Impacts of physical late effects on presenteeism in childhood cancer survivors

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Original Article

Impacts of Physical Late Effects on Presenteeism in Childhood Cancer Survivors

Running title: Late Effects and Presenteeism in CCSs

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Abstract

Background

Many childhood cancer survivors (CCSs) experience physical late effects related to their cancer types and treatment modalities. Physical late effects are an important factor in various occupational outcomes among CCSs. However, the relationship between physical late effects and presenteeism has remained unclear. This study aimed to estimate the impacts of physical late effects on presenteeism among employed CCSs.

Methods

CCSs replied to a questionnaire regarding presenteeism, and their attending physicians assessed their physical late effects between September 2014 and December 2015. The Work Limitations Questionnaire (WLQ) was used to measure presenteeism. Propensity score analysis and a generalized linear model (GLM) were used to adjust covariates related to physical late effects and/or presenteeism.

Results

Of the 125 questionnaires distributed, 114 were returned. The data from 61 employed CCSs were analyzed. After controlling for covariates by propensity score analysis and GLM, there were no significant differences in presenteeism between employed CCSs with either no or single physical late effects. However, employed CCSs with multiple physical late effects reported higher scores in Output (Estimate = 9.3, p = 0.041), Physical Demands (Estimate = 12.2, p = 0.020), and Productivity Loss Scores (Estimate = 2.4, p = 0.045) on the WLQ than employed CCSs with no physical late

effects.

Conclusions

Employed CCSs with multiple physical late effects were at an increased risk for presenteeism. Healthcare and social welfare systems should be established to provide vocational assistance for CCSs after being employed to alleviate presenteeism.

Introduction

The overall 5-year survival rate of childhood cancer patients improved from 50% in the 1970s to 70% in the 2000s [1]. This improved prognosis resulted in an increase in the number of childhood cancer survivors (CCSs). Even after successful treatments have ended, CCSs experience physical late effects depending on cancer sites, treatment modalities and intensities, and patient characteristics (e.g., age, gender, genotype) [2–4]. Seventy-three percent of adult CCSs reported physical late effects occurring up to 30 years after diagnosis, and 42% also suffered severe conditions or death due to physical late effects [4].

The impairment of job performance was one of work-related problems among employed CCSs. Job performance refers to absenteeism (absence from scheduled work because of employees' health problems) and presenteeism (impaired on-the-job performance because of employees' health problems) [5]. Thirty-one percent of employed CCSs were limited in the amount and kinds of work they could perform because of health problems [6]. Employed survivors of adolescent cancer also reported reduced work quantity compared to healthy controls [7]. Thus, presenteeism, particularly diminishing amount of work, seems to be a crucial problem among employed CCSs. However, few studies have evaluated presenteeism with valid and reliable measures.

Physical complications such as physical fatigue [8–10], pain [11], and hot flashes [12] were associated with presenteeism in employed survivors of adulthood cancer. Among CCSs, the onset of physical late effects are risk factors for work-related problems such as unemployment [13–15] and worries about future employment [16, 17]. Moreover, the risk for unemployment was higher

for CCSs with two or more medical co-morbidities compared to one medical co-morbidity [13]. As presenteeism was one of work-related difficulties, the presence and increased number of physical late effects can also cause worsening presenteeism in employed CCSs. Nevertheless, the nature of this influence has remained unclear in CCSs.

Previous studies reported that impairment of job performance decreased health-related quality of life in both workers with and without diseases [18–20]. Thus, in order to achieve high quality of life among employed CCSs, it would be essential to develop strategies for alleviating presenteeism. Although the provision of vocational rehabilitation services facilitated employment among CCSs [21], no intervention and rehabilitation programs have been established to improve presenteeism. Clarifying the relationship between physical late effects and presenteeism would be helpful in developing strategies ameliorating presenteeism. This study aimed to describe presenteeism and to clarify the impact of physical late effects on presenteeism in employed CCSs. We hypothesized that having multiple physical late effects in particular increased presenteeism among employed CCSs after controlling for confounders related to presenteeism and/or physical late effects.

