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Psychosocial Predictors of Smoking and Alcohol Use in Canadian Pediatric Cancer Survivors: Structural Equation Modeling

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Psychosocial Predictors of Smoking and Alcohol Use in Canadian Pediatric Cancer Survivors: Structural Equation Modeling

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Thesis submitted to the
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Abstract

Survivors of pediatric cancer should avoid smoking and heavy alcohol use due to health risks associated with intensive cancer treatments they received. Data were analyzed from a multi-centre, population-based study of pediatric cancer survivors in Canada (n=1231) and a frequency matched control group (n=1372). Logistic regression analyses showed that survivors were significantly less likely to be smokers and alcohol drinkers than the controls. Still, a substantial proportion of survivors were smokers (23%), binge drinkers (25%), alcohol drinkers (69%) and concurrent users (20%). Low education, poor life satisfaction, and high stress were the most consistent predictors of substance use. Results from the structural equation modeling analysis to describe pathways to concurrent smoking and alcohol use showed significant pathways from education and chronic stress to concurrent use in the cancer survivors. This study identifies potential risk factors for smoking and alcohol use in cancer survivors and suggests a need for preventive education.

Summary

Survivors of pediatric cancer are at risk for morbidities later in life and early mortality associated with intensive cancer treatments. For this reason survivors should be more cautious than their peers in avoiding health risk behaviours such as smoking and heavy alcohol use. The purposes of the current study were to determine the risks and predictors of smoking and alcohol use in pediatric cancer survivors and to develop and test a theoretical model describing pathways to concurrent use of alcohol and tobacco.

Data were analyzed from a multi-centre, population-based study of pediatric cancer survivors age 16 to 37 years from twelve pediatric oncology centres in Canada (n=1231) and a frequency matched control group (n=1372). Logistic regression analyses were performed to examine predictors of current smoking, alcohol use, binge drinking and concurrent use of alcohol and tobacco. Structural equation modeling was conducted to test a theoretical model describing pathways to concurrent smoking and alcohol use.

Survivors were significantly less likely to be current smokers (OR_{adj}=0.64, 95%CI=0.53-0.77), drinkers (OR_{adj}=0.73, 95%CI=0.60-0.88), binge drinkers (OR_{adj}=0.68, 95%CI=0.57-0.82) and concurrent users (OR_{adj}=0.65, 95%CI=0.53-0.78) than the control group. However, approximately one-fifth to one-quarter of survivors were engaging in health risk behaviours. Low education, poor life satisfaction and high stress were the most consistent predictors of smoking and alcohol use in both the cancer survivors and control group. Different predictors between the two groups included physical and mental health, special education and various clinical factors.

Structural equation modeling results showed significant pathways from education and chronic stress to concurrent use of alcohol and tobacco in the pediatric cancer survivors, with education being more strongly associated. In the control group satisfaction with life was a significant mediator between various health and psychosocial factors and concurrent use of alcohol and tobacco but this was not found for the cancer survivors.

Cancer survivors need to be educated about the health risks associated with smoking and heavy alcohol use and their vulnerability to developing health conditions. Interventions and policy targeted to helping pediatric cancer survivors improve their educational attainment and cope with chronic stress may also help improve their life satisfaction, self-esteem and reduce smoking and alcohol use in this population.

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List of Abbreviations

CCCSCP	Canadian Childhood Cancer Surveillance and Control Program
ALL	Acute Lymphoblastic Leukemia
CNS	Central Nervous System
LCH	Langerhans Cell Histiocytosis
ICCC	International Classification of Childhood Cancer
LD	Learning Disabled
CDC	Centers for Disease Control and Prevention
SEM	Structural Equation Modeling
CFA	Confirmatory Factor Analysis
RMSEA	Root Mean Square Error of Approximation
CFI	Comparative Fit Index
TLI	Tucker Lewis Index
WLSMV	Weighted Least Squares Mean and Variance adjusted
OR	Odds Ratio
CI	Confidence Interval
SD	Standard Deviation
SE	Standard Error
SWLS	Satisfaction With Life Scale
MAR	Missing At Random
MCAR	Missing Completely At Random

1.0 INTRODUCTION

Approximately 1,300 children and adolescents are diagnosed with cancer each year in Canada [1]. Due to improved treatments the five-year survival rate is approximately 80% for all types of pediatric cancer combined and has exceeded 70% for most cancers [2]. Although there is an improved survival rate there are a number of late effects associated with intensive cancer treatment and psychosocial consequences of having cancer that the survivors will face.

Pediatric cancer survivors are at increased risk for developing disease and early mortality. As a result, it has been recommended that they be more cautious than their peers in avoiding lifestyle behaviours such as smoking and heavy alcohol use and engage in health protective behaviours such as exercise and consumption of a healthy diet [3]. Although pediatric cancer survivors are at increased risk for developing health complications a number of early studies found that they were engaging in health risk behaviours at a similar rate as their peers [4, 5]. More recent studies found that pediatric cancer survivors were leading slightly healthier lifestyles than their peers. However, due to the health risks associated with smoking and heavy alcohol use educational programs, physician counselling and interventions are important to promote healthy lifestyles and support lifestyle changes in this sensitive population [6-9].

Most previous research has focused on the prevalence of health risk behaviours in pediatric cancer survivors, especially smoking. In order to design effective interventions it is also important to understand *why* survivors are engaging in these behaviours and if certain groups of survivors are at increased risk [3]. Identifying predictors of health risk behaviours in pediatric cancer survivors will aid in determining what types of interventions are needed and to whom they should be targeted [10].

There has been little research on alcohol use, or its concurrent use with tobacco in pediatric cancer survivors. Butterfield et al. [3] found that pediatric cancer survivors who had a higher intake of alcohol were more likely to smoke heavily. Studies of the general population have repeatedly found that there is a moderate to strong association between smoking and alcohol drinking where persons who smoke are more likely to drink alcohol, and vice versa. This suggests that there may be common risk factors for engaging in substance use making it informative to study concurrent tobacco and alcohol use [11].

This research aims to further our knowledge about important demographic, psychosocial, health and clinical factors associated with smoking and alcohol use in pediatric cancer survivors. It also aims to fill the gaps in knowledge about alcohol use and its concurrent use with tobacco in cancer survivors. This research determines the risks of smoking and alcohol use, their predictors and possible pathways among Canadian pediatric cancer survivors and age and sex matched controls from the general population. This research is important in order to guide policy and develop interventions to prevent or reduce smoking and alcohol use in pediatric cancer survivors who are at increased risk for negative health outcomes.

2.0 REVIEW OF THE LITERATURE

The purpose of this literature review was: 1) to provide a background on the late effects of cancer treatment in pediatric cancer survivors to affirm the importance of abstaining from smoking and heavy alcohol use in this population; 2) to identify and review studies on the prevalence and predictors of smoking and alcohol use in pediatric cancer survivors; 3) to provide a brief review of established theories of health risk behaviours; and 4) to review intervention studies for changing and promoting health behaviours in pediatric cancer survivors. A comprehensive literature search was performed in the PubMed, SCOPUS, Medline, PsychINFO and CINAHL databases to identify studies on smoking, alcohol use, binge drinking and health risk behaviours in pediatric cancer survivors. Literature published in English prior to August 2006 was included in the review. Key words included: p(a)ediatric, adolescent, child, childhood, survivor(s), neoplasm, cancer, childhood cancer, smoking, tobacco, alcohol, drinking, binge drinking, health behaviour(s), health behavior(s), and lifestyle. Literature was also identified from reference lists of published papers.

2.1 Late effects of cancer treatment and health risk behaviours

Late effects are health problems resulting from toxic cancer therapy that are absent or subclinical at the end of therapy but present later in life as the child develops and ages [12]. Late effects can be categorized by their time of occurrence from the end of treatment. Early late effects occur within five years, intermediate at five to twenty years and very late effects occur over twenty years after discontinuation of therapy [13]. Approximately 70% of pediatric cancer survivors report late effects related to their cancer treatment with one third being moderate to severe [14].

Treatment of cancer in children usually involves chemotherapy, radiotherapy, surgery or a combination of the three and are associated with various late effects [15]. Chemotherapy and radiotherapy have cytotoxic and mutagenic effects causing tissue damage that may result in organ dysfunctions later in life [12]. Surgery can also have side effects especially neuropsychological and cognitive difficulties in survivors of brain tumours [16]. Pediatric cancer survivors are at increased risk for early mortality and morbidities including: cardiac,

pulmonary, endocrine, renal, hepatic and gastrointestinal dysfunctions, hypertension and second malignancies, among others [16-18].

Pediatric cancer survivors are at risk for developing second malignant neoplasms due to the effects of treatment with radiation, particular chemotherapeutic agents or an underlying genetic predisposition [19-21]. Miké et al.[22] found that compared to the general population pediatric cancer survivors had a ten-fold or greater risk of developing a second malignant neoplasm within five to fifteen years of diagnosis and a cumulative incidence of 3.3% after twenty years. Being female, having a younger age at diagnosis, Hodgkin's disease, soft-tissue sarcoma, treatment with alkylating agents and relapse of initial cancer may be risk factors for developing second malignant neoplasms [17, 23-25]. Second malignant neoplasms may be one of the most distressing late effects for pediatric cancer survivors; they will have to undergo the difficult process of treatment and deal with the emotional and psychological aspects of having cancer yet again [15].

Cytotoxic cancer treatment also puts pediatric cancer survivors at increased risk for cardiovascular disease. Therapy with certain types of drugs including anthracyclines, alkylating agents, 5-fluorouracil (5-FU) and paclitaxel, are associated with cardiomyopathy, dysrhythmias, congestive heart failure and myocardial ischemia. Chest radiotherapy can also increase the risk for cardiovascular disease as it damages the cellular structures in the cardiac tissue [26]. Cardiac late effects are not uncommon in pediatric cancer survivors [27, 28] and there are a number of factors that can increase the risk of developing cardiovascular disease later in life such as growth hormone deficiency, excess body weight, low energy expenditure and altered cardiac structure or function. [29] Survivors of pediatric acute lymphoblastic leukemia and brain cancer were found to have risk factors for cardiovascular disease including growth hormone deficiencies, obesity, dyslipidemia, high blood pressure, and insulin resistance, which may be related to their cancer treatment. [30-33]. Cranial radiation and intensive chemotherapy may cause endocrine disruptions that affect the metabolism of survivors putting them at risk for obesity [32, 34].

Chest radiation and treatment with chemotherapeutic agents can also result in pulmonary dysfunctions [35, 36]. Mertens et al. [35] found that compared to their siblings pediatric cancer survivors had a greater risk of having self-reported lung fibrosis, recurrent pneumonia, chronic cough, pleurisy, abnormal chest wall, exercise-induced shortness of

breath, among other problems. Chest radiation and chemotherapeutic drugs such as bleomycin, busulfan, nitrosoureas and cyclophosphamide were associated with pulmonary dysfunction. Nysom et al. [36] found that younger age at treatment, intensive treatment with cranial irradiation, anthracyclines, cytosine arabinoside and intravenous cyclophosphamide were associated with compromised pulmonary function.

Osteoporosis and decreased bone mineral density is a late effect observed in survivors of pediatric cancer, especially survivors of acute lymphoblastic leukemia [37]. In a review of past literature Haddy et al. [37] identified leukemic invasion of the bone, corticosteroid and methotrexate therapy, cranial and local radiation, hormone deficiency, physical inactivity, nutritional deficiencies, male sex and being Caucasian as risk factors for osteoporosis in survivors of acute lymphoblastic leukemia.

Additional late effects observed in pediatric cancer survivors include liver disease, renal dysfunction and gastrointestinal disorders, among others. Hepatic fibrosis and cirrhosis are late effects that may occur and are related to treatment with abdominal radiation and certain chemotherapeutic agents. Blood transfusions also increase the risk for infection with Hepatitis C, which causes liver tissue damage. Radiation, chemotherapy and surgery can increase the risk for gastrointestinal late effects in pediatric cancer survivors. Intestinal fibrosis and enteritis are the most common and are associated with radiotherapy. Common to most late effects, renal dysfunction is dependent on the dose of agents used during chemotherapy, field and dose of radiotherapy, use of multiple treatment modalities and duration of treatment [12, 16, 38].

Pediatric cancer survivors have a higher mortality rate than persons of the same age in the general population [39, 40]. Mertens et al. [40] found that there was an eleven-fold excess of overall mortality in pediatric cancer survivors compared to the general population in the United States. The cumulative mortality rate was 14% twenty-five years after diagnosis. Deaths due to late effects of treatment accounted for 21.3% of deaths of which 12.7% were attributed to second malignancies, 4.5% to cardiac toxicity, 1.8% to pulmonary complications, and the remainder to other treatment related problems. Survivors who were treated with radiation and alkylating agents may be at increased risk for dying from causes other than primary cancer. [39]

In addition to compromised health, pediatric cancer survivors may have psychosocial late effects associated with their cancer experience and their psychosocial functioning may influence their health behaviours. Most research has found that the majority of pediatric cancer survivors have few psychological symptoms and are socially well adjusted [41] [42-46]. A systematic review by Eiser et al. [47] concluded that pediatric cancer survivors did not score worse than their peers or the general population on measures of anxiety, depression, and self-esteem. However, they did find that survivors of bone tumors had worse psychological outcomes than survivors with other types of cancer. Those with severe medical late effects, who had intensive treatments or cranial radiation may be at greater risk for psychosocial late effects [46-48]. Factors that have been associated with poor psychosocial adjustment in the general population also seem to be important in pediatric cancer survivors including socioeconomic status, educational attainment and gender [45, 49, 50].

Social and behavioural development may be more strongly affected by the cancer experience. In a study of 353 adult pediatric cancer survivors from the Netherlands Stam et al. [51] found that survivors were less likely to achieve developmental milestones or were achieving them at older ages. These milestones included: autonomy, social development and psychosexual development. Behavioural adjustment problems in pediatric cancer survivors may include anxiety, somatization, attention, adaptability and withdrawal [52]. In regards to social development Evans et al. [41] found that survivors were significantly less likely to receive higher education but were just as socially active as their siblings, achieved similar grades and had similar salaries.

In the general population smoking has been associated with an increased risk for developing cancer, pulmonary disease, cardiovascular disease, hypertension, osteoporosis and gastrointestinal disease, among others [53]. Heavy alcohol use has been associated with an increased risk for hypertension, liver disease, cardiovascular disease, and cancers of the upper gastrointestinal tract [54]. Lifestyle choices, compromised physiological systems, organ damage resulting from cancer treatment, genetic susceptibility to cancer and demographic factors may interact increasing the risk of morbidity and mortality in pediatric cancer survivors [55]. Abstaining from smoking and heavy alcohol use and engaging in positive health behaviours may be the only measure cancer survivors can take to try to prevent the development of health conditions to which they are predisposed.[9]

2.2 Prevalence of smoking and alcohol use in pediatric cancer survivors

There were twelve studies identified from a search of the literature that examined the prevalence of smoking, alcohol use or binge drinking in adult pediatric cancer survivors. A summary of characteristics of these studies and results are presented in Table 1. There were seven studies identified from a search of the literature that examined the prevalence of smoking, alcohol use or binge drinking in adolescent pediatric cancer survivors. A summary of characteristics of these studies and results are presented in Table 2.

