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Psychosocial Treatments for Bipolar Disorder in Children and Adolescents

Haley M. Brickman and Mary A. Fristad

Big Lots Behavioral Health Services and Division of Child and Family Psychiatry, Nationwide Children's Hospital, Columbus, Ohio, USA; email: haley.brickman@nationwidechildrens.org, mary.fristad@nationwidechildrens.org

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bipolar disorder, psychotherapy, youth, manic depression, child, adolescent

Abstract

Evidence suggests that adjunctive psychosocial intervention for the treatment of pediatric bipolar spectrum disorders (BPSDs) is effective, feasible, and highly accepted as both an acute and maintenance treatment for youth with BPSD diagnoses as well as a preventive treatment for high-risk youth who are either asymptomatic or exhibit subsyndromal mood symptoms. Here, we provide a comprehensive review of all known evidence-based interventions, including detailed descriptions of treatment targets and core components, results of clinical trials, and updated research on mediators and moderators of treatment efficacy. Treatments are presented systematically according to level of empirical support (i.e., well established, probably efficacious, possibly efficacious, experimental, or questionable); upcoming and ongoing trials are included when possible. In line with a staging approach, preventive interventions are presented separately. Recommendations for best practices based on age, stage, and additional evidence-based child and family factors shown to affect treatment outcomes are provided.

Contents

PSYCHOSOCIAL TREATMENTS FOR BIPOLAR SPECTRUM DISORDERS IN CHILDREN AND ADOLESCENTS

Bipolar spectrum disorders (BPSDs), which include bipolar disorder (BD) type 1 (BD1), bipolar disorder type 2 (BD2), cyclothymic disorder (CYC), and other specified bipolar and related disorders (OSBARD), are chronic, recurrent conditions associated with considerable impairment and reduced quality of life (Freeman et al. 2009) as well as high rates of hospitalization and suicidality (Hauser et al. 2013). Once considered primarily a disorder of adulthood, it is now recognized that BPSDs occur in youth as well as adults. Although BD1, or classic BD, has an average prevalence of only 0.6% in youth, when considering all BPSD subtypes, international prevalence increases to approximately 3.9% (Van Meter et al. 2019). Inclusion of OSBARD, the most prevalent subtype in youth, is meaningful because these youth exhibit similar levels of functional impairment compared to youth with BD1, and their likelihood of conversion to BD1 or BD2 over 5–8 years is approximately 30–50% (Axelson et al. 2011; Birmaher et al. 2009, 2018). Despite significant morbidity and mortality associated with BPSDs, approximately half of affected youth remain untreated (Khazanov et al. 2015, Merikangas et al. 2011).

Early identification and intervention are necessary to combat the often-disabling effects of BPSDs. Pharmacotherapy is generally considered first-line treatment (Yatham et al. 2018); however, efficacy trials of evidence-based treatments provide strong support for adjunctive psychosocial interventions, and guidelines and practice parameters recommend a combination approach (Kowatch et al. 2005, McClellan et al. 2007). Addition of psychosocial treatments to pharmacotherapy results in increased improvements in mood symptom severity, frequency, and recovery rates (for reviews, see Fristad 2016, Weinstein et al. 2013). Psychotherapy also targets circadian rhythms as well as environmental and psychosocial factors that medication alone cannot address—for example, by providing education, support, and skills necessary to create lasting improvements in family relations, school performance, and peer relations. Psychosocial treatments can also be individually tailored to address specific environmental challenges or co-occurring behavioral concerns. Finally, these treatments may improve medication adherence, resulting in improved overall functioning.

Early symptom onset (Birmaher et al. 2014, Estrada-Prat et al. 2019), increased frequency and severity of episodes (Youngstrom & Algorta 2014), and delayed treatment (Post et al. 2010) are all associated with a worse course of BPSD; thus, psychosocial interventions for BPSDs are likely to be particularly effective when provided early. In fact, preliminary evidence suggests that early intervention may decrease conversion rates to BPSDs in youth with subsyndromal symptoms (Miklowitz et al. 2013, Nadkarni & Fristad 2010). Delaying episode onset could have long-term effects on course and ultimate severity of BPSDs, as number of episodes has consistently been associated with poor prognosis (Magalhães et al. 2012) and treatment nonresponse (Peters et al. 2014). A major focus, then, is identification of early markers and risk factors that can be used to target high-risk individuals who would benefit from preventive interventions (Vieta et al. 2018).

Increased understanding of early indicators has allowed for increasingly early identification of high-risk youth based on genetic and environmental factors that often precede emergence of full bipolar symptoms (Faedda et al. 2019, Luby & Navsaria 2010). In addition, progression of BPSDs in high-risk youth frequently follows a predictable developmental course, beginning with early (prepubertal) nonmood symptoms (most commonly anxiety and sleep disturbance; Duffy et al. 2016, Levenson et al. 2015, Ritter et al. 2015) followed by emergence of nonspecific minor mood symptoms around puberty, depressive episodes in early adolescence, and, finally, onset of the first (hypo)manic episode, which often occurs several years following the first depressive episode (Duffy et al. 2017, Mesman et al. 2017). This conceptualization of a BPSD as a chronic, progressive illness lends itself well to a clinical staging approach. Indeed, several BPSD staging models have demonstrated preliminary prognostic validity (Benarous et al. 2016).

Traditionally used to classify and treat chronic medical illness, staging models place individuals along an illness continuum that ranges from stage 0 (high risk) to 4. In BPSD models, high risk generally refers to family history of BPSDs, which is the single strongest predictor of developing a BPSD: Approximately 25% of offspring of parents with BPSDs (OBD) eventually develop the disorder (Duffy et al. 2019). Stage 0 describes high-risk asymptomatic youth, stage 1 (prodromal stage) describes high-risk youth with subsyndromal symptoms, stage 2 represents first episode onset, and stages 3 and 4 represent recurrent, chronic mood episodes with significant impairment. In this review, we use the model proposed by Berk et al. (2017) because it is particularly relevant to the discussion of preventive interventions; Berk and colleagues' model separates out the prodromal stage into an earlier "heterotypic" prodrome (1a) characterized by nonspecific symptoms from a later, more advanced "homotypic" or "ultrahigh risk" prodrome (1b) characterized by BPSD-specific symptoms. One practical use of staging models is the ability to predict transition to subsequent stages and inform appropriate treatment options. In line with this approach, several preventive interventions are being developed for the earliest stages of BPSDs (see Perich & Mitchell 2019; for review, see Saraf et al. 2021).

The current article provides a comprehensive review of evidence-based psychosocial treatments for youth at all stages of BPSDs, including core components and empirical support, updated research regarding causal mechanisms and identification of individuals for whom interventions are likely to be most effective, and how this information can aid treatment decisions. In line with recent staging perspectives (Post et al. 2020), interventions developed for youth with BPSDs are presented separately from preventive interventions developed specifically for early-stage (stages 0 and 1a) youth. We conclude with a discussion of limitations, trends, and proposed future directions to address identified gaps in the literature.

EVIDENCE-BASED STATUS OF PSYCHOSOCIAL INTERVENTIONS FOR YOUTH WITH BIPOLAR SPECTRUM DISORDERS

For over two decades, researchers have conducted clinical trials testing the efficacy of psychosocial treatments for youth with BPSDs. Moreover, continued advances in our understanding of treatments have led to the development of additional interventions that remain to be tested in large-scale trials. Here, we present each evidence-based intervention developed for youth with BPSDs; modifications for high-risk youth are included if the sample included youth with OSBARD [previously called bipolar disorder not otherwise specified (BP-NOS)], CYC, or significant mood disturbance. Interventions are organized by level of empirical support; treatment classification (i.e., well established, probably efficacious, possibly efficacious, experimental, or questionable) is based on the Society for Clinical Child and Adolescent Psychology's adaptation of the Division 12 Task Force on Promotion and Dissemination of Psychological Procedures criteria used to evaluate evidence-based treatments (Southam-Gerow & Prinstein 2014). Currently, three interventions together compose a class of well-established treatments, meaning they have demonstrated efficacy through two or more research groups' independent, randomized controlled trials (RCTs). One intervention classified as possibly efficacious is predicted to advance to the classification of probably efficacious pending replication of treatment effects in an ongoing RCT. Similarly, several treatments currently classified as experimental, meaning they either have not yet been tested in an RCT or have been tested in studies not meeting methodological criteria necessary to be considered possibly efficacious, show promise and may prove to be efficacious through implementation of additional trials. For this reason, ongoing studies identified in clinical trial registries are noted throughout this section. **Table 1** provides a description of each treatment and its classification.

Well-Established Treatment: Family Psychoeducation Plus Skill Building

Several large, rigorous, single-blind RCTs have demonstrated the efficacy of three manualized treatments, all of which incorporate family-focused psychoeducation, cognitive behavioral therapy (CBT), and communication/problem solving training adjunctive to pharmacotherapy and/or other psychosocial services. These three manualized treatments fall under the umbrella of family psychoeducation plus skill building (FP + SB) and can be considered a well-established class of interventions. They include family-focused treatment for adolescents (FFT-A; Miklowitz et al. 2008, 2011, 2013), child- and family-focused CBT (CFF-CBT; Pavuluri et al. 2004; West et al. 2007, 2009, 2014), and psychoeducational psychotherapy (PEP; Fristad 2006; Fristad et al. 2002, 2003, 2009, 2015; Goldberg-Arnold et al. 1999).

