Supportive Care in Cancer (2019) 27:2665–2671
https://doi.org/10.1007/s00520-018-4555-9

ORIGINAL ARTICLE

Severely bothersome fatigue in children and adolescents with cancer and hematopoietic stem cell transplant recipients

Deborah Tomlinson[1] · Christina Baggott[2] · David Dix[3] · Paul Gibson[4] · Shannon Hyslop[1] · Donna L. Johnston[5] · Andrea Orsey[6] · Carol Portwine[7] · Victoria Price[8] · Magimairajan Vanan[9] · Susan Kuczynski[10] · Brenda Spiegler[11] · George A. Tomlinson[12] · L. Lee Dupuis[1,13,14] · Lillian Sung[1,15]

Received: 2 May 2018 / Accepted: 13 November 2018 / Published online: 26 November 2018

Abstract

Background Objectives were to describe bothersome fatigue in children with cancer and hematopoietic stem cell (HSCT) recipients and to identify factors associated with severely bothersome fatigue.

Methods We included children ages 8–18 years treated for cancer or HSCT recipients from three groups: [1] receiving active cancer treatment and admitted to hospital for at least 3 days, [2] attending outpatient clinic for acute lymphoblastic leukemia maintenance therapy, and [3] attending outpatient clinic following treatment completion. Fatigue was measured using the Symptom Screening in Pediatrics Tool (SSPedi); severely bothersome fatigue was defined as a lot or extremely bothersome fatigue (score of 3–4 on 0–4 scale). Factors associated with severely bothersome fatigue were examined using univariate and multiple logistic regression.

Results Of 502 children included, 414 (82.5%) reported some degree of bothersome fatigue (scores 1–4), and 123 (24.5%) reported severely bothersome fatigue (score 3 or 4). In multiple regression analysis, factors significantly associated with severely bothersome fatigue were child age 11–14 and 15–18 years vs 8–10 years (odds ratio (OR) 2.11, 95% confidence interval (CI) 1.21–3.77 and OR 2.96, 95% CI 1.66–5.44), and inpatients receiving cancer treatment vs outpatients who had completed therapy (OR 3.85, 95% CI 2.17–7.27).

Conclusions We found that 82.5% of children with cancer or HSCT recipients reported bothersome fatigue and 24.5% of children reported severely bothersome fatigue. Risk factors for severely bothersome fatigue were older age and

✉ Lillian Sung
lillian.sung@sickkids.ca

[1] Program in Child Health Evaluative Sciences, The Hospital for Sick Children, Peter Gilgan Centre for Research and Learning, 686 Bay Street, Toronto, ON M5G 0A4, Canada

[2] Pediatric Hematology/Oncology, Stanford University School of Medicine, 300 Pasteur Drive, Stanford, CA 94305, USA

[3] Division of Hematology/Oncology/BMT, Department of Pediatrics, BC Children's Hospital, 4480 Oak Street Room B315, Vancouver V6H 3V4, Canada

[4] Haematology/Oncology, Department of Pediatrics, London Health Sciences Centre, 800 Commissioners Road East, London, ON N6A 5W9, Canada

[5] Division of Hematology/Oncology, Children's Hospital of Eastern Ontario, 401 Smyth Road, Ottawa, ON K1H 8L1, Canada

[6] Division of Pediatric Hematology/Oncology, Connecticut Children's Medical Center, 282 Washington Street, Hartford, CT 06106, USA

[7] Division of Haematology/Oncology, McMaster Children's Hospital, Health Sciences Centre, 1280 Main Street West, Hamilton, ON L8S 4K1, Canada

[8] Division of Pediatric hematology/Oncology, Department of Pediatrics, IWK Health Centre, 5850/5980 University Avenue, Halifax, NS B3K 6R8, Canada

[9] Pediatric Hematology/Oncology/BMT, CancerCare Manitoba, Research Institute in Oncology and Hematology, Departments of Pediatrics and Child Health and Biochemistry and Medical Genetics, University of Manitoba, 675 McDermot Avenue, Winnipeg, MB R3E 0V9, Canada