Methods

Participants

CCSs were recruited through convenience sampling in the outpatient departments of four hospitals that provide treatment and follow-up for CCSs, between September 2014 and December

2015 in Japan. Participants were recruited if they met the following criteria: (a) older than 20 years of age at the time of the survey, (b) diagnosed with cancer at ≤ 18 years of age, (c) more than five years had passed since the diagnosis of cancer, (d) at least one year had passed since the completion of anti-cancer treatment, and (e) employed at the time of the survey. CCSs were further excluded from this study (a) if they could not understand the purposes of the study in Japanese or (b) if their attending physicians judged that they were otherwise ineligible for participation (e.g., psychiatric problems).

Sample Size Calculation

The primary aim of our study was to evaluate the effects of physical late effects on presenteeism in employed CCSs. Earlier studies on adulthood cancer survivors had shown a medium effect size for the relationship between physical fatigue and presenteeism in a multiple regression analysis ($f^2 = 0.28$) [9]. In our study, the effect size was conservatively set at $f^2 = 0.15$. We calculated the sample size with $\alpha = 0.05$, $\beta = 0.20$, and $f^2 = 0.15$ using G*Power version 3.1.9.5 for Mac OS X. The required sample size was N = 55.

Procedure

Researchers explained this study to 128 eligible CCSs when they visited the hospitals (Figure 1). Of these 128, 125 CCSs signed the consent forms to participate in the current study and then received a questionnaire about presenteeism, a written explanation of the study, and a self-

addressed, stamped envelope. Of the 125 questionnaires distributed, 114 CCSs (response rate 91%)

returned the questionnaires to the researchers. Researchers also obtained from their attending

physicians the medical histories of CCSs who returned the questionnaires. The focus of this study

was on presenteeism in employed CCSs. We therefore excluded the data from 49 unemployed CCSs

from the analysis of this study. Furthermore, data from four employed CCSs who did not answer

items on presenteeism were excluded. No CCSs were excluded from this study because of the

exclusion criteria. Finally, data from 61 employed CCSs were analyzed.

Measurements

Presenteeism

The Work Limitations Questionnaire (WLQ) was used to assess presenteeism among

employed CCSs [22, 23]. The WLQ includes four different subscales: Time Management (5 items),

Mental-Interpersonal (9 items), Output (5 items), and Physical Demands (6 items). The Time

Management, Mental-Interpersonal, and Output Demands scales assess the level of difficulty the

respondent has perceived over the past two weeks with respect to the particular demands of the

scale. The Physical Demands scale assesses the respondent's ability to perform physical demands

such as movement and flexibility. Response options are as follows: all of the time, a great deal of the

time, some of the time, a slight bit of the time, none of the time, and does not apply to my job. The

response option "does not apply to my job" is treated as a missing response. Subscale scores are

computed as the mean of the non-missing responses and converted to a score of 0 (not limited) to

100 (limited all of the time). If more than 50% of the items within each subscale are scored as missing responses, the subscale score is not calculated. Higher scores on the WLQ subscales indicate poorer performance on each facet of a job. The Productivity Loss Score is estimated using the weighted sum of the four subscale scores. This score indicates the percentage of at-work productivity loss for a given group or individuals as compared with a benchmark sample of healthy employees [22]. If the four subscale scores are not calculated, the Productivity Loss Score is not computed. Using data from workers selected randomly on the basis of the population composition of Japan, Takegami et al. confirmed the validity and reliability of the Japanese version of the WLQ [23]. Cronbach's alphas in this study were 0.88 for Time Management Demands, 0.92 for Mental/Interpersonal Demands, 0.92 for Output Demands, and 0.89 for Physical Demands.