FFT-A, CFF-CBT, and PEP are all manualized, family-based interventions that begin with psychoeducation and later shift to skill building, have foundations in CBT, are provided to families, and are intended to be adjunctive to pharmacotherapy. The theoretical basis for including the family in treatment is based on the known impact of family environment on symptoms and treatment outcomes in individuals with BPSDs. Negative family environments are associated with exacerbated symptoms and poor prognosis (Sullivan et al. 2012). Given that families of individuals with BPSDs exhibit increased rates of impairment in family functioning, as measured by high levels of conflict, control, and expressed emotion (EE; i.e., the amount of criticism, hostility, or emotional overinvolvement exhibited by family members) and lower levels of cohesion and expressiveness (Stapp et al. 2020), one major focus of these interventions is to improve the family environment with the goal of ultimately improving the symptoms, course, and outcome of the BPSD. Research also supports a strong emphasis on psychoeducation, which is consistently found to contribute to better short- and long-term outcomes (Miklowitz 2008). Finally, these

Table 1 Psychosocial interventions for youth with or at high risk for BPSDs

Treatment	Treatment population	Format	Length	Core components/modules	Classification
CFF-CBT	Youth with BPSDs and their families	Adjunctive to medication management; single-family: alternating parent, child, and family sessions; multifamily: concurrent parent and child groups	12 sessions over 3 months (acute phase) + maintenance phase booster sessions	Family psychoeducation + CBT-based skill building; RAINBOW: **R**outine; **a**ffect regulation; **I** can do it; **n**o negative thoughts/live in the **n**ow; **b**e a good friend/**b**alanced lifestyle; **o**h, how can we solve it?; and **w**ays to get support.	Together, CFF-CBT, FFT-A, and MF-PEP/IF-PEP form a class of well-established treatments
Family-focused treatment (FFT-A, FFT-HR)	Adolescents with BPSDs (FFT-A) or at high risk with mood symptoms (FFT-HR) and their families	Adjunctive to medication management; single-family	Twenty-one 50-min sessions over 9 months (FFT-A); 12 sessions over 4 months (FFT-HR)	Family psychoeducation + CBT-based skill building; three phases: psychoeducation, communication training, problem solving; components: encourage common understanding of disorder within family, decrease EE, psychoeducation regarding symptom management, stress/coping, mood charting, prevention planning	
PEP	Youth with mood disorders and their parents	Adjunctive to medication management; multifamily (MF-PEP) or single-family (IF-PEP)	Eight 90-min sessions of conjoint parent and youth groups (multifamily); seventeen to twenty-four 50-min sessions (single-family)	Family psychoeducation + CBT-based skill-building; components: psychoeducation, mood identification/monitoring, emotion regulation, cognitive restructuring, communication training, problem solving, in vivo social skills training; specific focus on equipping parents with knowledge and resources	
DBT	Adolescents with BPSDs; recently in acute episode	Adjunctive to medication management; weekly (acute phase) or biweekly (continuation phase) alternating individual therapy and family skill-building sessions	36 sessions (18 family skill building, 18 individual) over 1 year	Core modules: mindfulness, emotion regulation, distress tolerance, interpersonal effectiveness; psychoeducation; skill training; explicit focus on suicidal ideation/behaviors and treatment adherence/commitment	Possibly efficacious

(*Continued*)

Table 1 (*Continued*)

Treatment	Treatment population	Format	Length	Core components/modules	Classification
IPSRT-A	Adolescents with BPSDs	Adjunctive to medication management; primarily individual with limited family involvement	16–18 sessions over 20 weeks	Psychoeducation; improving relevant interpersonal problems; building structure, social routine, sleep regularity	Experimental
BMI	Adolescents and young adults aged 12–22 with BD1, BD2, or BP-NOS	Adjunctive; person-centered, individualized format; typically individual—parent or family involvement depends on individual preferences and appropriateness	Three 30-min sessions; two sessions over 4 weeks + booster session at 3 months	Core components: elicit thoughts and feelings about medication; psychoeducation; assess readiness for change/exploring ambivalence; create and evaluate adherence plan of action	Experimental
CBT for youth with BPSDs	Children and adolescents with BPSDs	Adjunctive to medication management; weekly sessions with parent check-ins at the end of every session	12 weekly sessions (nine individual, two family, one parent-only)	Psychoeducation, medication compliance, mood monitoring, identifying and modifying unhelpful thinking, stressor/trigger identification, sleep maintenance, family communication; optional modules for substance abuse, social skills, anger management, contingency management; CBT techniques	Experimental
RECOVER intervention	Adolescents and young adults aged 15–25 with BD1 who have recently experienced their first manic episode with psychotic features	Adjunctive to medication management and other interventions; primarily individual with optional family sessions	10–18 sessions delivered over 6 months	Six core modules—assessment and engagement, formulation, psychoeducation, specific CBT interventions, social rhythm regulation, and wellness planning—plus optional targeted modules (relationship issues/family work, substance abuse and comorbid disorders, medication, functional recovery)	Experimental

Abbreviations: BD1, bipolar disorder type 1; BD2, bipolar disorder type 2; BMI, brief motivational intervention; BP-NOS, bipolar disorder not otherwise specified; BPSD, bipolar spectrum disorder; CBT, cognitive behavioral therapy; CFF-CBT, child- and family-focused CBT; DBT, dialectical behavioral therapy; EE, expressed emotion; FFT-A, family-focused treatment for adolescents; FFT-HR, high-risk adaptation of FFT-A; IF-PEP, individual-family PEP; IPSRT-A, interpersonal and social rhythm therapy for adolescents; MF-PEP, multifamily PEP; PEP, psychoeducational psychotherapy; RECOVER, Research into Cognitive and Behavioural Versatility.

interventions place heavy emphasis on skill building, the primary goal of which is to increase the frequency of positive interactions and decrease EE in families by teaching skills necessary to engage in constructive communication and effective problem solving.

Several RCTs and other clinical trials have demonstrated the efficacy of single- and multiple-family FP + SB at improving outcomes for youth with BPSDs. FFT-A, CCF-CBT, and PEP have all been found to lead to lasting improvements in mood symptoms; secondary outcomes, such as psychosocial functioning and behavioral change, are also frequently reported (Boylan et al. 2013, Vesco et al. 2018). These interventions also directly influence family functioning by providing additional support for inclusion of family members in treatment. **Table 2** provides a list of clinical trials of well-established interventions.

Family-focused treatment for adolescents. FFT-A (Miklowitz et al. 2004) is an adaptation of a well-established treatment for adults with BPSDs—family-focused treatment (FFT)—modified to be developmentally appropriate for adolescents. Informed by research associating negative family environments with poor outcomes in individuals with BPSDs, the overarching goals of FFT-A are to encourage family members to develop a common understanding of the disorder, decrease EE, and provide psychoeducation regarding symptom management, stress and coping strategies, mood charting, and prevention planning. The three phases of FFT-A (psychoeducation, communication enhancement training, and problem solving) are delivered to adolescents, parents, and available siblings over 21 sessions.

In the initial open trial of FFT-A (Miklowitz et al. 2006), 20 adolescents with BPSDs demonstrated reduced mania, depression, total mood problems, and parent-rated problem behaviors following treatment and showed sustained improvements over 2 years. Since this development trial, two RCTs have been conducted. In the first (Miklowitz et al. 2008), 58 adolescents with BPSDs were randomly assigned to FFT-A plus pharmacotherapy or an enhanced care (EC) condition that consisted of three family psychoeducational sessions and pharmacotherapy. FFT-A was feasible, acceptable, and effective at decreasing mood severity, particularly with regard to depressive symptoms; participants recovered faster from baseline depressive symptoms, spent more time in remission, and exhibited a more favorable trajectory of depressive symptoms over 2 years.

Miklowitz et al. (2014) also conducted a multisite RCT ($N = 145$) comparing FFT-A plus pharmacotherapy to EC plus pharmacotherapy. In contrast to results of the initial RCT, FFT-A was not associated with improvements in depressive symptoms; however, adolescents who received FFT-A exhibited significantly reduced manic symptom severity during the second year of the study, indicating that FFT-A may be effective in long-term stabilization of mania. FFT-A was also associated with increased quality of family relationships during treatment and improved physical well-being at follow-up (O'Donnell et al. 2017); increased family cohesion persisted 2 years following treatment (O'Donnell et al. 2020). Ongoing trials of FFT-A, including an RCT in the United Kingdom that focuses on family functioning and well-being in adolescents and young adults, will continue to provide insight into treatment efficacy. Qualitative results from a recent feasibility trial of this 16-session UK FFT-A indicated feasibility, acceptability, and potential efficacy at improving family functioning (Sharma et al. 2020).

An abbreviated high-risk adaptation of FFT-A (FFT-HR) has demonstrated efficacy for youth with significant mood disturbance (including diagnoses of major depressive disorder, CYC, and OSBARD/BP-NOS) and positive family history of BPSDs. In an open trial of FFT-HR, 13 OBD youth demonstrated improvements in depressive symptoms, hypomanic symptoms, and global functioning; these were maintained at 1-year follow-up (Miklowitz et al. 2011). A subsequent RCT of 40 OBD youth demonstrated positive treatment effects, including faster recovery from mood episodes, longer remission periods, and improved (hypo)mania scores over 1 year (Miklowitz

Table 2 Clinical trials of well-established interventions for youth with BPSDs

Author(s) and year(s)	Intervention	Study design	Sample	Comparison group	Results	Comments/follow-up studies
Fristad et al. 2002, 2003; Goldberg-Arnold et al. 1999	MF-PEP + TAU	RCT with 6-month follow-up	35 children aged 8–11 with mood disorders (46% BPSD; 54% depressive disorder)	WLC + TAU	At 2- and 6-month follow-ups, improved family interactions and increased parent knowledge of mood disorders in MF-PEP + TAU families; at posttest and 4-month follow-up, increased knowledge, skills, and support; at 6-month follow-up, improved ability to obtain appropriate services, positive attitudinal shift in parents, and greater perceived social support from parents among youth	Positive consumer evaluations from parents and children
Pavuluri et al. 2004, West et al. 2007	Single-family CFF-CBT + study pharmacotherapy	Open trial with 3-year follow-up	34 youth aged 5–17 with BPSDs	NA	Significant improvements across all outcome measures (i.e., ADHD symptoms, aggression, mania, depression, psychosis, sleep disturbance, social and academic functioning) following acute treatment phase	High feasibility/ acceptability: 34/34 remained in treatment; symptom reduction and improvements in global functioning maintained at 3-year follow-up with delivery of booster sessions and pharmacotherapy
Miklowitz et al. 2004, 2006	FFT-A + study pharmacotherapy	Open trial with 1-year follow-up	20 adolescents (mean age = 15 years) with BPSDs	NA	Improvements in total mood symptoms, depressive symptoms, and problem behaviors at 1-year follow-up	Sustained improvements over 2 years
Fristad 2006	IF-PEP + TAU	RCT with 1-year follow-up	20 youth aged 8–11 with BPSDs	WLC + TAU	Immediate and long-term (1-year) improvements in children's mood symptoms in IF-PEP group (effect sizes favored IF-PEP, although not significantly greater than those seen in the WLC group); EE improved significantly in IF-PEP group compared to controls	Positive consumer evaluations from parents and children following treatment

