-based versus Nondirective supportive therapy	No	Dietz et al. (2015)	1. CBQ (parent-report) 2. CBQ (youth-report)	No	IPT did not reduce parent-reported parent-child conflict (NS trend), change in conflict not associated with depression symptoms IPT did not reduce youth-reported parent-child conflict, change in conflict not associated with depression symptoms
McCarty, Violette, Duong, Cruz, and McCauley (2013)	CBT group versus Nondirective supportive therapy	Yes	Duong et al. (2016)	Parent-Child Communication Scale—Parent Communication	No	CBT improved parent-child communication but communication not associated with change in depression symptoms; indirect effect NS
Rohde et al. (2004)	CBT group versus Case management	Yes	Kaufman et al. (2005)	Issues Checklist <sup>a</sup>	No	CBT did not improve parent-adolescent conflict
<i>Problem-Solving</i>						
Brent et al. (1997)	CBT individual versus Nondirective supportive therapy	Yes	Kolko et al. (2000)	1. FAD—Problem-Solving (parent-report) 2. FAD—Problem-Solving (youth-report) 3. FICS—Adolescent Problem-Solving scale	No	CBT did not reduce parent-reported family problem-solving CBT did not reduce youth-reported family problem-solving CBT improved adolescent problem-solving, which predicted higher remission rate; indirect effect only significant for youths whose mothers' pretreatment depression symptoms were low–moderate
TADS Team (2004)	CBT individual versus Pill placebo	No	Lewis et al. (2009)	SOCQ—Action scale <sup>b</sup>	Yes	CBT increased action stage of change, which mediated decreases in depression symptoms across four treatment conditions, but unclear if medication specific to CBT only versus control comparison
<i>Avoidance</i>						
TADS Team (2004)	CBT individual versus Pill placebo	No	Lewis et al. (2009)	SOCQ—Precontemplation scale	No	CBT did not change precontemplation
<i>Pleasant activities</i>						
Rohde et al. (2004)	CBT group versus Case management	Yes	Kaufman et al. (2005)	1. PES—Relaxation scale 2. PES—Pleasant Activities scale	No	CBT did not increase relaxation CBT did not increase pleasant activities

(Continues)

TABLE 2 (Continued)

Outcome Paper	Treatment Conditions	Treatment Effect?	Mediation Paper	Candidate Mediator	Significant Mediator?	Finding (treatment effects described reflect comparison to control)
Stice et al. (2008)	1. CBT group versus No treatment	Yes	Stice et al. (2010)	PES (brief)	Yes	CBT increased pleasant activities, which mediated decrease in depression symptoms, but change in negative thoughts did not precede change in outcome for most participants
	2. CBT bibliotherapy versus No treatment	No	Stice et al. (2010)	PES (brief)	No	CBT did not increase pleasant activities, but increased pleasant activities predicted decreases in depression symptoms
<i>Motivation to change</i>						
TADS Team (2004)	CBT individual versus Pill placebo	No	Lewis et al. (2009)	SOCQ—Contemplation scale	No	CBT did not change contemplation
<i>Expression of affect</i>						
Stice et al. (2008)	1. CBT group versus No treatment	Yes	Stice et al. (2010)	Emotional Expression scale	No	CBT increased emotional expression but authors did not continue mediation test
	2. CBT bibliotherapy versus No treatment	No	Stice et al. (2010)	Emotional Expression scale	No	CBT did not increase emotional expression
<i>Therapeutic Alliance</i>						
Rohde et al. (2004)	CBT group versus Case management	Yes	Kaufman et al. (2005)	Working Alliance Inventory	No	CBT improved alliance compared to control, but improved alliance did not predict decreases in depression symptoms
<i>Role Engagement</i>						
Brent et al. (1997)	CBT individual versus Nondirective supportive therapy	Yes	Dietz et al. (2014)	FICS—Adolescent Involvement	No	CBT did not reduce observed adolescent involvement
<i>Maintenance of Gains</i>						
TADS Team (2004)	CBT individual versus Pill placebo	No	Lewis et al. (2009)	SOCQ—Maintenance scale	No	CBT did not change maintenance
<i>Attitudes Toward School</i>						
McCarty et al. (2013)	CBT group versus Nondirective supportive therapy	Yes	Duong et al. (2016)	BASC-2 Attitudes Toward School scale	No	CBT improved attitudes toward school but attitudes not associated with change in depression symptoms; indirect effect NS
<i>Health Behaviors</i>						
McCarty et al. (2013)	CBT group versus Nondirective supportive therapy	Yes	Duong et al. (2016)	Health-Enhancing Behavior Index	No	CBT did not improve health behaviors, which were not associated with depression symptoms; indirect effect NS
<i>Group Cohesiveness</i>						

(Continues)

TABLE 2 (Continued)

