

## Fatigue, Sleep-wake Disturbances, and Quality of Life in Adolescents Receiving Chemotherapy

By: Jeanne M. Erickson, Susan L. Beck, Becky R. Christian, William PhD Dudley, Patricia J. Hollen, Karen A. Albritton, Margaret Sennett, Robyn L. Dillon, and Kamar Godder

Erickson, J.M., Beck, S.L., Christian, B.R., Dudley, W.N., Hollen, P.J., Albritton, K.A., Sennett, M., & Dillon, R.L. (2011). Fatigue, sleep-wake disturbances, and quality of life in adolescents receiving chemotherapy. *Journal of Pediatric Hematology/Oncology*, 33(1), e17–25. doi:10.1097/MPH.0b013e3181f46a46

**\*\*\*Note: This version of the document is not the copy of record. Made available courtesy of Lippincott, Williams & Wilkins. Link to Article: [http://journals.lww.com/jpho-online/Fulltext/2011/01000/Fatigue,\\_Sleep\\_wake\\_Disturbances,\\_and\\_Quality\\_of.27.aspx](http://journals.lww.com/jpho-online/Fulltext/2011/01000/Fatigue,_Sleep_wake_Disturbances,_and_Quality_of.27.aspx)**

### **Abstract:**

*Background:* Adolescents with cancer experience distressing physical and psychosocial symptoms, especially during treatment. Fatigue and sleep disturbances commonly affect adolescents' quality of life, but little is known about how adolescents experience these symptoms during an early month of chemotherapy. This study measured fatigue, sleep disturbances, and quality of life in 20 adolescents over 1 month while they were receiving chemotherapy.

*Methods:* Multidimensional fatigue and quality of life were measured weekly with modules from the PedsQL Measurement Model, and sleep disturbances were measured with the General Sleep Disturbance Scale.

*Results:* Adolescents experienced increased severity of fatigue and sleep disturbances during the week after treatment. Common sleep-wake problems included daytime sleepiness, decreased alertness, and poor sleep quality. Fatigue and sleep-wake disturbances were related symptoms, and both symptoms were associated with various domains of quality of life.

*Conclusions:* Fatigue and sleep-wake disturbances are significant problems for adolescents receiving chemotherapy and negatively affect the quality of life. Clinicians should routinely screen adolescent patients for fatigue and sleep disturbances and intervene to minimize their impact using pharmacologic and nonpharmacologic strategies.

### **Article:**

Quality of life is an important outcome measure for patients with cancer, incorporating domains of physical, emotional, social, and cognitive functioning.<sup>1</sup> For adolescents receiving cancer treatment, quality of life is based on their abilities to participate in usual teenage activities, maintain relationships with friends and family, and cope with the unpleasantness that comes with cancer treatment.<sup>2</sup> Unrelieved physical symptoms, such as fatigue and sleep disturbances, have the potential to interfere with activities of daily living and negatively impact the quality of life. A clear understanding of how physical symptoms affect the quality of life of the adolescents during

cancer therapy can assist cancer clinicians and researchers to design and implement effective interventions to enhance adolescents' well-being during their cancer experience.

Fatigue is a common and distressing symptom reported by adolescents at various stages of the cancer trajectory.<sup>3-6</sup> Studies show that cancer-related fatigue severity and distress in adolescents are highest in the early weeks of cancer treatment and gradually decline during and after therapy, and are affected by a number of factors including diagnosis, type of treatment, and treatment tolerance.<sup>7-10</sup> Fatigue can be a persistent symptom for some adolescent cancer survivors as they mature into adults, affecting social and career outcomes.<sup>11</sup> Posttreatment fatigue in young cancer survivors is associated with being female, unemployed, having symptoms of pain, depression, and sleeping problems, the presence of comorbidities, and risk behaviors, such as tobacco use.<sup>12-14</sup>

Sleep-wake disturbances frequently co-occur with fatigue in patients with cancer, including adolescents.<sup>3,15-18</sup> These symptoms, which include difficulty falling asleep, night-time awakenings, and daytime sleepiness, have been described alone and as components of symptom clusters in adults that also include depression, pain, anxiety, depressed daytime activity, and less robust circadian rhythms.<sup>9,19-23</sup> The exact nature of the relationship between fatigue and sleep-wake disturbances, however, is not known, but pediatric oncology patients with increased nighttime awakenings have reported more fatigue and longer but less efficient sleep.<sup>17</sup> More research is needed about how these 2 common symptoms are associated and vary over time in adolescents, especially during the periods of cancer treatment.

As survival rates for cancer increase, attention is shifting toward better symptom management to reduce the morbidity of cancer treatment. This is especially critical for adolescents who experience cancer at one of the most dynamic times of life, who receive intense multimodality cancer treatments, and who are likely to be long-term cancer survivors. Unfortunately, adolescents are often excluded from symptom and disease-focused research owing to a number of challenges and barriers, creating a disparity in survival and quality-of-life improvements that may be seen in other age groups with higher participation in research.<sup>24,25</sup> Adolescents receiving cancer therapy have a lower quality of life when compared with healthy peers, especially in domains that include physical complaints, compromised motor function and autonomy, and impaired emotional functioning and mood disturbances.<sup>26</sup> Older children and adolescents with cancer were found to have more problems with anxiety, emotional distress, mood disturbances, and altered self-perception, resulting in lower quality of life.<sup>27,28</sup> Specific cancer diagnoses and treatments are also factors that affect quality of life, with higher-risk disease and longer, more aggressive therapy associated with lower quality-of-life scores.<sup>29</sup>

Many of the studies related to symptom management and quality of life in adolescents are limited by samples that combine older and younger participants, by retrospective or cross-sectional study designs with 1 or 2 measurement points, and by symptom report data obtained from sources other than the adolescents themselves. To strengthen the evidence from earlier research, this prospective study measured fatigue, sleep-wake disturbances, and the quality of life in adolescents receiving first-line chemotherapy for 5 consecutive weeks using self-report. The aims of the study were to describe the relationship between fatigue and sleep-wake disturbances during 1 month of chemotherapy, to describe how the symptoms varied, and to

determine how these symptoms affected the quality of life for these adolescents. Demographic and treatment factors were also explored for their effect on the symptoms of fatigue and sleep-wake disturbances.

