Published in final edited form as:

Pediatr Blood Cancer. 2020 April ; 67(4): e28160. doi:10.1002/pbc.28160.

Expanding construct validity of established and new PROMIS Pediatric measures for children and adolescents receiving cancer treatment

Bryce B. Reeve¹, Molly McFatrigh¹, Jennifer W. Mack², Laura C. Pinheiro³, Shana S. Jacobs⁴, Justin N. Baker⁵, Janice S. Withycombe⁶, Li Lin¹, Courtney M. Mann¹, Katie R. Villabroza⁷, Pamela S. Hinds⁴

¹Duke University School of Medicine, Durham, North Carolina

²Dana-Farber Cancer Institute/Boston Children's Hospital, Boston, Massachusetts

³Well Cornell Medicine, New York, New York

⁴Children's National Health System, Washington, District of Columbia

⁵St. Jude Children's Research Hospital, Memphis, Tennessee

⁶Clemson University School of Nursing (formerly Emory University), Clemson, South Carolina

⁷Children's Hospital Los Angeles, Los Angeles, California

Abstract

Background: The Patient-Reported Outcomes Measurement Information System (PROMIS) Pediatric measures were designed to assess symptoms and functioning in children and adolescents. The study goal was to evaluate the validity and responsiveness of the PROMIS Pediatric measures in a diverse cohort of children with cancer.

Methods: Children (7–18 years) from nine pediatric oncology hospitals completed surveys at 72 hours preceding treatment initiation (T1) and at follow-up (T2) approximately 7 to 17 days later for chemotherapy, and 4+ weeks later for radiation. Children completed PROMIS Pediatric measures (Mobility, Pain Interference, Fatigue, Depressive Symptoms, Anxiety, Psychological Stress), Memorial Symptom Assessment Scale (MSAS), and global impressions of change (GIC) questions on their symptoms and functioning at T2 reflecting on T1. Parents completed the Lansky Play-Performance Status (PPS) scale and medication list for their child.

Results: The children ($n = 482$) were average age 12.9 years, 46% female, 60% Caucasian, and had diverse cancers and treatments. There were moderate to strong correlations between PROMIS

Correspondence: Bryce B. Reeve, Center for Health Measurement, Department of Population Health Sciences, Duke University School of Medicine, 215 Morris Street, Suite 230, Durham, NC 27701., Bryce.Reeve@Duke.edu.

DATA SHARING

A collaboration form is available upon request for those who are interested. Please email Pamela Hinds (pshinds@childrensnational.org) or Bryce Reeve (Bryce.reeve@duke.edu).

CONFLICTS OF INTEREST

All authors have no conflicts of interest to disclose.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Pediatric and MSAS, supporting convergent validity. In support for known-groups validity, the PROMIS Pediatric average scores were statistically different ($P < 0.05$) for most domains by PPS and if the child was on a medication (or not) for controlling a symptom. The PROMIS Pediatric measures were responsive over time in association with the GIC.

Conclusions: In a large, diverse sample of children and adolescents with cancer, there was strong evidence for the construct validity and responsiveness of the PROMIS Pediatric measures. This evidence supports PROMIS Pediatric measure use in pediatric oncology trials.

Keywords

function; oncology; pediatric; PROMIS; symptoms; validity

1 | INTRODUCTION

Each year in the United States, more than 16 000 children and adolescents receive a new cancer diagnosis, which has increased in incidence since 1975.^{1,2} Both cancer and its treatment have innumerable effects on health-related quality of life (HRQOL), including increased fatigue, nausea, vomiting, emotional distress, altered sleep quality, and poor social well-being and physical health.^{3–9} By measuring and understanding the scope of cancer- and treatment-related symptoms and their relationships with HRQOL domains, clinicians may adequately recognize and treat these adverse effects.

The National Institutes of Health (NIH) Patient-Reported Outcomes Measurement Information System (PROMIS) was designed to assess symptoms and functioning across a broad range of diseases and conditions and is now being used both in research and healthcare delivery settings.^{10,11} The wide-scale adoption of PROMIS measures is due to the rigorous process used to design and evaluate the measures through both qualitative and quantitative methods.^{12,13} Additionally, PROMIS is a flexible measurement system allowing investigators and clinicians to select HRQOL domains that are most relevant for their specific patient population or research question. In order to control questionnaire length, investigators can select an off-the-shelf short form in various lengths (e.g., 4-item or 8-item fatigue short form) or use the computerized-adaptive testing (CAT) approach, which tailors items to each participant based on how they answer each question.

Development of the PROMIS Pediatric measurement system used a broad range of patient populations that included children with cancer. Recently, Hinds et al examined the responsiveness of eight PROMIS Pediatric measures in a single-site cohort of 96 pediatric oncology patients between 13 and 18 years of age.¹⁴ They observed that the PROMIS Pediatric measures of depressive symptoms, fatigue, pain interference, and mobility correlated with similar items from the Symptom Distress Scale, providing support for PROMIS' convergent validity in pediatric cancer patients. Hinds et al also found evidence of responsiveness over time for all PROMIS Pediatric measures except upper extremity function.¹⁴ Hinds et al did not include the PROMIS Pediatric measure of psychological stress that is included in this study.¹⁵

It is critical that we continue to build a strong body of evidence regarding the validity of the PROMIS Pediatric measures for children and adolescents with cancer to support its use in clinical trials and healthcare delivery settings. Therefore, the goal of this study is to evaluate the construct validity of the PROMIS Pediatric measures in a much larger sample than previous studies of children and adolescents undergoing active cancer treatment.^{14,16} Additionally, we included children from a broad age range (ages 7–18 years) who were more diverse in respect of demographic characteristics, geographic location, cancer type, and treatment modality. We compared data from PROMIS Pediatric measures with other patient-reported and caregiver-reported measures, and evaluated responsiveness of the PROMIS Pediatric measures over time.

