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Symptom Screening Linked to Care Pathways for Pediatric Patients With Cancer

A Randomized Clinical Trial

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IMPORTANCE Pediatric patients with cancer commonly experience severely bothersome symptoms. The effectiveness of routine symptom screening with symptom feedback and symptom management care pathways is unknown.

OBJECTIVE To determine whether thrice-weekly symptom screening with symptom feedback and management care pathways, compared with usual care, improves overall self-reported symptom scores measured by the Symptom Screening in Pediatrics Tool (SSPedi) in pediatric patients with cancer.

DESIGN, SETTING, AND PARTICIPANTS This cluster randomized trial enrolled participants between July 2021 and August 2023 from 20 pediatric cancer centers in the US. Patients newly diagnosed with cancer aged 8 to 18 years receiving any cancer treatment were included. Twenty sites were randomized to provide symptom screening (n = 10) vs usual care (n = 10); 221 participants were enrolled at intervention sites and 224 participants at control sites. The date of final follow-up was October 18, 2023.

INTERVENTION Symptom screening included providing thrice-weekly symptom screening prompts to participants, email alerts to the health care team, and locally adapted symptom management care pathway implementation.

MAIN OUTCOMES AND MEASURES The primary outcome was self-reported total SSPedi score at week 8 (range, 0-60; higher scores indicate more bothersome). Secondary outcomes were Patient-Reported Outcomes Measurement Information System Fatigue score (mean [SD] score, 50 [10]; higher scores indicate more fatigue), Pediatric Quality of Life 3.0 Acute Cancer Module scores (range, 0-100; higher scores indicate better health), symptom documentation and interventions at week 8, and unplanned health care encounters.

RESULTS A total of 445 participants (median [range] age, 14.8 [8.1-18.9] years; 58.9% males) were enrolled. The mean (SD) 8-week SSPedi score was 7.9 (7.2) in the symptom screening group vs 11.4 (8.7) in the usual care group. Symptom screening was associated with significantly better 8-week total SSPedi scores (adjusted mean difference, -3.8 [95% CI, -6.4 to -1.2]) and less bothersome individual symptoms, with 12 of 15 symptoms being statistically significantly reduced. There was no difference in fatigue or quality of life. The mean (SD) number of emergency department visits was 0.77 (1.12) in the symptom screening group and 0.45 (0.81) in the usual care group. There were significantly more emergency department visits in the symptom screening group (rate ratio, 1.72 [95% CI, 1.03-2.87]).

CONCLUSIONS Symptom screening with symptom feedback and symptom management care pathways was associated with improved symptom scores and increased symptom-specific interventions. Future work should integrate symptom screening into routine clinical care.

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Pediatric patients with cancer experience severely bothersome symptoms.¹⁻⁸ Two approaches that may improve symptom control are routine symptom screening⁹ and clinical practice guideline-consistent care. To enable symptom screening, the Symptom Screening in Pediatrics Tool (SSPedi)¹⁰ and Supportive care Prioritization, Assessment and Recommendations for Kids (SPARK) were developed.¹¹ SSPedi is a validated self-report symptom assessment tool for patients aged 8 to 18 years receiving cancer treatments. SPARK is a web application that enables access to SSPedi, generates symptom reports, and distributes reports to the health care team. To increase guideline-consistent care, a process was developed to create and locally adapt symptom management care pathways.^{12,13}

In this cluster randomized clinical trial (RCT), the primary objective was to determine whether thrice-weekly symptom screening with symptom feedback and symptom management care pathways, compared with usual care, improves overall self-reported symptom scores in pediatric patients with cancer at 8 weeks.

Methods

This cluster RCT included patients from 20 pediatric oncology sites in the US (eTable 1 in [Supplement 2](#)). Sites were randomized to either intervention (symptom screening) or control groups. The intervention included participant prompts to complete symptom screening 3 times weekly via SPARK, provision of symptom reports to the health care team, and implementation of locally adapted care pathways for symptom management. The control group received usual care. The study was approved by The Hospital for Sick Children's research ethics board, the Western institutional review board, and institutional review boards from all participating sites. Patients and their guardians provided informed written consent and assent as appropriate. The study was registered with ClinicalTrials.gov (NCT04614662). This report follows the CONSORT reporting guideline for RCTs. The trial protocol is provided in [Supplement 1](#).

Participants

English- or Spanish-speaking pediatric patients newly diagnosed with cancer aged 8 to 18 years who were planned to undergo any chemotherapy, radiotherapy, or operation were eligible for inclusion. Participants were enrolled within 28 days after treatment initiation or cancer diagnosis, whichever occurred later. Exclusion criteria were recurrent disease, second malignancy, cognitive disability (attending lower than second grade or equivalent), or visual impairment (cannot see SPARK even with corrective lens). Cancer treatment may have begun prior to enrollment.

Procedures

Randomization

Once a site agreed that it would comply with both intervention and control group procedures, regulatory approvals were obtained and the site was randomized. Randomization was strati-

Key Points

Question Does thrice-weekly symptom screening with symptom feedback and symptom management care pathways reduce total symptom burden as measured by the Symptom Screening in Pediatrics Tool (SSPedi), compared with usual care, among pediatric patients newly diagnosed with cancer?

Findings The total 8-week SSPedi score (range, 0-60) was significantly better with symptom screening compared with usual care (7.9 vs 11.4, respectively; adjusted mean difference, -3.8).