Table 1: Studies examining the prevalence of smoking and alcohol use in adult pediatric cancer survivors

Authors Year	No. of Survivors	Country	Cohort (year of diagnosis)	Age (y)	Prevalence of current smokers	Prevalence of ever smokers	Prevalence of alcohol use	Prevalence of >5 drinks per occasion
Corkery et al. 1979 [4]	425	United States	Unknown	18+	Survivors: 30%			
Troyer & Holmes 1988 [5]	263	United States	1945-1975	21+	Survivors: 33.3% Siblings: 38.2%	Survivors: 13% Siblings: 16.5%		
Haupt et al. 1992 [56]	1289	United States	1945-1974	21+	Survivors: 28.6% Siblings: 30.5%	Survivors: 14.3% Siblings: 15.8%		
Mulhern et al. 1995 [57]	40	United States	Prior to 1988	18+	Survivors: 17.5%	Survivors: 47.5% ever tried smoking	Survivors: 72.5%	Survivors: 12.5%
Tao et al. 1998 [7]	592	U.S. & Canada	1970-1987	18+	Survivors: 14.0% Control: 20.3%	Survivors: 23.0% Control: 35.7%		
Verrill et al. 2000 [58]	26	United States	Unknown	~18	Survivors: 28% Control: 56%		Survivors: 54% Control: 65%	
Haddy et al. 2000 [59]	88	United States	1973-1993	18+ (8<18 y)	Survivors: 19.5%		Survivors: 65.1%	
Larcombe et al. 2002 [6]	113	United Kingdom	Prior to 1991	18-30	Survivors: 20% Control: 29%	Survivors: 29% Control: 45%	Survivors: 75% Control: 91%	Survivors: 37% Control: 42% Sibling: 43%
Emmons et al. 2002 [8]	9709	U.S. & Canada	1970-1986	18+	Survivors: 17%	Survivors: 28%		
Demark-Wahnfried et al. 2005 [60]	122	United States	Unknown	18+	Survivors: 17%	Survivors: 12%		
Bauld et al. 2005 [61]	72	Australia	Unknown	18-24	Survivors: 29%		Survivors: 90%	Survivors: 53%
Foster et al. 2006 [62]	HRb= 4441 NHRb= 395	United States	1914-1984	18+	HRb: 6.8% NHRb: 24.3%	HRb: 4.3% NHRb: 45.2%		

HRb= Hereditary Retinoblastoma
NHRB=Non-Hereditary Retinoblastoma

Table 2: Studies examining the prevalence of smoking and alcohol use in adolescent pediatric cancer survivors

Authors Year	No. of Survivors	Country	Cohort (year of diagnosis)	Age (y)	Prevalence of current smokers	Prevalence of ever smokers	Prevalence of alcohol use	Prevalence of >5 drinks per occasion
Hollen & Hobbie 1993 [63]	36	United States	Unknown	14-19	Survivors: 14%	Survivors: 53%	Survivors: 25%, 67% ever used alcohol	
Mulhern et al. 1995 [57]	110	United States	Prior to 1988	11-17	Survivors: <10%		Survivors: <10%	
Hollen & Hobbie 1996 [64]	52	United States	Unknown	14-19		Survivors: 48%	Survivors: 71% ever used alcohol	Survivors: 44% Control: 58%
Tyc et al. 2001 [65]	46	United States	Unknown	10-18	Survivors: 15.2%		Survivors: 27.3%	Survivors: 9.1%
Demark-Wahnfried et al. 2005 [60]	87	United States	Unknown	<18	Survivors: 1%	Survivors: 0%		
Bauld et al. [61] 2005	81	Australia	Unknown	13-17	Survivors: 16% Control : 31%		Survivors: 56% Control : 55%	Survivors: 16% Control: 25%
Tercyak et al. 2006 [66]	75	United States	Unknown	11-21		Survivors: 15% ever tried smoking		

Smoking

Early studies on smoking behaviours in pediatric cancer survivors found that survivors were smoking at similar rates as their siblings and the general population [4, 5]. A survey by Corkery et al. [4] found that 30% of pediatric cancer survivors over the age of 18 years reported being current smokers and smoked on average 21 cigarettes per day. Similarly, Troyer and Holmes [5] found in a study of cancer survivors over the age of 21 years that 33.3% smoked and 13.0% were former smokers. These prevalences were similar to the sibling controls where 38.2% were current smokers and 16.5% were former smokers. Haupt et al. [56] found that 28.6% of adult pediatric cancer survivors were current smokers, which was similar to their siblings (30.5%). In younger pediatric cancer survivors aged 12-19 years Hollen and Hobbie [63] found that the prevalence of ever smoking in survivors (53%) was comparable to that in the general population (52%). Their findings were replicated in a later study with a larger sample size where 48% of survivors reported ever smoking cigarettes [64]. These results may be expected as pediatric cancer survivors are challenged with the same social pressures as their peers to smoke and engage in health risk behaviours [67].

The prevalence of current smokers was much lower in the study by Hollen and Hobbie[63] (14%) compared to earlier studies by Troyer and Holmes[5], Corkery et al.[4] and Haupt et al.[56]. Hollen and Hobbie studied a population of adolescents whereas the other three studies were of adult survivors suggesting that smoking behaviours may increase with age. This is consistent with findings from a study by Demark-Wahnfried et al.[60] where survivors over the age of 18 years were significantly more likely to be current smokers (17%) than those under the age of 18 years (1%). In the general population it has been observed that there is an increase in smoking during adolescence, which peaks during young adulthood and then decreases slightly with older age [68].

Another explanation for the discrepancy in the prevalence of smoking is the year that the studies were conducted. The studies by Troyer and Holmes[5], Corkery et al.[4] and Haupt et al.[56] included cancer survivors that were adults in the late 1970's whereas Hollen and Hobbie[63] surveyed participants that were teenagers in the early 1990's. A birth cohort effect for smoking has been observed in both pediatric cancer survivors and in the general population where those born more recently are less likely to smoke as smoking is not as socially desirable as it was in the past [7, 8]. Hollen and Hobbie also had a small sample size

and only selected participants from one follow-up clinic so their results may not be a good representation of all adolescent survivors of pediatric cancer.

More recent studies suggest that pediatric cancer survivors are making healthier lifestyle choices. Stam et al. [51] found that survivors of pediatric cancer were significantly less likely to smoke than their peers both during and after finishing high school. Tao et al. [7] found that adult cancer survivors were significantly less likely to ever be daily smokers (19.1%) than their sibling controls (31.3%) and that they were smoking less than pediatric cancer survivors in earlier studies. Among pediatric cancer survivors significantly fewer (23%) reported that they had ever smoked compared to the sibling controls (35.7%). Similarly, Emmons et al.[8] found that 17% and 28% of adult survivors of pediatric cancer reported being current and ever smokers respectively and that they were smoking less than the general population. Foster et al.[62] found that adult survivors of retinoblastoma were smoking less than the general population of the same age in the United States and that survivors of hereditary retinoblastoma had a lower prevalence of current smoking than survivors of non-hereditary retinoblastoma (16.8% vs. 24.3%). Larcombe et al.[6] found that 20% and 9% of adult pediatric cancer survivors reported being current and ex-smokers respectively, which was significantly lower than the controls. A recent study of pediatric cancer survivors in Australia found that adult survivors age 18-24 years had a significantly lower prevalence of current smoking (29%) than the age matched control group (43%) [61]. Compared to earlier studies the rate of smoking in adult survivors of pediatric cancer dropped more dramatically than in the general population [6].

Adolescent survivors of pediatric cancer have a lower prevalence of smoking than their peers and also have a lower prevalence of smoking than adult survivors of pediatric cancer. Tyc et al.[69] found that 15.2% of pre-adolescent and adolescent pediatric cancer survivors reported using cigarettes and were smoking less than adolescents in the general population. Similarly, a study of pediatric cancer survivors in Australia found that 16% of adolescent survivors age 13-17 years reported being current smokers compared to 31% of age matched controls [61]. Mulhern et al.[57] found that in survivors under 18 years of age less than 10% reported being smokers and in survivors 18 years of age or over 17.5% reported being a smoker. Underreporting of tobacco use is possible in the group of cancer survivors

under 18 years of age as their parents completed the questionnaire on their child's health behaviours. Parents and guardians are often not aware of their child's substance use. [70]

The sample of pediatric cancer survivors in a study by Haddy et al.[59] contained both adult and a few adolescent survivors of non-Hodgkin's lymphoma. They found that the prevalence of current smoking was 19.5%, which is consistent with other studies of adult survivors. A study by Verrill et al.[58] did not find a significant difference in smoking behaviours between pediatric cancer survivors and matched controls. They found that both groups had a low prevalence of smoking. However, this study had a small sample size with only twenty-six survivors and twenty-six matched controls.

In studies of survivors of pediatric cancer that are less than 18 years of age the prevalence of current smoking ranged from 1% to 16% [57, 60, 61, 63, 69]. In recent studies of adult survivors of pediatric cancer the prevalence of current smoking ranged from 14% to 29% [6-8, 58, 60, 61]. Discrepancies in the prevalence of smoking in studies of pediatric cancer survivors may result from a birth cohort effect and differences in age of the survivors as well as other characteristics of the sample. Some study samples, especially small ones, may not be representative of the population of pediatric cancer survivors as a whole.

The prevalence of smoking may also differ by cancer diagnosis and treatment. The physical and psychosocial consequences of having cancer differ by the type of cancer and treatment where some survivors may be less likely to smoke than others [7]. In studies that looked at all types of cancer certain cancer types were underrepresented in the samples. Eligibility criteria for studies also varied. Some included the criteria that survivors must be in remission and had no treatment in the two years preceding the study while other studies had shorter time periods between treatment and recruitment [7, 61]. It is possible that survivors who underwent treatment more recently were less likely to smoke than survivors who had been off treatment for a longer period of time.

Regional differences could also explain discrepancies in the prevalence of smoking in pediatric cancer survivors. In the general population it has been found that persons are more or less likely to smoke depending where they live [68]. The studies reviewed here were mainly conducted in the United States. Some included survivors from all states while others were limited to smaller geographical regions. One study included in this review was of survivors in the United Kingdom[6] and another in Australia [61]. There were no studies of only survivors

from Canada although the Childhood Cancer Survivor Study (CCSS) study included survivors from the United States and a few oncology centres in Canada [3, 71].

Discrepancies in the reported prevalence of smoking in pediatric cancer survivors may also be due to differences in the definition of smoking and the way that authors measured smoking. The CDC definition of smoking [72] was most common but other questionnaires and scales were used.

Control group selection is important in comparison studies. In the studies reviewed here control groups included siblings, age-matched persons from the general population who had not had cancer and comparison with statistics of the general population. The use of siblings as a comparison group can be beneficial because they have been exposed to the same social environment including family members that smoke and share genetic factors. However, a sibling may also be likely to avoid health risk behaviours because they are often affected by their sibling's cancer experience [73]. Taking controls from the general population that have not had a sibling with cancer could therefore be beneficial.

Alcohol use

There have been few studies on the use of alcohol by pediatric cancer survivors. Mulhern et al.[57] reported that the percentage having ever used alcohol was less than 10% in pediatric cancer survivors under the age of 18 years and was 72.5% in those over 18 years of age, but that problem drinking was not often reported. Underreporting of alcohol use is likely in this study in the group of cancer survivors under 18 years of age as their parents completed the questionnaire on their child's health risk behaviours [70].

In a study by Tyc et al.[69] adolescent survivors self-completed questionnaires on health behaviours and the reported use of alcohol was higher than in the study by Mulhern et al.[57]. They found that the prevalence of ever using alcohol in preadolescent and adolescent pediatric cancer survivors was 27.3% with 9.1% drinking greater than five drinks per occasion (binge drinking) in the previous month and 0% drinking 60 or more drinks in the previous month (heavy drinking). Hollen and Hobbie [64] found a much higher prevalence of binge drinking in adolescent pediatric cancer survivors (44%) but they examined the number of survivors who had five or more drinks per occasion in the previous year, not one month.

Hollen and Hobbie [63] found that alcohol use in pediatric cancer survivors was similar to that in the general population. Sixty-seven percent of adolescent survivors reported ever

using alcohol and 25% did so within the previous month. In the general population 78% of adolescents reported ever using alcohol and 43% did so in the previous month. Their findings were replicated in a later study with a larger sample size where they found that 71% of adolescent survivors had ever used alcohol [64].

Larcombe et al.[6] found that adult pediatric cancer survivors were significantly less likely to drink alcohol than the controls where 75% were current drinkers compared to 91% of controls. Survivors were also less likely to drink alcohol than their siblings but this difference was not statistically significant. They found that both male and female survivors were more likely to be light drinkers than their peers and siblings. Binge drinking was also lower among survivors (37%) than the controls (42%) or their siblings (43%). Hollen and Hobbie[64] did not find a significant difference between adolescent cancer survivors and their peers in regards to binge drinking or number of times being drunk in the previous year.

Haddy et al.[59] studied predominantly adult survivors of non-Hodgkin's lymphoma. They found that the prevalence of current alcohol use was 65.1%, which is consistent with other studies of adult survivors. Verill et al.[58] did not find a statistically significant difference between pediatric cancer survivors (54%) and controls (65%) in terms of alcohol use but could have been due to a small sample size.

Unlike previous findings a recent study of adult pediatric cancer survivors from Australia found that survivors were equally or significantly more likely to be current alcohol drinkers than the age matched control group [61]. In survivors age 13-17, 56% reported being alcohol drinkers compared to 55% of controls and in survivors age 18-24, 90% reported being alcohol drinkers compared to 75% of controls. They found that survivors aged 13-17 years were less likely to be binge drinkers compared to controls (16% vs. 25%). In the 18-24 year age group the prevalence of binge drinking was the same for both groups (53%) [61]. These findings are not consistent with other studies of pediatric cancer survivors and may be due to regional differences as this study was conducted in only one pediatric oncology centre in Australia.

Four studies reviewed here reported the prevalence of alcohol use in adult pediatric cancer survivors ranged from 54% to 90% [6, 58, 59, 61]. In adolescent pediatric cancer survivors the prevalence of alcohol use ranged from less than 10% to 56% [57, 61, 63, 65]. The prevalence of binge drinking ranged from 12.5% to 53% in adult survivors [6, 57, 61] and 9.1% to 44% in

adolescents [61, 64, 65]. As with smoking behaviours the prevalence of alcohol use increased from adolescence to young adulthood. Stam et al.[51] found that pediatric cancer survivors were significantly less likely to consume alcohol than their peers during high school but were equally as likely to consume alcohol after they had completed high school. Discrepancies in the reported prevalence of alcohol use and binge drinking in studies of pediatric cancer survivors may be for the same reasons as discussed above with smoking: sample size, region, types of cancer, eligibility criteria, definition of alcohol use and the age distribution of survivors.

Concurrent smoking and alcohol use

Since few studies have examined alcohol use in pediatric cancer survivors there is even less information on the concurrent use of alcohol and tobacco in survivors. Butterfield et al.[3] found that there was a positive linear relationship between number of health risk behaviours and smoking in pediatric cancer survivors. Ninety-two percent of survivors who smoked also engaged in other health risk behaviours and those who smoked heavily were more likely to drink heavily. Studies of the general population have found that there is a moderate to strong association between smoking and alcohol drinking where those who consume alcohol are more likely to smoke cigarettes than those who do not, and vice versa. This suggests that there may be common factors that predispose someone to engage in health risk behaviours including smoking and drinking [11].

The lower prevalence of smoking and alcohol use in pediatric cancer survivors may be explained by better education and awareness of late effects but could also be expected, as the physical and social side effects of cancer treatment should be protective against health risk behaviours by limiting behavioural options [58].

2.3 Predictors of smoking and alcohol use in pediatric cancer survivors

There were ten studies identified from a search of the literature that examined covariates for smoking, alcohol use or health risk behaviours in adult pediatric cancer survivors. A summary of characteristics of these studies and results are presented in Table 3. There were ten studies identified from a search of the literature that examined covariates for smoking, alcohol use or health risk behaviours in adolescent pediatric cancer survivors. A summary of characteristics of these studies and results are presented in Table 4.

Table 3: Studies examining predictors of smoking, alcohol use and health risk behaviours in adult pediatric cancer survivors

Authors and year of publication	Predictors of smoking	
	Significant	Not significant
Corkery et al. 1979 [4]	- smoking in family	- history of chest irradiation
Haupt et al. 1992 [56]	- year of diagnosis	-Gender, age at diagnosis, treatment, type of cancer
Mulhern et al. 1995 [57]		- age, gender, age at diagnosis, race, family SES, time since therapy, duration of therapy, marital status
Tao et al. 1998 [7]	- older age, male gender, no college education	
Emmons et al. 2002 [8]	Smoking INITIATION: - older age at diagnosis, lower household income, lower education, not having pulmonary related treatment, not having brain radiation, race (non black)	
Emmons et al. 2003 [71]	- older age, lower education, more smokers in social network, more psychologic symptoms, those reporting support were less likely to quit	
Butterfield et al. 2004 [3]	- >3-4 servings of meat, more than recommended amount of alcohol, more likely to smoke heavily - engaging in more health risk behaviours	
Bauld et al. 2005 [61]		- age at diagnosis or time off and on treatment
Foster et al. 2006 [62]	- non-hereditary Rb, older age, being female, less education and use of other tobacco products significant	- Race, being hospitalized in past 5 years
Authors and year of publication	Predictors of alcohol use	
	Significant	Not significant
Mulhern et al. 1995 [57]		- age, gender, age at diagnosis, race, family SES, time since therapy, duration of therapy, marital status
Larcombe et al. 2002 [6]		-binge drinking higher in males but not significant
Bauld et al. 2005 [61]		- age at diagnosis, time off and on treatment
Authors and year of publication	Predictors of health risk behaviours	
	Significant	Not significant
Larcombe et al. 2002 [6]	- male gender, younger age, single	
Butterfield et al. 2004 [3]	- male gender, less than high school education	

Table 4: Studies examining predictors of smoking, alcohol use and health risk behaviours in adolescent pediatric cancer survivors

Authors Year	Predictors of smoking	
	Significant	Not significant
Mulhern et al. 1995 [57]		- age, gender, age at diagnosis, race, family SES, time since therapy, duration of therapy, marital status
Tyc et al 2001 [65]	INTENTIONS to smoke: - older age and knowledge of consequences	- perceived vulnerability
Tyc et al 2001 [69]	- older age	
Tyc et al 2006 [74]	INTENTIONS to smoke: - past tobacco use, perceived positive value of smoking in older survivors only	- gender, race, SES, diagnosis, time since diagnosis, peer and parent tobacco use, knowledge of consequences and perceived vulnerability
Bauld et al 2005 [61]		- age at diagnosis, time off and on treatment
Authors Year	Predictors of alcohol use	
	Significant	Not significant
Mulhern et al. 1995 [57]		- age, gender, age at diagnosis, race, family SES, time since therapy, duration of therapy, marital status
Bauld et al 2005 [61]		- age at diagnosis, time off and on treatment
Authors Year	Predictors of health risk behaviours	
	Significant	Not significant
Hollen & Hobbie 1993 [63]	- poor quality decision making	- prior CNS prophylactic leukemia therapy
Hollen & Hobbie 1996, 1997, 2001 [64, 75, 76]	- poor quality decision making - non-resiliency (non-even temperament, low self-esteem, low social support, and non-resistance to social pressure)	- age, gender, site of cancer, cognitive ability, treatment age, therapy with cognitive threat - negative modeling by parents and peers
Chen et al. 1998 [77]	- educational achievement	- negative mood
Tyc et al. 2001 [69]	Health PROTECTIVE behaviours: - younger age and higher SES were predictors of	- Gender, time since completion of treatment, perceived vulnerability, health protection and health locus of control
Cox et al. 2006 [78]	- higher grade in school, perceived susceptibility, worry	
Tercyak et al. 2006 [66]	- older age, depression and conflict with parents	- gender, race, type of cancer, time since diagnosis

Identifying risk factors for engaging in health related behaviours will aid in developing appropriate interventions and health promotion programs for pediatric cancer survivors [10]. Pediatric cancer survivors face the same pressures as their peers and therefore may make similar lifestyle choices; the same factors that put the general population at risk for engaging in health risk behaviours may also be important in cancer survivors [76].