2 | METHODS

2.1 | Participants

Children and adolescents participated in this study from nine pediatric oncology hospitals. Sites included Children's Healthcare of Atlanta, Children's Hospital Los Angeles, Children's Hospital of Pittsburgh of UPMC, Children's National Health System (Washington, DC), Dana-Farber Cancer Institute/Boston Children's Hospital, Duke University (Durham, NC), the Hospital for Sick Children (Toronto, Ontario, Canada), St. Jude Children's Research Hospital (Memphis, TN), and the University of North Carolina at Chapel Hill. All sites obtained institutional review board approval. Caregivers provided written informed consent, and children/adolescents provided assent. Participants received a \$10 gift card at each time point.

Eligible children were between the ages of 7 and 18 years, had a first diagnosis of cancer of any type, and were receiving frontline cancer therapy that included chemotherapy or radiation. Patients must have completed one month of frontline treatment before participating in this study. If surgery was part of the child's treatment, then 3 to 6 weeks must have passed from the date of surgery for the child to be eligible to participate. Additionally, the child must have been able to read (or listen to) and understand English, and have no clinically significant cognitive or memory impairment based on the judgment of the site investigator. Finally, the eligible child's caregiver must have agreed to participate in the study.

2.2 | Study design

Children and their caregivers completed questionnaires at two time points. The window of time between the first (T1) and second time point (T2) was selected to allow flexibility for various treatment schedules. The goal was to capture symptom burden and functional impact at distinct points along the cancer care continuum. One time point represented a point when the child was experiencing relatively low symptom burden and higher functional performance (at T1) and another point was when the child was experiencing relatively high symptom burden and functional limitations (at T2). Generally, for patients receiving chemotherapy, T1 was collected within 72 hours of beginning a chemotherapy cycle, and T2 was collected 7 to 17 days later. For patients receiving radiation therapy, T1 was collected

within 72 hours of starting the first day of radiation therapy and T2 was collected approximately 4+ weeks later.

Questionnaires were completed on tablet computers during healthcare visits. A study team member was present to assist both the child and the caregiver, and to ensure that the child and caregiver did not influence each other's answers on the questionnaires. This included reading the questions to the child if the child did not feel comfortable on their own. If the child and caregiver were not in clinic for their T2 assessment, electronic survey links were sent to the caregiver requesting that the caregiver and child complete the survey electronically. Approximately 14% of participants completed surveys from home at T2.

2.3 | Measures

Patient-Reported Outcomes Measurement Information System®: The PROMIS® Pediatric measures were administered using CAT and included measures of physical function-mobility,¹⁷ pain interference,¹⁸ fatigue,¹⁹ depressive symptoms,²⁰ anxiety,²⁰ and psychological stress experiences.^{15,21} Psychological stress is a relatively new PROMIS Pediatric measure and reflects feeling overwhelmed, perceived lack of control of capacity to manage one's life, and cognitive-perceptual disruption.^{15,21}

The CAT was set so that a child would answer five to six questions per domain based on the standard error of measurement. If the computer network was down or the participant preferred paper, static eight-item short forms were used. A previous study in children with juvenile arthritis found equivalence between the PROMIS Pediatric CAT and short forms.²² Each question's recall period was "the past 7 days," and the questions had five response categories. The PROMIS Pediatric scores were on a T-score metric with mean of 50 (standard deviation of 10) in the original calibration sample.^{15,17-21} Higher scores for symptom domains represented worse symptom experiences and for functioning domains represented better functioning. A difference or change score of three points on the PROMIS Pediatric scale was considered a minimally important difference (MID).²³

Memorial Symptom Assessment Scale (MSAS 7-12; MSAS 10-18): The MSAS 7-12 was completed by children in our study between 7 and 12 years of age.²⁴ It assessed eight symptoms with eight questions plus additional conditional questions if they reported having a symptom. For this study, the recall period was "the past week." The MSAS 10-18 was completed by adolescents in our study between 13 and 18 years of age.²⁵ It assessed 31 symptoms with 31 questions plus additional conditional questions if they reported having a symptom. The recall period was "the past week." Both the MSAS 7-12 and MSAS 10-18 asked about symptom frequency, severity, and/or bother/distress. Following scoring algorithms provided by the developer of the adult MSAS,²⁶ three summary measures were derived that incorporated symptom attributes of frequency, severity, and distress. The global distress index (GDI) assessed overall symptom distress for included physical and psychological symptoms. The physical symptom subscale (PHYS) included 15 common physical symptoms and the psychological symptom subscale (PSYCH) included six prevalent psychological symptoms. For convergent and discriminant validity, we expect the PROMIS Pediatric measures of mobility, pain interference, and fatigue to have higher correlations with the PHYS subscale than with the PSYCH subscale, and for the PROMIS

Pediatric measures of depressive symptoms, anxiety, and psychological stress to have higher correlations with the PSYCH subscale than with the PHYS subscale.

Lansky Play-Performance Scale²⁷ (PPS): This 11-point performance status tool was completed by caregivers. For the purposes of this study, we presented ranges from 10 (“No play, does not get out of bed”) to 100 (“Fully active, normal”), but did not present 0 (“unresponsive”) to caregivers. Following PPS recommendations,²⁷ we categorized performance status as “severe to moderate restriction” (PPS 10–40), “moderate to mild restriction” (PPS 50–70), and “normal activity” (PS 80–100). For known-groups validity, we expect all PROMIS Pediatric measures to reflect poorer scores for children with worsened restrictions in performance, but expected larger mean differences for PROMIS Pediatric measures of mobility, pain interference, and fatigue as the PPS focuses mostly on play activity.

Medications: Caregivers completed questions about the types of medications their child had taken in “the past 7 days” for specific symptoms. We asked about medications for insomnia, pain, mucositis, neuropathy, headache, depression, and anxiety. For known-groups validity, we expect children who took medications for symptom control will report poorer symptoms and functioning for conceptually related domains on the PROMIS Pediatric measures. For example, we would expect children receiving medications for neuropathy would self-report worse PROMIS Pediatric mobility and pain interference scores than children not taking medications for neuropathy.

