

**HHS PUBLIC ACCESS**

Author manuscript

Curr Drug Abuse Rev. Author manuscript; available in PMC 2016 April 04.

Published in final edited form as:

Curr Drug Abuse Rev. 2015 ; 8(1): 41–49.

Treatment of Adolescent Substance Use Disorders and Co-Occurring Internalizing Disorders: A Critical Review and Proposed Model

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Abstract

Background—The past several decades have seen dramatic growth in empirically supported treatments for adolescent substance use disorders (SUDs), yet even the most well-established approaches struggle to produce large or long-lasting improvements. These difficulties may stem, in part, from the high rates of comorbidity between SUDs and other psychiatric disorders.

Method—We critically reviewed the treatment outcome literature for adolescents with co-occurring SUDs and internalizing disorders.

Results—Our review identified components of existing treatments that might be included in an integrated, evidence-based approach to the treatment of SUDs and internalizing disorders. An effective program may involve careful assessment, inclusion of parents or guardians, and tailoring of interventions via a modular strategy.

Conclusions—The existing literature guides the development of a conceptual evidence-based, modular treatment model targeting adolescents with co-occurring internalizing and SUDs. With empirical study, such a model may better address treatment outcomes for both disorder types in adolescents.

Keywords

adolescent; substance use disorders; co-occurring psychiatric disorders; evidence-based treatments

INTRODUCTION

Recently summarized estimates from several large-scale epidemiological studies of US youth reveal an 8% lifetime prevalence of alcohol use disorders and 2–3% prevalence of illicit drug use disorders (1). The increase in prevalence from ages 13 to 18 and the strong association between early substance use and later substance use disorder (SUD) development (2, 3) highlight adolescence as a key period for SUD interventions. Treatments targeting this age group have the potential to impact the entire lifespan. In 1997, Stanton and Shadish's meta-analysis (4) lamented a “dearth of clinical trial-tested treatment options for

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CONFLICT OF INTEREST

No conflicts of interest are reported.

adolescent drug abusers” (p. 187). Fortunately, since then, the treatment outcome literature for adolescent SUDs has expanded dramatically. A recent review identified 45 experimental or quasi-experimental treatment studies and concluded that most empirically evaluated interventions “appear to be beneficial” (5). Psychosocial treatments receiving support from clinical trials fall into three general categories: cognitive behavioral therapy (CBT), motivational interviewing (MI), and family/systems approaches (FSA). Although intervention strategies and efficacies vary both across and within these categories (6), each has now reached a generally accepted level of empirical support for their use. Mutual-help approaches such as 12-step programs are also associated with improved outcomes among adolescents (7). These programs, however, are used less frequently among adolescents relative to adults, and their effectiveness among adolescents has received less empirical attention (8).

Despite the expansion of the treatment outcome literature, there remains room for improvement in at least two domains. First, the body of evidence from randomized clinical trials is still relatively small. This issue is particularly apparent in comparison with outcome studies for adult SUDs, which greatly outnumber adolescent treatment studies and include widely recognized, large-scale clinical trials such as Project MATCH and the COMBINE Study (9–13). Moreover, beyond the 45 adolescent outcome studies reviewed by Tanner-Smith and colleagues, more than 20 review articles have been published, an arguably disproportionate amount of scholarly discourse, particularly given the lack of demonstrably powerful and effective treatment options (4–6, 14–32). Clearly, the field would benefit from more empirical treatment outcome research.

Second, there is consensus that treatment gains in empirically supported treatments, though meaningful, are insufficient (21). As Wetherill and Tapert (14) noted, there is still a “lack of highly effective interventions for addictive behaviors among youth” (p. 398). In part, this consensus reflects the relatively modest effect sizes found in existing controlled trials (21), which are likely due to a range of factors related to patient motivation, compliance, response, retention, and relapse. More broadly, the substantive impact of interventions may be uncertain given that “well-controlled research on *long-term* treatment effects of [adolescent] drug treatment is virtually nonexistent” (p. 70, emphasis added) (15), although at least some have concluded that, following treatment, “a return to drug use (or relapse) is a fairly common occurrence among adolescents” (p. 419) (18).

Taken together, these two key issues—the need for further empirical study and the relatively modest impact of current treatments—reflect the extent to which outcomes for adolescents with SUDs can and should be improved. These conclusions are not new. In the present critical review, we seek to focus not only on the limitations of the existing literature but also on how it suggests ways to increase treatment gains. In particular, we emphasize psychiatric comorbidity, with internalizing (i.e., mood and anxiety) disorders specifically, as a key target for efforts to improve outcomes for adolescents with SUDs, and we draw from the literature to propose a conceptual model on which integrated, evidence-based treatment might be based (33). Thus, the focus and innovative aspect of this manuscript is to suggest improvements in the treatment of adolescent SUDs in the context of co-occurring internalizing disorders. We begin by establishing the presence of co-occurring psychiatric

and SUDs in adolescence and then explore etiological mechanisms unique to SUDs and internalizing disorders. We then review and critique existing co-occurring treatment models that incorporate internalizing disorders and close with a theoretical model for the treatment of co-occurring SUDs and internalizing disorders.

REVIEW

Adolescent SUD treatment in the presence of co-occurring disorders

In adolescent SUDs, *dual diagnosis*, or the presence of other *co-occurring* psychiatric disorders, is more common than not (30, 31, 34, 35), and prior reviews have highlighted the need to understand and address these high rates of comorbidity (21). Common co-occurring problems include conduct disorder (CD), attention-deficit/hyperactivity disorder (ADHD), mood disorders, and trauma-related disorders and symptoms (30). Approximately 11 – 48% of adolescents with SUDs in community samples have co-occurring internalizing disorders, with depression co-occurring more commonly than anxiety disorders (36). Rates of internalizing co-occurrence are even higher in clinical samples (36). A recent study of health records, for example, found that 29% of male and 49% of female adolescent patients with SUDs had co-occurring mood disorders, whereas 9% and 19% of male and female patients, respectively, had co-occurring anxiety disorders (37). Co-occurring disorders are also associated with increased SUD symptom severity, and co-occurring disruptive disorders in particular are associated with less successful treatment completion (35, 38).

Etiological Mechanisms Specific to Co-Occurring Internalizing and Substance Use Disorders

Developing more effective treatment programs will require an understanding of the specific etiological mechanisms that produce comorbid symptoms, particularly if co-occurring internalizing symptoms operate differently from co-occurring externalizing symptoms in their relationships to the development of SUDs. Although not the focus of this review, externalizing disorders frequently co-occur with one another and with SUDs, and a body of empirical evidence has developed examining this covariation, its structure, and its etiology (39–44). Evidence to date indicates that it may not be the case that externalizing disorders tend to lead to substance abuse or that SUDs promote externalizing behavior but rather that SUDs and externalizing disorders result from shared etiological forces—whether genetic, environmental, or both. In the absence of integrated treatment or a focus on underlying etiological mechanisms, addressing one class of symptoms may not substantially affect symptoms of the other disorder.

