

Running Head: Sleep Quality, Fatigue and HRQoL among TYA Cancer Survivors

Sleep Quality, Fatigue and Quality of Life among Teenage and Young Adult Cancer Survivors

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Abstract

Purpose: Teenage and young adult (TYA) cancer survivors experience a range of health-related problems during and beyond the active treatment period. This study examined associations between fatigue, sleep quality, and health-related quality of life (HR-QoL) among TYA survivors.

Methods: Self-reported data on sleep quality (Pittsburgh Sleep Quality Index), fatigue (Functional Assessment of Chronic Illness Therapy Fatigue) and HR-QoL (EuroQoL-5) were gathered from UK TYA survivors aged between 13 and 24 years. TYA survivors were stratified into those on (n=67) and off (n=135) treatment. Linear regression analyses were used with HR-QoL as the dependent variable to investigate potential associations. Fatigue and sleep were entered separately, and together in the same model. Age at survey and diagnosis, gender and ethnicity were included as covariates.

Results: 85.07% of TYAs on and 62.69% of TYAs off treatment had sleep quality scores suggestive of clinically significant sleep disorders. 56.72% of TYAs on and 26.67% of TYAs off treatment reported clinically significant levels of fatigue. Strong independent associations between sleep (B=0.05, 95% CI=0.03-0.07, $p<0.001$), fatigue (B=0.02, 95% CI=0.01-0.03, $p<0.001$), and HR-QoL were observed among TYA survivors on treatment. TYAs off treatment showed moderate to strong associations between sleep (B=0.04, 95% CI=0.02-0.05, $p<0.001$) and fatigue (B=0.02, 95% CI=0.01-0.02, $p<0.001$), and HR-QoL, when examined separately. Sleep was not independently associated with HR-QoL among TYAs off treatment (B=0.01, 95% CI=-0.01-0.02, $p=0.296$).

Conclusion: The significant associations reported suggest sleep quality and fatigue are potential modifiable factors associated with HR-QoL. Further research is warranted to understand the direction of associations.

Introduction

Each day seven young people aged between 13 and 24 years (TYA) are diagnosed with cancer in the United Kingdom (UK).¹ Advances in cancer therapies mean the five-year survival rate among TYAs is now >80%.² However, TYA survivors suffer significant impairments in health-related quality of life (HR-QoL) throughout and after treatment^{3,4} including psychosocial and physical limitations experienced up to ten years after treatment.⁵ Identifying potential modifiable factors associated with on and off treatment HR-QoL in TYA survivors is important as targeting these in interventions may in the long-term improve outcomes in this population.

More recently, there has been increasing interest in fatigue.⁶ Fatigue is defined as “a subjective, unpleasant symptom, which incorporates total body feelings ranging from tiredness to exhaustion creating an unrelenting overall condition which interferes with individuals’ ability to function to their normal capacity’.⁷ Fatigue experienced by cancer survivors i.e. cancer-related fatigue (CRF), is often of greater magnitude, disproportionate to activity levels, and cannot be resolved through resting.⁸ CRF may be caused by tumor-related productions of cytokines, pain and neuroendocrine factors, and by medication and treatment.^{9,10} A review of mainly quantitative observational cross-sectional and longitudinal studies suggests CRF is the most prevalent symptom of TYA cancer treatment,⁶ with more than 75% of cancer patients reporting the condition.¹¹ Across 22 studies included in the review, CRF was found to often result in distress, and to impact on TYA survivors’ cognitive and physical function.⁶ However, findings are limited in strength, as the studies conducted were of relatively low quality,⁶ and often evaluated fatigue mainly as a sub component of more general measures, such as the Memorial Symptom Assessment Scale Short Form (MSAS-SF).¹² Nevertheless cross-sectional studies involving survivors of childhood cancer and adult cancer survivors provide evidence for associations between CRF and HR-QoL. Fatigue was found to be associated with poorer

physical and psychosocial functioning in 86 survivors (age range= 8-18 years) of childhood cancer on average 7.8 years after treatment,¹³ and with poorer HR-QoL in 954 adult cancer patients with mixed cancer diagnoses.¹⁴