## METHODS

### *Design and Setting*

This prospective descriptive and correlational study measured fatigue, sleep-wake disturbances, and quality of life over 1 month using self-report measures in 20 adolescents receiving first-line chemotherapy. The 1-month study period was chosen to measure symptom trajectories before and after at least 1 administration of chemotherapy. Data collection began on a day of chemotherapy administration and continued for 28 days, with adolescents completing weekly reports of fatigue, sleep-wake disturbances, and quality of life. This feasibility study was conducted at the University of Virginia (UVa) Health System and the Virginia Commonwealth University (VCU) Health System.

### *Sample*

Participant inclusion criteria included adolescents who: (1) were age 12 to 19 years at the time of cancer diagnosis; (2) were receiving their second, third, fourth, or fifth month of chemotherapy; (3) assented to participate in the study; (4) had a parent who consented to the study if the adolescent was a minor; and (5) had the ability to read and write English. Patients receiving concurrent biotherapy or radiation therapy were not eligible. Every available adolescent who met the inclusion criteria at the 2 settings was invited to participate in the study.

### *Procedures*

The study was approved by the Cancer Center Protocol Review Committees (CCPRC) and the Institutional Review Boards (IRB) at the 2 study sites. A Certificate of Confidentiality from the National Institute of Nursing Research was obtained to protect the identities of adolescents who chose to self-report the use of illegal substances (tobacco, alcohol, or marijuana) on the sleep disturbance questionnaire. Patients who were interested in the study, and their parents if they were minors, learned about the study and completed assent/consent procedures in the outpatient setting. They were given the option to complete paper or electronic versions of the instruments.

### *Instruments*

Instruments that measure fatigue, sleep-wake disturbances, and quality of life with a 1-week recall were chosen for the study (Table 1). Three instruments were chosen from the PedsQL Measurement Model, which offers reliable and valid developmentally-designed modules to measure health-related quality of life and other symptoms in healthy and chronically-ill children and adolescents. The study used the teen self-report version of the PedsQL Multidimensional Fatigue Scale (MFS), developed for ages 13 to 18 years, to measure multidimensional fatigue.<sup>30</sup> Quality of life was measured with the PedsQL 4.0 Generic Core Scale (teen report) and the PedsQL 3.0 Cancer Module Acute Version (teen report) from the PedsQL Measurement Model System.<sup>30</sup> In this study, the school function items were dropped from the total and psychosocial subscale scores of the PedsQL 4.0 Generic Core Scale because they were not applicable for 7 of the participants. (Three of the 19-year-old participants completed high school, but were not in

college, and 4 of the younger teenagers were not regularly attending school because it was summer.)

**Table 1:** Instruments Used to Measure Fatigue, Sleep, and Quality of Life

<b>Instrument</b>	<b>Author/Year</b>	<b>Domains (# of Items)</b>	<b>Scoring</b>	<b>Reliability in this Study (Cronbach <math>\alpha</math>)</b>
PedsQL Multidimensional fatigue scale	Varni et al <sup>30</sup>	General fatigue (6) sleep/rest fatigue (6) cognitive fatigue (6)	5-point Likert scale; scores range from 0-100, and higher scores indicate fewer problems	Total scale = 0.92-0.95 general fatigue = 0.87-0.96 cognitive fatigue = 0.89-0.95
General sleep disturbance scale	Lee <sup>31</sup>	Sleep quality (10) daytime function (5) sleep aids (6)	8-point Likert scale for frequency of 0 (not at all) to 7 (every day); mean score > 3 is criteria for possible sleep disorder using DSM-IV criteria <sup>32</sup>	Sleep quality = 0.72-0.90 daytime function = 0.63-0.93
PedsQL 4.0 generic core scale	Varni et al <sup>30</sup>	Physical function (8) emotional function (5) social function (5) school function (5)	5-point Likert scale; scores range from 0-100, and higher scores indicate better quality of life	Physical function = 0.85-0.95 psychosocial function = 0.86-0.92
PedsQL 3.0 cancer module	Varni et al <sup>30</sup>	Pain (2) nausea (5) procedural anxiety (3) treatment anxiety (3) worry (3) cognitive problems (5) perceived physical appearance (3) communication (3)	5-point Likert scale; scores range from 0-100, and higher scores indicate better quality of life	Total scale = 0.83-0.93

The General Sleep Disturbance Scale (GSDS) was used to measure disturbances in sleep quantity and quality.<sup>31</sup> The GSDS has been reliable when used to measure sleep disturbances in healthy young adults and women infected with human immunodeficiency virus (HIV).<sup>33-35</sup> Evidence for concurrent validity of the GSDS was shown through correlations with actigraphy,<sup>35</sup> and evidence for construct validity was shown with groups of healthy adults working rotating shifts.<sup>31</sup> The sleep aids subscale of the GSDS was excluded in the analysis because all but 3 participants reported that they did not use any sleep aids.

Baseline demographic data and information about the cancer diagnosis and treatment plan were retrieved from the medical record at the time of participant enrollment. Ongoing treatment information was collected weekly during the study period.

### *Analyses*

Descriptive statistics were calculated for demographic and instrument variables. Because of the small sample size and distributions that were not normal for many variables, nonparametric statistics were used. Weekly scores were examined for changes over the 5 weekly time points using graphs and the Friedman test. Correlational analyses using Spearman coefficient examined the relationships between the symptoms of fatigue and sleep disturbances and between each symptom and quality of life (generic and cancer-specific). Correlational analyses determined the effects of age and length of time on chemotherapy on the symptoms of fatigue and sleep-wake disturbances. Data were also examined for the differences in symptom severity between groups based on sex and diagnosis at each time point using the nonparametric Mann-Whitney *U* test.

Data analyses were conducted using the Statistical Package for the Social Sciences (SPSS) version 15.0.

## RESULTS

Thirty-two adolescents were invited to participate in the study, and 7 adolescents declined to participate, for a 22% refusal rate. Four patients who enrolled in the study did not complete all of the self-report measures (16% attrition rate). Data from 1 patient is not included because she received only oral chemotherapy.