Outcome Paper	Treatment Conditions	Treatment Effect?	Mediation Paper	Candidate Mediator	Significant Mediator?	Finding (treatment effects described reflect comparison to control)
Rohde et al. (2004)	CBT group versus Case management	Yes	Kaufman et al. (2005)	Group Cohesiveness Questionnaire	No	CBT did not improve group cohesiveness
<i>Other<sup>c</sup></i>						
Dietz et al. (2015)	IPT individual family-based versus Nondirective supportive therapy	Yes	Dietz et al. (2015)	Self-Report for Childhood Anxiety Related Emotional Disorders (child- and parent-report)	No	IPT reduced anxiety symptoms, change in anxiety symptoms not associated with depression symptoms (NS trend)
Brent et al. (1997)	CBT individual versus Nondirective supportive therapy	Yes	Kolko et al. (2000)	Locke-Wallace Marital-Adjustment Test (parent-report)	No	CBT improved marital satisfaction, but authors did not continue mediation test as treatment effect was NS in mediation paper

Abbreviations: ACQ, Areas of Change Questionnaire; ATQ, Automatic Thoughts Questionnaire; BASC-2=Behavior Assessment Scale for Children-Second Edition; CASQ, Children's Attributional Style Questionnaire; CBCL-D, Child Behavior Checklist-Depression Scale; CBQ, Conflict Behavior Questionnaire; CBT, cognitive behavioral therapy; CDI, Child Depression Inventory; DAS, Dysfunctional Attitude Scale; FAD, Family Assessment Device; FICS, Family Interaction Coding System; HRSD, Hamilton Rating Scale for Depression; IPT, interpersonal psychotherapy; NS, not significant; PES, Pleasant Activities Schedule. SAS-SR, Social Adjustment Scale Self-Report; SOCC, Stages of Change Questionnaire.

<sup>a</sup>We categorized the *Issues Checklist* as Family Functioning rather than Problem-Solving as conceptualized by Kaufman et al. (2005) because the items resemble other measures of family functioning.

<sup>b</sup>We categorized SOCC Action scale as Problem-Solving rather than Motivation to Change because the items resemble other measures of problem-solving.

<sup>c</sup>These did not meet our criteria for candidate mediators (measured nondepressive symptoms or did not involve the youth or youth's relationships) but were tested as mediators by authors.

## 4 | DISCUSSION

To take stock of what is known about how therapies work for depressed children and adolescents, we conducted a systematic review of randomized trials testing CBT or IPT for youth depression, identifying 34 RCTs that measured any putative change process or change mechanism. Additionally, eight RCTs published reports of mediation testing. Overall, the numbers of RCTs of youth depression measuring any CM, and those testing CMs as mediators, have more than doubled since similar systematic and meta-analytic reviews were published more than a decade ago (Chu & Harrison, 2007; Weersing & Weisz, 2002). Despite this expansion of the evidence base, mediation tests remain rarely published—nearly three-quarters of RCTs measured some CM, whereas less than one-fifth of eligible RCTs also analyzed them as mediators of treatment outcome. Moreover, only half of the 26 mediator categories measured in RCTs were tested as treatment mediators. In short, our review shows a remarkably underutilized evidence base on CM, with enormous lost opportunity to (a) understand how therapies work to ameliorate youth depression and (b) improve the efficacy of those therapies. Next, we discuss what we were able to conclude from our findings about the mediators that are assessed, the mediation tests used, and the results of those tests. Finally, we offer five proposals for change in scientific practices and policies that could advance the search for treatment mediators of youth depression.

### 4.1 | Which mediators have been assessed, for which therapies, and how frequently?

Consistent with the preponderance of CBT trials in the study sample, most of the mediator categories measured in multiple RCTs are putative change mechanisms specific to CBT or to both CBT and IPT. Earlier reviews (Chu & Harrison, 2007; Weersing & Weisz, 2002) noted that CBT trial investigators had prioritized cognitive over behavioral measures. We found that this is still the case—there were 1.5–5 times more trials measuring negative cognition than those measuring other putative CBT/IPT change mechanisms.

In contrast to the earlier reviews, we made finer distinctions among cognitive and behavioral measures and found considerable variation. Negative cognition, which includes negative automatic thoughts, dysfunctional attitudes, pessimistic attributional style, hopelessness, and low self-esteem, was measured in 26 RCTs. On the other hand, reframing, which involves using cognitive skills or effort to address negative cognitions or stressors, such as secondary control engagement coping and positive problem orientation, was measured in only 6 RCTs. Moreover, social engagement was measured much more frequently (18 RCTs) than

problem-solving (8 RCTs), pleasant activities, and avoidance (5 RCTs each). Reframing, problem-solving, and pleasant activity scheduling are key skills that many CBT protocols aim to foster among depressed youths (see Ng, Eckshtain, & Weisz, 2016). Therefore, it is surprising that these skills were not more frequently assessed in CBT trials.

