European Journal of Oncology Nursing 38 (2019) 21–27

Contents lists available at ScienceDirect

European Journal of Oncology Nursing

journal homepage: www.elsevier.com/locate/ejon

Relationships among fatigue, physical activity, depressive symptoms, and quality of life in Chinese children and adolescents surviving cancer

Ka Yan Ho[a], William H.C. Li[a,*], Ka Wai Katherine Lam[a], Xia Wei[a], S.Y. Chiu[b], Chi-Fung Godfrey Chan[b], Oi Kwan Joyce Chung[a]

[a] School of Nursing, 4/F, William MW Mong Block, No 21 Sassoon Road, Pokfulam, Hong Kong
[b] Department of Adolescent Medicine, Room 115, New Clinical Building, Queen Mary Hospital, 102 Pokfulam Road, Hong Kong

ARTICLE INFO

Keywords:
Childhood cancer survivors
Fatigue
Physical activity
Quality of life
Severity
Occurrence

ABSTRACT

Purpose: Fatigue is the most common concern reported by childhood cancer survivors. Assessing its occurrence and severity is a prerequisite for planning and evaluating appropriate interventions. Nevertheless, there is a lack of large-scale surveys which examine the occurrence and severity of fatigue and its associated factors. The study aimed to shed light on this under researched area.

Methods: A cross-sectional study was used. A total of 400 childhood cancer survivors (7- to 18-year olds) were invited to participate in the study. The cancer-related fatigue, depressive symptoms, physical activity level, and quality of life of participants were assessed.

Results: An average of 46.4% of children and 48.4% of adolescents were found to display symptoms of cancer-related fatigue between "half the time" and "all the time" over the previous seven days. Besides, greater occurrence and severity of fatigue in childhood cancer survivors were associated with more self-reported depressive symptoms, lower level of physical activity and quality of life. In addition, the study revealed that physical activity level is a significant factor associated with cancer-related fatigue.

Conclusion: The findings provide further support that cancer and its treatment have adverse effects on survivors' fatigue, which can manifest months or even years after the completion of treatment. Importantly, this study reveals that physical activity is a significant factor associated with fatigue in children and adolescents. It is crucial for healthcare professionals to identify strategies that can help children and adolescents surviving cancer increase their adoption and maintenance of regular activity throughout their life.

1. Introduction

Recent advances in cancer screening and medical treatment have improved survival rates for all types of childhood cancer (WHO, 2016). Nevertheless, there is a large body of evidence that cancer and its treatments have long-term adverse effects on the physiological and psychological well-being of childhood cancer survivors, including fatigue, poor concentration and decreased attention span, memory loss, activity intolerance, depression, and lower self-esteem, all of which severely affect their quality of life (Zeltzer et al., 2009; Li et al., 2012; Dietz and Mulrooney, 2011). Of these, cancer-related fatigue is the most commonly identified concern (Kestler and LoBiondo-Wood, 2012; Yeh et al., 2011; Clanton et al., 2011). Western studies have indicated that between 19.2 and 30% of children who survive cancer experience fatigue (Meeske et al., 2007; Mulrooney et al., 2008). The symptom of cancer-related fatigue is generally defined as an individual's subjective feeling of long-term tiredness or exhaustion that cannot be relieved by rest (Stone and Minton, 2008). Though the cause of cancer-related fatigue remains unidentified, it is thought to be related to low-grade inflammatory responses resulting from chemotherapy and radiotherapy (Hamre et al., 2013).

There is strong evidence that regular physical activity can attenuate cancer-related fatigue, increase muscular strength, and help improve physical functioning (Lucía et al., 2003; Whitsett et al., 2008). It has, however, been found that many Hong Kong Chinese childhood cancer survivors are reluctant to engage in regular physical activity, resulting in a reduction of physical strength and endurance after remission (Li et al., 2011; Chung et al., 2014). In Hong Kong Chinese culture, the philosophy of Confucianism is a major influence, which emphasizes attaining balance and harmony in everyday living through the notions

* Corresponding author. 4/F, William M. W. Mong Block, 21 Sassoon Road, Pokfulam, School of Nursing, The University of Hong Kong, Hong Kong.
E-mail addresses: devilbb2@hku.hk (K.Y. Ho), william3@hku.hk (W.H.C. Li), kathins@gmail.com (K.W.K. Lam), u3003122@hku.hk (X. Wei), sychiu3@gmail.com (S.Y. Chiu), gcfchan@hku.hk (C.-F.G. Chan), joychung@hku.hk (O.K.J. Chung).

https://doi.org/10.1016/j.ejon.2018.11.007
Received 23 May 2018; Received in revised form 22 October 2018; Accepted 21 November 2018

of *chung* and *yung* (Li, 2009). In this philosophy, cancer or other chronic diseases are regarded as "bad spirits," and physical activity is believed to aggravate them further and violate the rule of harmony (Nisbett, 2004). Many parents of Chinese childhood cancer survivors may therefore advise further rest and to avoid any high energy-consuming activities, including physical exertion (Li et al., 2011). The recorded significant decline in the physical activity levels of Hong Kong Chinese childhood cancer survivors is proof of this; 92.2% did not meet the guidelines of the Centers for Disease Control and Prevention (Chung et al., 2014), compared to only 52.1% of survivors in the United States (Ness et al., 2009). The guidelines advocate 60 min or more per day of aerobic activity, mainly of moderate or vigorous intensity, and vigorous-intensity physical activity at least three days a week. Physical inactivity can in fact accelerate fatigue, as physical inactivity induces muscle catabolism and atrophy, which in turn may lead to a further decrease in functional capacity (Lucía et al., 2003; Braam et al., 2010).

