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## Modification of an Intervention to Improve Adherence in Adolescents and Young Adults With Bipolar Disorder

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### Abstract

**Objective:** Managing bipolar disorder (BD) is particularly challenging for adolescents and young adults (AYAs) ages 16 to 21. Few interventions exist that address self-management in AYAs with BD. Thus, this study aimed to modify the customized adherence enhancement behavioral intervention for AYAs through an iterative, patient-centered process.

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**Method:** The Obesity-Related Behavioral Intervention Trials (ORBIT) model was used for intervention development. In phase 1a, adherence barriers and facilitators were identified to refine intervention content. Phase 1b occurred following curriculum modification to ensure that the modified intervention was relevant and usable by the target population. Data were collected via focus groups and interviews with AYAs with BD, parents, and providers. Transcripts were analyzed using directed content analysis.

**Results:** Phase 1a included focus groups/interviews with AYAs (n = 10), parents (n = 4), and providers (n = 9) who described the difficulties and successes in managing BD symptoms, improving adherence, and transitioning care from caregivers. Phase 1b included an advisory board composed of 8 phase 1a participants who provided feedback on modified session activities, module delivery, and curriculum. Phase 1b involved usability testing with new participants (n = 8), revealing the need for modifiable language based on developmental level, more engaging visual images, and confirmation that topics were salient to AYAs with BD.

**Conclusion:** Though sample sizes were small and not representative of the population of AYAs with BD, the ORBIT methodology informed the adaptation of the customized adherence enhancement intervention to improve adherence in AYAs with BD. Important next steps are to conduct a pilot randomized clinical trial of customized adherence enhancement for AYAs.

## Keywords

adolescent; bipolar disorder; medication adherence; mental health services; young adult

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Pharmacotherapy is the primary treatment for adolescents and young adults (AYAs) with bipolar disorder (BD).<sup>1</sup> While an effective treatment for BD symptoms, suboptimal medication adherence occurs in approximately 65% of AYAs and is associated with lower rates of recovery, higher rates of relapse, and higher risk for substance use and suicide.<sup>2-4</sup> In a recent study conducted in collaboration with the Balanced Mind Parent Network of the Depression and Bipolar Support Alliance (DBSA) and the National Alliance on Mental Illness (NAMI), AYAs with BD identified several adherence barriers, including forgetting to take medication, side effects (eg, weight gain, sleepiness), interference with daily activities, feeling they did not need medication, and not liking to be told to take medicine.<sup>5</sup> Additionally, BD symptoms among AYAs occur at a developmentally vulnerable time when AYAs strive for greater autonomy from caregivers, seek peer affiliation, and negotiate independent decision making,<sup>6</sup> making them particularly vulnerable to suboptimal adherence. The allocation of treatment responsibility is critical during this developmental period, with caregivers transitioning the process to AYAs as they mature.<sup>7-9</sup> However, AYAs may experience worsening symptoms due to reduced/absent parental monitoring, increased family conflict, and increased risky behavior.<sup>10-12</sup>

AYAs are also transitioning from pediatric to adult mental health settings, where they are expected to take on more illness management responsibilities, often without adequate transitioning. Only a small percentage of AYAs successfully transition to adult care,<sup>13</sup> complicated by developmental transitions such as changes in residence, postsecondary education or training, and engagement in risky behavior.<sup>14</sup> During this time, caregivers cede responsibility to AYAs based on age-related developmental expectations without appropriate

preparation,<sup>15</sup> leading to insufficient understanding of their illness and treatments, poor self-regulation strategies, and worsening symptoms.<sup>2</sup> At times, caregivers may have to re-engage in the care management of AYAs at late stages in their development. As a result, the transition can be associated with a disruption in the continuity of care, leading to disengagement from care services and suboptimal health outcomes.<sup>16</sup> In contrast, successful care transition for AYAs has the potential to improve adherence; optimize educational, social, and vocational outcomes<sup>17</sup>; and reduce long-term adverse outcomes, such as hospitalization, incarceration, and premature mortality.<sup>18–20</sup>

Managing BD is a complex process for anyone, but is particularly challenging for AYAs, and only some interventions exist that address adherence and self-management in AYAs with BD.<sup>21</sup> A successful evidence-based adherence intervention and self-management program for adults with BD called customized adherence enhancement (CAE) focuses on addressing 4 critical barriers to adherence, including knowledge about BD and treatments, communication with providers, medication routines, and alcohol and drug use. CAE is delivered by an interventionist in 5 sessions and is an adjunct to regular mental health treatment.<sup>22,23</sup> A recent randomized controlled trial of the CAE intervention for adults found that the intervention was superior to BD-specific patient education, demonstrating improved medication adherence and increased global psychological functioning among participants.<sup>23</sup>

This study aimed to modify an existing evidence-based intervention (CAE) to improve medication adherence for AYAs with BD (CAE-AYA). We used the Obesity-Related Behavioral Intervention Trials (ORBIT) model, which recommends several phases of intervention development.<sup>24</sup> This study focused on the 2-part design phase of ORBIT. Phase 1a defines the foundational conceptual elements of the behavioral treatment. Phase 1b examines candidate modules to determine optimal methods of delivery. In this study, the aim of phase 1a was implemented in 2 steps. Step 1 was to identify barriers and facilitators of adherence for AYAs with BD, while step 2 sought to define and refine the intervention content. The aim of phase 1b was to ensure that the new CAE-AYA modules were relevant to and usable by our target population of AYAs with BD before preliminary testing (phase II) or efficacy/effectiveness trials (phase III and IV).<sup>24</sup>

## METHOD

In phase 1a, step 1 focus groups and individual interviews were conducted with AYAs with BD, caregivers of AYAs with BD, and health care providers who treat AYAs with BD.<sup>25,26</sup> In phase 1a, step 2, the modified content was reviewed by an advisory board (AB), who provided suggestions for further modifications. Phase 1b was then conducted with nonadherent AYAs with BD through usability testing.