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Table 2 (*Continued*)

Author(s) and year(s)	Intervention	Study design	Sample	Comparison group	Results	Comments/follow-up studies
Miklowitz et al. 2008, Sullivan et al. 2012	FFT-A + study pharmacotherapy	RCT with 2-year follow-up	58 adolescents ($n = 30$, FFT-A; $n = 28$, EC) aged 12–18 with BPSDs	EC	No difference in number of participants who met recovery criteria (91% of sample; did not differ by group) or weeks free of any mood symptoms; however, FFT-A adolescents recovered faster from baseline depressive symptoms (10.2 compared to 14.1 weeks), spent more time in remission from depressive symptoms, and exhibited a more favorable trajectory of depressive symptoms over 2-year follow-up; no group differences with regard to manic symptoms (e.g., recovery from mania, time spent free of manic symptoms)	Baseline high-conflict FFT-A families demonstrated greater reductions in conflict over time compared to baseline low-conflict families; decreases in parent-reported conflict predicted decreases in adolescents' manic symptoms over 2 years
Boylan et al. 2013, Cummings & Fristad 2012, Fristad et al. 2009, Mendenhall et al. 2009, Nadkarni & Fristad 2010	MF-PEP + TAU	RCT with 1-year follow-up	165 youth ($n = 78$, MF-PEP; $n = 87$, WLC) aged 8–11 with mood disorders (70% BPSD)	WLC + TAU	Significant improvement in mood (manic + depressive) symptom severity in MF-PEP group compared to WLC at 1-year follow-up; WLC group showed the same significant decrease after completing treatment (delayed)	MF-PEP improved quality of services used, which led to decreased mood symptom severity; high levels of baseline anxiety symptoms were associated with greater improvement in global functioning in MF-PEP participants; MF-PEP led to improvements in ADHD, ODD, and total disruptive behavior symptoms; disruptive behavior symptoms did not affect efficacy of MF-PEP on mood; lower conversion from depression with transient manic features to BPSD in MF-PEP

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Table 2 (*Continued*)

Author(s) and year(s)	Intervention	Study design	Sample	Comparison group	Results	Comments/follow-up studies
West et al. 2009	CFF-CBT multifamily format + study pharmacotherapy	Open trial	26 youth aged 6–12 with BPSDs	NA	Significant improvements in parent-rated manic symptoms and psychosocial functioning; no group differences for depressive symptoms; nonsignificant (trending) improvements in parent knowledge and perceived self-efficacy in coping	Multifamily format was feasible and acceptable; improved parental knowledge and perceived coping associated with improvements in children's emotional symptoms, conduct problems, total difficulties, hyperactivity; lower parental stress moderated effects of CFF-CBT on improvements in children's psychosocial functioning
Miklowitz et al. 2011	FFT-HR + TAU	Open trial with 1-year follow-up	13 youth aged 9–16 with depressive disorders, CYC, or BP-NOS and a parent with BD1 or BD2	NA	Improvements in both hypomanic and depressive symptoms and global functioning at 1-year follow-up	FFT-HR was feasible and acceptable to families (85% attended ≥9 of 12 sessions) and delivered with fidelity
Garrett et al. 2015, Miklowitz et al. 2013	FFT-HR + study pharmacotherapy	RCT with 1-year follow-up	40 youth ($n = 21$, FFT-HR; $n = 19$, FEC) aged 9–17 with MDD (42.5%), CYC (7.5%), or BP-NOS (50%) with a first-degree relative with a BPSD	FEC	In comparison to FEC group, FFT-HR had more weeks in remission (26.8 versus 19.5), more rapid recovery from initial mood (13 versus 21.3 weeks), shorter duration of depressive (9.2 versus 21.4 weeks) symptoms, more favorable trajectory of hypomanic symptoms, and fewer weeks in subthreshold states	Treatment effects of FFT-HR significantly higher among youth in high-EE (versus low-EE) families for weeks in remission and subthreshold states, nonsignificantly higher for weeks to recovery; mood symptom improvements associated with increased DL-PFC activation that occurred during treatment

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Table 2 (*Continued*)

Author(s) and year(s)	Intervention	Study design	Sample	Comparison group	Results	Comments/follow-up studies
B.I. Goldstein et al. 2014	FFT-SUD + TAU	Open trial/ feasibility study	10 adolescents (mean age = 16.9; six completed midtreatment assessments) with a BPSD and comorbid SUD	NA	Improvements in depressive and (hypo)manic symptoms and global functioning in the six adolescents who completed 6-month (midtreatment) assessments; substance use was not significantly affected	Parental active SUD associated with premature termination/noncompletion
MacPherson et al. 2014b	MF-PEP + TAU	Open trial/ feasibility of community outpatient setting	40 children aged 8–12 with depressive disorders or BPSDs (specific diagnoses not reported)	NA	Significant improvement in parental knowledge of mood disorders	Administration in community outpatient setting was feasible; participants and community clinicians reported high acceptability/satisfaction
Miklowitz et al. 2014; O'Donnell et al. 2017, 2020	FFT-A + TAU	RCT with 2-year follow-up	145 adolescents aged 9–18 with BD1 or BD2; compared to previous RCT (Miklowitz et al. 2008), participants were more likely to have BD2 and comorbid anxiety disorders and to enter in a manic or mixed episode	EC	No group differences in time to recovery, episode recurrence (manic, depressive, or any), or percentage of time euthymic during 9-month treatment period; however, FFT-A adolescents had increased stabilization of manic symptoms in the second year of the study (follow-up period); adolescents who lived with both biological parents had longer time to recurrence	No group differences in overall quality-of-life improvements, but FFT-A group had significant improvements compared to EC in terms of quality of family life during active treatment and physical well-being at 1-year follow-up; for quality of friendships, trajectory during treatment favored EC, but posttreatment trajectory favored FFT-A; greater adolescent-rated improvements in family cohesion (but not conflict or adaptability) between months 12 and 18 compared to EC

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Table 2 (*Continued*)

Author(s) and year(s)	Intervention	Study design	Sample	Comparison group	Results	Comments/follow-up studies
Weinstein et al. 2018, West et al. 2014	Single-family CFF-CBT	RCT with 6-month follow-up	69 youth ($n = 34$, CFF-CBT; $n = 35$, control) aged 7–13 with BPSDs	ETAU	After acute trial, CFF-CBT (compared to ETAU) had decreased parent-reported mania and depression; at follow-up, CFF-CBT had decreased depressive (but not manic) symptoms; 93% (versus 46%) of CFF-CBT youth scored below threshold for manic symptoms; global functioning did not differ between groups posttreatment, but scores improved significantly more for CFF-CBT families at 6-month follow-up	High feasibility and acceptability; average of 11.3 (versus 6.9) out of 12 acute treatment sessions attended, and higher reported satisfaction with treatment; no group differences in suicidality between CFF-CBT and TAU following treatment (both groups demonstrated significant improvements)
Fristad et al. 2015, Vesco et al. 2018, Roley-Roberts & Fristad 2021	IF-PEP (OATS)	12-week RCT; 2 × 2 design testing omega-3 fatty acid supplementation, IF-PEP, and combination IF-PEP + omega-3 treatment with 2- to 5-year follow-up	23 youth aged 7–14 with BP-NOS or CYC (omega-3 + PEP: $n = 5$; omega-3 + AM: $n = 5$; placebo + PEP: $n = 7$; placebo + AM: $n = 6$); unlike other PEP trials, participants not eligible if receiving psychotherapy or taking medications other than ADHD medication	Placebo pill; AM	Omega-3 side effects were uncommon and mild; improvements in executive functioning in both omega-3 alone and omega-3 + IF-PEP > placebo; combined IF-PEP + omega-3 resulted in improvements in depressive symptoms compared to placebo + AM; IF-PEP effect on depressive symptoms compared with AM was medium to large; effect of omega-3 was medium; no group differences in effects on manic symptoms (improved over time regardless of treatment)	High feasibility and satisfaction: 95% of IF-PEP participants reported they would recommend to others; 5 of 13 youth with BP-NOS or CYC at baseline who completed the 2- to 5-year follow-up converted to BD1 or BD2; treatment group not predictive of mood ratings or functioning at follow-up; continuation of omega-3 associated with decreased depression scores at follow-up; majority of IF-PEP parents and children reported improved coping and family functioning at 2- to 5-year follow-up

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Table 2 (*Continued*)

Author(s) and year(s)	Intervention	Study design	Sample	Comparison group	Results	Comments/follow-up studies
Knutsson et al. 2017	CFF-CBT multifamily format for adolescents	Open trial case series with 1-year follow-up testing feasibility of multifamily CFF-CBT format with adolescents	7 Swedish adolescents aged 13–18 with BPSDs	NA	Trend of improved parent-rated psychosocial functioning following treatment; parents' increased coping skills and knowledge about childhood BPSDs also increased and were maintained at 1-year follow-up; mixed results with regard to EE and BPSD symptoms—some families saw improvements that were maintained over follow-up	None
MacPherson et al. 2016a	MF-PEP	Multicenter open pilot effectiveness trial with 1-year follow-up	41 youth aged 7–12 with depressive disorders or BPSDs	NA	Improvements in depressive and manic symptoms, increased parental knowledge of mood disorders at 1-year follow-up; BPSD children and families with limited treatment history benefited most	Community MF-PEP was feasible and acceptable; overall mean group adherence = 72%
Miklowitz et al. 2020a,b	FFT-HR + TAU	Multisite RCT with average of 2-year follow-up	127 adolescents ($n = 61$, FFT-HR; $n = 66$, EC) aged 9–17 with MDD, CYC, or BP-NOS with a first- or second-degree relative with a BPSD	Intensive EC = six sessions over 4 months (compared to one to two sessions in EC)	No significant group differences in recovery times from initial episode (total mood symptoms, hypomania, depression) or rates of conversion to a syndromal BPSD; however, FFT-HR group exhibited longer intervals between euthymic periods and depressive episodes (but not manic/hypomanic episodes) compared to EC	Of participants with high baseline levels of SI, FFT-HR youth had lower levels of (and fewer weeks with) SI at follow-up compared to EC youth; FFT-HR youth also had longer intervals without suicidal behaviors; improvements in family conflict following treatment were associated with greater improvement in SI at follow-up; mood symptom improvements were associated with increased DL-PFC activation that occurred during treatment