Demographic factors including age, gender, race and socioeconomic status have been found to be important predictors of smoking in the general population [50, 68, 79-82]. In most studies of pediatric cancer survivors current age was found to be a significant predictor of smoking, alcohol use and health behaviours where older survivors were more likely to engage in risky behaviours [7, 62, 66, 69, 71]. In pediatric cancer survivors, male gender was associated with smoking, binge drinking and health risk behaviours [3, 6, 7]. However, a number of other studies did not find that gender was associated with health risk behaviours [56, 57, 66] and one study by Foster et al. [62] found that female gender was associated with current smoking in survivors of retinoblastoma. Race was found to be a significant predictor of smoking initiation in pediatric cancer survivors where non-black participants were more likely to begin smoking [8]. A recent study by Tercyack at el.[66] did not find that race was associated with health risk behaviours but the study included a fairly homogenous sample of white participants (75%). Terre et al. [50] found that socioeconomic status was the most consistent predictor of health behaviours in the general population, with those of lower socioeconomic status being more likely to engage in health risk behaviours. In a sample of pediatric cancer survivors, Emmons et al. [8] found that lower income and less education were associated with smoking initiation. Tyc et al. [69] found that younger adolescent survivors, and those of higher socioeconomic status were more likely to have healthy lifestyles. Older age, male gender and having less than a college education were significant predictors of smoking in adult survivors of pediatric Acute Lymphoblastic Leukemia [7].

Studies reported contradictory findings; demographic factors were not consistently related to substance use. Mulhern et al.[57] did not find that demographic factors such as gender, race, age or socioeconomic status were related to health behaviours or perceived vulnerability to negative health outcomes. Tyc et al. [74] did not find that gender, race, or socioeconomic status were related to intentions to use tobacco. It is not yet clear which demographic factors are risk factors for negative health behaviours in pediatric cancer

survivors but they may be similar to those in the general population. It is also not clear how to explain observed relationships such as the one between socioeconomic status and health behaviours.

A qualitative study Lindbladh et al. [83] explored the narrative of participants from the general population about decision-making and health related behaviour from both sociological and economic theoretical perspectives. They found that people in lower socioeconomic positions were more likely to rely on their habits, believed habits to be something good and were less likely to change their behaviour due to lack of resources. Those in lower socioeconomic positions were less likely to make decisions about their health behaviours and relied on habitual behavioural patterns.

Decision-making may be an important factor in determining health risk behaviour. Hollen and Hobbie [63, 64, 75] found that among adolescent pediatric cancer survivors those who were poor decision makers were more likely to engage in risk taking including smoking, alcohol and drug use. As well, treatment for central nervous system (CNS) cancer and poor academic achievement may be important predictors of poor quality decision-making and health risk behaviours but further studies with larger sample sizes are needed.

In a structural equation modeling analysis Chen et al.[77] found that intensive cancer treatment predicted educational achievement, which in turn predicted health behaviours. They suggest that neuropsychological deficits caused by cancer treatment may predict health behaviour. Educational achievement has been found to be an important predictor of health behaviours in a number of studies. Butterfield et al. [3] found that survivors who did not graduate from high school had more health risk behaviours than college graduates. Tao et al. [7] found that not having a college education was a significant predictor of smoking in both pediatric cancer survivors and their siblings. Emmons et al. [8, 71] found that lower education was also a significant predictor of smoking initiation and smoking dependence in pediatric cancer survivors. Wetter et al.[84] analysed the relationship between educational attainment and smoking status in working adults from the general population. In this sample they found that education was a strong independent predictor of smoking status even after adjusting for demographics, job status and job characteristics including salary. Further research is needed to determine how low educational attainment predicts smoking.

In addition to low educational attainment studies of adolescents in the general population found that having a learning disability was associated with substance abuse. Reasons for this association are not well understood but may be linked to low self-esteem, poor relationships with peers, social deficits as well as environmental and biological factors, among others [85, 86].

Poor academic success, low self-esteem, and social isolation from popular peers have been associated with an increased likelihood of smoking in the general population possibly due to the socialization of smoking behaviour [67]. In early studies adolescent survivors of pediatric cancer were found to have poorer self-esteem than their peers [48, 67]. However, in a more recent study it was found that self-esteem in pediatric cancer survivors was similar to their peers and that survivors were just as socially active and achieved their goals [41]. Tao et al.[7] did not find that pediatric cancer survivor's self-concept was an important predictor of smoking. However, Hollen and Hobbie [76] found that non-resiliency was associated with engaging in health risk behaviours and includes factors such as non-even temperament, low self-esteem, low social support, and non-resistance to social pressure.

In a study of Canadians aged 20-24 years from the National Population Health Survey, Allison et al.[87] found that males were 2.4 times more likely to drink heavily compared to females. Education was a significant predictor of daily smoking where those with less than high school education were more likely to smoke daily than those with a post-secondary education. The most consistent predictors of health behaviours were working status and chronic stress. Persons who worked were also more likely to smoke daily and drink heavily than persons who were in school. Chronic stress significantly predicted daily smoking, heavy alcohol use and health risk behaviour. They suggest that chronic stress may mediate the relationship between social factors such as working status and health risk behaviours. Chronic life stress and traumatic life events have been associated with both alcohol and tobacco use in the general population [88]. Tercyak et al.[66] suggested that conflict with parents and depression may be indictors of increased stress and found those factors to be associated with engaging in health risk behaviours in their study of adolescent pediatric cancer survivors.

There are many social factors that may influence whether someone engages in health risk behaviours. Having peers or family members who smoke has been identified as an

important predictor of smoking and alcohol use in adolescents from the general population [89-91]. In adult pediatric cancer survivors, especially women, Corkery et al.[4] found that smoking was more prevalent in those who had a family member who smoked. Emmons et al.[71] found that higher smoking rates were associated with having a higher proportion of smokers in the respondent's social network. In adolescent survivors peer and parent tobacco use was not associated with intentions to use tobacco in the future [74]. Hollen and Hobbie [76] also did not find that negative modeling was associated with engaging in health risk behaviours in adolescent survivors.

Emmons et al.[71] found that severity of psychological symptoms including: depression, anxiety and somatic symptoms were associated with an increase in smoking and dependence on tobacco in pediatric cancer survivors. In persons with higher levels of anxiety and depression nicotine and alcohol may be used as a form of self-medication to reduce these symptoms [88]. However, in adult survivors of leukemia Tao et al. [7] did not find that mood was an important predictor of smoking. Similarly, Chen et al. [77] did not find a significant pathway between negative mood and health compromising behaviour.

Although pediatric cancer survivors face the same pressures as their peers to make certain lifestyle choices their cancer experience and late effects of their treatment may influence their choices. General health, type of cancer, intensity of treatment and time since diagnosis are all factors that may influence whether or not they engage in health risk behaviours by changing their perception of their vulnerability to health consequences [92]. Most studies of adolescent survivors did not find any clinical factors to be associated with engaging in smoking, alcohol use or multiple health risk behaviours [57, 61, 63, 64, 66, 69]. Emmons et al.[8] found that older age at diagnosis, not having pulmonary-related cancer treatment, and not having brain radiation were factors that were associated with smoking initiation. Other studies that examined current smoking status rather than the initiation of smoking did not find these factors or other clinical factors to be important predictors [4, 56, 57, 61, 69, 74]. Health risk factors related to cancer treatment may be protective against the initiation of health risk behaviours such as smoking in pediatric cancer survivors but once they have begun to smoke these factors may no longer be important predictors of their behaviours. This would be consistent with the trend observed where pediatric cancer survivors are now smoking less than their peers and than those in the general population but

are equally likely or less to quit smoking once they have started [6, 7, 56]. However, one study by Emmons et al.[8] found that among smokers, pediatric cancer survivors were more likely to quit smoking.

A recent study by Foster et al.[62] found that survivors of hereditary retinoblastoma were less likely to be smokers than survivors of non-hereditary retinoblastoma and among survivors of hereditary retinoblastoma those with bilateral disease were less likely to smoke than those with only one eye affected. The authors suggest that survivors of hereditary and bilateral disease may smoke less due to greater vision impairments and blindness.

It is thought that having had cancer should be protective against engaging in health risk behaviours [58]. However, this has not always been observed and may be partially due to lack of knowledge in pediatric cancer survivors about their treatment, late effects and susceptibility to cancer. Bashore [93] found that only 84% of pediatric cancer survivors or their parent were able to list their diagnosis and 50% were able to list the chemotherapeutic drug they received. Similarly, Kadan-Lottick et al. [94] found that 72% of adult survivors were able to report their diagnosis with precision. Most survivors could remember the type of treatment they received but not the names of drugs or site of radiation. More concerning was that Bashore [93] found that only 30% of pediatric cancer survivors were aware of the late effects associated with their treatment. Lack of knowledge about the late effects of treatment may explain why some cancer survivors choose to engage in health risk behaviours even though they are at high risk for negative health outcomes.

Survivors may also lack knowledge about the increased health risks associated with smoking and heavy alcohol use. Tyc et al. [65] found that lack of knowledge about the adverse health consequences of smoking was a significant predictor of intentions to use tobacco in adolescent pediatric cancer survivors. Interestingly, Cox et al. [78] found that increased worry and perceived susceptibility to late effects of cancer treatment were associated with increased substance use. They suggest that survivors may be engaging in substance use as a coping method to reduce anxiety associated with having had cancer and the late effects of treatment.

2.4 Theories of health behaviour

Many theories have been developed to explain health risk behaviours in the general population but few have been proposed for pediatric cancer survivors. Social cognitive models that are based on the social cognitive theory are commonly used to explain health behaviour and have been implemented in health education. The social cognitive theory is based on the concept that people interact with their environment and acquire behaviours through learning processes, but that they also have a strong ability to control their own behaviours.[95] Determinants of behaviours identified by Bandura [96] in the social cognitive theory include knowledge of health risks and benefits, perceived self-efficacy to control ones own behaviours, health goals and facilitators and barriers to achieve these goals. Social cognitive models are based on the theory that a person perceives or has an actual threat to their health and seek to understand the reasons for actions taken or ignored [97]. The end goal is to take knowledge gained from models of determinants of health behaviour and to apply this to health education and promotion practices [96].

Other models of health behaviour have similar constructs to the social cognitive theory. The Health Belief model is based on the concept that one's perceptions about the seriousness and severity of a health outcome and their susceptibility to an outcome will predict their motivations and behaviours [98, 99]. Rose [98] discusses how the Health Belief Model (HBM) by Rosenstock could be applied to cancer survivors to determine why they engage in particular health behaviours. In cancer survivors past experiences with cancer may alter their beliefs about their susceptibility to and seriousness of diseases consequentially affecting their motivations and health behaviours [98]. Perceived susceptibility to a negative health outcome is a factor that is part of the Health Belief Model but is also common to other cognitive models of health behaviour such as the Theory of Reasoned Action, Protection Motivation Theory and Subjective Expected Utility Theory [100].

Hollen [101] developed a model of predictors of health risk behaviours in pediatric cancer survivors. In this model decision making acted as a mediator between clinical and sociodemographic variables and health behaviours. Risk motivation or attitude about health risk behaviours is a moderator in this model altering the relationship between decision making and risk behaviours. Studies of pediatric cancer survivors by Hollen and Hobbie [63,

[64, 75] found that poor quality decision making was associated with engaging in health risk behaviours which supports one aspect of the model.

Cox [102] refers to structural equation modeling as a useful analytical method that can be used to test models of health behaviour with mediators and moderators, testing the ability of the model to explain health behaviour. Chen et al. [77] used structural equation modeling to test a model of health behaviours in pediatric cancer survivors where treatment intensity predicted health risk behaviour with mood and educational achievement acting as mediators. They hypothesized that those with more intensive treatment would be more likely engage in health risk behaviours as these survivors are at greater risk for negative psychological and cognitive outcomes. Results partially supported the hypothesis as intensive treatment was found to predict health risk behaviours through lower educational achievement but not mood.

Many theories of health behaviour try to explain the development and predictors of health behaviour but neglect to incorporate intervention strategies into their models to explain how they will affect health behaviours. Cox [102] discusses the Interaction Model of Client Health Behaviour and how this model which has guided previous intervention studies may be applied to pediatric cancer survivors. The model is constructed of three main components: client singularity, client-professional interaction and health outcomes. Client singularity is comprised of background variables such as gender and dynamic variables that are subject to change, such as knowledge, cognitive appraisal and motivation. The interaction between the pediatric cancer patient and health care provider can be useful in changing these dynamic factors to change health behaviours. Pediatric oncology patients often build a strong bond with their health care provider during treatment however, after the completion of their treatment they typically see a general practitioner. Health care providers can provide support and information to pediatric cancer survivors to enable them to make healthy lifestyle choices [102].

2.5 Health promotion and prevention of health risk behaviours

Theories of health behaviour can be used as the basis for intervention strategies. Theories such as the social cognitive approach focus on the determinants of health behaviours and the prevention of disease rather than on treatment. In our current health care system the needs of the population are far outweighing the supply meaning that strategies focusing on health promotion and disease prevention, especially chronic disease are important to sustain the health of our nation and a well functioning health care system [96].

Hudson et al.[103] used the Health Belief model as a basis for the development and implementation of a health promotion intervention to reduce health risk behaviours in pediatric cancer survivors, entitled the Protect Study. The intervention in the Protect Study was educational risk counselling provided by health care practitioners that focused on the late effects of cancer treatment. Changes in health knowledge, perceptions of seriousness and susceptibility to negative health outcomes as well as perceived benefits and barriers to health behaviours were assessed. They found that female survivors of pediatric cancer had higher scores in knowledge following intervention than males and the control group. Survivors who chose specific health goals to focus on also had improved health behaviour. No other significant changes were observed following the intervention. The authors suggest that future interventions consider gender and target specific health behaviours.

A secondary analysis of the Protect Study examined each health protective and health risk behaviour separately [104]. When looking at separate health behaviours Cox et al. [104] found that knowledge about breast self examination and testicular self examination improved. Perceptions about the need to change behaviour and to stay healthy also improved following the intervention. Health behaviour changes were also observed in the treatment group. Smoking abstinence was maintained and junk food consumption decreased. Gender and age differences in practices of health behaviours were observed. In a later analysis Cox et al.[78] found that the intervention predicted survivors' perceived need to change behaviours that resulted in a desire to change health behaviours and consequentially decreased substance use. Cox et al.[104] suggest that health risk and health protective behaviours should be measured and analysed separately.

Tyc et al. [105] designed an intervention to target perceived vulnerability to health risks associated with tobacco use in pediatric cancer survivors. This intervention involved risk

counselling in the form of a video and follow-up telephone calls and measured changes in knowledge, perceived vulnerability, intentions and perceived positive effects of tobacco use. After one year they found that compared to the standard care control group the treatment group had significantly higher knowledge of the adverse consequences of tobacco use, perceived vulnerability to health risks and lower intentions to use tobacco. This effect was not seen at six months suggesting that changes in beliefs and motivations to engage in health risk behaviours may take place over longer periods of time through reinforcement.

Hollen et al. [106] designed an intervention in the form of a one day camp workshop to improve decision making skills and provide information about survivorship and risk behaviours and social support for pediatric cancer survivors. The effectiveness of the intervention was assessed by questionnaires of decision making quality, risk motivation and substance use. Significant changes following the intervention were a decreased motivation toward alcohol use at one month and higher decision making scores at one and twelve months compared to survivors who did not receive the intervention. The authors suggest that a larger sample size and a longer intervention period may be needed.

A recent intervention study by Emmons et al.[107] was the first published study to target smoking cessation in pediatric cancer survivors. One group received a self-help letter from physicians outlining the importance of smoking cessation in reducing the risk of secondary cancers. The second group received motivational telephone counselling from other cancer survivors. Results indicated that the group that received peer counselling had significantly higher cessation rates, almost double the group that received health risk information ($p<0.01$) [107]. A secondary analysis of the data found that intervention dose was related to smoking cessation. Survivors who received more phone calls were significantly more likely to quit with four to six calls being an effective number [108]. Both interventions that target smoking and alcohol use cessation and prevention are important in reducing the rate of smoking and alcohol use in survivors [107].

2.6 Conclusions

Pediatric cancer survivors are engaging in smoking and alcohol consumption at similar or slightly lower rates than their peers. Cancer treatment puts them at greater risk for negative health outcomes associated with smoking and alcohol use and therefore further research into the determinants of health behaviours in this group and the design and implementation of interventions are needed. Although cancer survivors may engage in health risk behaviours for the same reasons their peers do, the health and psychosocial late effects of cancer treatment create a need for research and interventions to be oriented specifically towards this group. The development of models to explain health behaviour in pediatric cancer survivors can provide the foundation and theoretical framework for an intervention program.

3.0 AIMS AND OBJECTIVES

The overall objective of this thesis was to investigate factors associated with tobacco use, alcohol use and their concurrent use in pediatric cancer survivors, a high risk sub-population for negative health outcomes. More specific objectives were to:

1. Describe the prevalences of alcohol use, tobacco use and their concurrent use in a study population of Canadian pediatric cancer survivors and make a comparison to a population-based control group.