While interest in investigating fatigue among TYA survivors has been increasing, there has been less emphasis on sleep quality. In general, engagement in poor sleep hygiene behaviors means many young people suffer from sleep problems.¹⁵ Among TYA survivors poor sleep may be associated both with increased fatigue and impaired HR-QoL. Sleep problems in cancer survivors may arise as a direct effect of the cancer, and be caused by indirect effects, including aspects of poor HR-QoL such as pain and anxiety.¹⁶ Within one small longitudinal study of 20 TYAs receiving chemotherapy (mean age=16.12 years) significant associations were found between poor sleep quality and poor cancer-related quality of life, including cognitive problems, pain and anxiety.¹⁷ Another study found significant associations between poor sleep and impaired HR-QoL in a sample of 61 TYA survivors (age range= 12-25 years) who had finished all treatment ($r=-0.57$, $p>0.001$).¹⁸ Poor sleep quality was also correlated with bodily pain and impaired vitality, in a sample of 72 adult breast cancer survivors.¹⁹ Additionally, poor sleep in TYA survivors often occurs simultaneously with fatigue,²⁰ and the adult literature suggests a reciprocal relationship.¹²

Given that adolescence and young adulthood are characterised by unique psychosocial developmental changes, including increasing independence and transitions in school and work settings, good HR-QoL is important. Thus, it is essential to explore potential modifiable factors associated with poor HR-QoL in TYA survivors. Fatigue and poor sleep quality are suggested as such factors. However, findings that indicate associations within the TYA survivor population are limited in reliability, as studies suggesting an association between fatigue and

HR-QoL have mainly been of low quality⁶ and studies investigating sleep quality used predominantly small samples sizes.¹⁷ Furthermore, TYA survivors are a unique group in terms of tumor type and prognosis.²¹ While the majority of TYA survivors receive their cancer diagnosis during adolescence or young adulthood, survivors of childhood cancer will have been diagnosed during childhood. Evidence coming from this group, or adult cancer survivors can thus not be directly extrapolated to TYA-aged survivors. Using distinct and detailed measures the aim of this study was therefore to examine associations between sleep quality, fatigue, and HR-QoL in a large sample of TYA survivors. It was hypothesised that there are associations between sleep quality, fatigue, and HR-QoL in the TYA survivor population.

Methods

Study design, procedure, and participants

In 2015-2016 TYA survivors were recruited to participate in a cross-sectional survey study investigating their health behaviors, well-being and interest in lifestyle advice. Detailed information regarding the recruitment procedure can be found in a previous publication.²² TYA survivors were eligible if they had a diagnosis of cancer at any point within their lifetime; have had, have, or were going to receive active treatment for their cancer; were aged between 13 and 24 years; were living in the UK during the time of data collection; and understood spoken and written English. TYAs with terminal cancer, receiving palliative care or unable to provide consent themselves were excluded from the study. Interested participants were given an information sheet outlining the purpose of the study. All eligible TYAs could consent themselves independent of their age; interested young people were assumed to have Gillick competence.²³ Participants who agreed to participate were offered either a paper-version of the survey, or a link where it could be completed online. After finishing the questionnaire participants could fill in their personal details to be included in a prize draw to win vouchers

worth £15-£50. Ethical approval was obtained from UCL Research Ethics Committee (project number: 6206/001) and London Hampstead NHS Research Ethics Committee (reference: 15/LO/0764).

Measures

Demographic information and health characteristics

Self-reported data on age, gender and ethnicity were collected alongside self-reported data on health characteristics including cancer type, cancer stage, treatment type, treatment stage and age at diagnosis. Since chemotherapy and radiotherapy are known to have a negative impact on sleep and fatigue²⁰, TYA survivors were classified as having received/receiving chemotherapy and/or radiotherapy or having received/receiving neither of the two. Additionally, information on health problems other than the primary cancer was gathered. Participants were asked to indicate whether they have had any health problems in addition to their primary cancer, including osteoporosis, diabetes, asthma, irregular heart rhythm, extreme fatigue, mental health problems, lung disease, arthritis, any other heart trouble, another cancer, sensory impairments or specified other problems. Responses were categorized into 'no health problem present' and 'health problem present' (\geq one additional health problem present).