Three other categories were relatively frequently assessed: family functioning, measured in CBT and IPT trials albeit being an IPT-specific putative change mechanism (18 RCTs); treatment expectancy, a common factor client change process (8 RCTs); and motivation to change, a common factor change mechanism (3 RCTs).

## 4.2 | Have researchers been using improved mediation tests?

Researchers have incorporated methodological improvements into their mediation tests. Articles published up till the early 2000s used Baron and Kenny (1986) causal steps approach, whereas those that followed employed a significance test of the indirect effect. Advanced statistical procedures used in the later articles include bias-corrected bootstrapping, which maximizes power to test the indirect effect (Fritz & MacKinnon, 2007), and assessing conditional indirect effects (see Preacher, Rucker, & Hayes, 2007). The latter approach, also known as moderated mediation, assesses mediation within subsamples or in the context of differential mediator–outcome relationships between treatment conditions. More rigorous logical criteria were also used—change in statistical mediators was assessed for temporal precedence.

However, all but one of the mediation studies involved some form of causal steps approach, which, albeit helpful in conceptualizing mediation as a series of logical criteria to be met, has the lowest power among existing mediation tests (Fritz & MacKinnon, 2007). This is because each step requires conducting a separate significance test, and each test carries some degree of error, thus higher-powered tests involve a single significance test of the mediation effect to minimize error (Hayes, 2009). Nearly all the reviewed CMs were nonsignificant by virtue of having failed one of the steps. Kolko et al. (2000), for example, did not complete mediation analyses for cognitive distortions and family functioning due to a lack of significant treatment effect in the mediation paper, even though the primary outcome paper (Brent et al., 1997) found a significant treatment effect with a different outcome measure. In addition, Kaufman et al. (2005) did not continue testing pleasant activities as a mediator because the treatment effect on this CM was just above the significance cutoff. One wonders how more mediators would have been identified with a higher-powered mediation test that is not conditional on meeting causal steps criteria. Hence, quantitative

researchers (Hayes, 2009) recommend significance testing of indirect effects *without* the causal steps approach.

## 4.3 | Can we draw meaningful conclusions on how therapies treat youth depression?

We acknowledge substantial challenges to drawing meaningful conclusions about the findings reviewed. Besides the low power and heterogenous mediation tests used, other questions arise. How representative of the evidence base of EBPs for youth depression are the eight RCTs that tested mediation? CBT in individual, group, and bibliotherapy formats are represented, but only one included RCT tested IPT using a new family-based format. Since the literature search and review procedures were conducted, mediation analyses were published beyond the range of dates examined for one more included RCT assessing individual IPT (Reyes-Portillo, McGlinchey, Yanes-Lukin, Turner, & Mufson, 2017)—even if counted, only two RCTs examining different formats of IPT have tested mediation, and the proportion of all RCTs that analyzed any CM as a mediator remains under 20 percent. In addition, empirical support for all four mediator categories is mixed, but how exactly should contradictory evidence be accounted for? It is possible that findings are mixed because mediation may be present only for a specific measure, EBP, or delivery format, in the context of certain study characteristics. Unfortunately, the small sample makes it impossible to distinguish systematic from chance variation in findings. A conservative approach would be to state that findings are inconclusive. Alternatively, a more liberal approach would be to draw very tentative conclusions, keeping in mind the limitations of the evidence base, including the small number of included IPT trials. Recent efforts have focused on streamlining EBP protocols to improve the disseminability of evidence-based practices in everyday clinical settings (Weisz, Kuppens, et al., 2017). Although imperfect, these two suggested frameworks provide an empirical basis for guiding current decisions about which therapy practices to disseminate and examine further—at least until more rigorous evidence is available.

A simple way to draw conclusions is to count the number of trials with significant mediation findings (i.e., vote counting). The identification of negative cognition as a mediator across four CBT trials affirms that cognitive restructuring is likely a key active ingredient that should be emphasized in therapy. The identification of problem-solving and pleasant activities as mediators in two and one CBT trials, respectively, suggests that these behavioral targets may also drive symptom reduction. These findings support cognitive behavioral theory that changing maladaptive thoughts and behaviors to more adaptive ones should lead to symptom reduction (Clarke & DeBar, 2010). In contrast, IPT theory

posits that positive social relationships are important for emotional well-being; thus, it focuses on helping youth build interpersonal skills to improve relationships with peers, romantic partners, or parents to reduce their depression symptoms (Jacobson & Mufson, 2010; Rosselló & Bernal, 1999). Consistent with this theory, social engagement was a significant mediator, though family functioning was not, in the sole IPT trial within the present review that tested mediation (Dietz et al., 2015), and both peer and family functioning were significant mediators among Latino adolescents in the other IPT trial (Reyes-Portillo et al., 2017). One could argue that there is most evidence for cognitive change, then problem-solving and pleasant activity scheduling within CBT, and only for social engagement within IPT, and prioritize addressing them in research and practice accordingly.