2. Examine whether the prevalences of alcohol use, tobacco use and their concurrent use within pediatric cancer survivors were associated with important clinical factors including cancer diagnosis, treatment received, age at diagnosis and relapse.

3. Compare tobacco use, alcohol use and their concurrent use in pediatric cancer survivors to controls after adjusting for important covariates.

4. Examine predictors of tobacco use, alcohol use and their concurrent use in both pediatric cancer survivors and controls.

5. Investigate psychosocial pathways that lead to alcohol and tobacco use in pediatric cancer survivors in comparison with controls using structural equation modeling.

3.1 Theoretical Model

Based on a review of the literature and available data a theoretical model was specified to investigate how psychosocial factors may contribute to the development of smoking and alcohol drinking behaviours in pediatric cancer survivors. Structural equation modeling involves the testing of a theoretical pathway model that describes the development of an outcome. It is similar to factor analysis, multiple regression or path analysis but it is more powerful because it allows for the examination of multiple, correlated predictor and outcome variables. Structural equation modeling also allows for the testing of complex hypotheses and is more comprehensive than other modeling methods [109, 110].

The application of structural equation modeling in behavioural oncology has important implications for lowering cancer morbidity and mortality and for improving psychological well-being and quality of life in cancer survivors [111]. Structural equation modeling was a useful method of analysis for the current study to help to explain the complex relationships between demographic, psychosocial, health factors and alcohol and tobacco use in pediatric cancer survivors. The structural equation modeling for this study was largely exploratory and model generating. A possible theoretical model was specified prior to data analysis. If it did not fit the data the model was modified based on the data and theoretical justification and then retested [112].

In the specified model (Figure 1) the outcome variable was concurrent use of alcohol and tobacco. Concurrent use of alcohol and tobacco was selected as the outcome as 90% of participants who smoked in the current study also drank alcohol. There may be common factors that predispose someone to substance use. In the model it was hypothesized that satisfaction with life would partially mediate the relationship between various psychosocial and health factors and concurrent use of alcohol and tobacco. A mediator is a variable through which a predictor variable can influence the outcome variable [113]. It was hypothesized that poor physical and mental health, lower educational attainment, increased stressful life events and chronic stress as well as poor self-esteem would be associated with increased life dissatisfaction.

In order for life satisfaction to be a mediator several criteria must be met. The mediator variable must be associated with both the predictor and outcome variables. There must be a significant indirect path from the predictor variable to the outcome variable

through the mediating variable. If there is mediation the direct path from the predictor variable to the outcome variable should be reduced or non-significant [114, 115].

It was hypothesized that life satisfaction would be associated with the outcome in the model, concurrent use of alcohol and tobacco, where those who had greater life dissatisfaction would be more likely to engage in substance use. A previous study by Zullig et al.[116] found that greater life dissatisfaction was associated with substance use in a population of high school students.

It was hypothesized that persons with lower self-esteem would have a greater dissatisfaction with life and would be more likely to engage in concurrent use of alcohol and tobacco. Self-esteem has been found to have high correlations with life satisfaction and to be an important predictor of life satisfaction in several populations [117]. Studies from the general population have also suggested that low self-esteem is a predictor of smoking possibly due to the socialization of smoking behaviour [67, 118]. Individuals with low self-esteem may also have low self-efficacy and poor coping abilities increasing their risk for engaging in health risk behaviours [119].

It was also hypothesized that poor physical and mental health and lower educational attainment would be associated with lower self-esteem. Poor mental health, physical health and educational attainment have been shown in previous studies of the general population to be associated with low self-esteem and that the directionality of the relationships may be in either direction [119]. In this model it was hypothesized that lower educational attainment and poor physical and mental health would be predictors of low self-esteem. In child and adolescent cancer survivors, low self-esteem was associated with increased educational problems compared to those with high self-esteem [120]. Survivors of bone tumours were found to have low self-esteem scores, possibly due to changes in physical appearance and the presence of surgical scars [121].

It was hypothesized that higher levels of stress including both chronic and acute stressors would be associated with decreased life satisfaction and that those with higher perceived levels of stress would be more likely to engage in concurrent use of alcohol and tobacco. A study of the general population found that perceived stress was an important predictor of life satisfaction in young and older adults [122]. Chronic life stress and traumatic life events have also been associated with both alcohol and tobacco use in the general

population [88]. It has been suggested that when under stress persons may engage in tobacco and alcohol use as a coping function [88, 89, 118].

It was hypothesized that physical health would be associated with life satisfaction where those with poorer physical health including: increased bodily pain, lower physical functioning and ability to do daily activities would be more dissatisfied with life. Decreased mobility and poor perceived health were associated with lower life satisfaction in a spinal cord injury cohort [123].

It was hypothesized that physical health would be associated with concurrent use of alcohol and tobacco. Smoking and alcohol drinking in the general population were associated with poor physical and mental health scores on the SF-36 scale and other measures of quality of life [124-126]. Other researchers have hypothesized that poor physical health would be a protective factor for engaging in health risk behaviours in pediatric cancer survivors by changing their perceived vulnerability to health consequences [92].

It was hypothesized that mental health would be associated with life satisfaction where those with poorer mental health would have greater dissatisfaction with life. In a previous study of the general population life dissatisfaction was strongly associated with depression and moderately correlated with anxiety [127].

It was hypothesized that mental health would be an important predictor of concurrent use of alcohol and tobacco. One study of pediatric cancer survivors found that more severe psychological symptoms including depression, anxiety and somatic symptoms were associated with current smoking and dependence on tobacco [71]. However, two other studies did not find that mood was associated with smoking and health risk behaviour [7, 77].

It was hypothesized that those with a lower educational attainment would have greater life dissatisfaction and would be more likely to engage in concurrent use of alcohol and tobacco. In several studies of different populations low socioeconomic status was associated with greater dissatisfaction with life [123, 127]. Low education has been shown to have a strong independent relationship with smoking in the general population after adjusting for other factors related to socioeconomic status and an important predictor of smoking and health risk behaviours in pediatric cancer survivors [3, 7, 8, 71, 77, 84].

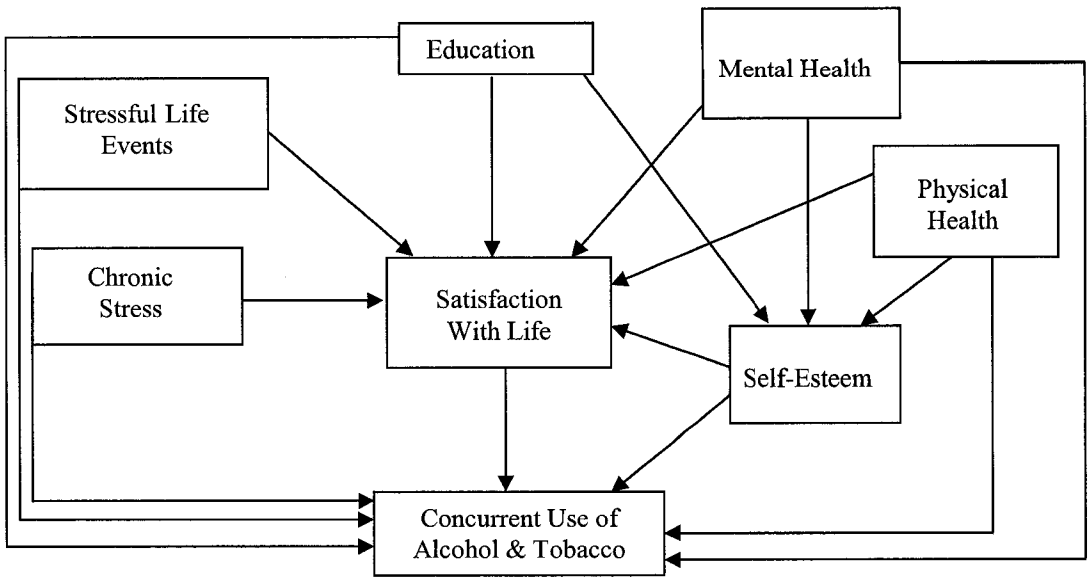


Figure 1: Hypothesized mediational model of the relationship between psychosocial, health and demographic factors with concurrent use of alcohol and tobacco in pediatric cancer survivors.

4.0 METHODS

4.1 Study Design

Data were analyzed from the Canadian Late Effects Study that was designed to assess long term psychosocial and physical outcomes in survivors of childhood cancer and a frequency matched population based control group. Details of the study methods have been published elsewhere [128]. Data were collected between January 1997 and February 2000 using a mailed out questionnaire. Inclusion criteria for the cancer survivors were: 1) to be diagnosed with a first malignancy between 1981 and 1990; have survived at least five years after diagnosis; 2) to be under 20 years at age of diagnosis; 3) alive at the time of study; and 4) have sufficient English or French language skills to complete the questionnaire.

Participants included 2,152 cancer survivors who were selected randomly from twelve participating pediatric oncology centres or cancer registries representing each province and territory in Canada. Population-based controls included 2,432 respondents who were randomly selected through provincial health insurance agencies or by random digit dialling in provinces with restrictions to access to health insurance information. Inclusion criteria for controls were: 1) no self-reported previous cancer diagnosis; 2) sufficient English or French language skills to complete the questionnaire; and 3) to have been a Canadian resident from at least December 31, 1990. Controls were frequency matched to cancer survivors by age and sex within each province [128].

Each participating centre contacted subjects to complete the questionnaire. Two types of questionnaires were administered: one for participants 16 years of age or over and one for those under 16 years. Participants greater than 16 years of age completed a self-report questionnaire, while a parent or guardian completed the questionnaire for those under 16 years of age [128]. For the current study only data on participants that were 16 years or greater was used to reduce misclassification of respondents by outcome as parents and guardians are often not aware that their child uses alcohol or tobacco [70]. The sample size for pediatric cancer survivors over the age of 16 years who completed the questionnaire was 1,352, with a response rate of 60.2% and for the control group was 1,509 with a response rate of 49% [128].

Access to the late effects database, part of the Canadian Pediatric Cancer Surveillance and Control Program (CCCSCP)[129], was obtained through the Public Health Agency of

Canada. Ethical approval for this study was obtained from the Ottawa Hospital Research Ethics Board on August 9, 2005. Data analysis was conducted entirely at the Public Health Agency of Canada site at 120 Colonnade Road and no data that could identify a patient's name, hospital or physician were removed from that site. Individual identifiers that identify the patient's name, hospital or physician were also removed prior to the investigator's access to the data.

4.2 Variable Selection and Development

Outcome Variables

Smoking was categorized as never smokers, current smokers and former smokers. A never smoker was defined as someone who had not smoked at least 100 cigarettes in their life. Respondents were asked "Have you ever smoked at least 100 cigarettes in your entire life?" A current smoker was defined as someone who had smoked at least 100 cigarettes in their life and reported that they smoked now. Respondents were also asked "Do you smoke cigarettes now?" A former smoker was defined as someone who had smoked at least 100 cigarettes in their life but reported that they did not smoke now. Smoking was also categorized into current and non-current smokers. A current smoker was any participant that was defined as a current smoker above. A non-current smoker was anyone who was a former or never smoker as defined above.

These questions and definitions are similar to those used in the National Health Interview Survey (NHIS) by the Centers for Disease Control (CDC) in the United States. The only difference being that the CDC now classifies a current smoker as respondents who reported smoking at least 100 cigarettes in their entire life and who report smoking every day or some days [72]. The questionnaire used in the current study did not ask the participants the frequency that they smoked. By not restricting the current smokers to those who smoke on some days or every day we also captured a group of smokers that smoked more infrequently.

Thirteen participants reported that they had smoked greater than 100 cigarettes in their life but did not report whether they smoked now. Whether or not they were a former or current smoker was deduced by examining their answer to the question regarding an age at which they quit smoking. Three participants reported that they were current smokers but did not report whether they had smoked at least 100 cigarettes in their lives. All were estimated

to have smoked greater than 100 cigarettes after examining how many cigarettes they reported smoking on average per day and for how many years they had smoked. Three persons reported that they were not current smokers but did not report whether they had smoked at least 100 cigarettes in their lives. Their smoking status was deduced by looking at their answers to questions regarding the age that they quit smoking and how many cigarettes they smoked on average per day. There were eleven cases who reported having had at least 100 cigarettes in their life but did not report whether they smoked now or the age at which they started smoking or quit smoking making it impossible to determine whether they were a former or a current smoker. Since the participants had smoked at least 100 cigarettes in their life it was assumed that they were current smokers.

There were 15 respondents (0.53%) that provided no information about their smoking status and were therefore deleted from the dataset. Of the deleted cases 8 (53%) were cancer survivors and 7 (47%) were from the control group. Seven (47%) were 16-20 years of age, 3 (20%) were 21-25, 4 (27%) were 26-30 and 1 (7%) was 31-37. Eight (53%) were male and 7 (47%) were female. Three (20%) did not report their level of education, 2 (13%) had less than a high school education, 5 (33%) had completed high school and 5 (33%) had greater than a high school education. The demographic characteristics of the deleted cases were similar to the entire study population (Table 5).

Alcohol use was categorized by the frequency and amount of alcoholic drinks consumed. An abstainer was defined as a person who had never had at least twelve drinks of any kind of alcoholic beverage in their life or who had, on average, less than one drink of wine, beer or mixed drink per month in the previous twelve months. Respondents were asked "In your entire life, have you ever had at least 12 drinks of any kind of alcoholic beverage?" and "During the past 12 months, on average, how often did you drink the following per month: wine (4 oz. Glass), beer (12 oz. Can), mixed drink (1 shot) (if less than 1 drink enter 0)?" Light alcohol users were defined as those who reported drinking 1-13 drinks of beer, wine or mixed drink per month. Moderate alcohol users were defined as those who reported drinking 14-60 drinks of beer, wine or mixed drinks per month. Heavy alcohol users were defined as those who reported drinking greater than 60 drinks of beer wine or mixed drink per month. However, for the current study moderate and heavy drinkers were regrouped into one category, as the prevalence of heavy drinkers was low with only 41 (3.2%) cancer survivors

and 58 (4.1%) controls reporting being heavy drinkers. Alcohol use was also dichotomized into drinkers and abstainers. An abstainer included anyone who was categorized as an abstainer as defined above. A drinker was anyone who was categorized as a light or moderate to heavy drinker as defined above.

The number of drinks a participant had on average, per month, in the previous 12 months was first summed. A numerical field and a text field both contained relevant information. The text field was manually changed to numerical values. If the respondent did not answer whether they had at least 12 alcoholic drinks in their lives but did answer how many drinks they had, on average, per month in the previous 12 months they were coded as light and moderate to heavy drinkers as defined above. There were 12 participants who responded that they had not had at least 12 drinks in their lives but in the questions following they answered as though they had more than 12 drinks in their life. It was assumed that they had answered the first question incorrectly and they were coded as light and moderate to heavy drinkers.

There were 118 respondents (4.2%) who did not provide answers to either of the questions on alcohol use and were therefore deleted from the dataset. Of those deleted 57 (48%) were cancer survivors and 61 (52%) were from the control group. Thirty (25%) were 16-20 years of age, 34 (29%) were 21-25, 40 (34%) were 26-30 and 14 (12%) were 31-37. Forty-one (35%) were male and 77 (65%) female. Five (4%) did not report their education level, 28 (25%) had less than a high school education, 39 (33%) had completed high school, 46 (39%) had greater than a high school education. There were slightly more females than males who did not report how much alcohol they consumed but otherwise the demographic characteristics of the deleted cases were similar to the entire study population (Table5).

There is no consensus on how to define alcohol use or even what constitutes moderate drinking, which has been associated with health benefits [130]. The definitions of alcohol use for the current study were adapted from the dietary guidelines published by the U.S. Department of Health and Human Services (USDHHS) and U.S. Department of Agriculture (USDA) [131] as well as definitions from Dawson and Room [132] and Dufour [130]. The USDHHS and USDA defined moderate alcohol consumption as up to one drink per day for women and up to two drinks per day for men. A drink was defined as 12 oz. of regular beer, 5 oz. of wine, or 1.5 oz. of 80-proof distilled spirits. However, they caution that this is

the amount consumed per day and is not meant to be an average over many days, as consuming more than two drinks per day increases the risk for health problems and injury. Dawson et al.[132] defined an abstainer as someone who had less than 12 drinks in the previous year, a light drinker as a person who drinks 1 to 13 drinks per month, a moderate drinker as someone who drinks 4 to 14 drinks per week and a heavier drinker as someone who has more than two drinks per day.

A problem with the proposed definition was that it did not capture binge drinkers. It is possible that someone could have an average of 50 drinks per month, which would be considered moderate consumption by the previous definition but had five or more drinks per occasion, which is considered hazardous drinking. Having more than 60g of ethanol per day for men and 40g for women has been a threshold set to define hazardous drinking. Sixty grams of ethanol is equivalent to approximately five drinks in the United States [132]. In order to take into account hazardous drinking of alcohol the current study also examined binge drinking as an outcome.

Binge drinking was defined as having 5 or more drinks on average on days that respondent drinks. Respondents were asked, "On the days that you drink, on average, how many drinks do you have?"

If the participant did not answer the question regarding binge drinking and were defined as an abstainer they were coded as a non-binge drinker; those who reported abstaining from alcohol use were not intended to answer this question. When participants did not answer the question about binge drinking but responded that they had on average, less than four drinks per month in the previous 12 months they were also coded as non-binge drinkers as binge drinking requires that they have five drinks or more per occasion.

Concurrent use of alcohol and tobacco was defined as those who are current smokers and are also light or moderate to heavy alcohol users as defined above.