Fatigue

Fatigue was measured as the total score of the 13-item fatigue subscale of the Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-F) questionnaire. On a five-point Likert scale, the questionnaire assesses the intensity of fatigue and its impact on daily life over the past seven days.¹⁶ Examples of items included in the scale are "I feel fatigued", "I feel tired" and "I have to limit my social activity because I am tired". After reverse scoring items seven ("I have energy") and eight ("I am able to do my usual activities"), a global score ranging from zero to 52 is obtained. Higher scores indicate greater levels of fatigue. The FACIT-F is widely accepted as a measure of fatigue in cancer patients,²⁴ with high internal validity

(Cronbach's $\alpha=0.96$)(1) and good test-retest reliability ($r=0.90$).(1) Scores above 22 are considered as clinically significant fatigue.²⁶

Sleep

Sleep quality over the past month was measured using the Pittsburgh Sleep Quality Index (PSQI). The 19-question scale has seven dimensions: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication and daytime dysfunction. The individual dimensions can be evaluated separately, or combined to give a global score ranging from zero to 21, with greater scores indicating poorer sleep quality. The PSQI was validated for cancer patients (Cronbach's $\alpha=0.81$),²⁷ and shows good reliability ($r=0.85$).²⁷ The cut-off score is set at five, to identify cases with clinical sleep disorders.²⁸

HR-QoL

HR-QoL was measured with the EuroQoL-5, a valid (Cronbach's $\alpha=0.71$) and reliable ($r>0.7$) measure of health status that is widely used in cancer research.²⁹ The five-item questionnaire assesses mobility, self-care, daily activities, discomfort/pain, and anxiety/depression at the day of survey on a five-point Likert scale.²⁹ Individual dimension scores are added to give a global score ranging from five to 25. Higher scores indicate poorer HR-QoL.

Statistical analyses

Participants who started the survey but did not complete any items contained within either the HR-QoL, sleep or fatigue measures were excluded from all analyses. Where participants completed outcome measures partially, missing data were imputed using expectation maximization algorithm.³⁰ Data were not imputed for any demographic variables or health characteristics, and pairwise deletion was applied to minimize loss of data.³¹

Descriptive statistics were calculated for all variables. Following the advice of the TYA clinical team and after testing for an interaction by treatment status ($B=0.01$, $\beta=0.62$, 95% CI=0.01-0.02, $p<0.001$ for treatment status * fatigue interaction; $B=0.03$, $\beta=0.46$, 95% CI=0.02-0.04, $p<0.001$ for treatment status * sleep interaction) TYA survivors were stratified into those on and off treatment. In the UK a TYA survivor is defined as any young person between the ages of 13 and 24 years living with or beyond cancer.³² Both groups are consequently widely referred to as TYA survivors,³³ yet they differ in their needs.³⁴ TYAs undergoing treatment struggle with hospitalization and treatment-related side effects such as nausea, whilst TYA survivors off treatment are faced with challenges regaining a sense of normalcy to their lives. TYAs who reported undergoing active treatment at survey were classified as TYA survivors on treatment. TYAs who reported not having started treatment or to have finished all active treatment were categorized as TYA survivors off treatment.

Prior to main analyses associations between sleep and fatigue were explored. HR-QoL was log transformed to account for the non-normality of data. Simple linear regressions were run to test for unadjusted associations between sleep and HR-QoL, and fatigue and HR-QoL with HR-QoL as the dependent variable. Then models adjusting for covariates were run, with demographics and age at diagnosis entered as covariates, and sleep or fatigue as variables of main interest. Separate regressions were run for sleep and fatigue. To investigate whether sleep and fatigue were independently associated with HR-QoL additional analyses were carried out that included sleep and fatigue in the same model. TYA survivors on and off treatment commonly reported to suffer from extreme fatigue and mental health problems such as anxiety, in addition to their cancer. To avoid overlap with the measures included in this study the presence of an additional health problem was not adjusted for. Other cancer-specific health

characteristics such as cancer type were not controlled for, as no significant associations between these and any of the key variables were found in preliminary analyses.