Another way is to apply the criteria for identifying empirically supported therapies (ESTs) to mediator categories (Chambless & Hollon, 1998; Southam-Gerow & Prinstein, 2014). These criteria accord higher empirical support for trials conducted by independent research teams, that used an alternative treatment or placebo control, and with fewer contradictory findings. Applying a liberal cutoff requiring half the mediation tests/measures to be significant in the expected direction, one could designate negative cognition, problem-solving, and social engagement as “probable mediators” as they were significant in at least half the mediation tests within one or more trials with an active control, conducted by nonindependent teams. Pleasant activities could be designated as a “possible mediator,” as it was significant in at least half the tests within a trial with a no treatment control. All categories not tested as mediators could be classified as “experimental” and those tested and found not to mediate outcome in one or more trials could be labeled as “questionable.” Evidence level can vary by treatment—social engagement would be a probable mediator for IPT but questionable for CBT.

#### 4.4 | What can we do to advance the search for treatment mediators of youth depression?

Although we have suggested ways to draw tentative conclusions from the available evidence, the glaring fact remains that these conclusions are severely limited by findings that are sparse, conflicting, and come from a small proportion of relevant studies that were not optimally designed to investigate change processes and mechanisms. If psychotherapy researchers continue this pattern of studying and reporting on treatment mediators, the field may see little progress in developing the most effective treatments for youth depression. To advance the search for treatment mediators of youth depression, we offer several proposals for discussion and debate.

#### 4.4.1 | Exploit existing data using meta-analysis

Perhaps our most striking finding is that completed RCTs are a substantial source of untested CMs. Individual participant data (IPD) meta-analysis (Cooper & Patall, 2009) and meta-analytic structural equation modeling (MASEM; Cheung & Hafdahl, 2016) can quantify mean conjoint pathways from treatment condition to mediator and mediator to outcome and thus may be bestsuited to studying treatment mediation. The former synthesizes raw participant-level data, whereas the latter first synthesizes group-level statistics into a pooled correlation or covariance matrix and then uses the matrix to fit models of interest. Meta-analysis would not only greatly expand the size and representativeness of the study sample and of the mediator categories tested, but also resolve conflicting findings by estimating mean effects across trials, with larger samples and more precise effects weighted more heavily. Moreover, mean mediation effects are standardized, which would facilitate comparison between mediator categories when the trial investigators used different mediation tests or did not test mediation at all. Meta-analysis would also increase power to detect mediation via pooling of RCT samples and using a single significance test of indirect effects. Both IPD meta-analysis and MASEM are beginning to be applied to psychotherapy data (Gu, Strauss, Bond, & Cavanagh, 2015; Manassis et al., 2014).

#### 4.4.2 | Investigate moderated mediation

Most mediation analyses described in the present review assume that a treatment works the same way in all participants, but it is plausible that change mechanisms and processes vary according to patient characteristics. Consider that changes in CMs preceded improvement in only some depressed youth (Stice et al., 2010), problem-solving mediated outcome in the subgroup of depressed youths whose mothers were not severely depressed (Dietz et al., 2014), and peer and family functioning mediated outcome among Latino youth, who may place more value on personal and family relationships over youth from other cultures (Reyes-Portillo et al., 2017). The increased power from meta-analysis would be especially advantageous in detecting moderated mediation—mediation effects that vary by individual characteristics could guide researchers to explore how treatments may work differently across subgroups based on demographic, clinical, family, or other psychological characteristics. In particular, age or pubertal status may be especially relevant to investigate as potential moderators of mediation effects in youth. Given the neural, physical, cognitive, and socioemotional changes that take place during adolescence (Dahl, Allen, Wilbrecht, & Suleiman, 2018), change mechanisms may plausibly differ

across developmental stages. Indeed, our recent meta-analysis (Cuijpers et al., 2020) of psychotherapy outcomes for depression across the lifespan found that treatment effects were small–medium for children, medium for adolescents, and very large for young adults, suggesting that existing treatment strategies are differentially effective, and may perhaps work differently, across developmental stages. Also consistent with the notion of individual differences in change mechanisms are the findings that depressed adults differ in their optimal treatment (e.g., CBT, IPT, antidepressants) depending on their particular constellation of personal characteristics (Cohen & DeRubeis, 2018).

