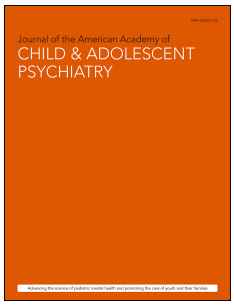

Article:
Monga, Suneeta, Desai, Riddhi, Anthony, Samantha J. et al. (27 more authors) (2023) Study Preregistration:Measuring What Matters: Development and Dissemination of a Core Outcome Set for Pediatric Anxiety Disorders Clinical Trials. Journal of the american academy of child and adolescent psychiatry. pp. 696-698. ISSN: 0890-8567

https://doi.org/10.1016/j.jaac.2023.01.016



Measuring What Matters: Development and Dissemination of a Core Outcome Set for Pediatric Anxiety Disorder Trials

Suneeta Monga, MD, FRCPC, Riddhi Desai, MSc, Samantha J. Anthony, PhD, MSW, Paul D. Arnold, MD, PhD, FRCPC, Alexa Bagnell, MD, FRCPC, Boris Birmaher, MD, Leslie Anne Campbell, PhD, RN, Rachel Churchill, PhD, Kristin Cleverley, PhD, CPMHN(C), Darren B. Courtney, MD, FRCPC, Gina Dimitropoulos, PhD, Sarah E. Hetrick, DPsych, Karolin R. Krause, PhD, Lidwine B. Mokkink, PhD, Scott B. Patten, MD, PhD, Megan C. Patton, HBASc, Matthew J. Prebeg, HBSc, Beth K. Potter, PhD, Erin Romanchych, PhD, Jai L. Shah, MD, FRCPC, Maureen Smith, MEd, S. Evelyn Stewart, MD, FRCPC, Peter Szatmari, MD, RSC, Andrea C. Tricco, PhD, Peter Tugwell, MD, FRCPC, John T. Walkup, MD, Vivian A. Welch, PhD, Bonnie T. Zima, MD, MPH, Nancy J. Butcher, PhD, Martin Offringa, MD, PhD

PII: S0890-8567(23)00064-3

DOI: https://doi.org/10.1016/j.jaac.2023.01.016

Reference: JAAC 4146

To appear in: *Journal of the American Academy of Child & Adolescent Psychiatry*

Received Date: 12 September 2022

Revised Date: 29 December 2022

Accepted Date: 6 January 2023

Please cite this article as: Monga S, Desai R, Anthony SJ, Arnold PD, Bagnell A, Birmaher B, Campbell LA, Churchill R, Cleverley K, Courtney DB, Dimitropoulos G, Hetrick SE, Krause KR, Mokkink LB, Patten SB, Patton MC, Prebeg MJ, Potter BK, Romanchych E, Shah JL, Smith M, Stewart SE, Szatmari P, Tricco AC, Tugwell P, Walkup JT, Welch VA, Zima BT, Butcher NJ, Offringa M, Measuring What Matters: Development and Dissemination of a Core Outcome Set for Pediatric Anxiety Disorder Trials, *Journal of the American Academy of Child & Adolescent Psychiatry* (2023), doi: https://doi.org/10.1016/j.jaac.2023.01.016.

Measuring What Matters: Development and Dissemination of a Core Outcome Set for Pediatric Anxiety Disorder Trials

RH = Measuring What Matters

Suneeta Monga, MD, FRCPC, Riddhi Desai, MSc, Samantha J. Anthony, PhD, MSW, Paul D. Arnold, MD, PhD, FRCPC, Alexa Bagnell, MD, FRCPC, Boris Birmaher, MD, Leslie Anne Campbell, PhD, RN, Rachel Churchill, PhD, Kristin Cleverley, PhD, CPMHN(C), Darren B. Courtney, MD, FRCPC, Gina Dimitropoulos, PhD, Sarah E. Hetrick, DPsych, Karolin R. Krause, PhD, Lidwine B. Mokkink, PhD, Scott B. Patten, MD, PhD, Megan C. Patton, HBASc, Matthew J. Prebeg, HBSc, Beth K. Potter, PhD, Erin Romanchych, PhD, Jai L. Shah, MD, FRCPC, Maureen Smith, MEd, S. Evelyn Stewart, MD, FRCPC, Peter Szatmari, MD, RSC, Andrea C. Tricco, PhD, Peter Tugwell, MD, FRCPC, John T. Walkup, MD, Vivian A. Welch, PhD, Bonnie T. Zima, MD, MPH, Nancy J. Butcher, PhD, Martin Offringa, MD, PhD

DEI
Supplemental Material

Accepted February 15, 2023

Drs. Monga, Anthony, Butcher, and Offringa are with the Hospital for Sick Children, and the University of Toronto, Ontario, Canada. Dr. Romanchych, Ms. Desai, Ms. Patton, and Mr. Prebeg are with the Hospital for Sick Children, Toronto, Ontario, Canada. Drs. Krause and Szatmari are with The Cundill Centre for Child and Youth Depression, Centre for Addiction and Mental Health, Toronto, Ontario, Canada. Ms. Smith is a patient partner from Ottawa, Ontario, Canada. Dr. Bagnell is with IWK Health Centre, Halifax, Nova Scotia, Canada. Dr. Campbell is with Dalhousie University, Halifax, Nova Scotia, Canada. Drs. Cleverley and Courtney are with the Centre for Addiction and Mental Health, and the University of Toronto, Toronto, Ontario, Canada. Dr. Tugwell and Dr. Potter are with the University of Ottawa, Ottawa, Ontario, Canada. Drs. Arnold, Dimitropoulos and Patten are with the University of Calgary, Calgary, Alberta, Canada. Dr. Shah is with the Douglas Mental Health University Institute, and McGill University, Montreal, Quebec, Canada. Dr. Tricco is with Unity Health Toronto, Toronto, Ontario, Canada. Dr. Stewart is with the University of British Columbia, Vancouver, British Columbia, Canada. Dr. Birmaher is with the University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, USA. Dr. Hetrick is with the University of Auckland, Auckland, New Zealand. Dr. Churchill is with the University of York, Heslington, England, United Kingdom. Dr. Mokkink is with the UMC, Virje Universiteit Amsterdam, Amsterdam, The Netherlands. Dr. Walkup is with the Ann and Robert H Lurie Children's Hospital Chicago, Chicago, Illinois, USA. Dr. Welch is with the Bruyère Research Institute, Ottawa, Ontario, Canada. Dr. Zima is with the University of California, Los Angeles (UCLA), Los Angeles, California, USA.