Physical Late Effects

The CCSs' attending physicians subjectively evaluated for each of them whether physical late effects related to their cancer and required therapies were clinically problematic. They rated the following physical complications: cardiovascular, pulmonary, endocrine, renal, bone or muscle, skin, neurocognitive, gastrointestinal, hepatic, and immunological dysfunctions; second cancer; chronic infection; and others in this study. We categorized CCSs into the following three groups by the number of physical late effects: CCSs with no, single, and multiple (≥ 2) physical late effects. This assessment for physical late effects is based on the method in previous studies evaluating physical late effects [2, 3].

Demographic and Clinical Characteristics

The employed CCSs completed items regarding age at the time of the survey, gender, educational level, employment status, occupational types, and job stress. Regarding employment status, employed CCSs were asked to select from full-time, part-time, and self-employed. Occupational types were chosen from professional (e.g., teacher and doctor), managerial (e.g., board member at a company), clerical, sales, production, services, security, and others. The following item was used to assess job stress: "How often do you think your current work situation puts you under too much stress?" [8–10]. The possible responses were "Often" (3), "Sometimes" (2), "Seldom" (1), and "Never" (0). A higher score on this item was determined to indicate more stress. The information about age at diagnosis, diagnosis, treatment modalities (chemotherapy, radiotherapy, stem cell transplant (SCT), and surgery), age at treatment completion, and relapse were extracted from the medical histories of the employed CCSs.

Statistical Analyses

All analyses were performed using IBM SPSS software, Version 21 (SPSS, Inc., Chicago, IL, USA). The level of significance was set at 0.05. Frequencies, percentages, means, and standard deviations were calculated for all variables used to describe characteristics in employed CCSs with no, single, and multiple physical late effects.

We estimated differences in presenteeism between employed CCSs with either no or single, and between employed CCSs with either no or multiple physical late effects. These differences may also be confounded by demographic and clinical characteristics, such as gender and

treatment modalities. We eliminated imbalances of demographic and clinical characteristics using the inverse propensity score weighting (IPW) method [24, 25]. Many studies have conducted multiple regression analysis using possible confounders as independent variables to account for these differences between groups [26]. However, multiple regression analysis adjusting for many confounders requires a large sample size and causes multicollinearity [27, 28]. Propensity score analysis is robust in adjusting for confounders in the case of seven or fewer observations per confounder variable [29]. Therefore, the IPW method was appropriate for this study to effectively eliminate imbalances in confounders.

First, propensity scores were calculated from a multinomial logistic regression in which the demographic and clinical variables predicted categories of physical late effects; that is, no, single, and multiple physical late effects. All variables potentially predictive of physical late effects and/or presenteeism were entered into a multinomial logistic regression regardless of statistical significance to estimate accurately the relationship between physical late effects and presenteeism [30]. Previous studies reported that cancer type, age at diagnosis and treatment completion, treatment modalities, and relapse were related to the onset of physical late effects [2, 3]. Previous systematic review also reported that age at the time of the survey, gender, educational level, employment status, occupational type, job stress, and treatment modalities were related to presenteeism in adulthood cancer survivors [31]. We therefore selected the following variables: age at the time of the survey, gender, educational level, employment status, occupational types, job stress, age at diagnosis, diagnosis, chemotherapy, radiotherapy, SCT, surgery, age at treatment

completion, and relapse. The propensity scores were the estimated predicted probabilities of

assignment to each category of physical late effects calculated for each employed CCSs. The

Nagelkerke pseudo R^2 of the multinomial logistic regression in this study was 58.2%.

Second, we assessed the degree of imbalance in characteristics between employed CCSs

with no, single, and multiple physical late effects. Standardized bias was used to assess these

imbalances [32]. Standardized bias was defined as the absolute value of the difference in means of

each of the paired groups divided by the standard deviation of the mean for all groups [32].