Meaning Among pediatric patients newly diagnosed with cancer, symptom screening with symptom feedback and symptom management care pathways was associated with improved total SSPedi scores compared with usual care.

fied on 2 site characteristics split at their medians: anticipated number of eligible patients who speak English or Spanish and historical percentage of patients with private insurance. Randomization sequence was computer-generated (block size of 2: 1 intervention and 1 control) and concealed from all participants and the health care and research teams. Once 2 or 4 sites within a stratum were ready for randomization, they were randomized in the order they became ready. Randomization of sites occurred from March 26, 2021, to February 17, 2022.

Site Preparation and Patient Enrollment

Before patient enrollment could be activated at the recently randomized intervention and control sites within each stratum, intervention sites had to accomplish 2 tasks: email configuration and care pathway adaptation. First, email configuration was required because patient symptom reports were distributed to the health care team by emails generated from that institution's email domain. This approach was taken to reduce the likelihood that users would mistake the emails as spam. Configuration was accomplished in collaboration with each institution's information technology team. Second, care pathway adaptation was required; the procedures used to develop template care pathways based on clinical practice guidelines¹² and to adapt them for each intervention institution in consideration of their values, preferences, and resources have been previously described.¹³ Overall, 40.8% of template care pathway statements were adopted, 48.7% were adapted, and 6.4% were rejected across all intervention sites. eTable 2 in [Supplement 2](#) shows examples of locally adapted care pathway statements for each SSPedi symptom and eTable 3 in [Supplement 2](#) shows decisions made by individual intervention sites. The percentage of statements rejected ranged from 3.7% to 18.5% per site. The finalized care pathways were uploaded to SPARK.

Once these 2 steps were completed, the recently randomized intervention and control sites proceeded concurrently to activate their site to enrollment. Eligible participants were sequentially identified by site personnel with a goal to approach all potentially eligible patients. Those who declined to complete SSPedi and other patient-reported outcomes were asked if they would permit medical record review only. Demographic

characteristics, including sex, age, race, ethnicity, cancer diagnosis, metastatic disease, planned or received treatment (chemotherapy, radiotherapy, or surgery), inpatient at enrollment, first language, and family socioeconomic information were collected from the participant's family and medical record. Race and ethnicity were collected by parent report.

Intervention

Soon after site activation, the finalized locally adapted care pathways were widely disseminated to health care professionals and an implementation toolkit was provided to promote care pathway-consistent care. Sites could choose from the following items: training slides; materials that displayed a QR code to the local care pathways, including posters, pens, booklets, stickers, and magnets; and instruction for creating a shortcut to the local care pathways on devices or computers. These care pathways were in place before patients were enrolled and for the entire study duration.

Enrolled participants were prompted to complete symptom screening 3 times weekly via SPARK. Participants selected whether they wanted to receive reminders by text or email and whether they wanted a guardian to receive a concurrent reminder. They also chose the days and times of reminders. Participants used their own smartphone, tablet, or computer to perform symptom screening. If participants did not have a device, one was loaned to them for the study duration.

If participants reported at least 1 severely bothersome symptom (score of 3 or 4 on a scale ranging from 0-4), a symptom report containing the SSPedi symptom bar graph¹¹ was emailed to the health care team. The local health care team determined who would receive the emails and the recipient(s) could change over time for an individual participant. The report included a link to the locally adapted symptom management care pathways.

Evaluations

For both groups, patient-reported outcomes consisting of SSPedi, Patient-Reported Outcomes Measurement Information System (PROMIS) Fatigue scale, and Pediatric Quality of Life (PedsQL) 3.0 Acute Cancer Module were administered in person or remotely by site clinical research associates at baseline, week 4 (± 1 week), and week 8 (± 1 week). Symptom documentation and interventions were abstracted from the medical record using procedures we developed.¹ Abstractions were performed in duplicate by 2 independent clinical research associates. Findings were compared and disagreements were resolved by consensus. An arbitrator (L.S.) resolved cases in which consensus could not be achieved. Unplanned health care encounters were also abstracted from the medical record. At weeks 4 and 8, guardians were asked about health care visits to ensure that encounters outside the primary institution were captured.

Outcomes

The primary outcome was the 8-week self-reported total SSPedi score, which is the sum of the 15 SSPedi item scores. The total score ranges from 0 (no bothersome symptoms) to 60 (most bothersome symptoms). The recall period is "yesterday or today."

SSPedi is reliable, valid, and responsive to change in patients receiving cancer treatments aged 8 to 18 years.¹⁰ The designated 4- and 8-week SSPedi scores were obtained on the day the other patient-reported outcomes were obtained to distinguish SSPedi as an outcome rather than as part of the intervention.

Secondary outcomes were the 15 self-reported individual SSPedi symptom scores (range, 0-4), fatigue, and quality of life. Fatigue was measured using PROMIS Ped Bank v2.0-Fatigue scale (scaled to have mean [SD] score of 50 [10] against the US general population),¹⁴ where the recall period was the last 7 days. It is reliable and valid in patients with cancer aged 8 to 18 years.¹⁵ Higher scores indicate more fatigue. Quality of life was measured using the PedsQL 3.0 Acute Cancer Module, which produces 8 domain scores on a scale ranging from 0 to 100,¹⁶ where the recall period was the last 7 days. It is reliable and valid in patients with cancer aged 8 to 18 years.¹⁶ Higher scores indicate better health. All measures are validated for use in English and Spanish language.^{17,18}

Other secondary outcomes were symptom documentation, symptom interventions (prophylactic or therapeutic), and the number of unplanned health care encounters (emergency department visits, unplanned clinic visits, and unplanned hospitalizations) over the 8-week period. For documentation and interventions, the abstraction window was a 3-day period extending from 1 day before to 1 day after the 4- and 8-week assessment points. Two intervention types were evaluated. Any intervention, regardless of attribution, was abstracted from a list of potential, previously defined interventions for specific symptoms.¹ For example, acetaminophen was considered an intervention for pain even if it was administered for fever or an unknown reason and a child life specialist visit was considered an intervention for sadness, anxiety, and anger, regardless of visit reason. In contrast, a symptom-specific intervention was abstracted where the clinical documentation clearly noted that provision was for that symptom. These outcomes were specific to each of the 15 SSPedi symptoms and were binary variables (yes or no).