### Study Population

**Phase 1a.**—Participants in step 1 focus groups or interviews included 10 AYAs (ages 16–21) diagnosed with BD I or II, 4 caregivers of AYAs with BD, and 9 health care professionals with experience treating BD in AYAs (N = 23). Most AYAs and parent participants were referred by transition care or adult psychiatry clinics in the Department

of Psychiatry at Case Western Reserve University/University Hospitals (1 participant responded to a recruitment flyer). See Table 1 for demographic data.

AYAs met the following inclusion criteria: between the ages of 16 and 21, self-reported diagnosis of BD I or II, written assent and consent of legal guardian if younger than age 18, and fluent in English. Given the intent for the CAE-AYA intervention to broadly apply to most AYAs with any BD, we used a self-reported BD diagnosis premised on a longitudinal clinical evaluation. AYAs with and without a history of medication adherence difficulties were included to gain perspective from participants who were both successful and unsuccessful with disease management. AYAs were excluded if they were not receiving care in an outpatient setting, had a diagnosis of an autism spectrum or primary psychotic disorder, or had a documented IQ of less than 70. Parents/guardians were included in the study if they were involved in the care of the AYA or lived with the AYA who met the study criteria. Similarly, providers were included if they were physicians, therapists, pharmacists, or nurses caring for AYAs with BD. Participants in the second step of phase 1a included AB members composed of 3 AYAs and 5 care providers recruited from participants in step 1.

**Phase 1b.**—Usability testing occurred with 8 AYAs (4 participants each identified as female and male, respectively) who were not participants in phase 1a (Table 1). Usability participants met the following inclusion criteria: between the ages of 16 and 21; self-reported *DSM-5* diagnosis of BD I or II; suboptimal adherence, defined as having at least 20% of days with missed doses of a prescribed evidence-based BD medication in past week or month, as measured by the Tablets Routine Questionnaire (TRQ); written assent and consent of legal guardian if younger than age 18; and fluent in English. Exclusion criteria were identical to phase 1a. Participants in the usability testing group were recruited from the Department of Psychiatry at Case Western Reserve University/University Hospitals and the University of Cincinnati College of Medicine.

## Procedures

The study used an open system of recruitment that prioritized self-referral and clinician referral and consisted of institutional review board–approved flyers posted in locations where AYAs might see them (health center waiting rooms, coffee shops/restaurants, bulletin boards on school campuses) and presentations to local and regional clinicians who provide care to AYAs with a request/solicitation for referrals. Health care professionals from phase 1a were asked to refer AYAs from their practices. A trained research assistant contacted participants who met eligibility criteria and provided a thorough overview of the study procedures, including risks and benefits. When participants could not meet in person, consent was conducted remotely over videoconferencing with REDCap/electronic written consent/assent as approved by University Hospitals of Cleveland Institutional Review Board 20190554.

Recruitment and enrollment in the study was conducted between November 23, 2019, and May 20, 2020. Initial focus groups were conducted face-to-face but transitioned to a videoconferencing platform or telephone call-in when public health restrictions were

implemented due to the COVID-19 pandemic. Participants enrolled but unavailable for group sessions completed individual interviews using the same prompts.

### Qualitative Data Collection

Qualitative research remains instrumental in collecting indepth information from participants to guide the development of health interventions in special populations.<sup>27</sup> This study used focus groups/interviews to collect qualitative data from key stakeholders in both phases. This allowed participants to share their experiences and perspectives on BD symptoms and medication management in their own words.

**Phase 1a.**—Before participation, participants completed a demographic form. A licensed psychiatrist or psychologist conducted the focus groups/interviews based on a structured interview guide with 3 broad foci: knowledge of BD, current symptoms, and quality of self-management; perceived barriers and facilitators to medication adherence and medication routines; and relationships with parents and providers and their role in medication adherence. Participants were given \$20 to compensate them for their time and effort.

Selected members of focus groups/interviews (n = 8) participated in 2 meetings of an AB convened after the focus groups/interviews were completed. At the first AB meeting, attendees were presented with a summary of the perceived barriers and facilitators from focus groups/interviews, asked for additional suggestions on barriers/facilitators, and presented with a draft of the modified CAE intervention, called CAE-AYA. Participants provided feedback on the 4 CAE-AYA intervention modules (psychoeducation, communication, medication routines, substance use/risky behavior), customized into low- and high-intensity formats. In the second AB meeting, attendees reviewed the revised CAE-AYA intervention and provided additional input for a final product. AB members were also given \$20 for their time and effort.

**Phase 1b.**—Participants in usability testing (n = 8) were separate and distinct from the participants in the initial phases of the study. After completing a demographics form, a trained facilitator with expertise in the adult CAE intervention guided each participant through 1 or 2 modules. The usability of the newly adapted CAE-AYA was evaluated via a think aloud procedure, which involved verbalizing thoughts. At the same time, the interventionist delivered the modules and shared the patient-facing materials.<sup>28</sup> The participants also had a copy of the manual to follow. Each session was limited to 60 to 75 minutes to minimize participant burden. Each module was reviewed by 2 or 3 AYAs. Each participant viewed the written materials and graphics, navigated through 1 or 2 modules, and discussed their thinking in real time, emphasizing suggestions for improving acceptability and ease of use. Specifically, acceptability, comprehensibility, and relevance of each CAE module were evaluated. In addition to open-ended feedback, participants were asked the following questions: Is the content relevant for the age range (16–21)? How difficult/easy is it to understand the module? Is the language appropriate? Are there ways to improve?