The Chinese cultural context is markedly different from that of the West, so the experience of illness and symptoms for children and adolescents, particularly the effect of cancer and its treatments, is likely to differ considerably in the two regions (Chung et al., 2014). Before any appropriate interventions to help promote regular physical activity and minimize cancer-related fatigue can be recommended for Chinese children and adolescents surviving cancer, it is essential to assess the occurrence and severity of the fatigue. In a study using a semi-structured interview to examine the effect of cancer on the physical and psychological well-being of Hong Kong Chinese childhood cancer survivors, most participants expressed that their major concern was fatigue and that they tired easily, even after adequate rest (Li et al., 2013a). However, a review of the literature finds a lack of large-scale surveys assessing the occurrence and severity of fatigue in Hong Kong Chinese childhood cancer survivors. This study used a larger sample size to assess the occurrence and severity of fatigue manifested by these survivors. The factors associated with fatigue in Chinese children and adolescents surviving cancer were also examined.

2. Methods

2.1. Study design and sample

A cross-sectional study was used. Hong Kong Chinese childhood cancer survivors who attended medical follow-up at the outpatient clinic of a public acute-care hospital in Hong Kong, and who met the inclusion criteria were invited to participate. Participants were also recruited through the Sunshine Parents Club, a non-profit voluntary organization providing education and psychological support to parents of Hong Kong Chinese childhood cancer survivors. The inclusion criteria were: (1) cancer survivors who had completed treatment at least six months; (2) aged between 7 and 18; and (3) able to speak Cantonese and read Chinese. We excluded survivors with evidence of recurrence or second malignancies and those with cognitive and learning problems, as identified from their medical records.

In Hong Kong, the incidence of cancer in children is about 10 per 100,000 children, with approximately 170 new cases diagnosed each year (Hospital Authority: Hong Kong Cancer Registry, 2016). To increase the generalizability of the findings, we recruited 200 participants aged between 7 and 12 years old and another 200 of between 13 and 18 years old.

2.2. Study instruments

2.2.1. Chinese version of the fatigue scale – child (FS-C)

The Chinese version of the FS-C was used to measure cancer-related fatigue of the participants aged 7–12. It contains 12 items rated on a 5-point Likert scale (1 = "not at all", 2 = "a little", 3 = "some", 4 = "quite a bit", 5 = "a lot"). Its scores range from 12 to 60, with higher scores demonstrating higher levels of fatigue. The evaluation of its psychometric properties demonstrated high internal consistency and test-retest reliability, as well as reasonable convergent, discriminant and known-group validity (Chiang et al., 2008a).

2.2.2. Chinese version of the fatigue scale – adolescent (FS-A)

The Chinese version of the FS-A was used to measure cancer-related fatigue of the participants aged 13–18. It consists of 12 items which are evaluated on a 5-point Likert scale (1 = "not at all", 2 = "a little", 3 = "some", 4 = "quite a bit", 5 = "a lot"). The possible range of scores is from 12 to 60, with higher scores representing higher level of fatigue. The psychometric properties of the Chinese version of the FS-A were examined, showing adequate internal consistency reliability, good content validity, and excellent construct validity (Chiang et al., 2008b).

2.2.3. The Chinese version of the center for epidemiology studies depression scale for children (CES-DC)

The participants' depressive symptoms were documented by the CES-DC. This instrument contains 20 items, evaluated on a four-point Likert scale in relation to the experience of last week. The scores range from 0 to 60, and higher scores represent the greater numbers of depressive symptoms. The cut-off score is 16, which shows the children currently experiencing a significant number of depressive symptoms. The psychometric properties of the Chinese version of the CES-DC were examined, showing good internal consistency, and reasonable convergent and discriminant validity (Li et al., 2010).

2.2.4. The Chinese University of Hong Kong: physical activity rating for children and youth (CUHK-PARCY)

The CUHK-PARCY was used to measure the participants' physical activity level. It is a comprehensive checklist which asks the participants to rate their average physical activity level over the past year from 0 (no physical exercise at all) to 10 (having vigorous exercise almost every day) by considering the frequency, duration and intensity of the activity. Scores of 0–2, 3 to 6 and 7 to 10 are interpreted as low, moderate and high physical activity levels, respectively. The psychometric properties of the CUHK-PARCY were examined, showing good internal consistency and test-retest reliability (Chung et al., 2014).

2.2.5. Chinese version of the paediatric quality of life inventory 4.0 generic core scales (PedsQL 4.0)

The participants' quality of life was assessed by the PedsQL. This instrument contains 23 items which can be further categorized into four subscales, named physical functioning, emotional functioning, social functioning and school functioning. The PedsQL scores range from 0 to 100, with higher scores representing better health-related quality of life. The psychometric properties of the Chinese version of the PedsQL were tested, showing acceptable internal consistency, test-retest reliability, and known-group validity (Chan et al., 2005).