Standardized bias is not affected by sample size, and is recommended to evaluate imbalances in

characteristics between groups [32]. Standardized bias greater than 0.25 represent

meaningful imbalances [32]. In this study, the imbalance in characteristics between employed CCSs

with no and single physical late effects, and between employed CCSs with no and multiple physical

late effects, were assessed separately. Standardized biases were calculated before and after IPW. In

the IPW method, for example, observations in employed CCSs with no physical late effects were

weighted by the inverse of the probability of having no physical late effects. The IPW method

creates distributions of characteristics for each group that resemble the full sample, thus equating the

groups [25].

Finally, we compared presenteeism between employed CCSs with no, single, and

multiple physical late effects using a generalized linear model (GLM) after IPW. The four subscales

and Productivity Loss Score on the WLQ were set separately as the dependent variables in the GLM.

We entered two dummy variables of physical late effects (no physical late effects as the reference

category) as the independent variables into the GLM. If there were demographic and clinical

variables for which imbalances were not eliminated after IPW, these variables were also entered as

independent variables. The estimates, these standard errors (SE), and Wald 95% confidence intervals

(CI) for variables on physical late effects were calculated. The statistical significance of these

estimates were confirmed by Wald chi-square test. We also calculated r correlation coefficients for

these estimates as effect sizes ($r \geq 0.1$, small; 0.3, medium; 0.5, large) [33, 34].

Ethical Considerations

Our study was approved by the ethics committee of the principal investigator's institution

(The University of Tokyo, approved No. 10594) and the local ethics committees of all the

participating hospitals. In consideration of the Japanese socio-cultural environment, we avoided

using the terms such as "cancer" and "leukemia," and instead used the term "your disease" in the

written explanation of the study, the informed consent document, and questionnaires.

Results

Of 61 employed CCSs, 21 had single and 10 had multiple physical late effects (Table 1).

The most common physical late effect was endocrine dysfunction in both employed CCSs with

single (n = 11, 52%) and multiple physical late effects (n = 5, 50%). Few employed CCSs had

neurocognitive, gastrointestinal, hepatic, and immunological dysfunction, and second cancer.

Tables 2 and 3 show the demographic and clinical characteristics in employed CCSs. The

standardized biases between employed CCSs with no and single physical late effects were > 0.25 in

age at the time of the survey, occupational types, radiotherapy, SCT, and relapse before IPW. The

standard biases between employed CCSs with no and multiple physical late effects were also > 0.25

in gender, age at diagnosis, diagnosis, radiotherapy, SCT, surgery, and age at treatment completion.

After IPW, the standard biases in characteristics excluding age at the time of the survey (Standard

bias = 0.497), occupational types (Standard bias = 0.419), and SCT (Standard bias = 0.465) between

employed CCSs with no and multiple physical late effects were more than 0.25.

Table 4 shows unadjusted means and standard deviations of the four subscales and

Productivity Loss Score on the WLQ. The Productivity Loss Score in employed CCSs with no,

single, and multiple late effects indicated 2.5, 3.5, and 5.8, respectively. Four subscale scores also

increased in the order of increasing number of physical late effects.

Table 5 shows the results from GLM after IPW. The imbalances of the variables in age at

the time of the survey, occupational types, and SCT were not eliminated after IPW. These variables

were also entered into the GLM as independent variables. Although employed CCSs with single

physical late effect reported higher score in the Productivity Loss Score and four subscales on the

WLQ, these differences were not significant. Meanwhile, the Productivity Loss Score among

employed CCSs with multiple physical late effects was significantly higher than that among

employed CCSs with no physical late effects (Estimate = 2.4, Wald 95%CI = 0.1–4.8, p = 0.045).

This difference represented a small effect size (r = 0.261). Moreover, the estimates for the variable

on multiple physical late effects were statistically significant and had small to medium effect sizes in

Output (Estimate = 9.3, Wald 95%CI = 0.4–18.3, p = 0.041, r = 0.266) and Physical Demands

(Estimate = 12.2, Wald 95%CI = 2.0–22.5, p = 0.020, r = 0.300).