Sessions took place via videoconferencing due to public health restrictions. Participants received \$30 to compensate them for their time and effort.

## Qualitative Data Analysis

Phase 1a focus groups and interviews were transcribed from recordings or virtual meeting transcripts. Two research assistants trained in directed content analysis<sup>29</sup> conducted the initial coding. Past research on medication adherence barriers, facilitators, and AYA developmental characteristics provided the foundation for the initial codes used in the analysis. Barriers were defined as feelings, beliefs, attitudes, or actions that reduce the likelihood of taking medications as prescribed. Facilitators were defined as feelings, beliefs, attitudes, and actions that increase adherence to a medication schedule. Developmental characteristics refer to intra-personal and interpersonal medication adherence characteristics that are developmentally typical for AYAs. As coding proceeded, data that did not fit existing codes were assigned new codes and descriptions. Approximately one-third of the transcripts were independently coded by both coders, who then met to review their coding for consistency and accuracy. Discrepancies in applying or describing existing or new codes were resolved through consensus among the coders and two lead investigators with expertise in qualitative content analysis. Once initial coding was completed, two lead investigators consolidated the codes into categories based on similarity in content and continuity with existing research. The categories mapped onto underlying themes.

AB meetings and phase 1b usability sessions were video recorded, and the facilitator took notes. The recordings were transcribed verbatim (any reference to names or other protective health information was removed/coded to ensure deidentification) and analyzed by study team members.

## CAE Intervention

Adherence is a multicomponent process involving knowledge of what is needed to manage a medical condition and implement a self-management plan. In addition, it requires communicating with health care professionals and caregivers to manage a care plan effectively. The original CAE intervention for adults consisted of 4 psychosocial treatment modules based on an adult's unique adherence barriers: psychoeducation on BD medications, communication with providers, strategies to enhance medication routines, and targeting of substance use problems with modified motivational enhancement therapy.<sup>22,23</sup> Each module can be delivered in 45- to 60-minute sessions.

## RESULTS

### Phase 1a: Focus Group/Individual Interviews

Two focus groups and 5 interviews were conducted with AYAs, 1 focus group and 2 interviews were conducted with parents, and 2 focus groups were conducted with health care providers (N = 23). Across participants, 3 significant themes characterized the management of BD and its symptoms among AYAs (Tables 2, 3, and 4).

**Theme 1: Difficulties With Mood Symptoms.**—All participants noted the difficulty that AYAs have in coping with BD symptoms. An AYA said, “I’m crying over literally nothing,” while a parent/caregiver noted that their child is “very erratic, she’s all over the place emotionally.” Providers indicated that unpredictable emotions may lead to anxiety



because “It’s not knowing what’s next.” Associated with the challenges of managing BD symptoms, participants described several perceived barriers to medication adherence, including memory, attention, and motivation; denial of BD; stigma from peers/family; medication side effects; and negative relationship with their provider. Several AYAs noted difficulty remembering to take medications because they “just get distracted by life and everything that’s going on.” Others noted difficulties with motivation or laziness. One parent stated, “... when she’s been in deep depression, she’ll just turn them [reminders] off.” Providers expressed that AYAs with inconsistent schedules are more likely to have difficulties. School, work, play, and sleep are less regular compared with adults, which may lead to problems with memory or attention.

Participants also noted that AYAs often have difficulty accepting the diagnosis early in the disease recognition process. Denial was common. One AYA said: “[I] definitely denied that I had bipolar. Denied it for a month, two months ... I was like they’re wrong, I don’t have this.” Another parent/caregiver described how “seeing her sister and grandmother [with BD], I think it was hard for her. And then she knew she had it and she kept denying it.” Providers described the issues of not believing in the problem. It was noted that AYAs lack insight or self-examination to acknowledge the symptoms that they fear.

AYAs were also aware of stigma from peers and family members. One AYA stated, “it’s gotten hard at school because a bunch of kids found out that I’m being treated for a disease ... they don’t understand.” Parents noted this concern and discussed how they try to help the child cope with the anxiety and differential treatment by peers. Providers also recognized the dilemma, with one provider noting, “I agree, I think the concern about the stigma, how do you talk about that with your peers or even should I talk about that with my peers.”

Another common complaint among AYAs was difficulty with side effects. The most common side effects reported by AYAs included loss of appetite, weight gain, blurred vision, loss of balance, stomach upset, restless legs, trouble sleeping, anxiety, and suicidal thoughts. One AYA noted that “my body couldn’t handle the side effects. I think medications are frustrating and difficult.” When the side effects were perceived by AYAs as more harmful than the symptoms, they were less likely to take medications.

Finally, a few AYAs and their parent/caregivers reported difficulties with providers that may impact medication adherence. Specifically, poor communication was cited as a problem, including feeling like providers did not listen to their concerns regarding medications and side effects. One AYA noted, “I just changed my psychiatrist because my other one ... she just went along with what [psychiatric facility] had to say with everything, and she didn’t really try anything else.” A caregiver noted that her child’s therapist is “not very talkative ... and I don’t know if [my child] feels safe with the therapist.”