The convenience sample included 20 adolescents diagnosed with cancer, age 12 to 19 years (mean age=16.12 y, SD=2.13) (Table 2). Half of the participants were female, and most (85%) were White. The most common diagnoses were acute lymphoblastic leukemia (ALL) and non-Hodgkin lymphoma. The participants' length of time since the initiation of chemotherapy to study entry ranged from 5 to 17 weeks (mean time on therapy=8.71 wk, SD=3.56). The group of adolescents was being treated with 10 different treatment regimens, specific to their cancer diagnosis. These regimens included intravenous (IV), intrathecal (IT), and oral chemotherapy agents, given every week, every 2 weeks, or every 3 weeks, and some treatments that occurred over several consecutive days.

**Table 2:** Demographics of Adolescents in Study

Variable	N (20)	%
Sex		
Female	10	50
Male	10	50
Race		
White	17	85
African American	3	15
Diagnosis		
ALL	7	35
Hodgkin lymphoma	6	30
Non-Hodgkin lymphoma	2	10
Sarcoma	2	10
AML	1	5
Rhabdomyosarcoma	1	5
Neuroblastoma	1	5

Twelve adolescents received their chemotherapy on an outpatient basis and required no hospitalization during the study period. Four adolescents each had 1 short unscheduled (2 to 3 d) hospitalization for complications, including neutropenic fevers and an allergic reaction. Four adolescents had scheduled hospitalizations (4 to 5 d) to receive all or part of their chemotherapy.

### *Fatigue*

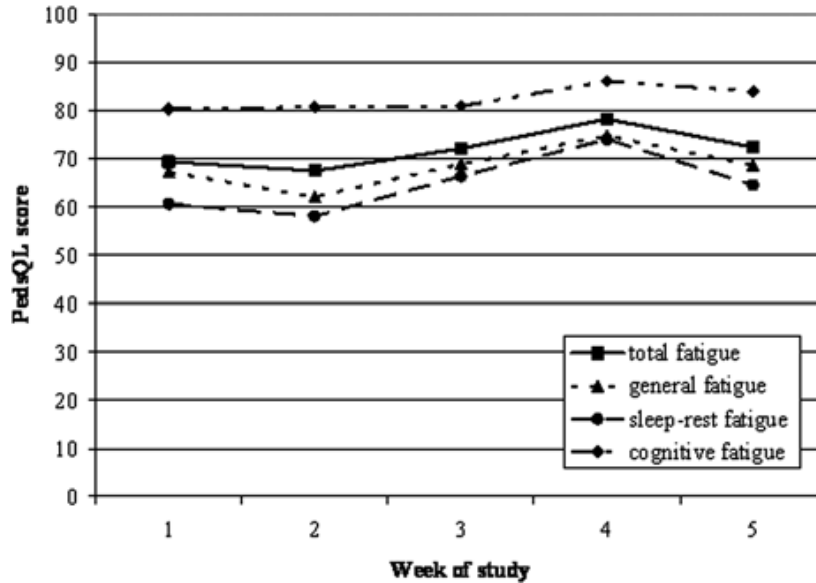
Across the 5 weeks of the study, up to 75% of adolescents reported that “feeling tired” was a problem “sometimes,” “often,” or “almost always” on the PedsQL MFS. Participants reported the least problems with cognitive fatigue and the most problems with sleep/rest fatigue (Table 3, Fig. 1). The highest fatigue levels (lowest scores) were reported at week 2 for the total scale, for the general fatigue subscale, and for the sleep/rest fatigue subscale. Changes in PedsQL MFS total scores were not found to be significantly different over time when examined with the Friedman test ( $P=0.82$ ).

**Table 3:** Means and Standard Deviations for PedsQL Multidimensional Fatigue Reports from 20 Adolescents Receiving Chemotherapy

	Week 1 (Baseline)		Week 2		Week 3		Week 4		Week 5	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Total fatigue	69.45	17.30	67.56	19.55	72.17	18.71	78.30	20.10	72.45	20.02
General fatigue	67.29	21.13	62.13	24.98	68.96	23.36	74.77	26.60	68.75	27.72
Sleep/rest fatigue	60.67	20.38	58.11	23.43	66.42	24.16	74.07	23.11	64.58	25.28
Cognitive fatigue	80.42	17.10	80.83	16.85	81.04	16.75	86.20	15.42	84.03	14.74

Possible range of scores is 0-100. Higher scores indicate fewer problems with fatigue.

**Figure 1:** Mean Values of PedsQL Multidimensional Fatigue Scores for 20 Adolescents Receiving Chemotherapy



### Sleep-wake Disturbances

Nearly all (95%) of the adolescents recalled at least 1 sleep-wake disturbance at a frequency of 3 days per week or more. Items approaching clinical significance based on DSM-IV criteria included not feeling rested (mean=3.19, SD=2.37), not feeling alert during the day (mean=3.14, SD=1.93), feeling sleepy during the day (mean=2.97, SD=1.96), not feeling satisfied with sleep quality (mean=2.93, SD=2.25), and feeling tired (mean=2.59, SD=2.07).