Discussion

We described presenteeism using a valid and reliable measure, and examined the impacts

on presenteeism of the number of physical late effects among employed CCSs. Our results support

our hypothesis that multiple physical late effects in particular increased presenteeism. Physical

complications aggravated employment [13–15] and worries about future employment [16, 17] in

CCSs. Our findings indicate that CCSs with multiple physical late effects in particular struggle with

work-related difficulties even after getting a job.

Our results indicate that employed CCSs with no, single, and multiple physical late

effects had 2.5%, 3.5%, and 5.8% lower job performance, respectively, compared to healthy

employees. The Productivity Loss Score among employed CCSs with no and single physical late

effects were similar to Japanese workers (mean = 3.4) [23] and better than American survivors of

adolescent cancer (mean = 4.5) [7]. Meanwhile, employed CCSs with multiple physical late effects

reported worse presenteeism than Japanese employees and American survivors of adolescent cancer.

Furthermore, the Productivity Loss Score in employed CCSs may be underestimated because of

various biases. For instance, previous studies found that older age at the survey was a risk factor for

presenteeism among adulthood cancer survivors [35, 36]. Employed CCSs in this study were

younger than Japanese employees (mean age 47 years) in the study by Takegami et al [23]. Such

biases in characteristics may have resulted in estimating lower presenteeism.

Our results corresponded with previous findings that physical complications impaired presenteeism in employed survivors of adulthood survivors [8–12]. These previous studies estimated separately the effect of each physical complication on presenteeism. Our findings highlight the synergistic influences of multiple physical late effects on presenteeism. Future studies should pay attention to a combined effect as well as an independent effect of physical late effects on presenteeism.

Our results suggest that multiple physical late effects in particular limited employed CCSs to managing heavy workloads. Employed CCSs and adolescent cancer survivors were limited in their amount of work because of health problems compared to controls without cancer experiences [6, 7]. In addition to these previous findings, our results indicate that multiple physical late effects greatly elevate the risk for diminished work quantity. Meanwhile, employed survivors of adolescent cancer have better performance on tasks involving bodily strength, movement, endurance, coordination, and flexibility compared to controls without cancer experiences [7]. Our result identified a subgroup of employed CCSs with low performance on physical job tasks from the viewpoint of number of physical late effects.

Employed CCSs with multiple physical late effects in particular should be provided work-related follow-up to alleviate their presenteeism. Physical complications related to childhood cancer and its treatment could be improved when long-term follow-up care for CCSs is available and implemented [37]. Tamminga et al. also suggested that sharing information about medical conditions

at a workplace could ameliorate job performance in adulthood cancer survivors [38]. Employed

CCSs with multiple physical late effects should be provided assistance in communication about their

conditions with their co-workers and supervisors to coordinate the amount and kinds of their tasks.

In this study, employed CCSs with multiple physical late effects had the greatest difficulties on tasks

involving bodily strength, movement, endurance, coordination, and flexibility. To ameliorate

employed CCSs' presenteeism, it would be of value to adjust the amount and kinds of physically

demanding tasks in particular.

This study had several limitations. First, our study recruited employed CCSs receiving

medical follow-up. Healthcare professionals provided various kinds of support including screening

and management of physical late effects in a follow-up setting [39]. These supports may weaken the

relationship between physical late effects and presenteeism in employed CCSs. Second, this study

had a cross-sectional observational design. We were cautious in interpreting the associations

between physical late effects and job performance as indicative of prognostic relationships. Third,

CCSs' attending physicians evaluated physical late effects subjectively on the basis of the method

used in previous research [2, 3]; however, this evaluation may not be accurate. In addition, this study

could not evaluate the severity of physical late effects and did not clarify its relationship with

presenteeism. Future research should investigate objectively physical late effects using standardized

evaluation methods such as the Common Terminology Criteria for Adverse Events. Finally, the small

sample size limited our ability to clarify differences in job performance between the various types of

physical late effects. Future research needs larger samples of employed CCSs to clarify this

differences.