#### 4.4.3 | Conduct intensive longitudinal and idiographic assessments

We found few trials with even one mid-treatment assessment of CMs, and only Stice et al. (2010) explicitly assessed temporal order of change in CMs and outcome measures. They reported that for most participants, changes in negative thoughts and pleasant activities did not occur before symptom reduction at post-treatment—but this finding does not preclude the outcome from changing concurrently with the CM. Intensive measurements of CMs and outcomes at multiple time points during treatment are required to establish temporal precedence of the CM and could be analyzed across and within individuals. Intensive longitudinal measurements have also begun to demonstrate idiographic patterns of within-person temporal relationships among depressive symptoms and related emotions and behaviors (Fisher, Reeves, Lawyer, Medaglia, & Rubel, 2017)—which may explain individual differences in treatment response. Intensive and idiographic assessment are rare in youth psychotherapy research but should become more feasible with the widespread and frequent use of smartphones and wearable technology among youths, and with active development of apps to capture both self-report and behavioral data (Silk et al., 2020).

#### 4.4.4 | Measure a wider range of candidate mediators

Very few measures reviewed were specific to IPT. Support for the theoretical model of IPT may be bolstered by assessing a variety of relevant change mechanisms (e.g., insight into self and interpersonal patterns, understanding and finding meaning in loss and change) and change processes (i.e., therapist IPT strategies). Although more varied, CMs of CBT were largely reliant on subjective report; multiple methods of assessing these CMs would strengthen support for the CBT

model. Thus, we re-iterate Weersing and Weisz's (2002) recommendation to assess information processing measures of negative cognition (e.g., bias for recalling negative memories, impaired mood repair using positive memories). Indeed, cognitive tasks are beginning to be used in treatment contexts (Cha & DiVasto, 2017), as are measures of biological mechanisms (Messina, Sambin, Palmieri, & Viviani, 2013). These developments have occurred primarily in the adult psychotherapy literature but would potentially be very valuable for understanding youth psychotherapy as well.

#### 4.4.5 | Adjust journal and funder policies to promote research on change processes and mechanisms

The above proposals will remain largely unrealized aspirations unless journals and funding agencies adjust their policies to incentivize and facilitate conducting such research. Collecting data frequently on multiple CMs, using multiple methods adds significant cost to an already expensive treatment trial, and highly specialized statistical skills are required to conduct intensive longitudinal and idiographic analyses. Increased funding would give a much needed boost to these research directions. Meta-analysis demands considerable time and effort not only from the meta-analyst but also from trial investigators to provide the required data. When attempting to obtain summary statistics for our own meta-analytic work, most investigators have responded, many have generously shared their data, some were able to do so by accepting modest compensation to cover expenses, one pointed us to a data archive from which we requested the data, and several simply lacked the time or resources to retrieve the data given other responsibilities. Accelerating our understanding of how treatments work may necessitate designating funding for meta-analysis and requiring trial investigators to publish raw data or summary statistics of all CMs and outcomes, whether tested or not. In the spirit of open science, many journals now offer authors the option to share their data, syntax, and other materials, and platforms have been designed to facilitate such sharing, such as the National Institute of Mental Health Data Archive (<https://nda.nih.gov/>) and the Open Science Framework ([osf.io](https://osf.io)). Routine data sharing would go a long way toward a collective understanding of what the field has or has not learned about how therapies for youth depression work.

## 5 | CONCLUSION

Reviewing 30 years of RCT research on EBPs for youth depression, we discovered that candidate change processes

and mechanisms are measured frequently among RCTs, but seldom tested as treatment mediators. Although significant mediators were identified, findings are sparse, conflicting, and clouded by methodological issues. Advancing the field will involve shifts in scientific practices and policies to exploit existing data using meta-analysis, measure a wider range of CMs, and conduct intensive and idiographic assessments.

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## ENDNOTE

<sup>1</sup> We acknowledge that the numerical mid-point of treatment duration may not necessarily correspond with the mid-point of treatment content delivered. For example, in one of the included studies (Mufson et al., 2004) testing an IPT protocol, most of the active ingredients were delivered after session 4 (L. Mufson, personal communication, June 2, 2020, June 17, 2020), which was the assessment time point closest to the numerical mid-point of sessions attended (10.5 total sessions for IPT, 7.9 total sessions for control).

