



Understanding Key Evidence Gaps in the Treatment of Anxiety Disorders in Children, Adolescents, and Young Adults: Workshop Meeting Summary

Overview

On July 26, 2017, PCORI convened a multi-stakeholder workshop to explore opportunities for funding comparative effectiveness research (CER) that would increase the actionable evidence base for the treatment and management of anxiety disorders in youth. The population of interest was children, adolescents, and young adults with anxiety disorders, as well as their families. Workshop participants included patient advocates, clinicians, researchers, and representatives of federal and private research funding organizations, clinical societies, and public and private payers. The meeting was open to the public via webinar.

Before the workshop, PCORI staff conducted informational interviews with stakeholders to identify important evidence gaps, areas of research where PCORI could have an impact, and potential CER questions. Additionally, workshop participants were asked to rank the importance of five topics within the field of treating anxiety disorders in youth.

The two topics that ranked the highest among participants were identified to inform the content of two simultaneous breakout sessions at the workshop. The two highest-ranking topics were: 1) stepped therapy, including combination approaches and discontinuation of treatment, and 2) addressing access to care, including the format and delivery of cognitive behavioral therapy (CBT). After the breakout sessions took place, workshop participants reconvened to synthesize the information discussed in each session, and to further refine the research areas and questions for PCORI to consider for future funding announcements.

Box 1: Two Highest-Ranking Topics from Survey Distributed to Workshop Participants

<i>Topic 1: Stepped Therapy, Including Combination Approaches and Discontinuation of Treatment</i>	<i>Topic 2: Addressing Access to Care, Including Format and Delivery of CBT</i>
<ul style="list-style-type: none">• What is the appropriate starting point for treatment of anxiety disorders?• Which treatments would you add if the first treatment is not effective?• When do you add additional interventions?	<ul style="list-style-type: none">• What are the strengths and limitations of various formats and delivery settings for CBT (e.g., face-to-face, digital approaches, primary care, school-based settings)? Do these vary by patient characteristics (e.g., severity, age)?

<ul style="list-style-type: none"> Under what circumstances would you initiate treatment with an intervention other than CBT? 	<ul style="list-style-type: none"> What level and type of therapist involvement is needed to deliver CBT effectively? Is reimbursement or confidentiality for telehealth visits a consideration in the scalability of research?
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Introduction

Anxiety disorders are the most common psychiatric disorders with childhood-onset in the United States, with prevalence estimates ranging from 10 to 30 percent.¹ Childhood anxiety disorders typically follow a progressive course and hinder the social, emotional, and academic development of youth. Early intervention can modify the trajectory of the disorder and prevent significant impairment.^{2,3} When these disorders are not treated sufficiently, they often persist into adulthood and are associated with depression, substance abuse, functional and occupational impairments, and suicidal behavior.^{3,4,5}

There are a range of effective treatments for childhood anxiety disorders, including psychological, pharmacologic, and combined treatment approaches. Among the psychological interventions, CBT is the most widely studied and has the strongest evidence of effectiveness.^{2,5} However, patients and families experience numerous barriers to accessing CBT, including time constraints, lack of insurance coverage, and difficulty navigating the healthcare system.

Digital health interventions (DHIs), particularly computerized CBT interventions, have been shown to be effective for improving anxiety symptoms in adolescents and young adults with mild-to-moderate anxiety. DHIs may help address some of the access issues around face-to-face CBT; however, it is still unclear whether computerized CBT is effective for younger children or for youth with more severe anxiety. Also, additional research is needed to assess the level and type of human support that may be required for DHIs to be clinically effective.⁶

Among the pharmacologic therapies, selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) have the strongest evidence of effectiveness; however, there is a lack of evidence for head-to-head comparisons of individual medications, as well as optimal strategies for the discontinuation of pharmacotherapy.² Additionally, evidence is lacking for comparisons of CBT versus medications, combination therapy versus monotherapy, treatment sequencing approaches, and various models of care delivery.^{2,3}

Thus, despite the range of available treatments, patients, families, and clinicians are faced with many uncertainties when making treatment decisions. Given the high prevalence and burden of anxiety disorders in youth—and the lack of evidence regarding the most effective interventions, treatment sequencing approaches, and models of care delivery—PCORI has a unique role to play in funding patient-centered outcomes research that advances the evidence base for the treatment and management of childhood anxiety disorders.

PCORI convened this multi-stakeholder workshop to better understand the most pressing issues faced by patients, families, and clinicians in making treatment decisions for children and young adults with

anxiety disorders, and to identify opportunities for funding patient-centered CER. The workshop began with introductions and an overview presentation by Dr. Evelyn Whitlock, Chief Science Officer at PCORI, and Dr. Kristin Carman, Director of Public and Patient Engagement at PCORI. After Dr. Whitlock described the purpose of the workshop and PCORI's work to date on the topic, she then invited workshop participants to raise some of the critical issues and evidence gaps in the treatment of childhood anxiety disorders.