Psychosocial factors and other predictors

Demographic, psychosocial and health variables that were identified in a review of the literature and were available in the dataset to be examined as potentially important risk factors for smoking, alcohol use and their concurrent use included: age, gender, ethnicity, education, special education/learning disabled, personal income, self-esteem, chronic stress, stressful life events, satisfaction with life, mental and physical health. The current study also examined clinical factors as important predictors of smoking, alcohol use, binge drinking and their concurrent use including: cancer diagnosis, type of treatment, age at diagnosis, and whether or not a relapse occurred.

Age

The survey was designed to include participants aged 16 years and older. Fifty participants reported being age fifteen, of which 18 were cancer survivors and 32 were controls. Reasons for inclusion of these fifteen year olds were unknown and were therefore deleted from the dataset reducing the sample size to 2,811. Participants were categorized into approximately four-year age groups: 16-20, 21-25, 26-30 and 31-37. There was no missing data for this variable.

Gender

Participants were categorized as male or female. Reported gender data from the questionnaire was verified with data collected from medical charts. There was no missing data for this variable.

Ethnicity

Participants were asked, "To which ethnic or cultural group(s) did your ancestors belong?" and were required to check from a list of ethnicities the ones to which their father's and mother's ancestors belonged. Ethnicity was categorized as white, non-white, Aboriginal and mixed. This categorization was selected because studies of the general population found that Aboriginals were more likely to be smokers than other groups and whites were more likely to be smokers than non-whites [89, 118]. The non-white category includes respondents who would be defined as visible minorities in Canada. They include all respondents who are

non-Caucasian in ethnicity, other than Aboriginal people [133]. Grouping all visible minorities together disregards individual group differences however, the majority of cancer survivors (84%) and controls (80%) were white thus small sample sizes restricted further categorization of the ethnicity variable [133].

If the participant reported that both their mother and father's ancestors were white or Aboriginal, they were coded as white and Aboriginal respectively. If the participant reported that both their mother and father's ancestors were of the same non-white ethnicity, they were coded as non-white. If the participant reported that their mother and father's ancestors were of different ethnicities, they were coded as mixed. If the participant only reported the ethnicity of one parent's ancestors they were coded according to that response. An option when answering the question was to check "other" and to specify an ethnic or cultural group. Some of the participants chose to do so and were recoded into the appropriate ethnic category.

There were 72 respondents (2.6%) who reported that they did not know their mother and father's ancestor's ethnicities or they left the question blank and were imputed as being white. Thirty (42%) were cancer survivors and 42 (58.3%) were from the control group. The reason for inclusion of participants with unknown ethnicities in the white category is that approximately 84% of the population of cancer survivors and 80% of controls participating in the study were white meaning that if data were missing at random there was a high probability that the respondents who left the question blank were also white.

Income

Questions pertaining to both total yearly household and personal income before taxes were included in the questionnaire. All participants were asked to check the appropriate category that included their total yearly personal income before taxes ranging from none to $70,000 or more. Possible responses for household income ranged from less than $10,000 to $70,000 or more. However, those that were reliant on their parents for income were not asked to report their household income. Those who were not reliant on their parents for income were asked to report both their total yearly household income and their total yearly personal income before taxes.

Household income was the measure of interest as it is a measure of socioeconomic status that has been associated with substance use in pediatric cancer survivors [7, 8]. However, because of the study design, only approximately half of the population answered this question and personal income was used. Personal income was categorized based on the frequency distribution of the data into three groups: $0-$4,999, $5,000-$19,999 and $20,000 or greater. This measure may not represent socioeconomic status well as a large portion of the participants reported being reliant on their parents for income but would better represent disposable income. Participants who did not know their personal income or left the question blank were recoded into the median category as having a total personal income of $5,000-$19,000 per year before taxes.

There were 358 respondents (13.6%) who had an unknown personal income and were imputed into the median category of which, 164 (45.8%) were cancer survivors and 194 (54.2%) were from the control group. Recoding participants with unknown personal income into this category was done to be conservative as theoretically this group should be at high risk for substance use. In adolescents, higher disposable income has been associated with substance use and in adults lower income has been associated with substance use [118]. Adolescents dependent on their parents for income would have a higher disposable income if they were in this group ($5,000-$19,000) and adults independent of their parents would have a lower personal income. The low income cutoff estimated by Statistics Canada in 2000 for a single adult living in Canada was $12,696 to $18,371 depending on whether they lived in a rural or urban area [134].

Education

Education was categorized as having less than a high school education, having completed high school and having greater than a high school education. Participants were asked, "What is the highest grade of school you have completed?" Options included less than eight years, eight to twelve years, completed high school, completed vocational/technical training, completed college/university and completed graduate school. Participants who reported having less than eight years or eight to twelve years of education were coded as 'less than high school'. Participants who reported having completed high

school were coded as 'high school' and those with vocational/technical training, completed college/university or completed graduate school were coded as 'greater than high school'.

Respondents who left the question blank were imputed as having less than a high school education. Fifty-three (2%) participants did not report their level of education obtained, of which 31 (58%) were cancer survivors and 22 (42%) were from the control group. Recoding participants with unknown education into the less than high school education category was done to be conservative as lower educational attainment has been associated with substance use [3, 7, 8, 8, 71, 77, 84].

Special Education/Learning Disabled Programs

Participants were asked, "In elementary or high school were you ever in any of the following programs?" Options included learning disabled, special education, gifted or talented and other. If participants responded that they were in a learning disabled or special education program they were categorized as 'Yes'. If they responded that they were not in either a special education or learning disabled program they were categorized as 'No'. If the participant responded that they were not in a special education program and did not answer whether they were in a learning disabled program they were assumed to have not been in either and were categorized as 'No'. If the participant responded that they were not in a learning disabled program and did not answer whether they were in a special education program they were assumed to have not been in either and were categorized as 'No'. If the participant left both questions blank it was assumed that they had not been in either a learning disabled or special education program and they were coded as 'No'.

There were 145 participants who responded that they did not know if they were in a special education or learning disabled program or left the questions blank. It was assumed that these 145 participants were not in a special education or learning disabled program and they were recoded as "No". Of those missing data 75 (52%) were cancer survivors and 70 (48%) were from the control group.

Physical and Mental Health

The SF-36 scale was developed to measure general health concepts of patients from any disease or treatment group and can be administered to patients over the age of fourteen through self-administration or a variety of other methods [136]. There are two summary measures that comprise the SF-36 questionnaire: physical health and mental health. Four multiple item Likert type scales best represent each of these constructs, with higher scores indicating better health. The physical health construct is represented by the physical functioning, role limitations due to physical health problems, bodily pain and general health perceptions scales. The mental health construct is represented by the social functioning, role limitations due to emotional health, mental health and vitality scales [137, 138].

Medical Outcome Trust provides a standardized method of scoring the SF-36 that can be found in the SF-36 manual [139]. The authors suggested that deviating from the standardized methods might jeopardize the validity of the scale and comparability with other studies. For these reasons the standard scoring method was used. The method for treating missing data involved mean imputation by case where greater than 50% of the items were answered for each multiple item scale [139]. Following imputation and scoring of the SF-36, cases with greater than 50% of the data missing on any multiple item scale were deleted from the dataset. Physical and mental health variables were created using the physical and mental health summary measures from the SF-36 and were categorized into five categories each based on the frequency distribution of the data.

The SF-36 has been shown to have good reliability and validity in different populations including adult survivors of childhood cancer [135,138, 140]. The Cronbach alpha test for internal consistency for physical health scale in the current study population was 0.77 for cancer survivors and 0.71 for the control group. For the mental health scale the Cronbach alpha was 0.82 in cancer survivors and 0.81 in the control group (Appendix 1). Internal consistency is a measure of reliability of a scale and whether the items on the scale are measuring a unidimensional construct.[141] These scores were over 0.70 indicating acceptable internal consistency. Total scores on the physical health component of the SF-36 scale were negatively skewed in both cancer survivors (skewness= -1.42, kurtosis=2.12) and the control group (skewness= -1.46, kurtosis= 3.14) suggesting most respondents had good physical health. Total scores on the mental health component were also negatively skewed in both

cancer survivors (skewness=-1.05, kurtosis=0.59) and the control group (skewness= -1.13, kurtosis=1.07) suggesting most respondents had good mental health.

There were forty-seven respondents (1.75%) who were missing data on greater than 50% of the items on at least one of the SF-36 scales and were therefore deleted from the dataset. Of those missing data 26 (55%) were cancer survivors and 21 (45%) were from the control group. Twenty-one (45%) were 16-20 years of age, 9 (19%) were 21-25, 14 (30%) were 26-30 and 3 (6%) were 31-37. Twenty-four (51%) were male and 23(49%) were female. Nine (19%) had less than a high school education, 21 (45%) had completed high school, 15 (32%) had greater than a high school education and 2 (4%) did not report their education level. The demographic characteristics of the deleted cases were similar to the entire study population (Table 5).

Satisfaction with life

The Satisfaction With Life Scale (SWLS) by Diener et al.[142] was used as a measure of global life satisfaction in the Late Effects study questionnaire. The SWLS consists of five statements about the participant's global life satisfaction and asks the participant to rate their agreement with the statements on a seven point Likert scale ranging from strongly disagree to strongly agree. Previous research found this scale to have a high test-retest reliability (0.82) and high internal consistency (α=0.87). Additionally, this scale was found to be appropriate for use in different age, cultural and clinical groups and had a moderate to high correlation with other measures of subjective well being [142, 143]. The Cronbach alpha test for internal consistency for the satisfaction with life scale in the current study population was 0.90 in cancer survivors and 0.91 in the control group suggesting high internal consistency (Appendix 1).

Scores were calculated by first performing mean imputation by case when participants responded to greater than 50% of the statements. This method was chosen for consistency as the SF-36 scale included in this study used this method in their standard scoring procedure. After imputation scores were checked for any values outside of the possible range of one to seven. The five items were then summed to provide an overall score with a possible minimum of five and maximum of thirty-five. On this scale twenty is considered neutral with those scoring below being dissatisfied with life and those above

being satisfied with life [143]. Total scores on this scale were negatively skewed in both cancer survivors (skewness= -0.69, kurtosis=-0.30) and the control group (skewness= -0.61, kurtosis=-0.49) meaning that most participants were more satisfied with life (Appendix 1). Participants who scored between 5 and 19 were categorized as 'dissatisfied' and those who were satisfied with life were further categorized into two groups based on the frequency distribution of the data as scoring 20-29 and 29 or greater.

There were 15 respondents (0.6%) who did not respond to at least 50% of the items and were deleted from the dataset. Four (27%) of these respondents were cancer survivors and 11 (83%) were from the control group. Eight (53%) were 16-20 years of age, 3 (20%) were 21-25, and 4 (27%) were 26-30. Six (40%) were male and 9 (60%) were female. One participant did not report their level of education, 4 (27%) had less than a high school education, 3 (20%) had completed high school and 7 (47%) had greater than a high school education. There were slightly more controls who missing data but otherwise the demographic characteristics of the deleted cases were similar to the entire study population (Table 5).

Self-Esteem

Rosenberg's self-esteem scale was a Guttman scale consisting of ten items asking respondents to rank their agreement with each statement as strongly agree, agree, disagree or strongly disagree [144]. A Guttman type scale consists of items that measure one construct and are presented on a continuum, in this case ranging from low self-esteem to high self-esteem. [144] In the Late Effects study questionnaire a short-form version of the original Rosenberg self-esteem scale was used that consisted of six items scored as a five point Likert type scale ranging from strongly disagree to strongly agree. Similar results are produced when the Rosenberg self-esteem scale is scored using a Likert, rather than Guttman type method [144].

Scores were calculated by first reverse coding the last item and then performing mean imputation by case when participants responded to greater than 50% of the statements. After imputation, scores were checked for any values out of the possible range of one to five. The six items were then summed to provide an overall score with a possible minimum of six and maximum of thirty. On this scale the midpoint indicates a neutral score with those scoring above having a theoretically positive self-esteem and those scoring below having a negative

self-esteem [145]. In the late effects study a score of fifteen was a neutral score. The self-esteem variable was categorized based on the frequency distribution of scores into four categories: 6-23, 24-26, 27-29 and 30. The self-esteem variable was categorized based on the frequency distribution. Scores were negatively skewed in both the cancer survivors (skewness=-1.37, kurtosis=1.91) and control group (skewness= -1.40, kurtosis=2.06) suggesting that reported self-esteem was high in both groups (Appendix 1). Schmitt and Allik [145] found that positive self-evaluations and mean scores above the theoretical midpoint for the Rosenberg self-esteem scale were common across cultural groups. The Cronbach alpha test for internal consistency for the self-esteem scale in the current study population was 0.83 for cancer survivors and 0.85 for controls suggesting good internal consistency (Appendix 1). There were nineteen participants that provided answers to less than 50% of the items on the self-esteem scale and were therefore deleted from the dataset.

There were 19 respondents (0.71%) that provided answers to less than 50% of the items on the self-esteem scale and were therefore deleted from the dataset. Nine (47%) were cancer survivors and 10 (53%) were from the control group. Six (31%) were 16-20 years of age, 4 (21%) were 21-25, 7 (37%) were 26-30 and 2 (10%) were 31-35. Nine (47%) were male and 10 (53%) were female. Two (10%) did not report their level of education, 5 (26%) had less than a high school education, 5 (26%) had completed high school and 7 (37%) had greater than a high school education. The demographic characteristics of the deleted cases were similar to the entire study population (Table 5).

Chronic Stress

A modified, shortened version of Wheaton's chronic stress inventory was used as a measure of chronic stress in the Late Effects Study [146]. The shortened version consisted of 30 items from the original Wheaton inventory. Participants were asked to rank their agreement with statements about chronic stressors that may have occurred over the previous twelve months as not true, somewhat true, very true or not applicable to themselves. Not applicable and not true were equivalent to no stress or a score of zero, somewhat true corresponded to a score of one and very true corresponded to a score of two. Participants who left any item of the chronic stress inventory blank were assumed to have meant not true or not applicable and received a score of zero for that item. Scores on the thirty items were

summed to provide a total score. The minimum score for the scale is zero, meaning no stress and the maximum is 60, meaning high stress.

The chronic stress variable was categorized for the logistic regression analysis based on the frequency distribution of total scores into three categories: 1-5, 6-11, 12-45. The chronic stress variable was categorized based on the frequency distribution for the logistic regression analysis. Scores were positively skewed in both cancer survivors (skewness=1.15, kurtosis=1.60) and the control group (skewness=0.89, kurtosis=0.73) suggesting that respondents generally had lower levels of chronic stress (Appendix 1). The Cronbach alpha test for internal consistency for chronic stress scale in the current study population was 0.83 in cancer survivors and 0.81 in the control group suggesting good internal consistency (Appendix 1). There were 133 respondents (5%) who did not answer at least one of the questions on the inventory, of which 71 (53%) were cancer survivors and 62 (47%) were from the control group. It was assumed that if the respondent left the question blank they did not have the event. The method of mean imputation by case for missing data when participants responded to greater than 50% of the items was not used for this inventory because scoring on each item was dependent on whether an event occurred and would not reflect scores on other items.

Stressful Life Events

Turner and Avison's Stressful Life Events Scale was used as an additional measure of stress in the Late Effects Study. This measure of stress reflects life events and the perceived severity of the acute stressors that occur whereas Wheaton's Chronic Stress inventory is designed to capture stress that would occur over a continuum [146, 147]. The Late Effects study used items from the Quebec Health Survey on stressful life events combined with Turner and Avison's scale to create an eleven item inventory. Three items in the scale came from Turner and Avison's Stressful Life Events Scale and the remaining eight items from the Quebec Health Survey. Participants were first asked to report whether the stressful event had happened to them in the previous twelve months. If the event had occurred they were then asked to rank the severity of the event on a four point Likert scale from not at all stressful to extremely stressful.

If the participant reported that they had not had the event they received a score of zero for that item. If the participant reported that they had the event they received a score of one to four based on their severity ranking. If the participant did not report whether they had the event but reported a severity score it was assumed that the event had occurred and they received the appropriate score. If the participant did not report a severity score it was assumed that the event had not occurred. Scores on the eleven items were summed to provide a total score. The minimum score for the scale was zero, meaning no stressful life events and the maximum was 44, meaning high stress.

The stressful life events variable was categorized based on the frequency distribution of total scores into three categories: 0 (no stressful life events), a score of 1-4 and 5 or greater. Scores were positively skewed in both cancer survivors (skewness=1.54, kurtosis=2.79) and the control group (skewness=1.62, kurtosis=2.11) suggesting that respondents generally had fewer stressful life events or perceived them to be less severe (Appendix 1). The Cronbach alpha test for internal consistency for the stressful life events scale in the cancer survivors was 0.53 and in the control group was 0.42 suggesting low internal consistency. A low internal consistency on this scale would be expected, as it is not measuring a unidimensional construct but rather different events that could happen in ones life [148, 149]. Previous examinations of stressful life event scales have also found low test-retest reliability and it is suspected that timing of administration of the questionnaire strongly affects respondents' ability to recall events but do not invalidate the use of these inventories [148].

There were 46 respondents (2%) who did not answer at least one of the questions on the inventory, of which 27 (59%) were cancer survivors and 19 (41%) were from the control group. It was assumed that if the respondent did not answer the question they did not have the event. The method of mean imputation by case for missing data when participants responded to greater than 50% of the items was not used for this inventory because scoring on each item was dependent on whether an event occurred and would not reflect scores on other items.