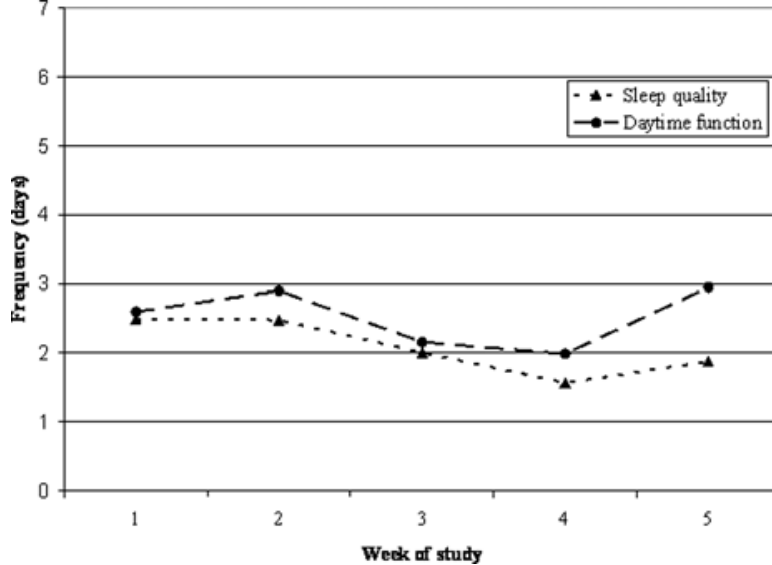
Average daytime function subscale scores were higher (worse) than sleep quality subscale scores across all the time points (Table 4). Daytime function scores worsened from baseline to week 2, then improved for the next 2 time points before increasing in severity again at week 5 (Fig. 2). Using the Friedman test, these changes in daytime function were not found to be significantly different over time ( $P=0.46$ ). Sleep quality subscale scores improved over the first 4 time points, before worsening again at week 5. Using the Friedman test, changes in sleep quality scores were not significantly different over time ( $P=0.41$ ).

**Table 4:** Means and Standard Deviations for GSDS Subscale Reports from 20 Adolescents Receiving Chemotherapy

	Week 1 (Baseline)		Week 2		Week 3		Week 4		Week 5	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Daytime function	2.60	1.32	2.90	1.59	2.16	1.36	1.99	1.47	2.95	2.01
Mean sleep quality	2.50	1.68	2.48	1.63	2.01	1.24	1.57	1.26	1.88	1.14

Possible scores range from 0 to 7. Higher scores indicate more frequent sleep-wake disturbances. For example, mean of 2.6=daytime function disturbances occurred 2.6 days in the earlier week.

**Figure 2:** Mean values for GSDS daytime function and sleep quality scores for 20 adolescents receiving chemotherapy



### Quality of Life

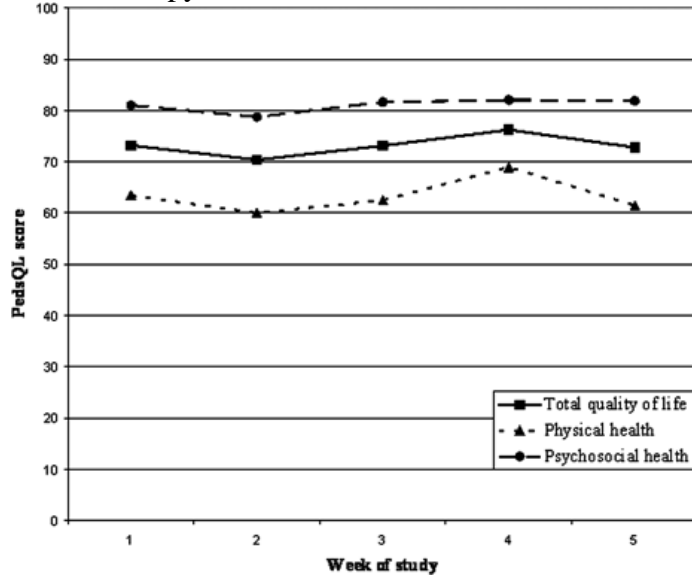
Across the 5 measurement points, scores in the physical domain of quality of life were lower (worse) than scores in the psychosocial domain, as measured with the PedsQL 4.0 Generic Core. The PedsQL 4.0 Generic Core total scale and subscale scores were lowest (worst) at week 2. For the PedsQL Cancer Module, scores were lowest at week 4 (Table 5). Changes in scores for the PedsQL Generic Core and PedsQL Cancer Module were not statistically different over time when examined with the Friedman test,  $P=0.31$  and  $P=0.71$ , respectively (Figs. 3 and 4).

**Table 5:** Means and Standard Deviations for PedsQL Generic Quality of Life and Cancer-related Quality of Life Reports from 20 Adolescents Receiving Chemotherapy

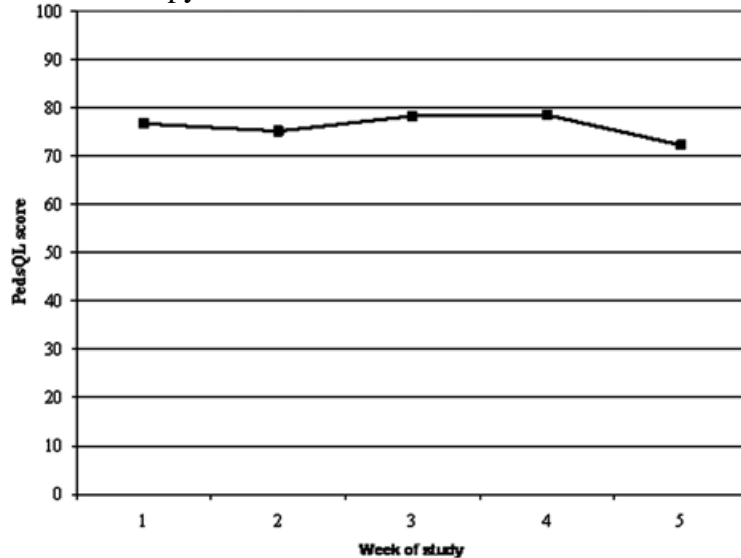
	Week 1 (Baseline)		Week 2		Week 3		Week 4		Week 5	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
PedsQL 4.0 generic core										
Total	73.19	17.78	70.37	20.42	73.13	18.67	76.23	21.29	72.80	20.98
Physical health	63.44	23.85	60.00	26.53	62.50	26.17	68.93	27.16	61.48	29.52
Psychosocial health	81.00	14.86	78.76	17.67	81.63	14.26	82.06	18.08	81.88	15.78
PedsQL cancer module										
Total	76.63	12.16	75.11	15.46	78.22	13.30	78.41	16.26	72.22	17.32

Possible scores range from 0 to 100. Higher scores indicate better quality of life.