[10] Ontario Parents Advocating for Children with Cancer (OPACC), 99 Citation Drive, Toronto, ON M2K 1S9, Canada

[11] Department of Psychology, The Hospital for Sick Children, 555 University Avenue, Toronto, ON M5G 1X8, Canada

[12] Department of Medicine, Toronto General Hospital, 200 Elizabeth Street, Toronto, ON M5G 2C4, Canada

[13] Department of Pharmacy, The Hospital for Sick Children, 555 University Avenue, Toronto, ON M5G 1X8, Canada

[14] Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, Canada

[15] Division of Haematology/Oncology, The Hospital for Sick Children, 555 University Avenue, Toronto, ON M5G 1X8, Canada

inpatients receiving active cancer treatment. Future work should evaluate systematic symptom screening in clinical practice and apply interventions to reduce fatigue.

Keywords Fatigue · Children · Adolescents · Oncology · Hematopoietic stem cell transplantation

Background

Cancer-related fatigue is a subjective feeling of physical, emotional, or cognitive tiredness that can be distressing and persistent. [1, 2] Research has focused on fatigue in adult cancer patients, and in this population, it occurs in 80–90% of chemotherapy or radiotherapy recipients. [3–5] Fatigue is important because it can be extremely bothersome and it is known to reduce quality of life (QoL). [6, 7] Guidelines from the National Comprehensive Cancer Network suggest that patients with cancer should be routinely screened for fatigue and that fatigue should be managed according to clinical practice guidelines. [2] However, less is known about fatigue in children with cancer.

Because fatigue is subjective, measuring fatigue from the patient's perspective is important. Several reliable and valid approaches for measuring fatigue in children with cancer have been developed [8] including the Patient-Reported Outcomes Measurement Information System [9], the Pediatric Quality of Life Multidimensional Fatigue Scale [10], and the Fatigue Scale Child and Adolescent. [11, 12] While these are all appropriate approaches to measuring fatigue for the purpose of clinical trials, we recently developed a symptom screening tool for the purpose of clinical implementation named the Symptom Screening in Pediatrics Tool (SSPedi). [13–15] We recently found that SSPedi displays internal consistency, test re-test and inter-rater reliability, construct validity, and responsiveness to change in a prospective study of 502 children with cancer or hematopoietic stem cell transplantation (HSCT) recipients. [16] This data set then afforded the opportunity to describe fatigue in this population.

Consequently, our objectives were to describe bothersome fatigue in children with cancer and HSCT recipients and to identify factors associated with severely bothersome fatigue.

Methods

This is a sub-analysis of a primary study designed to evaluate the reliability, validity, and responsiveness of SSPedi. [16]

Subjects Respondents were English-speaking children and adolescents ages 8–18 years treated for cancer or HSCT recipients. Three groups of respondents were enrolled for the purpose of psychometric evaluation: [1] children receiving active treatment for cancer or undergoing HSCT, admitted to hospital, and expected to be in hospital or in clinic 3 days later; [2] children with non-relapsed acute lymphoblastic leukemia (ALL) during a routine clinic visit following initiation of at least 6 months of maintenance chemotherapy and clinically well with no procedure planned that day; and [3] survivors in follow-up during a routine clinic visit at least 3 months after completion of cancer treatment that did not include HSCT and clinically well. The rationale behind these three groups was to establish known groups construct validity by hypothesizing that inpatients should have higher total SSPedi scores (more bothersome symptoms) compared to children with ALL in maintenance therapy and children who had completed therapy. We excluded those with illness severity, cognitive disability, or visual impairment that precluded completion of SSPedi according to the primary healthcare team.

Procedures Nine sites in Canada and the USA (Appendix 1 Table 3) participated in this study. Research Ethics Board approval was obtained from the coordinating site (The Hospital for Sick Children) and all other participating sites. Child participants and their parents provided informed consent or assent as appropriate.

