Integrating the Child's Voice in Adverse Event Reporting in Oncology Trials: Cognitive Interview Findings from the Multisite Pediatric PRO-CTCAE Initiative

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AIMS

Over 60% of children with cancer in the U.S. participate in a clinical trial. Collection of adverse events (AEs) is legally mandated. Although many AEs are subjective (e.g., fatigue), the current standard for AE collection is clinician report. Our overarching goal is to design a child self-report measure of subjective AEs to inform AE reporting for the National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE). The CTCAE is the standard lexicon for grading AEs in oncology trials. This cognitive interview study evaluated children's understanding and ability to provide valid responses to the PRO-CTCAE measures to inform questionnaire refinements. More specifically, the interviews evaluated:

- What is the appropriate wording of the question stems?
- Do children at different age levels interpret symptom terms in the same way?
- What is an easily comprehensible response scale?
- How well do children understand the 7-day recall period?

METHODS

The newly-developed pediatric PRO-CTCAE (and parent-proxy version) was evaluated separately in 7-8 and 9-12 year olds, and the previously-developed adult PRO-CTCAE was evaluated in 13-15 and 16-20 year olds. Because of the length of the PRO-CTCAE item library (130 items measuring 63 AEs), multiple forms were created to reduce participant burden. Across 7 pediatric hospitals, trained interviewers conducted cognitive interviews with the child (and parent separately) after the child/parent completed the assigned PRO-CTCAE forms independently.

Examples of Pediatric PRO-CTCAE questionnaire wording changes based on cognitive interviews with children:

CTCAE v4.0 Term	Symptom Attributes (severity, frequency, interference, etc.)	Round 1 Wording	Round 2 Wording
Abdominal distention	Presence	Did you have a swollen belly?	Did you have a bigger belly than usual?
	Interference	How much did having a swollen belly keep you from doing things you usually do?	How much did having a bigger belly than usual keep you from doing the things you usually do?
Hot flashes	Frequency	How often did you feel hot for no reason?	How often did you feel hot all of a sudden (hot flashes)?
	Severity	How bad was your worst feeling hot for no reason?	How bad was your feeling hot all of a sudden (hot flashes)?
	Interference	How much did feeling hot for no reason keep you from doing things you usually do?	How much did feeling hot all of a sudden (hot flashes) keep you from doing things you usually do?
Palpitations	Frequency	How often did you have a pounding or racing heart?	How often did you have a racing heart beat?
	Severity	How bad was your worst pounding or racing heart?	How bad was your racing heart beat?
Tinnitus	Severity	How bad was the worst ringing in your ears?	How bad was the ringing or buzzing in your ears?
	Interference	How much did ringing in your ears keep you from doing things you usually do?	How much did the ringing or buzzing in your ears keep you from doing things you usually do?

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RESULTS

Ninety-six children (59% female) with cancer (and their parents) participated in Round 1 cognitive interviews. The adult PRO-CTCAE performed well in 16-20 year olds; however comprehension of some question stems (e.g., using the word "severity") and certain AE terms (e.g., anxiety) was difficult among 13-15 year olds. This finding led us to recommend the use of the pediatric PRO-CTCAE in the 13-15 year old age group. With younger age groups, problems with items from the pediatric PRO-CTCAE increased, including describing "past 7 days". Most seven year olds required the interviewer to read the questionnaire aloud. Following Round 1, the AE severity stem and 14 AE terms were revised for further evaluation in Round 2. Thirty-six children (44% female) with cancer participated in Round 2 of cognitive interviews.

CONCLUSIONS

Overall, most participants had little to no problem completing PRO-CTCAE on their own. The data from Round 2 of interviews is currently being analyzed. Next, the pediatric PRO-CTCAE will be longitudinally validated. The availability of a valid and reliable system for children to self-report symptom toxicities will enhance AE reporting and improve care for children with cancer.

Next Step: Longitudinal Validation Study

Evaluate psychometric properties and agreement among child, proxy, and clinicians

PRO-CTCAE Responsiveness Study

Time 1 (T1) Less symptomatic → Time 2 (T2) More symptomatic

(Child, Proxy, and Clinician data collected at T1 &T2)
(Children stratified by age: 7-12, 13-15, 16-20 years)

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