Global Prioritization of Survivorship Symptoms by Healthcare Providers to Inform a Standardized PRO Assessment Tool

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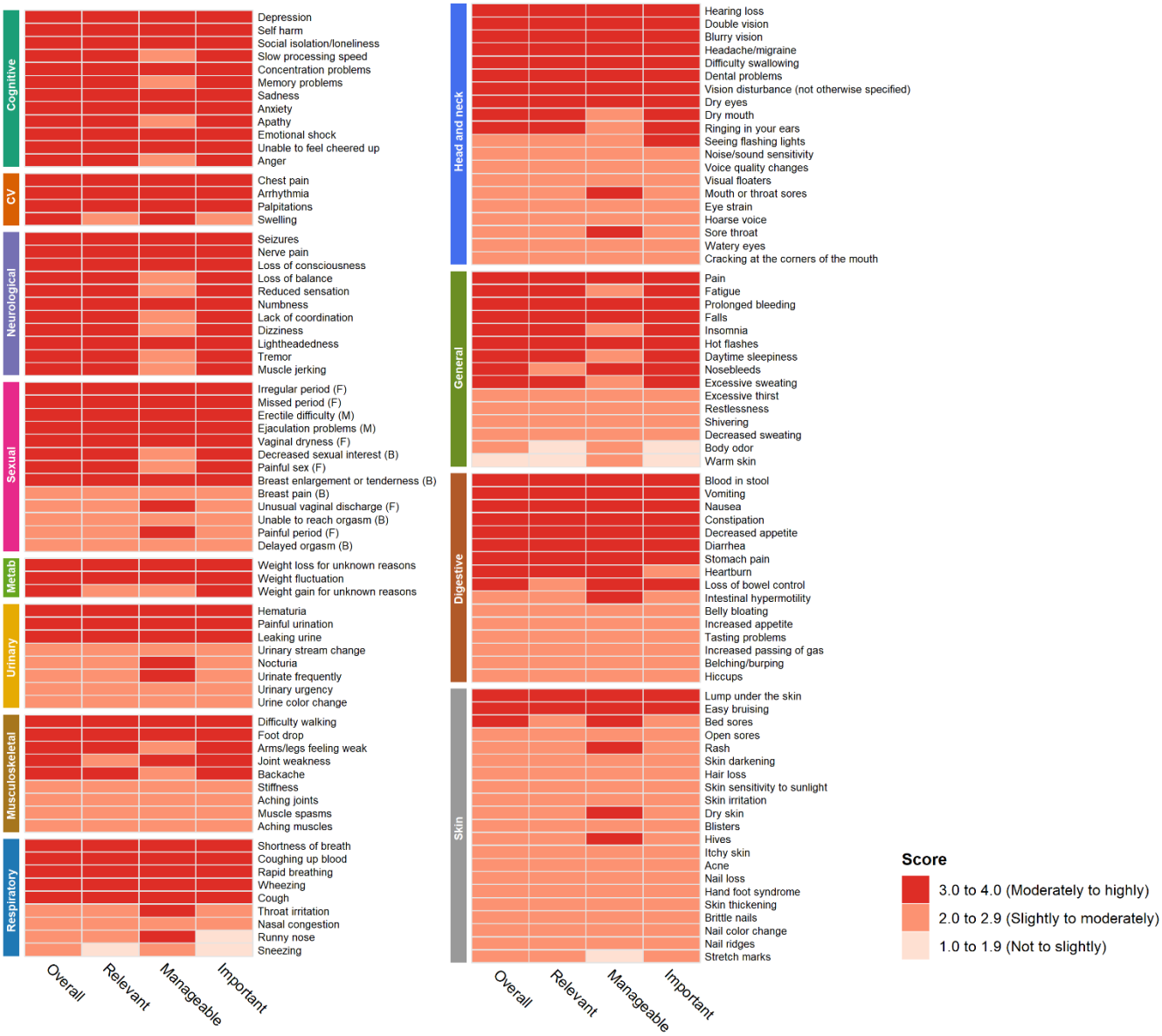
Background: We recently developed a 141-item symptom instrument, the Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events for Childhood Cancer Survivors (PRO-CTCAE-SCC). This study aims to identify survivorship-relevant, clinically-manageable, and assessment-important symptoms rated by healthcare providers across 21 countries on 4 continents to inform the global use of the PRO-CTCAE-SCC.