All data were analysed using IBM SPSS Version 24.0. The significance level was set at $\alpha=0.05$ for all analyses. 95% confidence intervals (95% CI), and standardized regression coefficients (β) as effect size estimates, were reported (with $\beta<0.2$ =small, $0.2<\beta<0.5$ =medium, $\beta>0.5$ =strong).³⁵ Due to a lack of effect sizes reported in studies suggesting an association between fatigue and HR-QoL among TYA cancer survivors sample size calculations for the present study were based on a recent quantitative study which found a large significant correlation ($r=-0.57$) between sleep quality and HR-QoL among TYA survivors in the first year post treatment.¹⁸ Power calculations suggested samples of minimum 55 participants were required to observe associations (linear regressions, large effect size, power of 80%, $\alpha=0.05$).

Results

Response rate

In total, 295 eligible TYA survivors began the survey, 85 of whom did not complete any items contained within either HR-QoL, sleep or fatigue measures. They were thus excluded from analyses. Sixty-seven TYAs reported to currently receive active cancer treatment, and 135 TYAs said to be off treatment. The remaining eight survivors did not indicate their treatment status.

Sample and health characteristics

Table 1 and Table 2 provide an overview of the demographic information of the study population, and their health characteristics, respectively. The average age at survey for TYA survivors on treatment was 19.57 years (SD=3.14), and 20.17 years (SD=2.86) for survivors

off treatment. The majority of participants were female (64.18% for on treatment, 65.19% for off treatment) and White (85.07% for on treatment, 86.67% for off treatment).

TYA survivors on treatment (mean age=17.80 years, SD=3.25) were significantly older at diagnosis compared to survivors off treatment (mean age=16.27 years, SD=4.31) ($p=0.015$). The majority of TYAs on (67.16%) and off treatment (60.74%) reported the presence of an additional health problem. The two groups differed in cancer type ($p=0.015$). Almost all TYAs on (95.52%) and off treatment (94.81%) reported to have received/receive chemotherapy and/or radiotherapy as cancer treatment. Most survivors on (47.76%) and off treatment (40.74%) were unsure about the stage of cancer they had been diagnosed with. The majority of TYAs off treatment (45.19%) had finished their treatment between one and five years prior to survey.

Table 3 lists the mean scores for sleep, fatigue and HR-QoL. 85.07% of TYAs on treatment and 62.96% of TYAs off treatment had PSQI sleep quality scores above five, suggesting possible clinically significant sleep disorders.²⁸ 56.72% of TYAs on and 26.67% of TYAs off treatment had fatigue scores indicating clinically significant levels of fatigue.⁽³⁾ Sleep quality and fatigue were significantly associated among TYA survivors on ($\beta=0.41$, 95% CI=0.54-1.98, $B=1.26$, $p=0.001$) and off treatment ($\beta=0.54$, 95% CI=1.21-2.17, $B=1.69$, $p<0.001$).

Associations with HR-QoL

Table 4 presents results of regression analyses among TYA survivors on treatment. In separate adjusted analyses sleep quality ($\beta=0.49$, 95% CI=0.03-0.07, $B=0.05$, $p<0.001$) and fatigue ($\beta=0.55$, 95% CI=0.01-0.03, $B=0.02$, $p<0.001$) were strongly associated with HR-QoL. When entering sleep quality and fatigue into the same model both variables showed strong

independent associations with HR-QoL ($\beta=0.32$, 95% CI=0.01-0.06, B=0.03, $p=0.009$ for sleep quality, $\beta=0.41$, 95% CI=0.01-0.02, B=0.01, $p=0.002$ for fatigue).

Table 5 lists results of analyses including TYA survivors off treatment. Moderate to strong associations were found between sleep quality and HR-QoL ($\beta=0.43$ 95% CI=0.02-0.05, B=0.04, $p<0.001$), and fatigue and HR-QoL ($\beta=0.67$, 95% CI=0.01-0.02, B=0.02, $p<0.001$). After entering sleep quality and fatigue into the same model fatigue was strongly associated with HR-QoL ($\beta=0.63$, 95% CI=0.01-0.02, B=0.02, $p<0.001$) but no association was found between sleep quality and HR-QoL ($\beta=0.08$, 95% CI=-0.01-0.02, B=0.01, $p=0.296$).

