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PSYCHOSOCIAL AND SUPPORTIVE CARE: RESEARCH ARTICLE

Internet-delivered insomnia intervention improves sleep and quality of life for adolescent and young adult cancer survivors

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Abstract

Background: Insomnia is common among adolescent and young adult (AYA) cancer survivors. Cognitive-behavioral therapy for insomnia (CBT-I) is considered the gold standard treatment. Standard CBT-I was designed for adults and not adapted to the unique medical, psychosocial, and developmental needs of AYA cancer survivors, which can exacerbate their insomnia. Further, the vast majority of cancer centers do not have a behavioral sleep medicine expert on staff. Our study objective was to examine the efficacy of an Internet-delivered CBT-I program that was tailored for AYA cancer survivors (NCT03279055).

Procedure: Twenty-two AYA cancer survivors (mean age 20.4; range 14-25) with insomnia enrolled in an automated CBT-I program modified for AYA cancer survivors following stakeholder feedback. Participants were blood cancer (54.5%) and solid tumor (45.5%) survivors, an average of 9.7 years postdiagnosis. Sleep health, fatigue, and quality of life were assessed at baseline and at two follow up timepoints (8 and 16 weeks postbaseline).

Results: Significant improvements in insomnia severity, daytime sleepiness, fatigue, and quality of life were reported at both follow up timepoints. However, most participants (72.7%) did not complete all of the six study sessions, with a mean completion rate of 3.2 sessions. Participants who completed at least two sessions reported better sleep (insomnia severity index total score) than those who did not.

Conclusions: An Internet-delivered insomnia intervention adapted for AYA cancer survivors was efficacious. This has important implications for access to evidence-based clinical care for this growing population. Future efforts should study stepped care models of care and ways to improve treatment adherence.

KEYWORDS
adolescent and young adult cancer survivors, cognitive-behavioral therapy for insomnia, insomnia disorder, online intervention

1 | INTRODUCTION

Adolescent and young adult (AYA) cancer survivors are at significant risk for medical and psychological disorders as a result of their cancer-directed therapies.[1] One common problem is insomnia: many AYA cancer survivors struggle with falling and/or staying asleep, resulting in

Abbreviations: AYA, adolescent and young adult; CBT-I, cognitive-behavioral therapy for insomnia; ISI, insomnia severity index; PDSS, pediatric daytime sleepiness scale; PedsQL, pediatric quality-of-life inventory; SHUTi, sleep healthy using the internet; SHUTi-AYA, sleep healthy using the internet for adolescents and young adults

daytime impairment following cancer treatment.[2] Unfortunately, this often persists with over 25% of childhood cancer survivors suffering from insomnia symptoms up to 20 years later,[3-5] compared to approximately 12% in general population adolescents.[6] We know that chronic insomnia is associated with the development or exacerbation of many behavioral, physical, and psychological health problems[7-12] in a patient population already at risk for health morbidities. Given its prevalence and impact on key health outcomes, there is a clear need for evidence-based treatment.

Cognitive-behavioral therapy for insomnia (CBT-I) is a multicomponent intervention (sleep restriction, stimulus control, sleep hygiene, cognitive restructuring, and relaxation training)[13] and is considered "front-line treatment."[14] Research has demonstrated that CBT-I is highly effective in many patient populations, including in adult cancer survivors.[15-18] Unfortunately, very few studies have been about CBT-I in the AYA cancer survivor group. This is a problem because adult CBT-I protocols may not address key factors that can impact the sleep of AYA cancer survivors. This includes developmentally normative delays in when they sleep, different sleep duration requirements,[19-22] and social and sleep environment constraints (eg, inflexible school start times, disruptive roommates, etc). Further, standard (noncancer specific) CBT-I protocols typically do not take into account common long-term sequelae that interfere with sleep (eg, pain and fatigue).[23] Previously, we demonstrated that CBT-I tailored to be developmentally and disease-appropriate for AYA cancer survivors was efficacious at improving insomnia and quality of life.[24] However, it required an interventionist to deliver CBT-I.

A notable barrier to insomnia treatment is a shortage of trained CBT-I providers.[25] This includes limited access to CBT-I at cancer centers across the country.[26] Consequently, a recent review concluded that "it is imperative to develop alternatives to face-to-face sessions for the treatment of insomnia in patients with cancer."[27] Internet-delivered CBT-I holds great promise, with considerable evidence demonstrating efficacy that is comparable to face-to-face CBT-I.[28] There is an additional benefit that these programs are often fully automated and require few resources in order to be able to offer it to patients with insomnia. One such program is SHUTi (sleep healthy using the internet), which improves insomnia and other health outcomes across a wide range of healthy and comorbid populations, including cancer survivors.[29-34] However, these studies have only been conducted in adults.