Global Impressions of Change (GIC): At T2 only, children completed seven GIC questions. The questions asked children to rate changes in their health “compared to the last time you completed this survey.” Questions asked about overall health, pain, fatigue, anxiety, depression, stress, and mobility on a five-point scale ranging from “much better now,” “a little better now,” “the same now,” “a little worse,” and “much worse now.” For sample size purposes, we created a three-level variable collapsing the two “better” categories together and the two “worse” categories together. The GIC has been used previously to assess responsiveness of patient-reported outcome (PRO) measures in children.²⁸ For responsiveness, we expect poorer PROMIS Pediatric scores for children in the “worse now” categories than the “better now” categories.

2.4 | Analyses

We assessed three aspects of construct validity. The first was convergent and discriminant validity, which examined the extent to which PROMIS Pediatric measures correlated with the MSAS symptom measures for symptoms in common (e.g., fatigue with fatigue) and symptoms not in common (e.g., fatigue and pain). Polyserial correlations were estimated with magnitudes classified as small (0.10–0.29), moderate (0.30–0.49), strong (0.50–0.69), and very strong (>0.70).^{29,30}

The second was known-groups validity, which examined the extent to which the PROMIS Pediatric measures differentiated among groups of children who are “known” to be different based on previous data or theory. Known-groups validity was examined for both performance status and medication use. Means and 95% confidence intervals (95% CIs) are

provided for each assessment. When the 95% CIs do not overlap, then the groups are statistically different from each other ($P < 0.05$). A three-point difference was used as a threshold for MID.²³

The third type of construct validity was responsiveness, which examined the extent that PROMIS Pediatric measures were able to show change over time in accordance with the child's GIC items. Means and 95% CIs are provided for children who self-reported their HRQOL as "better now," "same now," or "worse now." A three-point difference was used as a threshold for MID.

For cross-sectional analyses, we present results for only T2 as this is when the child was expected to be more symptomatic in response to their treatments. We also examined results at T1 to make sure findings were consistent (results available upon request). Additionally, we explored T1 and T2 results by age group (7–12, 13–15, 16–18 years) to examine differences based on developmental stages. When there are no differences by age, we present the aggregated data.

3 | RESULTS

3.1 | Patient characteristics

Five hundred eighty child-caregiver dyads were approached for study participation, 88 (15.2%) declined, and 10 (1.7%) withdrew before completing the T1 survey, for a participation rate of 83.1%. Characteristics of the 482 patients by child age group are presented in Table 1. The patient sample included a diverse balance of gender (46% female), race/ethnicity (60% Caucasian), cancer types, and treatment modalities. The average number of days between T1 and T2 for children receiving chemotherapy was 10 days (range, 7–17 days) and for children receiving radiation was 30 days (range, 26–40 days). The survey was completed on paper by 11% of children at T1 and 22% of children at T2.

3.2 | Correlations among PROMIS Pediatric domains

Table 2 presents the Pearson correlations among the six PROMIS Pediatric measures at T2 (collapsed across age groups). We saw similar patterns at T1 and when examining by age groups (7–12, 13–15, 16–18 years), although the older age group had slightly stronger correlations than the younger age groups. Psychological stress had strong associations with depressive symptoms ($r = 0.79$), anxiety ($r = 0.75$), and fatigue ($r = 0.70$).

3.3 | Convergent and discriminant validity: PROMIS Pediatric and MSAS

Table 3 provides correlations between the six PROMIS Pediatric measures and the MSAS summary measures of GDI, PHYS, and PSYCH for 13–18 year olds at T2 (correlations were consistent at T1 and for other age groups). Mobility and pain interference had the highest correlations with PHYS. Fatigue was strongly associated with all summary scales. Psychological stress, depressive symptoms, and anxiety had strong associations with GDI and PSYCH.

Supporting Information Tables S1–6 provide the correlations of the six PROMIS Pediatric measures with the ~26 symptoms assessed by MSAS at T2 by age group. PROMIS and

MSAS indicators of the same symptom had higher correlations than indicators of different symptoms. The PROMIS Psychological Stress measure was strongly associated with the MSAS items of worry, anxiety, and sadness. Additionally, the “bother” questions for MSAS showed stronger associations with the PROMIS Psychological Stress measure than the “frequency” or “severity” questions.

3.4 | Known-groups validity: PROMIS Pediatric and Lansky PPS

Table 4 provides the means and 95% CIs for the PROMIS Pediatric scores by the three categories of caregiver-reported Lansky PPS at T2 (aggregated across child age groups). Children in the “normal activity” PPS level had statistically better HRQOL scores than the other two groups for PROMIS Pediatric measures of mobility, pain interference, and fatigue. Children in the “normal activity” PPS level had statistically better HRQOL scores than the children in the “severe to moderate limitations” PPS level for PROMIS Pediatric measures of depressive symptoms and psychological stress. All statistically significant associations outlined here had mean differences that exceeded the MID of three points.

3.5 | Known-groups validity: PROMIS Pediatric and medications

Table 5 provides the means and 95% CIs for the PROMIS Pediatric scores at T2 for both children who did not and who did take medications for symptom control in the past seven days (aggregated across child age groups). Although we did not formally test all PROMIS domains versus every medication, our clinician investigators selected domains that would be expected to vary by medication use. The children who took medications were statistically significantly different from those who did not take the medications for all comparisons in Table 5 except for PROMIS anxiety and depressive symptom scores for children who took medications for anxiety. However, all mean differences exceeded the MID of three points.

3.6 | Responsiveness over time: PROMIS Pediatric and GIC

Table 6 provides the mean change scores over time for the PROMIS Pediatric measures categorized by the child’s self-report of change for specific symptoms or functioning since the last time they completed the survey (the GIC items). In Table 6, we also present the correlations between the PROMIS Pediatric change scores and the GIC items. These associations were small in magnitude. For all GIC items, the “worse now” group (comparing T2 with T1) had statistically worse PROMIS Pediatric change scores than the “better now” group. For the GIC items of mobility, pain, fatigue, and depression, the “worse now” group (comparing T2 with T1) had statistically worse PROMIS Pediatric change scores than the “same now” group. As example, for the GIC for mobility, the PROMIS Pediatric mobility score was worse by 5.10 points at T2 (compared with T1) for the “worse now” group which was statistically different from the “same now” (−0.41 points) and “better now” (2.53 points) groups.