**Theme 2: Management of BD Symptoms and Improving Adherence.**—AYAs provided insight into the ways they successfully manage their BD symptoms and maintain medication adherence (Table 2). Successful management of BD symptoms fell into 3 categories: correct knowledge of BD and treatment; strong beliefs that the medication benefits far outweighed the costs; and positive relationships with caregivers, peers, and

providers. Several AYAs reported that they were aware of the primary symptoms of BD and that medication is a primary form of treatment. For example, one AYA noted, “I actually have done a lot of research, and I go to a lot of therapy groups about bipolar disorder.” However, providers cautioned that often the knowledge is insufficient and includes lay knowledge that may be detrimental to their treatment (Table 4). At the same time, many AYAs held strong beliefs that the medication benefits far outweigh the costs. Several noted that they had tried multiple medications over time to find ones that both treat their specific symptoms and have the least side effects. Even though they tried several medications, they always believed that the benefits were worth it in the long run. One AYA stated, “I think the benefits definitely outweigh the not taking them just because I am psychotic without it. So like I enjoy not feeling like someone is [out to get] me.”

Positive relationships with caregivers, peers, and providers were also instrumental in managing BD symptoms. AYAs described how family members may have the same or similar diagnosis and can help with coping, medication regimens, and transportation to appointments (Table 2). One young adult stated that on initial diagnosis in adolescence, “... so my mom was hand and hand with me, she made sure I was on the medication, made sure I was going to therapy and would hold my hand.” In addition, some AYAs reported that disclosure to peers was also helpful in maintaining mental health and remaining on medication schedules, particularly peers with a mental health diagnosis. A provider noted, “if they ... have a social network, I think that can be really helpful for that age group that they openly talk about ‘I take medication, it’s okay, I’m diagnosed,’ that kind of thing.” Finally, positive relationships with providers were another contributor. Comments from AYAs included, “it’s just good to talk to someone”; “She makes me feel comfortable”; “She’s the first psychiatrist that has ever listened to me.” Some reported that participation in group therapy helped manage emotions, helped improve coping skills, and provided drug and alcohol counseling to avoid self-medicating (Table 2).

Among the specific facilitators of medication adherence, participants identified planning/ routines and reminders (Table 2). For example, if staying at a friend’s house, AYAs would pack the necessary medications. At the same time, others used visual reminders, including setting a time on their phone or placing the medications in a conspicuous location (eg, a nightstand or next to a toothbrush). While many reported that parents tended to remind them occasionally, older AYAs (older than 18) noted transitioning to taking responsibility themselves.

**Theme 3: Transition to Care.**—The last category included the transition of care from parent to child. Themes reflected the developmental process of individuating from one’s family of origin. AYAs described either their independence from parents in treatment decision making actively or negotiating with their parents about taking more responsibility. Young adults told how they would talk with their parents about taking more responsibility and becoming more self-sufficient. However, adolescents (younger than 18) continued to rely heavily on their parents. One AYA parent reported, “I’m the one that makes sure she takes her meds every day, I’m the one that gets her to her appointments, makes the appointments, has conversations with her psychiatrist and therapist.” While this level of involvement may be uncomfortable for AYAs, it is not entirely unwelcome. An AYA noted,



“I feel like, uh, they have a very high level of control over my life just because I get so mentally ill sometimes that I can’t really be as independent as I guess I should be or want to be, so my parents are big, they’re my rock.”

### **Phase 1a: AB Review**

AYAs, parents, and care providers from focus groups and individual interviews who represented a range of ages and types of clinical practice and who were interested in providing more input on the CAE intervention refinement were prioritized for recruitment to the AB. A summary of the perceived barriers and facilitators from phase 1a focus groups/interviews was presented at the first of 2 AB meetings. The AB identified additional barriers, including access to medication while traveling, self-care while caring for ill family or friends, and sudden changes in routine. Facilitators focused on relationships with family and friends with recommendations to include parents/caregivers, roommates, or other loved ones in session or through psychoeducational materials that the participant can share. AB members also recommended that individual sessions be at most 50 to 60 minutes in length and that offering sessions virtually is appropriate but may be feasible only for some participants who may have access to adequate bandwidth. In a second AB meeting, following initial revisions to the CAE-AYA intervention described in the discussion, participants provided additional feedback, including modifications to session activities, worksheets, and homework assignments; recommendations for improving module delivery and active learning; and suggestions for additions to the psychoeducational curriculum and use of technology.

### **Phase 1b: Usability Testing**

Usability testing of the resultant CAE-AYA modules revealed that while the content was relevant for AYAs between ages 16 and 21, language modifications were needed based on the participant’s developmental level (eg, teenager vs young adult). Almost all participants said the content was easy to understand, that 60 minutes was an appropriate length for each session, and that the information was “just right.” Recommendations to improve on the modules included the need for more visual images with color and vibrancy to engage participants as well as having therapists who review the materials to use the words and language of the participant (eg, less clinical language) and consider the impact of the materials on everyday functioning. Another suggestion from 2 participants was to modify our module regarding inhibition, where we provide a “STOP and THINK” exercise. This was perceived as a “PBS special” and not reviewed favorably. Modifications were made to the modules (ie, use of more visual images and updated contemporary-looking forms, revision of the “STOP and THINK” exercise) and therapist manual (ie, guidance about developmentally appropriate language based on age and maturity) following these recommendations for use in the pilot randomized trial.

## **DISCUSSION**

The overarching goal of the current study was to modify an existing adherence intervention developed for adults with BD for use with AYAs with BD to accommodate developmental differences in disease and symptom management, side effects, substance use, and

communication. Engaging relevant groups of stakeholders in modifying an evidence-based BD adherence intervention allowed the researchers to compare experiences, perceptions, and insights from various sources.