Respondents were approached in the inpatient or outpatient setting by a member of the research team. For those who agreed to participate, demographic information were obtained from the respondent, parent, and from the medical records. Children self-reported SSPedi on an iPad. Those admitted to hospital completed SSPedi a second time for the purpose of test-re-test reliability and responsiveness evaluations.

Fatigue is one of the 15 SSPedi items and it is worded as "feeling tired". The degree of bothersome fatigue was rated on a 5-point Likert scale that ranged from 0 = "not at all bothered" to 4 = "extremely bothered". Severely bothersome fatigue was categorized as those who rated fatigue as a score of 3 (a lot bothered) or 4 (extremely bothered).

Statistics The total SSPedi score is calculated by summing each of the 15 items' Likert scores that range from 0 to 4 for a total score that ranges from 0 (none) to 60 (worst possible). We calculated the proportion of the total SSPedi score due to fatigue.

To compare baseline demographics between the severely bothersome fatigue and not severely bothersome fatigue

Table 1 Demographics of the study cohort

Characteristic	Severely bothersome fatigue (score 3 or 4) ($N = 123$)	Not severely bothersome fatigue (scores 0–2) ($N = 379$)	P value
Child characteristics			
Gender			0.920
Male	75 (24.4%)	233 (75.6%)	
Female	48 (24.7%)	146 (75.3%)	
Median age in years			0.002
8–10.99	22 (14.7%)	128 (85.3%)	
11–14.99	54 (26.7%)	148 (73.3%)	
15–18.99	47 (31.3%)	103 (68.7%)	
Diagnosis			0.115
Leukemia/lymphoma	80 (22.6%)	274 (77.4%)	
Solid tumor	34 (27.9%)	88 (72.1%)	
Brain tumor	8 (44.4%)	10 (55.6%)	
Other	1 (12.5%)	7 (87.5%)	
Diagnosis ALL			0.002
Yes	42 (18.2%)	189 (81.8%)	
No	81 (29.9%)	190 (70.1%)	
Diagnosis AML			0.078
Yes	15 (35.7%)	27 (64.3%)	
No	108 (23.5%)	352 (76.5%)	
Metastatic disease	26 (27.1%)	70 (72.9%)	0.504
Relapse			0.133
Yes	18 (32.7%)	37 (62.3%)	
No	105 (23.5%)	342 (76.5%)	
Stem cell transplantation			0.009
Yes	14 (43.8%)	18 (56.3%)	
No	109 (23.2%)	361 (76.81%)	
In school			0.240
Yes	101 (23.5%)	329 (76.5%)	
No	49 (70.0%)	21 (30.0%)	
First language			0.178
English	109 (25.7%)	316 (74.4%)	
Non-English	14 (18.4%)	62 (81.6%)	
SSPedi group			< 0.0001
Admitted to hospital	99 (32.8%)	203 (67.2%)	
ALL in maintenance	9 (14.1%)	55 (85.9%)	
Off treatment	15 (11.0%)	121 (89.0%)	
Reason for visit chemotherapy			0.002
Yes	85 (29.6%)	202 (70.4%)	
No	38 (17.7%)	177 (82.3%)	
Parent characteristics			
Parent gender			0.430
Male	82 (25.7%)	237 (74.3%)	
Female	26 (22.0%)	92 (78.0%)	
Married			0.610
Yes	83 (23.9%)	265 (76.2%)	
No	40 (26.0%)	114 (74.0%)	
College or University Education			0.717
Yes	60 (23.8%)	192 (76.2%)	
No	63 (25.2%)	187 (74.8%)	
Parent works full time			0.968
Yes	59 (24.6%)	181 (75.4%)	
No	64 (24.4%)	198 (75.6%)	

groups, we used the Chi-square test for categorical variables. To determine factors associated with severely bothersome fatigue, we conducted univariate and multiple logistic regression analysis. Factors significant in univariate analysis were evaluated in multiple regression. Statistical significance was considered a P value < 0.05. Analyses were conducted using the SAS statistical program (SAS-PC, version 9.4; SAS Institute Inc., Cary, North Carolina).