4 | DISCUSSION

This longitudinal validation study provides critical evidence for the construct validity and responsiveness of six domains of PROMIS Pediatric measures in children and adolescents undergoing frontline cancer treatment. A strength of this study is that it includes one of the

largest pediatric oncology patient samples to evaluate the PROMIS Pediatric measures. The sample was quite diverse in terms of race/ethnicity, cancer type, treatment modality, and geographic area, which allows for greater generalizability of our findings. Additionally, we compared the PROMIS Pediatric measures both cross-sectionally and longitudinally against multiple data sources, as there is no single gold-standard HRQOL measure as a comparator. We also examined the data in narrow age bands (7–12, 13–15, 16–18 years), when possible, to ensure that patterns were consistent for both younger and older children in our study.

To date, the PROMIS Pediatric Psychological Stress measure has not been evaluated in children with cancer. However, children with cancer experience significant psychological distress during their treatments and beyond, with more than half of children reporting anxiety and depression during the early days after diagnosis.³¹ In 2015, an interdisciplinary group of psychosocial experts developed The Standards of Psychosocial Care for Children with Cancer and Their Families.^{32,33} However, these standards are not routinely integrated across institutions and significant gaps exist in the implementation of the standards. Psychological distress remains underappreciated and underreported by clinicians; thus, this domain exemplifies the need for robust child self-report measures. We found that the PROMIS Pediatric Psychological Stress measure was highly associated with depression ($r = 0.79$), anxiety ($r = 0.75$), and fatigue ($r = 0.70$). It correlated generally higher with the symptom attribute of “bother” than symptom frequency or severity (see Supporting Information Table S6), and psychological stress was higher among children with moderate to high limitations in performance status relative to children with normal performance status. Children taking medications for anxiety or depression had statistically significantly more psychological stress than children not taking such medications. However, the GIC item on stress was weakly correlated with change in PROMIS Pediatric Psychological Stress over time ($r = 0.17$) and was only statistically significant with improvements in psychological stress for the “better now” group. A limitation of this study is that the PROMIS Pediatric measures of psychological stress, depressive symptoms, and anxiety performed similarly and were highly correlated with each other; thus, we were unable to distinguish the PROMIS measures with external measures. This may reflect a common overall psychological distress experience among children under treatment for cancer.^{31,34,35} Further work should focus on differentiating these concepts in pediatric cancer settings.

The PROMIS Pediatric Fatigue measure had strong evidence of construct validity with all data sources. This is critical for pediatric oncology as children report that fatigue is both a prevalent and intense illness- and treatment-related adverse event experienced during therapy.^{36–38} The most intense fatigue scores documented to date were reported by children and adolescents during scheduled admissions for chemotherapy.^{39–42}

The PROMIS pain interference scores from T1 to T2 showed a large change when the children self-reported their pain getting worse (7.5 points), but no change for children getting better (see Table 6). This is likely due to many children at T1 being near the measure’s floor, meaning they had no pain and no pain interference; thus, there was little room to show improvement. If we only look at those children who report their pain as “much better now,” we do see a reduction in pain interference scores of 1.68 points, which is statistically different from 0.

The evidence for construct validity was consistent across the age bands of 7- to 12-year-olds, 13- to 15-year-olds, and 16- to 18-year-olds, although the older age group tended to have slightly stronger associations or group differences. The current recommended age group for PROMIS Pediatric measures is from 8 to 17 years. Our study was able to include children as young as seven years; however, they were more likely to need assistance when completing the questionnaires, such as having the questions read to them. We believe it is critically important to look for opportunities to include the younger children in research as long as we can feel confident we can get valid reports. For children less than seven or eight years, it is currently recommended to use the proxy versions of the PROMIS Pediatric measures; however, one could consider using self-report if assistance with reading was provided. The validity of this approach would need to be investigated.

The study was limited to children who spoke English and resided in the United States or Canada, and would benefit from more evaluation in other countries. This study likely does not represent the sickest pediatric oncology patients, as it only included patients receiving curative treatment with a first diagnosis of cancer, who were able to complete a 30+ minute survey. A large majority of children received chemotherapy; thus, the sample does not generalize to the larger pediatric oncology population. The associations of PROMIS Pediatric measures with the GIC were weaker than expected. Given the strong associations of PROMIS Pediatric measures with other sources within this data set and in the literature, we believe the GIC may not be a good system to judge recall of HRQOL changes over time in children. The recall period for the GIC is “Compared to the last time you completed this survey,” and this request may be difficult for younger children or children participating in multiple research studies, where it may be difficult to remember which survey we are referencing. A related limitation is that the assessment points were selected by clinicians to reflect a worsening change in HRQOL from T1 (prior to treatment) to T2 (post-treatment); however, children’s HRQOL scores appear to be equally poor at both time points as measured by PROMIS and MSAS measures.

Combined with previous literature,^{14,43–45} this study offers strong evidence for the construct validity and responsiveness of PROMIS Pediatric measures in children and adolescents with cancer.¹⁴ We believe there is sufficient evidence for use of the PROMIS Pediatric measures in clinical trials, where there are few existing PRO measures that have been as extensively evaluated as PROMIS Pediatric measures.⁴⁶ Use of PRO measures of symptoms and functioning in oncology trials has been regarded by the Food and Drug Administration as the gold standard for assessing the benefits and risks of cancer therapies, but historically child reports have been underutilized due to a lack of available robust PRO measures.⁴⁷ The PROMIS Pediatric measures offer an opportunity to elicit child voices directly so that symptom reports reflect their individual experiences, without the filter of a parent or clinician proxy. Ultimately, the use of such measures can enhance the focus on the patient experience in oncology trials.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGMENTS

We would like to especially thank the children, adolescents, and their families for participating in this study and giving us their time to help us create better measures to capture their experiences.