**Figure 3:** Mean Values of PedsQL Genetic Quality of Life for 20 Adolescents Receiving Chemotherapy



**Figure 4:** Mean Values of PedsQL Cancer-Related Quality of Life for 20 Adolescents Receiving Chemotherapy



*Correlations Between Fatigue, Sleep-wake Disturbances, and Quality of Life*

Data at each weekly time point were explored for associations between sleep-wake disturbances (GSDS subscale scores of daytime function and sleep quality), fatigue (PedsQL MFS total score and subscale scores of general and cognitive fatigue), cancer-related QOL (PedsQL Cancer Module scores), and generic QOL (PedsQL 4.0 Generic Core physical and psychosocial health subscale summary scores) using nonparametric statistics. Items that overlapped on scales were excluded before each analysis.



Table 6 lists moderately strong associations ( $r \geq 0.49$ ,  $P < 0.01$ ) between pairs of variables at each weekly time point. At baseline, fatigue was associated with poor sleep quality and worse psychosocial QOL, and daytime function and sleep quality problems were associated with worse physical QOL. At week 1, recalling the week after chemotherapy administration, problems with daytime function and sleep quality were associated with worse cancer-related QOL. The final 2 weeks showed associations between daytime function problems and worse psychosocial QOL.

**Table 6:** Moderately Strong Correlations by Week between Fatigue, Sleep-Wake Disturbances, and Quality Life in 20 Adolescents Receiving Chemotherapy

Bivariate Pairs of Study Variables	Week 1 (Baseline)	Week 2	Week 3	Week 4	Week 5
General fatigue and Sleep quality	-0.49	—	—	—	—
Cognitive fatigue and Daytime function	—	-0.53	—	—	—
Sleep quality	-0.54	—	—	—	—
Total fatigue and Psychosocial QOL	0.51	—	—	—	—
Daytime function and Cancer-related QOL	—	-0.55	—	—	—
Physical QOL	-0.49	—	—	—	—
Psychosocial QOL	—	—	—	-0.59	-0.59
Sleep quality and Cancer-related QOL	—	-0.51	-0.54	—	—
Physical QOL	-0.55	—	—	—	—

Daytime function and sleep quality: Higher scores indicate more frequent complaints.

Fatigue and QOL: Higher scores indicate better QOL and fewer problems.

$P < 0.01$  (2-tailed). —, not significant.

### *Differences between Groups*

Data were explored at week 2 (highest symptom severity) to determine whether age and length of time on chemotherapy affected the symptoms of fatigue and sleep-wake disturbances. Age was not associated with PedsQL MFS total scores, GSDS daytime function subscale scores, or GSDS sleep quality subscale scores. No significant associations were found between the length of time on chemotherapy and PedsQL MFS total scores, GSDS daytime function subscale scores, or GSDS sleep quality subscale scores.

Mann-Whitney U tests were used to examine differences in fatigue and sleep-wake disturbances between male and female adolescents and between groups based on diagnosis (leukemia and lymphoma versus solid tumor) at week 2. No significant sex or diagnostic group differences were found in fatigue severity, GSDS daytime function subscale scores, or GSDS sleep quality subscale scores.

### CONCLUSIONS

This study explored self-reports of fatigue, sleep-wake disturbances, and quality of life from 20 adolescents over 1 month during first-line chemotherapy. These adolescents were undergoing chemotherapy for the most common cancer diagnoses in this age group, including acute lymphoblastic leukemia, lymphoma, and sarcoma. The sample was mostly White (85%) with equal numbers of males and female patients, and the participants represented every age between 12 and 19 years. The 7 patients who declined to participate were all White, both males and females, and significantly younger than the study sample (mean age=13.9 y,  $t=2.47$ ,  $P < 0.05$ ). Six were receiving treatment for a hematologic cancer. Although their most frequent reasons for not participating included “not interested” and “sounds like too much work,” it is possible that the nonparticipants chose not to participate because of the effects of fatigue. These study results, therefore, may not capture the experience of younger adolescent patients who may be significantly limited by fatigue.

## *Fatigue*

The majority of adolescents in this sample reported fatigue during the month of chemotherapy. Weekly scores for this adolescent sample (mean age=16 y) reflected more problems with fatigue than the younger children with cancer (mean age=8.72 y) but less fatigue than college-age young adults (mean age=20.04 y) with a variety of self-reported chronic illnesses.<sup>30,37</sup> This finding is consistent with other evidence that adolescents with cancer are more bothered by fatigue than younger children.<sup>8,17</sup> Possible explanations for this developmental difference include hormonal changes during puberty and a greater awareness and reporting of fatigue in adolescents than children.<sup>36</sup> Another explanation is that the consequence of greater social and academic involvement for adolescents is increased fatigue.<sup>3,10</sup> Fatigue severity in young adults with cancer has yet to be explored. Adolescents in this study reported fewer problems with cognitive fatigue (difficulty remembering, paying attention, and thinking quickly) than both the younger oncology sample and the sample of young adults with chronic illness.<sup>30,37</sup> These adolescents were either less likely to acknowledge problems with mental fatigue or they maintained their cognitive ability despite complaints of generalized fatigue.

The 5 weekly PedsQL MFS scores did not significantly change across the month of chemotherapy, but the most problems with fatigue (lowest scores) occurred after the first week, when the entire sample received chemotherapy. Other studies with adolescents and adults confirm a pattern of increased fatigue 2 to 4 days after chemotherapy.<sup>38-43</sup>

## *Sleep-wake Disturbances*

These adolescents reported that they were frequently bothered by sleep-wake disturbances, especially daytime symptoms related to not feeling rested, not feeling alert, and feeling sleepy. It is possible that teenagers in this study did not discriminate between self-report of “sleepiness” and “fatigue” and that the instruments did not adequately distinguish between these 2 symptoms. Daytime sleepiness is defined by sleep researchers as “poor vigilance, lack of alertness, and the tendency to fall asleep” and is driven by an increasing sleep debt owing to insufficient sleep.<sup>44</sup> The National Comprehensive Cancer Network (NCCN) defines fatigue as a “sense of tiredness or exhaustion not proportional to recent activity.”<sup>45</sup> Further discussion and research is needed about the measurement challenges related to distinguishing between the symptoms of sleepiness and fatigue. If sleepiness is the desired construct, measurement using an instrument specific to daytime sleepiness, such as the Epworth Sleepiness Scale<sup>46</sup> or the Sleepiness Diary,<sup>47</sup> should be explored. Participants in this study who reported the highest frequency of problems with daytime sleepiness were more likely to be female and to be in the consolidation phase of chemotherapy for ALL. These characteristics should be explored as contributing factors or risk factors for increased symptom severity.

