Creating a Child Self-Report Measure of Adverse Events Related to Cancer Treatment; Providing a Voice for the Child

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36 children are diagnosed with cancer every day
40,000 children receive cancer treatment each year
60% of those children with cancer will participate in a clinical trial
Children’s Oncology Group (COG) is the national cooperative clinical trial study group for pediatric cancer
Research has turned children’s cancer from a virtually incurable disease 40 years ago to one with an overall cure rate of 78% today

www.curesearch.org
Curing cancer often requires intensive treatment which results in many side effects.

Most frequent side effects reported by children include fatigue, pain, nausea, cough, psychological symptoms.

For children enrolled on clinical trials, reporting adverse events is a federal requirement.

Ensures patient safety and provides data to patients, clinicians, sponsors, & regulators about the treatment effects.
“...any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medical treatment or procedure that may or may not be considered related to the medical treatment or procedure” (National Cancer Institute 2010)
Common Terminology Criteria for Adverse Events (CTCAE)

β NCI’s Standard lexicon for grading and reporting AE’s
β Includes 790 items
β AE’s Graded and reported by clinician; including subjective AE’s such as pain, fatigue, nausea, depression, and anxiety
β Adult studies show this approach under-reports prevalence and severity of subjective symptoms (Basch 2010)

<table>
<thead>
<tr>
<th>Gastrointestinal disorders</th>
<th>Grade</th>
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<tbody>
<tr>
<td><strong>Adverse Event</strong></td>
<td>1</td>
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<tr>
<td>Nausea</td>
<td>Loss of appetite without alteration in eating habits</td>
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Definition: A disorder characterized by a queasy sensation and/or the urge to vomit.
NCI has initiated a large multi-site 7 year study to develop and test an electronic system for capturing and summarizing subjective AE data directly from adult cancer patients – Patient Reported Outcome (PRO)-CTCAE

Study is limited the adults 21 years of age and older

Need for pediatric PRO-CTCAE instrument
Framework

Development Science (Magnusson & Cairns, 1996)

- Recognizes that cognitive, psychological, physiological and physical components involve reciprocal interactions to form a dynamic, continual process of development.

- In this framework, all the components may influence each other as well as be affected by cancer and its treatment.

- Research measurements must not only be developmentally appropriate but also, when conducting a longitudinal study, must accommodate developmental advances that occur over time.
Content Validation Study of the CTCAE for the Pediatric version of the PRO-CTCAE

- Study Aim: Perform a content validation exercise in which expert opinions are invited to identify which adverse events from NCI’s CTCAE are amendable to self-report by children or their family caregiver proxies.

- 7 COG institution sites
- Surveyed 189 clinicians – MD’s, APRN’s, RN’s
- 2 lists – each had 131 AE’s (total 262 AE’s)
- Clinicians asked to identify which AE’s (from 1 list of 131 items) could be reported by a child age 7 or older

- Funded by Alex’s Lemonade Stand Foundation
Content Validation Study of the CTCAE for the Pediatric version of the PRO-CTCAE

- Modified Delphi Approach
- Analyses of the survey data were based on reviewing agreement levels among the clinicians.
- Survey 1 – 78% response rate – 79 CTCAE terms remained
- Survey 2 – just completed – 66% response rate – CTCAE terms being selected as amenable to self-report by children, were subjective in nature, and relevant for measuring in pediatric clinical trials.
Next Steps
Submit Study Proposal

**Aim 1:** Translate subjective AEs into child-friendly terms in English and Spanish to form the PRO-CTCAE.

**Aim 2:** Conduct cognitive interviews with both children and proxies to establish, evaluate and refine the PRO-CTCAE measures (Pediatric, Adult, and Proxy) to be clear, comprehensible, and relevant for capturing AEs.

**Aim 3:** Conduct a longitudinal study to evaluate the psychometric properties of the PRO-CTCAE measures with newly diagnosed children in cancer treatment, stratified by different age ranges and cancer types.
Aim 2: Conducting Cognitive Interviews

- PRO-CTCAE questions will undergo extensive qualitative evaluation using cognitive interviews with both children and their caregivers.
- Evaluate children and their proxy’s comprehension of the questions in the PRO-CTCAE.
- Critical issues:
  - Appropriate wording of the stem of the questions for assessing subjective AE experiences.
  - The interpretation and comprehension of symptom terms (e.g., tiredness, pain, or sadness) in children of different age levels.
  - Easiest comprehensible response scale for the questions.
  - The affect of recall period on responses.
Aim 3: Evaluate the psychometric properties of the PRO-CTCAE

600 child and caregiver proxy pairs will participate from across our 8 COG sites.

Child between 7 and 20 years
- newly diagnosed with a first cancer of any type
- receiving curative therapy that includes non-biological agents
- completed at least one month of treatment but not more than two months that included chemotherapy

Caregiver proxy must be able to read and respond to questionnaires in English or Spanish.
Aim 3: Evaluate the psychometric properties of the PRO-CTCAE

- Child and proxy will be given a tablet in a private area of the clinic (not side by side) to complete the questionnaire.
- No child will respond to questions for all 79 subjective AEs; forms will be tailored by study investigators to include relevant AEs based on the child’s disease and/or treatment type.
- All children and proxies will answer the “core” AEs.
- Children will also respond to the Memorial Symptom Assessment Scale (MSAS) to allow comparison (Collins et al 2000; Collins et al 2002)
### Study Sites

<table>
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<tr>
<th>Lead Site Investigator</th>
<th>Institution</th>
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<tbody>
<tr>
<td>Justin Baker, MD, FAAP</td>
<td>St. Jude Children’s Research Hospital</td>
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<td>David Freyer, DO, MS</td>
<td>Children's Hospital Los Angeles</td>
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<tr>
<td>Steven Joffe, MD, MPH</td>
<td>Dana-Farber Cancer Institute/</td>
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<td>Boston Children's Hospital</td>
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<tr>
<td>Bryce Reeve, PhD</td>
<td>University of North Carolina/</td>
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<td>NC Cancer Hospital (UNC)</td>
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<tr>
<td>Lillian Sung, MD, PhD</td>
<td>The Hospital for Sick Children</td>
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<tr>
<td>Janice Withycombe, RN, MN, CCRP</td>
<td>Palmetto Health Children’s Hospital</td>
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As pediatric cancer clinical trials continue to advance the treatment of children with cancer, understanding the child’s toxicity experience becomes increasingly important. This will help us to:

- Compare treatment arms in relation to patient reported toxicity
- Identify developmental differences in toxicities which merit further investigation (i.e., adolescents compared to young children)
- Develop priorities for studying interventions to relieve symptom distress
This will help us to support positive life experiences that advance children along the developmental continuum to a healthy future
Thank you.

Questions?

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