Funding information

Research reported in this publication was supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases under award number U19AR069522 and the NIH including the NCI under award number R01CA175759.

Abbreviations:

CAT	computerized-adaptive testing
CI	confidence interval
GDI	global distress index (MSAS)
GIC	global impressions of change
HRQOL	health-related quality of life
MID	minimally important difference
MSAS	Memorial Symptom Assessment Scale
PHYS	physical symptom subscale (MSAS)
PPS	play-performance status (Lansky)
PRO	patient-reported outcomes
PROMIS	Patient-Reported Outcomes Measurement Information System
PSYCH	psychological symptom subscale (MSAS)
T1	Time 1
T2	Time 2

REFERENCES

1. American Cancer Society. Cancer facts and figures 2019 <https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/cancer-facts-figures-2019.html>. Accessed August 23, 2019.
2. Ward E, DeSantis C, Robbins A, Kohler B, Jemal A. Childhood and adolescent cancer statistics, 2014. *CA Cancer J Clin*. 2014;64(2):83–103. 10.3322/caac.21219. [PubMed: 24488779]
3. Jones E, Isom S, Kemper KJ, McLean TW. Acupressure for chemotherapy-associated nausea and vomiting in children. *J Soc Integr Oncol*. 2008;6(4):141–145. [PubMed: 19134445]
4. Cheng KK-F. Association of plasma methotrexate, neutropenia, hepatic dysfunction, nausea/vomiting and oral mucositis in children with cancer. *Eur J Cancer Care (Engl)*. 2008;17(3):306–311. 10.1111/j.1365-2354.2007.00843.x. [PubMed: 18419635]
5. Hinds PS, Billups CA, Cao X, et al. Health-related quality of life in adolescents at the time of diagnosis with osteosarcoma or acute myeloid leukemia. *Eur J Oncol Nurs*. 2009;13(3):156–163. 10.1016/j.ejon.2008.08.003. [PubMed: 18926773]

6. Dupuis LL, Tamura RN, Kelly KM, et al. Risk factors for chemotherapy-induced nausea in pediatric patients receiving highly emetogenic chemotherapy. *Pediatr Blood Cancer*. 2019;66(4):e27584 10.1002/pbc.27584. [PubMed: 30561134]
7. Ullrich CK, Dussel V, Orellana L, et al. Self-reported fatigue in children with advanced cancer: results of the PediQUEST study: child-reported fatigue in cancer. *Cancer*. 2018;124(18):3776–3783. 10.1002/cncr.31639. [PubMed: 30291811]
8. Crabtree VM, Rach AM, Schellinger KB, Russell KM, Hammarback T, Mandrell BN. Changes in sleep and fatigue in newly treated pediatric oncology patients. *Support Care Cancer*. 2015;23(2):393–401. 10.1007/s00520-014-2356-3. [PubMed: 25112560]
9. Wolfe J, Orellana L, Ullrich C, et al. Symptoms and distress in children with advanced cancer: prospective patient-reported outcomes from the PediQUEST study. *J Clin Oncol*. 2015;33(17):1928–1935. 10.1200/JCO.2014.59.1222. [PubMed: 25918277]
10. Cella D, Yount S, Rothrock N, et al. The Patient-Reported Outcomes Measurement Information System (PROMIS): progress of an NIH roadmap cooperative group during its first two years. *Med Care*. 2007;45(5 Suppl 1):S3–S11. 10.1097/01.mlr.0000258615.42478.55.
11. Cella D, Riley W, Stone A, et al. The Patient-Reported Outcomes Measurement Information System (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005–2008. *J Clin Epidemiol*. 2010;63(11):1179–1194. 10.1016/j.jclinepi.2010.04.011. [PubMed: 20685078]
12. DeWalt DA, Rothrock N, Yount S, Stone AA. Evaluation of item candidates: the PROMIS qualitative item review. *Med Care*. 2007;45(Suppl 1):S12–S21. 10.1097/01.mlr.0000254567.79743.e2. [PubMed: 17443114]
13. Reeve BB, Hays RD, Bjorner JB, et al. Psychometric evaluation and calibration of health-related quality of life item banks: plans for the Patient-Reported Outcomes Measurement Information System (PROMIS). *Med Care*. 2007;45(5 Suppl 1):S22–S31. 10.1097/01.mlr.0000250483.85507.04. [PubMed: 17443115]
14. Hinds PS, Wang J, Cheng YI, et al. PROMIS pediatric measures validated in a longitudinal study design in pediatric oncology. *Pediatr Blood Cancer*. 2019;66(5):e27606 10.1002/pbc.27606. [PubMed: 30663254]
15. Bevans KB, Gardner W, Pajer KA, et al. Psychometric evaluation of the PROMIS pediatric psychological and physical stress experiences measures. *J Pediatr Psychol*. 2018;43(6):678–692. 10.1093/jpepsy/jsy010. [PubMed: 29490050]
16. Lai J-S, Kupst MJ, Beaumont JL, et al. Using the Patient-Reported Outcomes Measurement Information System (PROMIS) to measure symptom burden reported by patients with brain tumors. *Pediatr Blood Cancer*. 2019;66(3):e27526 10.1002/pbc.27526. [PubMed: 30426667]
17. DeWitt EM, Stucky BD, Thissen D, et al. Construction of the eight-item patient-reported outcomes measurement information system pediatric physical function scales: built using item response theory. *J Clin Epidemiol*. 2011;64(7):794–804. 10.1016/j.jclinepi.2010.10.012. [PubMed: 21292444]
18. Quinn H, Thissen D, Liu Y, et al. Using item response theory to enrich and expand the PROMIS® pediatric self report banks. *Health Qual Life Outcomes*. 2014;12(1):160 10.1186/s12955-014-0160-x. [PubMed: 25344155]
19. Lai J-S, Stucky BD, Thissen D, et al. Development and psychometric properties of the PROMIS pediatric fatigue item banks. *Qual Life Res*. 2013;22(9):2417–2427. 10.1007/s11136-013-0357-1. [PubMed: 23378106]
20. Irwin DE, Stucky B, Langer MM, et al. An item response analysis of the pediatric PROMIS anxiety and depressive symptoms scales. *Qual Life Res*. 2010;19(4):595–607. 10.1007/s11136-010-9619-3. [PubMed: 20213516]
21. Bevans KB, Gardner W, Pajer K, Riley AW, Forrest CB. Qualitative development of the PROMIS(R) pediatric stress response item banks. *J Pediatr Psychol*. 2013;38(2):173–191. 10.1093/jpepsy/jss107. [PubMed: 23124904]
22. Brandon TG, Becker BD, Bevans KB, Weiss PF. Patient-reported outcomes measurement information system tools for collecting patient-reported outcomes in children with juvenile