Results

As previously reported, between November 11, 2014 and June 5, 2017, 624 children were assessed for eligibility. [16] There were 61 who did not meet eligibility criteria and 61 who declined to participate, thus leaving 502 children who were enrolled in the study. Of the 61 who declined, all were parents who declined on behalf

Table 2 Factors Associated with Severely Bothersome Fatigue

Characteristic	Odds ratio	95% CI	*P* value
Child characteristics			
Male gender	0.98	0.65 to 1.49	0.921
Median age in years			0.003
8–10.99	REF		
11–14.99	2.12	1.24 to 3.74	0.007
15–18.99	2.66	1.52 to 4.76	0.0008
Diagnosis			0.131
Leukemia/lymphoma	0.76	0.48 to 1.22	0.240
Solid tumor	REF		
Brain tumor	2.07	0.74 to 5.69	0.158
Other	0.37	0.02 to 2.19	0.361
Diagnosis ALL	0.52	0.34 to 0.79	0.003
Diagnosis AML	1.81	0.91 to 3.49	0.081
Metastatic disease	1.19	0.71 to 1.95	0.504
Relapse	1.59	0.85 to 2.86	0.135
Stem cell transplantation	2.58	1.22 to 5.33	0.011
In school	0.72	0.42 to 1.27	0.241
First language English	1.53	0.84 to 2.94	0.180
SSPedi group			< 0.0001
Admitted to hospital	3.93	2.25 to 7.33	< 0.0001
ALL in maintenance	1.32	0.53 to 3.16	0.539
Off treatment	REF		
Reason for visit chemotherapy	1.96	1.28 to 3.05	0.002
Parent characteristics			
Parent gender male	0.82	0.49 to 1.34	0.430
Married	0.89	0.58 to 1.39	0.610
College or University Education	0.93	0.62 to 1.39	0.717
Parent works full time	1.00	0.67 to 1.52	0.968

REF reference category, *CI* confidence interval, *ALL* acute lymphoblastic leukemia, *AML* acute myeloid leukemia, *SSPedi* Symptom Screening in Pediatrics Tool

of their child. Reasons for declining were as follows: not interested ($n = 52$), too busy ($n = 5$), too sick ($n = 2$), and too overwhelmed ($n = 2$). There were no significant differences between participants enrolled and those that declined by gender, age group, or diagnosis (data not shown).

From the three groups, there were 302 inpatients receiving active cancer treatment, 64 outpatients with ALL in maintenance, and 136 outpatients who had completed cancer treatment. Among the 502 participants, 414 (82.5%) reported some degree of bothersome fatigue meaning that only 88 (17.5%) stated fatigue was not bothersome. In terms of the degree of bothersome fatigue, 98 (19.5%) rated the fatigue score as "a lot bothered" (score of 3) and 25 (5.0%) rated the fatigue score as "extremely bothered" (score of 4) and thus, 123 (24.5%) rated fatigue as severely bothersome. Table 1 shows the demographics of the cohort stratified by those who stated fatigue was severely bothersome (score of 3 or 4) and those who stated fatigue was not severely bothersome (scores 0 to 2).