Results demonstrate the critical need for multi-informant investigations into barriers and facilitators to medication adherence.<sup>2,30</sup> While adherence barriers in AYAs with BD overlap considerably with barriers identified by adults with BD and other pediatric chronic conditions,<sup>31</sup> there were a few exceptions. Most notably, BD challenges, barriers, and facilitators associated with relationships with peers, partners, parents, and providers were particularly important to AYAs in this study. All 3 groups of participants (eg, AYAs, caregivers, providers) noted the challenges that a BD diagnosis can have on symptom management and medication adherence, including disruption in peer relationships, peer stigma, caregiver overinvolvement, and lack of trust in their health care providers. While changes in interpersonal relationships are a normative developmental process as adolescents transition into young adulthood,<sup>6</sup> the non-normative stressors associated with BD management, such as mood dysregulation, medication side effects, attention problems, and poor memory, may disrupt the accomplishment of these crucial developmental tasks.<sup>8</sup> Negotiating these barriers and stressors requires developing effective communication with providers, caregivers, and peers and addressing the impact of stigma by peers and family.

Preliminary findings suggest that parental involvement and overinvolvement in illness management have less to do with AYA age and more to do with the skills and competencies of the AYA. While there was an implicit expectation that with increasing age, AYAs would assume more responsibility for illness management, the transition of care from parent to child was not always on the expected timetable. While younger AYAs were more likely to rely on parents for medication and treatment management, parents were mindful of the cognitive and behavioral capacity of AYAs to assume responsibility, which is critical. This suggests that while there are cultural expectations of autonomy and legal obligations for health management, the transition of care may not occur on the expected age or developmental path. It is also notable that transition is not always a linear path and that re-engagement by parents may be necessary in the face of increased symptoms or stressors. To accommodate individual differences based on development, modifications to CAE-AYA included both low- and high-intensity modules to address the specific needs of the AYAs.

In the modified CAE for AYAs, the communication module was updated to focus on basic communication skills, including optimal ways to communicate with the support network, issues of disclosure, allocation of treatment responsibility, and initial stages of transition from a triadic partnership for care to a dyadic one. The communication module was modified to include 2 versions based on the individual needs of the AYAs: low vs high intensity. The higher intensity version targets AYAs who identify difficulty in communication with peers, parents, and/or providers. They receive instruction on basic communication skills (eg, do's and don't's), including optimal ways to communicate with their support network, issues of disclosure, and allocation of treatment responsibility. The lower-intensity version focuses more exclusively on communication with clinicians and anticipatory guidance on transitioning from a triadic partnership for care to a dyadic one.

Similarly, low- and high-intensity versions were created for the medicine routines and the risky behavior modules. For medication routines, a higher-intensity version was developed for participants who either have no caregiver input or have few medication reminder strategies. Participants complete a medication profile to help them be more confident and knowledgeable when they talk to caregivers and practitioners. In addition, participants complete a medication routines activity for “remembering to take your medication.” The lower-intensity version is for participants who independently manage their medications or have many strategies to remember to take their medications. Finally, in the risky behavior module, the higher-intensity version is for participants with a history of using drugs or alcohol. It uses a modified motivational enhancement therapy approach to help participants understand the effect of substance use on BP in general and on adherence to the BD regimen. The lower-intensity version is for participants who have no or minimal experience with alcohol or drugs, providing anticipatory guidance about patterns of risky behavior that impact BD self-management, such as staying out late.

A fifth session of the CAE-AYA was developed to go into more detail on one of two topics, psychoeducation about BD, including a plan for relapse prevention, or modified motivational interviewing to address substance use/risky behaviors. The rationale for including the booster session was twofold: to reduce the amount of information covered in any one session and to further customize the intervention by going into more depth for particularly challenging barriers.

While our findings have implications for informing care delivery for AYAs with BD, there are some limitations. Although the sample size used in phase 1a was within the suggested range for inductive analytic approaches,<sup>32</sup> it remains small and not necessarily representative of the broad population of AYAs with BD. Implementing the later phases of ORBIT intervention development may mitigate these initial phase limitations.<sup>33</sup> Likewise, the racial composition of the sample was primarily White and female, further limiting the generalizability of the results. Additionally, as the study strongly relied on self-referral or clinician referral for recruitment, findings may not be generalizable to AYAs who are less likely to seek help. The self-reported BD diagnosis was an additional limitation. However, most study referrals came from clinicians for patients in their clinical practices, making it more likely that diagnoses were based on longitudinal clinical evaluation. Finally, phase 1a included participants who self-reported to be highly adherent; thus, the endorsed barriers may be more conservative. However, it is notable that the barriers and facilitators experienced by participants in phase 1a are also supported in the broader literature.<sup>5</sup> Despite these limitations, this exploratory study demonstrated that using qualitative methods to examine characteristics unique to AYAs with BD could provide valuable insights into adherence difficulties for the adaptation and modification of an intervention.

Overall, our results demonstrate that the ORBIT phase 1a and 1b design was effective in providing stakeholder feedback to optimize CAE to address the unique developmental challenges of AYAs with BD.<sup>24</sup> Using the iterative procedure, we were able to engage patients, caregivers, and clinicians to provide critical feedback that resulted in a more developmentally and contextually appropriate final CAE-AYA intervention. Developmental issues were addressed by removing jargon and improving module delivery by modifying

activities to more accurately reflect the lived experiences of AYAs. On the other hand, AYAs demonstrated a nonlinear path to autonomous illness management, which was addressed in our modifications by developing modules that accommodate the specific needs of AYAs, regardless of age. With increased confidence that the intervention addresses the unique developmental and contextual needs of AYAs with BD, we are conducting a pilot randomized controlled trial of CAE-AYA vs enhanced treatment as usual.<sup>33</sup> The long-term goal of the modified CAE for AYAs is to demonstrate improved medication adherence, BD symptoms, and quality of life.