After this initial discussion, workshop participants were organized by interest and expertise into the two breakout sessions: 1) stepped therapy, including combination approaches and discontinuation of treatment, and 2) addressing access to care, including format and delivery of CBT. After these breakout sessions, the participants reconvened to summarize the information discussed in each session, and to further refine the research areas and questions for prioritization.

Breakout Sessions

The purpose of the breakout sessions was to have a focused discussion on topics within the field of childhood anxiety disorders that were identified by participants as being highly important. PCORI staff facilitated each of the breakout sessions by prompting participants to consider topics within the context of important comparators, outcomes of interest to patients and families, and areas of key research focus.

Stepped Therapy, Including Combination Approaches and Discontinuation of Treatment

This breakout session was focused on the issues surrounding the initiation, sequencing, and discontinuation of treatments for anxiety disorders in youth. The session was facilitated by Dr. Laura Esmail, Program Officer for the Clinical Effectiveness and Decision Science Program at PCORI. Dr. Esmail started the conversation by highlighting some of the key uncertainties related to this topic, including the appropriate starting point for the treatment of childhood anxiety disorders, what treatments should be added, when they should be added if the first treatment is not effective, and what the best strategies are for discontinuing treatment and preventing relapse. Additionally, Dr. Esmail invited participants to comment on other critical issues and research areas within this topic that may be important for improving patient-centered and family outcomes.

In response to these questions, workshop participants discussed the need for evidence on the following subtopics: population-based prevention strategies, screening for early identification and intervention, addressing parental anxiety and involving parents in the management of their children's anxiety, the impact of delayed or limited access to CBT, initiation of medication therapy and the potential of pharmacogenomic testing, optimal sequencing of treatments based on patient and family characteristics, remaining uncertainties around discontinuation of treatment, and strategies for preventing relapse.

Moreover, participants discussed how various factors—including age, severity of symptoms, functional impairment, and family demographics— influence these treatment considerations. For instance, participants emphasized that the severity of anxiety symptoms and functional impairment should be assessed to inform decisions regarding the initiation of treatment, such as whether to start treatment with computerized CBT, face-to-face CBT, medication, a combination of CBT and medication, or some

other modality. Also, participants stressed the importance of considering sociocultural factors, and using assessment tools and interventions that are culturally and linguistically appropriate.

Lastly, participants discussed the outcomes that matter most to patients and families. In addition to the reduction of anxiety symptoms, participants noted the importance of various functional outcomes, including academic and social functioning, the ability to cope with challenging situations, and reaching developmental milestones. Also, participants emphasized the significance of family-based outcomes, such as family burden and work days lost.

Addressing Access to Care, Including Format and Delivery of CBT

This breakout session was focused on addressing access-to-care issues for the treatment and management of childhood anxiety disorders. The session was facilitated by Dr. Carly Parry, Senior Advisor for the Healthcare Delivery and Disparities Research Program at PCORI. Dr. Parry began the conversation by asking how access to care—or lack thereof—impacts the issues faced by patients, families, and clinicians in treating and managing childhood anxiety disorders.

In response, participants noted that childhood anxiety disorders are significantly under-identified, and that numerous challenges remain around early identification and screening for these disorders in primary care settings. Also, participants discussed how a lack of access to non-technical, high-quality information about childhood anxiety disorders exacerbates the uncertainties faced by patients and families, and that the stigma associated with mental health conditions often inhibits the identification and appropriate treatment of these disorders.

In terms of the factors that impact access to care, participants emphasized the high costs associated with CBT and the insufficient supply of trained mental healthcare providers. Several primary care providers described the challenges they face in delivering care, such as being pressed for adequate time with patients and the inability to refer patients for treatment given the insufficient supply of providers. The group also discussed various strategies for improving access to and delivery of care. In particular, participants described how non-mental-health specialists, such as teachers, school nurses, and community health workers, can be trained to provide CBT and refer patients to mental healthcare specialists when necessary. The importance of leveraging community resources and expanding the delivery of care into schools and other community-based settings was also emphasized. As in the other breakout session, participants in this session noted the need to consider sociocultural factors when designing and implementing assessment tools and interventions for youth with anxiety disorders.