Methods: Participants included 232 providers involved in childhood cancer survivorship care, recruited from ISLCCC meeting attendees and the St Jude Global Alliance database. We grouped 141 symptoms into 12 domains (cardiovascular, digestive, head/neck, musculoskeletal, sexual, cognitive/psychological, respiratory, neurological, urinary, metabolic, skin, general). Two survey forms were used, each including approximately 70 items across six domains. Providers were randomly assigned to complete one form, rating each symptom across 3 dimensions (survivorship relevance, clinical manageability, assessment importance) using a 4-point ordinal scale. A dimension-specific score for each symptom was calculated as the mean of all provider responses. An overall score was derived by averaging the scores of 3 dimensions. Providers reported personal characteristics, including attained age, sex, practice type (oncologists, primary care physicians [PCPs], nurses), practice years, and practice focus (more research vs clinical care). Country-level factors from the 2019 WHO dataset included age-standardized all-cancer mortality, physician density, and out-of-pocket expenditure as a % of total health expenditure (OOP%). Associations between each symptom rating and personal and country factors were assessed using chi-square tests.

Results: The response rate was 71%. Respondents were predominantly oncologists (67%), followed by nurses (22%) and PCPs (9%). Most providers practiced in high-income countries (87%), countries with age-standardized cancer mortality >100 per 100,000 population (86%), and health systems with ≤20% OOP% (74%). Across symptoms, survivorship relevance and assessment importance dimensions received consistently higher scores than clinical manageability (see **Figure**). The highest-scoring domains were cognitive/psychological (3.4), cardiovascular (3.4), and neurological (3.4). The top-rated symptoms included depression (3.7), self-harm (3.7), and social isolation/loneliness (3.5) in cognitive/psychological domain; chest pain (3.6), arrhythmia (3.5), and palpitations (3.4) in cardiovascular domain; and seizures (3.7), nerve pain (3.6), and loss of consciousness (3.6) in neurological domain. Most symptoms were rated consistently across physician (85-94%) and country (75-86%) factors. Symptoms showing significant associations across 2-3 dimensions were uncommon (1.4-3.5% by provider and 2.1-8.5% by country factors). Cardiovascular symptoms were emphasized in higher-mortality or lower-resource settings, whereas symptoms from head/neck, musculoskeletal, and sexual domains were prioritized in lower-mortality or higher-capacity health systems ($P<0.05$).

Conclusion: Provider and country factors had limited influence on symptom prioritization across survivorship relevance, clinical manageability, and assessment importance. The largely consistent prioritization across providers, with expected context-specific variation, provides key evidence for the next phase of clinical validation of the PRO-CTCAE-SCC tool for global survivorship care.

Figure: Provider ratings across three dimensions (survivorship relevance, clinical manageability, and assessment importance) of 141 symptoms spanning 12 symptom domains



Notes:

1. CV: Cardiovascular; Metab: Metabolic; Relevant: Survivorship Relevance; Manageable: Clinical Manageability; Important: Assessment Importance.
2. The heatmap displays descriptive ratings and does not indicate statistical significance.
3. Each cell represents an individual symptom.
4. Overall represents the mean of the three dimension-specific scores for each symptom.
5. Dimension-specific scores were calculated as the mean of provider responses per symptom.
6. Symptom domains are ranked by the overall scores of all symptoms within each domain. Individual symptoms of each domain are ranked according to their overall scores.
7. Similar color intensity across symptoms indicates consistency in provider ratings.