- arthritis. *Arthritis Care Res (Hoboken)*. 2017;69(3):393–402. 10.1002/acr.22937. [PubMed: 27159889]
23. Thissen D, Liu Y, Magnus B, et al. Estimating minimally important difference (MID) in PROMIS pediatric measures using the scale-judgment method. *Qual Life Res*. 2016;25(1):13–23. 10.1007/s11136-015-1058-8. [PubMed: 26118768]
  24. Collins JJ, Devine TD, Dick GS, et al. The measurement of symptoms in young children with cancer: the validation of the Memorial Symptom Assessment Scale in children aged 7–12. *J Pain Symptom Manage*. 2002;23(1):10–16. 10.1016/s0885-3924(01)00375-x. [PubMed: 11779663]
  25. Collins JJ, Byrnes ME, Dunkel IJ, et al. The measurement of symptoms in children with cancer. *J Pain Symptom Manage*. 2000;19(5):363–377. 10.1016/s0885-3924(00)00127-5. [PubMed: 10869877]
  26. Portenoy RK, Thaler HT, Kornblith AB, et al. The Memorial Symptom Assessment Scale: an instrument for the evaluation of symptom prevalence, characteristics and distress. *Eur J Cancer*. 1994;30A(9):1326–1336. 10.1016/0959-8049(94)90182-1. [PubMed: 7999421]
  27. Lansky SB, List MA, Lansky LL, Ritter-Sterr C, Miller DR. The measurement of performance in childhood cancer patients. *Cancer*. 1987;60(7):1651–1656. 10.1002/1097-0142(19871001)60:7<1651::aid-cnrcr2820600738>3.0.co;2-j. [PubMed: 3621134]
  28. Juniper EF, Guyatt GH, Feeny DH, Ferrie PJ, Griffith LE, Townsend M. Measuring quality of life in children with asthma. *Qual Life Res*. 1996;5(1):35–46. [PubMed: 8901365]
  29. Cohen J A power primer. *Psychol Bull*. 1992;112(1):155–159. [PubMed: 19565683]
  30. Cohen J Statistical Power Analysis for the Behavioral Sciences. 2nd ed. Hillsdale, NJ: L. Erlbaum Associates; 1988.
  31. Levine DR, Mandrell BN, Sykes A, et al. Patients' and parents' needs, attitudes, and perceptions about early palliative care integration in pediatric oncology. *JAMA Oncol*. 2017;3(9):1214–1220. 10.1001/jamaoncol.2017.0368. [PubMed: 28278329]
  32. Jones B, Currin-McCulloch J, Pelletier W, Sardi-Brown V, Brown P, Wiener L. Psychosocial standards of care for children with cancer and their families: a national survey of pediatric oncology social workers. *Soc Work Health Care*. 2018;57(4):221–249. 10.1080/00981389.2018.1441212. [PubMed: 29498614]
  33. Wiener L, Kazak AE, Noll RB, Patenaude AF, Kupst MJ. Standards for the psychosocial care of children with cancer and their families: an introduction to the special issue. *Pediatr Blood Cancer*. 2015;62(Suppl 5):S419–424. 10.1002/pbc.25675. [PubMed: 26397836]
  34. Abrams AN, Hazen EP, Penson RT. Psychosocial issues in adolescents with cancer. *Cancer Treat Rev*. 2007;33(7):622–630. 10.1016/j.ctrv.2006.12.006. [PubMed: 17434265]
  35. Compas BE, Desjardins L, Vannatta K, et al. Children and adolescents coping with cancer: self- and parent reports of coping and anxiety/depression. *Health Psychol*. 2014;33(8):853–861. 10.1037/hea0000083. [PubMed: 25068455]
  36. Hockenberry M. Fatigue in children and adolescents with cancer. *J Pediatr Oncol Nurs*. 1998;15(3):172–182. 10.1016/S1043-4542(98)90086-8. [PubMed: 9699454]
  37. Hinds PS, Quargnenti A, Bush AJ, et al. An evaluation of the impact of a self-care coping intervention on psychological and clinical outcomes in adolescents with newly diagnosed cancer. *Eur J Oncol Nurs*. 2000;4(1):6–17. 10.1054/ejon.1999.0051. [PubMed: 12849624]
  38. Hinds PS, Schum L, Srivastava DK. Is clinical relevance sometimes lost in summative scores. *West J Nurs Res*. 2002;24(4):345–353. 10.1177/01945902024004004. [PubMed: 12035909]
  39. Hockenberry MJ, Hinds PS, Barrera P, et al. Three instruments to assess fatigue in children with cancer: the child, parent and staff perspectives. *J Pain Symptom Manage*. 2003;25(4):319–328. [PubMed: 12691683]
  40. Hinds PS, Hockenberry MJ, Gattuso JS, et al. Dexamethasone alters sleep and fatigue in pediatric patients with acute lymphoblastic leukemia. *Cancer*. 2007;110(10):2321–2330. 10.1002/cncr.23039. [PubMed: 17926333]
  41. Hinds PS, Hockenberry M, Tong X, et al. Validity and reliability of a new instrument to measure cancer-related fatigue in adolescents. *J Pain Symptom Manage*. 2007;34(6):607–618. 10.1016/j.jpainsymman.2007.01.009. [PubMed: 17629669]