Statistical Analysis

The primary outcome was the 8-week total SSPedi score. We planned to enroll 444 participants to achieve 85% power assuming a minimal clinically important difference of 3, within-cluster SD of 8.8, intracluster correlation coefficient of 0.021 (all based on data from the SSPedi validation study),¹⁰ $\alpha = .05$, a baseline covariate explaining 20% of variance, and 10% missing data.

The primary analysis used the patient-level 8-week total SSPedi score as the outcome in a mixed linear regression model with a random effect for site; fixed effects for treatment assignment, patient age (8-10, 11-14, and 15-18 years), and diagnosis group (leukemia/lymphoma, solid tumor and brain tumor); and 2 binary fixed effects at the cluster level for randomization stratification variables (see [Supplement 2](#)). The treatment effect was expressed as the covariate-adjusted mean difference between the groups with the 95% CI. The *P* value was based on the difference in mean week-8 score, not a difference in mean change in score. We did not plan to adjust the model for baseline total SSPedi score because some care

pathway interventions might affect symptoms prior to enrollment and the baseline score may already reflect some benefit of the cluster's treatment assignment. However, a sensitivity analysis that adjusted for baseline total SSPedi score was performed. We also evaluated the change in score (baseline to week 8) in a fully adjusted model that included baseline as recommended to control for potential imbalance.¹⁹⁻²¹ To account for potential differential enrollment of patients only undergoing an operation (who might not be cared for by oncology teams) between intervention vs control sites, we conducted a sensitivity analysis restricted to patients who received systemic chemotherapy. An ad hoc analysis also compared baseline total SSPedi score between the groups using the fully adjusted model.

For the secondary analysis comparing 8-week individual SSPedi symptoms in which each was considered an ordinal outcome (scored 0-4), a mixed effects proportional odds model was fit with random effect for site and fixed effects for treatment assignment and the 2 stratification variables. The treatment effect was expressed as the odds ratio (OR) with the 95% CI. The secondary outcomes of 8-week PROMIS Fatigue scale and PedsQL 3.0 Acute Cancer Module domain scores were analyzed using the same approach as the primary outcome.

For comparing secondary outcomes of documentation of symptoms, any intervention, and symptom-specific intervention between groups, we fit a mixed or fixed effects logistic regression model (details in eText in [Supplement 2](#)). Treatment effects were estimated using the OR and 95% CI. We took 3 approaches to this analysis. The first compared documentation and interventions for all participants. However, symptoms might be less common in the symptom screening group if the approach was effective at reducing symptoms. Thus, we also compared documentation and interventions among participants with a symptom-specific SSPedi score greater than or equal to 1 (any degree of bother) and greater than or equal to 3 (severely bothersome). The denominators in these analyses differed by symptom.

For secondary outcomes of unplanned health care encounters, the number of events per patient was counted over the 8-week period and compared between groups using mixed effects Poisson regression analyses, with a random effect for site and fixed effects for the 2 stratification variables. Robustness of these results was checked through analogous negative binomial models (eText in [Supplement 2](#)).

We did not plan interim or subgroup analyses. If more than 10% of data were missing, we planned multiple imputation. Sensitivity analyses and approach to missing data are shown in eFigure 1 in [Supplement 2](#). The statistical analysis plan was uploaded to ClinicalTrials.gov before the analysis began. All analyses were performed using R, version 4.3.2 (R Foundation). All tests of significance were 2-sided and a *P* value < .05 was considered statistically significant.

Results

Between July 27, 2021, and August 22, 2023, a total of 687 patients were assessed for eligibility, 530 were approached, and

445 were enrolled: 221 at intervention sites and 224 at control sites. Fifteen enrolled as medical record review-only participants. **Figure 1** illustrates site randomization, enrollment, and flow through the trial. The eText in [Supplement 2](#) shows comparisons of those who agreed vs declined participation and those excluded due to physician preference. There was no significant difference in the percentage of patients who declined participation between intervention and control sites (16.6% vs 15.5%; *P* = .81). The number of missing 8-week SSPedi scores was 38 of 445 (8.5%) overall and 23 of 430 (5.3%) among nonmedical record review-only participants. The observed posterior distribution of intracluster correlation coefficient for 8-week total SSPedi scores was a median of 0.06 (95% credible interval, 0.01-0.16) and the coefficient of variation of site size was 0.61.