This trial is funded by the Canadian Institutes of Health Research (CIHR).

Diversity & Inclusion Statement: We worked to ensure sex and gender balance in the recruitment of human participants. We worked to ensure race, ethnic, and/or other types of diversity in the recruitment of human participants. We worked to ensure that the study questionnaires were prepared in an inclusive way. One or more of the authors of this paper self-identifies as a

member of one or more historically underrepresented racial and/or ethnic groups in science. One or more of the authors of this paper self-identifies as a member of one or more historically underrepresented sexual and/or gender groups in science. We actively worked to promote sex and gender balance in our author group. We actively worked to promote inclusion of historically underrepresented racial and/or ethnic groups in science in our author group. The author list of this paper includes contributors from the location and/or community where the research was conducted who participated in the data collection, design, analysis, and/or interpretation of the work.

The research was performed with permission from The Hospital for Sick Children Research Ethics Board.

This work has been prospectively registered: http://www.comet-initiative.org/Studies/Details/1701.

Author Contributions
Conceptualization: Monga, Desai, Churchill, Hetrick, Krause, Potter, Szatmari, Tugwell, Butcher, Offringa
Data curation: Monga, Desai, Hetrick, Krause, Patton, Prebeg
Formal analysis: Monga, Desai, Campbell, Cleverley, Krause, Mokkink, Patten, Patton, Prebeg, Potter, Butcher, Offringa
Funding acquisition: Monga, Desai, Anthony, Tugwell, Butcher, Offringa
Investigation: Monga, Romanchych, Offringa
Methodology: Monga, Anthony, Churchill, Cleverley, Courtney, Dimitropoulos, Hetrick, Krause, Mokkink, Potter, Smith, Szatmari, Tricco, Tugwell, Welch, Butcher, Offringa
Project administration: Monga, Desai
Resources: Monga, Arnold, Bagnell, Birmaher, Campbell, Churchill, Courtney, Dimitropoulos, Hetrick, Romanchych, Smith, Stewart, Welch, Zima
Supervision: Monga, Desai, Bagnell, Dimitropoulos, Mokkink, Patton, Prebeg, Smith, Butcher
Validation: Monga
Writing – original draft: Monga, Desai, Butcher, Offringa
Writing – review and editing: Monga, Desai, Anthony, Arnold, Bagnell, Birmaher, Campbell, Churchill, Cleverley, Courtney, Dimitropoulos, Hetrick, Krause, Mokkink, Patten, Patton, Prebeg, Potter, Romanchych, Shah, Smith, Stewart, Szatmari, Tricco, Tugwell, Walkup, Welch, Zima, Butcher, Offringa

Disclosure: Dr. Monga has reported receiving grant support from the TD Bank Financial Group Chair in Child and Adolescent Psychiatry, Canadian Institutes of Health Research (CIHR), and the Cundill Centre for Child and Youth Depression at the Centre for Addiction and Mental Health and royalties from Springer Publishing for her book, *Assessing and Treating Anxiety Disorders in Young Children*. Dr. Arnold has reported receiving grant support from the Alberta Innovates Translational Health Chair in Child and Youth Mental Health, CIHR, Canadian Foundation for Innovation, and the Alberta Children's Hospital Foundation; research support from Biohaven Pharmaceuticals; and has served as a consultant (unpaid) for Headversity. Dr. Birmaher has received research support from the National Institute of Mental Health and royalties from Random House, UpToDate, and Lippincott, Williams and Wilkins. Dr. Campbell

has reported receiving salary support from the Sobey Family Chair in Child and Adolescent Mental Health Outcomes; grant support from CIHR and Research Nova Scotia; and an honorarium for chairing the Canadian Agency for Drugs and Technologies in Health (CADTH) Health Technology Expert Review Panel. Dr. Cleverley has reported receiving grant support from the CAMH Chair in Mental Health Nursing Research, Operating Grants from CIHR, Ontario Early Research Award from Government of Ontario, and the Connaught Global Challenge Award, University of Toronto. Dr. Courtney has reported receiving grant support from CIHR and salary support from the Cundill Centre for Child and Youth Depression and Academic Scholars Award from the Department of Psychiatry at the University of Toronto. Dr. Hetrick has reported being the coordinating editor for the Cochrane Common Mental Health Disorders Group and the Principal Clinical Advisor for the Suicide Prevention Office, Ministry of Health, New Zealand. Dr. Krause has reported receiving grant support from CIHR and from AIM Youth Mental Health, as well as advising the International Alliance of Mental Health Research Funders (IAMHRF) on the adoption of common measures in mental health research and has received fees from the International Consortium for Health Outcomes Measurement (ICHOM) for acting as a research fellow. Dr. Potter has reported receiving grant support from CIHR, as well as grant support from the following matched partners for a CIHR-funded rare disease clinical trials network (see www.informrare.ca): Biomarin, Cambrooke Ajinomoto, the National Food Distribution Centre, Nutricia, Perkin Elmer, Roche, Takeda, Ultragenyx, and Vitaflo. Dr. Shah has reported receiving grant funding from CIHR, the National Institutes of Health, and SickKids Foundation as well as salary support from the Fonds de Recherche du Québec - Santé. Dr. Stewart has reported receiving grant/research support from CIHR, Social Sciences and Humanities Research Council (Canada), BC Ministry of Health COVID-19 Research Priorities Fund, BC Centre for Disease Control, University of British Columbia Faculty of Medicine (Strategic Investment Fund), British Columbia Children's Hospital, and BC Mental Health and Substance Use Services Research Institute; has served on advisory boards/DSMB / Speakers Bureau / travel expenses from the International OCD Foundation (IOCDF); has served on the advisory boards/DSMB of Anxiety Canada, Youth Development Instrument Provincial Practice and Policy Group, and British Columbia Ministry of Mental Health and Addictions; has served as consultant / honoraria from Misophonia Research Foundation and Milken Institute; has served on the editorial board of *Canadian Journal of Psychiatry* and *Annals of Clinical Psychiatry*; has reported authorship of assessment tools: Abramovitch A, Abramowitz JS, McKay D, Cham H, Anderson KS, Farrell L, Geller DA, Hanna GL, Mathieu S, McGuire JF, Rosenberg DR, Stewart SE, Storch EA, Wilhelm S. A Revision of the Obsessive-Compulsive Inventory – Child Version: The OCI-CV-R. Journal of Anxiety Disorders (accepted manuscript, January 2022). Dr. Szatmari has reported receiving grant funding from CIHR; salary support from the Centre for Addiction and Mental Health, the Department of Psychiatry at the University of Toronto, and the Hospital for Sick Children; and royalties from Guilford Press for his book *A Mind Apart: Understanding Children with Autism and Asperger Syndrome* and from Simon & Schuster Publishers for his co-authored book *Start Here: A Parent's Guide to Helping Children and Teens Through Mental Health Challenges*. Dr. Tugwell has reported receiving an honorarium as a member of an independent advisory panel for the Reformulary Group and as a member of a Safety and Monitoring Committee for a biologic for Parexel International and has reported co-chairing the OMERACT executive committee. Dr. Walkup has reported serving on the advisory board and Speaker's Bureau of the Tourette Association of America and has received royalties from Oxford Press, Guilford Press, and Wolters Kluwer. Dr. Zima has reported receiving grant/research