Table 2 shows factors associated with severely bothersome fatigue at the first assessment. Children who were 11 to 14 years of age and adolescents who were 15 to 18 years of age were more likely to report severely bothersome fatigue compared to children 8 to 10 years of age (odds ratio (OR) 2.12, 95% confidence interval (CI) 1.24 to 3.74; $P = 0.007$ and OR 2.66, 95% CI 1.52 to 4.76; $P = 0.0008$), respectively. Children with ALL were less likely to report severely bothersome fatigue (OR 0.52, 95% CI 0.34 to 0.79; $P = 0.003$) compared to those without ALL. In addition, HSCT recipients were more likely to report severely bothersome fatigue (OR 2.58, 95% CI 1.22 to 5.33; $P = 0.011$). Compared to outpatients who had completed cancer therapy, those actively receiving cancer treatments, admitted to hospital and expected to be in hospital or in clinic 3 days later, had an almost 4-fold increased odds of severely bothersome fatigue (OR 3.93, 95% CI 2.25 to 7.33; $P < 0.0001$). Finally, those for whom the primary purpose of their admission was chemotherapy administration were more likely to report severely bothersome fatigue ($P = 0.002$). Child gender and parent characteristics were not associated with severely bothersome fatigue.

For multiple regression, SSPedi study group (admission to hospital, ALL in maintenance, and off treatment) was highly correlated with ALL (Spearman correlation 0.42, $P < 0.0001$) and reason for visit was chemotherapy (Spearman correlation 0.62, $P < 0.0001$). Thus, among these three variables, only SSPedi study group was retained. In the multiple regression analysis which included child age, HSCT, and SSPedi study group, independent risk factors were age 11 to 14 years and age 15 to 18 years, relative to 8 to 10 years (OR 2.11, 95% CI 1.21 to 3.77; $P = 0.010$ and OR 2.96, 95% CI 1.66 to 5.44; $P = 0.0003$, respectively) and inpatients receiving cancer treatment vs outpatients who had completed therapy (OR 3.85, 95% CI 2.17 to 7.27; $P < 0.0001$).

The median total SSPedi score among the entire group was 9 (interquartile range (IQR) 4 to 16). The median proportion of the total symptom burden or total SSPedi score due to fatigue was 14.3% (IQR 8.3 to 23.1%). Figure 1 shows the distribution of change in fatigue scores between the 2 days (3 days apart) among the 282 participants who submitted two SSPedi assessments. While 134 (47.5%) did not report a change in bother due to fatigue, 101 (23.8%) reported that bothersome fatigue was better while 47 (16.7%) reported that bothersome fatigue was worse 3 days later.