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APPENDIX 1

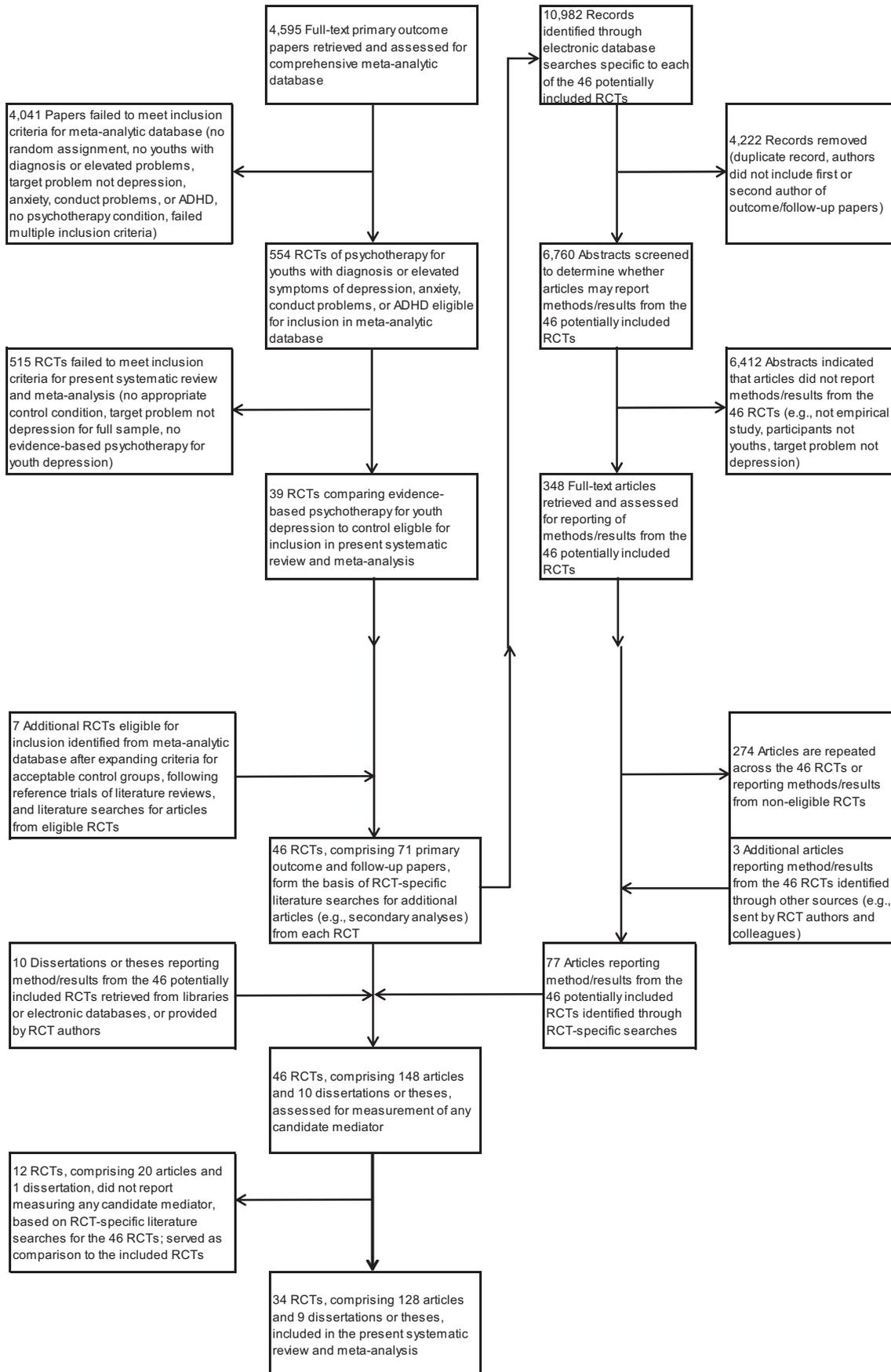


FIGURE A1 Flowchart detailing retrieval, inclusion, and exclusion of randomized controlled trials (RCTs)

## APPENDIX 2

This Appendix lists articles, dissertations, and theses of included RCTs except those cited in Table 2, which are included in the main References section of the paper and marked with an asterisk.

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APPENDIX 3

TABLE A1 Study Sample, Treatment Conditions, and Candidate Mediators and their Categories

Outcome Paper	N	Mean Age (years)	Diagnosis Required?	EBP	Control	COG	SOC	FAM	PRO	EXP	REF	AVO	ACT	Other
Ackerson et al. (1998)	30	15.9	No	CBT bibliotherapy	Waitlist	X								Role Engagement
Asarnow et al. (2005)	418	17.2	No	CBT individual (enhanced collaborative primary care)	Usual care (in primary care + brief provider training)		X	X		X				Perceived Stigma
Asarnow, Scott, & Mintz (2002)	23	10.0	No	CBT group	Waitlist	X	X		X			X		
Brent et al. (1997)	72	15.6	Yes, MDD	CBT individual	Nondirective supportive therapy	X		X	X	X				Role Engagement
De Cuyper, Timbremont, Braet, De Backer, & Wullaert (2004)	22	10.0	No	CBT group	Waitlist	X								
Dietz et al. (2015)	42	10.6	Yes, MDD, DYS, or DD-NOS	IPT individual family-based	Nondirective supportive therapy		X		X					
Fleming, Dixon, Frampton & Merry (2012)	32	14.9	No	CBT computerized	Waitlist	X								
Garber et al. (2009)	316	14.8	No	CBT group + usual care	Usual care (allowed to seek nonstudy services)	X			X					