2.3. Data collection methods

This study was approved by the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster (UW 16-026). To attract participants who had survived cancer, posters with detailed information about the research were put up in the paediatric outpatient clinic. Those who were interested to participate could express their willingness to the nurse in-charge. After confirming that they were eligible, their parent or guardian was asked to sign a consent form. They were given the option of allowing or refusing their child's involvement in the study. Children were also invited to put their names on a special individual assent form and were told that their participation was voluntary. Both of them were assured that their participation was totally voluntary and were given an option to withdraw at any time without penalty. Parents were asked to complete a demographic sheet, whereas the participants were asked to respond to the Chinese version of the FS-C/FS-A, CES-DC, CUHK-PARCY and PedsQL. A leaflet about

this study, consent form and questionnaires were mailed to each eligible members of the Sunshine Parent Club. Those who were interested to join were asked to return the consent forms and completed questionnaires using the enclosed envelopes.

2.4. Data analysis

The statistical Package for Social Science (SPSS: Version 20.0; SPSS Inc., Chicago, IL, USA) for Windows was used for data analysis. Descriptive statistics were applied to summarize the demographic characteristics of the participants, and their occurrence and severity of fatigue. The associations of all variables (age, sex, diagnosis, treatment received, time since treatment completed, number of depressive symptoms, physical activity levels and quality of life) with cancer-related fatigue were first explored using the univariate linear regression analyses. Multiple linear regression analyses were used to further examine the factors associated with cancer-related fatigue after adjusting for confounders. The multivariate model was built using a theoretical-driven approach. Variables that were potentially associated fatigue according to previous literature were entered into the model. These variables were physical activity levels, depressive symptoms, type of treatment received and time since treatment completed (Basen-Engquist et al., 2009; Cella et al., 1998; Ray, 1991). Age, gender and diagnosis that might confound the multivariate analyses were controlled (Reuter et al., 2006). In both the univariate and multivariate linear regression analyses, the age, number of depressive symptoms, and physical activity levels were operationalized as a continuous variable, while the sex, diagnosis (leukemia, lymphoma, brain tumor, osteosarcoma, kidney tumor and germ-cell tumor), type of treatment received (surgery, chemotherapy, bone marrow transplant and mixed methods) and times since treatment completed (6–12 months, 13–24 months, 25–36 months, 37–48 months, 49–60 months, > 60 months) were as categorical variables in the regression models. To account for the possible effect of collinearity on the multivariate linear regression model, principal components analysis was applied. The FS-C and FS-A were used to measure the cancer-related fatigue of participants aged 7-12 and 13-18, respectively. Data analyses were therefore performed separately for the two age groups.

3. Results

Data collection was conducted between January 2014 and March 2015. During this period, we approached 472 eligible childhood cancer survivors, 72 refused to participate. A total of 400 survivors of childhood cancer was successfully recruited, giving a response rate of 84.7%. The reasons of refusal included no interest (n = 46) and a busy schedule (n = 26). The demographic characteristics, medical history, and the mean and standard deviation of the FS-C, FS-A, CES-DC, CUHK-PARCY, and PedsQL of the participants are shown in Table 1. About 53.3% was male and the most common type of cancer was leukemia (39.5%). Most participants (44.8%) received chemotherapy, followed by a combined treatment of surgery and chemotherapy (10.0%). More than half (55.9%) had completed the entire medical treatment within 3 years, with only 55 children (13.5%) continuing for more than 5 years.

The distribution of the reported occurrence and severity of fatigue for children (aged 7 -12) and adolescent (aged 13 -18) is shown in Tables 2 and 3, respectively. Tables 4 and 5 present the summary of univariate linear regression for variables associated with cancer-related fatigue in children and adolescents surviving cancer. The results showed that number of depressive symptoms (children: $\beta = 0.52$, $p < .01$; adolescents: $\beta = 0.56$, $p < .01$) had a significantly positive association with fatigue in children and adolescents surviving cancer. The results also showed that times since treatment completed (children: $\beta = -0.19$, $p = .01$; adolescents: $\beta = -0.20$, $p = .01$), quality of life (children: $\beta = -0.61$, $p < .01$; adolescents: $\beta = -0.60$, $p < .01$) and physical activity levels (children: $\beta = -0.68$ $p < .01$; adolescents: $\beta = -0.62$, $p < .01$) were significantly negatively associated with fatigue in children and adolescents surviving cancer.