In this trial, we sought to build upon our pilot CBT-I program developed for AYA cancer survivors by adapting SHUTi for this unique patient population. We present data from our single arm efficacy trial of SHUTi adapted for AYA cancer survivors (SHUTi-AYA).

2 | METHODS

2.1 | Participants

To be eligible for this study, participants had to: (a) be between 14 and 25 years of age; (b) have a cancer history; (c) have completed cancer-directed therapy ≥3 months ago; (d) be able to access the internet at home; (e) meet diagnostic criteria for insomnia disorder[35]; and (f) have a total insomnia severity index (ISI)[36] score ≥11. Potential participants were excluded if they: (a) had planned cancer therapy in the next 6 months; (b) reported an untreated sleep disorder other than insomnia; (c) worked overnight or rotating shifts; (d) reported frequent travel across time zones; (e) had been diagnosed with bipolar disorder, seizure disorder, or experienced a seizure within the past year; (f) routinely consumed ≥15 alcoholic beverages per week; (g) planned to adjust their use of any sleep-related medications; or (h) had previously attempted CBT-I. Potential participants were recruited via one of the following four ways: (a) research staff approached patients at the time of their medical appointment; (b) referral from the patient's medical provider; (c) mailed letter to a longitudinal cohort of childhood cancer survivors at our cancer center[4,5,37-39]; or (d) recruitment at a national conference for young adult cancer survivors conference. The study was approved by the cancer center's institutional review board and informed consent of participants (or their parents for those <18 years of age) was obtained for all participants. This trial was registered at clinicaltrials.gov (NCT03279055).

Of the 59 potential participants screened for eligibility, eight declined participation, and 29 were excluded (not meeting insomnia criteria [16]; medical and/or psychiatric comorbidities [five]; personal circumstances that would interfere with participation [three]; upcoming cancer-directed treatments [two]; excessive alcohol use [one]; irregular work schedule [one]; and a history of CBT-I [one]). A total of 22 AYA cancer survivors enrolled.

2.2 | Intervention

Standard SHUTi is comprised of six intervention sessions designed to be delivered over the course of approximately 6-8 weeks. SHUTi content is based on fundamental CBT-I intervention strategies including sleep restriction, stimulus control, cognitive therapy, sleep hygiene, and relapse prevention to treat the underlying factors perpetuating the insomnia. It is a fully automated program designed to not require external support once a participant has started treatment and includes a variety of interactive features, including personalized goal setting, graphical feedback based on insomnia symptom severity, patient vignettes, and video-based expert explanations.

The standard version of SHUTi, designed for adults without a cancer history, was tailored to the AYA cancer survivor population based upon feedback received from key stakeholders (AYA cancer survivor, pediatric oncologist, pediatric sleep medicine physician, pediatric psychosocial clinician, and behavioral sleep medicine expert) after reviewing SHUTi content. Notable adaptations to the content of standard SHUTi program included: (a) psychoeducation regarding the prevalence and precipitants of insomnia in the context of a cancer history; (b) discussion of the impact of common medical (fatigue, pain, and medication side effects) and psychological (fear of recurrence) factors that could cause/worsen insomnia; (c) explanation of circadian tendencies

in AYAs and its potential contribution to difficulty with sleep initiation; (d) information about the negative impact of alcohol consumption on sleep maintenance and quality; and (e) suggestions for how to engage the participant's family and/or friends (particularly roommates) in supporting the insomnia intervention. Further changes were made to the visual appearance of the program, which included: (a) replacing images of older adults in the standard SHUTi program with images of AYAs in the study age range; (b) introducing images of our cancer center clinics; and (c) updating the expert videos to include the study's principal investigator.

2.3 | Procedures

Participants were provided with personalized login information granting them access to SHUTi-AYA. Each session of the six-session automated program was designed with a 1-week break between sessions to allow participants to implement intervention strategies. Our study participants were instructed to complete SHUTi-AYA with an 8-week window, with program access shut off after 8 weeks. SHUTi-AYA was delivered without any research staff engagement once participants were instructed on how to successfully log in and navigate the website. SHUTi-AYA automatically sent out reminder emails to participants in order to maintain user engagement.