Whereas less research has addressed the topic, co-occurrence between SUDs and internalizing disorders may result from differing developmental processes. O’Neil and colleagues (36) recently presented a review of research on SUDs and internalizing disorders. Integrating findings regarding comorbidity, risk relationships, and the tendency toward temporal precedence of internalizing symptoms over SUDs, these authors concluded that internalizing disorders may, in some cases, serve as an etiological pathway to SUDs in youth. As an example, Hussong and colleagues speculate that early childhood internalizing symptoms may result in interpersonal skills deficits as well as expectancies about drugs of

abuse, both of which may motivate substance use to cope with negative affect, thereby increasing use and risk for SUDs (45). While this perspective is enticing in that it implies that identifying and ameliorating internalizing disorders early could prevent the eventual emergence of some SUDs, the literature suggests several major caveats to this proposal. As O'Neil and colleagues (36) note, "though the majority of the evidence supports a unidirectional model in which childhood internalizing disorders increase risk for later SUDs, there is also evidence that substance use disorders may increase risk for internalizing disorders, or that the association may be explained by common risk factors" (p. 111). Indeed, genetically informed research has revealed a complex web of interrelationships among internalizing disorders and SUDs (42). For example, there are both genetic and environmental correlations between depressive symptoms and alcohol use across adolescence, supporting the role of common risk factors (46).

Taken together, the reviewed literature suggests several conclusions regarding treatment of adolescents with SUDs and co-occurring internalizing disorders. First, dual diagnosis with internalizing disorders may be qualitatively different from dual diagnosis with externalizing disorders, indicating that unique treatment approaches may be needed. Second, although the possible etiological role of early internalizing disorders in adolescent SUDs suggests that treating primary internalizing symptoms holds promise in addressing some SUDs, doing so will likely be insufficient to fully prevent or treat all co-occurrence (47). Thus, integrated treatments, in which both disorders are targets of intervention are likely the best approach (31, 48). Fortunately, several integrated treatment options have been developed, and below, we review these psychotherapeutic approaches with a focus on how they might inform current evidence-based practice as well as the development of new interventions. We confine our review to psychosocial interventions but note the robust literature on effective psychopharmacologic treatments for adolescent internalizing disorders (49, 50), particularly in dually diagnosed populations (51, 52).

Existing treatments for adolescents with co-occurring suds and internalizing disorders

Several approaches have been developed for treatment of adolescents with SUDs and co-occurring disorders (29–32). The Substance Abuse and Mental Health Services Administration (SAMHSA)'s National Registry of Evidence-based Programs and Practices (NREPP) lists 18 adolescent substance use treatment programs (53). Of these, 10 have evidence supporting their use in treating any type of co-occurring psychiatric disorders (Adolescent Community Reinforcement Approach, Chestnut Health Systems-Bloomington Adolescent Outpatient and Intensive Outpatient Treatment Model, Family Behavior Therapy, Family Support Network [which comprises 12-sessions of Motivational Enhancement Therapy/Cognitive Behavioral Therapy, a family component, and case management], Multidimensional Family Therapy, Multisystemic Therapy, Parenting with Love and Limits, Phoenix House Academy, The Seven Challenges, and Seeking Safety). Two other programs listed under co-occurring disorders, Moral Reconciliation Therapy and Trauma Affect Regulation: Guide for Education and Therapy (TARGET), are additionally recognized as beneficial in this context, although their impact on substance use or abuse has not yet been described in NREPP.

Unfortunately, these treatments for co-occurring SUDs and psychiatric disorders share the limited efficacy and substantial relapse risk of other adolescent SUD interventions. As Hawkins (31) noted, despite the promise of some positive outcomes, “virtually all of the [co-occurring treatment] models share modest reductions in symptoms, difficulties maintaining treatment gains, and high relapse rates” (p. 215). Given the high prevalence of co-occurring disorders, improving treatment approaches that impact co-occurring disorders therefore offers the potential for substantial improvement over the current status quo. Notably, greater empirical attention should be paid to the extent to which differing categories of co-occurring disorders—such as externalizing (i.e., attention-deficit/hyperactivity disorder, conduct disorder, oppositional defiant disorder) and internalizing disorders—might necessitate different approaches to intervention (31). That is, not all co-occurrence should be treated equally. Although recognition and exploitation of this issue has recently led to the development of an effective adolescent substance use *prevention* program targeting specific personality risk profiles (i.e., anxiety sensitivity, hopelessness, impulsivity, and sensation seeking) (54–56), further consideration in the treatment literature is needed as well.

There has been less attention focused on treatment programs targeting adolescents with co-occurring SUDs and *internalizing* disorders (vs. externalizing). This gap is especially striking given the relatively stronger efficacy of treatments for internalizing disorders relative to those for externalizing disorders (36). Of the treatments listed in NREPP for co-occurring disorders, only five (Adolescent Community Reinforcement Approach, Family Behavior Therapy, Phoenix House Academy, The Seven Challenges, and Seeking Safety) have been identified for use with teens with any internalizing disorders. Beyond these existing programs, research is also ongoing to develop treatments for adolescents with SUDs and internalizing disorders. For example, a search of the NIH RePORTER database (projectreporter.nih.gov/reporter.cfm) on March 11, 2014 for projects funded through NCI, NIAAA, NIDA, NIMH, SAMHSA, or the VA with the search terms *adolescent, treatment, substance, AND [internalizing, trauma, depression, OR anxiety]* revealed five interventions, at varying stages of development, targeting the co-occurrence of SUDs and post-traumatic stress disorder, major depressive disorder (or depressive symptoms), and general internalizing symptoms. These treatment programs and ongoing research projects represent important steps toward improving outcomes for adolescents, yet given the limited effectiveness of current approaches (31), the field may additionally benefit from a broader search for interventions. We now turn to specific treatment components of existing models which address co-occurring internalizing disorders.

CBT and behavioral therapies have been identified as strong approaches for co-occurring disorders treatment (30). Macgowan and Engle (19), for example, recommend the use of behavioral interventions when adolescents with SUDs present with comorbidity or greater symptom severity. Indeed, an integrated CBT has been developed specifically for adolescents with SUDs and suicidality (57). CBT’s strengths in the context of co-occurring internalizing disorders include its extensive body of support for efficacy in treating anxiety and depressive disorders. Goal-directed techniques such as role-playing and modeling, self-monitoring of behavior outside the therapy session, challenging maladaptive beliefs, and conducting behavioral exposures or experiments have the potential to generalize across target behaviors. Contingency management strategies to reinforce abstinence and other

therapy compliance have emerged as promising behavioral components among adolescents as well (58), at least when combined with CBT or other evidence-based interventions (59).