support from the California Mental Health Service Act, the National Institute on Drug Abuse, the Betty Moore Foundation, and the California Cannabis Bureau. Dr. Butcher has reported receiving research funding from CIHR and consulting fees from Nobias Therapeutics Inc. Drs. Anthony, Bagnell, Churchill, Dimitropoulos, Mokkink, Patten, Romanchych, Tricco, Welch, and Offringa, Mss. Desai and Patton, Mr. Prebeg, and Ms. Smith have reported no biomedical financial interests or potential conflicts of interest.

Correspondence to Suneeta Monga, MD, FRCPC, 555 University Avenue, Toronto, Ontario M5G 1X8; e-mail: suneeta.monga@sickkids.ca

INTRODUCTION:

Prevalence rates for pediatric anxiety disorders vary from 9.4% to 20.5% worldwide.[1-3] With a median age of onset of 11 years,[4,5] pediatric anxiety disorders significantly impact all aspects of a child's life, including their social, academic and family functioning.[6,7] They are chronic disorders, with significant co-morbidity, often persisting into adulthood, resulting in impairments in adult social, educational, and occupational functioning.[5-9] Although evidence supports the most commonly used psychological treatments, (e.g., cognitive behaviour therapy [CBT]), or pharmacological treatments (e.g., selective serotonin reuptake inhibitors), there are notable concerns with the research to date, which include the relatively small body of evidence, the brief follow-up time of most trials, as well as the use of many different symptom rating scales across studies to assess improvement.[6,10]

A major concern across trials in all areas of medicine is the wide variability that exists in outcome selection, measurement, analysis, and reporting.[11-14] Amongst mental health trials, there is little overlap in selected outcome measurement instruments (OMIs) measuring major concepts such as symptom severity or functioning.[15,16] Research results from one trial therefore, may be unique to the particular OMI used, or to the specific construct measured by the questionnaire or scale,[15,16] further impairing comparison of results between studies. Additionally, when it comes to measurement across pediatic anxiety disorders, capturing dimensionality across the various anxiety disorders, fluctuation of symptoms over time, as well as the longitudinal stability of symptoms are all critically important. Current heterogeneity in outcome selection and measurement across trials limits the comparison of treatment effects, evidence synthesis, and ultimately hinders the translation of research into clinical practice,[11-14,17] highlighting the need for outcome standardization and the importance of identifying one OMI for any selected outcome.[16,18,19]

Across both pediatric mental health clinical care and research, there is also growing awareness of the value of multi-informant perspectives on symptom change and the need to ensure a meaningful difference for patients beyond reporting statistically significant differences in treatment groups.[12,14,20-22] As such, patients and families are increasingly engaged in defining what is meaningful change to them and selecting what are important outcomes to measure in their care as well as in trials.[12,14,21,23]

Recognition of the need for and importance of outcome standardization in pediatric mental health disorders is evolving and there are several initiatives of importance to note. The International Consortium for Health Outcomes Measurement (ICHOM) has developed standard outcome sets for use in routine clinical treatment of various mental health conditions including anxiety, depression, obsessive compulsive disorder, and post-traumatic stress disorder in children and adolescents[24] and adults.[25] These standardized sets for routine clinical care focus on easy implementation in a variety of contexts (e.g., low-income countries); feasibility (e.g., single set of outcomes across four diagnoses); and acceptability (e.g., prioritizing OMIs that are short, widely translated, and free of charge).[26] Many widely used OMIs (e.g., Beck Anxiety Inventory), of note, were not chosen due to not meeting these criteria (e.g., costs).[27]

Importantly, the context and requirements of clinical trials are quite distinct from those of routine care. For example, academic or industry funding is typically available to support assessor training and OMI licensing, if needed; there is typically dedicated, compensated time in trials for obtaining comprehensive, sensitive outcome assessments; and clinical trial OMIs must meet specific (e.g., regulatory) requirements to ensure that the validity, reliability, and responsiveness of measurements are maximized. Amongst clinical trials in other areas of medicine, development of a Core Outcome Set (COS) has been a solution to address heterogeneity in outcome selection and measurement. A COS, as defined by the Core Outcome Measures in Effectiveness Trials Initiative (COMET), is an agreed upon, standardized minimum set of

outcomes that should be measured and reported in all trials in specific areas of health or health care, while not precluding the inclusion of other outcomes.[28,29] In other areas of medicine (e.g., rheumatology), the development of a COS has allowed for (a) increased consistency across trials; (b) maximized potential for a trial to contribute to systematic reviews of key outcomes; (c) increased measurement of outcomes important to knowledge users, including patients and their families; and (d) reduced selective outcome reporting, which can lead to biased estimates of treatment effects.[29,30] Pediatric mental health trials; however, critically lag behind.