In conclusion, this study was one of very few studies describing job performance and clarifying a correlate of job performance in employed CCSs. Multiple physical late effects contributed greatly to presenteeism. In particular, employed CCSs with multiple physical late effects had diminished work amounts and performance of tasks with physical demands. Employed CCSs should be provided vocational assistance after starting their jobs to alleviate their presenteeism.

Disclosure

The authors declare no conflict of interest.

Author Contributions

T.S., I. S., and K.K. contributed to the conception and design of this study; T.S., J.T., K.K., T.K., H.I., and S.O. collected data; T.S. performed the statistical analysis and drafted the manuscript; K.K. critically reviewed the manuscript and supervised the whole study process. All authors read and approved the final manuscript.

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Figure legend

Figure 1. Summary of the recruitment procedure and number of participants

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┌─────────────────────────────────────────────────┐
│ Selected Survivors within the criteria          │
│ Explained this study to survivors               │
│ N = 128                                          │
└─────────────────────────────────────────────────┘
            │
            │        ┌─────────────────────────────────────────┐
            ├───────▶│ Declined participation in this study     │
            │        │ n = 3                                    │
            │        └─────────────────────────────────────────┘
            ▼
┌─────────────────────────────────────────────────┐
│ Distributed questionnaires to participants       │
│ n = 125                                          │
└─────────────────────────────────────────────────┘
            │
            │        ┌─────────────────────────────────────────┐
            ├───────▶│ Questionnaires not returned              │
            │        │ n = 11                                   │
            │        └─────────────────────────────────────────┘
            ▼
┌─────────────────────────────────────────────────┐
│ Returned questionnaires to researchers and       │
│ obtained medical histories of survivors          │
│ n = 114                                          │
└─────────────────────────────────────────────────┘
            │
            │        ┌─────────────────────────────────────────┐
            ├───────▶│ Unemployed survivors                     │
            │        │ (32 students, 8 homemakers, and 9 others)│
            │        │ n = 49                                   │
            │        └─────────────────────────────────────────┘
            ▼
┌─────────────────────────────────────────────────┐
│ Employed survivors                               │
│ n = 65                                           │
└─────────────────────────────────────────────────┘
            │
            │        ┌─────────────────────────────────────────┐
            ├───────▶│ Incomplete items on work performance     │
            │        │ n = 4                                    │
            │        └─────────────────────────────────────────┘
            ▼
┌─────────────────────────────────────────────────┐
│ Analyzed data from questionnaires                │
│ n = 61                                           │
└─────────────────────────────────────────────────┘
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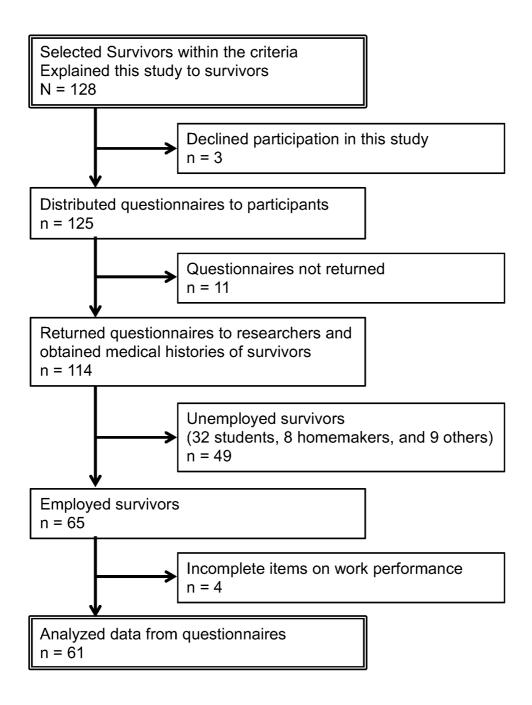
Table 1. Frequency of physical late effects in employed CCSs