Discussion

A cross-sectional survey design was used to test for associations between fatigue, sleep quality, and HR-QoL among TYA survivors. High prevalence of clinical sleep problems and fatigue were observed across the sample. After stratification by treatment status moderate to strong associations were observed between sleep quality, fatigue and HR-QoL among TYA survivors on and off treatment. While fatigue was found to be independently associated with HR-QoL in both groups independent associations between sleep quality and HR-QoL were found in TYA survivors on treatment, but not among survivors off treatment.

The high prevalence of sleep problems and fatigue observed among TYA survivors is in line with past research that found sleep onset latency suggestive of insomnia in 41% of TYA survivors in their first year post treatment.¹⁸ Another study found increased fatigue among TYA survivors on treatment compared to general population TYAs.³ While poor sleep quality is common also among TYAs from the general population³⁶ the high percentage found in this study is particularly concerning as sleep disruption can cause circadian rhythm dysregulation

which is linked to poor health outcomes including poorer cancer prognosis.^{37,38} Additionally, fatigue hinders the development of adolescent key needs, including autonomy and close peer relationships.³⁹

The significant associations found between fatigue and HR-QoL in TYAs on and off treatment are supported by findings of a review that suggests fatigue in TYA survivors was associated with increased levels of distress and reduced mobility.⁶ Using the MSAS, which allows comparisons of the level of distress caused by each symptom, fatigue was found in the top half in the majority of studies included in the review. Another review of mainly qualitative studies described the impact of fatigue on children and adolescents with cancer as an increased need to sleep and rest, and therefore to not being able to take part in regular activities.⁴⁰

The finding that sleep quality was strongly associated with HR-QoL among TYA survivors is in line with past research involving TYA and adult cancer survivors. Associations between increased sleep-wake disturbances and impaired cancer-related quality of life were observed in a small sample of TYAs receiving chemotherapy.¹⁷ Another study found associations between poor sleep quality and impaired HR-QoL among TYA survivors in the first year post treatment. Moreover, diminished sleep quality was associated with impaired cognitive functioning and poorer functional status in 115 adult lung cancer patients undergoing chemotherapy.⁴¹

Strong associations were found between sleep quality and fatigue both in TYA survivors on and off treatment. However, sleep quality among those on treatment is likely to be additionally impacted by treatment-specific factors such as hospitalization.⁹ This may explain why sleep was found to be associated with HR-QoL independent of fatigue in TYA survivors on treatment but not among those off treatment.

Several limitations need to be addressed when interpreting the findings of this study. First, as this study is a cross-sectional design, assumptions about causal relationships between sleep, fatigue and HR-QoL cannot be made. Second, the study used self-report measures, thus introducing potential biases including over- or underestimation of certain outcomes such as sleep duration.⁴² Inclusion of objective tools, such as actigraphy⁴³ would have been valuable. Third, to reduce the burden related to study participation it was decided to include the EuroQoL-5 as a brief measure of HR-QoL, yet a more detailed measure may have yielded in more insightful findings. Fourth, this study used a UK sample of TYA survivors aged between 13 and 24 years. Findings are therefore limited in generalizability to TYAs from countries that apply different age ranges to define TYA survivors.⁴⁴ Despite aforementioned limitations, the present study had important strengths. Although a large number of TYA survivors, particularly those on treatment, appears to suffer from sleep disorders, and our findings suggest poor sleep quality to be strongly associated with impaired HR-QoL in this group, only one study has to date investigated sleep quality among TYA survivors.¹⁸ Additionally, this study included exclusively TYA survivors in the first year after having finished treatment.¹⁸ The present study is thus the first sufficiently powered quantitative study to examine associations between sleep quality and HR-QoL, and to describe the prevalence of sleep disorders among TYA survivors on treatment. Moreover, previous studies that examined associations between fatigue and HR-QoL⁶ evaluated fatigue mainly as a sub component of more general measures.¹² The present study in contrast used a distinct and detailed measure of fatigue.²⁵ Furthermore, it was the first study to investigate whether sleep quality and fatigue are independently associated with HR-QoL among TYA survivors on and off treatment.