The use of CBT in co-occurring internalizing disorders treatment is also supported by research among adults. For example, a meta-analysis found that both CBT and antidepressant medications modestly improved outcomes for both alcohol use and internalizing disorders among alcohol use disorder patients (60). Treatment gains were greater for CBT relative to medication and for anxiety over depressive symptoms. More recent adult studies provide additional evidence in support of CBT. A six-hour, group-delivered CBT program for anxiety and anxiety-coping-related alcohol use decreased alcohol consumption—although not anxiety symptoms—among residential alcohol use disorder patients (61). Similarly, a group-based CBT for depression and depression-related substance use improved depressive *and* SUD symptoms in a quasi-randomized study of residential treatments (62). These findings are tempered, however, by the fact that, like adolescent interventions, adult co-occurring disorder treatments have generally had difficulty producing meaningful and replicable benefits (63).

Motivational Interviewing (MI) is a conceptually distinct approach that is frequently combined with CBT (64). The MI therapeutic style is intended to increase motivation to change behavior. It employs a non-confrontational and validating yet directive mode of discussion that strives to enhance desire and self-efficacy by aligning patients' substance-related goals with their broader values (65). In the absence of concrete skill building or interventions against internalizing symptoms, MI is unlikely to be sufficient on its own with co-occurring disorders (24, 30). However, motivation to change is clearly quite important in SUD treatment and should be a target in developing improved co-occurring disorders interventions.

Other treatment programs that draw from CBT, including Dialectical Behavior Therapy (DBT) and Seeking Safety (SS), have also been recommended for use in adolescents with co-occurring SUDs and other psychiatric problems. DBT was first developed for individuals with borderline personality disorder and has been extended to treat a range of other disorders (66–69). DBT conceptualizes substance abuse as a response to mood dysregulation, and it combines traditional CBT-based skills training with acceptance and mindfulness practices (30, 31). As Hawkins (31) notes, it holds promise for treating co-occurring mood and anxiety disorders. To date, however, we are not aware of any trials of DBT for adolescent SUDs with or without co-occurring internalizing disorders. Further evidence is therefore needed to evaluate its potential value in this population.

SS also draws from CBT and was developed specifically for individuals with comorbid SUDs and trauma-related conditions such as post-traumatic stress disorder (PTSD). Among adults, SS has received considerable empirical support in treating symptoms of both PTSD and SUD (70). As reviewed by Hawkins (31), strengths of SS for adolescent SUDs and PTSD treatment may include its use of integrated CBT skills development and emphasis on the interplay between substance use and coping with PTSD symptoms. It should be noted, however, that to our knowledge SS has only been found efficacious among adolescents in one small controlled trial (71).

Finally, FSA interventions, incorporating parental training and monitoring skills, also hold promise for use with co-occurring disorders. As reviewed by Rowe (15), FSA treatments such as Multidimensional Family Therapy (MDFT) are efficacious in treating adolescent SUDs, and there are strong links between indices of parental functioning and a range of offspring problems. Studies employing rigorous, quasi-experimental designs have found strong evidence that environmental factors associated with parental functioning, including marital instability and teen childbirth, may causally increase their offspring's propensities for not only SUDs but also internalizing and externalizing symptoms (72, 73). Thus, a truly effective co-occurring internalizing disorders treatment will likely require the involvement of family, perhaps including interventions to directly target parenting behaviors.

In sum, existing interventions targeting co-occurring SUDs and internalizing disorders have been shown to impact internalizing symptoms, although indirectly. None have directly addressed internalizing symptoms as a primary focus of the treatment. We conclude that new treatment programs can draw from components of existing efficacious treatments, with an emphasis on targeting possible mechanisms of change that might generalize across SUDs and internalizing disorders. This strategy is akin to a modularity approach to treatment, in which components common to multiple empirically supported treatments are identified and then applied as appropriate (74). Such an approach has been developed for a wide range of youth mental health concerns (75, 76). Although it has been recommended for use in this population, the limited current empirical support for modular interventions for SUDs and co-occurring disorders has impeded its implementation (77).

Conceptual Model for Co-Occurring Internalizing Disorder Treatment

Drawing from the results of our review, we conclude by proposing a conceptual model for treating co-occurring internalizing and substance use disorders. The model is built on individual CBT but incorporates MI, FSA, contingency management, and, where applicable, psychopharmacological interventions. It is designed to guide empirically informed practice but should not be considered authoritative given the absence of sufficiently strong evidence.

Our conceptual proposal rests on three principles. First, comprehensive psychiatric and SUD assessment is necessary to tailor an effective integrated treatment. As reviewed above, there are likely multiple mechanisms through which SUDs may co-occur with internalizing disorders. Comprehensive assessment can generate an accurate clinical conceptualization of their interplay and help guide treatment targeting. Second, as recommended by Hawkins (31), interventions for SUD and internalizing disorders should be integrated into a single treatment program. We recommend an approach in which integrated treatment is tailored by combining selected therapeutic modules and in which adolescents receive full doses of the components (e.g., exposure-based therapy for anxiety disorders) thought necessary to meliorate their symptoms (75, 77). Third, treatment should be multi-faceted, with CBT, motivational, parental, and, where relevant, psychopharmacological components (78, 79). Previous reviews have noted that there are multiple critical targets for interventions in co-occurring disorders (30), and our model assumes an interdisciplinary approach in which each of these components plays a meaningful role.

Given the clinical necessity of understanding specific comorbidities and their interplay, we suggest an approach with three phases and two major decision points (Fig. 1). The first phase would be a formal diagnostic evaluation session with adolescents and their parent(s) or guardian(s) that employs a structured or semi-structured diagnostic interview (e.g., K-SADS-PL (80)). After diagnoses are made, providers may determine that some adolescents may be best treated through other services (e.g., inpatient hospitalization).

For candidate adolescents, the second phase of the intervention can begin. First, medication for mood or anxiety disorders (e.g., sertraline) and SUDs (e.g., buprenorphine), where indicated, may be started. Second, adolescents can begin to provide weekly follow-up measures in order to evaluate progress regarding both substance use and internalizing symptoms. These assessments could include the Timeline Follow-Back for substance use, the Children's Depression Rating Scale, and the Multidimensional Anxiety Scale for Children, in addition to weekly drug screens (81–83). To reinforce their attendance and negative drug screens, adolescents would receive contingency management, which may be particularly valuable for those adolescents with co-occurring conduct or defiance symptoms or who are otherwise less motivated for treatment. Third, this model extends the benefits of current cognitive behavioral and motivational enhancement therapies by allowing for up to four additional assessment sessions to fully conceptualize the interplay between internalizing disorder symptoms and substance related behaviors that may not emerge until a closer therapeutic alliance has been formed. One component of this assessment is a functional analysis in which close examination of the bidirectional relationship between triggers precipitating use (internal motives and external motives) and reinforcing consequences of use (both positive and negative) can be understood.