Table 1
Demographic characteristics, and the mean scores of depressive symptoms, physical activity and quality of life of the participants ($N = 400$).

	n (%)
Sex	
Male	213 (53.3)
Female	187 (46.7)
Parents' Educational Attainment	
Primary school or below	53 (13.3)
Lower secondary school	130 (32.5)
Upper secondary school	142 (36.3)
Tertiary education	75 (17.9)
Diagnosis	
Leukemia	158 (39.5)
Lymphoma	103 (25.8)
Brain tumor	68 (17.0)
Osteosarcoma	35 (8.8)
Kidney tumor	19 (4.8)
Germ-cell tumor	17 (4.1)
Treatment received	
Surgery	39 (9.8)
Chemotherapy	179 (44.8)
Bone Marrow Transplant	38 (9.5)
Mixed method:	
Chemotherapy and radiotherapy	27 (6.8)
Surgery and chemotherapy	40 (10.0)
Chemotherapy and bone marrow transplantation	53 (13.3)
Radiotherapy and surgery	24 (5.8)
Time since treatment completed	
6–12 months	87 (21.8)
13–24 months	69 (17.3)
25–36 months	67 (16.8)
37–48 months	69 (17.3)
49–60 months	53 (13.3)
> 60 months	55 (13.5)
	Mean (S.D.)
Age	
7–12 years	9.4 (1.7)
13–18 years	15.9 (1.6)
Outcomes	
FS-C	29.0 (7.3)
FS-A	28.1 (6.9)
CES-DC	37.9 (8.8)
PARCY	4.34 (2.7)
PedsQL	77.44 (15.7)

A summary of multiple regression analysis for variables associated with cancer-related fatigue is presented in Table 6 (aged 7 -12) and Table 7 (aged 13–18) after controlling for age, gender and diagnosis. Three variables (time since treatment completed, physical activity levels and depressive symptoms) were found to be statistically significantly associated with cancer-related fatigue of children and adolescents. In particular, number of depressive symptoms (children: $\beta = 0.21$, $p = .01$; adolescents: $\beta = 0.23$, $p = .02$) had a significantly positive association with fatigue in children and adolescents surviving cancer. While times since treatment completed (children: $\beta = -0.14$, $p = .04$; adolescents: $\beta = -0.13$, $p = .05$), and physical activity levels (children: $\beta = -0.56$, $p < .01$; adolescents: $\beta = -0.51$, $p < .01$) were significantly negatively associated with fatigue in children and adolescents surviving cancer.

4. Discussion

Cancer-related fatigue is the most common and debilitating late-effect symptom of cancer treatment reported by childhood survivors. To the best of our knowledge, this is the first study to examine the occurrence and severity of fatigue in Hong Kong Chinese childhood cancer survivors. Research into the factors specifically associated with fatigue in a Chinese population is essential, given the different cultural context

Table 2
Distribution of responses to the items of the FS-C for participants Aged 7–12 (n = 200).

Item	Severity					Mean Severity	Range
	Not at all = 1	A little = 2	Half the time = 3	Quite a bit = 4	All the time = 5		
I have been tired	20.5	19.9	24.7	26.7	8.2	2.8	1–5
My body has felt different	31.8	21.5	20.5	15.5	10.7	1.9	1–5
Tired in the morning	19.9	28.8	29.5	15.8	6.2	2.6	1–5
I have needed a nap	16.2	35.1	22.6	15.5	10.7	2.3	1–5
Too tired to play	16.2	31.6	20.5	18.1	13.6	2.8	1–5
I have been lying around	36.2	20.6	20.5	13.4	9.4	1.9	1–5
I have been sad	6.2	41.8	27.4	21.2	3.4	2.7	1–5
Stop and rest when walking	32.5	25.1	20.8	17.5	4.1	2.0	1–5
Too tired to do my usual activities 0.1	13.0	41.2	22.6	16.2	7.1	2.3	1–5
Too tired to run	26.7	29.5	28.8	8.9	6.2	2.4	1–5
Hard to keep eyes open	41.5	25.1	17.1	10.7	5.7	1.3	1–5
I slept more at night	28.1	26.5	25.8	13.9	5.7	2.2	1–5
I have trouble thinking	39.1	21.7	21.0	12.7	5.5	1.8	1–5

Note: The table shows (in addition to the mean severity column) also the distribution of responses, thus the columns corresponding to the 1- to 5- point ratings indicate the symptom severity reported by this sample.

from that of the West. Understanding the associated factors is an important step toward designing appropriate interventions to attenuate cancer-related fatigue.

Similar to previous studies conducted in the West (Kestler and LoBiondo-Wood, 2012; Yeh et al., 2011; Meeske et al., 2007; Mulrooney et al., 2008), a considerable number of childhood cancer survivors were found to display symptoms of cancer-related fatigue. An average of 46.4% of children and 48.4% of adolescents in our study reported that the occurrence and severity of fatigue was between “half the time” and “all the time” over the previous seven days. Western studies have indicated that between 19.2 and 30% (Meeske et al., 2007; Mulrooney et al., 2008) of childhood cancer survivors experience fatigue, whereas in this study it was found that about 46% of children and 38% of adolescents surviving cancer scored at or above the cut-off scores for some symptoms of fatigue, as measured by the FS-C and FS-A, respectively. These higher levels may be due to the lower level of physical activity among Hong Kong Chinese children and adolescents surviving cancer, as it has been documented that they perform less physical activity than their Western counterparts (Chung et al., 2014; Ness et al., 2009). The results provide further support that a lower level of physical activity is associated with higher levels of fatigue in children and adolescents.

Consistent with a previous local study (Li et al., 2012) and studies from the West (Zeltzer et al., 2009; Dietz and Mulrooney, 2011), the mean CES-DC score of our participants was 37.9 which is higher than the cut-off. This is suggested that a majority of children and adolescents surviving cancer are potentially at risk of depression. The results also indicate that more self-reported depressive symptoms and a lower physical activity level were associated with greater occurrence and severity of fatigue in children and adolescents. This is understandable, as fatigue can severely limit the capacity to perform ordinary daily

Table 4
Summary of univariate linear regression for variables contributing to fatigue in children surviving cancer (n = 200).