	Employed CCSs with single physical LE (N = 21)		Employed CCSs with multiple physical LEs (N = 10) †	
	n	%	n	%
Cardiovascular dysfunction	0	0	0	0
Pulmonary dysfunction	0	0	2	20
Endocrine dysfunction	11	52	5	50
Renal dysfunction	1	5	2	20
Bone/muscle dysfunction	4	19	3	30
Skin dysfunction	0	0	2	20
Neurocognitive dysfunction	1	5	1	10
Gastrointestinal dysfunction	1	5	0	0
Hepatic dysfunction	1	5	1	10
Immunological dysfunction	0	0	0	0
Second cancer	0	0	1	10
Chronic infection	0	0	0	0
Others ‡	2	10	4	40

Note. CCS, childhood cancer survivor; LE, late effect.

† Multiple answers allowed.

‡ Included obesity, gonadal dysfunction, paralysis, and hearing loss.

Table 2. Demographic characteristics in employed CCSs

	Employed CCSs with no physical LE (N = 30)		Employed CCSs with single physical LE (N = 21)		Standardized bias †		Employed CCSs with multiple physical LEs (N = 10)		Standardized bias ‡	
	Mean or n	SD or %	Mean or n	SD or %	Unadjusted	IPW Adjusted	Mean or n	SD or %	Unadjusted	IPW Adjusted
Age at the time of the survey [years]	25.7	4.2	27.2	5.1	0.340	0.168	24.7	4.7	0.209	0.497
Female gender	18	60	13	62	0.039	0.081	8	80	0.413	0.229
Educational level					0.099	0.202			0.138	0.017
Junior-high and high school	10	33	8	38			4	40		
Vocational school, college, university, and graduate school	20	67	13	62			6	60		
Employment status					0.099	0.154			0.138	0.102
Full-time	20	67	13	62			6	60		
Part-time and self-employed	10	33	8	38			4	40		
Occupational type					0.292	0.160			0.068	0.419
Professional, service, sales, and production	20	67	11	52			7	70		
Managerial, clerical, security, and others	10	33	10	48			3	30		
Job stress	2.4	0.8	2.3	1.0	0.081	0.137	2.4	0.8	0.243	0.183

Note. CCS, childhood cancer survivor; IPW, Inverse probability weighting; LE, Late effect; SD, Standard deviation.

† Between survivors with no and single late effects.

‡ Between survivors with no and multiple late effects.

Table 3. Clinical characteristics in employed CCSs

	Employed CCSs with no physical LE (N = 30)		Employed CCSs with single physical LE (N = 21)		Standardized bias †		Employed CCSs with multiple physical LEs (N = 10)		Standardized bias ‡	
	Mean or n	SD or %	Mean or n	SD or %	Unadjusted	IPW Adjusted	Mean or n	SD or %	Unadjusted	IPW Adjusted
Age at diagnosis [years]	8.8	4.8	8.3	4.6	0.112	0.116	11.2	4.1	0.500	0.204
Diagnosis §					0.132	0.179			1.305	0.197
Hematological malignancy	26	87	17	81			3	30		
ALL	17	57	10	48			2	20		
AML	2	7	3	14			1	10		
CML	1	3	0	0			0	0		
APL	1	3	0	0			0	0		
NHL	5	17	4	19			0	0		
Solid tumor	4	13	4	19			7	70		
Brain Tumor	1	3	1	5			1	10		
Neuroblastoma	1	3	0	0			0	0		
Osteosarcoma	1	3	3	14			2	20		
Ewing's Sarcoma	0	0	0	0			1	10		
Extracranial germ cell tumor	0	0	0	0			1	10		
Undifferentiated sarcoma	1	3	0	0			0	0		