All study measures were collected at baseline (prior to intervention), follow up 1 (8 weeks postbaseline), and follow up 2 (16 weeks postbaseline). Once participants completed their baseline assessment, they were provided with packets containing the follow up assessments and stamped addressed return envelopes. Phone calls were scheduled for each of their follow up assessments. During each of the follow up assessment phone calls, research staff asked participants to provide their responses for the ISI to ensure data collection for our primary study outcome, and then asked participants to return the full completed assessment packet by mail (including the ISI).

2.4 | Measures

Demographics and medical history: Demographic information, as well as medical information including cancer diagnosis and treatment, were collected by medical record review as well as direct participant report at the baseline assessment only.

ISI[36]: The ISI served as our primary study outcome measure and is the most commonly used measure in insomnia research. It has been validated in cancer populations.[40] In a community-based adult sample, mean ISI scores are 7.3,[41] and the average is 8.7 in a sample of adult breast cancer patients.[40] The ISI has demonstrated adequate internal consistency, and is sensitive to detect changes in perceived sleep difficulties with treatment. A clinically meaningful improvement to insomnia symptoms is seen when there is a ≥6-point reduction in the ISI total score.[42] In clinical samples, ISI scores of ≥11 is associated with 100% specificity for detecting insomnia cases.[43] Internal consistency for the ISI (Cronbach's α = .93) was excellent.

Pediatric daytime sleepiness scale (PDSS)[44]: The PDSS is an eight-item questionnaire designed to assess excessive daytime sleepiness (EDS) in adolescents. EDS encompasses subjective experiences of daytime sleepiness and drowsiness in a variety of settings throughout the day. Internal consistency for the PDSS (Cronbach's α = .64) was acceptable.

Pediatric quality-of-life inventory (PedsQL)[45]: The PedsQL is a modular system designed to assess health-related quality of life in populations under 26 years of age. The 23-item PedsQL generic core scale comprises four multidimensional scales: physical, emotional, social, and school functioning. Internal consistency for the PedsQL (Cronbach's α = .90) was excellent.

Pediatric quality-of-life inventory multidimensional fatigue scale (PedsQL multidimensional fatigue scale)[45]: The PedsQL multidimensional fatigue scale is an 18-item measure designed to measure fatigue in pediatric cancer populations. It encompasses three subscales: general fatigue, sleep/rest fatigue, and cognitive fatigue. Internal consistency for the PedsQL multidimensional fatigue scale (Cronbach's α = .91) was excellent.

Sleep diaries: Sleep diaries were collected by SHUTi-AYA beginning in session 2. They inquired about time to bed, sleep onset latency, night wakings, wake after sleep onset, and wake times. The participant's total sleep duration and sleep efficiency (commonly used by sleep clinicians; computed by dividing total time spent in bed by total sleep duration with 85% conventionally considered the clinically significant cutoff[46]) were calculated from this information.

Intervention adherence: SHUTi-AYA automatically collected data on the number of intervention scores that each participant completed during the course of the trial.

2.5 | Statistical analysis

Descriptive statistics were calculated for study demographic, disease specific, sleep (ISI and sleep diary), and intervention adherence data. The primary analysis of comparing ISI total scores between baseline and the two follow up assessments and between each of the follow up assessments was conducted using two-sided paired samples *t*-tests. Similarly, two-sided paired samples *t*-tests were conducted to compare baseline and the two follow up assessments for secondary measures including the PDSS, PedsQL, and PedsQL multidimensional fatigue scale. Cohen's *d* was calculated as a measure of effect size relative to baseline data. One-way ANOVAs were calculated to evaluate whether a minimum core completion was associated with change in ISI scores between baseline and the follow up assessments, as well as for assessing whether time since treatment was associated with baseline and follow up ISI and intervention completion. Pearson correlation coefficients were calculated for the relationship between time since diagnosis and baseline and follow up ISI and intervention completion. Missing data were addressed using listwise deletion.

TABLE 1 Demographic and cancer-related descriptives (N = 22)

	$\bar{x}$ (SD)	N (%)
Demographic		
Age (years)	20.4 (3.6)	
Gender		
Male		12 (54.5)
Female		10 (45.5)
Ethnicity		
Non-Hispanic White		17 (77.3)
Hispanic		3 (13.6)
African-American		2 (9.1)
Education		
≤High school diploma		11 (50.0)
≥College education		11 (50.0)
Cancer related		
Primary diagnosis		
Blood cancer		12 (54.5)
Solid tumor		10 (45.5)
Time since diagnosis (years)	9.7 (7.2)	
Time since treatment (years)		
<1 year		2 (9.1)
1-5 years		10 (45.5)
6-10 years		4 (18.2)
11-20 years		5 (22.7)
>20 years		1 (4.5)
Chemotherapy		
Yes		22 (100)
No		0
Radiation therapy		
Yes		11 (50.0)
No		11 (50.0)
Surgery		
Yes		12 (54.5)
No		10 (45.5)
Transplant		
Yes		3 (13.6)
No		19 (86.4)