Variables contributing to fatigue	*SE B*	*β*	*p*-value
Age[a]	0.35	0.01	.95
Sex[b]	2.53	0.03	.67
Diagnosis[b]	0.29	0.08	.32
Treatment received[b]	0.74	−0.22	.00*
Times since treatment completed[b]	1.28	−0.19	.01
Number of depressive symptoms[a]	0.07	0.52	.00*
Physical activity levels[a]	0.19	−0.68	.00*
Quality of life[a]	0.04	−0.61	.00*

Notes: The diagnosis included leukemia, lymphoma, brain tumor, osteosarcoma, kidney tumor and germ-cell tumor; Treatment received contained surgery, chemotherapy, bone marrow transplant and mixed methods; Times since treatment completed contained 6–12 months, 13–24 months, 25–36 months, 37–48 months, 49–60 months, > 60 months.
SE B = standard error of unstandardized coefficient; β = standardized coefficient; *Significant at $P < .01$.
[a] Operationalized as a continuous variable.
[b] Operationalized as a categorical variable.

Table 3
Distribution of responses to the items of the FS-A for participants aged 13–18 (n = 200).

Item	Severity					Mean Severity	Range
	Not at all = 1	A little = 2	Half the time = 3	Quite a bit = 4	All the time = 5		
My body has felt tired	16.7	21.2	27.5	27.1	7.4	2.9	1–5
My mind has felt worn out	24.9	24.9	30.9	16.0	3.3	2.5	1–5
I move more slowly	37.4	22.8	19.2	14.0	6.6	1.8	1–5
I want to rest more	20.4	19.0	27.9	21.6	11.2	2.8	1–5
I sleep more often	24.2	13.8	29.7	21.2	11.2	2.8	1–5
I don't feel like doing much	34.2	22.3	25.3	16.3	1.9	2.1	1–5
My body hasn't kept up with others	33.1	24.7	21.2	15.0	5.9	2.3	1–5
Unable to do my usual activities	29.4	23.9	19.0	16.8	10.9	3.9	1–5
I have not felt like talking	30.9	22.3	22.1	14.8	9.9	1.9	1–5
I need help to do my usual activities	33.7	24.7	18.9	15.7	6.9	1.6	1–5
I don't feel like being with others	34.9	24.0	17.4	14.6	9.1	1.6	1–5
I have to work harder to do my usual activities	33.5	22.0	18.4	16.3	9.9	1.9	1–5

Note: The table shows (in addition to the mean severity column) also the distribution of responses, thus the columns corresponding to the 1- to 5- point ratings indicate the symptom severity reported by this sample.

Table 5
Summary of univariate linear regression for variables contributing to fatigue in adolescents surviving cancer (n = 200).

Variables contributing to fatigue	*SE B*	*β*	*p*-value
Age[a]	0.54	0.03	.87
Sex[b]	1.30	0.15	.08
Diagnosis[b]	0.27	−0.11	.22
Treatment received[b]	0.31	0.14	.05
Times since treatment completed[b]	1.12	−0.20	.01
Number of depressive symptoms[a]	0.09	0.56	.00*
Physical activity levels[a]	0.19	−0.62	.00*
Quality of life[a]	0.04	−0.60	.00*

Notes: The diagnosis included leukemia, lymphoma, brain tumor, osteosarcoma, kidney tumor and germ-cell tumor; Ttreatment received contained surgery, chemotherapy, bone marrow transplant and mixed methods; Times since treatment completed contained 6–12 months, 13–24 months, 25–36 months, 37–48 months, 49–60 months, > 60 months.
SE B = standard error of unstandardized coefficient; β = standardized coefficient; *Significant at $P < .01$.
[a] Operationalized as a continuous variable.
[b] Operationalized as a categorical variable.

Table 6
Summary of multiple regression for variables contributing to fatigue in children surviving cancer (n = 200).

Variables contributing to fatigue	*SE B*	*β*	*p*-value
Step 1			
Age[a]	0.35	0.01	.88
Sex[b]	2.57	0.02	.86
Diagnosis[b]	0.31	0.08	.38
Step 2			
Age[a]	0.27	−0.09	.18
Sex[b]	1.95	−0.03	.64
Diagnosis[b]	0.24	−0.01	.87
Treatment received[b]	0.53	−0.11	.10
Times since treatment completed[b]	1.19	−0.14	.04
Number of depressive symptoms[a]	0.09	0.21	.01
Physical activity levels[a]	0.21	−0.56	.00*
$R^2 = 0.53$			
Adjusted $R^2 = 0.51$			
R^2 change = 0.49			

Notes: The diagnosis included leukemia, lymphoma, brain tumor, osteosarcoma, kidney tumor and germ-cell tumor; Treatment received contained surgery, chemotherapy, bone marrow transplant and mixed methods; Times since treatment completed contained 6–12 months, 13–24 months, 25–36 months, 37–48 months, 49–60 months, > 60 months.
SE B = standard error of unstandardized coefficient; β = standardized coefficient; *Significant at $P < .01$.
[a] Operationalized as a continuous variable.
[b] Operationalized as a categorical variable.

activities such as reading and studying, watching television, playing computer/electronic games, and particularly outdoor leisure activities, which adversely affects mood states and quality of life (Chung et al., 2014; Paxton et al., 2010). Physical activity is known to produce beneficial effects on both physical and psychological well-being (WHO, 1995), with some evidence that increased physical activity reduces depressive symptoms and enhances the quality of life (Paxton et al., 2010). It is therefore of paramount importance to promote physical activity in children and adolescents who survive cancer.