Next, patients could begin a third treatment phase, which would add final treatment components: modular individual CBT and parent training. Using the results of the functional analysis, specific treatment modules can be organized into interventions tailored to an individual adolescent's co-occurring internalizing symptoms. These tailored interventions can be roughly grouped into tracks for co-occurring trauma-related symptoms, depression, and non-trauma anxiety, and their length can be determined at this time. Recognizing that effectively addressing both the internalizing and substance use disorders takes time, our model attempts to strike a balance between undue treatment length and sufficient treatment duration. Since most CBT trials for adolescent depression fall within the 12–20 session range, we suggest a maximum of 20 sessions of individual CBT in the third phase. However, given the dearth of research on the topic, future investigations or clinical experience may ultimately dictate otherwise. For trauma, treatment components from SS may be the ideal third phase approach. For depression, behavioral activation strategies (84), for example, might be modified to promote pro-social, non-substance-related activities. For other anxiety disorders, treatments may focus on behavioral exposures that include substance-relevant cues. Socially anxious adolescents who engage in substance use to meliorate their discomfort in social gatherings might benefit, for instance, from exposures to “party” stimuli that combine substance-related and social cues. Finally, the third phase would also begin parent training independent of the adolescent's tracking. Recent research has found that contingency management approaches with parents can help improve adolescents' long-term abstinence-related behaviors (85, 86).

The proposed model for empirically informed intervention has advantages and disadvantages. Improving motivation for change has been identified as a key component in SUD treatment, and to the extent that internalizing symptoms are more distressing than are SUD symptoms, integrated treatments may see motivational gains if they can promise internalizing symptom relief. Additionally, in cases where internalizing symptoms are etiologically involved in the development of SUDs, secondary gain from the treatment of those internalizing symptoms may produce greater SUD symptom improvement (36). These potential benefits are offset by what may be substantial costs. Most notably, this approach would require greater time and resources than might some existing empirically supported treatments. Given that adolescent co-occurring disorders are associated with increased severity, however, it is likely that these individuals may require more intensive (and perhaps longer) treatments, and to the extent that this model could reduce relapse rates, it may prove financially beneficial in the long run.

Implications for future research

Consideration of our proposed model of integrated treatment should be tempered by the recognition that the empirical literature does not yet provide absolute recommendations for clinical practice. Existing gaps in the literature, however, provide key opportunities for future studies to clarify recommendations for clinicians. First, as described above, the existing body of randomized, controlled trials is not large, particularly when considering co-occurring disorders. More trials, particularly well-powered trials using appropriate, active control conditions, will help resolve current uncertainty. Second, studies using dismantling designs and other systematic means of identifying mechanisms of change will provide insight into ways of improving existing interventions (87). They additionally may help in selecting treatment components for inclusion in a modular integrated treatment. Contemporary CBT packages for SUDs and co-occurring disorders often include a wide range of interventions, including self-monitoring, psychoeducation, refusal skills, cognitive restructuring, and contingency management (79). Randomized, controlled trials with dismantling designs could examine the impact of each intervention and thereby provide evidence that one or more serves as an essential ingredient.

Third, the intervention literature will benefit from developmentally informed research into causal factors that are implicated in both SUD and internalizing disorders. Although there is much observational research on SUDs in youth, third variable confounding, transactional interplay among personal and environmental factors, and differences in the onset timing of different disorders raise serious questions regarding the inferences that can be drawn from traditional etiological research, even when temporal precedence can be demonstrated (36). Given the challenges of untangling complex developmental pathways, quasi-experimental designs may be valuable in clarifying causal relationships and selecting potential targets for intervention (88). Comparisons of twins or siblings within families, for example, can provide strong tests of childhood environmental exposures (89–91). Additionally, children of twins or siblings designs can add similar methodological rigor when testing the roles of parenting factors shared by siblings in offspring development (92).

Fourth, the present review and proposed model focused on a single SUD sub-group, adolescents with co-occurring internalizing disorders. Additional sources of variability among those needing treatment for SUDs also merit further consideration. Indeed, the co-occurring internalizing disorders population itself is likely far from homogenous, with many adolescents carrying additional internalizing and externalizing disorders or other medical comorbidities that may have implications for treatment. Other individual differences across and within these subgroups should be addressed in future research as well. One estimate, for example, suggested that only 6% of adolescent SUD treatment trials have tested for moderation by ethnicity (93).

Finally, our model draws heavily from behavioral and CBT intervention techniques, which is consistent with recommendations from previous reviews of this area (19, 30). CBT is effective in treating a range of internalizing disorders and is increasingly recognized as an efficacious treatment for adolescent SUDs. Nevertheless, when other efficacious approaches are developed, they may be able to replace or augment CBT as the central psychotherapy component in an integrated treatment model. As Wetherill and Tapert (14) note, mindfulness-based interventions may provide an alternative to CBT, and further evidence will help determine their level of efficacy. If new and more powerful treatments for co-occurring internalizing disorders are to be integrated and inclusive, they will rely upon advances in the etiological and treatment-outcome literatures to identify the most crucial targets and interventions.

Acknowledgments

We would like to thank Nicole Silva, MD for assistance with literature searching and Alisha Baker for assistance with figures. Funding sources were the National Institute on Alcohol Abuse and Alcoholism (F31AA020725 for PQ's effort), the Waggoner Center for Alcohol and Addiction Research at the University of Texas at Austin (for PQ's effort) and the National Institute of Drug Abuse (K12DA00035 for LH's effort).