3 | RESULTS

Enrolled study participants (12 males, 10 females) were an average of 20.4 years of age (SD 3.6 years; range 14.0-25.0 years) and primarily non-Hispanic White (77.3%) (Table 1). Fifty percent of the sample had completed at least some postsecondary education. The participants were primarily survivors of blood cancer (54.5%), an average of 9.7 years postdiagnosis (SD 7.1 years; range 1.0-23.0 years) and between 1 and 5 years posttreatment (45.5%). Eight of the 22 enrolled participants (36.4%) reported they were taking a medication for sleep (eg, clonazepam, mirtazapine, hydroxyzine, melatonin, and diphenhydramine).

Participants completed an average of 3.2 SHUTi-AYA sessions (SD 2.3; range 0-6). As seen in Figure 1, there was a range in session completion. For example, three participants (13.6%) completed 0 sessions while six participants (27.3%) completed all six sessions. Time since diagnosis and time since treatment were not significantly associated with the number of sessions completed.

At the follow up 1 assessment, participants reported statistically significant improvements in the primary study outcome (ISI) and secondary study outcomes (PDSS, PedsQL, and PedsQL multidimensional fatigue scale scores; Table 2). These gains were maintained at their follow up 2 assessment across all study measures (ISI, PDSS, PedsQL, and PedsQL multidimensional fatigue scale). At the follow up 1 assessment, 50.0% of participants reported their ISI score had decreased by 6.0 points or greater. At the follow up 2 assessment this proportion increased to 71.4% of participants. Time since diagnosis and time since treatment were not significantly associated with ISI scores at baseline or either follow up. Among participants completing at least two SHUTi-AYA sessions (n = 15), their ISI scores decreased 5.1 points between baseline to follow up 1 and decreased 10.0 points from baseline to follow up 2. The average ISI change from baseline to follow up 1 for participants who completed at least two sessions was significantly greater than those who did not. Participants who completed at least three SHUTi-AYA sessions (n = 12) saw their ISI score decrease from baseline by 7.5 points at follow up 1 and by 10.9 points at follow up 2 (Table 3). Improvements to the participant's sleep were also noted in the sleep diary outcomes collected by SHUTi-AYA. The first week of sleep diaries collected by SHUTi-AYA during session 2 showed an average participant sleep efficiency of 80.3%, which is clinically indicative of insomnia. This was prior to any behavioral sleep change recommendations by SHUTi-AYA. This improved throughout the intervention, culminating in a sleep efficiency of 90.9% in session 6 (Figure 2).

4 | DISCUSSION

Sleep is essential for physical, psychological, emotional, and overall health in AYAs. Many AYA cancer survivors struggle with insomnia, in addition to the multitude of physical and psychological late effects of their cancer treatments. Despite the knowledge that CBT-I is an effective treatment for insomnia in the adult population, there is scant evidence demonstrating its efficacy in AYA cancer populations. This is important because they experience unique developmental and cancer-related challenges that impact sleep, which should be addressed in their insomnia treatment.

Our results demonstrate that an internet-delivered CBT-I program targeting AYA cancer survivors improved their insomnia, daytime sleepiness, fatigue, and quality of life, and these improvements were maintained up to 2 months following the intervention. The majority of participants reported a clinically meaningful improvement to their insomnia at both follow up timepoints. Notably, our participants'