A longer period of time after the completion of treatment was found to be associated with lower fatigue levels, and though it could be argued that the adverse effect of cancer and its treatment on survivors' fatigue will diminish over time, caution must be taken when interpreting these findings. The univariate analysis showed that the standardized beta coefficients in the associations between the level of fatigue and the time since treatment was completed were – 0.19 and – 0.20 for children and adolescents, respectively. Despite attaining

Table 7
Summary of multiple regression for variables contributing to fatigue in adolescents surviving cancer (n = 200).

Variables contributing to fatigue	*SE B*	*β*	*p*-value
Step 1			
Age[a]	0.54	0.03	.71
Sex[b]	1.30	0.16	.07
Diagnosis[b]	0.27	−0.12	.19
Step 2			
Age[a]	0.44	0.01	.88
Sex[b]	1.01	0.06	.42
Diagnosis[b]	0.22	−0.05	.46
Treatment received[b]	0.10	0.08	.27
Times since treatment completed[b]	1.01	−0.13	.05
Number of depressive symptoms[a]	0.08	0.23	.02
Physical activity levels[a]	0.20	−0.51	.00*
$R^2 = 0.48$			
Adjusted $R^2 = 0.47$			
R^2 change = 0.44			

Notes: The diagnosis included leukemia, lymphoma, brain tumor, osteosarcoma, kidney tumor and germ-cell tumor; Treatment received contained surgery, chemotherapy, bone marrow transplant and mixed methods; Times since treatment completed contained 6–12 months, 13–24 months, 25–36 months, 37–48 months, 49–60 months, > 60 months.
SE B = standard error of unstandardized coefficient; β = standardized coefficient; *Significant at $P < .01$.
[a] Operationalized as a continuous variable.
[b] Operationalized as a categorical variable.

statistical significance, the actual associations between these two variables were quite small when compared with the other variables with statistical significance. In fact even very small associations between variables can obtain a significant result in large samples, but this does not mean the associations have any theoretical or practical significance.

A multiple linear regression analysis was performed separately on children and adolescents, to examine whether participants' physical activity level, depressive symptoms, the type of treatment received, and the time since treatment was completed were significant associated factors with the occurrence and severity of fatigue in childhood cancer survivors. The overall models explained 53% (children) and 48% (adolescents) of the variance. After controlling for the possible effects of age, gender, and diagnosis, it was found that the R^2 change values were 0.49 (children) and 0.44 (adolescents)—that is, physical activity level, depressive symptoms, the type of treatment received, and the time since treatment was completed explained an additional 49% and 44% of the variance in fatigue levels of children and adolescents, respectively. With all variables entered into the equation, three—physical activity level, depressive symptoms, and the time since treatment—were statistically significant ($P < .05$), implying that these factors were still associated with the level of fatigue in children and adolescents after controlling for possible confounders. However, β coefficients for the time since treatment, depressive symptoms, and physical activity level were −0.14, 0.21, and −0.56, respectively for children, and −0.13, 0.23, and −0.51, respectively for adolescents, indicating that physical activity level was the strongest factor associated with fatigue. The findings offer further evidence that physical activity can attenuate cancer-related fatigue, and conversely that physical inactivity can accelerate fatigue (Lucía et al., 2003; Whitsett et al., 2008).

4.1. Limitations

This study had several major limitations. First, given the cross-sectional study design, we are not able to conclude any causal relationship between physical activity and fatigue among survivors of childhood cancer. Second, the subject recruitment was carried out in only one hospital, undermining the generalizability of the results. Third, our study sample was biased since recruitment required children who were

interested in participating let their nurses know about their interest. It was likely that those with fatigue were therefore differentially recruited. Fourth, we did not use any objective measure, such as pedometers and accelerometers to assess physical activity. This potentially affects the reliability and validity of our results.

4.2. Implications for research and clinical practice

A significant number of Hong Kong Chinese children and adolescents surviving cancer were found to experience cancer-related fatigue. Most importantly, this study reveals that physical activity level is a significant factor associated with fatigue, and a lower level is associated with higher levels of fatigue, greater symptoms of depression, and poorer quality of life in children and adolescents. Given the health benefits of regular physical activity, in particular to ameliorate fatigue, it is crucial for healthcare professionals to correct the misconceptions about physical activity and illness, and to increase awareness of the importance of physical activity in childhood cancer survivors and their parents.