Future research should aim to identify the direction of associations between sleep quality, fatigue and HR-QoL. Equally, longitudinal repeated-measures study should identify the underlying mechanisms of poor sleep and HR-QoL, and fatigue in TYA survivors on and off treatment. Once the direction of associations has been clarified studies including large numbers of participants per cancer and treatment type are required to investigate potential cancer/treatment- and demographic-related differences among TYA survivors to identify those who are in greatest need of potential interventions.

The present study suggests potentially high prevalence of sleep disorders and fatigue, and has identified probable associations between sleep and fatigue, and HR-QoL among TYA survivors. Poor sleep quality and fatigue are suggested as potential modifiable factors associated with poor HR-QoL among TYA survivors on and off treatment. Targeting sleep and fatigue in tailored interventions may therefore improve on and off treatment HR-QoL outcomes. Furthermore, the finding that sleep quality was independently associated with HR-QoL among TYA survivors on treatment but not among those off treatment suggests that interventions TYA survivors on and off treatment may benefit from different interventions. However, the causes of poor sleep and HR-QoL, and fatigue among TYA survivors are complex and yet to be understood. Large-scale longitudinal studies using subjective and objective measures are needed to understand the exact mechanisms underlying fatigue, and poor sleep and HR-QoL before starting the development of potential interventions.

Author Disclosure Statement

No competing financial interests exist.

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TABLE 1 Sociodemographic information of the study population

	TYA survivors on treatment (n=67)	TYA survivors off treatment (n=135)	p-value
Age at survey, mean (SD)	19.57 (3.14)	20.17 (2.86)	0.174
<i>13-18 years, % (n)</i>	29.85 (20)	30.37 (41)	
<i>19-24 years, % (n)</i>	70.15 (47)	69.63 (94)	
Female, % (n)	64.18 (43)	65.19 (88)	0.888
Ethnicity, % (n)			0.980
<i>White</i>	85.07 (57)	86.67 (117)	
<i>Black</i>	7.46 (5)	7.41 (10)	
<i>Asian</i>	2.99 (2)	2.22 (3)	
<i>Mixed</i>	4.48 (3)	3.70 (5)	