(Continues)

Outcome Paper	N	Mean Age (years)	Diagnosis Required?	EBP	Control	COG	SOC	FAM	PRO	EXP	REF	AVO	ACT	Other
Gillham et al. (2012)	408	12.5	No	1. CBT group 2. CBT group + parent group	Usual care ("school-usual")	X		X	X					
Gillham, Hamilton, Freres, Patton, & Gallop (2006)	271	11.5	No	CBT group	Usual care (unspecified)	X								
Kahn, Kehle, Jenson, & Clark (1990)	34	12.1	No	CBT group + parent group	Waitlist	X								
Lewinsohn, Clarke, Hops, & Andrews (1990)	74	16.2	Yes, MDD, mDD, or IDD	1. CBT group 2. CBT group + parent group	Waitlist	X	X	X			X		X	
Liddle & Spence (1990)	31	9.2	No	CBT group	1. Waitlist 2. Attention placebo (group drama program)		X		X					
McCarty et al. (2013)	120	12.7	No	CBT group	Attention placebo (individual support)	X	X	X						Attitudes Toward School, Health Behaviors
Merry et al. (2012)	187	15.6	No	CBT computerized	Usual care (services at youth clinics, schools, or primary care)	X								
Mufson et al., (2004) <sup>a</sup>	63	15.1	Yes, MDD, DYS, DD-NOS, or ADJ	IPT individual	Usual care (school counseling)	X	X	X						
Mufson, Myrna, Weissman, Moreau, & Garfinkel (1999)	48	15.8	Yes, MDD	IPT individual	Attention placebo (clinical monitoring)	X	X	X	X		X	X		Impulsive Coping

(Continues)

TABLE A1 (Continued)

Outcome Paper	N	Mean Age (years)	Diagnosis Required?	EBP	Control	COG	SOC	FAM	PRO	EXP	REF	AVO	ACT	Other
Reed (1994)	18	16.5	Yes, MDD or DYS	CBT group	Attention placebo (art and imagery exercises, creative and verbal expression)	X	X							
Reynolds & Coats (1986)	19	15.7	No	CBT group	Waitlist	X								
Rohde et al. (2004)	93	15.1	Yes, MDD + conduct disorder	CBT group	Case management	X	X	X			X		X	Therapeutic Alliance, Group Cohesiveness
Rohde, Stice, Shaw, & Brière (2014)	378	15.5	No	1. CBT group 2. CBT bibliotherapy	No treatment (educational brochure)	X	X			X				Motivation to Change
Rosselló and Bernal (1999)	71	14.7	Yes, MDD or DYS	1. CBT individual 2. IPT individual	Waitlist	X	X	X						
Santomauro, Sheffield, & Sofronoff (2016)	23	15.8	No, but autism spectrum disorder was required	CBT group	Waitlist		X				X			Expression of Affect, Alexithymia, Executive Functioning, Theory of Mind
Stark, Reynolds, & Kaslow (1987)	19	11.2	No	CBT group	Waitlist	X	X			X				
Stasiak, Hatcher, Frampton & Merry (2014)	34	15.2	No	CBT computerized	Attention placebo (computerized psychoeducation)			X				X		
Stice et al. (2008)	253	15.6	No	1. CBT group 2. CBT bibliotherapy	No treatment (education brochure)	X	X	X		X			X	Motivation to Change, Expression of Affect
Szigethy et al. (2007)	41	15.0	No	CBT individual	Waitlist	X							X	

(Continues)

TABLE A1 (Continued)

Outcome Paper	N	Mean Age (years)	Diagnosis Required?	EBP	Control	COG	SOC	FAM	PRO	EXP	REF	AVO	ACT	Other
Tang, Jou, Ko, Huang, & Yen (2009)	73	15.3	No	IPT individual	Usual care (school counseling)	X								
Treatment for Adolescents with Depression Study Team (2004)	223	14.6	Yes, MDD	CBT individual	Pill placebo	X	X	X	X	X	X	X		Motivation to Change, Impulsive Coping, Maintenance of Gains, Research Understanding
Vostanis, Feehan, & Bickerton (1996b)	57	12.7	Yes, MDD, mDD, or DYS	CBT individual	Attention placebo	X	X	X	X	X			X	Role Engagement
Weisz et al. (2009)	57	11.8	Yes, MDD, mDD, or DYS	CBT individual	Usual care	X			X	X	X	X		Therapeutic Alliance, Therapist Strategies - CBT, Client-centered, Family Systems, and Psychodynamic
Young, Mufson, & Davies (2006)	41	13.4	No	IPT group	Usual care (school counseling)							X		
Young, Mufson & Gallop (2010)	57	14.5	No	IPT group	Usual care (school counseling)							X		
Yu and Seligman (2002)	220	11.8	No	CBT group	Waitlist								X	