The teens' complaints of daytime sleepiness may result from an insufficient quantity of restorative sleep, confirmed by common responses indicating problems with difficulty falling asleep, getting too little sleep, waking during the night, and waking too early. Insomnia, the complaint of an inadequate quantity and quality of sleep, is the most common sleep-related problem in adults with cancer, reported to affect more than half of the population with cancer.<sup>48,49</sup> Incidence and prevalence rates of cancer-related insomnia need to be described in adolescents, including the specific types of insomnia (eg, initiation insomnia versus maintenance insomnia) they experience. Many factors influence cancer-related insomnia, especially

hospitalization and other symptoms, such as pain.<sup>6,17</sup> The majority of adolescents in this study, however, were not hospitalized, and their sleep-wake disturbances reflect sleeping problems in their home environments. Disease-related and treatment-related factors likely add to preexisting lifestyle factors and biological changes in pubertal sleep that lead to disrupted sleep in adolescents with cancer.<sup>50-52</sup>

In this study, few teenagers reported the use of prescribed and over-the-counter or other substances to relieve their sleep problems and chemotherapy-related side effects. It would be helpful to explore what strategies, if any, the adolescents use to facilitate sleep and what sleep-promoting recommendations they receive from health care providers.

### *Relationship between Fatigue, Sleep-wake Disturbances, and the Quality of Life*

At the time of chemotherapy administration, fatigue was associated with problems with sleep quality and daytime function, which in turn were associated with physical aspects of QOL. The association between fatigue and sleep disturbances has been established in several studies.<sup>23,53,54</sup> Hinds et al<sup>17</sup> confirmed the relationship between fragmented sleep and fatigue in a sample of children and adolescents, suggesting a cycle in which sleep interruptions contribute to increased daytime fatigue, leading to longer but less efficient sleep periods. Longer periods of sleep lead to decreased daytime activities and disrupted sleep on subsequent nights, which over time may result in less robust circadian activity rhythms. Such depressed activity rhythms are considered an undesirable outcome and have been linked to higher fatigue levels in adults with cancer.<sup>20,55,56</sup> Strategies that enhance efficient sleep and help teenagers maintain robust activity patterns need to be explored as interventions to relieve both sleep-wake disturbances and fatigue.

In the weeks after chemotherapy administration, findings suggest associations between daytime function, cancer-related symptoms, and psychosocial QOL and between sleep quality and cancer-related symptoms. On the PedsQL Cancer Module, these teenagers reported treatment-related symptoms, such as nausea, pain, worry, and anxiety, which may have affected their affected sleep, mood, and interpersonal activities. Adolescents who are too tired to see friends and participate in the social and school activities are unlikely to feel a sense of well-being and satisfaction with their quality of life. Studies with adult oncology patients confirm the profound negative impact of fatigue and sleep-wake disturbances on health-related outcomes and quality of life throughout the cancer trajectory.<sup>57-59</sup> In addition, studies have linked insufficient sleep in healthy adolescents with multiple negative outcomes, including poor school performance, behavior and mood problems, and unintentional injuries, chronic illness, and death from accidents.<sup>50</sup> Co-occurring fatigue, sleep-wake disturbances, depression, and other symptoms need further study in adolescents with cancer, to explore common underlying physiologic pathways and their impact on developmental aspects of physical, emotional, and social performance.<sup>60,22</sup>

### *Limitations*

This research has several limitations that need to be considered when interpreting the results. This study reports subjective findings from a small convenience sample of adolescents receiving chemotherapy without a control or a comparison group. As this sample of teenagers had a variety of cancer diagnoses and were receiving various chemotherapy regimens and schedules, no conclusions about symptom responses can be drawn about specific cancer diagnoses or

chemotherapy regimens. The PedsQL instruments have psychometric data to support their use with adolescents, but self-report instruments to measure sleep-wake disturbances in adolescents with cancer need further development. This study provided initial evidence for acceptable reliability of 2 of 3 subscales (sleep quality and daytime function) of the GSDS when used with adolescents.

### *Recommendations for Practice and Research*

Clinicians should not underestimate the impact of fatigue and sleep-wake disturbances on the quality of life of adolescents who are receiving chemotherapy. As fatigue and sleep-wake disturbances are so common, they should be included in routine assessments during cancer therapy, especially during the week of chemotherapy administration, when symptom severity is high. Clinicians can screen adolescent patients for fatigue severity using the numerical rating scale recommended in the NCCN guidelines.<sup>45</sup> A number of screening tools are also available for clinicians to use to identify adolescents with sleep-wake disturbances. The “BEARS” screening tool is one practical guide recommended for sleep screening and assessment that includes questions that assess 5 major sleep domains: “B” is for bedtime problems, “E” is for excessive daytime sleepiness, “A” is for night-time awakenings, “R” is for regularity of sleep, and “S” is for sleep-disordered breathing.<sup>61</sup>

Causes of fatigue and sleep disruption, whether associated with cancer treatment, hospitalization, or with the adolescents' lifestyle, should be identified and considered important points for intervention to facilitate optimal activity/rest patterns for teenagers with cancer. Scheduling restorative sleep during chemotherapy may play a critical role in minimizing fatigue and other physical and psychosocial symptoms. Clinicians need to stress the importance of optimizing daily periods of activity and rest and strategize with adolescents about ways to maintain regular schedules and involvement in developmentally critical activities despite the irregularities that accompany rigorous chemotherapy regimens. Clinicians may consult resources on the website of the Oncology Nursing Society (ONS) (<http://www.ons.org/outcomes>) for evidence-based interventions that have been evaluated to relieve fatigue and sleep-wake disturbances in adults with cancer. Interventions to prevent and manage fatigue and sleep-wake disturbances include a variety of cognitive-behavioral therapies, complementary therapies, psychoeducational and information interventions, energy conservation and activity management, and exercise.<sup>58,62</sup> The benefits and risks of pharmacologic management of common sleep-problems in adolescents should also be considered.<sup>63</sup>

Prospective research with both subjective and objective sleep measurement is needed with larger samples of adolescents to investigate the specific sleep-wake disturbances of adolescents with cancer, especially related to insomnia, daytime symptoms such as sleepiness and irritability, and daily patterns of activity and rest. Interventions that show evidence for effective symptom management, both pharmacologic and nonpharmacologic, are needed to decrease the symptom burden of fatigue and sleep-wake disturbances for adolescents during cancer chemotherapy and improve their quality of life.