(*Continued*)

Table 2 (*Continued*)

Author(s) and year(s)	Intervention	Study design	Sample	Comparison group	Results	Comments/follow-up studies
Sharma et al. 2020	UK FFT-A	Feasibility open trial (randomized, nonmasked) with WLC design; 16 sessions over 6 months with a 6-month follow-up	27 adolescents ($n = 14$, immediate; $n = 13$, delayed) aged 11–17 with BPSDs	WLC (delayed arm); 12-month delay	Qualitative feedback suggested satisfaction/acceptability, and families reported benefits to family relationships; quantitative analyses (collected at baseline, 6 months, and 12 months) were not reported	None
D.J. Miklowitz et al. in progress[a] (NCT03913013)	FFT-MCC: technology-enhanced FFT-HR using MCC phone application	RCT with 6-month follow-up	69 adolescents aged 12–18 with (*a*) mood symptoms, (*b*) a parent with a BPSD or MDD, and (*c*) one parent high in EE	FFT-Assess: FFT with MCC assessments only (no skill coaching or psychoeducation)	RCT in progress: currently collecting 6-month follow-up	Outcome measures: EE, mood instability, quality of life; MCC application will collect real-time speech samples and mood assessments; in FFT-MCC participants, data from real-time assessments will be used for clinicians to push recommendations through app to parents and adolescents

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; AM, active monitoring; BD1, bipolar disorder type 1; BD2, bipolar disorder type 2; BP-NOS, bipolar disorder not otherwise specified; BPSD, bipolar spectrum disorder; CFF-CBT, child- and family-focused cognitive behavioral therapy; CYC, cyclothymic disorder; DL-PFC, dorsolateral prefrontal cortex; EC, enhanced care (condition consisting of three family psychoeducational sessions and pharmacotherapy); EE, expressed emotion; ETAU, enhanced TAU [participants received psychotherapy (not CFF-CBT) and pharmacotherapy services from study outpatient clinic]; FEC, family educational control (1–2 family psychoeducational sessions plus study pharmacotherapy, crisis sessions, referrals as needed); FFT-A, family-focused treatment for adolescents; FFT-HR, high-risk adaptation of FFT-A; FFT-SUD, adaptation of FFT-A for adolescents with a BPSD and comorbid SUD; IF-PEP, individual-family PEP; MCC, MyCoachConnect (mobile application that includes assessments, skill training, and psychoeducation); MDD, major depressive disorder; MF-PEP, multifamily PEP; NA, not applicable; OATS, omega-3 and therapy studies; ODD, oppositional defiant disorder; PEP, psychoeducational psychotherapy; RCT, randomized controlled trial; SI, suicidal ideation; SUD, substance use disorder; TAU, treatment as usual [standard of care treatment received in outpatient setting (psychotherapy and pharmacotherapy)]; WLC, wait-list control (serves as control group during delayed treatment period; receives intervention following study completion).

[a] In-progress study: information from ClinicalTrials.gov (NCT listed above) and personal communication with investigator.

et al. 2013). Most recently, a large RCT ($N = 127$) found that of youth who entered treatment with high baseline levels of suicidal ideation (SI), those who received FFT-HR demonstrated reduced SI frequency and longer intervals without suicidal behaviors at follow-up (Miklowitz et al. 2020a). Notably, neuroimaging studies suggest that FFT-HR may exert treatment effects through alteration of emotion regulation networks. Two studies demonstrated that improvements in mood symptoms were associated with increased dorsolateral prefrontal cortex activation that occurred during treatment (Garrett et al. 2015, 2021).

Finally, FFT-SUD, an adaptation for adolescents with BPSDs and comorbid substance use disorder (SUD), has demonstrated preliminary feasibility and efficacy. In an open trial (B.I. Goldstein et al. 2014), the 21-session treatment resulted in improved depression, (hypo)manic symptoms, and global functioning in the six adolescents who completed the midpoint assessment. Notably, substance use was not affected, and pilot data suggest difficulty with participant retention when primary caregivers also have SUD.

Child- and family-focused cognitive behavioral therapy. CFF-CBT (Pavuluri et al. 2004) is a family-based intervention incorporating similar family-focused, psychoeducational, and skills-based content tailored to meet the developmentally specific needs of younger children with BPSDs. The acute phase consists of 12 alternating parent, child, and family sessions; booster sessions are available during a maintenance phase. Treatment components include affect regulation, cognitive restructuring, social skills, healthy habits, and family support. Although originally designed as a single-family treatment, CFF-CBT has been adapted to a multifamily format.

Pavuluri et al. (2004) conducted an open trial of single-family CFF-CBT in 34 youth with BPSDs. Participants exhibited significant improvements in attention-deficit/hyperactivity disorder (ADHD) symptoms, aggression, mania, depression, psychosis, sleep disturbance, and social and academic functioning following acute treatment. A feasibility study of the maintenance model (i.e., monthly booster sessions) was then conducted (West et al. 2007). After 3 years of acute and maintenance treatment, symptom reduction and improvements in global functioning were maintained.

Weinstein et al. (2018) conducted an RCT ($N = 69$) comparing CFF-CBT against an enhanced treatment as usual (ETAU) condition. CFF-CBT demonstrated high feasibility and acceptability; there was significantly higher retention in the CFF-CBT group, whose members attended an average of 11.3 (compared to 6.9) treatment sessions. Parent-reported manic and depressive symptoms for CFF-CBT youth improved following treatment; significant group differences in depressive symptoms were maintained 6 months following treatment. Although long-term trajectories in manic symptoms did not differ between conditions, 93% of CFF-CBT youth scored below threshold by 6-month follow-up compared to 46% of ETAU youth. Global functioning did not differ between groups immediately following treatment; however, CFF-CBT families had significantly more improvement compared to ETAU families at the 6-month follow-up. No group differences regarding suicidality were found.

Two open trials of a multifamily group format have also been conducted. In a sample of 26 youth, multifamily CFF-CBT was associated with improved parent-rated manic symptoms and psychosocial functioning (West et al. 2009). Parents also reported nonsignificant improvements in their own functioning, which were associated with their children's improved psychosocial functioning. Knutsson et al. (2017) adapted the multifamily format to adolescents with BPSDs in an open trial case series design with seven Swedish adolescents; they reported a trend of improvements in therapist and parent ratings.

Psychoeducational psychotherapy. Similar to FFT-A and CFF-CBT, PEP (Fristad et al. 1998) is an adjunctive, manualized treatment that targets psychosocial contributors to mood disorders (i.e., EE, relationship conflicts) by employing a family-based psychoeducational approach and cognitive

behavioral techniques. Treatment components and specific skills include psychoeducation about mood symptoms, mood identification/monitoring, emotion regulation strategies, coping skills, cognitive restructuring, communication training, problem solving, and in vivo social skills training. An additional targeted focus is to equip parents with the knowledge, resources, and empowerment to become more effective advocates for their children. PEP has also been modified for adolescents (Fristad et al. 2019).

PEP can be delivered in a multifamily group (MF-PEP) or an individual-family format (IF-PEP; Fristad 2006). MF-PEP and IF-PEP session content is nearly identical; differences include session structure (8 concurrent parent and child groups versus 20–24 single-family sessions) and a few unique features of IF-PEP made possible by its individualized format (e.g., targeted sibling and school consultation sessions; greater focus on sleep, nutrition, and exercise). High feasibility and acceptability of PEP have been demonstrated in both research and clinical outpatient community mental health settings (Fristad 2006, Leffler et al. 2010, MacPherson et al. 2014b, 2016a).

Several randomized trials have supported the efficacy of both MF-PEP and IF-PEP in improving long-term mood symptom severity, family functioning, and coping/emotion regulation skills (Fristad 2006; Fristad et al. 2003, 2009, 2021). In a large, rigorous RCT comparing MF-PEP plus treatment as usual (TAU) versus a 1-year wait-list control group (WLC) plus TAU for 165 youth with mood disorders, youth in the immediate MF-PEP condition demonstrated significantly reduced symptom severity 1 year following treatment; improvements were maintained at 18-month follow-up. Notably, the WLC + TAU group showed similar improvements after receiving MF-PEP (Fristad et al. 2009). This study also was the first to demonstrate potential for FP + SB interventions to delay or prevent conversion to a BPSD in early-stage youth; participants with depression and transient manic symptoms who received MF-PEP were nearly four times less likely to receive a diagnosis of a BPSD at 1-year follow-up (Nadkarni & Fristad 2010). Using similar methodology, a small ($N = 20$) pilot RCT of IF-PEP indicated that IF-PEP led to long-term (1-year) improvements in youth's mood symptoms. Although group differences were not statistically significant given the small sample size, effect sizes favored IF-PEP (Fristad 2006).

The omega-3 and therapy studies (OATS) were two RCTs conducted to examine the individual and combined efficacy of IF-PEP and omega-3 fatty acids compared to placebo/active monitoring (AM) at improving mood symptoms in youth with depression (Fristad et al. 2019) and BP-NOS/CYC (Fristad et al. 2015). In the BP-NOS/CYC trial, 23 youth were randomly assigned to a 12-week trial of one of four conditions: omega-3 plus IF-PEP, omega-3 plus AM, placebo plus PEP, or placebo plus AM. IF-PEP, both as a stand-alone treatment and in combination with omega-3 supplementation, was effective (Fristad et al. 2015). Combined group participants exhibited reduced depression compared to those who received placebo and/or AM; IF-PEP monotherapy yielded a large effect size on depressive symptoms. There were no significant benefits of combined therapy over IF-PEP alone, and there were no group differences in manic symptoms, which declined in each group over treatment.

There is also evidence that participation in PEP directly influences family functioning. Findings from a small RCT ($N = 35$) comparing MF-PEP + TAU versus WLC + TAU in children with mood disorders demonstrated efficacy of MF-PEP in improving family interactions, increasing perceived parental support, and increasing parents' understanding of mood symptoms and use of quality services (Fristad et al. 2002, 2003). In addition, IF-PEP (compared to a WLC group) was associated with improved family communication and decreased EE (Fristad 2006, Leffler et al. 2010). Finally, a recent follow-up indicated that improvements in family functioning were maintained up to 5 years following treatment (Fristad et al. 2021).