Abbreviations: ACT, pleasant activities; ADJ, adjustment disorder with depressed mood; AVO, avoidance; CBT, cognitive behavioral therapy; COG, negative cognition; DD-NOS, depressive disorder—not otherwise specified; DYS, dysthymia; EBP, evidence-based psychotherapy; EXP, treatment expectancy; FAM, family functioning; HMO, health maintenance organization; IDD, intermittent depressive disorder; IPT, interpersonal psychotherapy; MDD, major depressive disorder; mDD, minor depressive disorder; PRO, problem-solving; REF, reframing; SOC, social engagement.

<sup>a</sup>In this trial, randomization occurred at the level of the clinician for a small subset ( $n = 7$ ) of youths, and at the level of both clinician and youth for the rest of the sample, because the subset of youths were recruited from one school that restricted each clinician to treating students on a particular floor.

#### APPENDIX 4

This Appendix lists primary outcome papers of randomized controlled trials that did not report measuring any candidate mediator but met all other inclusion criteria for the present review.

Bolton, P., Bass, J., Betancourt, T., Speelman, L., Onyango, G., Clougherty, K. F., ... Verdeli, H. (2007). Interventions for depression symptoms among adolescent survivors of war and displacement in northern Uganda: A randomized controlled trial. *JAMA*, *298*(5), 519–527. <https://doi.org/10.1001/jama.298.5.519>

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Clarke, G. N., Hornbrook, M., Lynch, F., Polen, M., Gale, J., Beardslee, W., ... Seeley, J. (2001). A randomized trial of a group cognitive intervention for preventing depression in adolescent offspring of depressed parents. *Archives of General Psychiatry*, *58*(12), 1127–1134. <https://doi.org/10.1001/archpsyc.58.12.1127>

Clarke, G. N., Hornbrook, M., Lynch, F., Polen, M., Gale, J., O'Connor, E., ... Debar, L. (2002). Group cognitive-behavioral treatment for depressed adolescent offspring of depressed parents in a health maintenance organization. *Journal of the American Academy of Child & Adolescent Psychiatry*, *41*, 305–313. <https://doi.org/10.1097/00004583-200203000-00010>

Clarke, G. N., Rohde, P., Lewinsohn, P. M., Hops, H., & Seeley, J. R. (1999). Cognitive-behavioral treatment of

adolescent depression: Efficacy of acute group treatment and booster sessions. *Journal of the American Academy of Child & Adolescent Psychiatry*, *38*, 272–279. <https://doi.org/10.1097/00004583-199903000-00014>

Gillham, J. E., Hamilton, J., Freres, D. R., Patton, K., & Gallop, R. (2006). Preventing depression among early adolescents in the primary care setting: A randomized controlled study of the Penn Resiliency Program. *Journal of Abnormal Child Psychology*, *34*, 195–211. <https://doi.org/10.1007/s10802-005-9014-7>

Listug-Lunde, L., Vogeltanz-Holm, N., & Collins, J. (2013). A cognitive-behavioral treatment for depression in rural American Indian middle school students. *American Indian Alaskan Native Mental Health Research*, *20*, 16–34. <https://doi.org/10.5820/aian.2001.2013.16>

Stice, E., Burton, E., Bearman, S. K., & Rohde, P. (2007). Randomized trial of a brief depression prevention program: An elusive search for a psychosocial placebo control condition. *Behaviour Research and Therapy*, *45*(5), 863–876. <https://doi.org/10.1016/j.brat.2006.08.008>

Szigethy, E., Bujoreanu, S. I., Youk, A. O., Weisz, J., Benhayon, D., Fairclough, D., ... DeMaso, D. R. (2014). Randomized efficacy trial of two psychotherapies for depression in youth with inflammatory bowel disease. *Journal of the American Academy of Child and Adolescent Psychiatry*, *53*, 726–735. <http://doi.org/10.1016/j.jaac.2014.04.014>

Weisz, J. R., Thurber, C. A., Sweeney, L., Proffitt, V. D., & LeGagnoux, G. L. (1997). Brief treatment of mild-to-moderate child depression using primary and secondary control enhancement training. *Journal of Consulting and Clinical Psychology*, *65*, 703–707. <https://doi.org/10.1037/0022-006X.65.4.703>

Young, J. F., Benas, J. S., Schuler, C. M., Gallop, R., Gillham, J. E., & Mufson, L. (2016). A randomized depression prevention trial comparing Interpersonal Psychotherapy–Adolescent Skills Training to group counseling in schools. *Prevention Science*, *17*, 314–324. <https://doi.org/10.1007/s11121-015-0620-51>