Highlighting the growing interest among funders and regulators to establish common measures across trials, the International Alliance of Mental Health Funders[31] have begun to advocate for the use of the Revised Child and Adolescent Anxiety and Depression Scale Short Form (RCADS-25)[32] in youth anxiety and depression research they fund.[33,34] Use of this one OMI across two complex and heterogenous disorders without clarity as to what outcome it is meant to measure, its relevance and meaning to youth and families,[35] or its fitness as a trial OMI, however, does not fully address the need for a tailored and comprehensive COS for trials across the spectrum of pediatric anxiety disorders.[12,19]

OBJECTIVES

The objective of the COMPACT (Core Outcomes and Measures in Pediatric Anxiety Clinical Trials) Initiative is to develop a harmonized, evidence- and consensus-based COS that is meaningful to youth and families for use in future trials in pediatric anxiety disorders. The study will identify "what" outcomes, at a minimum, should be measured and reported in all future trials in pediatric anxiety disorders following the framework of COMET[29] and OMERACT Filter 2.1 for COS development[36] and will identify "how" endorsed outcomes should be measured by identifying fit-for-purpose OMIs (e.g., valid, reliable, responsive, and feasible) using COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) standards[37,38] and international recommendations for guiding the selection of OMIs for COS.[37-39]

METHODS

Study Design: An integrated mixed-methods design, including literature scoping review, and quantitative and qualitative consensus approaches, with a focus on meaningful engagement of youth and families as full research partners will be used. The COMPACT Initiative will follow international best-practice guidelines for developing[40,41] and reporting[42] COSs, adapted from COMET,[28,29] OMERACT[30,38,39] and COSMIN[43-46] guidance for COS development. This project is registered with COMET.[47] Important protocol amendments, if made, will be documented on Open Science Framework.[48] See Supplementary Table 1 for the Core Outcome Set-Standardised Protocol Items (COS-STAP) checklist.[41]

Process:

Step 1 - Identification and Prioritization of Outcomes: Identification of what outcomes to measure will be carried out in three phases following recommendations from the Core Outcome Set-STAndards for Development framework[29,40] as outlined below. See Figure 1 for an overview of planned steps.

Phase 1a Identification of Candidate Outcomes Through a Scoping Review: Following the COMET framework,[28,29] we will conduct a scoping review of the literature to systematically identify candidate outcomes and OMIs through a comprehensive search of electronic bibliographic databases to identify published trials in pediatric anxiety disorders in the last 10 years. Citations retrieved will be screened against prespecified inclusion/exclusion criteria by two independent reviewers with the aim to extract reported candidate outcomes and OMIs used.

Phase 1b Identification of Youth and Family Outcomes: In parallel to the scoping review, virtual workshops will be conducted through a secure virtual platform to identify outcomes important to youth with anxiety disorders' lived experience and family members of youth with anxiety disorders' lived experience. Upon appropriate Research Ethics Board approval, international recruitment of youth aged 8 to 24 years with anxiety disorders' lived experience and family members of youth 4 to 18 years with anxiety disorders' lived experience for participation in workshops will be through 1) clinical sites and 2) patient engagement partners and their networks. We will use a variety of platforms including posters, social media, and project website to ensure diverse engagement of youth and families. We will also establish a national committee of youth and family members to serve as active research partners through the entire project course and who will advise on all aspects of youth and family engagement and recruitment (e.g., informed consent, educational materials, co-facilitate youth and family workshops, attend consensus meetings, etc.).

Workshop Design: Four workshops of 8 to 10 participants each will be held separately for: 1) younger youth (8 to 12 years); 2) older youth (13 to 17 years); 3) transition-aged youth (18 to 24 years); and 4) family members, for a total of 30 to 40 participants per each of the four participant groups (120 to 160 total). Purposive sampling will be employed to ensure wide representation across participant characteristics (e.g., age, sex and gender, race), as outcomes of importance may differ across characteristics. As the aim of these workshops are to invite youth and families to identify treatment outcomes that matter to them, and not meant to assert the prevalence of preferences of outcomes in populations, we anticipate that between 20 to 40 purposively sampled participants in each group (younger youth, older youth, transition-aged youth, and family members) will result in saturation of outcomes being identified.

Our Youth and Family Advisory Committee will co-design and co-facilitate developmentally appropriate workshops for use with each group, which will include fun and engaging ice-breaker activities. As part of these workshops, we will provide education on outcomes and outcome selection in clinical research and facilitate age-appropriate discussion about outcomes that participants feel are important to select and measure.

Workshop Data Synthesis: Workshops will be transcribed verbatim and analyzed using a reflexive thematic analysis approach.[49] To authentically capture the experiences of workshop participants, a thematic approach will be conducted inductively. Transcripts will be independently coded by three reviewers, with regular analysis meetings to reach consensus. Emerging themes will be verified by research team members with professional experience (e.g., clinicians and researchers) and members of our youth and family advisory committees with lived experience with the goal of generating youth and family outcomes.

Outcomes generated through the workshops will be carried forward to an outcome synthesis meeting with our Youth and Family Advisory Committee, who will review all workshop outcomes, de-duplicate outcomes, and finalize definitions and wording of outcomes.

Phase 2 Delphi Study - Identification and Prioritization of Outcomes: In order to identify and prioritize outcomes generated from Phase 1, as recommended for COS development,[50-52] we will conduct an international, web-based Delphi Study using an iterative systematic multistage process that facilitates consensus through engagement of knowledge users inclusive of youth and family members.[36,50-53] Candidate outcomes generated from both the scoping review and workshops will be merged into one list for the Delphi and identified as coming from the scoping review, or youth and families.

Delphi Study Description: We will recruit a wide and international group of knowledge users and stakeholders, including clinicians, trialists, methodologists, and others, as a "Clinicians/Researchers Delphi Group", all of whom will help to further disseminate invitations through their expansive professional contacts, networks, and affiliations. Participants will be purposefully sampled using combined snowball sampling and purposive criterion sampling[54] to ensure adequate geographical and demographic representation.[54] Recruitment of a "Youth and Family Delphi Group" will be facilitated through clinical sites and national youth/family engagement partners. Our Youth and Family Advisory Committee will co-design educational materials for use with youth and families in preparation for Delphi participation, and will pilot-test the Delphi to ensure language and structure are youth and family-friendly.[23] Participant confidentiality will be maintained for all analyses through the course of the study.

Although there is no consensus on the number of Delphi participants required,[55] the majority of COSs developed to date have achieved samples in the 100 to 200 participant range for their Delphi studies.[56] Delphi participants will be asked to rate the importance of each outcome within the context of clinical effectiveness trials on a 9-point Likert scale with ratings 1 to 3 identifying outcome is of limited importance to measure, 4 to 6 representing moderate importance, and 7 to 9 representing critical importance.[29] Free-text boxes will allow participants to provide comments on candidate outcomes in each round. In the first round only, participants will be asked to suggest new candidate outcomes. Anonymized feedback (e.g., quantitative counts and qualitative response from textboxes) from previous rounds will be fed back to participants in subsequent rounds, allowing participants to re-consider and adjust their individual judgements in light of trends emerging within the wider group.[29] If necessary, a third round will be held to evaluate any new candidate outcomes introduced in round 1 and only rated in round 2, thereby ensuring all items are evaluated twice.