FIGURE 1 Study intervention session completion

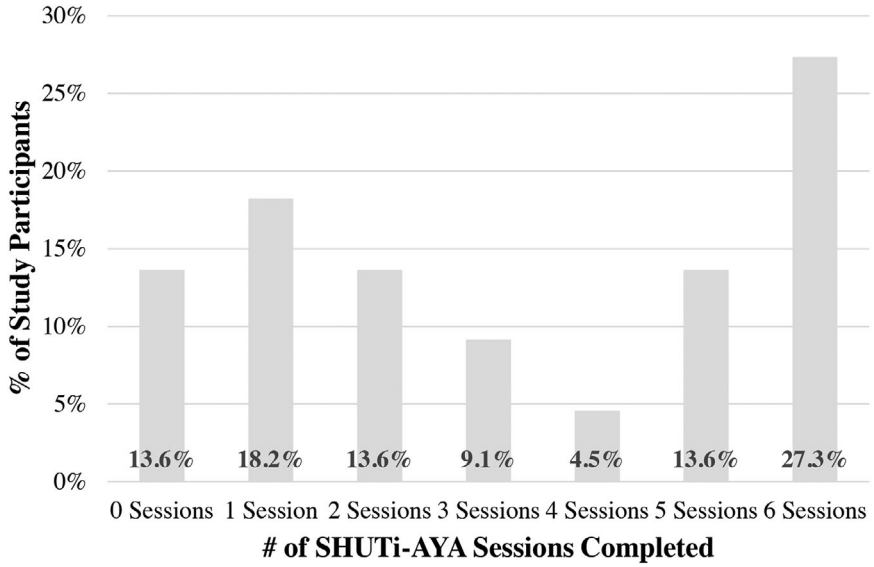

TABLE 2 Sleep and health changes following the intervention

	Baseline (N = 22)	Follow up 1 (n = 16)		Follow up 2 (n = 14)	
	Mean (SD)	Mean (SD)	Effect size (*d*)	Mean (SD)	Effect size (*d*)
Insomnia severity index					
Total summary score	15.2 (2.4)	9.6 (6.7)[a]	1.1	6.0 (4.5)[a,b]	2.5
Pediatric daytime sleepiness scale					
Total summary score	18.8 (4.1)	15.5 (5.1)[a]	0.7	13.0 (4.3)[a]	1.5
PedsQL multidimensional fatigue scale					
Total summary score	46.1 (16.7)	63.2 (22.5)[a]	0.7	70.9 (22.2)[a]	1.2
Pediatric quality-of-life inventory					
Physical function	69.3 (21.6)	76.6 (21.3)[a]	0.3	79.9 (22.8)[a]	0.6
Emotional function	52.7 (19.7)	65.6 (25.3)[a]	0.6	65.4 (27.4)[a]	0.6
Total summary score	64.2 (17.5)	73.0 (20.3)[a]	0.4	75.1 (22.4)[a]	0.5

Note. Follow up 1 occurred 8 weeks postbaseline; Follow up 2 occurred 16 weeks postbaseline.
[a]Follow up 1 or follow up 2 values that are significantly different ($P < .05$) from baseline.
[b]Follow up 2 values that are significantly different ($P < .05$) from follow up 1.

insomnia severity continued to get better after the intervention had ended, suggesting that they continued to make sleep-related decisions that helped their sleep even after the intervention period. The robust effect size seen in our data is comparable to our prior trial of clinician-delivered CBT-I for AYA cancer survivors.[24] This is meaningful as access to CBT-I at cancer centers across the country is limited,[26] whereas the ability for an AYA cancer survivor to log on to our adapted SHUTi-AYA program is essentially limited only by their awareness of the intervention and interest in engaging in insomnia treatment.

Though asynchronous online interventions promise to dramatically expand access to behavioral treatments including CBT-I, these automated interventions are also vulnerable to challenges to adherence. Most AYA cancer survivors in our trial only completed half of the program's six sessions. While a prior trial of the standard SHUTi program delivered to an adult cancer survivor sample (mean age 56.7 years) reported 86% of participants completed all six SHUTi sessions,[33] the much lower level of adherence we found is consistent with data suggesting AYAs are "less adherent than younger or older patients with cancer, even when treated on similar protocols for similar diseases."[49] Adherence in our sample is comparable to a large trial of a different internet-delivered CBT-I intervention (Sleepio) conducted in a similarly aged population (mean age 26.7 years).[50] The average participant in that trial completed 2.8 out of six intervention sessions, with an even higher proportion not completing a single session (31% vs 14% in our sample). Ultimately, interventions cannot be effective as adherence is associated with outcomes. Our data indicated that if a participant completed at least two sessions, they were more likely to benefit more from the program than those who did not, indicating that there may be a minimum "dosage" that is required. As prior trials of SHUTi have suggested that this cutoff may be four sessions,[30] working toward

TABLE 3 Number of SHUTi sessions completed and mean insomnia severity index (ISI) total summary score change

	ISI change from baseline to follow up 1	n	ISI change from baseline to follow up 2	n
≥2 Sessions completed?				
Yes	−5.1*	12	−10.0**	12
No	0	4	−3.0	2
≥3 Sessions completed?				
Yes	−7.5**	10	−10.9	10
No	−2.0	6	−6.8	4

Note. Decreasing scores indicate improving insomnia. Follow up 1 occurred 8 weeks postbaseline; follow up 2 occurred 16 weeks postbaseline.
*$P < .05$. **$P < .10$.