42. Lai J-S, Cella D, Kupst MJ, et al. Measuring fatigue for children with cancer: development and validation of the pediatric Functional Assessment of Chronic Illness Therapy-Fatigue (pedsFACIT-F). *J Pediatr Hematol Oncol*. 2007;29(7):471–479. 10.1097/MPH.0b013e318095057a. [PubMed: 17609625]
43. Hinds PS, Nuss SL, Ruccione KS, et al. PROMIS pediatric measures in pediatric oncology: valid and clinically feasible indicators of patient-reported outcomes. *Pediatr Blood Cancer*. 2013;60(3):402–408. 10.1002/pbc.24233. [PubMed: 22829446]
44. Menard JC, Hinds PS, Jacobs SS, et al. Feasibility and acceptability of the patient-reported outcomes measurement information system measures in children and adolescents in active cancer treatment and survivorship. *Cancer Nurs*. 2014;37(1):66–74. 10.1097/NCC.0b013e3182a0e23d. [PubMed: 24036439]
45. DeWalt DA, Gross HE, Gipson DS, et al. PROMIS(®) pediatric self-report scales distinguish subgroups of children within and across six common pediatric chronic health conditions. *Qual Life Res*. 2015;24(9):2195–2208. 10.1007/s11136-015-0953-3. [PubMed: 25715946]
46. Pinheiro LC, McFatrigh M, Lucas N, et al. Child and adolescent self-report symptom measurement in pediatric oncology research: a systematic literature review. *Qual Life Res*. 2018;27(2):291–319. 10.1007/s11136-017-1692-4. [PubMed: 28879501]
47. Kluetz PG, Slagle A, Papadopoulos EJ, et al. Focusing on core patient-reported outcomes in cancer clinical trials: symptomatic adverse events, physical function, and disease-related symptoms. *Clin Cancer Res*. 2016;22(7):1553–1558. 10.1158/1078-0432.CCR-15-2035. [PubMed: 26758559]

TABLE 1

Characteristics of the children and adolescents being treated for cancer by age group

	7–12 years (n = 203)	13–15 years (n = 144)	16–18 years (n = 135)	Total (n = 482)
Age (mean, SD)	9.5, 1.7	14.2, 0.8	16.9, 0.8	12.9, 3.4
Gender—female	97 (48%)	67 (47%)	56 (42%)	220 (46%)
Race				
White	141 (69%)	99 (69%)	88 (65%)	328 (68%)
Black	35 (17%)	17 (12%)	28 (21%)	80 (17%)
Asian	9 (4%)	8 (6%)	5 (4%)	22 (5%)
Other	16 (8%)	17 (12%)	13 (10%)	46 (10%)
Ethnicity—Hispanic	29 (15%)	24 (16%)	18 (14%)	71 (15%)
Cancer type				
Leukemia/lymphoma	107 (53%)	67 (47%)	89 (66%)	263 (55%)
Solid tumor	49 (24%)	52 (36%)	34 (25%)	135 (28%)
Neuro-oncology	41 (20%)	19 (13%)	11 (8%)	71 (15%)
Bone marrow transplant	4 (2%)	5 (4%)	0	9 (2%)
Treatment received				
Chemotherapy	179 (89%)	127 (89%)	130 (97%)	436 (91%)
Radiation	18 (9%)	11 (8%)	4 (3%)	33 (7%)
Bone marrow transplant	4 (2%)	5 (4%)	0	9 (2%)

Note: Each variable had a small amount of missing data (<5%), and we assume the data are missing at random.

Abbreviation: SD, standard deviation.

TABLE 2

Pearson correlations among PROMIS Pediatric measures at time 2 ($N = 421$)

	Pain interference	Mobility	Depressive symptoms	Anxiety	Fatigue
Mobility	-0.53				
Depressive symptoms	0.52	-0.36			
Anxiety	0.51	-0.35	0.74		
Fatigue	0.65	-0.59	0.64	0.61	
Psychological stress	0.54	-0.39	0.79	0.75	0.70

Note: Correlations were similar across age groups and at time 1. Magnitudes of correlation are classified as small (0.10–0.29), moderate (0.30–0.49), strong (0.50–0.69), and very strong (> 0.70).

Abbreviations: PROMIS, Patient-Reported Outcomes Measurement Information System.

TABLE 3

Pearson correlation of PROMIS Pediatric measures with the MSAS summary measures at time 2 for 13- to 18-year-olds ($N = 240$)

	Global distress index	Physical symptom subscale	Psychological symptom subscale
Mobility	−0.38	−0.46	−0.31
Pain interference	0.57	0.63	0.40
Fatigue	0.66	0.68	0.58
Depressive symptoms	0.69	0.46	0.72
Anxiety	0.69	0.45	0.72
Psychological stress	0.70	0.50	0.72

Note: Magnitudes of correlation are classified as small (0.10–0.29), moderate (0.30–0.49), strong (0.50–0.69), and very strong (>0.70). Data for children between ages 7 and 12 years are not available because they completed a much shorter MSAS 7–12 version. GDI is the average of both frequency of four psychological symptoms (feeling sad, worrying, feeling irritable, and feeling nervous), and distress of six physical symptoms (lack of appetite, lack of energy, pain, feeling drowsy, constipation, dry mouth). PHYS is the average of frequency, severity, and distress associated with 15 physical symptoms (lack of appetite, lack of energy, pain, feeling drowsy, constipation, dry mouth, nausea, vomiting, change in taste, weight loss, dizziness, cough, numbness/tingling, headache, mouth sores). PSYCH is the average of the frequency, severity, and distress associated with six psychological symptoms (worrying, feeling sad, feeling nervous, difficulty sleeping, feeling irritable, and difficulty concentrating). The correlations by age group and at time 1 were similar to the correlations presented above. Abbreviations: GDI, global distress index; MSAS, Memorial Symptom Assessment Scale; PHYS, physical symptom subscale; PSYCH, psychological symptom subscale; PROMIS, Patient-Reported Outcomes Measurement Information System.