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## REFERENCES

1. McClellan J, Kowatch R, Findling RL; Work Group on Quality Issues. Practice parameter for the assessment and treatment of children and adolescents with bipolar disorder. *J Am Acad Child Adolesc Psychiatry*. 2007;46(1):107–125. 10.1097/01.chi.0000242240.69678.c4 [PubMed: 17195735]
2. Coletti DJ, Leigh E, Gallelli KA, Kafantaris V. Patterns of adherence to treatment in adolescents with bipolar disorder. *J Child Adolesc Psychopharmacol*. 2005;15(6): 913–917. 10.1089/cap.2005.15.913 [PubMed: 16379511]
3. DelBello MP, Hanseman D, Adler CM, Fleck DE, Strakowski SM. Twelve-month outcome of adolescents with bipolar disorder following first hospitalization for a manic or mixed episode. *Am J Psychiatry*. 2007;164(4):582–590. 10.1176/ajp.2007.164.4.582 [PubMed: 17403971]
4. Gonzalez-Pinto A, Mosquera F, Alonso M, et al. Suicidal risk in bipolar I disorder patients and adherence to long-term lithium treatment. *Bipolar Disord*. 2006;8(5 Pt 2): 618–624. 10.1111/j.1399-5618.2006.00368.x [PubMed: 17042834]
5. Klein CC, Topalian AG, Starr B, et al. The importance of second-generation antipsychotic-related weight gain and adherence barriers in youth with bipolar disorders: patient, parent, and provider perspectives. *J Child Adolesc Psychopharmacol*. 2020;30(6): 376–380. Published correction appears in *J Child Adolesc Psychopharmacol*. Published online March 23. 10.1089/cap.2019.0184 [PubMed: 32423240]

6. Tanner JL, Arnett JJ. The emergence of emerging adulthood: the new life stage between adolescence and young adulthood. In: Furlong A, ed. *Routledge Handbook of Youth and Young Adulthood*. 2nd ed. New York: Routledge; 2016:50–56. 10.4324/9781315753058-13
7. Creary SE, Modi AC, Stanek JR, et al. Allocation of treatment responsibility and adherence to hydroxyurea among adolescents with sickle cell disease. *J Pediatr Psychol*. 2019;44(10):1196–1204. 10.1093/jpepsy/jsz061 [PubMed: 31403687]
8. Holbein CE, Smith AW, Peugh J, Modi AC. Allocation of treatment responsibility in adolescents with epilepsy: associations with cognitive skills and medication adherence. *J Pediatr Psychol*. 2019;44(1):72–83. 10.1093/jpepsy/jsy006 [PubMed: 29447360]
9. Modi AC, Marciel KK, Slater SK, Drotar D, Quittner AL. The influence of parental supervision on medical adherence in adolescents with cystic fibrosis: developmental shifts from pre to late adolescence. *Child Health Care*. 2008;37(1):78–92. 10.1080/02739610701766925
10. Dean AJ, Wragg J, Draper J, McDermott BM. Predictors of medication adherence in children receiving psychotropic medication. *J Paediatr Child Health*. 2011;47(6): 350–355. 10.1111/J.1440-1754.2010.01985.x [PubMed: 21309880]
11. Holtzman JN, Miller S, Hooshmand F, et al. Childhood-compared to adolescent-onset bipolar disorder has more statistically significant clinical correlates. *J Affect Disord*. 2015; 179:114–120. 10.1016/J.JAD.2015.03.019 [PubMed: 25863906]
12. Townsend LD, Demeter CA, Youngstrom E, Drotar D, Findling RL. Family conflict moderates response to pharmacological intervention in pediatric bipolar disorder. *J Child Adolesc Psychopharmacol*. 2007;17(6):843–852. 10.1089/cap.2007.0046 [PubMed: 18315455]
13. Appleton R, Connell C, Fairclough E, Tuomainen H, Singh SP. Outcomes of young people who reach the transition boundary of child and adolescent mental health services: a systematic review. *Eur Child Adolesc Psychiatry*. 2019;28(11):1431–1446. 10.1007/S00787-019-01307-7 [PubMed: 30850925]
14. Broad KL, Sandhu VK, Sunderji N, Charach A. Youth experiences of transition from child mental health services to adult mental health services: a qualitative thematic synthesis. *BMC Psychiatry*. 2017;17:1–11. 10.1186/S12888-017-1538-1 [PubMed: 28049496]
15. Paul M, Street C, Wheeler N, Singh SP. Transition to adult services for young people with mental health needs: a systematic review. *Clin Child Psychol Psychiatry*. 2015; 20(3):436–457. 10.1177/1359104514526603 [PubMed: 24711585]
16. Singh SP. Transition of care from child to adult mental health services: the great divide. *Curr Opin Psychiatry*. 2009;22(4):386–390. 10.1097/YCO.0B013e32832c9221 [PubMed: 19417667]
17. Robb A, Findling RL. Challenges in the transition of care for adolescents with attention-deficit/hyperactivity disorder. *Postgrad Med*. 2015;125(4):131–140. 10.3810/pgm.2013.07.2685
18. Hong J, Reed C, Novick D, Haro JM, Aguado J. Clinical and economic consequences of medication non-adherence in the treatment of patients with a manic/mixed episode of bipolar disorder: results from the European Mania in Bipolar Longitudinal Evaluation of Medication (EMBLEM) study. *Psychiatry Res*. 2011;190(1):110–114. 10.1016/j.psychres.2011.04.016 [PubMed: 21571375]
19. Copeland LA, Miller AL, Welsh DE, McCarthy JF, Zeber JE, Kilbourne AM. Clinical and demographic factors associated with homelessness and incarceration among VA patients with bipolar disorder. *Am J Public Health*. 2009;99(5):871–877. 10.2105/AJPH.2008.149989 [PubMed: 19299667]
20. Robertson AG, Swanson JW, van Dorn RA, Swartz MS. Treatment participation and medication adherence: effects on criminal justice costs of persons with mental illness. *Psychiatr Serv*. 2014;65(10):1189–1191. 10.1176/appi.ps.201400247 [PubMed: 25270494]
21. Goldstein TR, Krantz ML, Fersch-Podrat RK, et al. A brief motivational intervention for enhancing medication adherence for adolescents with bipolar disorder: a pilot randomized trial. *J Affect Disord*. 2020;265:1–9. 10.1016/j.jad.2020.01.015 [PubMed: 31957686]
22. Sajatovic M, Levin J, Tatsuoka C, et al. Six-month outcomes of Customized Adherence Enhancement (CAE) therapy in bipolar disorder. *Bipolar Disord*. 2012;14(3):291–300. 10.1111/j.1399-5618.2012.01010.x [PubMed: 22548902]