Cancer Diagnosis

The second edition of the International Classification of Childhood Cancer, which is based on the ICD-O-2, was used to categorize pediatric cancer types. The ICCC classifies types of cancer into twelve categories: leukemia; lymphoma and reticuloendothelial neoplasms; central nervous system and miscellaneous intracranial and intraspinal neoplasms; sympathetic nervous system tumors; retinoblastoma; renal tumors; hepatic tumors; malignant bone tumors; soft-tissue sarcomas; germ-cell, trophoblastic and other gonadal neoplasms; carcinomas and other malignant epithelial neoplasms; other and unspecified malignant neoplasms [150]. In the current study there were no cases of other and unspecified malignant neoplasms. There were also very few cases of retinoblastoma, hepatic and sympathetic nervous system cancers so they were combined into one category called 'other'. In the analyses leukemia was chosen as the reference category as it was the most common type of cancer diagnosis.

The current study also included nineteen cases of Langerhans cell histiocytosis (LCH) that were categorized as lymphoma and reticuloendothelial neoplasms. The ICCC no longer considers LCH to be a neoplastic disease and therefore excludes it from its classification system [150]. However, whether or not LCH is a neoplastic or immunological disease remains under debate and may actually be a combination of immune dysregulation and oncogenesis [151, 152]. Regardless of whether it is a neoplastic disease or not survivors of LCH were included in the current study because they have similar clinical histories and are at risk for late effects of treatment like pediatric cancer survivors. Langerhans cell histiocytosis can be a fatal disease [153]. Children with LCH are often treated with chemotherapy and radiation therapy at oncology centers [153]. The late effects associated with Langerhans cell histiocytosis and its treatment include endocrine, neurological, orthopedic and second cancers, among others, which are similar to those observed in pediatric cancer survivors [154].

Type of Treatment

Data on the type of cancer treatments received were obtained from medical charts. The types of treatment that cancer survivors had were categorized as chemotherapy, radiation, surgery, chemotherapy and radiation, chemotherapy and surgery, radiation and surgery and all three. If no treatment was reported they were categorized as such.

Age at Diagnosis

Data on age at diagnosis with cancer were collected from medical charts. The age at diagnosis variable was categorized into four 5-year categories: 0-4, 5-9, 10-14 and 15-19 years. There was no missing data for this variable.

Relapse

Data on whether a relapse of the initial cancer occurred were collected from medical charts; a maximum of three relapses were recorded. The relapse variable was dichotomized into 'Yes', having had a relapse and 'No', having had no relapse. It was not informative to have more than two categories as only a small portion of survivors had more than one relapse. If the question was left blank it was assumed that the participant had not had a relapse.

4.3 Treatment of Missing Data

There are different types of missing data; data can be missing completely at random (MCAR), missing at random (MAR) or non-ignorable. MCAR assumes that probability of missing data on a variable is unrelated to the value of all other variables including the variable itself. Data are MAR when the probability of missing data on an independent variable can depend on other variables but not on the value of the variable itself. When the value of the missing data depends on the value of the variable itself it is considered non-ignorable and special modeling methods are required [155]. A summary of the quantity of missing data by variable and the method for dealing with the missing data is found in Appendix 3.

Listwise Deletion

Listwise deletion is a conventional method to deal with missing data. The advantages of this method are that it can be used for any types of statistical analysis and does not require special computational methods or software. If data are missing completely at random (MCAR) then parameter estimates will be unbiased as the listwise deleted dataset will be a random sample of the original study population. Standard errors will be larger in the listwise

deleted dataset due to a reduced sample size [155]. Listwise deletion can be biased if deleted cases are unrepresentative of the entire population [156].

One hundred and thirty-three or 4.7% of respondents in the dataset were deleted due to missing data on the outcome variables, smoking and/or alcohol use. The outcomes of smoking and alcohol use were categorical type variables. Chen and Astebro [157] examined six missing data methods for categorical data. They found that listwise deletion was the better missing data technique for categorical data under the MAR or MCAR assumption but would present a problem if there were a lot of variables missing greater than 10-20% of data due to loss of information and statistical power.

An additional 75 participants were deleted from the dataset as they were missing greater than 50% of responses on the SF-36, Rosenberg Self-Esteem or Satisfaction With Life scales and mean imputation could not be performed. A total of 208 cases or 7.4% of the sample population were deleted from the dataset due to missing data.

Person Mean Imputation

Listwise deletion was not performed on all variables as approximately 38% of respondents were missing data on at least one variable. This would drastically reduce the sample size and may not be representative of the population. Large sample sizes were also required for the structural equation modeling analysis. Person mean imputation is a missing data method that imputes the mean of completed items and was used for Likert type scales when greater than 50% of the items were answered. This is a standard procedure used for scoring the SF-36 scale and for consistency was also used for missing data on the self-esteem and satisfaction with life scales [139]. A study by Downey and King [158] found that person mean imputation represented the original data well when the number of respondents with missing data and the number of items missing were 20% or less. If greater than 20% they found that the reliability estimates tended to be inflated. For the self-esteem and satisfaction with life variables the percent of respondents missing data prior to imputation was less than 2%.

Single Imputation

In the final analysis participants missing data on the education, personal income, ethnicity, chronic stress, stressful life events and special education variables were regrouped

into other categories. Single imputation of missing data can result in underestimated standard errors and overestimated test statistics [155]. However, the amount of missing data on each of these variables was under 7% except for personal income, which had approximately 13% of respondents missing data.

Multiple Imputation

It is not possible to know whether missing data are MAR, MCAR or non-ignorable and whether the assumptions of the missing data technique are appropriate [155]. Therefore a multiple imputation procedure for missing data was also performed and results from logistic regression analyses were compared to results from the logistic regressions using missing data procedures discussed above.

Multiple imputation is a method that creates multiple datasets each with a different imputed value representing a random sample of missing values, which accounts for the uncertainty about the correct value to impute. Each dataset is analyzed separately and then results are combined to provide overall estimates and standard errors [156, 159]. This method is advantageous to other missing data techniques as it creates a complete dataset without affecting sample size and produces consistent estimates that are efficient and normal when data are MAR [155, 156].

The Monte Carlo Marcov Chain (MCMC) Bayesian multiple imputation procedure (PROC MI) from SAS version 8.02 was used, as it was determined from the multiple imputation output that the data had an arbitrary missing data pattern. Multiple imputation using the MCMC method assumes that data are from a continuous multivariate normal distribution and that each variable is a linear function of all other variables. However, it is also robust to violations of normality [155, 159]. For each variable that contains missing data the variable is regressed on all other variables. The regression equations are used to generate predicted values for missing data and a random draw from the residual normal distribution for that variable is added to account for uncertainty. In SAS a single chain is run of data augmentation cycles creating five datasets. The number of burn in iterations performed before the imputation was 500 and 200 iterations between imputations. Multiple imputation of data was performed by case and control groups to account for group differences [155, 159].

In SAS autocorrelations and time series plot for bivariate tables were produced to examine if convergence was reached with the number of iterations used. The time series plots of means did not display any long term trends suggesting that convergence was reached. The autocorrelation plots for means reached zero also suggesting convergence [155, 159] (Appendix 4).

Missing data were imputed for the sum scores on the satisfaction with life, self-esteem, chronic stress and stressful life events scales as continuous variables setting a maximum and minimum score. After imputation the continuous variables were categorized for the logistic regression analysis. The personal income variable was imputed as a continuous variable to avoid biases created by imputing data as a categorical variable by first setting each score to the median of the category included in the questionnaire. Ethnicity was imputed using the initial grouping of parent's ancestors into 16 categories included in the questionnaire with plausible values ranging from 1-16. Education was imputed as the original 6 categories included in the questionnaire with plausible values ranging from 1-6. For the categorical variables imputation was performed with a minimum set to one and following imputation scores were rounded to avoid implausible values [155]. All variables were recategorized following imputation for the logistic regression analysis.

The PROC MI ANALYZE procedure in SAS was used to combine results from the five imputed datasets [160]. Logistic regression analyses must be done for each of the five imputed datasets and results are combined using PROC MIANALYZE. The output contains regression coefficients and their associated covariance matrix but not chi-square test statistics. These must be computed by hand which is computationally demanding [155, 160]. Other limitations of multiple imputation are that you get slightly different parameter estimates each time you do a multiple imputation procedure and imputation of categorical data followed by rounding may result in biased parameter estimates [155, 161]. Parameter estimates from the logistic regression analysis of multiply imputed data were similar to results from the logistic regression analysis using other missing data procedures as discussed above. Due to the complexity, time required to perform logistic regression analyses on multiply imputed datasets and violations of normality, the simpler missing data procedures were used. Additionally, listwise deletion has been shown to be more robust than multiple imputation when the MAR assumption is violated [155].

4.4 Statistical Analysis

SAS version 8.02 for Windows software was used to organize and manage data, to perform missing data procedures, to calculate descriptive statistics and to perform multivariate logistic regression analyses [162]. The statistical modeling software Mplus version 3.13 by Muthén and Muthén [163] was used for structural equation modeling (SEM) analyses.

4.4.1 Descriptive Statistics

Descriptive statistics were used to describe smoking and alcohol use, psychosocial, demographic, health and clinical characteristics of the population of pediatric cancer survivors and the controls. Frequency distributions and percentages were calculated for smoking, alcohol use and their concurrent use in both survivors and controls. The prevalence of smoking, alcohol use, and their concurrent use were calculated for both survivors and controls by the covariates. Chi-square tests were used to compare proportions. Means and standard deviations were calculated to describe continuous variables. Tests for normality were conducted which produced tests for skewness and kurtosis where values of zero represented a normal distribution. Cronbach alphas were also calculated to describe the internal consistency of the psychological scales. Internal consistency is a measure of reliability and assesses the extent to which items on the scale correlate with each other. An alpha of 0.70 was considered adequate internal consistency [141].

Bivariate correlations were calculated for variables used in the SEM analysis. Pearson Product moment correlations were calculated for two continuous variables; Polychoric correlations were calculated for two categorical variables; and Kendall's tau-b correlations were calculated for a continuous variable with an ordered categorical variable. Point biserial correlations were calculated for a continuous variable with a dichotomous variable using the SAS Macro for biserial correlations [164].

Stratified analyses were performed to test for confounders and effect modifiers of the relationship between pediatric cancer survivors and controls on the outcomes of smoking and alcohol use. The Breslow-Day test for homogeneity was used to test for effect modification at the 0.05 level of significance. The Mantel Haenszel odds ratios and 95% confidence intervals were used to adjust for potential confounding variables and were compared to the

crude odds ratios. Results from the stratified analyses were later compared to the multivariate logistic regression analyses.

Univariate logistic regression models were fit between each covariate and the outcome variables in pediatric cancer survivors and controls separately to obtain odds ratios, 95% confidence intervals, likelihood ratio and Wald chi-square test statistics for the significance of the relationship using SAS PROC LOGISTIC.

4.4.2 Multivariate Analysis

Multivariate logistic regression analyses were performed using SAS PROC LOGISTIC to compare tobacco use, alcohol use and their concurrent use in pediatric cancer survivors to the controls taking into consideration potential confounders and effect modifiers. Variables that could potentially be an intermediate step in the causal pathway from being a cancer survivor to smoking and alcohol use were not included in one of the adjusted models and was compared to other models [165].

Multivariate logistic regression analyses were also performed to determine the important predictors of smoking, alcohol use and their concurrent use in both pediatric cancer survivors and the control group independently. The outcomes of smoking and alcohol use were categorical and initially contained more than two categories necessitating that polytomous logistic regression modeling be performed. However, due to small sample sizes and zero cells resulting from the stratification of outcomes by covariates multivariate analyses were only performed on dichotomized outcome variables. Covariates that were found to be significant at the 0.25 level of significance in the univariate logistic regression analyses were included in the full multivariate model. Variables were removed from the model at the 0.05 level of significance. Interaction terms that were significant at the 0.10 level of significance were included in the model and removed at the 0.05 level of significance. Interaction terms had to also be biologically plausible to be included in the final model and the most parsimonious, statistically significant models were selected [166].

Model parameters were estimated using maximum likelihood estimates. The Wald chi-square and log likelihood ratio chi-square test were used to determine the importance of each variable in the multivariate models [167, 168]. The disadvantage of the Wald chi-square statistic is that if there are large logistic regression coefficients the standard error will be

inflated increasing the likelihood of making a Type II error; failing to reject the null hypothesis when it is false [167]. Pampel [168] suggests that log likelihood statistics also be examined to determine significance and if they show a significant p-value for a model with a large effect size then good model fit is assumed even if the Wald statistics are opposing.

Analyses were also performed to test for collinearity among variables in the multivariate models. The Tolerance statistic (TOL) and the Variance Inflation Factor (VIF) were calculated in SAS PROC REG using the same dependent and independent variables as the logistic regression analysis. If the tolerance statistic was less than 0.20 collinearity was considered and a value less than 0.10 indicated serious collinearity. There is no standard criteria for the Variance Inflation Factor but a conservative value of 2.5 was used to consider collinearity among variables [167]. The only variables found to be potentially collinear were age and age at diagnosis (Appendix 2). Therefore, they were never included together in a multivariate model.

4.4.3 Structural Equation Modeling

The following steps are involved in structural equation modeling:[109, 169]

1) Theory development;
2) Model Specification;
3) Parameter estimation;
4) Evaluating model fit;
5) Model modification (trimming or building); and
6) Testing the structural model against others.

Model Specification

In the model specification stage a model to be tested was developed based on theory and was represented in a diagrammatic form (Figure 2). There are two types of variables in the model: measured variables and latent variables. An important advantage of structural equation modeling is that it attempts to reduce bias in estimates created by measurement error. Latent constructs are variables that we cannot directly or precisely measure. In structural equation modeling multiple indicator variables can be used to measure a latent construct to attempt to better estimate its true value [170].

Latent constructs were represented in the diagrammatic model (Figure 2) as ellipses and their indicators as squares or rectangles. Circles also indicated error terms, as they are not directly measured. Any single indicator or measured variables were represented by squares or rectangles [170]. There are two parts to a structural equation model: the measurement model and the structural model. The measurement model specifies the relationships between latent constructs and their measured indicators as well as correlations between constructs. Whereas the structural model includes latent constructs and measured variables with directional pathways among variables [171].

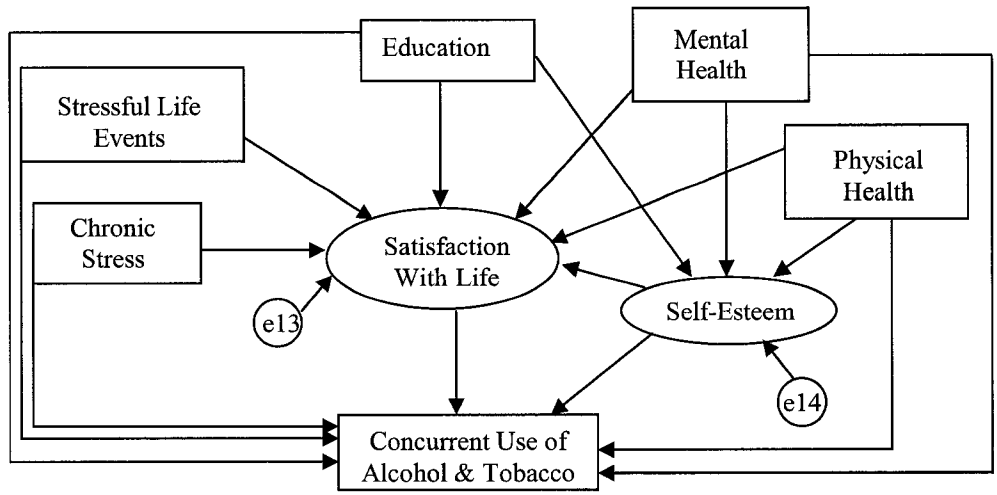


Figure 2: Structural model to test the relationship between psychosocial, health, demographic factors and concurrent use of alcohol and tobacco mediated by satisfaction with life.

In the specified measurement model for this thesis there were two latent constructs: satisfaction with life and self-esteem, with directional pathways to their indicators, error terms for each indicator and a covariance term between the two constructs (Figure 3). A covariance term was included between the two constructs as they are independent variables in the measurement model and are known to be correlated [117]. Latent constructs were created for the self-esteem and satisfaction with life variables using the items from each psychological scale included in the Late Effects study. The self-esteem construct had six ordinal indicators and the satisfaction with life had five (Figure 3). Items included from the Self-Esteem scale and Satisfaction With Life scale can be found in Appendices 5 and 6 respectively.

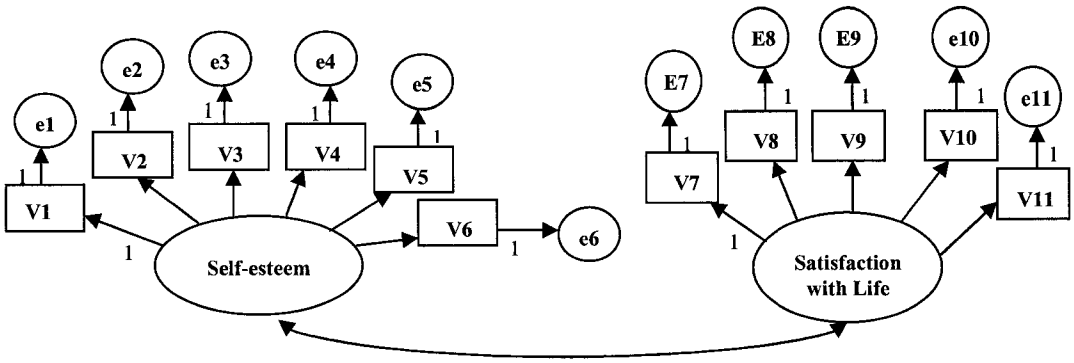


Figure 3: Measurement model with two latent constructs, eleven measured dependent indicator variables and a covariance between the latent constructs.