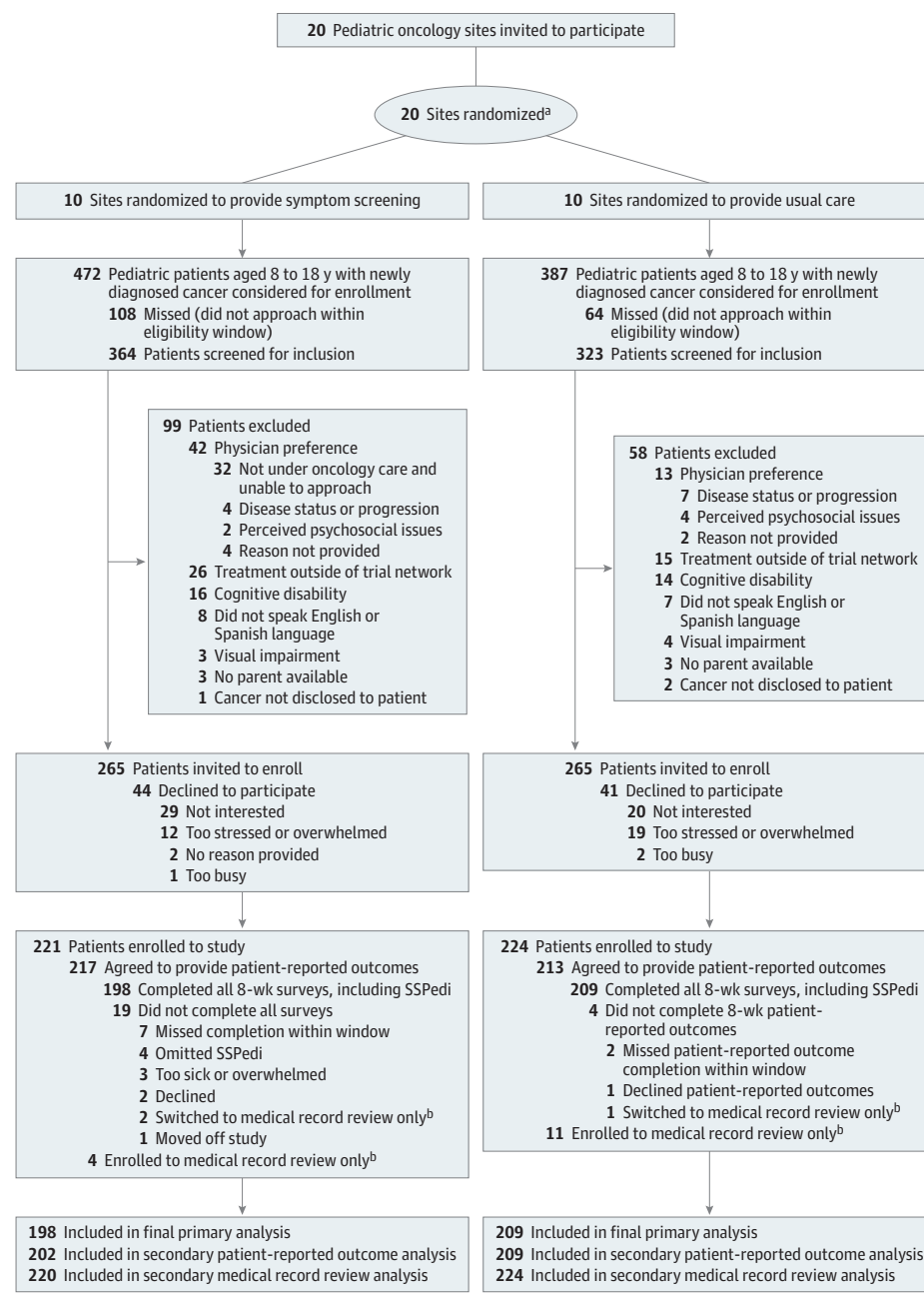
Table 1 shows baseline participant characteristics; the median (range) age was 14.8 (8.1-18.9) years and 262 participants (58.9%) were male. eTable 4 in [Supplement 2](#) shows reasons participants stopped conducting symptom screening or providing study observations. Only 1 participant did not complete the planned observations. eTable 5 in [Supplement 2](#) shows the number of participants who completed the SSPedi and other patient-reported outcomes at weeks 4 and 8. In the symptom screening group, the numbers of participants who completed the SSPedi were 216 at baseline, 208 at week 4, and 198 at week 8. In the usual care group, the numbers of participants who completed the SSPedi were 213 at baseline, 207 at week 4, and 209 at week 8.

The mean (SD) 8-week SSPedi score was 7.9 (7.2) in the symptom screening group and 11.4 (8.7) in the usual care group. **Table 2** and eTable 6 in [Supplement 2](#) show that the adjusted 8-week total SSPedi scores were significantly better in the intervention group than in the control group (adjusted mean difference, -3.8 [95% CI, -6.4 to -1.2]; *P* = .007). Sensitivity analyses did not alter these findings (eFigure 1 in [Supplement 2](#)). eTable 7 in [Supplement 2](#) shows that the baseline total SSPedi scores were significantly better in the intervention group (adjusted mean difference, -1.8 [95% CI, -3.5 to -0.1]; *P* = .04). Symptom screening improved 8-week total SSPedi scores even after inclusion of baseline SSPedi score in the model (eFigure 1 in [Supplement 2](#)). More specifically, when comparing the difference in scores from baseline between groups, symptom screening remained associated with better outcomes (mean difference, -3.0 [95% CI, -5.2 to -0.8]).

Table 2, **Figure 2**, and eTable 8, eTable 9, and eFigure 2 in [Supplement 2](#) show comparisons of individual SSPedi symptoms between groups. Symptom screening reduced the odds of higher scores for all symptoms; this reduction was statistically significant for 12 of 15 symptoms. **Table 2** also shows that there was no significant difference in PROMIS Fatigue scores between the groups. **Table 2** and eFigure 3 in [Supplement 2](#) show that all adjusted mean differences for PedsQL 3.0 Acute Cancer Module domain scores were greater than 0, although none were statistically significant.

eTables 10 and 11 in [Supplement 2](#) show results related to symptom documentation, any intervention, and symptom-specific interventions. Among the symptom screening and usual care groups, fatigue (43/220 [19.5%] vs 61/224 [27.2%])

Figure 1. Site Randomization, Enrollment, and Flow Through the Trial of Symptom Screening



and changes in hunger (22/220 [10.0%] vs 37/224 [16.5%]) were documented in the symptom screening and usual care groups. Documentation was significantly more common in the usual care group for these symptoms ($P = .04$ for fatigue and $P = .03$ for changes in hunger). Further, intervention was provided in the symptom screening and usual care group for sadness (52/220 [23.6%] vs 82/224 [36.6%]) and anxiety (54/220 [24.5%] vs 96/224 [42.9%]) but was significantly more common in the usual care group for these symptoms ($P = .05$ for sadness and $P = .01$ for anxiety).