Two trials thus far have demonstrated feasibility and preliminary efficacy of MF-PEP in community outpatient settings. In the first trial ($N = 40$), community therapists administered MF-PEP

to youth with depressive disorders or BPSDs with adequate fidelity; both participants and clinicians reported high satisfaction, and parents evidenced a significant improvement in their knowledge of mood disorders (MacPherson et al. 2014b). Using similar enrollment criteria, MacPherson et al. (2016a) then conducted a multicenter effectiveness trial of MF-PEP ($N = 41$) with a 1-year follow-up. Again, MF-PEP was feasible and acceptable, with adequate group adherence, and improvements in mood symptoms (manic and depressive) and parental knowledge of mood disorders were found at follow-up.

Possibly Efficacious Treatment: Dialectical Behavioral Therapy

Dialectical behavioral therapy (DBT) is currently considered possibly efficacious in treating adolescents with BPSDs. Several ongoing trials, including a large RCT ($N = 100$) with a 2-year follow-up, are being conducted. Given that findings thus far have provided consistent support for DBT's efficacy at reducing depressive symptoms and suicidality in adolescents with BPSDs, it is expected that DBT will soon meet the criteria to be classified as probably efficacious. **Table 3** provides a list of clinical trials of possibly efficacious interventions.

Modified from a DBT protocol for suicidal adolescents (Miller et al. 2007), DBT for adolescents with BPSDs is a manualized treatment that addresses illness-specific aspects of BPSDs using a DBT framework. Weekly (acute phase) and biweekly (continuation phase) alternating family skill training and individual therapy sessions cover the four core DBT modules (i.e., mindfulness, emotion regulation, distress tolerance, and interpersonal effectiveness); content from the "walking the middle path" module is also addressed. DBT was created to be adjunctive to pharmacotherapy and is appropriate for adolescents who have recently experienced an acute episode. Aside from adding psychoeducation on BPSDs, modifications include a longer length of treatment (1 year), a single-family skill training format, skills and activities tailored to the BPSD, and a focus on the importance of sleep and treatment adherence. One particular benefit of this treatment is its explicit focus on suicidality.

In an open trial, Goldstein et al. (2007) demonstrated feasibility, acceptability, and preliminary evidence for efficacy of DBT (adjunctive to pharmacotherapy) in improving targeted symptom outcomes in this population. Participating adolescents exhibited improvements in depressive symptoms, SI, and emotional dysregulation. No significant improvements in mania or interpersonal functioning were reported. Additional support was demonstrated in a small RCT comparing DBT versus standard outpatient care (SOC) (Goldstein et al. 2015). Compared to the SOC group ($n = 6$), DBT adolescents ($n = 14$) exhibited increased treatment adherence, had decreased depressive symptoms, and were approximately three times more likely to demonstrate decreased SI; 83% of DBT adolescents exhibited decreased SI, whereas 50% of TAU adolescents exhibited increased SI. In addition, adolescents who received DBT spent twice as much time in euthymic states and demonstrated improvements in manic symptoms and emotion regulation.

Although DBT for adolescents with BPSDs has not been studied as extensively as FP + SB, growing research demonstrates efficacy, particularly regarding depressive symptoms and suicidality. Additionally, its active treatment components share many similarities to FP + SB. As noted above, several ongoing trials of DBT are expected to provide additional support for its use in this population. Aside from replicating findings, these studies intend to address mediators, moderators, and predictors of treatment response, including neural mechanisms that may underlie effects.

Experimental Treatments

Several interventions developed for youth with BPSDs are considered experimental. Of these, three—interpersonal and social rhythm therapy (IPSRT) for adolescents (IPSRT-A; Hlastala et al.

Table 3 Clinical trials of possibly efficacious interventions for youth with BPSDs

Author and year	Intervention	Study design	Sample	Comparison group	Results	Comments
Goldstein et al. 2007	DBT + study pharmacotherapy	1-year open trial; participants received 36 DBT sessions with in vivo telephone skills training	10 adolescents aged 14–18 with BPSDs	NA	Significantly reduced suicidality, depressive symptoms, and emotion dysregulation; no significant improvements in manic symptoms	High adherence and satisfaction; 9 of 10 participants completed 90% of sessions over 1 year
Goldstein et al. 2015	DBT + study pharmacotherapy	RCT; patients and parents completed quarterly assessments by a masked evaluator over 1 year	20 adolescents ($n = 14$, DBT; $n = 6$, SOC) aged 12–18 with BPSDs	SOC: included study pharmacotherapy	DBT adolescents exhibited better treatment adherence, decreased depressive symptoms, and improvements in SI; SI in DBT adolescents decreased 83% (versus 50% increase in SOC adolescents); DBT adolescents spent twice as much time in a euthymic state and demonstrated improvements in manic symptoms and emotional dysregulation (SOC group did not)	None
T.R. Goldstein et al. in progress[a] (NCT04815239)	DBT + study pharmacotherapy	RCT with 2-year follow-up; patients and parents completed quarterly assessments by a masked evaluator over 1 year	100 adolescents aged 12–18 with BPSDs	SOC: included study pharmacotherapy	RCT recently completed; manuscript in preparation	Primary outcomes: suicidality and mood symptoms; also examined feasibility/cost-effectiveness, mediators/moderators/predictors of treatment response

Abbreviations: BPSD, bipolar spectrum disorder; DBT, dialectical behavioral therapy; NA, not applicable; RCT, randomized controlled trial; SI, suicidal ideation; SOC, standard outpatient care.
[a]In-progress study: information from ClinicalTrials.gov (NCT listed above) and personal communication with investigator.

2010), brief motivational intervention (BMI; Goldstein et al. 2020), and Research into Cognitive and Behavioural Versatility (RECOVER) CBT (Cotton et al. 2019)—are intended for adolescents, whereas one (CBT; Feeny et al. 2006) was developed for ages 10–17. Pilot trials have provided preliminary support for their treatment efficacy, indicating the need for future RCTs, which in some instances are underway. **Table 4** lists published and in-progress trials of experimental treatments.

Interpersonal and social rhythm therapy for adolescents. IPSRT-A is a developmentally modified version of adult IPSRT (Frank 2005), an empirically supported treatment for adults with BPSDs. Based on the social zeitgeber theory of mood disorders (Ehlers et al. 1988), which posits that mood episode onset and exacerbation may be due to disruptions in sleep and social routines that result from psychosocial stressors, IPSRT combines fundamental elements of interpersonal therapy for depression (Klerman et al. 1984) with added components of social rhythm therapy. Thus, main targets of IPSRT-A include psychoeducation, interpersonal problems, and building structure into social routines and the sleep–wake cycle. This is accomplished through 16–20 sessions conducted primarily with adolescents, with limited family engagement in psychoeducation. Notably, IPSRT-A has also been modified for use with OBD who do not meet criteria for BPSDs (T.R. Goldstein et al. 2014, 2018); those trials are presented in the following section.

Hlastala et al. (2010) conducted a pilot open trial of IPSRT-A as an adjunctive treatment to SOC pharmacotherapy. Feasibility and acceptability were high, with 97% of sessions attended. Improvements were present on all outcome measures (general psychiatric symptom severity, depression, mania, and global functioning) following treatment.

Brief motivational intervention. Given low rates of medication compliance and detrimental effects of missed doses or termination in youth with BPSDs, Goldstein et al. (2016, 2020) developed an intervention targeting medication adherence. BMI is a three-session (two treatment sessions, one booster session) intervention for adolescents and young adults with BPSDs. Core treatment components include eliciting thoughts and feelings about medication, providing psychoeducation, assessing readiness for change/exploring ambivalence, and creating and evaluating an adherence plan. Consistent with motivational interviewing, BMI is individualized and person-centered; one major aim is to foster a sense of responsibility and control. Treatment components are delivered flexibly within sessions, and the format (e.g., degree of parental involvement) may vary.

Preliminary support for BMI has come from a pilot randomized trial (Goldstein et al. 2020), which tested SOC versus SOC + BMI. Participants ($N = 43$) were receiving outpatient pharmacotherapy for BPSDs. Medication adherence was measured by a Bluetooth-enabled electronic pill box (MedTracker), which allowed researchers to track when medications were taken. Mood symptoms were assessed at intake, 3 months (booster session), and 6 months. Results indicated that BMI was feasible and acceptable; an average 2.9 out of 3 sessions were completed. It was also effective: Participation led to increased medication adherence, which, in contrast, decreased in SOC individuals. Moreover, participants who were medication adherent more than 60% of the time in a week had a threefold decreased chance of exhibiting depressive symptoms in the subsequent 2 weeks. Notably, another intervention targeting medication adherence in this population, customized adherence enhancement for adolescents and young adults, currently has an RCT in progress (NCT04348604).