The Late Effects study also included previously validated psychological scales to measure physical health, mental health, chronic stress and stressful life events constructs. Each of these scales contained multiple items that could have been used as indicators of their latent constructs. The items for the chronic stress and stressful life events scales were found to be inappropriate for use as indicators as they were not measuring a unidimensional construct but rather different events that could occur in ones life [148, 149].

The physical and mental health scales contained 20 and 14 ordinal items respectively, that could have been used as indicators for the physical and mental health latent constructs. However, this many indicators for each latent construct would have increased model complexity and worsened the model fit as a high item to subject ratio increases the instability of the factor solution [172]. It also would have been possible to use the four subscales for each mental and physical health scales as indicators. However, these subscales were found to have very high ceiling effects where a substantial number of subjects scored the highest possible value on the scale. Austin and Brunner [173] showed that high ceiling effects increases the chance of making a type I error where we would conclude that there was a significant relationship when there truly was not.

Another option would have been to select a few indictors to represent the physical and mental health constructs by performing an exploratory factor analysis. However, the SF-36 scale has been validated in several populations and the authors warn against altering the scale as it may affect the validity and comparability with other studies [139]. Therefore, the continuous summary scores for the physical and mental health scales as well as the chronic stress and stressful life events scales were used as single indicators of the latent constructs.

The limitation of using a single indicator is that we must assume zero measurement error, which can bias estimates of relationships among constructs [170].

The structural model specified for this thesis contained the measurement model as discussed above and six measured variables. Figure 2 shows the full structural model that was tested. In this model there were three dependent variables: satisfaction with life, self-esteem and concurrent use of alcohol and tobacco, as well as the dependent factor indicators for the latent constructs. Concurrent use of alcohol and tobacco was the outcome of interest in the model. The satisfaction with life latent construct was tested as a mediator in the model. There were direct paths from all of the variables to the outcome variable. There were indirect paths from all of the observed continuous measured variables and the self-esteem latent construct to concurrent use of alcohol and tobacco through satisfaction with life. In the model education was a measured categorical exogenous variable that was dichotomized into two dummy variables and regressed on satisfaction with life, self-esteem and concurrent use of alcohol and tobacco. Error terms were included for each measured variable and latent constructs but were set at zero for the measured variables. For the theoretical explanation behind each included structural parameter see Chapter 3 section 1 on the theoretical development of the model.

The WLSMV estimator was used in Mplus and with this estimator it was not possible to estimate covariances between observed exogenous variables and latent exogenous variables. Therefore, it was necessary to regress self-esteem onto mental health, physical health and education to account for the relationship between these variables [174].

In Mplus the model is estimated conditioned on the observed exogenous variables when using the WLMSV estimator. Therefore the means, variances and covariances of the observed exogenous variables are not estimated as part of the model. The benefit of this is that we do not have to assume that the variables are normally distributed. Although the covariances among exogenous variables are not specified or estimated as part of the model, they are also not fixed at zero and are allowed to freely correlate [174].

Model Identification

Another important aspect of the model specification process is to ensure that the specified model is identified so that one has enough information from the components of the

covariance matrix to obtain a unique solution for parameters in the model. There are three possibilities for model identification. A model can be underidentified where there are more unknown parameters than available information; just identified where the number of unknown parameters is equal to available information; and overidentified where there are more information available than unknown parameters. A model needs to be just identified or overidentified in SEM to obtain a proper solution. It is preferred for a model to be overidentified so that model tests can be performed. The number of degrees of freedom for model testing is the number of nonredundant elements in a covariance matrix minus the number of parameters to be estimated [175]. In Mplus degrees of freedom when using WLSMV are not calculated in this way and the formula can be found in the Mplus technical appendices [176].

In the measurement portion of the model one factor loading from each latent construct is fixed to one for identification purposes. All other factor loadings and variances are free parameters to be estimated [177].

In a single group analysis in Mplus the default is that for each continuous latent construct means and intercepts are fixed to zero. Intercepts and thresholds of observed categorical dependent variables are free to be estimated. When using Theta parameterization variances and residual variances of latent variables with categorical factor indicators are fixed to one [178].

In a multiple group analyses in Mplus the default is that means and intercepts of continuous latent constructs are fixed to zero in the first group and are unequal and free to be estimated in the second group. Intercepts and thresholds of observed categorical factor indicators of continuous latent constructs are free and held equal across groups. When using Theta parameterization variances and residual variances of latent variables with categorical factor indicators are fixed to one in the first group and are free and unequal in the second group [178].

Parameter estimation in Mplus

Standard SEM utilizes maximum likelihood methods to estimate model parameters and test statistics with the assumption that observations are drawn from a continuous, multivariate normal population. The use of categorical and non-normally distributed

variables in the current study violates this assumption. Non-normality of data has been shown to not affect parameter estimates but underestimates standard errors and can lead to substantial overestimation of likelihood ratio chi-square goodness-of-fit statistics [169].

Muthén [179, 180] proposed a general structural equation model termed CVM (continuous/categorical variable methodology) that allows for dichotomous, ordered polytomous and continuous measured variables to be analysed. CVM results in unbiased and consistent parameter estimates for ordered categorical data. It is based on the assumption that each measured variable has an underlying continuous normally distributed latent variable [181]. Model parameters are estimated by polychoric correlations between measured variables using Weighted Least Squares (WLS) [110]. Muthén and Muthén developed a statistical modeling software Mplus [163] based on the CVM approach that is able to perform structural equation modeling with categorical, dichotomous and continuous data [182].

Measurement Model: Multiple Group Confirmatory Factor Analysis

A multiple group confirmatory factor analysis (CFA) was used to test the measurement model for validity of its indicators and invariance across the cancer survivor and control groups. Often in research that involves multiple groups it is simply assumed that measurement invariance is present; that a measurement instrument will be measuring the same construct in both groups, but this is rarely tested statistically [183]. In Mplus the default estimator used for a CFA with ordered categorical indicator variables is robust weighted least squares (WLSMV) using polychoric correlations. The weighted least square parameter estimates were produced using a diagonal weight matrix with standard errors. A mean and variance adjusted chi-square test statistic was produced using a full weight matrix. With this estimator probit regressions of the latent construct on the measured ordinal indicators were estimated. Since factor indicators were ordered categorical, thresholds were modeled rather than intercepts or means and were equal to the number of categories minus one. Theta parameterization was used for the multiple group analysis. With theta parameterization residual variances for the latent response variables were allowed to be parameters in the model and were fixed to one in the first group and are free to be estimated in the other groups for identification purposes [178].

When the CFA model was first run the output specified that there was a "zero cell problem" for the bivariate tables of the ordinal indicator variables. In order to avoid zero bivariate frequencies the ordinal variables were collapsed into three categories; disagree, neither disagree nor agree, and agree [180].

After the multiple group CFA was estimated and model fit was found to be satisfactory the model was tested for measurement invariance across groups. Testing for equivalent factor loadings is considered necessary to determine that factors are measuring the same constructs across groups [183]. Measurement invariance for ordinal categorical outcomes does not require invariance of the factor means or factor covariance matrices but just the measurement parameters, the thresholds and factor loadings [177, 184, 185]. Testing for invariance of error variances and covariances is generally considered too restrictive and unnecessary [183]. Here, the measurement model included the latent construct self-esteem with six ordered categorical indicators, the latent construct satisfaction with life with five ordered categorical indicators, and a covariance between the two latent constructs. Measurement invariance was tested for the factor loadings and thresholds.

First the model was estimated where thresholds and factor loadings were constrained to be equal across groups; residual variances were fixed to one in the control group and free in the cancer survivors; factor means were fixed to zero in the control group and free in the cancer survivors (default in Mplus). This model was then compared to a less restrictive model where thresholds and factor loadings were allowed to be free across groups; residual variances were fixed to one in all groups and factor means were fixed to zero in all groups. With categorical outcomes the thresholds and factor loadings must be constrained together because the item probability curve is influenced by both parameters [186]. A chi-square difference test was calculated to determine if constraining the factor loadings and thresholds significantly worsened model fit compared to the less restrictive model. A non-significant chi-square would indicate that it did not. However, because chi-square difference tests are affected by sample size alternative goodness-of fit indices should be used to test for invariance [187]. Cheung and Rensvold found that the difference in CFI from the constrained to unconstrained model was a powerful procedure for detecting group differences and was used in the current study. A change in CFI less than or equal to –0.01 was used to indicate that the null hypothesis of invariance across groups should not be rejected [187].

In Mplus, when using WLSMV estimator a chi-square difference test cannot be calculated by simply subtracting the chi-square values from the two nested models because with this estimator the chi-square values are not distributed as chi-square. Instead the DIFFTEST option in Mplus was used to obtain a correct chi-square difference test [178].

Multiple Group Structural Equation Model

Measurement invariance was found for measurement model across cancer survivor and the control groups. After measurement invariance was found the full structural model was tested. A multiple group analysis was performed with the WLSMV estimator and theta parameterization in Mplus. For continuous latent dependent variables the regression coefficients produced were simple linear regression coefficients. For observed categorical dependent variables the regression coefficients produced were probit coefficients. Significance of regression coefficients was determined by dividing the estimate by the standard error. This test has approximately a normal distribution in large samples and therefore a value greater than 1.96 was considered significant for a two-tailed test at the 0.05 level [178]. The full structural model was found to have satisfactory fit with the data but there were a number of pathways that were significant in the control group and not in the cancer survivors suggesting structural non-invariance. Structural invariance is where the relations between constructs or parameter estimates are equal across groups [183]. Here structural invariance did not hold, therefore the model was estimated separately in cancer survivors and controls and non-significant paths were removed.

Mplus provides both standardized and unstandardized parameter estimates as well as 95% confidence intervals. The standardized coefficients were standardized using the variances of the latent and observed variables so that variances were equal to one. This allows for comparison of parameters in the model [169]. The unstandardized solutions were used to compare models across groups.

Testing for Mediation

The models were tested for mediation using the MODEL INDIRECT command in Mplus. The approach used in Mplus to test the significance of the mediating variable is to multiply the coefficient for the relationship between the independent variable and the

mediating variable by the coefficient for the relationship between the mediating variable and the dependent variable and dividing it by the standard error. This value is then compared to a standard normal distribution to test for significance [188]. Confidence limits were included for the indirect effects to examine sampling variability. If the confidence limits included zero it provided evidence that the effect was not larger than expected by chance [189].

Assumptions

One assumption of the SEM method proposed by Muthén is that the underlying latent construct is continuous. When using ordinal indicators that are non-normally distributed we violate this assumption. However, Flora and Curran [190] found that estimation of CFA models with ordinal indicators using Weighted Least Squares and polychoric correlations was robust to moderate levels of non-normality of the latent response variables. They found that the parameter estimates were only slightly inflated and there was no effect on the test statistics or standard error estimates.

Other assumptions of SEM are that the sample is obtained randomly from the population of interest, that there is no missing data, no specification errors or relevant variables left out of the model and that there is weak exogeneity of exogenous variables or that the exogenous variable is not explained by previous values of the dependent variable [169].

Evaluating model fit

Mplus provides chi-square square test statistics and has a number of alternative fit indices available to assess model fit. The chi-square test alone is not enough to determine model fit as it is sensitive the distribution of the data and sample size. A large sample can result in the rejection of a model based on only small differences between the model and sample covariance or correlation matrix resulting a Type II error [191]. Hoyle and Panter [192] recommend reporting at least two incremental fit indices along with the model chi-square test statistic. Incremental fit indices are less sensitive to sample size and compare the model to be tested with a nested baseline model. The baseline model is more restrictive as it is the model where all observed variables are uncorrelated [191]. For this study the two incremental fit indices that were reported were the Comparative Fit Index (CFI) and the Tucker Lewis

Index (TLI). As well an additional fit index, the Root Mean Square Error of Approximation (RMSEA), was reported.

The CFI and TLI are incremental fit indices that range from 0 to 1. Conventionally a value of 0.90 was suggested to indicate adequate model fit. More recently Hu and Bentler recommended that a value of 0.95 be used to minimize type I and type II errors, especially with small sample sizes [191, 193].

Generally, as the number of parameters in the model increases, model fit decreases. The RMSEA is an alternative fit index that accounts for model complexity or the degrees of freedom in the model [112]. The RMSEA can range from 0 to infinity; Brown and Cudeck [194] recommended that an RMSEA value of 0.05 or less indicates close fit and up to 0.08 indicates reasonable fit of the model to the data.

Yu [195] found that the cut-off values recommended by Hu and Bentler [193] were also appropriate for categorical data. All of these criteria are only guidelines and may differ depending on the characteristics of the study. Smaller sample sizes are of concern but as sample size increases the test statistics are appropriate measures of model fit [191].

Mplus also provides an R^2 statistic that represents the variance in the latent construct that is accounted for by the exogenous variables. With categorical dependent variables the pseudo R^2 is interpreted as a standard deviation change in the underlying continuous latent construct for a change in the exogenous variable from 0 to 1 [176].

Model modification

Modification indices were provided by the Mplus program and can be used to modify a model if it does not fit the data well. It provides information on the expected reduction in the likelihood ratio chi-square statistic if the parameter is freed [176]. Modification indices were not used in the current study, as model fit was acceptable, modification indices were low and did not make theoretical sense. Although model fit was acceptable there were a number of non-significant paths, especially for the cancer survivor group. Models were modified by removing non-significant paths sequentially beginning with the least significant.

Test the structural model against others

The trimmed models with non-significant paths removed were compared to the originally specified model using the chi-square difference test (DIFFTEST in Mplus).

5.0 RESULTS

5.1 Population characteristics

There were 1231 pediatric cancer survivors (47.3%) and 1372 controls (52.7%) included in the current study. The frequency distribution of age and gender were similar between the cancer survivors and controls. The majority of respondents were under 25 years of age and there were slightly more females than males. Cancer survivors had a higher proportion of participants with lower income and education and poorer mental health and physical health compared to the controls ($p<0.05$). They also had a higher proportion of white participants and participants that had been in a special education or learning disabled program ($p<0.01$). Cancer survivors and controls had a similar distribution of self-esteem and satisfaction with life scores. Survivors had a higher proportion of participants reporting low chronic stress and stressful life events compared to the control group (<0.05) (Table 5).

Table 5: Distribution of demographic, psychosocial and health characteristics of pediatric cancer survivors and controls.

Characteristic	Cancer survivors (n=1231) n (%)	Controls (n=1372) n (%)	
Age (years)			
16-20	485 (39.4)	497 (36.2)	
21-25	343 (27.9)	386 (28.1)	
26-30	276 (22.4)	308 (22.5)	
31-37	127 (10.3)	181 (13.2)	
Gender			
Male	594 (48.3)	628 (45.8)	
Female	637 (51.7)	744 (54.2)	
Personal Income			
$0 to $4,999	429 (34.8)	382 (27.8)	**
$5,000 to $19,999	460 (37.4)	576 (42.0)	
$20,000+	342 (27.8)	414 (30.2)	
Education			
Less than high school	338 (27.5)	329 (24.0)	**
High school	461 (37.4)	460 (33.5)	
Greater than high school	432 (35.1)	583 (42.5)	
Ethnicity			
White	1059 (86.0)	1123 (81.8)	**
Non-white	45 (3.7)	90 (6.6)	
Aboriginal	22 (1.8)	15 (1.1)	
Mixed	105 (8.5)	144 (10.5)	

Continues

Table 5 continued

Mental Health Score †			
5-39	247 (20.1)	252 (18.4)	*
40-48	233 (18.9)	316 (23.0)	
49-53	250 (20.3)	288 (21.0)	
54-56	213 (17.3)	241 (17.6)	
57-70	288 (23.4)	275 (20.0)	
Physical Health Score †			
15-48	278 (22.6)	232 (16.9)	**
49-53	213 (17.3)	246 (17.9)	
54-56	246 (20.0)	316 (23.0)	
57-58	238 (19.3)	270 (19.7)	
59-73	256 (20.8)	308 (22.5)	
Satisfaction with Life Score			
5-19 (Dissatisfied)	319 (25.9)	361 (26.3)	
20-28 (Satisfied)	498 (40.5)	541 (39.4)	
29-35 (More satisfied)	414 (33.6)	470 (34.3)	
Self-Esteem Score ‡			
6-23	288 (23.4)	297 (21.6)	
24-26	257 (20.9)	298 (21.7)	
27-29	376 (30.5)	425 (31.0)	
30	310 (25.2)	352 (25.7)	
Chronic Stress Score §			
0-5	412 (33.5)	389 (28.3)	*
6-11	436 (35.4)	499 (36.4)	
12-45	383 (31.1)	484 (35.3)	
Stressful Life Events Score §			
0	448 (36.4)	426 (31.0)	*
1-4	395 (32.1)	491 (35.8)	
5+	388 (31.5)	455 (33.2)	
Special Education/ LD Program			
No	1040 (84.5)	1260 (91.8)	**
Yes	191 (15.5)	112 (8.2)	

* $p<0.05$, ** $p<0.01$
† Higher score indicates better health.
‡ Higher score indicates greater self-esteem.
§ Higher score indicates greater stress.