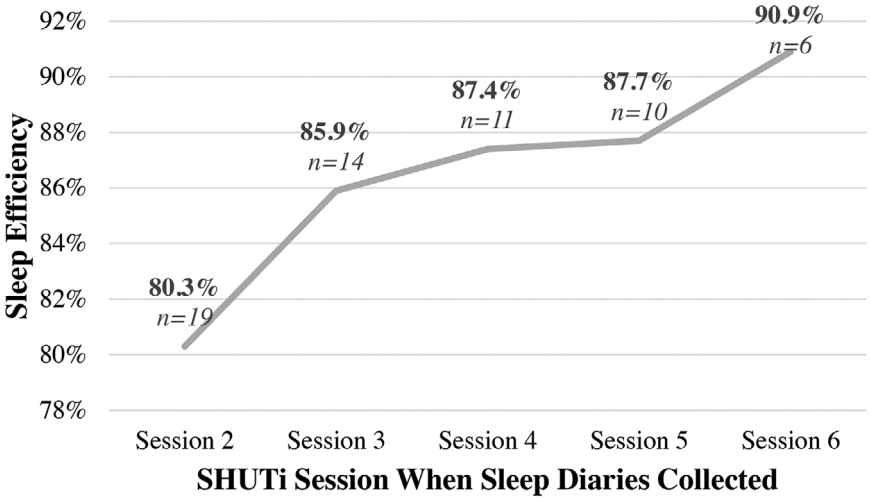

FIGURE 2 Sleep efficiency throughout the intervention
Note: Participants were instructed following their first session to initiate sleep diaries. Therefore, the first set of sleep diary data collected by SHUTi-AYA was in session 2

optimization of the intervention will be important.[51] It is crucial that future trials involving automated interventions in AYA population, test ways to improve adherence. For example, identifying those at higher risk of nonadherence at baseline, incorporating follow up phone calls or text messages, providing more incentives, or using an adaptive intervention design (eg, sequential, multiple assignment, randomized trials[52]) could all be considered. Alternatively, there have been recent efforts to deliver brief insomnia interventions over a one to three sessions that are efficacious.[53,54] Additional efforts to better understand which AYA cancer survivors would benefit from a briefer course of insomnia treatment is an intriguing direction of research.

4.1 | Study limitations

We acknowledge several study limitations that should be addressed in future research. First, our sample was recruited primarily from a single cancer center and comprised primarily of non-Hispanic Whites. A multicenter trial with efforts to recruit a more diverse patient population would ensure that these findings can be generalizable to the broader AYA cancer survivor population. Second, as this study did not include a control arm, we cannot exclude the possibility that insomnia would not have resolved without any active program. It is possible that screening positive for insomnia disorder could have impacted the participant's sleep-related behaviors. Further, we acknowledge that we did not collect sleep diaries at the baseline assessment, and it is possible that the participant's sleep improved between the period from study enrollment to SHUTi-AYA session 2 when sleep diaries were first collected. Conducting a randomized controlled trial, with earlier sleep diary data collection and an appropriate control condition, will be important. Next, we did not collect actigraphy data from our sample. Future research should include objective sleep assessments. In addition, a longer follow up period would be helpful to understand if the positive sleep behavior changes persisted among AYA cancer survivors. Finally, we note that scores in our sample on the PedsQL quality of life and fatigue scales were lower compared to other samples of cancer survivors. For example, the PedsQL total summary score in our sample at baseline was 64.2, while this was 76.0 in a validation study of the scale in AYA cancer survivors,[55] and the PedsQL fatigue total summary score in our sample at baseline was 46.1, while this was 71.5 in a validation study of the scale in adult survivors of childhood cancer.[56] Thus, our sample may not be representative of all AYA cancer survivors.

4.2 | Conclusion

We believe that our novel intervention holds great promise to help treat insomnia in AYA cancer survivors. Internet-delivered insomnia

treatments can be readily disseminated and have the potential to be offered to survivors at any cancer center across the country, with limited burden on that institution's staff. Based on our findings, there are specific next steps that should occur to advance our clinical research, with the ultimate goal of better management of insomnia in the AYA cancer survivor population. Cancer centers providing care for AYA survivors should consider committing resources to routinely screen for sleep disorders and to support patient access to evidence-based insomnia treatment.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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