Symptom-specific interventions (provision clearly for the symptom) were provided for pain (40 patients [18.2%] in

the symptom screening group vs 9 [4.0%] in the usual care group), peripheral neuropathy (8 patients [3.6%] in the symptom screening group), changes in hunger (10 [4.5%] in the symptom screening group), and constipation (15 [6.8%] in the symptom screening group vs 5 [2.2%] in the usual care group). Among those with any symptoms, symptom-specific interventions were provided for pain (25/73 [34.2%] vs 5/95 [5.3%]), peripheral neuropathy (6/57 [10.5%] vs 0/70), and changes in hunger (6/111 [5.4%] vs 0/130) in the symptom screening and usual care groups. Further, among those with severely bothersome symptoms, symptom-specific interventions were provided for feeling sad (4/5 [80.0%] vs 2/11 [18.2%]) and nausea

Table 1. Baseline Demographic Characteristics by Group

Characteristic	No. (%)	
	Symptom screening (n = 221)	Usual care (n = 224)
Sex		
Male	133 (60.2)	129 (57.6)
Female	88 (39.8)	95 (42.4)
Age, median (range), y	15.0 (8.1-18.9)	14.7 (8.1-18.9)
Age group, y		
8-10	33 (14.9)	37 (16.5)
11-14	77 (34.8)	85 (37.9)
15-18	111 (50.2)	102 (45.5)
Race ^a	n = 177	n = 183
American Indian or Alaska Native	2 (1.1)	4 (2.2)
Asian	13 (7.3)	7 (3.8)
Black or African American	13 (7.3)	14 (7.7)
Native Hawaiian or Other Pacific Islander	14 (7.9)	1 (0.5)
White	113 (63.8)	145 (79.2)
More than 1 race	22 (12.4)	12 (6.6)
Ethnicity	n = 208	n = 202
Hispanic or Latino	85 (40.9)	63 (31.2)
Not Hispanic or Latino	123 (59.1)	139 (68.8)
First language English or Spanish	211 (95.5)	197 (87.9)
Inpatient at enrollment	88 (39.8)	88 (39.3)
Preferred language for patient-reported outcomes		
English	203 (91.9)	201 (89.7)
Spanish	13 (5.9)	12 (5.4)
Not applicable or not available ^b	5 (2.3)	11 (4.9)
Guardian married	138 (62.4)	141 (62.9)
Guardian employed full or part time	125 (56.6)	127 (56.7)
Guardian graduated from college or higher	120 (54.3)	133 (59.4)
Annual household income ≥\$60 000	78 (35.3)	103 (46.0)
Cancer diagnosis		
Leukemia	89 (40.3)	62 (27.7)
Solid tumor	73 (33.0)	86 (38.4)
Lymphoma	50 (22.6)	61 (27.2)
Brain tumor	9 (4.1)	15 (6.7)
Metastatic disease	45 (20.4)	80 (35.7)
Cancer diagnosis to enrollment, median (IQR), d	23 (16-29)	21 (13-28)
Planned or received treatment		
Chemotherapy	210 (95.0)	207 (92.4)
Radiotherapy	20 (9.0)	18 (8.0)
Surgical procedure	23 (10.4)	36 (16.1)

^a Race and ethnicity were collected by parent report using limited categories; choosing more than 1 race was an option.

^b Preferred language for patient-reported outcomes was not applicable for participants enrolled as medical record review only and was not available for the 1 participant who withdrew from the study immediately after enrollment.

and vomiting (7/19 [36.8%] vs 2/27 [7.4%]) in the symptom screening and usual care group. Overall, symptom-specific intervention was significantly more common in the symptom screening group for pain, peripheral neuropathy and changes

in hunger among all participants and among those with SSPedi score greater than or equal to 1. Symptom-specific intervention was also more common in the symptom screening group for constipation among all participants and for sadness, pain, and nausea/vomiting among those with SSPedi score greater than or equal to 3.

Table 3 and eTable 12 in Supplement 2 show the comparison of unplanned health care encounters between the groups. The mean (SD) number of emergency department visits was 0.77 (1.12) in the symptom screening group and 0.45 (0.81) in the usual care group. There were significantly more emergency department visits in the intervention group than the usual care group (rate ratio, 1.72 [95% CI, 1.03-2.87]), with no significant differences in unplanned clinic visits and hospitalizations.

Discussion

In this cluster RCT, symptom screening with provision of symptom reports to the health care team and locally adapted symptom management care pathway implementation significantly reduced overall symptom scores compared with usual care. The study provides high-quality evidence that an intervention including symptom screening improves symptom control, a finding consistent with adult clinical trials.^{9,22,23}

Although symptom screening improved SSPedi symptoms, it did not improve PROMIS Fatigue or PedsQL domain scores. This may have occurred because these instruments measure different constructs: SSPedi focuses on degree of symptom-related bother, while PROMIS and PedsQL focus on symptom frequency. Increased documentation and any intervention for some symptoms in participants in the usual care group suggest they were experiencing more symptoms compared with those in the symptom screening group. It is also possible that repeated administration of SSPedi leads to habituation and decreased symptom perception. Alternatively, simply administering SSPedi repeatedly may reduce bothersome symptoms, which could, in itself, make the intervention worthwhile even if the desired outcome was achieved via a different mechanism than originally hypothesized.