### REFERENCES

1. Di Gallo A, Felder-Puig R, Topf RJ. Quality of life from research and clinical perspectives: an example from paediatric psycho-oncology *Clin Child Psychol Psychiatry*. 2007;12:599–610

2. Hinds PS, Gattuso JS, Fletcher A, et al. Quality of life as conveyed by pediatric patients with cancer *Qual Life Res.* 2004;13:761–772
3. Gibson F, Mulhall AB, Richardson A, et al. A phenomenologic study of fatigue in adolescents receiving treatment for cancer *Oncol Nurs Forum.* 2005;32:651–660
4. Hedstrom M, Ljungman G, von Essen L. Perceptions of distress among adolescents recently diagnosed with cancer *J Pediatr Hematol Oncol.* 2005;27:15–22
5. Hockenberry-Eaton M, Hinds PS, Alcoser P, et al. Fatigue in children and adolescents with cancer *J Pediatr Oncol Nurs.* 1998;15:172–182
6. Jalmsell L, Kreicbergs U, Onelov E, et al. Symptoms affecting children with malignancies during the last month of life: a nationwide follow-up *Pediatrics.* 2006;117:1314–1320
7. Hinds P, Scholes S, Gattuso J, et al. Adaptation to illness in adolescents with cancer *J Pediatr Oncol Nurs.* 1990;7:64–65
8. Meeske K, Katz ER, Palmer SN, et al. Parent proxy-reported health-related quality of life and fatigue in pediatric patients diagnosed with brain tumors and acute lymphoblastic leukemia *Cancer.* 2004;101:2116–2125
9. Phipps S, Dunavant M, Garvie PA, et al. Acute health-related quality of life in children undergoing stem cell transplant: I. Descriptive outcomes *Bone Marrow Transplant.* 2002;29:425–434
10. Ream E, Gibson F, Edwards J, et al. Experience of fatigue in adolescents living with cancer *Cancer Nurs.* 2006;29:317–326
11. Langeveld N, Ubbink M, Smets E. “I don't have any energy”: the experience of fatigue in young adult survivors of childhood cancer *Eur J Oncol Nurs.* 2000;4:20–28
12. Langeveld NE, Grootenhuis MA, Voute PA, et al. No excess fatigue in young adult survivors of childhood cancer *Eur J Cancer.* 2003;39:204–124
13. Meeske KA, Siegel SE, Globe DR, et al. Prevalence and correlates of fatigue in long-term survivors of childhood leukemia *J Clin Oncol.* 2005;24:5501–5509
14. Ng A, Si S, Recklitis C, et al. A comparison between long-term survivors of Hodgkin's disease and their siblings on fatigue level and factors predicting for increased fatigue *Ann Oncol.* 2005;16:1949–1955
15. Davies B, Whitsett SF, Bruce A, et al. A typology of fatigue in children with cancer *J Pediatr Oncol Nurs.* 2002;19:12–21
16. Gedaly-Duff V, Lee KA, Nail LM, et al. Pain, sleep disturbance, and fatigue in children with leukemia and their parents: a pilot study *Oncol Nurs Forum.* 2006;33:641–646
17. Hinds PS, Hockenberry M, Rai SN, et al. Nocturnal awakenings, sleep environment interruptions, and fatigue in hospitalized children with cancer *Oncol Nurs Forum.* 2007;34:393–402
18. Hinds P, Hockenberry M, Srivastava DK, et al. Sleep, fatigue, and dexamethasone in children and adolescents with acute lymphocytic leukemia (ALL) *Oncol Nurs Forum.* 2007;34:199

19. Barsevick AM. The elusive concept of the symptom cluster *Oncol Nurs Forum*. 2007;34:971–980
20. Berger AM, Parker KP, Young-McCaughan S, et al. Sleep-wake disturbances in people with cancer and their caregivers: state of the science *Oncol Nurs Forum*. 2005;32:E98–E126
21. Dodd MJ, Miaskowski C, Lee KA. Occurrence of symptom clusters *J Natl Cancer Inst*. 2004;32:76–78
22. Hockenberry M, Hooke MC. Symptom clusters in children with cancer *Semin Oncol Nurs*. 2007;23:152–157
23. Roscoe JA, Kaufman ME, Matteson-Rusby SE, et al. Cancer-related fatigue and sleep disorders *Oncologist*. 2007;12:35–42
24. Albritton K, Bleyer WA. The management of cancer in the older adolescent *Eur J Cancer*. 2003;39:2584–2599
25. Anderson B, Albritton K, et al. Bleyer A, O'Leary M, Barr R Foreword *Cancer epidemiology in older adolescents and young adults 15 to 29 years of age, including SEER incidence and survival: 1975 to 2000* 2006 Bethesda, MD National Cancer Institute
26. Landolt MA, Vollrath M, Niggli FK, et al. Health-related quality of life in children with newly diagnosed cancer: a one year follow-up study *Health Qual Life Outcomes*. 2006;4:63–70
27. Challinor JM, Miaskowski CA, Franck LS, et al. Somatization, anxiety, and depression as measures of health-related quality of life children/adolescents with cancer *Int J Cancer*. 1999;12S:52–27
28. Magal-Vardi L, Laor N, Toren A, et al. Psychiatric morbidity and quality of life in children with malignancies and their parents *J Nerv Ment Dis*. 2004;192:872–875
29. Bhat SR, Goodwin TL, Burwinkle TM, et al. Profile of daily life in children with brain tumors: an assessment of health-related quality of life *J Clin Oncol*. 2005;24:5493–5500
30. Varni JW, Burwinkle TM, Katz ER, et al. 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*. 2002;94:2090–2106
31. Lee KA. Self-reported sleep disturbances in employed women *Sleep*. 1992;15:493–498
32. American Psychiatric Association *The Diagnostic and Statistical Manual of Mental Disorders* 2000 4th ed Washington, DC American Psychiatric Association
33. Lee KA, DeJoseph JF. Sleep disturbances, vitality, and fatigue among a select group of employed childbearing women *Birth*. 1992;19:208–213
34. Lee KA, Portillo CJ, Miramontes H. The fatigue experience for women with human immunodeficiency virus *J Obstet Gynecol Neonatal Nurs*. 1999;28:193–200
35. Lee S. Validating the general sleep disturbance scale among Chinese American parents with hospitalized infants *J Transcult Nurs*. 2007;18:111–117
36. Wolbeek M, van Doornen LJ, Kavelaars A, et al. Severe fatigue in adolescents: a common phenomenon? *Pediatrics*. 2006;117:e1078–e1086