TABLE 4

PROMIS Pediatric T-scores by parent-reported Lansky PPS at time 2

	Moderate to severe restriction PPS 10–40, <i>n</i> = 51 Mean (95% CI)	Mild to moderate restriction PPS 50–70, <i>n</i> = 184 Mean (95% CI)	Normal activity PPS 80–100, <i>n</i> = 228 Mean (95% CI)
Mobility ^{a,b}	39.92 (37.30–42.53)	42.01 (40.56–43.46)	50.41 (48.99–51.84)
Pain interference ^{a,b}	47.41 (44.51–50.30)	43.59 (42.24–44.94)	40.69 (39.52–41.85)
Fatigue ^{a,b}	49.98 (45.63–54.33)	45.31 (43.56–47.05)	39.60 (37.94–41.26)
Depressive symptoms ^a	46.41 (43.37–49.45)	43.93 (42.36–45.50)	41.38 (39.94–42.83)
Anxiety ^b	43.34 (40.29–46.40)	42.89 (41.27–44.51)	39.25 (38.01–40.49)
Psychological stress ^a	49.27 (46.41–52.14)	46.99 (45.58–48.41)	44.51 (43.16–45.86)

Note: The results are similar by age group and at time 1.

Abbreviations: CI confidence interval; PPS, play-performance status; PROMIS, Patient-Reported Outcomes Measurement Information System.

^aStatistically significant differences ($\alpha = 0.05$) between “moderate to severe restriction” and “normal activity” groups.^bStatistically significant differences ($\alpha = 0.05$) between “mild to moderate restriction” and “normal activity” groups.

TABLE 5

PROMIS Pediatric T-scores by medications taken over the past seven days at time 2

Medication taken for	PROMIS Pediatric measure	Did not take medication in past 7 days		Took medication in past 7 days	
		<i>n</i>	Mean (95% CI)	<i>n</i>	Mean (95% CI)
Insomnia	Depressive symptoms ^a	330	42.53 (41.44–43.62)	85	46.49 (43.94–49.03)
	Anxiety ^a	330	40.75 (39.70–41.80)	84	44.29 (41.84–46.74)
	Fatigue ^a	330	42.25 (40.92–43.59)	85	49.19 (46.30–52.07)
Depression	Psychological stress ^a	328	45.39 (44.39–46.39)	85	49.60 (47.36–51.84)
	Depressive symptoms ^a	377	42.74 (41.70–43.77)	37	48.71 (44.93–52.50)
	Psychological stress ^a	376	45.70 (44.77–46.64)	36	52.29 (48.73–55.85)
Anxiety	Anxiety ^a	376	40.95 (39.97–41.93)	37	46.79 (42.77–50.81)
	Anxiety	347	40.99 (39.96–42.02)	69	44.12 (41.33–46.91)
	Psychological stress ^a	346	45.69 (44.70–46.68)	69	49.34 (46.88–51.79)
Pain	Depressive symptoms	348	42.77 (41.67–43.86)	69	45.98 (43.40–48.55)
	Pain interference ^a	326	41.56 (40.67–42.46)	89	48.08 (45.90–50.27)
	Pain interference ^a	299	41.53 (40.58–42.49)	117	46.66 (44.85–48.47)
Headache	Pain interference ^a	326	41.60 (40.72–42.48)	91	47.85 (45.57–50.13)
	Pain interference ^a	342	42.29 (41.35–43.23)	74	46.23 (43.89–48.58)
	Pain interference ^a	342	45.84 (44.71–46.97)	74	41.92 (39.42–44.42)

Note: The results are similar at time 1.

Abbreviations: CI, confidence interval; PROMIS, Patient-Reported Outcomes Measurement Information System.

^aStatistically significant differences ($\alpha = 0.05$) between no medication and medication groups.

Responsiveness of PROMIS Pediatric T-scores over time by child-reported GIC for specific domains at time 2

TABLE 6

Compared with the last time you completed this survey, how would you rate your...	Corresponding PROMIS pediatric domain	Worse now		Same now		Better now		Polyserial correlation
		n	Mean (95% CI)	n	Mean (95% CI)	n	Mean (95% CI)	
Ease to walk, run, play now?	Mobility ^{a,b,c}	58	-5.10 (-7.10, -3.09)	196	-0.41 (-1.41, 0.58)	157	2.53 (1.32, 3.74)	-0.34
Pain now?	Pain interference ^{a,b}	49	7.54 (4.91, 10.17)	146	-0.61 (-1.83, 0.61)	220	-0.61 (-1.77, 0.55)	0.26
Tired feelings now?	Fatigue ^{a,b}	88	4.37 (1.88, 6.86)	152	-0.30 (-2.08, 1.48)	177	-3.12 (-4.79, -1.45)	0.25
Sad/unhappy feelings now?	Dep. symptoms ^{a,b}	39	4.41 (1.75, 7.08)	188	-1.80 (-2.99, -0.62)	186	-2.41 (-3.77, -1.06)	0.18
Worried/nervous feelings now?	Anxiety ^a	36	2.90 (-0.18, 5.99)	191	-1.16 (-2.24, -0.08)	189	-2.67 (-3.94, -1.40)	0.18
Stress now?	Psych stress ^a	40	1.54 (-0.93, 4.00)	192	-1.33 (-2.33, -0.34)	184	-2.35 (-3.60, -1.10)	0.17

Note:

^aText abbreviated for table.

Abbreviations: CI, confidence interval; GIC, Global Impressions of Change; PROMIS, Patient-Reported Outcomes Measurement Information System.

^aStatistically significant differences ($\alpha = 0.05$) between "worse now" and "better now" groups.

^bStatistically significant differences ($\alpha = 0.05$) between "worse now" and "same now" groups.

^cStatistically significant differences ($\alpha = 0.05$) between "same now" and "better now" groups.