TABLE 2 Health characteristics of the study population

	TYA survivors on treatment (n=67)	TYA survivors off treatment (n=135)	p-value
Sleep, mean (SD)	8.91 (3.36)	7.27 (3.55)	
Age at diagnosis, mean (SD)	17.80 (3.25)	16.27 (4.31)	0.015
Fatigue, mean (SD)	23.20 (7.86)	15.56 (6.98)	0.791
Health problem present, % (n)	67 (100)	82 (60.74)	
ORQOL score, mean (SD)	9.90 (3.48)	7.86 (2.76)	
<i>Diabetes</i>	7.46 (5)	1.48 (2)	
<i>Asthma</i>	10.45 (7)	10.37 (14)	
<i>Irregular heart rhythm</i>	7.46 (5)	5.19 (7)	
<i>Extreme fatigue</i>	35.82 (24)	29.63 (40)	
<i>Mental health problems</i>	16.42 (11)	20.00 (27)	
<i>Lung disease</i>	0 (0)	0.74 (1)	
<i>Arthritis</i>	1.49 (1)	2.96 (4)	
<i>Any other heart trouble</i>	1.49 (1)	2.22 (3)	
<i>Another cancer</i>	2.98 (2)	1.48 (1)	
<i>Sensory impairment</i>	1.49 (1)	3.70 (5)	
<i>Other</i>	19.40 (13)	19.25 (26)	
Treatment type, % (n)			0.827
<i>Chemotherapy or radiotherapy</i>	95.52 (64)	94.81 (128)	
<i>No chemotherapy or radiotherapy</i>	4.48 (3)	5.19 (7)	
Cancer type, % (n)			0.015
<i>Leukemia</i>	32.84 (22)	24.44 (33)	
<i>Lymphoma</i>	26.87 (18)	35.56 (48)	
<i>Carcinoma</i>	0 (0)	4.44 (6)	
<i>Germ cell tumor</i>	0 (0)	3.70 (5)	
<i>CNS tumor</i>	0 (0)	2.22 (3)	
<i>Melanoma</i>	1.49 (1)	0.74 (1)	
<i>Bone tumor</i>	4.48 (3)	9.63 (13)	
<i>Soft tissue tumor</i>	14.92 (10)	3.70 (5)	
<i>Other</i>	17.91 (12)	14.07 (19)	
<i>Missing</i>	1.49 (1)	1.48 (2)	
Cancer stage at diagnosis, % (n)			0.222
<i>0</i>	0 (0)	0.74 (1)	
<i>I</i>	11.94 (8)	6.67 (9)	
<i>II</i>	11.94 (8)	20.00 (27)	
<i>III</i>	11.94 (8)	16.30 (22)	
<i>IV</i>	13.4 (9)	11.85 (16)	
<i>Don't know</i>	47.76 (32)	40.74 (55)	
<i>Don't want to answer</i>	0 (0)	0.74 (1)	
<i>Missing</i>	2.99 (2)	2.96 (4)	
Time since active treatment, % (n)			
<i>Less than 3 months</i>		14.08 (19)	
<i>Between 4 and 11 months</i>		20.00 (27)	
<i>Between 1 and 5 years</i>		45.19 (61)	
<i>On active surveillance</i>		12.59 (17)	
<i>More than 5 years</i>		3.70 (5)	
<i>Missing</i>		4.44 (6)	

TABLE 3 Mean scores of sleep, fatigue, and HR-QoL of TYA survivors

	TYA survivors on treatment (n=67)	TYA survivors off treatment (n=135)
Sleep, mean (SD)	8.91 (3.36)	7.27 (3.55)
Fatigue, mean (SD)	23.20 (10.86)	15.56 (10.98)
HR-QoL, mean (SD)	9.90 (3.68)	7.86 (2.76)

TABLE 4 Linear regression analyses of TYA survivors on treatment

	Unadjusted	Adjusted ^a
Sleep quality		
β	0.52	0.49
B (95% CI)	0.05 (0.03 - 0.07)	0.05 (0.03 - 0.07)
p-value	<0.001	<0.001
Fatigue		
β	0.55	0.55
B (95% CI)	0.02 (0.01 - 0.03)	0.02 (0.01 - 0.03)
p-value	<0.001	<0.001
Sleep quality & Fatigue		
Sleep quality		
β	0.33	0.32
B (95% CI)	0.03 (0.01 - 0.06)	0.03 (0.01 - 0.06)
p-value	0.005	0.009
Fatigue		
β	0.38	0.41
B (95% CI)	0.01 (0.01 - 0.02)	0.01 (0.01 - 0.02)
p-value	0.001	0.002

^a Regressions adjusted for age at survey, age at diagnosis, gender and ethnicity (n= 61)

TABLE 5 Linear regression analyses of TYA survivors off treatment

	Unadjusted	Adjusted ^a
Sleep quality		
β	0.43	0.43
B (95% CI)	0.04 (0.02 - 0.05)	0.04 (0.02 - 0.05)
p-value	<0.001	<0.001
Fatigue		
β	0.69	0.67
B (95% CI)	0.02 (0.01 - 0.02)	0.02 (0.01 - 0.02)
p-value	<0.001	<0.001
Sleep quality & Fatigue		
Sleep quality		
β	0.07	0.08
B (95% CI)	0.01 (-0.01 - 0.02)	0.01 (-0.01 - 0.02)
p-value	0.334	0.296
Fatigue		
β	0.64	0.63
B (95% CI)	0.02 (0.01 - 0.02)	0.02 (0.01 - 0.02)
p-value	<0.001	<0.001

^a Regressions adjusted for age at survey, age at diagnosis, gender and ethnicity (n= 131)