Delphi Data Analysis: Using COMET,[28,29] *a priori* decisions from each Delphi round on outcome prioritization criteria have been established: "Outcome In" occurs when $\geq$70% of participants score an outcome at 7-9 and <15% score an outcome at 1-3; while "Outcome Out" occurs when $\geq$ 70% participants score an outcome at 1-3 and <15% score an outcome at 7-9. All other results are considered to receive "No Consensus" on whether the outcome is sufficiently important to be part of a COS, or if it should be dropped from further consideration. As per COMET recommendations,[28,29] final analyses of responses will include aggregate overall group results and weighted results stratified by the two primary knowledge user groups ("clinicians/researchers" and "youth/family") to ensure equal representation via coding of responses for each self-reported knowledge user representation.

Phase 3 COS Outcome Finalization: Following best practices for COS development, an expert virtual meeting, will be held to review the Delphi findings and reach consensus on a final COS that is acceptable and feasible for use. To allow for round-table discussion we will invite a maximum of 30 participants that will include youth and families, in addition to clinicians/researchers, clinical trialists (academic and industry), and other stakeholders who can support or mandate COS use, (e.g., funders, regulators, and journal editors).

"No Consensus" outcomes (e.g., outcomes that do not reach consensus in the Delphi study) will be presented with the goal of conducting moderated round table discussion amongst meeting attendees followed by anonymous real-time voting as to "Include in COS" or "Exclude from COS. Outcomes deemed "Outcome In" or "Outcome out" will only be brought forward for discussion if attendees feel strongly that they warrant discussion at the meeting.

Meeting Data Analysis: After discussion and real-time anonymous voting during the meeting, outcomes reaching consensus for inclusion will be defined *a priori* as ≥ 70% of participants voting "Include in COS" while exclusion of outcomes will be defined as ≥ 70% of participants voting "Exclude from COS".[29] A second round of moderated round table discussion and anonymous voting will take place for outcomes that remain "No Consensus" after the first round of voting. Published pediatric COSs have typically included between 6 to 9 outcomes,[57] a benchmark for how many outcomes should be carried forward from the meeting.

Step 2 - Identification of Outcome Measurement Instruments for the COS: Identification of how to measure final selected outcomes will be carried out in three sequential phases following internationally developed and recognized standards set by COSMIN[37,44,45] as outlined below.

Phase 1 Screening of OMIs: To ensure that there are no new OMIs developed in the interim from the time of the scoping review, we will perform a rapid review for any new OMIs developed, including searching relevant measurement databases (e.g., PROMIS Pediatric Instrument Banks).[58] The large list of candidate OMIs will be reviewed against the selected core outcomes to evaluate for: (i) content validity and (ii) feasibility of use. Those that pass this screen will move forward for a more comprehensive, albeit brief psychometric evaluation in Phase 2.

Phase 2 Psychometric Appraisal of Short-listed OMIs: The focus of this phase is to systematically identify and provide an overall synthesis of the breadth and quality of evidence on the measurement properties of the short-listed candidate OMIs following internationally endorsed standard COSMIN methodology.[19,37,38] With the aim of establishing one OMI with sufficient measurement properties for each outcome in the final COS, we will complete a focused assessment of commonly used OMIs to briefly review key measurement properties (e.g., validity, reliability, and responsiveness to change) and evaluate the quality of evidence for these key measurement properties.

Phase 3 Expert Meeting to Review and Endorse OMIs: An expert virtual meeting will be held to review the findings of the quality review of candidate OMIs and reach consensus on the final OMI recommendations. To allow for round-table discussion and anonymous voting, we will invite a maximum of 30 key knowledge users, including experts in measurement science, pediatric anxiety disorders (clinicians and researchers), clinical trialists, funders and regulators through purposeful sampling and invitation. Youth and Family Advisory Committee members will also be invited to attend. Round table discussion will take place with a goal to achieve consensus as to which OMI should be used for each outcome through anonymous real-time voting. To ensure widespread involvement in the final consensus decision on the OMIs, we will also have an open, international review period of the final recommendations from the expert group posted on Open Science Framework[48] with a call for written comments thereby allowing for scientific, and youth and family community input before the OMIs are finalized and disseminated.

It is possible that specific outcomes identified in the developed final COS will either not have an OMI with sufficient measurement properties to adequately measure the outcome, or there may not be an existing OMI to measure the outcome. For example, if there are outcomes deemed critical but for which there are no valid, reliable, relevant, and feasible OMIs, these outcomes will be highlighted in the final COS report as requiring urgent development of measurement instruments.[38,57]

Step 3 – COS Dissemination:
Knowledge translational and dissemination activities will be guided in collaboration with our Youth and Family Advisory Committees and other international knowledge users through all phases of the study.

Educational materials co-developed with our Youth and Family Advisory Committee for this project, will enable us to create an open-access COS Educational Manual consisting of capacity-building educational deliverables and "best-practice" resources for use by COS developers in future pediatric mental health COS development. These resources will further advance how youth and families are engaged in pediatric mental health COS development, given the importance placed on this by the COMET Initiative.[29]

The freely and widely available COS, inclusive of outcomes and OMIs, will be hosted on the COMET database,[28] which collates and hosts all developed COSs, and which trialists and knowledge users search to find relevant COSs for their population of interest. We will raise awareness of the COS via dissemination through our advisory committee members, project partners and their networks, community stakeholders and the larger academic/scientific community via a variety of media platforms (e.g., journal papers and academic presentations, press releases, virtual webinars, social media platforms, infographics, video animations, policy briefs, web content and plain language summaries). Greater outcome standardization across future trials in pediatric anxiety disorders will ultimately enhance the development of evidence-based clinical practice guidelines.