Adventure-based training has recently been used to enhance physical activity levels, self-efficacy, and quality of life among Hong Kong childhood cancer survivors (Li et al., 2013b; Chung et al., 2015). It was previously found that childhood cancer survivors who joined a 4-day integrated adventure-based training and health education program reported statistically significant differences in the stages of change in physical activity than those who did not at 18 months follow-up, along with higher levels of physical activity, self-efficacy, and quality of life (Chung et al., 2015). The participants' level of fatigue was not, however, measured, and consequently it is unclear whether engaging in regular physical activity can help attenuate cancer-related fatigue. More rigorous empirical scrutiny is needed to determine the effectiveness of such a training program before it can be used to ease fatigue.

5. Conclusion

This study has addressed a gap in the literature by examining the occurrence and severity of fatigue manifested by Hong Kong Chinese childhood cancer survivors, which is essential for the development of appropriate interventions to help minimize their cancer-related fatigue. The findings provide further support that cancer and its treatment have adverse effects on survivors' fatigue, which can manifest months or even years after the completion of the treatment. In addition, physical activity was found to be a significant factor associated with fatigue in children and adolescents. It is therefore crucial for healthcare professionals to develop and evaluate interventions which can encourage children and adolescents surviving cancer to adopt and maintain regular physical activity throughout their live.

Conflict of interest

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

Ethics approval and consent to participate

This study was approved by Institutional Review Board of the University of Hong Kong and Hospital Authority Hong Kong West Cluster (reference UW 16-026). To ensure the rights of all participants were protected, especially for the vulnerable subjects such as children in this study, the researchers strictly adhered to the Declaration of Helsinki (http://www.wma.net/en/30publications/10policies/b3/index.html.pdf?print-media-type&footer-right=[page]/[toPage]) and the ethical principles in designing and conducting clinical research. Written consent was sought from the children's parents or guardians. Children were also invited to put their names on a special individual assent form to indicate that their participation was voluntary.

Acknowledgments

The authors acknowledge all the children and adolescents, in particular those young cancer patients, for participating in this study.

References

Basen-Engquist, K., Scruggs, S., Jhingran, A., Bodurka, D.C., Lu, K., Ramondetta, L., Hughes, D., Carmack Taylor, C., 2009. Physical activity and obesity in endometrial cancer survivors: associations with pain, fatigue, and physical functioning. Am. J. Obstet. Gynecol. 200 (3), 288.

Braam, K.I., van Dijk, E.M., Veening, M.A., Bierings, M.B., Merks, J.H., Grootenhuis, M.A., Chinapaw, M.J., Sinnema, G., Takken, T., Huisman, J., Kaspers, G.J., 2010. Design of the Quality of Life in Motion (QLIM) study: a randomized controlled trial to evaluate the effectiveness and cost-effectiveness of a combined physical exercise and psychosocial training program to improve physical fitness in children with cancer. BMC Canc. 10 (1), 624.

Cella, D., Peterman, A., Passik, S., Jacobsen, P., Breitbart, W., 1998. Progress toward guidelines for the management of fatigue. Oncology 12 (11A), 369–377.

Chan, L.F., Chow, S.M., Lo, S.K., 2005. Preliminary validation of the Chinese version of the pediatric quality of life inventory. Int. J. Rehabil. Res. 28 (3), 219–227.

Chiang, Y.C., Hinds, P.S., Yeh, C.H., Yang, C.P., 2008a. Development and psychometric testing of a Chinese version of the fatigue scale - children in Taiwan. J. Clin. Nurs. 17 (9), 1201–1210.

Chiang, Y.C., Hinds, P.S., Yeh, C.H., Yang, C.P., Srivastava, D.K., 2008b. Reliability and validity of the Chinese version of the fatigue scale-adolescent. Cancer Nurs. 31 (3), E1–E8.

Chung, O.J., Li, H.C.W., Chiu, S.Y., Ho, K.Y.E., Lopez, V., 2014. The impact of cancer and its treatment on physical activity levels and behavior in Hong Kong Chinese childhood cancer survivors. Cancer Nurs. 37 (3), E43–E51.

Chung, O.K.J., Li, H.C.W., Chiu, S.Y., Ho, K.Y., Lopez, V., 2015. Sustainability of an integrated adventure-based training and health education program to enhance quality of life among Chinese childhood cancer survivors: a randomized controlled trial. Cancer Nurs. 38 (5), 366–374.

Clanton, N.R., Klosky, J.L., Li, C., Jain, N., Srivastava, D.K., Mulrooney, D., Zeltzer, L., Stovall, M., Robison, L.L., Krull, K.R., 2011. Fatigue, vitality, sleep, and neurocognitive functioning in adult survivors of childhood cancer. Cancer 117 (11), 2559–2568.

Dietz, A.C., Mulrooney, D.A., 2011. Life beyond the disease: relationships, parenting, and quality of life among survivors of childhood cancer. Haematologica 96, 643–645.

Hamre, H., Zeller, B., Kanellopoulos, A., Kiserud, C.E., Aakhus, S., Lund, M.B., Loge, G.H., Fosså, S.D., Ruud, E., 2013. High prevalence of chronic fatigue in adult long-term survivors of acute lymphoblastic leukemia and lymphoma during childhood and adolescence. J. Adolesc. Young Adult Oncol. 2 (1), 2–9.