The number of participants in the symptom screening group who received care pathway-consistent interventions was surprisingly low. It was previously demonstrated that interventions are rare for symptom management in patients with pediatric cancer overall.¹ It is possible that low rates of care pathway-consistent care were observed because SSPedi symptoms are not prioritized by clinicians or because sites' care pathway implementation efforts were inadequate. This suggests that symptom control needs to be explicitly prioritized by institutional leadership and that achievement of care pathway-consistent supportive care delivery requires purposeful, targeted implementation that includes systems for tracking symptoms, rates of care pathway-consistent intervention, and associated patient outcomes.²⁴

This study used SSPedi as both the intervention and outcome. The primary rationale was that the purpose of the intervention was to reduce symptom bother rather than frequency or severity. SSPedi was the only validated instrument

Table 2. Primary and Secondary Patient-Reported Outcomes at Baseline and Week 8 by Group^a

	Baseline		Week 8		Mean difference or odds ratio (95% CI) ^b		Adjusted P value ^c
	Symptom screening (n = 216)	Usual care (n = 213)	Symptom screening (n = 198)	Usual care (n = 209)	Unadjusted	Adjusted	
Primary outcome							
Total SSPedi score, mean (SD) ^a	11.8 (8.2)	13.5 (8.2)	7.9 (7.2)	11.4 (8.7)	-3.7 (-6.3 to -1.1)	-3.8 (-6.4 to -1.2)	.007
Secondary outcomes							
Severely bothersome SSPedi symptoms (score of 3-4), No. (%)							
Feeling disappointed or sad	12 (5.6)	15 (7.0)	5 (2.5)	11 (5.3)	0.46 (0.24 to 0.89)	0.46 (0.26 to 0.83)	.01
Feeling scared or worried	11 (5.1)	23 (10.8)	6 (3.0)	7 (3.3)	0.58 (0.38 to 0.88)	0.57 (0.38 to 0.85)	.005
Feeling cranky or angry	9 (4.2)	10 (4.7)	5 (2.5)	12 (5.7)	0.43 (0.29 to 0.63)	0.43 (0.29 to 0.63)	<.001
Problems with thinking or remembering things	15 (6.9)	11 (5.2)	7 (3.5)	14 (6.7)	0.60 (0.38 to 0.95)	0.62 (0.42 to 0.90)	.01
Changes in how your body or face look	23 (10.6)	24 (11.3)	4 (2.0)	21 (10.0)	0.51 (0.30 to 0.89)	0.52 (0.31 to 0.88)	.01
Feeling tired	57 (26.4)	74 (34.7)	28 (14.1)	52 (24.9)	0.52 (0.36 to 0.74)	0.52 (0.36 to 0.74)	<.001
Mouth sores	8 (3.7)	12 (5.6)	0 (0.0)	8 (3.8)	0.49 (0.28 to 0.86)	0.48 (0.27 to 0.85)	.01
Headache	8 (3.7)	21 (9.9)	10 (5.1)	10 (4.8)	0.60 (0.41 to 0.89)	0.61 (0.41 to 0.90)	.01
Hurt or pain (other than headache)	10 (4.6)	16 (7.5)	11 (5.6)	11 (5.3)	0.70 (0.48 to 1.03)	0.69 (0.47 to 1.01)	.06
Tingly or numb hands or feet	10 (4.6)	11 (5.2)	4 (2.0)	10 (4.8)	0.76 (0.50 to 1.15)	0.76 (0.50 to 1.15)	.19
Throwing up or feeling like you may throw up	23 (10.6)	29 (13.6)	19 (9.6)	27 (12.9)	0.81 (0.50 to 1.34)	0.80 (0.51 to 1.26)	.34
Feeling more or less hungry than you usually do	49 (22.7)	51 (23.9)	15 (7.6)	35 (16.7)	0.63 (0.43 to 0.94)	0.63 (0.44 to 0.90)	.01
Changes in taste	31 (14.4)	34 (16.0)	11 (5.6)	25 (12.0)	0.56 (0.33 to 0.93)	0.56 (0.34 to 0.90)	.02
Constipation	16 (7.4)	20 (9.4)	2 (1.0)	9 (4.3)	0.53 (0.27 to 1.06)	0.55 (0.31 to 0.95)	.03
Diarrhea	18 (8.3)	10 (4.7)	4 (2.0)	6 (2.9)	0.38 (0.19 to 0.75)	0.37 (0.19 to 0.73)	.004
Other PROs	n = 216	n = 213	n = 202	n = 209			
PROMIS Fatigue scores, mean (SD) ^a	53.9 (12.1)	54.6 (12.1)	49.3 (13.3)	49.8 (12.9)	-0.5 (-3.5 to 2.4)	-0.7 (-4.0 to 2.5)	.64
PedsQL 3.0 domain score, mean (SD) ^a							
Pain and hurt	69.8 (26.6)	68.8 (24.8)	76.2 (26.5)	76.1 (24.2)	-0.1 (-6.1 to 6.0)	0.2 (-5.9 to 6.2)	.95
Nausea	73.9 (23.4)	69.2 (20.7)	71.1 (23.1)	70.4 (23.3)	0.9 (-5.7 to 7.6)	1.3 (-4.9 to 7.6)	.66
Procedural anxiety	66.4 (30.3)	62.8 (29.1)	75.8 (27.9)	71.1 (26.1)	3.5 (-4.5 to 11.4)	3.0 (-4.5 to 10.5)	.41
Treatment anxiety	77.7 (26.3)	76.0 (23.4)	83.9 (22.2)	80.4 (23.0)	2.9 (-3.4 to 9.3)	2.9 (-3.4 to 9.1)	.34
Worry	64.7 (26.6)	62.8 (22.8)	72.9 (24.4)	69.5 (24.4)	3.1 (-2.8 to 9.1)	3.6 (-2.4 to 9.6)	.22
Cognitive problems	70.3 (21.2)	69.1 (20.6)	75.3 (21.5)	74.5 (21.4)	0.9 (-5.4 to 7.2)	1.2 (-5.5 to 7.9)	.71
Perceived physical appearance	74.7 (25.0)	73.2 (26.4)	77.6 (23.8)	77.3 (24.6)	0.2 (-5.1 to 5.4)	0.6 (-5.0 to 6.1)	.83
Communication	77.8 (21.3)	73.2 (21.7)	79.6 (21.2)	77.8 (21.2)	1.8 (-2.6 to 6.3)	1.8 (-3.1 to 6.6)	.45