References

1. Merikangas KR, McClair VL. Epidemiology of substance use disorders. *Hum Genet.* 2012; 131(6): 779–89. [PubMed: 22543841]
2. Anthony JC, Petronis KR. Early-onset drug use and risk of later drug problems. *Drug and alcohol dependence.* 1995; 40(1):9–15. [PubMed: 8746919]
3. Grant BF, Dawson DA. Age of onset of drug use and its association with DSM-IV drug abuse and dependence: results from the National Longitudinal Alcohol Epidemiologic Survey. *Journal of substance abuse.* 1998; 10(2):163–73. [PubMed: 9854701]
4. Stanton MD, Shadish WR. Outcome, attrition, and family–couples treatment for drug abuse: A meta-analysis and review of the controlled, comparative studies. *Psychol Bull.* 1997; 122(2):170–91. [PubMed: 9283299]
5. Tanner-Smith EE, Wilson SJ, Lipsey MW. The comparative effectiveness of outpatient treatment for adolescent substance abuse: A meta-analysis. *J Subst Abuse Treat.* 2013; 44(2):145–58. [PubMed: 22763198]
6. Becker SJ, Curry JF. Outpatient interventions for adolescent substance abuse: A quality of evidence review. *J Consult Clin Psychol.* 2008; 76(4):531–43. [PubMed: 18665683]
7. Kelly JF, Urbanoski K. Youth recovery contexts: the incremental effects of 12-step attendance and involvement on adolescent outpatient outcomes. *Alcohol Clin Exp Res.* 2012; 36(7):1219–29. [PubMed: 22509904]

8. Donovan DM, Ingalsbe MH, Benbow J, Daley DC. 12-step interventions and mutual support programs for Substance Use Disorders: An overview. *Soc Work Public Health*. 2013; 28(3–4):313–32. [PubMed: 23731422]
9. Magill M, Ray LA. Cognitive-behavioral treatment with adult alcohol and illicit drug users: A meta-analysis of randomized controlled trials. *J Stud Alcohol Drugs*. 2009; 70(4):516–27. [PubMed: 19515291]
10. Miller WR, Wilbourne PL. Mesa Grande: a methodological analysis of clinical trials of treatments for alcohol use disorders. *Addiction*. 2002; 97(3):265–77. [PubMed: 11964100]
11. Project MATCH Research Group. Matching alcoholism treatments to client heterogeneity: Project MATCH Posttreatment drinking outcomes. *J Stud Alcohol*. 1997; 58(1):7–29. [PubMed: 8979210]
12. Anton RF, O'Malley SS, Ciraulo DA, Cisler RA, Couper D, Donovan DM, et al. Combined pharmacotherapies and behavioral interventions for alcohol dependence. *J Am Med Assoc*. 2006; 295(17):2003–17.
13. Project MATCH Research Group. Matching alcoholism treatments to client heterogeneity: Project MATCH three-year outcomes. *Alcohol Clin Exp Res*. 1998; 22:1300–11. [PubMed: 9756046]
14. Wetherill R, Tapert SF. Adolescent brain development, substance use, and psychotherapeutic change. *Psychol Addict Behav*. 2013; 27(2):393–402. [PubMed: 22732057]
15. Rowe CL. Family therapy for drug abuse: Review and updates 2003–2010. *J Marital Fam Ther*. 2012; 38(1):59–81. [PubMed: 22283381]
16. Barnett E, Sussman S, Smith C, Rohrbach LA, Spruijt-Metz D. Motivational Interviewing for adolescent substance use: A review of the literature. *Addict Behav*. 2012; 37(12):1325–34. [PubMed: 22958865]
17. Jensen CD, Cushing CC, Aylward BS, Craig JT, Sorell DM, Steele RG. Effectiveness of motivational interviewing interventions for adolescent substance use behavior change: A meta-analytic review. *J Consult Clin Psychol*. 2011; 79(4):433–40. [PubMed: 21728400]
18. Winters KC, Botzet AM, Fahnhorst T. Advances in adolescent substance abuse treatment. *Curr Psychiatry Rep*. 2011; 13(5):416–21. [PubMed: 21701838]
19. Macgowan MJ, Engle B. Evidence for optimism: behavior therapies and motivational interviewing in adolescent substance abuse treatment. *Child Adolesc Psychiatr Clin N Am*. 2010; 19(3):527–45. [PubMed: 20682219]
20. Tripodi SJ, Bender K, Litschge C, Vaughn MG. Interventions for reducing adolescent alcohol abuse: A meta-analytic review. *Arch Pediatr Adolesc Med*. 2010; 164(1):85–91. [PubMed: 20048247]
21. Waldron HB, Turner CW. Evidence-based psychosocial treatments for adolescent substance abuse. *J Clin Child Adolesc Psychol*. 2008; 37(1):238–61. [PubMed: 18444060]
22. Toumbourou JW, Stockwell T, Neighbors C, Marlatt GA, Sturge J, Rehm J. Interventions to reduce harm associated with adolescent substance use. *Lancet*. 2007; 369(9570):1391–401. [PubMed: 17448826]
23. Waldron HB, Kaminer Y. On the learning curve: The emerging evidence supporting cognitive-behavioral therapies for adolescent substance abuse. *Addiction*. 2004; 99(Suppl2):93–105. [PubMed: 15488108]
24. O'Leary Tevyaw T, Monti PM. Motivational enhancement and other brief interventions for adolescent substance abuse: Foundations, applications and evaluations. *Addiction*. 2004; 99(Suppl2):63–75. [PubMed: 15488106]
25. Little HA. Family-based therapies for adolescent alcohol and drug use: Research contributions and future research needs. *Addiction*. 2004; 99(Suppl2):76–92. [PubMed: 15488107]
26. Deas D, Thomas SE. An overview of controlled studies of adolescent substance abuse treatment. *Am J Addict*. 2001; 10(2):178–89. [PubMed: 11444159]
27. Williams RJ, Chang SY, Addiction Centre Adolescent Research Group. A comprehensive and comparative review of adolescent substance abuse treatment outcome. *Clin Psychol Sci Pr*. 2000; 7(2):138–66.
28. Weinberg NZ, Rahdert E, Colliver JD, Glantz MD. Adolescent substance abuse: A review of the past 10 years. *J Am Acad Child Adolesc Psychiatry*. 1998; 37(3):252–61. [PubMed: 9519629]