Hospital Authority: Hong Kong Cancer Registry, 2016. 10 Most Common Cancers in Hong Kong in 2015. http://www3.ha.org.hk/cancereg/statistics.html, Accessed date: 10 May 2018.

Kestler, S.A., LoBiondo-Wood, G., 2012. Review of symptom experiences in children and adolescents with cancer. Cancer Nurs. 35 (2), E31–E49.

Li, W.H.C., 2009. The Importance of Incorporating Cultural Issues into Nursing Interventions for Chinese Populations. Strategies in Evaluation of Complex Health Care Interventions for People with Physical or Mental Health Issues.

Li, H.C.W., Chung, O.K.J., Ho, K.Y., 2010. Center for epidemiologic studies depression scale for children: psychometric testing of the Chinese version. J. Adv. Nurs. 66 (11), 2582–2591.

Li, H.W., Lopez, V., Chung, O.J., Ho, K.Y., Chiu, S.Y., 2013a. The impact of cancer on the physical, psychological and social well-being of childhood cancer survivors. Eur. J. Oncol. Nurs. 17 (2), 214–219.

Li, H.C., Chung, O.K.J., Ho, K.Y., Chiu, S.Y., Lopez, V., 2013b. Effectiveness of an integrated adventure-based training and health education program in promoting regular physical activity among childhood cancer survivors. Psycho Oncol. 22 (11), 2601–2610.

Li, H.C.W., Chung, O.K.J., Ho, K.Y.E., Chiu, S.Y., Lopez, V., 2012. A descriptive study of the psychosocial well-being and quality of life of childhood cancer survivors in Hong Kong. Cancer Nurs. 35 (6), 447–455.

Li, W.H., Chung, J.O., Ho, E.K., 2011. The effectiveness of therapeutic play, using virtual reality computer games, in promoting the psychological well-being of children hospitalised with cancer. J. Clin. Nurs. 20 (15–16), 2135–2143.

Lucía, A., Earnest, C., Pérez, M., 2003. Cancer–related fatigue: can exercise physiology assist oncologists? Lancet Oncol. 4 (10), 616–625.

Meeske, K.A., Patel, S.K., Palmer, S.N., Nelson, M.B., Parow, A.M., 2007. Factors associated with health-related quality of life in pediatric cancer survivors. Pediatr. Blood Canc. 49 (3), 298–305.

Mulrooney, D.A., Ness, K.K., Neglia, J.P., Whitton, J.A., Green, D.M., Zeltzer, L.K., Robison, L.L., Mertens, A.C., 2008. Fatigue and sleep disturbance in adult survivors of childhood cancer: a report from the childhood cancer survivor study (CCSS). Sleep 31 (2), 271–281.

Ness, K.K., Leisenring, W.M., Huang, S., Hudson, M.M., Gurney, J.G., Whelan, K., Wendy, L., Hobbie, W.L., Armstrong, G.T., Robison, L.L., Oeffinger, K.C., 2009. Predictors of inactive lifestyle among adult survivors of childhood cancer. Cancer 115 (9), 1984–1994.

Nisbett, R., 2004. The Geography of Thought: How Asians and Westerners Think Differently and Why. Simon and Schuster, New York.
Paxton, R.J., Jones, L.W., Rosoff, P.M., Bonner, M., Ater, J.L., Demark-Wahnefried, W., 2010. Associations between leisure-time physical activity and health-related quality of life among adolescent and adult survivors of childhood cancers. Psycho Oncol. 19 (9), 997–1003.
Ray, C., 1991. Chronic fatigue syndrome and depression: conceptual and methodological ambiguities. Psychol. Med. 21 (1), 1–9.
Reuter, K., Classen, C.C., Roscoe, J.A., Morrow, G.R., Kirshner, J.J., Rosenbluth, R., Flynn, P.J., Shedlock, K., Spiegel, D., 2006. Association of coping style, pain, age and depression with fatigue in women with primary breast cancer. Psycho Oncol. 15 (9), 772–779.
Stone, P.C., Minton, O., 2008. Cancer-related fatigue. Eur. J. Canc. 44, 1097–1104.
Whitsett, S.F., Gudmundsdottir, M., Davies, B., McCarthy, P., Friedman, D., 2008. Chemotherapy-related fatigue in childhood cancer: correlates, consequences, and coping strategies. J. Pediatr. Oncol. Nurs. 25 (2), 86–96.
World Health Organization, 1995. Exercise for health. WHO/FIMS Committee on physical activity for health. Bull WHO 73, 135–136.
World Health Organization, 2016. WHO Cancer Mortality Database. http://www-dep.iarc.fr/WHOdb/WHOdb.htm, Accessed date: 17 May 2018.
Yeh, C.H., Wai, J.P.M., Lin, U.S., Chiang, Y.C., 2011. A pilot study to examine the feasibility and effects of a home-based aerobic program on reducing fatigue in children with acute lymphoblastic leukemia. Cancer Nurs. 34 (1), 3–12.
Zeltzer, L.K., Recklitis, C., Buchbinder, D., Zebrack, B., Casillas, J., Tsao, J.C.I., Lu, Q., Krull, K., 2009. Psychological status in childhood cancer survivors: a report from the childhood cancer survivor study. J. Clin. Oncol. 27 (14), 2396–2404.