23. Sajatovic M, Tatsuoka C, Cassidy KA, et al. A 6-month, prospective, randomized controlled trial of customized adherence enhancement versus bipolar-specific educational control in poorly adherent individuals with bipolar disorder. *J Clin Psychiatry*. 2018; 79(6):17m12036. 10.4088/JCP.17m12036
24. Czajkowski SM, Powell LH, Adler N, et al. From ideas to efficacy: the ORBIT model for developing behavioral treatments for chronic diseases. *Health Psychol*. 2015;34(10): 971–982. 10.1037/HEA0000161 [PubMed: 25642841]
25. Strauss A *Qualitative Analysis for Social Scientists*. Cambridge: Cambridge University Press; 1988.
26. Patton MQ. Enhancing the quality and credibility of qualitative analysis. *Health Serv Res*. 1999;34(5 Pt 2):1189–1208. [PubMed: 10591279]
27. Farquhar SA, Parker EA, Schulz AJ, Israel BA. Application of qualitative methods in program planning for health promotion interventions. *Health Promot Pract*. 2006;7(2): 234–242. 10.1177/1524839905278915 [PubMed: 16585146]
28. Ericsson KA, Simon HA. *Protocol Analysis: Verbal Reports as Data*. Rev ed. Cambridge, MA: MIT Press; 1993.
29. Hsieh HF, Shannon SE. Three approaches to qualitative content analysis. *Qual Health Res*. 2005;15(9):1277–1288. 10.1177/1049732305276687 [PubMed: 16204405]
30. Goldstein TR, Krantz M, Merranko J, et al. Medication adherence among adolescents with bipolar disorder. *J Child Adolesc Psychopharmacol*. 2016;26(10):864–872. 10.1089/cap.2016.0030 [PubMed: 27419273]
31. Prajapati AR, Dima A, Mosa G, et al. Mapping modifiable determinants of medication adherence in bipolar disorder (BD) to the theoretical domains framework (TDF): a systematic review. *Psychol Med*. 2021;51(7):1082–1098. 10.1017/S0033291721001446 [PubMed: 34006337]
32. Creswell JW, Poth CN. *Qualitative Inquiry and Research Design*. Thousand Oaks, CA: Sage; 2017.
33. McVoy M, Delbello M, Levin J, et al. A customized adherence enhancement program for adolescents and young adults with suboptimal adherence and bipolar disorder: trial design and methodological report. *Contemp Clin Trials*. 2022;115:106729. 10.1016/j.cct.2022.106729 [PubMed: 35278693]



**TABLE 1**

**Participant Demographics and Adolescent and Young Adult (AYA) Disease Characteristics**

	AYA focus group/individual interviews (n = 10)		Caregiver focus group/individual interviews (n = 4)		Health care provider focus group (n = 9)		Usability testing group (n = 8)	
	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)
Participant age, y	18.7	(1.89)	45.3	(8.33) <sup>a</sup>	N/A	N/A	19	(1.31)
AYA age of diagnosis, y	15.9	(2.88)	15.3	(0.5)	N/A	N/A	10.5	(4.72)
AYA age of first significant mood symptoms,	14.1	(3.60)	13.5	(1.73)	N/A	N/A	4.9	(6.17)
Living situation								
AYA lives with caregiver/guardians	10		4		N/A	N/A	6	
AYA lives with others, eg, roommate	0		0		N/A	N/A	2	
Highest education level								
Less than high school diploma	4		1		N/A	N/A	2	
High school diploma/GED	1		2		N/A	N/A	0	
Some college	5		0		N/A	N/A	7	
College degree	0		1		N/A	N/A	0	
AYA was hospitalized for BD								
Yes	7		3		N/A	N/A	6	
No	3		1		N/A	N/A	2	
Prescribed BD medication on daily basis								
Yes	9		4		N/A	N/A	7	
No	1		0		N/A	N/A	1	
Difficulty with missing doses								
Never/hardly miss doses	8		3		N/A	N/A	2	
Miss doses 2 times per week	2		1		N/A	N/A	6	
Sex								
Male	2		1		2	2	4	
Female	8		3		7	7	4	
Race/ethnicity								
	<b>Mean</b>	<b>(SD)</b>	<b>Mean</b>	<b>(SD)</b>	<b>Mean</b>	<b>(SD)</b>	<b>Mean</b>	<b>(SD)</b>