29. Bender K, Springer DW, Kim JS. Treatment effectiveness with dually diagnosed adolescents: A systematic review. *Brief Treat Crisis Interv.* 2006; 6(3):177–205.
30. Bukstein OG, Horner MS. Management of the adolescent with Substance Use Disorders and comorbid psychopathology. *Child Adolesc Psychiatr Clin N Am.* 2010; 19(3):609–23. [PubMed: 20682224]
31. Hawkins EH. A tale of two systems: Co-occurring mental health and substance abuse disorders treatment for adolescents. *Annu Rev Psychol.* 2009; 60(1):197–227. [PubMed: 19035824]
32. Torrens M, Rossi PC, Martinez-Riera R, Martinez-Sanvisens D, Bulbena A. Psychiatric comorbidity and Substance Use Disorders: Treatment in parallel systems or in one integrated system? *Subst Use Misuse.* 2012; 47(8–9):1005–14. [PubMed: 22676568]
33. APA Presidential Task Force on Evidence-Based Practice. Evidence-based practice in psychology. *Am Psychol.* 2006; 61(4):271–85. [PubMed: 16719673]
34. Armstrong TD, Costello EJ. Community studies on adolescent substance use, abuse, or dependence and psychiatric comorbidity. *J Consult Clin Psychol.* 2002; 70(6):1224–39. [PubMed: 12472299]
35. Chan Y-F, Dennis ML, Funk RR. Prevalence and comorbidity of major internalizing and externalizing problems among adolescents and adults presenting to substance abuse treatment. *J Subst Abuse Treat.* 2008; 34(1):14–24. [PubMed: 17574804]
36. O’Neil KA, Conner BT, Kendall PC. Internalizing disorders and substance use disorders in youth: Comorbidity, risk, temporal order, and implications for intervention. *Clin Psychol Rev.* 2011; 31(1):104–12. [PubMed: 20817371]
37. Wu L-T, Gersing K, Burchett B, Woody GE, Blazer DG. Substance use disorders and comorbid Axis I and II psychiatric disorders among young psychiatric patients: Findings from a large electronic health records database. *J Psychiatr Res.* 2011; 45(11):1453–62. [PubMed: 21742345]
38. Wise BK, Cuffe SP, Fischer T. Dual diagnosis and successful participation of adolescents in substance abuse treatment. *J Subst Abuse Treat.* 2001; 21(3):161–5. [PubMed: 11728790]
39. Witkiewitz K, King K, McMahon RJ, Wu J, Luk J, Bierman KL, et al. Evidence for a multi-dimensional latent structural model of externalizing disorders. *J Abnorm Child Psychol.* 2013; 41(2):223–37. [PubMed: 22936218]
40. Krueger RF, Markon KE, Patrick CJ, Benning SD, Kramer MD. Linking antisocial behavior, substance use, and personality: An integrative quantitative model of the adult externalizing spectrum. *J Abnorm Psychol.* 2007; 116(4):645–66. [PubMed: 18020714]
41. Krueger RF, Hicks BM, Patrick CJ, Carlson SR, Iacono WG, McGue M. Etiologic connections among substance dependence, antisocial behavior and personality: Modeling the externalizing spectrum. *J Abnorm Psychol.* 2002; 111(3):411–24. [PubMed: 12150417]
42. Kendler KS, Aggen SH, Knudsen GP, Røysamb E, Neale MC, Reichborn-Kjennerud T. The structure of genetic and environmental risk factors for syndromal and subsyndromal common DSM-IV Axis I and all Axis II disorders. *Am J Psychiatry.* 2011; 168(1):29–39. [PubMed: 20952461]
43. Kendler KS, Chen X, Dick D, Maes H, Gillespie N, Neale MC, et al. Recent advances in the genetic epidemiology and molecular genetics of substance use disorders. *Nat Neurosci.* 2012; 15(2):181–9. [PubMed: 22281715]
44. Rose RJ, Dick DM, Viken RJ, Pulkkinen L, Kaprio J. Genetic and environmental effects on Conduct Disorder and Alcohol Dependence symptoms and their covariation at age 14. *Alcohol Clin Exp Res.* 2004; 28(10):1541–8. [PubMed: 15597087]
45. Hussong AM, Jones DJ, Stein GL, Baucom DH, Boeding S. An internalizing pathway to alcohol use and disorder. *Psychology of addictive behaviors: journal of the Society of Psychologists in Addictive Behaviors.* 2011; 25(3):390–404. [PubMed: 21823762]
46. Edwards AC, Sihvola E, Korhonen T, Pulkkinen L, Moilanen I, Kaprio J, et al. Depressive symptoms and alcohol use are genetically and environmentally correlated across adolescence. *Behav Genet.* 2011; 41(4):476–87. [PubMed: 20890653]
47. Glantz MD, Anthony JC, Berglund PA, Degenhardt L, Dierker L, Kalaydjian A, et al. Mental disorders as risk factors for later substance dependence: Estimates of optimal prevention and treatment benefits. *Psychol Med.* 2009; 39(08):1365–77. [PubMed: 19046473]

48. Mueser KT, Drake RE, Wallach MA. Dual diagnosis: A review of etiological theories. *Addict Behav.* 1998; 23(6):717–34. [PubMed: 9801712]
49. Emslie GJ. The psychopharmacology of adolescent depression. *Journal of child and adolescent psychopharmacology.* 2012; 22(1):2–4. [PubMed: 22339610]
50. Blazquez A, Mas S, Plana MT, Gasso P, Mendez I, Torra M, et al. Plasma fluoxetine concentrations and clinical improvement in an adolescent sample diagnosed with major depressive disorder, obsessive-compulsive disorder, or generalized anxiety disorder. *Journal of clinical psychopharmacology.* 2014; 34(3):318–26. [PubMed: 24743718]
51. Riggs PD, Mikulich-Gilbertson SK, Davies RD, Lohman M, Klein C, Stover SK. A randomized controlled trial of fluoxetine and cognitive behavioral therapy in adolescents with major depression, behavior problems, and substance use disorders. *Archives of pediatrics & adolescent medicine.* 2007; 161(11):1026–34. [PubMed: 17984403]
52. Warden D, Riggs PD, Min SJ, Mikulich-Gilbertson SK, Tamm L, Trello-Rishel K, et al. Major depression and treatment response in adolescents with ADHD and substance use disorder. *Drug and alcohol dependence.* 2012; 120(1–3):214–9. [PubMed: 21885210]
53. Substance Abuse and Mental Health Services Administration. National Registry of Evidence-based Programs and Practices (NREPP). Sep 9. 2013 [September 12, 2013]. Available from: <http://www.nrepp.samhsa.gov/>
54. Conrod PJ, Castellanos N, Mackie C. Personality-targeted interventions delay the growth of adolescent drinking and binge drinking. *J Child Psychol Psychiatry.* 2008; 49(2):181–90. [PubMed: 18211277]
55. Conrod PJ, Castellanos-Ryan N, Strang J. Brief, personality-targeted coping skills interventions and survival as a non-drug user over a 2-year period during adolescence. *Arch Gen Psychiatry.* 2010; 67(1):85–93. [PubMed: 20048226]
56. Conrod PJ, O’Leary-Barrett M, Newton N, Topper L, Castellanos-Ryan N, Mackie C, et al. Effectiveness of a selective, personality-targeted prevention program for adolescent alcohol use and misuse: A cluster randomized controlled trial. *JAMA Psychiatry.* 2013; 70(3):334–42. [PubMed: 23344135]
57. Esposito-Smythers C, Spirito A, Kahler CW, Hunt J, Monti P. Treatment of co-occurring substance abuse and suicidality among adolescents: A randomized trial. *J Consult Clin Psychol.* 2011; 79(6):728–39. [PubMed: 22004303]
58. Stanger C, Budney AJ. Contingency management approaches for adolescent substance use disorders. *Child Adolesc Psychiatr Clin N Am.* 2010; 19(3):547–62. [PubMed: 20682220]
59. Killeen TK, McRae-Clark AL, Waldrop AE, Upadhyaya H, Brady KT. Contingency management in community programs treating adolescent substance abuse: A feasibility study. *J Child Adolesc Psychiatr Nurs.* 2012; 25(1):33–41. [PubMed: 22299805]
60. Hobbs JDJ, Kushner MG, Lee SS, Reardon SM, Maurer EW. Meta-analysis of supplemental treatment for depressive and anxiety disorders in patients being treated for Alcohol Dependence. *Am J Addict.* 2011; 20(4):319–29. [PubMed: 21679263]
61. Kushner MG, Maurer EW, Thuras P, Donahue C, Frye B, Menary KR, et al. Hybrid cognitive behavioral therapy versus relaxation training for co-occurring anxiety and alcohol disorder: A randomized clinical trial. *J Consult Clin Psychol.* 2013; 81(3):429–42. [PubMed: 23276124]
62. Watkins KE, Hunter SB, Hepner KA, Paddock SM, Cruz Edl, Zhou AJ, et al. An effectiveness trial of group cognitive behavioral therapy for patients with persistent depressive symptoms in substance abuse treatment. *Arch Gen Psychiatry.* 2011; 68(6):577–84. [PubMed: 21646576]
63. Tiet QQ, Mausbach B. Treatments for patients with dual diagnosis: A review. *Alcohol Clin Exp Res.* 2007; 31(4):513–36. [PubMed: 17374031]
64. Dennis M, Godley SH, Diamond G, Tims FM, Babor T, Donaldson J, et al. The Cannabis Youth Treatment (CYT) Study: Main findings from two randomized trials. *J Subst Abuse Treat.* 2004; 27(3):197–213. [PubMed: 15501373]
65. Naar-King, S.; Suarez, M. *Motivational interviewing with adolescents and young adults.* New York: Guilford Press; 2011.
66. Linehan, MM. *Cognitive behavioral treatment of borderline personality disorder.* New York: Guilford Press; 1993.