REFERENCES

1. Bitsko RH, Claussen AH, Lichstein J, et al. Mental Health Surveillance Among Children — United States, 2013–2019. MMWR Suppl 2022; 71(Suppl-2):1-42. doi: 10.15585/mmwr.su7102a1.
2. Racine N, McArthur BA, Cooke JE, Eirich R, Zhu J, Madigan S. Global prevalence of depressive and anxiety symptoms in children and adolescents during COVID-19: a meta-analysis. *JAMA pediatrics.* 2021;175(11):1142-1150. doi: 10.1001/jamapediatrics.2021.2482
3. Mohammadi MR, Ahmadi N, Yazdi FR, et al. Prevalence, comorbidity and predictors of anxiety disorders among children and adolescents. *Asian journal of psychiatry.* 2020;53:102059. doi: 10.1016/j.janxdis.2020.102234
4. Polanczyk GV, Salum GA, Sugaya LS, Caye A, Rohde LA. Annual research review: A meta-analysis of the worldwide prevalence of mental disorders in children and adolescents. *J Psychol Psychiatry.* 2015;56(3):345-365. doi: 10.1111/jcpp.12381
5. Kessler RC, Avenevoli S, Costello EJ, et al. Prevalence, persistence, and sociodemographic correlates of DSM-IV disorders in the National Comorbidity Survey Replication Adolescent Supplement. *Arch Gen Psychiatry.* 2012;69(4):372-380. doi: 10.1001/archgenpsychiatry.2011.160
6. Walter HJ, Bukstein OG, Abright AR, et al. Clinical Practice Guideline for the Assessment and Treatment of Children and Adolescents With Anxiety Disorders. *J Am Acad Child Adolesc Psychiatry.* 2020;59(10):1107-1124. doi: 10.1016/j.jaac.2020.05.005
7. Connolly SD, Bernstein GA. Practice parameter for the assessment and treatment of children and adolescents with anxiety disorders. *J Am Acad Child Adolesc Psychiatry.* 2007;46(2):267-283. doi: 10.1097/01.chi.0000246070.23695.06
8. Copeland WE, Angold A, Shanahan L, Costello EJ. Longitudinal patterns of anxiety from childhood to adulthood: the Great Smoky Mountains Study. *J Am Acad Child Adolesc Psychiatry.* 2014;53(1):21-33. doi: 10.1016/j.jaac.2013.09.017
9. Costello EJ, Mustillo S, Erkanli A, Keeler G, Angold A. Prevalence and development of psychiatric disorders in childhood and adolescence. *Arch Gen Psychiatry.* 2003;60(8):837-844. doi: 10.1001/archpsyc.60.8.837

10. Schwartz C, Barican JL, Yung D, Zheng Y, Waddell C. Six decades of preventing and treating childhood anxiety disorders: a systematic review and meta-analysis to inform policy and practice. *Evid Based Ment Health.* 2019;22(3):103-110. doi: 10.1136/ebmental-2019-300096
11. Szatmari P, Offringa M, Butcher NJ, Monga S. Counting what counts: The case for harmonized outcomes in child and youth mental health research. *J Am Acad Child Adolesc Psychiatry.* 2019;58(7):656-658. doi: 10.1016/j.jaac.2019.02.016
12. Monga S, Offringa M, Butcher NJ, Szatmari P. From research to practice: The importance of appropriate outcome selection, measurement, and reporting in pediatric mental health research. *J Am Acad Child Adolesc Psychiatry.* 2020;59(4):497-500. doi: 10.1016/j.jaac.2019.08.468
13. Mew EJ, Monsour A, Saeed L, et al. Systematic scoping review identifies heterogeneity in outcomes measured in adolescent depression clinical trials. *J Clin Epidemiol.* 2020;126:71-79. doi: 10.1016/j.jclinepi.2020.06.013
14. Krause K, Bear H, Edbrooke-Childs J, Wolpert M. What outcomes count? Outcomes measured for adolescent depression between 2007 and 2017. *J Am Acad Child Adolesc Psychiatry.* doi: 2019;58(1):61-71. doi: 10.1016/j.jaac.2018.07.893
15. Weisz JR, Kuppens S, Ng MY, et al. What five decades of research tells us about the effects of youth psychological therapy: A multilevel meta-analysis and implications for science and practice. *Am Psychol* 2017;72(2):79-117. doi: 10.1037/a0040360
16. Fried EI. The 52 symptoms of major depression: Lack of content overlap among seven common depression scales. *J Affect Disord.* 2017;208:191-197. doi: 10.1016/j.jad.2016.10.019
17. Mayo-Wilson E, Fusco N, Li T, et al. Multiple outcomes and analyses in clinical trials create challenges for interpretation and research synthesis. *J Clin Epidemiol.* 2017;86:39-50. doi: 10.1016/j.jclinepi.2017.05.007
18. Newson JJ, Hunter D, Thiagarajan T. The heterogeneity of mental health assessment. *Front Psychiatry.* 2020;11:76. doi: 10.3389/fpsyt.2020.00076
19. Beaton DE, Maxwell LJ, Shea BJ, et al. Instrument selection using the OMERACT filter 2.1: the OMERACT methodology. *J Rheumatol.* 2019;46(8):1028-1035. doi: 10.3899/jrheum.181218
20. Monga S, Monsour A, Stallwood E, et al. Core outcome set development for adolescent major depressive disorder clinical trials: a registered report. *J Am Acad Child Adolesc Psychiatry.* 2020; 59(11):1297-1298. doi: 10.1016/j.jaac.2020.07.905
21. De Los Reyes A, Augenstein TM, Wang M, et al. The validity of the multi-informant approach to assessing child and adolescent mental health. *Psychol Bull.* 2015;141(4):858-900. doi: 10.1037/a0038498
22. The Lancet P. Measuring success: the problem with primary outcomes. *Lancet Psychiat.* 2020;7(1):1. doi: 10.1016/S2215-0366(1019)30483-30483.
23. Sherratt FC, Bagley H, Stones SR, et al. Ensuring young voices are heard in core outcome set development: international workshops with 70 children and young people. *Res Involv Engagem.* 2020;6:19. doi: 10.1186/s40900-020-00202-9
24. ICHOM Standard Set for Depression & Anxiety Working Group. *Children & Young People with Anxiety & Depression, Including OCD & PTSD Data Collection Reference Guide.* London, UK: ICHOM;2020.
25. Obbarius A, van Maasakkers L, Baer L, et al. Standardization of health outcomes assessment for depression and anxiety: recommendations from the ICHOM Depression and Anxiety Working Group. *Qual Life Res.* 2017;26(12):3211-3225. doi: 10.1007/s11136-017-1659-5
26. Krause K, Chung S, Adewuya A, et al. Measuring response to clinical care in children and young people with anxiety, depression, OCD, or PTSD: An international standard set of outcome measures. *Lancet Psychiat.* In Press.