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	AYA focus group/individual interviews (n = 10)	Caregiver focus group/individual interviews (n = 4)	Health care provider focus group (n = 9)	Usability testing group (n = 8)
Asian	1	0	2	1
Black/African American	2	2	1	0
White Hispanic	0	0	1	0
White non-Hispanic	7	2	5	7
Caregiver type				
Mother	N/A	2	N/A	N/A
Father	N/A	1	N/A	N/A
Other	N/A	1	N/A	N/A
Health care provider				
Psychiatrist/physician	N/A	N/A	3	N/A
Nurse/nurse practitioner	N/A	N/A	2	N/A
Mental health counselor/therapist	N/A	N/A	3	N/A
Pharmacist	N/A	N/A	1	N/A
Practice setting				
Community mental health clinic	N/A	N/A	2	N/A
Private practice	N/A	N/A	0	N/A
Academic setting	N/A	N/A	5	N/A
Other	N/A	N/A	2	N/A
Years in practice	Mean N/A	Mean N/A	Mean 2.67 (8.65)	Mean N/A

Note: N/A refers to variables for which the category does not apply. BD = bipolar disorder; GED = General Educational Development test.

<sup>a</sup> n=3 as one of the ages was missing.

**TABLE 2**

**Focus Group Categories and Themes for Adolescent and Young Adults (AYAs)**

<b>Theme 1: Difficulties with mood symptoms</b>	
Difficult mood symptoms	Uncertainty
	Changing emotions
Relationships with others	Trouble dating
	Trouble holding a steady job
	Trouble with parents
Stigma	Treated differently by others after diagnosis
	Others comparing this diagnosis to other diagnoses/people
	Self-acceptance
<b>Theme 2: Management of BD symptoms and improving adherence</b>	
Barriers/challenges with medication adherence	Laziness
Memory, attention, motivation	Forgetfulness
Denial of BD	Denial
Side effects	Loss of appetite or weight gain
	Blurred vision
	Loss of balance
	Stomach upset
	Restless legs
	Trouble sleeping
	Anxiety
	Suicidal thoughts
	Communication
	Change provider
Negative relationship with provider	
Facilitators/management of BD diagnosis/symptoms	Family history
Knowledge of BD diagnosis/symptoms	Genetic predisposition
	Symptoms (depression, mania)
	Treatment (medication)
	Reduce symptoms
Beliefs regarding benefits	

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- Side effects manageable
- Benefits outweigh costs
- Someone to talk to Listens
- Respectful
- Comfortable
- Art and music therapy
- Coping skills learned
- Drug and alcohol abuse, mental illness counselor
- Close friends
- Trusted individuals
- Parent has same diagnosis
- Supportive but allow autonomy
- Supportive and involved
- Parent on the child's side
- Make up for a missed dose
- Planning, routine
- Keeps medication with them
- Visual reminders
- Independent
- Self-sufficient
- Child vs parent control
- Schedule and medication
- Overinvolvement

Positive relationship with provider

Counseling/therapy/group support

Self-disclosure/peer social support

Caregiver support and involvement

Planning/routine

Reminders

**Theme 3: Transition of care**

Individuation from caregivers

Caregiver (over)involvement

**Note:** BD = bipolar disorder.

**TABLE 3**

**Focus Group Categories and Themes for Caregivers**

<b>Theme 1: Difficulties with mood symptoms</b>	
Difficult mood symptoms	Unmotivated
Relationships with others	Isolation
Stigma	Impact of fighting with peers/significant others
	Did not want the child to be treated differently
	Helping child through stigma
	Family secret
<b>Theme 2: Management of BD symptoms and improving adherence</b>	
Barriers/challenges with medication adherence	Lack of drive
Memory, attention, motivation	Forgetfulness
Denial of BD	Denial
Side effects	None
Negative relationship with provider	Communication
Facilitators/management of BD diagnosis/symptoms	Family history
Knowledge of BD diagnosis/symptoms	Symptoms (depression, mania)
Beliefs regarding benefits	Reduce symptoms
Positive relationship with provider	Improve behavior
Counseling/therapy/group support	Comfortable
Self-disclosure/peer social support	Regular meetings
Caregiver support and involvement	Coping skills learned
Facilitators/management of medication adherence	Close friends
Planning/routine	Supportive and involved
Reminders	None
<b>Theme 3: Transition of care</b>	Visual reminders
Individuation from caregivers	Independent
	Self-sufficient

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Overinvolvement

Caregiver (over)involvement

**Note:** BD = bipolar disorder.



**TABLE 4**

Focus Group Categories and Themes for Health Care Providers

<b>Theme 1: Difficulties with mood symptoms</b>	
Difficult mood symptoms	Fear of uncertainty
Relationships with others	None
Stigma	Peer judgment
<b>Theme 2: Management of BD symptoms and improving adherence</b>	
Barriers/challenges with medication adherence	
Memory, attention, motivation	Forgetfulness
Denial of BD	Inconsistent schedules
Side effects	Belief/insight
Negative relationship with provider	Journey to understand side effects/benefits
Facilitators/management of BD diagnosis/symptoms	Lack of positive connection
Knowledge of BD diagnosis/symptoms	Knowledge, incomplete/inaccurate
Beliefs regarding benefits	Symptoms (depression, mania)
Positive relationship with provider	Benefits outweigh costs
	Listens, open-minded
	Regular contact
	Communication
Counseling/therapy/group support	Regular meetings
	Coping skills taught
Self-disclosure/peer social support	Close friends
Caregiver support and involvement	Caregiver supervision
Planning/routine	Planning, routine
Reminders	Visual reminders
	Caregiver reminders
	Phone reminders
<b>Theme 3: Transition of care</b>	
Individuation from caregivers	Child vs parent control
	Doctor-patient confidentiality issues
Caregiver (over)involvement	Involvement

Note: BD = bipolar disorder.

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