Abbreviations: PedsQL, Pediatric Quality of Life Inventory; PROMIS, Patient-Reported Outcomes Measurement Information System; SSPedi, Symptom Screening in Pediatrics Tool.

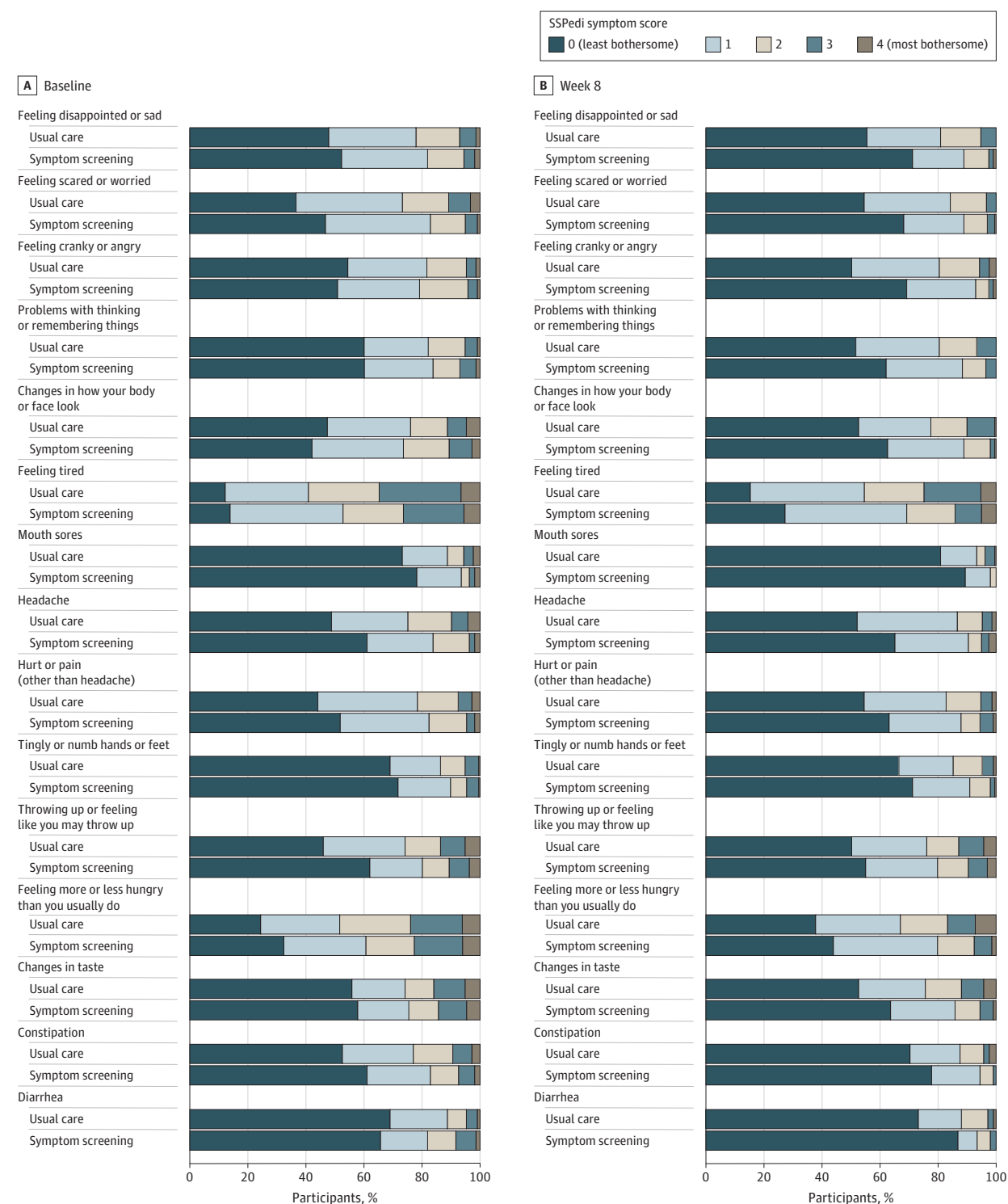
^a The 8-week self-reported total SSPedi score (range, 0-60; higher scores indicate more bothersome symptoms) is the sum of 15 SSPedi item scores (range, 0-4); recall period is "yesterday or today." Fatigue was measured using PROMIS v2.0-Fatigue (recall period of past 7 days); higher scores represent more fatigue. Quality of life was measured using the PedsQL 3.0 Acute Cancer Module, which produces 8 domain scores on a scale ranging from 0-100 (recall period of past 7 days). Higher scores indicate better health.