27. Ulusoy M, Sahin NH, Erkmen H. The Beck anxiety inventory: psychometric properties. *J Cogn Psychother.* 1998;12(2):163-172.
28. COMET Initiative Website. http://www.comet-initiative.org/. Published 2019. Accessed May 10 2019.
29. Williamson PR, Altman DG, Bagley H, et al. The COMET Handbook: Version 1.0. *Trials.* 2017;18(Suppl 3):280. doi: 10.1186/s13063-017-1978-4
30. Boers M, Kirwan JR, Wells G, et al. Developing core outcome measurement sets for clinical trials: OMERACT filter 2.0. *J Clin Epidemiol.* 2014;67(7):745-753. doi: 10.1016/j.jclinepi.2013.11.01
31. International Alliance of Mental Health Funders. https://iamhrf.org/. Published 2021. Accessed March 29 2021.
32. Chorpita BF, Yim L, Moffitt C, Umemoto LA, Francis SE. Assessment of symptoms of DSM-IV anxiety and depression in children: A revised child anxiety and depression scale. *Behav Res Ther.* 2000;38(8):835-855. doi: 10.1016/s0005-7967(99)00130-8
33. Notice Announcing the National Institute of Mental Health (NIMH) Expectations for Collection of Common Data Elements. https://grants.nih.gov/grants/guide/notice-files/NOT-MH-20-067.html. Published 2020. Accessed March 29 2021.
34. Wolpert M. Funders agree first common metrics for mental health science. https://www.linkedin.com/pulse/funders-agree-first-common-metrics-mental-healthscience-wolpert. Published 2020. Accessed October 12, 2020.
35. Patalay P, Fried EI. Editorial Perspective: Prescribing measures: unintended negative consequences of mandating standardized mental health measurement. *J Child Psychol Psychiatry.* 2020;62(8):1032-1036. doi: 10.1111/jcpp.13333
36. Maxwell LJ, Beaton DE, Shea BJ, et al. Core domain set selection according to OMERACT filter 2.1: the OMERACT methodology. *J Rheumatol.* 2019;46(8):1014-1020. doi: 10.3899/jrheum.181097
37. Prinsen C, Vohra S, MR. R, et al. Guideline for selecting outcome measurement instruments for outcomes included in a Core Outcome Set. https://cosmin.nl/wp-content/uploads/COSMIN-guideline-selecting-outcome-measurement-COS.pdf. Published 2016. Accessed August 23, 2019.
38. Gorst SL, Prinsen CAC, Salcher-Konrad M, Matvienko-Sikar K, Williamson PR, Terwee CB. Methods used in the selection of instruments for outcomes included in core outcome sets have improved since the publication of the COSMIN/COMET guideline. *J Clin Epidemiol.* 2020;125:64-75. doi: 10.1016/j.jclinepi.2020.05.021
39. OMERACT Handbook. https://omeracthandbook.org/handbook. Published 2021. Accessed March 29 2021.
40. Kirkham JJ, Davis K, Altman DG, et al. Core Outcome Set-STAndards for Development: The COS-STAD recommendations. *PLoS medicine.* 2017;14(11):e1002447. doi: 10.1371/journal.pmed.1002447
41. Kirkham JJ, Gorst S, Altman DG, et al. Core Outcome Set-STAndardised Protocol items: The COS-STAP statement. *Trials.* 2019;20(1):116. doi: 10.1186/s13063-019-3230-x
42. Kirkham JJ, Gorst S, Altman DG, et al. Core outcome set–STAndards for reporting: the COS-STAR statement. *PLoS medicine.* 2016;13(10):e1002148. doi: 10.1371/journal.pmed.1002148
43. Mokkink LB, De Vet HC, Prinsen CA, et al. COSMIN risk of bias checklist for systematic reviews of patient-reported outcome measures. *Qual Life Res.* 2018;27(5):1171-1179. doi: 10.1007/s11136-017-1765-4
44. Lidwine Mokkink Orcid Page. https://orcid.org/0000-0001-6489-2827 Published 2021. Accessed March 29, 2021.
45. COSMIN Website. https://www.cosmin.nl/. Published 2021. Accessed March 29 2021.

46. Prinsen CA, Vohra S, Rose MR, et al. How to select outcome measurement instruments for outcomes included in a "Core Outcome Set"–a practical guideline. *Trials.* 2016;17(1):1-10. doi: 10.1186/s13063-016-1555-2
47. Monga S, Butcher N, Offringa M, et al. Measuring What Matters: Development and Implementation of a Core Outcome Set (COS) for Child and Adolescent Anxiety Disorders. COMET Initiative. http://www.comet-initiative.org/Studies/Details/1701. Published 2020. Accessed October 12, 2020.
48. Foster ED, Deardorff A. Open science framework (OSF). *J Med Libr Assoc.* 2017;105(2):203. doi: 10.5195/jmla.2017.88
49. Braun V, Clarke V. Using thematic analysis in psychology. *Qual Res Psychol.* 2006;3(2):77-101. doi: 10.1191/1478088706qp063oa
50. Hasson F, Keeney S, McKenna H. Research guidelines for the Delphi survey technique. *J Adv Nurs.* 2000;32(4):1008-1015. doi: 10.1046/j.1365-2648.2000.t01-1-01567.x
51. von der Gracht HA. Consensus measurement in Delphi studies. *Technol Forecast Soc Change* 2012;79(8):1525-1536. doi: 10.1016/j.techfore.2012.04.013
52. Humphrey-Murto S, Crew R, Shea B, et al. Consensus building in OMERACT: recommendations for use of the Delphi for core outcome set development. *J Rheumatol.* 2019;46(8):1041-1046. doi: 10.3899/jrheum.181094
53. Sinha IP, Smyth RL, Williamson PR. Using the Delphi technique to determine which outcomes to measure in clinical trials: recommendations for the future based on a systematic review of existing studies. *PLoS medicine.* 2011;8(1):e1000393. doi: 10.1371/journal.pmed.1000393
54. Palinkas LA, Horwitz SM, Green CA, Wisdom JP, Duan N, Hoagwood K. Purposeful sampling for qualitative data collection and analysis in mixed method implementation research. *Adm Policy Ment Health.* 2015;42(5):533-544. doi: 10.1007/s10488-013-0528-y
55. Knaapen M, Hall NJ, van der Lee JH, et al. Establishing a core outcome set for treatment of uncomplicated appendicitis in children: study protocol for an international Delphi survey. *BMJ Open.* 2019;9(5):e028861. doi: 10.1136/bmjopen-2018-028861
56. Gargon E, Gorst SL, Williamson PR. Choosing important health outcomes for comparative effectiveness research: 5th annual update to a systematic review of core outcome sets for research. *PLoS ONE.* 2019;14(12):e0225980. doi: 10.1371/journal.pone.0225980
57. Potter BK, Hutton B, Clifford TJ, et al. Establishing core outcome sets for phenylketonuria (PKU) and medium-chain Acyl-CoA dehydrogenase (MCAD) deficiency in children: study protocol for systematic reviews and Delphi surveys. *Trials.* 2017;18(1):603. doi: 10.1186/s13063-017-2327-3
58. HealthMeasures. https://www.healthmeasures.net/search-view-measures Published 2020. Accessed June 5, 2020.