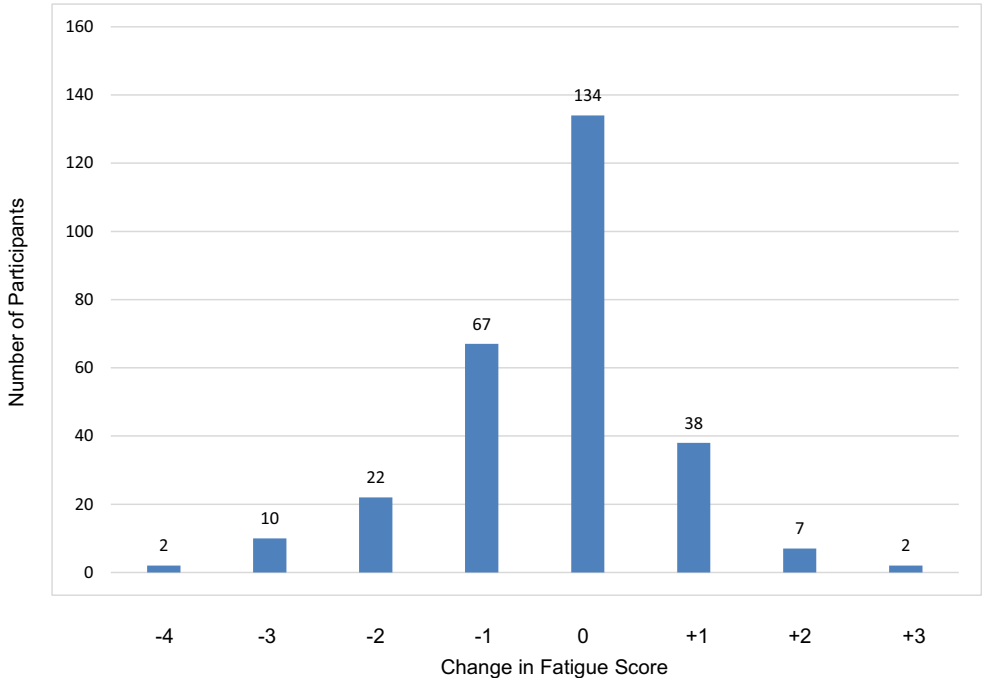

Fig. 1 Change in SSPedi Fatigue Scores. Legend: figure shows the number of participants who had a change in fatigue scores between two assessments conducted 3 days apart where negative numbers indicate improvement in fatigue

Discussion

We found that bothersome fatigue affected 82.5% of children enrolled on this study and it was severely bothersome in 24.5% of child and adolescent participants. Factors associated with severely bothersome fatigue were older age and inpatients receiving active cancer treatment. Three days after the initial assessment, we found that at least half of the cohort had a change in fatigue perception. These findings are important as they suggest that fatigue is both very common and very bothersome in children and adolescents with cancer. Given that there are evidence-based interventions that can be used for fatigue management in children with cancer and pediatric HSCT recipients including physical activity, relaxation, and mindfulness, [17] reduction of bothersome fatigue is an attainable goal.

The prevalence of fatigue in our study was higher than in other pediatric series. Three cross-sectional studies conducted in children 10 to 18 years of age found that lack of energy occurred in 50% to 76%. [18–20] This discrepancy is particularly interesting since we purposefully enriched our cohort for children who were anticipated to have lower symptom burden, namely those who were off therapy and those with ALL receiving maintenance chemotherapy. In terms of risk factors for fatigue, our study is consistent with two studies that showed that children who were inpatients had significantly more symptoms than outpatients [19, 21] and, in particular, tiredness was more common in children who had received chemotherapy in the preceding 7 days ($P = 0.023$). [21] Our findings are also consistent with a study that described severe fatigue in patients with acute leukemia and HSCT recipients who were expected to be inpatients for at least 3 weeks. [22]

Among inpatients, we found that about half of the cohort had a change in the degree of bothersome fatigue when measured 3 days apart. This finding suggests that fatigue scores change rapidly and that assessments should be frequent. These data also suggest that there is an opportunity to improve fatigue in this setting, with an opportunity to realize immediate gains with interventions aimed at reducing fatigue. Clinical implementation of routine symptom screening and application of evidence-based interventions for fatigue control are both important toward improving QoL in children receiving cancer therapies. Based upon a recent clinical practice guideline developed specifically for children receiving cancer treatments, physical activity, relaxation, and mindfulness are strongly recommended for the management of fatigue for this population. [17]

A strength of this study is that we measured bothersome fatigue from the child's perspective using a validated tool. Another strength is that we enrolled children from multiple sites which improve the generalizability of our finding. However, our results should be interpreted in light of the limitations of our study. We did not randomly sample from children with all types of cancer and specifically selected subgroups relevant for psychometric evaluation. In particular, since we enriched the sample for those expected to have fewer

symptoms, we may have underestimated the burden of fatigue in this study. Second, we used a symptom screening approach to fatigue assessment, and thus, we did not capture specific domains of fatigue such as cognitive fatigue and sleep/rest fatigue. Correlations between sleep/rest fatigue and sleep duration have been described [23]; this additional information may thus aid in the choice of intervention for fatigue.

In summary, we found that 82.5% of children with cancer or HSCT recipients reported bothersome fatigue and 24.5% of children reported severely bothersome fatigue. Risk factors for severely bothersome fatigue were older age and inpatients receiving active cancer treatment. Future work should evaluate systematic symptom screening in clinical practice and apply interventions to reduce fatigue.

Acknowledgements We are grateful for the generosity of the patients and parents who participated in this study. We wish to thank all the clinical research associates and nurses who were involved in this study at each site.