Cognitive behavioral therapy. CBT for adolescents with BPSDs is a manualized CBT protocol (Danielson et al. 2004) developed largely from other CBT manuals, with additions of components found to be effective in BPSD treatments. Twelve sessions cover core modules, including psychoeducation, medication compliance, mood monitoring, identifying and modifying unhelpful

Table 4 Clinical trials of experimental interventions for youth with BPSDs

Author and year	Intervention	Study design	Sample	Comparison group	Results	Comments
Feeny et al. 2006	CBT	Open trial; 12-week treatment with 8-week follow-up	16 youth (8 treatment, 8 control) aged 10–17 with BPSDs	Matched historical control receiving medication management	Self-report outcomes indicated no between-group differences in mood symptoms at posttreatment or follow-up, but moderate to large between-group effect sizes favored CBT for manic and depressive symptoms at both time points; parents of CBT youth reported observing significant improvements in depression and mania following treatment; differences in depressive symptoms remained at follow-up	None
Hlastala et al. 2010	IPSRT-A	Open trial; 20-week treatment	12 adolescents aged 13–17 with BPSDs	NA	Improvements from baseline scores on all outcome measures (general psychiatric symptom severity, depression, mania, and global functioning) following treatment	High feasibility and acceptability: 97% of sessions attended and high adolescent-rated satisfaction and treatment completion (11 of 12); 11 of 12 participants also received adjunctive pharmacotherapy
Macneil et al. 2012	RECOVER	18-month open trial	40 adolescents and young adults aged 15–25 (20 RECOVER participants, 20 controls) with BD1 with psychotic features enrolled from an SEI program	TAU matched by sex, age, symptom severity, and substance use; receiving services provided by SEI (case management, pharmacotherapy)	RECOVER participants evidenced decreased depression scores and significantly lower symptom severity at 18 months, and better global, social, and occupational functioning compared to TAU group; no group differences for manic symptoms	Both RECOVER and TAU exhibited improvements on all outcome measures (mania, depression, symptom severity, adaptive functioning) during the study

(*Continued*)

Table 4 (*Continued*)

Author and year	Intervention	Study design	Sample	Comparison group	Results	Comments
Goldstein et al. 2020	BMI	Open trial; mood symptoms assessed at baseline, 3 months (booster session), and 6 months; medication adherence assessed for 6 months through a Bluetooth-enabled electronic pillbox (MedTracker)	43 adolescents and young adults (aged 12–22) receiving medication management for BPSDs	SOC receiving medication management	Increased medication adherence (1% increase per month) in participants who received BMI compared to SOC, whose adherence decreased by 5% per month; increased adherence led to decreased mood symptoms; participants adherent >60% in a week had a more than threefold decreased chance of exhibiting depressive symptoms in the subsequent 2 weeks	Individuals with higher expectations of treatment efficacy improved more quickly than participants with lower expectations; efficacy of BMI was greater for participants with high medication adherence
Delbello et al. in progress[a] (NCT04348604)	CAE-AYA	RCT of 6-month treatment with 1-year follow-up	40 adolescents and young adults aged 16–21 with BD1 or BD2 receive four weekly in-person sessions plus one booster session	ETAU: usual clinical care (psychotherapy and pharmacotherapy) plus psychoeducational written material on BPSDs and six follow-up telephone calls to review materials	RCT in progress; expected completion May 2022	Target outcomes: medication adherence, as measured subjectively by self-report and objectively by electronic pillbox
S.M. Cotton et al. in progress[a] (see Cotton et al. 2019 for details)	RECOVER	RCT of 6-month treatment with 1-year follow-up	Expected 122 adolescents and young adults aged 15–25 (61 RECOVER participants, 61 controls) with BD1; first time seeking treatment for manic episode	TAU: receiving services provided by SEI (case management, pharmacotherapy)	RCT in progress; began enrollment January 2019; expected completion 2022	Target outcomes: global functioning following treatment and at 1-year follow-up; manic and depressive symptomatology, quality of life; will also involve measures of medication adherence and actigraphy to measure sleep/circadian rhythm patterns

Abbreviations: BD1, bipolar disorder type 1; BD2, bipolar disorder type 2; BMI, brief motivational intervention; BPSD, bipolar spectrum disorder; CAE-AYA, customized adherence enhancement for adolescents and young adults; CBT, cognitive behavioral therapy; ETAU, enhanced TAU; IPSRT-A, interpersonal and social rhythm therapy for adolescents; NA, not applicable; RCT, randomized controlled trial; RECOVER, Research into Cognitive and Behavioural Versatility; SEI, special early intervention; SOC, standard outpatient care; TAU, treatment as usual.

[a]In-progress studies: information from ClinicalTrials.gov (NCT listed above) and personal communication with investigators.

thinking, stressor/trigger identification, sleep maintenance, and family communication, as well as optional modules targeting substance abuse, social skills, anger management, and contingency management. This CBT protocol differs from FP + SB interventions in that family involvement is limited (i.e., 9 out of 12 sessions are individual).

Feeny et al. (2006) conducted an open trial pilot study comparing eight youth with BPSDs who received CBT to matched historical controls. Results provided preliminary evidence for efficacy of individual CBT with limited family involvement in addressing mood symptoms in youth with BPSDs. Although interview and self-report outcomes did not indicate significant between-group differences posttreatment or at 8-week follow-up, moderate-to-large between-group effect sizes favored CBT. In addition, parents of CBT youth reported observing significant improvements in depression and mania at posttreatment. Of these, only differences in depressive symptoms remained significant at follow-up.

Cognitive behavioral therapy for adolescents and young adults. The RECOVER intervention is an adjunctive, manualized, psychosocial treatment for adolescents and young adults in early stages of BD1 (Macneil et al. 2012). Specifically, RECOVER is intended for individuals aged 15–25 years who have experienced their first manic episode with psychotic features and are already receiving medication and case management services. RECOVER was developed based on research demonstrating efficacy of psychoeducation, CBT-based skill training, social rhythm therapy, and family work in treating BPSDs; thus, the six core modules address these topics, along with assessment/engagement and wellness planning, in the first two phases of treatment (10 sessions total). Phase 3, which is meant to be flexibly tailored based on individual needs, consists of up to eight sessions that can include further focus on previous core modules from phases 1 and 2, or may incorporate relevant optional targeted modules (i.e., relationship issues and family work; alcohol, substance use, and other comorbid disorders; exploring medication; functional recovery). Given the target age range and phase-specific nature of RECOVER, modules are designed to be developmentally appropriate for the individual's stage of illness as well as their transition from adolescence to early adulthood. Thus, developmentally tailored cognitive behavioral strategies and a focus on functional outcomes and autonomy are major targets of the intervention.

Initial support for RECOVER has come from an 18-month open-label pilot study of 40 patients already enrolled in a special early intervention (SEI) program (Macneil et al. 2012). Twenty patients who received RECOVER alongside TAU (SEI program), which included pharmacotherapy and case management, were matched to TAU patients. Notably, both groups exhibited improvements on all outcomes (mania, depression, symptom severity, adaptive functioning) during the study; however, compared to the TAU group, participants who received RECOVER evidenced reduced depression and symptom severity at 18 months as well as higher levels of global, social, and occupational functioning. Given these preliminary results, a prospective RCT with 1-year follow-up using actigraphy to measure sleep/circadian rhythm cycles is underway (Cotton et al. 2019).

Preventive Psychosocial Treatments for High-Risk Youth Without a Bipolar Spectrum Disorder Diagnosis

Increased understanding of the importance of early intervention as well as growing interest in staging models of BPSDs has led to development of preventive interventions for youth at the very earliest stages of the disorder (stages 0–1a). **Table 5** provides a list of trials of preventive interventions for high-risk youth without BPSD diagnoses. In contrast to high-risk studies of modified versions of well-established treatments detailed above, these interventions target youth

Table 5 Clinical trials of preventive interventions for high-risk youth without significant mood symptoms

Author(s) and year(s)	Intervention	Study design	Sample	Comparison group	Results	Comments
T.R. Goldstein et al. 2014	Brief IPSRT-A for high-risk adolescents	Open trial; 12 sessions over 6 months	13 adolescents aged 12–18 with a parent ($n = 12$) or sibling ($n = 1$) with BD1 or BD2; could have mood symptoms (including depressive disorders) but excluded if history of (hypo)mania	NA	Participants exhibited significant improvements in sleep and circadian patterns (i.e., less oversleeping on weekends)	None
Goldstein et al. 2018	Brief IPSRT-A for high-risk adolescents	Pilot RCT with 3- and 6-month follow-up; self-reports and parent reports completed every 6 weeks	42 adolescent OBD aged 12–18 ($n = 21$, IPSRT-A + DIR; $n = 21$, DIR alone)	DIR: referral for community treatment for any identified psychiatric condition	No significant differences in subjective measures of sleep and social rhythms, sleep timing, or sleep variability as measured by actigraph; one objective measure (wake after sleep onset) decreased following IPSRT-A; no group differences in self- or parent-rated psychological symptoms	None
Cotton et al. 2016, Strawn et al. 2016	MBCT-C	Open trial	10 youth OBD with separation, social, and/or generalized anxiety disorders but no affective disorders; two groups divided by age ($n = 5$, ages 9–12; $n = 5$, ages 13–17)	NA	Clinicians and youth rated improvements in anxiety; parents rated improvements in youth emotional regulation; no significant improvements in mindfulness, but when present, increases were associated with decreased anxiety	Following MBCT-C, youth demonstrated increased activation of several brain structures implicated in emotional processing (i.e., bilateral insula, lentiform nucleus, thalamus, and left anterior cingulate), which were associated with decreased anxiety

(*Continued*)

Table 5 (*Continued*)

Author(s) and year(s)	Intervention	Study design	Sample	Comparison group	Results	Comments
Cotton et al. 2020	MBCT-C	WLC pilot trial	24 youth OBD aged 9–18 with diagnosed anxiety disorder and no current or historical symptoms indicative of a BPSD (including depressive symptoms); four groups divided by age; one group received treatment immediately, and the other three groups were wait-listed	WLC	Overall clinical severity improved following MBCT-C; no differences between intervention and wait-list periods regarding anxiety, emotional regulation, or mindfulness; increased mindfulness that occurred during treatment (but not during the wait-list period) was associated with decreased anxiety and improved emotional regulation	None
Serravalle et al. 2021	RUSH	Pilot trial; 12-week treatment with a 6-month follow-up	$N = 55$; 26 OBD aged 6–11 without current or history of an affective, psychotic, or developmental disorder; 90% of affected parents receiving RUSH had BD1	29 offspring of parents without a history of affective disorder who did not receive RUSH	RUSH led to increased positivity, decreased negativity, and improved dyadic mutuality on an observational task; improvements maintained at 6-month follow-up	Decreases in parental negativity following treatment were associated with lower parent-rated internalizing symptoms at 6-month follow-up

Abbreviations: BD1, bipolar disorder type 1; BD2, bipolar disorder type 2; BPSD, bipolar spectrum disorder; DIR, data-informed referral; IPSRT-A, interpersonal and social rhythm therapy for adolescents; MBCT-C, mindfulness-based cognitive therapy for children; NA, not applicable; OBD, offspring of parents with BPSDs; RCT, randomized controlled trial; RUSH, reducing unwanted stress in the home; WLC, wait-list control [received 12 weeks of psychoeducational material before beginning treatment (wait-list period)].

who do not yet exhibit symptoms of BPSDs. The three treatments described below were designed to be implemented with OBD; clinical trials specifically excluded youth with any signs of current or past (hypo)manic symptoms.