^b Estimated difference between the groups in 8-wk outcomes treated as continuous variables. Unadjusted models included only the stratification

variables used for randomization (number of patients with cancer and percentage of patients with private insurance). Adjusted models: for continuous outcomes, treatment effect is the covariate-adjusted mean difference using a mixed linear regression model with a random effect for site, fixed effects for treatment assignment, patient age and diagnosis group and 2 binary fixed effects at the cluster level for stratification variables; for individual SSPedi symptoms, treatment effect is the odds ratio using a mixed effects proportional odds model with a random effect for site and fixed effects for treatment assignment and 2 stratification variables.

^c Based on the difference in mean 8-week score, not a difference in mean change in score.

Figure 2. Symptoms Included in SSPedi by Group at Baseline and Week 8



The number of participants is 198 in the symptom screening group and 209 in the usual care group. The 15 individual Symptom Screening in Pediatrics Tool (SSPedi) symptoms were scored from 0 to 4, where 0 indicates "not at all

bothered" and 4 indicates "extremely bothered." The recall period is "yesterday or today."

Table 3. Number of Unplanned Health Care Encounters by Group^a

Unplanned encounter type	Symptom screening (n = 220)	Usual care (n = 224)	Absolute difference (95% CrI) ^b	Rate ratio (95% CI) ^b	Adjusted P value
Total emergency department visits and unplanned clinic visits and admissions					
Mean (SD)	1.82 (2.34)	1.12 (1.62)	6.13 (−1.56 to 14.51)	1.46 (0.97 to 2.19)	.07
Rate per 100 patient-weeks	22.8	14.0			
No. of encounters, No. (%)					
0	95 (43.2)	117 (52.2)			
1	22 (10.0)	40 (17.9)			
2	42 (19.1)	34 (15.2)			
3	22 (10.0)	11 (4.9)			
4	17 (7.7)	11 (4.9)			
5	5 (2.3)	6 (2.7)			
≥6	17 (7.7)	5 (2.2)			
Emergency department visits					
Mean (SD)	0.77 (1.12)	0.45 (0.81)	3.38 (−0.57 to 7.94)	1.72 (1.03 to 2.87)	.04
Rate per 100 patient-weeks	9.6	5.6			
No. of encounters, No. (%)					
0	126 (57.3)	155 (69.2)			
1	49 (22.3)	48 (21.4)			
2	25 (11.4)	14 (6.2)			
3	12 (5.5)	5 (2.2)			
4	7 (3.2)	1 (0.4)			
5	0	1 (0.4)			
≥6	1 (0.5)	0			
Unplanned clinic visits					
Mean (SD)	0.40 (1.09)	0.24 (0.58)	−0.01 (−3.23 to 3.04)	1.01 (0.41 to 2.50)	.99
Rate per 100 patient-weeks	5.1	3.0			
No. of encounters, No. (%)					
0	174 (79.1)	182 (81.2)			
1	27 (12.3)	34 (15.2)			
2	11 (5.0)	5 (2.2)			
≥3	8 (3.6)	3 (1.3)			
Unplanned hospital admissions					
Mean (SD)	0.65 (0.93)	0.43 (0.81)	2.28 (−0.59 to 5.16)	1.40 (0.96 to 2.03)	.08
Rate per 100 patient-weeks	8.1	5.4			
No. of encounters, No. (%)					
0	130 (59.1)	161 (71.9)			
1	51 (23.2)	40 (17.9)			
2	28 (12.7)	13 (5.8)			
3	8 (3.6)	9 (4.0)			
4	3 (1.4)	1 (0.4)			

Abbreviations: CrI, credible interval.

^a No participant had less than 8 weeks of follow-up.^b Treatment effect was the rate ratio with 95% CI estimated using mixed effects Poisson regression with treatment, random effect for site, and 2 stratification variables based on the anticipated number of eligible patients who speak English or Spanish and historical percentage of patients with private insurance. The absolute rate difference per 100 patient-weeks was estimated by marginalizing over a mixed effects Poisson regression that included only treatment and a random effect for site.

to measure this construct in a fashion suitable for pediatric patients when the study was developed,²⁵ justifying this approach.

The symptom screening group was more likely to receive symptom-specific intervention, but also visited the emergency department more often. It was anticipated that symptom screening would identify symptoms early and result in prompt management. Thus, it was hypothesized that symptom screening would reduce unplanned encounters. The contrasting finding suggests that symptoms that require medical attention are being identified more frequently, likely by parents,

with symptom screening. Although this result was unexpected, it does not influence the interpretation of the study outcomes and results. Future work should focus on better symptom prevention strategies and better outpatient supports to reduce emergency department visits.

In the original statistical analysis plan, it was hypothesized that baseline total SSPedi score might reflect the cluster's treatment assignment because care pathway implementation could reduce symptoms prior to enrollment. The analysis shows that baseline total SSPedi score was significantly

better in the intervention group, suggesting that exposure to care pathways independently improves symptoms.

Strengths of this study include the cluster RCT design, the pairing of symptom identification and management, and use of 2 reviewers to abstract documentation and interventions from the medical records.

Limitations

This study has several limitations. First, although a reduction in total SSPedi scores of 3.8 associated with the intervention was demonstrated, more work is required to better understand the clinical relevance of SSPedi score differences. Second, granular interventions, such as specific medication administrations at baseline or follow-up, were not compared. Third, documen-

tation and interventions were measured during a 3-day window around 4- and 8-week assessments. It is possible that documentation and intervention rates outside of these windows would have shown divergence between the groups.

Conclusions

Symptom screening with symptom feedback and symptom management care pathways improved SSPedi scores and increased symptom-specific interventions among pediatric patients with cancer. These findings provide strong support for integrating symptom screening and care pathways into routine clinical care.

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