67. Linehan, MM. Skills training manual for treating borderline personality disorder. New York: Guilford Press; 1993.
68. Linehan MM, Armstrong HE, Suarez A, Allmon D, Heard HL. Cognitive-behavioral treatment of chronically parasuicidal borderline patients. *Arch Gen Psychiatry*. 1991; 48(12):1060–4. [PubMed: 1845222]
69. Lynch TR, Trost WT, Salsman N, Linehan MM. Dialectical behavior therapy for borderline personality disorder. *Annu Rev Clin Psychol*. 2007; 3:181–205. [PubMed: 17716053]
70. Najavits LM, Hien D. Helping vulnerable populations: A comprehensive review of the treatment outcome literature on Substance Use Disorder and PTSD. *J Clin Psychol*. 2013; 69(5):433–79. [PubMed: 23592045]
71. Najavits LM, Gallop RJ, Weiss RD. Seeking safety therapy for adolescent girls with PTSD and substance use disorder: A randomized controlled trial. *J Behav Health Serv Res*. 2006; 33(4):453–63. [PubMed: 16858633]
72. D’Onofrio BM, Turkheimer E, Emery RE, Slutske WS, Heath AC, Madden PA, et al. A genetically informed study of marital instability and its association with offspring psychopathology. *J Abnorm Psychol*. 2005; 114(4):570–86. [PubMed: 16351381]
73. Harden KP, Lynch SK, Turkheimer E, Emery RE, D’Onofrio BM, Slutske WS, et al. A behavior genetic investigation of adolescent motherhood and offspring mental health problems. *J Abnorm Psychol*. 2007; 116(4):667–83. [PubMed: 18020715]
74. Rotheram-Borus MJ, Swendeman D, Chorpita BF. Disruptive innovations for designing and diffusing evidence-based interventions. *Am Psychol*. 2012; 67(6):463–76. [PubMed: 22545596]
75. Weisz JR, Chorpita BF, Palinkas LA, Schoenwald SK, Miranda J, Bearman SK, et al. Testing standard and modular designs for psychotherapy treating depression, anxiety, and conduct problems in youth: A randomized effectiveness trial. *Arch Gen Psychiatry*. 2012; 69(3):274–82. [PubMed: 22065252]
76. Chorpita BF, Daleiden EL. Mapping evidence-based treatments for children and adolescents: Application of the distillation and matching model to 615 treatments from 322 randomized trials. *J Consult Clin Psychol*. 2009; 77(3):566–79. [PubMed: 19485596]
77. Mitchell PF. Designing evidence-based treatments for youth with multiple and complex needs: A modular practice elements approach. *Adv Dual Diagn*. 2012; 5(3):122–36.
78. Riggs PD, Mikulich-Gilbertson SK, Davies RD, Lohman M, Klein C, Stover SK. A randomized controlled trial of fluoxetine and cognitive behavioral therapy in adolescents with major depression, behavior problems, and substance use disorders. *Arch Pediatr Adolesc Med*. 2007; 161(11):1026–34. [PubMed: 17984403]
79. Riggs PD, Winhusen T, Davies RD, Leimberger JD, Mikulich-Gilbertson S, Klein C, et al. Randomized controlled trial of osmotic-release methylphenidate with cognitive-behavioral therapy in adolescents with attention-deficit/hyperactivity disorder and substance use disorders. *J Am Acad Child Adolesc Psychiatry*. 2011; 50(9):903–14. [PubMed: 21871372]
80. Kaufman J, Birmaher B, Brent D, Rao U, Flynn C, Moreci P, et al. Schedule for affective disorders and schizophrenia for school-age children-present and lifetime version (K-SADS-PL): Initial reliability and validity data. *J Am Acad Child Adolesc Psychiatry*. 1997; 36(7):980–8. [PubMed: 9204677]
81. Poznanski, EO.; Mokros, HB. Children’s depression rating scale, revised (CDRS-R): manual. Los Angeles, CA: Western Psychological Services; 1996.
82. Sobell, LC.; Sobell, MB. Timeline Follow-Back: A technique for assessing self-reported ethanol consumption. In: Allen, J.; Litten, RZ., editors. *Measuring alcohol consumption: Psychosocial and biological methods*. Totowa, NJ: Humana Press; 1992. p. 41-72.
83. March JS, Parker JD, Sullivan K, Stallings P, Conners CK. The Multidimensional Anxiety Scale for Children (MASC): Factor structure, reliability, and validity. *J Am Acad Child Adolesc Psychiatry*. 1997; 36(4):554–65. [PubMed: 9100431]
84. Dimidjian S, Barrera M Jr, Martell C, Muñoz RF, Lewinsohn PM. The origins and current status of behavioral activation treatments for depression. *Annu Rev Clin Psychol*. 2011; 7:1–38. [PubMed: 21275642]