Brief interpersonal and social rhythm therapy for adolescents at risk for bipolar disorder. T.R. Goldstein et al. (2014) developed a modified IPSRT-A model for adolescents with an immediate family member with a BPSD. Similar to IPSRT-A, the OBD version targets sleep, social rhythm disturbance, and psychoeducation; modifications include an interpersonal component of treatment focusing on psychoeducation and support surrounding the topic of having a loved one with a BPSD, as well as reduced treatment length (12 sessions versus 16–20). In the initial phase, adolescents and their parents are introduced to the biopsychosocial model of BPSDs, are provided psychoeducation about symptoms and risk factors, and create a family tree to discuss prevalence and impact of BPSDs on the family. Intermediate and termination phases explore feelings about being at risk, target sleep and social rhythm regularity, and facilitate creation of a symptom identification and management plan.

Results of two open trials indicate high participant satisfaction but low attendance (50–67%) rates. Findings regarding treatment effects on psychological symptoms and sleep and social rhythm factors are inconclusive. In the first open trial, adolescents reported significant improvements in sleep and circadian patterns (i.e., less oversleeping on weekends) (T.R. Goldstein et al. 2014). However, a later pilot RCT (Goldstein et al. 2018) revealed no differences in subjective measures of sleep and social rhythms in adolescents who received brief IPSRT-A versus those who did not, nor were there differences in sleep timing or variability as measured by actigraph, although one objective measure (wake after sleep onset) decreased in the IPSRT-A group. There were also no group differences found in self- or parent-rated psychological symptoms. Notably, a single-blind RCT ($N = 120$) to be delivered via telehealth is currently underway (NCT04815239).

Mindfulness-based cognitive therapy for children. Originally developed for adults as mindfulness-based cognitive therapy (MBCT) and later modified for youth, MBCT for children (MBCT-C) incorporates mindfulness training and cognitive behavioral techniques to target anxiety symptoms and improve emotional regulation. MBCT-C is delivered in a group format over 12 weekly sessions; in-class and assigned mindfulness exercises (e.g., meditation practice, breath training, body scans) teach youth to stay in the moment by remaining mindful of thoughts, emotions, and bodily sensations. Given MBCT's effectiveness at decreasing symptoms of anxiety and depression in adults (including adults with BPSDs; Hofmann et al. 2017, Perich et al. 2013) and youth (Semple et al. 2010), a manualized intervention of MBCT-C for anxiety (Semple & Lee 2011) has been implemented for OBD with anxiety disorders.

Two trials have demonstrated feasibility, acceptability, and preliminary support for MBCT-C in anxious children at high familial risk for BPSDs. In an open pilot study of 10 OBD youth (two groups divided by age: $n = 5$, ages 9–12; $n = 5$, ages 13–17), MBCT-C was associated with improved clinician- and child-rated anxiety symptoms as well as parent-rated emotional regulation (Cotton et al. 2016). Increased mindfulness was associated with decreased anxiety. Notably, preliminary neuroimaging data from 9 of the 10 participants suggested that MBCT-C may be effective at decreasing anxiety through resulting alterations in brain activation; following MBCT-C, youth demonstrated increased activation of brain structures implicated in emotion processing (i.e., bilateral insula, lentiform nucleus, thalamus, and left anterior cingulate), which was in turn associated with decreased anxiety (Strawn et al. 2016).

A more recent trial of MBCT-C employed a WLC design with 24 OBD youth with anxiety (Cotton et al. 2020). Participants were excluded if they were receiving concurrent treatment

(medication or psychosocial) or exhibited significant depressive or (hypo)manic symptoms. As in the initial pilot trial, youth were separated by age to ensure developmental appropriateness of the intervention, given the wide age range of the sample (9–18 years old; mean age = 13.6). One of the four groups ($n = 5$) received the intervention immediately, whereas the other three groups ($n = 19$; WLC group) received 12 weeks of psychoeducational material before beginning MBCT-C. Improvements in overall clinical severity were demonstrated following MBCT-C (compared to during the wait-list period); however, no differences were seen with regard to anxiety, emotion regulation, or mindfulness. Although significant improvements in mindfulness were not found following MBCT-C, direct effects of increased mindfulness were demonstrated during treatment. Increased mindfulness that occurred during the treatment period (but not during the wait-list period) was associated with decreased anxiety and improved emotional regulation.

Reducing unwanted stress in the home program. One recent preventive intervention, the reducing unwanted stress in the home (RUSH) program (Serravalle et al. 2021), was developed specifically for the earliest stage (0) of BPSDs. Similar to other preventive treatments, RUSH is a structured, manualized intervention for OBD that incorporates skills-based coping and a cognitive behavioral approach. However, rather than focusing on symptom management, RUSH targets risk factors in the family environment that are associated with negative outcomes in OBD. RUSH consists of 12 weekly concurrent child (ages 6–11) and parent group sessions. Parent sessions focus on communication, problem solving, and behavioral/household management skills such as implementing structure, organization, and consistency; youth sessions include CBT-based skills such as emotion and thought identification, relaxation techniques, and other coping skills.

Serravalle et al. (2021) recently completed a pilot study of RUSH that examined effects on the parent–child relationship and the development of internalizing and externalizing symptoms in OBD. Twenty-six OBD–parent dyads who participated in RUSH were compared with 29 offspring of parents without a history of affective disorder who did not receive the intervention. Results indicated that RUSH is feasible, acceptable, and potentially effective at improving parent–child relationships in OBD. RUSH parents exhibited increased positivity, decreased negativity, and improved dyadic mutuality in observer-rated interactions, and these effects were maintained at 6-month follow-up. Moreover, improvements in parental negativity mediated the effect of RUSH on improvements in OBD internalizing symptoms at 6-month follow-up.

MEDIATORS, MODERATORS, AND PREDICTORS OF TREATMENT RESPONSE

Although the efficacy trials described above provide valuable information regarding which treatments are effective and which general components may be necessary, research on factors associated with treatment response, moderators, and mechanisms of change is limited. Experts agree that identifying these factors is a necessary next step to improve treatment outcomes and have called for prioritizing such studies to determine core components of interventions and to allow clinicians to match patients to appropriate treatments (Fristad & Algorta 2013, Goldstein et al. 2017).

Studies of FP + SB interventions have identified several mediating factors that play a significant role in treatment outcomes. Positive outcomes appear to occur through the interventions' effects on parenting and family factors. For example, parent-reported knowledge and understanding of BPSDs, as well as increased skills and coping, mediate effects of CFF-CBT on children's emotional and behavioral symptoms and overall global functioning (MacPherson et al. 2016b, West et al. 2009), and parents' beliefs about treatment mediate effects of MF-PEP by increasing

the use of quality services, which in turn leads to improved child outcomes (Mendenhall et al. 2009). Finally, improvements in family variables, including maternal EE (Miklowitz et al. 2006) and family conflict (Miklowitz et al. 2020b), appear to underlie treatment effects of FFT-A on decreased mood symptoms (including SI) in adolescents with BPSDs (Miklowitz et al. 2020b).

Each well-established intervention has examined potential moderators of treatment efficacy (Roley-Roberts & Fristad 2021), and this continues to be a main research priority in ongoing and upcoming trials. Through this research, the field has gained a better understanding of potential child, parent/family, and comorbidity factors that do not appear to affect treatment efficacy, as well as insight into potential factors that may play a role in differential treatment response.

Child sex, age, and race do not appear to affect treatment efficacy (MacPherson et al. 2014a, Weinstein et al. 2015). Level of impairment appears to moderate treatment effects; children with more severe baseline impairment (i.e., impaired global functioning, high levels of stress, trauma, and SI) tend to show greater improvements following participation in MF-PEP and FFT-HR (Macpherson et al. 2014a, Miklowitz et al. 2020a). However, Weinstein et al. (2015) reported more pronounced treatment effects of CFF-CBT for youth with lower baseline depressive symptom severity and higher self-esteem. Moderating effects of SI and suicidal behaviors are also inconclusive and may differ by age. Severely ill youth aged 9–17 with high levels of SI appear to preferentially benefit from FFT-HR compared to youth with lower levels of SI (Miklowitz et al. 2020a); however, neither SI nor nonsuicidal self-injury moderated effects of CFF-CBT in younger children, a finding that may be due to lower rates of SI and nonsuicidal self-injury in youth younger than 9 (Weinstein et al. 2015). Biological and cognitive factors may also serve as moderators. Higher baseline levels of interleukin have been associated with reduced adolescent depressive symptoms following group CBT (Pearlstein et al. 2020), and effects of BMI in adolescents were moderated by baseline patient expectations of treatment efficacy (Goldstein et al. 2020).

Diagnostic comorbidity may also moderate FP + SB treatment effects. Weintraub et al. (2019) examined the impact of comorbid ADHD, disruptive behavior disorders (DBD), and anxiety disorders on treatment outcomes of FFT-A. Comorbid ADHD (but not DBD) moderated treatment effects; adolescents with BPSDs with comorbid (unmedicated) ADHD who received FFT-A demonstrated greater reduction of (hypo)manic symptoms compared to adolescents without ADHD. In addition, comorbid anxiety disorders predicted more time with depressive symptoms, more severe (hypo)manic symptoms, and fewer improvements in family conflict. However, studies with younger samples have not indicated moderating effects of comorbid anxiety disorders (Cummings & Fristad 2012, Weinstein et al. 2015).

Studies examining effects of parent and family factors have reported mixed results. Some parental psychopathology (in particular, personality disorder or substance dependency) may predict treatment nonresponse and premature termination (B.I. Goldstein et al. 2014, MacPherson et al. 2014b, Miklowitz et al. 2014), whereas depressive symptoms either predicted increased improvements following CFF-CBT (Weinstein et al. 2015) or did not moderate treatment response in PEP (MacPherson et al. 2014b). High levels of family conflict or EE produce varying outcomes, including increased treatment drop-out and relapse (Geller et al. 2008) and greater treatment response (Joyce et al. 2016). Effects may vary by age (Roley-Roberts & Fristad 2021). Studies of adolescents using two different samples have reported that high-conflict families demonstrate significantly reduced conflict following FFT-A, whereas low-conflict families do not (O'Donnell et al. 2020, Sullivan et al. 2012). Similarly, adolescents from families with high levels of parental EE appear to show larger treatment response to FFT-A (Miklowitz et al. 2008, 2009, 2013). In contrast, studies of younger children receiving PEP and CFF-CBT have not demonstrated moderating effects of EE (MacPherson et al. 2014a, Weinstein et al. 2015). In fact, CFF-CBT was more

effective for highly cohesive families, suggesting that a positive family environment may predict stronger treatment response (Weinstein et al. 2015). Socioeconomic status has also been posited as a moderator of treatment response, although findings are mixed. Weinstein et al. (2015) found that low-income families may benefit most from CFF-CBT; however, studies of MF-PEP have reported no difference in treatment efficacy based on family income or other such demographic variables (Fristad et al. 2009, MacPherson et al. 2014a).