37. Varni JW, Limbers CA. The PedsQL™ Multidimensional Fatigue Scale in young adults: feasibility, reliability and validity in a University student population *Qual Life Res.* 2008;17:105–114
38. Erickson JM *Fatigue and Sleep Disturbances in Adolescents Receiving Chemotherapy.* Unpublished Doctoral Dissertation 2008 Salt Lake City University of Utah
39. Yeh C, Chiang Y, Yang C, et al. Clinical factors associated with fatigue over time in paediatric oncology patients receiving chemotherapy *Br J Cancer.* 2008;99:23–29
40. Berger AM. Patterns of fatigue and activity and rest during adjuvant breast cancer chemotherapy *Oncol Nurs Forum.* 1998;25:51–62
41. Miller M, Maguire R, Kearney N. Patterns of fatigue during a course of chemotherapy: Results from a multi-centre study *Eur J Oncol Nurs.* 2007;11:126–132
42. Schwartz A. Daily fatigue patterns and effect of exercise in women with breast cancer *Cancer Pract.* 2000;8:16–24
43. Stasi R, Abriani L, Beccaglia P, et al. Cancer-related fatigue: evolving concepts in evaluation and treatment *Cancer.* 2003;98:1786–1801
44. Partinen M, Hublin CKryger MH, Roth T, Dement WC. Epidemiology of sleep disorders *Principles and Practice of Sleep Medicine* 20054th ed Philadelphia Elsevier- Saunders:626–647
45. National Comprehensive Cancer Network. Cancer-related fatigue. Version 2. Retrieved from [www.nccn.org/on](http://www.nccn.org/on) April 30, 2007.
46. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale *Sleep.* 1991;14:540–545
47. National Sleep Foundation. Sleepiness diary. Retrieved January 2, 2007, from [http://www.sleepfoundation.org/site/c.huIXKjM0IxF/b.2419099/k.9DD7/Sleepiness\\_Diary.htm](http://www.sleepfoundation.org/site/c.huIXKjM0IxF/b.2419099/k.9DD7/Sleepiness_Diary.htm).
48. Graci G. Pathogenesis and management of cancer-related insomnia *J Support Oncol.* 2005;3:349–359
49. Lee K, Cho M, Miaskowski C, et al. Impaired sleep and rhythms in persons with cancer *Sleep Med Rev.* 2004;8:199–212
50. National Sleep Foundation *Adolescent Sleep Needs and Patterns* 2000 Washington, DC National Sleep Foundation
51. Millman RP. Excessive sleepiness in adolescents and young adults: causes, consequences, and treatment strategies *Pediatrics.* 2005;115:1774–1786
52. Carskadon MA, Vieri C, Acebo C. Association between puberty and delayed phase preference *Sleep.* 1993;16:258–262
53. Davidson JR, MacLean AW, Brundage MD, et al. Sleep disturbance in cancer patients *Soc Sci Med.* 2002;54:1309–1321
54. Servaes P, Verhagen C, Bleijender G. Fatigue in cancer patients during and after treatment: prevalence, correlates, and interventions *Eur J Cancer.* 2002;38:27–43

55. Levin RD, Daehler MA, Grutsch JF, et al. Circadian function in patients with advanced non-small-cell lung cancer *Br J Cancer*. 2005;93:1202–1208
56. Rich T, Innominato PF, Boerner J, et al. Elevated serum cytokines correlated with altered behavior, serum cortisol rhythm, and dampened 24-hour rest-activity patterns in patients with metastatic colorectal cancer *Clin Cancer Res*. 2005;11:1757–1764
57. Hofman M, Ryan JL, Figueroa-Moseley CD, et al. Cancer-related fatigue: the scale of the problem *Oncologist*. 2007;12S:4–10
58. Mitchell SA, Beck SL, Hood LE, et al. Putting evidence into practice: evidence-based interventions for fatigue during and following cancer and its treatment *Clin J Oncol Nurs*. 2007;11:99–113
59. Clark J, Cunningham M, McMillan S, et al. Sleep-wake disturbances in people with cancer. Part II: evaluating the evidence for clinical decision making *Oncol Nurs Forum*. 2004;31:747–768
60. Miaskowski C, Aouizerat BE, Dodd M, et al. Conceptual issues in symptom clusters research and their implications for quality-of-life assessment in patients with cancer *J Natl Cancer Inst*. 2007;37:39–46
61. Owens JA, Dalzell V. Use of the “BEARS” sleep screening tool in a pediatric residents' continuity clinic: a pilot study *Sleep Med*. 2005;6:63–69
62. Page MS, Berger AM, Johnson LB. Putting evidence into practice: evidence-based interventions for sleep-wake disturbances *Clin J Oncol Nurs*. 2006;10:753–767
63. Mindell JA, Emslie G, Blumer J, et al. Pharmacologic management of insomnia in children and adolescents: consensus statement *Pediatrics*. 2006;117:e1223–e1232