Synovial sarcoma	0	0	1	5			0	0		
Rhabdoid tumor	0	0	0	0			1	10		
Renal cell carcinoma	0	0	0	0			1	10		
Treatment modalities c)										
Chemotherapy	30	100	21	100	0.000	0.000	10	100	0.000	0.000
Radiotherapy	11	37	15	71	0.692	0.056	7	70	0.663	0.079
SCT	5	17	9	43	0.570	0.012	4	40	0.507	0.465
Surgery	4	13	4	19	0.132	0.179	7	70	1.305	0.197
Age at treatment completion [years]	11.2	4.9	11.3	4.7	0.014	0.057	12.9	3.1	0.370	0.098
Relapse	3	10	7	33	0.582	0.139	2	20	0.249	0.115

Note. ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; APL, Acute promyelocytic leukemia; CCS, childhood cancer survivor; CML, chronic myeloid leukemia; IPW, Inverse probability weighting; LE, late effect; NHL, non-Hodgkin lymphoma; SCT, stem cell transplantation; SD, standard deviation.

† Between survivors with no and single late effects.

‡ Between survivors with no and multiple late effects.

§ The standardized bias for the difference in the rate of hematological malignancies between employed CCSs with no, single, and multiple physical late effects were calculated.

Table 4. Presenteeism in employed CCSs

	Employed CCSs with no physical LE (N = 30)			Employed CCSs with single physical LE (N = 21)			Employed CCSs with multiple physical LEs (N = 10)		
	Mean	SD	Range	Mean	SD	Range	Mean	SD	Range
WLQ									
Productivity Loss Score	2.5	2.0	0.0–6.8	3.5	3.7	0.0–11.6	5.8	4.1	2.1–13.2
Time Management	5.9	6.7	0.0–25.0	12.7	15.6	0.0–45.0	16.1	20.6	0.0–60.0
Mental-Interpersonal	7.9	9.2	0.0–35.0	11.9	14.1	0.0–43.8	22.4	19.4	2.8–66.7
Output	7.6	8.6	0.0–30.0	14.5	17.6	0.0–60.0	20.0	17.5	0.0–50.0
Physical	9.1	14.8	0.0–41.7	18.1	20.3	0.0–66.7	28.3	21.9	0.0–66.7

Note. CCS, childhood cancer survivor; LE, Late effect; SD, Standard deviation; WLQ, Work Limitations Questionnaire.

Table 5. Impacts of physical late effects on presenteeism in employed CCSs estimated by a generalized linear model †

		WLQ				
		Productivity Loss Score	Time Management	Mental-Interpersonal	Output	Physical
Employed CCSs with single physical LE	Estimate ‡	0.2	3.2	-0.3	2.4	5.3
	SE	0.9	3.6	3.3	3.9	5.0
	Wald 95% CI					
	Upper	1.9	10.2	6.1	10.1	15.2
	Lower	-1.5	-3.9	-6.7	-5.3	-4.5
	Wald χ^2 §	0.046	0.779	0.007	0.383	1.116
	p	0.830	0.377	0.933	0.536	0.291
	r	0.029	0.118	0.011	0.083	0.141
Employed CCSs with multiple physical LEs	Estimate ‡	2.4	6.4	7.8	9.3	12.2
	SE	1.2	8.0	5.0	4.6	5.2
	Wald 95% CI					
	Upper	4.8	22.2	17.6	18.3	22.5
	Lower	0.1	-9.3	-2.0	0.4	2.0
	Wald χ^2 §	4.007	0.641	2.463	4.180	5.445
	p	0.045	0.423	0.117	0.041	0.020

	r	0.261	0.107	0.207	0.266	0.300

Note. CCS, childhood cancer survivor; CI, Confidence interval; LE, Late effect; SE, Standard error; WLQ, Work Limitations Questionnaire.

† A generalized linear model adjusted age at the time of the survey, occupational types, and SCT as confounders.

‡ Reference is survivors with no late effects.

§ Degree of freedom is 1.