Funding information This research was funded by The Pedal for Hope Impact Grant of the Canadian Cancer Society (grant #702295). The authors have declared no conflicts of interest.

Compliance with ethical standards

Research Ethics Board approval was obtained from the coordinating site (The Hospital for Sick Children) and all other participating sites. Child participants and their parents provided informed consent or assent as appropriate.

Conflict of interest The authors declare that they have no conflict of interest.

Appendix

Table 3 Participating sites

Site	Location	Principal investigator(s)
BC Children's Hospital	Vancouver, Canada	David Dix
CancerCare Manitoba	Winnipeg, Canada	Magimairajan Vanan
Children's Hospital, London Health Sciences Centre	London, Canada	Paul Gibson
Children's Hospital of Eastern Ontario	Ottawa, Canada	Donna Johnston
Connecticut Children's Medical Center	Hartford, United States	Andrea Orsey
IWK Health Centre	Halifax, Canada	Vicky Price
McMaster Children's Hospital	Hamilton, Canada	Carol Portwine
Stanford University School of Medicine	Palo Alto, United States	Christina Baggott
The Hospital for Sick Children	Toronto, Canada	Lillian Sung, Lee Dupuis

References

1. Mortimer JE, Barsevick AM, Bennett CL, Berger AM, Cleeland C, DeVader SR, Escalante C, Gilreath J, Hurria A, Mendoza TR, Rugo HS (2010) Studying Cancer-related fatigue: report of the NCCN scientific research committee. J Natl Compr Cancer Netw 8: 1331–1339
2. (2018) National Comprehensive Cancer Network. Fatigue. https://www.nccn.org/patients/resources/life_with_cancer/managing_symptoms/fatigue.aspx (Accessed May 2018)
3. Hofman M, Ryan JL, Figueroa-Moseley CD, Jean-Pierre P, Morrow GR (2007) Cancer-related fatigue: the scale of the problem. Oncologist 12(Suppl 1):4–10
4. Henry DH, Viswanathan HN, Elkin EP, Traina S, Wade S, Cella D (2008) Symptoms and treatment burden associated with cancer treatment: results from a cross-sectional national survey in the U.S. Support Care Cancer 16:791–801
5. Higginson IJ, Armes J, Krishnasamy M (2004) Introduction, in fatigue in Cancer. In: Armes J, Krishnasamy M, Higginson IJ (eds) Fatigue in Cancer. Oxford University Press, Oxford, pp xvii–xxxi
6. Wilson IB, Cleary PD (1995) Linking clinical variables with health-related quality of life. A conceptual model of patient outcomes. JAMA 273:59–65
7. Meeske K, Katz ER, Palmer SN, Burwinkle T, Varni JW (2004) Parent proxy-reported health-related quality of life and fatigue in pediatric patients diagnosed with brain tumors and acute lymphoblastic leukemia. Cancer 101:2116–2125
8. Tomlinson D, Hinds PS, Ethier MC, Ness KK, Zupanec S, Sung L (2013) Psychometric properties of instruments used to measure fatigue in children and adolescents with cancer: a systematic review. J Pain Symptom Manag 45:83–91
9. Hinds PS, Nuss SL, Ruccione KS, Withycombe JS, Jacobs S, DeLuca H, Faulkner C, Liu Y, Cheng YI, Gross HE, Wang J, DeWalt DA (2013) PROMIS pediatric measures in pediatric oncology: valid and clinically feasible indicators of patient-reported outcomes. Pediatr Blood Cancer 60:402–408
10. Varni JW, Burwinkle TM, Katz ER, Meeske K, Dickinson P (2002) The PedsQL in pediatric cancer: reliability and validity of the Pediatric Quality of Life Inventory Generic Core Scales, Multidimensional Fatigue Scale, and Cancer Module. Cancer 94:2090–2106