Figure 1. Timeline for completion of the study.

STUDY SYNOPSIS

Introduction Summary

Pediatric anxiety disorders (AD) are prevalent disorders impacting all aspects of a child's life and functioning.[1] Although evidence supports commonly used treatments, there are notable concerns with the research to date.[2] Heterogeneity in outcome selection, measurement, analysis, and reporting is a contributing factor to the hinderance of the translation of research into clinical practice.[3]

Recognition for outcome standardization in pediatric mental health disorders is evolving and there are several initiatives of importance, including The International Consortium for Health Outcomes Measurement (ICHOM), which has developed standardized outcome sets for use in the routine clinical mental health treatment of children and adolescents.[4] Similarly, the International Alliance of Mental Health Funders[5] advocate for use of one specific outcome measurement instrument (OMI) in youth mental health research they fund.

Development of a Core Outcome Set (COS), a minimal set of outcomes that should be measured and reported in clinical trials, has been a solution in other areas of medicine to address heterogeneity in outcome selection and measurement across trials.[6] The COMPACT (Core Outcomes and Measures in Pediatric Anxiety Clinical Trials) Initiative will develop a harmonized, evidence- and consensus-based COS that is meaningful to youth and families for use in future trials in pediatric AD.

Method Summary

An integrated mixed-methods design, including literature scoping review, quantitative, and qualitative consensus approaches, with a focus on meaningful engagement of youth and families as full research

partners will be used. We will follow international best-practice guidelines for developing and reporting COSs, adapted from COMET,[6] and COSMIN[7] guidance for COS development. This project is registered with COMET.[8]

First, we will conduct a scoping review of the literature by completing a comprehensive search of electronic bibliographic databases to identify published trials in pediatric AD in the last 10 years, with the goal to systematically identify candidate outcomes and outcome measurement instruments (OMIs) used across trials to date. In parallel, virtual workshops will be conducted through a secure virtual platform to identify outcomes important to youth with anxiety disorders' lived experience aged 8 to 24 years and family members of youth aged 4 to 18 years with anxiety disorders' lived experience. We will establish a national committee of youth and family members to serve as active research partners through the entire project, who will advise on all aspects of youth and family engagement and recruitment. Workshops will be held separately for youth of different age groups and separately for family members. The aim of these workshops is to understand what treatment outcomes matter to youth and families. Our Youth and Family Advisory Committee will co-design and co-facilitate developmentally appropriate workshops for use with each group and review all workshop outcomes to finalize outcome definitions and wording.

We will then conduct an international, web-based Delphi study using an iterative systematic multistage process that facilitates consensus through engagement of knowledge users inclusive of youth and family members.[9] Candidate outcomes generated from the scoping review and workshops will be merged into one list and identified as coming from the scoping review, or youth and families. Following COMET[6] guidelines, *a priori* decisions from each Delphi round for "Outcome In" and "Outcome Out" will be established. An expert virtual meeting will be held to review Delphi findings and reach consensus on acceptable and feasible for use outcomes that will make up the final COS.

In a second step, we will identify how each outcome in the final COS is to be measured. We will perform a rapid review of relevant measurement databases to ensure no new OMIs were developed since the scoping review. The list of candidate OMIs will be reviewed against the selected core outcomes to evaluate for: (i) content validity and (ii) feasibility of use. We will identify and synthesize aspects of the quality of evidence on the measurement properties of the short-listed candidate OMIs to inform the ultimate selection of one valid, reliable, and responsive for use OMI for each outcome in the COS for future trials in pediatric AD. An expert virtual meeting will be held to review the findings of the brief quality review of candidate OMIs and reach consensus on final OMI recommendations.

Significance Summary

Knowledge translational and dissemination activities will be guided in collaboration with our Youth and Family Advisory Committee and other international knowledge users through all phases of the study. The freely and widely available COS will be hosted on the COMET database.[10] Greater outcome standardization across trials in pediatric AD will ultimately enhance the development of evidence-based clinical practice guidelines.

REFERENCES

1. Connolly SD, Bernstein GA. Practice parameter for the assessment and treatment of children and adolescents with anxiety disorders. *J Am Acad Child Adolesc Psychiatry.* 2007;46(2):267-283. https://doi.org/10.1097/01.chi.0000246070.23695.06
2. Walter HJ, Bukstein OG, Abright AR, et al. Clinical Practice Guideline for the Assessment and Treatment of Children and Adolescents With Anxiety Disorders. *J Am Acad Child Adolesc Psychiatry.* 2020;59(10):1107-1124. https://doi.org/10.1016/j.jaac.2020.05.005
3. Mayo-Wilson E, Fusco N, Li T, et al. Multiple outcomes and analyses in clinical trials create challenges for interpretation and research synthesis. *J Clin Epidemiol.* 2017;86:39-50. https://doi.org/10.1016/j.jclinepi.2017.05.007
4. ICHOM Standard Set for Depression & Anxiety Working Group. *Children & Young People with Anxiety & Depression, Including OCD & PTSD Data Collection Reference Guide.* London, UK: ICHOM;2020.
5. International Alliance of Mental Health Funders. https://iamhrf.org/. Published 2021. AccessedMarch 29 2021.
6. Williamson PR, Altman DG, Bagley H, et al. The COMET Handbook: Version 1.0. *Trials.* 2017;18(Suppl 3):280.
7. Prinsen CA, Vohra S, Rose MR, et al. How to select outcome measurement instruments for outcomes included in a "Core Outcome Set"–a practical guideline. *Trials.* 2016;17(1):1-10. https://doi.org/10.1186/s13063-016-1555-2
8. Monga S, Butcher N, Offringa M, et al. Measuring What Matters: Development and Implementation of a Core Outcome Set (COS) for Child and Adolescent Anxiety Disorders. COMET Initiative. http://www.comet-initiative.org/Studies/Details/1701. Published 2020. Accessed October 12, 2020.
9. Humphrey-Murto S, Crew R, Shea B, et al. Consensus building in OMERACT: recommendations for use of the Delphi for core outcome set development. *J Rheumatol.* 2019;46(8):1041-1046. https://doi.org/10.3899/jrheum.181094
10. COMET Initiative Website. http://www.comet-initiative.org/. Published 2019. Accessed May 10 2019.