CLINICAL IMPLICATIONS AND RECOMMENDATIONS FOR BEST PRACTICE

Evidence suggests that adjunctive psychosocial interventions are effective, feasible, and highly accepted for all stages of BPSDs in youth. FP + SB is a well-established class of interventions; interventions classified as probable, possible, or experimental share many features with FP + SB, and with further study they are likely to also become well established. While pharmacotherapy is considered the first line of intervention for BPSDs, psychosocial interventions address environmental factors known to contribute to onset and course of BPSDs. They provide youth and their families education, support, and skills necessary for symptom identification, relapse management, and medication adherence, as well as improved family relationships and academic, occupational, and social functioning that can have long-term effects on overall quality of life.

The aforementioned efficacy trials and analyses of potential mediating and moderating factors can aid in determining appropriate treatments and in identifying youth for whom certain interventions may not be effective. With this information, youth can be matched based on child and family factors, such as symptom severity, course, presentation, and family environment characteristics, to ensure the highest chance of treatment success. Early and comprehensive assessment is key; research on risk factors and prodromal symptoms of BPSDs has revealed the importance of assessing for manic symptoms and sleep disturbance in youth presenting with depression, particularly when there is a family history of BPSDs. Comprehensive assessment of symptom severity and suicidality even in prepubescent youth is also critical, given the high proportion of youth with BPSDs reporting SI (Weinstein et al. 2018). Finally, clinicians should conduct a thorough assessment of family factors. A detailed family history of mental illness and characteristics of primary caregivers and family environment (e.g., family relationship dynamics; levels of conflict, cohesion, and EE) should be comprehensively evaluated as these factors may contribute to treatment efficacy. Obtaining commitment and buy-in to treatment is crucial because patient and parent expectations and beliefs about treatment may serve as both mediators and moderators of treatment efficacy (Goldstein et al. 2020, Mendenhall et al. 2009). Early intervention with a low-risk treatment is recommended to delay illness onset and provide skills to improve the course of BPSDs. Thus, a primary consideration in determining appropriate treatment depends on stage and severity of illness.

For high-risk youth who have not yet exhibited BPSD-specific symptoms, MBCT-C, IPSRT-A, and RUSH appear to be safe, low-risk treatment options. Although no RCTs have been conducted, RUSH appears to lead to improvements in parent–child relationships in unaffected OBD (Serravalle et al. 2021), MBCT has exhibited high acceptance/feasibility and preliminary efficacy for decreasing anxiety and increasing emotion regulation abilities in OBD youth with anxiety disorders (Cotton et al. 2016, 2020), and IPSRT-A for high-risk youth may improve sleep and circadian rhythms, although these results have been mixed and difficulties in participant retention and attendance have been noted (T.R. Goldstein et al. 2014, 2018). For high-risk youth in later stages who exhibit significant mood symptoms (i.e., stage 1b), a targeted high-risk FP + SB intervention may be most effective.

Significantly more research has examined treatments for later-stage youth with BPSD diagnoses. For these youth, the well-established class of FP + SB interventions (i.e., FFT-A, CFF-CBT, and PEP) holds the most empirical support and should be considered first. Although no dismantling studies have been conducted, active treatment components common to these interventions include family psychoeducation, incorporation of CBT-based skill training surrounding communication, problem solving, sleep and social rhythms, emotion regulation skills, and relapse prevention strategies.

Considerations in deciding which empirically supported treatment is appropriate for a specific youth include child and family factors, such as the child's age, symptom presentation and severity, and the family environment. Of the well-established treatments, CFF-CBT and PEP have demonstrated efficacy for younger children with BPSDs, and FFT-A is indicated for adolescents. Although ongoing replication studies are necessary, DBT has also demonstrated efficacy at reducing depressive symptoms in adolescents with BPSDs and shows potential to be a favorable treatment for adolescents with high levels of suicidality and emotional dysregulation.

As noted above, several experimental interventions have ongoing efficacy trials and may prove to be viable treatment options. A pilot study of RECOVER for adolescents and young adults with first-episode BD1 demonstrates promise as a future treatment for this population, and BMI has demonstrated preliminary efficacy for improving medication adherence in adolescents (Goldstein et al. 2020); however, future RCTs will be needed before these interventions can be considered efficacious.

LIMITATIONS AND FUTURE DIRECTIONS

Although considerable advances have been made regarding our knowledge and understanding of treating BPSDs in youth, several critical questions remain. Given our increased confidence in well-established treatments at improving mood symptoms, dismantling studies and identifying how and for whom interventions are effective should be prioritized. Importantly, significantly fewer efficacy trials have evidenced improvements in manic symptoms compared to depressive symptoms, indicating a need to further investigate treatment components that may target mania. The implementation of mania-specific treatment components, such as those targeting sleep and circadian rhythm patterns and bipolar-specific medication management, may be most effective at decreasing manic symptoms. Large-scale RCTs of DBT and experimental interventions will also be necessary. Common limitations such as subjectivity and recall bias should be avoided, when possible, through implementation of objective measures and ecological momentary assessment (EMA). Finally, there are currently no clear guidelines for treating early-stage BPSDs (Chia et al. 2019); further study of low-risk preventive interventions is needed.

Fortunately, current research is addressing identified gaps in the literature. Consistent with recent recommendations (Goldstein et al. 2017), ongoing trials are increasingly prioritizing identification of mediators, moderators, and predictors of treatment efficacy. More studies are using functional magnetic resonance imaging to assess potential neurological changes associated with interventions. Targeted treatment outcomes are emphasizing functional improvements and increased quality of life rather than merely examining symptom changes. Additional relevant outcomes, including suicidality, physical/cardiovascular health, medication adherence, and comorbid conditions (e.g., trauma), are being examined, per review of trial registries.

Technological advances have allowed for development and implementation of clinical tools to augment, deliver, and evaluate psychosocial treatments. The increasingly common implementation of EMA appears to be a feasible and acceptable method of collecting real-time data in youth with mood disorders while minimizing recall bias (Baltasar-Tello et al. 2018). Several mobile

applications have been specifically developed for youth mental health (Grist et al. 2017); however, research is needed to validate and establish standards regarding appropriate application of these methods. Passive monitoring measures, such as actigraphy to collect data on circadian rhythms and sleep, are also beneficial, particularly when combined with EMA (Dunster et al. 2021). Notably, per ClinicalTrials.gov registry entries, most ongoing and upcoming efficacy trials are using monitoring methods to maximize ecological validity and minimize recall bias. For example, an RCT ($N = 69$) of a "technology-enhanced FFT-HR" intervention will supplement FFT-HR sessions with the MyCoachConnect mobile application to track and provide feedback and recommendations to families in real time, the MedTracker pillbox tool is being used in multiple upcoming studies on medication adherence, and actigraphy is being used in interventions that target sleep and circadian rhythm. Finally, an RCT of IPSRT-A for high-risk youth is evaluating telehealth delivery (NCT04815239).

Regarding prevention and early intervention research, much has been accomplished in the past 5 years. Staging models specific to BPSDs have been created and used to develop novel preventive interventions, and advances in our understanding of prodromal symptoms and markers of BPSDs have led to the development of risk calculators that, although experimental, may move the field closer to the goal of personalized prevention and early intervention (Birmaher et al. 2018, Hafeman et al. 2017, Van Meter et al. 2021). However, for staging models and tools to be clinically useful, clear, universal guidelines regarding terminology, operationalization, and treatment implementation will be necessary (Vallarino et al. 2015). This will require continued efforts to improve and compare the accuracy and predictive validity of models in both clinical and community samples and to further develop and test evidence-based treatments for this population. Advanced genetic analyses to identify biomarkers that may be specific to BPSDs will be helpful in this domain.

Finally, for psychosocial treatments to be useful, dissemination efforts are critical. Currently, even the well-established treatments are primarily implemented in academic facilities (Van Meter & Cosgrove 2019), limiting the ability to determine if observed effects are generalizable to real-world settings. As more RCTs are conducted, it will be important to conduct more effectiveness and postimplementation trials to examine the interventions' effects in community samples, and to develop training and consultation methods to facilitate broad use by clinicians.

SUMMARY POINTS

1. Research spanning several decades supports the implementation of manualized, empirically supported psychosocial interventions for the treatment of pediatric bipolar disorder. The addition of psychosocial treatments to pharmacotherapy results in increased improvements in mood symptom severity, frequency, and recovery rates; secondary outcomes, such as improved psychosocial functioning and behavioral change, are also frequently reported.
2. Psychosocial treatments for children with bipolar disorder can be categorized based on level of empirical support (i.e., well established, probably efficacious, possibly efficacious, experimental, or questionable); interventions with the most support include family psychoeducation plus skill building (FP + SB). Three manualized treatments (family-focused treatment for adolescents, child- and family-focused cognitive behavioral therapy, and psychoeducational psychotherapy) make up a well-established class of FP + SB interventions.

3. In line with a clinical staging model, preventive interventions for children at high risk for developing bipolar disorder are being developed, and studies show that early intervention may delay illness onset and provide skills to ultimately decrease conversion in children with subsyndromal symptoms.
4. Choosing the appropriate empirically supported intervention for a particular child should include consideration of both child and family factors, such as the child's age, symptom presentation and severity, and family environment. Continued research on mediators, moderators, and predictors of treatment can aid in this decision-making process to help ensure the highest chance of treatment success.
5. Technological advances allow for increased dissemination of interventions and the collection of real-time data to evaluate target treatment outcomes; however, effectiveness trials are still needed to determine the generalizability of app-based interventions.

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