11. Hinds PS, Yang J, Gattuso JS, Hockenberry M, Jones H, Zupanec S, Li C, McLaughlin Crabtree V, Mandrell BN, Schoumacher RA, Vallance K, Sanford S, Srivastava DK (2010) Psychometric and clinical assessment of the 10-item reduced version of the Fatigue Scale-child instrument. J Pain Symptom Manag 39:572–578
12. Hinds PS, Hockenberry M, Tong X, Rai SN, Gattuso JS, McCarthy K, Pui CH, Srivastava DK (2007) Validity and reliability of a new instrument to measure cancer-related fatigue in adolescents. J Pain Symptom Manag 34:607–618
13. Tomlinson D, Dupuis LL, Gibson P, Johnston DL, Portwine C, Baggott C, Zupanec S, Watson J, Spiegler B, Kuczynski S, Macartney G, Sung L (2014) Initial development of the Symptom Screening in Pediatrics tool (SSPedi). Support Care Cancer 22:71–75
14. O'Sullivan C, Lee Dupuis L, Gibson P, Johnston DL, Baggott C, Portwine C, Spiegler B, Kuczynski S, Tomlinson D, Tomlinson GA, Sung L (2018) Evaluation of the electronic self-report Symptom Screening in Pediatrics tool (SSPedi). BMJ Support Palliat Care 8:110–116
15. O'Sullivan C, Dupuis LL, Gibson P, Johnston DL, Baggott C, Portwine C, Spiegler B, Kuczynski S, Tomlinson D, de Mol Van Otterloo S, Tomlinson GA, Sung L (2014) Refinement of the Symptom Screening in Pediatrics tool (SSPedi). Br J Cancer 111: 1262–1268
16. Dupuis LL, Johnston DL, Baggott C, Hyslop S, Tomlinson D, Gibson P, Orsey A, Dix D, Price V, Vanan M, Portwine C, Kuczynski S, Spiegler B, Tomlinson GA, Sung L (2018) Validation of the Symptom Screening in Pediatrics tool in children receiving Cancer treatments. J Natl Cancer Inst 110:661–668
17. Robinson PD, Oberoi S, Tomlinson D, Duong N, Davis H, Cataudella D, Culos-Reed N, Gibson F, Götte M, Hinds P, Nijhof SL, van der Torre P, Cabral S, Dupuis LL, Sung L. (2018) Management of fatigue in children and adolescents with cancer and in paediatric recipients of haemopoietic stem-cell transplants: a clinical practice guideline. Lancet Child Adolesc Health. 2(5): 371–378.
18. Baggott C, Dodd M, Kennedy C, Marina N, Matthay KK, Cooper BA, Miaskowski C (2010) Changes in children's reports of symptom occurrence and severity during a course of myelosuppressive chemotherapy. J Pediatr Oncol Nurs 27:307–315
19. Collins JJ, Byrnes ME, Dunkel IJ, Lapin J, Nadel T, Thaler HT, Polyak T, Rapkin B, Portenoy RK (2000) The measurement of symptoms in children with cancer. J Pain Symptom Manag 19: 363–377
20. Walker AJ, Gedaly-Duff V, Miaskowski C, Nail L (2010) Differences in symptom occurrence, frequency, intensity, and distress in adolescents prior to and one week after the administration of chemotherapy. J Pediatr Oncol Nurs 27:259–265
21. Collins JJ, Devine TD, Dick GS, Johnson EA, Kilham HA, Pinkerton CR, Stevens MM, Thaler HT, Portenoy RK (2002) 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 Manag 23:10–16
22. Diorio C, Schechter T, Lee M, O'Sullivan C, Hesser T, Tomlinson D, Piscione J, Armstrong C, Tomlinson G, Sung L (2015) A pilot study to evaluate the feasibility of individualized yoga for inpatient children receiving intensive chemotherapy. BMC Complement Altern Med 15:2
23. Walter LM, Nixon GM, Davey MJ, Downie PA, Horne RS (2015) Sleep and fatigue in pediatric oncology: a review of the literature. Sleep Med Rev 24:71–82