Furthermore, participants discussed the evidence base for digital applications of CBT, and the need to include some face-to-face involvement of a provider in addition to the digital components. The group also underscored the need to consider complementary and alternative interventions, such as yoga, mindfulness, and other self-help strategies, particularly when access to CBT is significantly limited. Finally, participants explained how the level of care should be tiered based on various factors, including the patient's age, severity of symptoms, and functional impairment, as well as family preferences and the mode of care delivery.

As in the other breakout session, participants in this session also discussed the outcomes that are of greatest interest to patients and their families. Participants noted the importance of measuring various functional and family-based outcomes. Additionally, participants described the need to measure

provider competence and fidelity to treatment models, process and utilization outcomes, and family engagement and satisfaction with care.

Report Back Session

After the breakout sessions and lunch break, the workshop participants reconvened to review the key points and themes discussed in each session, and to further refine the research areas for PCORI to consider for future funding announcements. Dr. Evelyn Whitlock and Dr. Kristin Carman facilitated this final discussion session by highlighting the important areas of research and outcomes that were discussed in each breakout session.

First, Dr. Whitlock presented an overview of the key points that were discussed in the breakout session on stepped therapy. She reviewed the major research areas that emerged in this session, which included: population-based prevention strategies, screening for early identification, appropriate treatment choices and sequences of care, strategies for discontinuation of treatment, and approaches to prevent relapse. Additionally, Dr. Whitlock reviewed the outcomes that participants described as being most important for patients and families, which included: the patient's anxiety symptoms, academic and social functioning, and ability to reach developmental milestones and cope with difficult situations, as well as the family's burden and distress.

Dr. Kristin Carman then presented an overview of the research areas and outcomes that were discussed in the breakout session on addressing access to care. This overview revealed that several of the research areas discussed in the session on addressing access to care overlapped with those discussed in the session on stepped therapy. In particular, the numerous barriers to accessing evidence-based treatments, as well as strategies for improving access to and delivery of care, were discussed in both sessions. The issues regarding insufficient identification of childhood anxiety disorders, and approaches for improving early identification, were also discussed in both sessions. Furthermore, participants emphasized the importance of considering various contextual and cultural factors when designing and choosing assessment tools, interventions, and models of care delivery.

The breakout session overviews by Drs. Whitlock and Carman also revealed significant overlap in the patient-centered and family outcomes that were discussed in each session. For example, the importance of measuring age- and developmentally-appropriate functional outcomes, in addition to anxiety symptoms, was underscored in both sessions. After presenting these overviews, Drs. Whitlock and Carman then invited participants to further elaborate on the critical research areas and additional outcomes that PCORI should consider for future funding announcements. Participants discussed measures of intervention feasibility and acceptability, family engagement and satisfaction with care, provider competence and fidelity to treatment models, provider workflow, and healthcare service utilization rates. Lastly, participants and PCORI staff discussed existing models of care for childhood anxiety disorders and other mental health conditions that may warrant additional research, as well as the potential for unintended harms and consequences associated with various interventions and models of care.

Next Steps

PCORI program staff will work to conduct further analyses and refinement of the research areas that were emphasized by workshop participants. These prioritized research areas and deliberations from the workshop will also be shared with PCORI leadership and PCORI governance to determine the next steps for funding patient-centered CER that would increase the evidence base for the treatment and management of childhood anxiety disorders.

¹ Bennett, S. & Walkup, J.T. (2016). Anxiety Disorders in Children and Adolescents: Epidemiology, Pathogenesis, Clinical Manifestations, and Course. *UpToDate*. Accessed on March 15, 2017.

² Anxiety in Children, Draft Comparative Effectiveness Review. (2017). Prepared for: Agency for Healthcare Research and Quality.

³ James, A.C., James G., Cowdrey, F.A., Soler A., & Choke, A. (2015). Cognitive Behavioural Therapy for Anxiety Disorders in Children and Adolescents. *Cochrane Database of Systematic Reviews*. Issue 2, Art. No.: CD004690.

⁴ Glazier, K., Puliafico, A., Na, P., & Rynn, M. (2015). Pharmacotherapy for Anxiety Disorders in Children and Adolescents. *UpToDate*. Accessed on March 15, 2017.

⁵ Higa-McMillan, C.K., Francis, S.E., Najarian L.R., & Chorpita, B.F. (2016). Evidence Base Update: 50 Years of Research on Treatment for Child and Adolescent Anxiety. *Journal of Clinical Child & Adolescent Psychology*, 45:2, 91-113.

⁶ Hollis, C., Falconer, C.J., Martin, J.L., Whittington, C., Stockton, S., Glazebrook, C., & Davies, E.B. (2017). Annual Research Review: Digital Health Interventions for Children and Young People with Mental Health Problems – A Systematic and Meta-Review. *Journal of Child Psychology and Psychiatry*, 58(4), 474-503.