85. Ryan SR, Stanger C, Thostenson J, Whitmore JJ, Budney AJ. The impact of disruptive behavior disorder on substance use treatment outcome in adolescents. *J Subst Abuse Treat.* 2013; 44(5): 506–14. [PubMed: 23228436]
86. Stanger C, Budney AJ, Kamon JL, Thostensen J. A randomized trial of contingency management for adolescent marijuana abuse and dependence. *Drug Alcohol Depend.* 2009; 105(3):240–7. [PubMed: 19717250]
87. Hamby S, Grych J. Evidence-based interventions need to be more systematic, not more disruptive. *Am Psychol.* 2013; 68(6):476–7. [PubMed: 24016126]
88. Rutter M. Proceeding from observed correlation to causal inference: The use of natural experiments. *Perspect Psychol Sci.* 2007; 2(4):377–95. [PubMed: 26151974]
89. Lahey BB, D’Onofrio BM. All in the family: Comparing siblings to test causal hypotheses regarding environmental influences on behavior. *Curr Dir Psychol Sci.* 2010; 19(5):319–23. [PubMed: 23645975]
90. Dick DM, Johnson JK, Viken RJ, Rose RJ. Testing between-family associations in within-family comparisons. *Psychol Sci.* 2000; 11(5):409–13. [PubMed: 11228913]
91. Johnson W, Turkheimer E, Gottesman II, Bouchard TJ Jr. Beyond heritability: Twin studies in behavioral research. *Curr Dir Psychol Sci.* 2009; 18(4):217–20. [PubMed: 20625474]
92. D’Onofrio BM, Turkheimer EN, Eaves LJ, Corey LA, Berg K, Solaas MH, et al. The role of the Children of Twins design in elucidating causal relations between parent characteristics and child outcomes. *J Child Psychol Psychiatry.* 2003; 44(8):1130–44. [PubMed: 14626455]
93. Strada MJ, Donohue B, Lefforge NL. Examination of ethnicity in controlled treatment outcome studies involving adolescent substance abusers: A comprehensive literature review. *Psychol Addict Behav.* 2006; 20(1):11–27. [PubMed: 16536661]

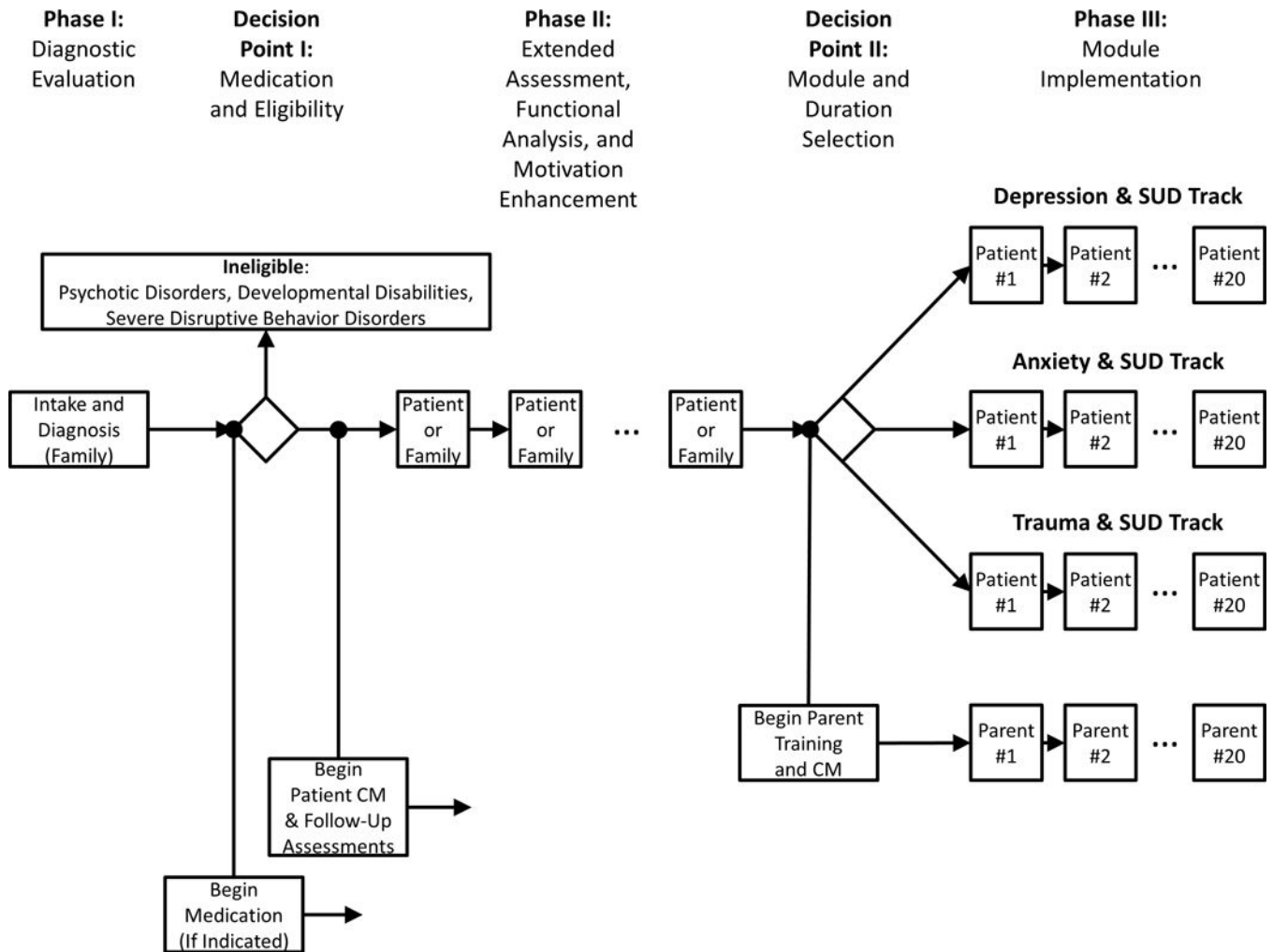


Figure 1. Conceptual model of integrated, family-inclusive CBT for adolescent SUDs and co-occurring internalizing disorders. Phase III tracking (i.e., depression, non-trauma anxiety, and trauma tracks) would be determined by the extended assessment and should include modules as indicated in the functional assessment. CM = contingency management for retention and negative drug screens (patient) and adherence (parents and/or guardian).