Table 6 shows the distribution of clinical characteristics of the pediatric cancer survivors. There were a lower proportion of survivors who were diagnosed with cancer in the 0-4 year age group (18.4%) compared to the other age groups. Most survivors were treated with chemotherapy and radiation (20.0%) or chemotherapy, radiation and surgery (19.3%). The proportion of survivors who received only radiation (2.9%) or had no treatment reported (1.6%) was small. Leukemia was the most common type of cancer diagnosis in survivors (25.5%) followed by cancer of the central nervous system (17.5%). The least common cancers included retinoblastoma, hepatic and cancers of the sympathetic

nervous system, which combined accounted for only 3.4% of cases. Most survivors (88.6%) had not had a relapse of their initial cancer (Table 6).

Table 6: Distribution of clinical characteristics of pediatric cancer survivors.

Characteristic	n (%)
Age at Diagnosis (years)	
0-4	227 (18.4)
5-9	327 (26.6)
10-14	333 (27.1)
15-19	344 (27.9)
Type of Cancer Treatment	
Chemotherapy	125 (10.1)
Radiation	36 (2.9)
Surgery	206 (16.7)
Chemotherapy & Radiation	246 (20.0)
Chemotherapy & Surgery	207 (16.8)
Radiation & Surgery	154 (12.5)
Chemotherapy & Radiation & Surgery	237 (19.3)
No Treatment Reported	20 (1.6)
Cancer Diagnosis	
Leukemia	314 (25.5)
Hodgkin's Lymphoma	189 (15.4)
Non-Hodgkin's Lymphoma *	99 (8.0)
Central Nervous System	216 (17.5)
Renal	62 (5.0)
Bone tumours	74 (6.0)
Soft Tissue Sarcomas	85 (6.9)
Germ cell/Gonadal	68 (5.5)
Carcinomas	82 (6.7)
Other †	42 (3.4)
Relapse	
No	1091 (88.6)
Yes	140 (11.4)

* Including reticuloendothelial neoplasms and Langerhans cell histiocytosis.
† Other cancers include: retinoblastoma, hepatic and sympathetic nervous system.

Table 7 shows the prevalence of current smokers, alcohol drinkers, binge drinkers and concurrent users of alcohol and tobacco in pediatric cancer survivors and the control group. The prevalence of current and former smokers was lower in the cancer survivors than the control group (current: 22.8% vs. 30.2% and former: 10.6% vs. 13.0%). Alcohol use was also lower in the childhood cancer survivors with a prevalence of 31.4% of survivors abstaining from alcohol use compared to only 24.2% of controls. The prevalence of light alcohol use was slightly lower in cancer survivors (41.8%) compared to control group (44.0%). Moderate to heavy alcohol use was lower in childhood cancer survivors (26.8%)

compared to controls (31.8%). The prevalence of binge drinking was similar to the prevalence of moderate to heavy drinking in both the survivor (24.9%) and control (31.0%) groups. Concurrent use of alcohol and tobacco was also lower in childhood cancer survivors (20.4%) compared to controls (27.3%). The prevalence of binge drinking was higher in the controls than the cancer survivors for all age groups except in the 26-30 year old age group where the controls had a lower prevalence (controls:19.5% , survivors: 24.6%) (Table 7).

Table 7: Prevalence of current smokers, alcohol drinkers, binge drinkers and concurrent users of alcohol and tobacco in pediatric cancer survivors and controls

	Survivors n (%)	Controls n (%)	
Smoking			
Never	820 (66.6)	779 (56.8)	*
Former	130 (10.6)	178 (13.0)	
Current	281 (22.8)	415 (30.2)	
Alcohol Use			
Abstain	387 (31.4)	332 (24.2)	*
Light	514 (41.8)	604 (44.0)	
Moderate to Heavy	330 (26.8)	436 (31.8)	
Current Smoker			
Yes	281 (22.8)	415 (30.2)	*
No	950 (77.2)	957 (69.8)	
Alcohol Drinker			
Drinker	844 (68.6)	1040 (75.8)	*
Non-Drinker	387 (31.4)	332 (24.2)	
Concurrent use			
Yes	251 (20.4)	375 (27.3)	*
No	980 (79.6)	997 (72.7)	
Binge Drinking			
Yes	307 (24.9)	425 (31.0)	*
No	924 (75.1)	947 (69.0)	
Binge Drinking Stratified by age †			
16-20	133 (27.4)	203 (40.8)	
21-25	87 (25.4)	121 (31.3)	
26-30	68 (24.6)	60 (19.5)	
31-37	19 (15.0)	41 (22.6)	

* $p < 0.001$

† Age was found to be a significant effect modifier by the Breslow-Day test for homogeneity ($\chi^2 = 14.44$, $= 0.002$).

Table 8 shows crude and adjusted odds ratios and their 95% confidence intervals for current smoking, alcohol drinking and the concurrent use of alcohol and tobacco in cancer survivors compared to controls. For the outcomes of smoking, alcohol drinking and

concurrent use no significant effect modifiers were found. Odds ratios were adjusted for potential confounders that could not be intermediate variables in the causal pathway and for all potential confounders in separate models. The odds ratios adjusted for all potential confounders did not differ greatly from the crude odds ratios and odds ratios adjusted only for variables that could not be intermediate in the causal pathway (Table 8). Pediatric cancer survivors were significantly less likely to be current smokers (OR_{adj}=0.64, 95%CI=0.53, 0.77), alcohol drinkers (OR_{adj}=0.73, 95%CI=0.60, 0.88) and concurrent users of alcohol and tobacco (OR_{adj}=0.65, 95%CI=0.53,0.78) compared to the control group.

The odds ratio for binge drinking in cancer survivors compared to controls was modified by age (Breslow-Day test for homogeneity: χ^2=14.44, p=0.002). Age specific crude odds ratios and adjusted odds ratios are presented in Table 8. Although not statistically significant the 26-30 year old group appeared to differ from the other age groups with cancer survivors having higher odds of being binge drinkers than the controls in the stratified analysis (OR=1.35, 95% CI=0.91, 2.00). In all other age groups cancer survivors were significantly less likely to be binge drinkers than the controls (Table 8).

Table 8: Crude odds ratios (ORs), adjusted odds ratios (ORs) and their 95% confidence intervals (95%CI) for current smoking, alcohol drinking, concurrent use and binge drinking in pediatric cancer survivors compared to the control group.

	Crude OR (95% CI)	OR_{Adj} (95% CI) †	OR_{Adj} (95% CI) ‡
Current Smoker	0.68 (0.57, 0.81)	0.64 (0.53, 0.77)	0.67 (0.56, 0.80)
Alcohol Drinker	0.70 (0.59, 0.83)	0.73 (0.60, 0.88)	0.67 (0.56, 0.80)
Concurrent user	0.68 (0.57, 0.82)	0.65 (0.53, 0.78)	0.67 (0.56, 0.80)
Binge Drinker	0.74 (0.62, 0.88)	0.68 (0.57, 0.82)	0.68 (0.57, 0.81)
Binge Drinker Stratified by age *			
16-20	0.55 (0.42, 0.71)	0.54 (0.40, 0.72)	0.53 (0.40, 0.69)
21-25	0.74 (0.54, 1.03)	0.66 (0.46, 0.95)	0.67 (0.48, 0.94)
26-30	1.35 (0.91, 2.00)	1.23 (0.79, 1.92)	1.27 (0.84, 1.91)
31-37	0.60 (0.33, 1.09)	0.51 (0.25, 1.03)	0.53 (0.28, 0.98)

Note: Reference group is the control group

* Age was found to be a significant effect modifier by the Breslow-Day test for homogeneity (χ^2=14.44, p=0.002).

† Adjusted for all potential confounders: age, gender, education, special education, ethnicity, physical health, mental health, self-esteem, satisfaction with life, chronic stress and stressful life events. Odds ratios stratified by age are not adjusted for age.

‡ Adjusted for age, gender and ethnicity as these variables could not be in the causal pathway. Odds ratios stratified by age are not adjusted for age.

5.2 Current Smoking

Table 9 shows crude odds ratios and 95% confidence internals for current smoking associated with various predictors in cancer survivors and controls. Respondents with less than a high school education were more likely to be current smokers than those with greater than a high school education in both the cancer survivor (OR=2.05, 95%CI=1.46, 2.88) and control groups (OR=2.05, 95%CI=1.53, 2.74). In the control group those with a high school education were also more likely to be current smokers than those with greater than a high school education (OR=1.43, 95%CI=1.09, 1.88). Respondents of Aboriginal ethnicity were more likely to be current smokers than those who were white in both the cancer survivor (OR=2.30, 95%CI=1.97, 5.45) and control groups (OR=3.41, 95%CI=1.20, 9.66). In the control group respondents of non-white ethnicity were significantly less likely to be current smokers than white respondents (OR=0.49, 95%CI=0.28, 0.86). Controls in the lowest mental health category were more likely to be current smokers than those in the highest mental health category (OR=2.14, 95%CI=1.49, 3.09). In both the cancer survivors and the control group, respondents who scored in the lowest physical health categories were more likely to be current smokers than those in the highest physical health category. As satisfaction with life and self-esteem scores decreased respondents were more likely to be current smokers than those with high satisfaction with life and self-esteem in both the cancer survivor and control groups. As chronic stress and stressful life events scores increased respondents were more likely to be current smokers in both the cancer survivor and control groups (Table 9).

Table 9: Prevalence, crude odds ratios (ORs) and 95% confidence intervals (95%CIs) for current smoking by demographic, psychosocial and health factors in pediatric cancer survivors and controls.

	Cancer Survivors		Controls	
	Current Smoker n(%)	OR (95%CI)	Current Smoker n(%)	OR (95%CI)
Age (years)				
16-20	109 (22.5)	1.00	136 (27.4)	1.00
21-25	73 (21.3)	0.93 (0.67, 1.30)	121 (31.4)	1.21 (0.90, 1.62)
26-30	62 (22.5)	1.00 (0.70, 1.42)	96 (31.2)	1.20 (0.88, 1.64)
31-37	37 (29.1)	1.42 (0.92, 2.20)	62 (34.3)	1.38 (0.96, 1.99)
Gender				
Male	135 (22.7)	1.00	180 (28.7)	1.00
Female	146 (22.9)	1.01 (0.77, 1.32)	235 (31.6)	1.15 (0.91, 1.45)

Continues

Table 9 continued

Personal Income				
$0 to $4,999	86 (20.0)	0.91 (0.64, 1.29)	113 (29.6)	1.08 (0.79, 1.47)
$5,000 to $19,999	121 (26.3)	1.29 (0.93, 1.80)	186 (32.3)	1.22 (0.93, 1.62)
$20,000+	74 (21.6)	1.00	116 (28.0)	1.00
Educational Attainment				
Less than high school	103 (30.5)	2.05 (1.46, 2.88) *	130 (39.5)	2.05 (1.53, 2.74) *
High school	102 (22.1)	1.33 (0.96, 1.85)	144 (31.3)	1.43 (1.09, 1.88) *
Greater than high school	76 (17.6)	1.00	141 (24.2)	1.00
Ethnicity				
White	245 (23.1)	1.00	343 (30.5)	1.00
Non-white	5 (11.1)	0.42 (0.16, 1.06)	16 (17.8)	0.49 (0.28, 0.86) *
Aboriginal	9 (40.9)	2.30 (1.97, 5.45) *	9 (60.0)	3.41 (1.20, 9.66) *
Mixed	22 (20.9)	0.88 (0.54, 1.44)	47 (32.6)	1.10 (0.76, 1.60)
Special Education/ LD Program				
No	225 (21.6)	1.00	381 (30.2)	1.00
Yes	56 (29.3)	1.50 (1.06, 2.12) *	34 (30.4)	1.01 (0.66, 1.53)
Mental Health Score †				
5-39	82 (33.2)	2.25 (1.51, 3.37) *	110 (43.6)	2.14 (1.49, 3.09) *
40-48	47 (20.2)	1.15 (0.74, 1.78)	97 (30.7)	1.23 (0.86, 1.75)
49-53	53 (21.2)	1.22 (0.80, 1.87)	79 (27.4)	1.05 (0.72, 1.52)
54-56	47 (22.1)	1.28 (0.83, 2.00)	56 (23.2)	0.84 (0.56, 1.25)
57-70	52 (18.1)	1.00	73 (26.5)	1.00
Physical Health Score †				
15-48	84 (30.2)	2.03 (1.35, 3.06) *	87 (37.5)	1.83 (1.26, 2.65) *
49-53	47 (22.1)	1.33 (0.84, 2.10)	95 (38.6)	1.92 (1.33, 2.77) *
54-56	60 (24.4)	1.51 (0.98, 2.33)	88 (27.8)	1.18 (0.82, 1.68)
57-58	45 (18.9)	1.09 (0.69, 1.73)	69 (25.6)	1.05 (0.72, 1.53)
59-73	45 (17.6)	1.00	76 (24.7)	1.00
Satisfaction with Life				
5-20 (Dissatisfied)	100 (31.4)	2.69 (1.88, 3.87) *	150 (41.5)	2.56 (1.89, 3.47) *
21-28 (Satisfied)	121 (24.3)	1.89 (1.34, 2.66) *	163 (30.1)	1.56 (1.17, 2.07) *
29-35 (More satisfied)	60 (14.5)	1.00	102 (21.7)	1.00
Self-Esteem ‡				
6-23	83 (28.8)	1.84 (1.25, 2.70) *	104 (35.0)	1.75 (1.24, 2.46) *
24-26	67 (26.1)	1.60 (1.07, 2.39) *	101 (33.9)	1.66 (1.18, 2.34) *
27-29	75 (20.0)	1.13 (0.77, 1.66)	127 (29.9)	1.38 (1.00, 1.91)
30	56 (18.1)	1.00	83 (23.6)	1.00
Chronic Stress Score §				
0-5	60 (14.6)	1.00	86 (22.1)	1.00
6-11	97 (22.3)	1.68 (1.18, 2.39) *	147 (29.5)	1.47 (1.08, 2.00) *
12-45	124 (32.4)	2.81 (1.98, 3.98) *	182 (37.6)	2.12 (1.57, 2.87) *
Stressful Life Events Score §				
None	75 (16.7)	1.00	105 (24.6)	1.00
1-4	93 (23.5)	1.53 (1.09, 2.15) *	145 (29.5)	1.28 (0.95, 1.72)
5+	113 (29.1)	2.04 (1.47, 2.84) *	165 (36.3)	1.74 (1.30, 2.33) *

*$p<0.05$

† Higher score indicates better health.

‡ Higher score indicates greater self-esteem.

§ Higher score indicates greater stress.

Table 10 shows that the prevalence of current smoking was highest in those diagnosed with cancer between ages ten and fourteen years (25.2%), patients who had received only chemotherapy (26.4%), who were diagnosed with carcinomas (30.5%) and who had not had a relapse of their initial cancer (23.5%). The prevalence of current smoking was lowest in participants diagnosed with cancer at zero to four years of age (18.5%), those who had received radiation therapy (13.9%) or radiation in combination with other types of therapy and in participants with central nervous system tumours (18.5%). However, all differences among the clinical groups were not significantly significant.

Table 10: Prevalence, crude odds ratios (ORs) and 95% confidence intervals (95%CIs) for current smoking by clinical factors in pediatric cancer survivors.

	Current Smoker n(%)	OR (95% CI)
Age at Diagnosis (years)		
0-4	42 (18.5)	1.00
5-9	73 (22.3)	1.27 (0.83, 1.94)
10-14	84 (25.2)	1.49 (0.98, 2.25)
15-19	82 (23.8)	1.38 (0.91, 2.09)
Type of Cancer Treatment		
Chemotherapy	33 (26.4)	1.00
Radiation	5 (13.9)	0.45 (0.16, 1.25)
Surgery	52 (25.2)	0.94 (0.57, 1.56)
Chemotherapy & Radiation	56 (22.8)	0.82 (0.50, 1.35)
Chemotherapy & Surgery	51 (24.6)	0.91 (0.55, 1.51)
Radiation & Surgery	31 (20.1)	0.70 (0.40, 1.23)
Chemotherapy & Radiation & Surgery	48 (20.3)	0.71 (0.43, 1.18)
No Treatment Reported	5 (25.0)	0.93 (0.31, 2.76)
Cancer Diagnosis		
Leukemia	71 (22.6)	1.00
Hodgkin's Lymphoma	47 (24.9)	1.13 (0.74, 1.73)
Non-Hodgkin's Lymphoma *	21 (21.2)	0.92 (0.53, 1.60)
Central Nervous System	40 (18.5)	0.78 (0.50, 1.20)
Renal	15 (24.2)	1.09 (0.58, 2.07)
Bone tumours	18 (24.3)	1.10 (0.61, 1.99)
Soft Tissue Sarcomas	18 (21.2)	0.92 (0.51, 1.65)
Germ cell/Gonadal	16 (23.5)	1.05 (0.57, 1.96)
Carcinomas	25 (30.5)	1.50 (0.88, 2.58)
Other †	10 (23.8)	1.07 (0.50, 2.28)
Relapse		
No	256 (23.5)	1.00
Yes	25 (17.9)	0.71 (0.45, 1.12)

* Including reticuloendothelial neoplasms and Langerhans cell histiocytosis.
† Other cancers include: retinoblastoma, hepatic and sympathetic nervous system.

Results of the multivariate logistic regression analysis to examine important predictors of current smoking in pediatric cancer survivors are presented in Table 11. Education, satisfaction with life, stressful life events and chronic stress were all found to be significant predictors of current smoking ($p<0.05$). Respondents with less than a high school education were significantly more likely to be current smokers than those with greater than a high school education (OR=2.22, 95%CI=1.55, 3.16). As satisfaction with life scores decreased respondents were more likely to be current smokers. Respondents who were dissatisfied with life were more likely to be current smokers than those who scored highest on the satisfaction with life scale (OR=1.82, 95%CI=1.23, 2.68). The odds of current smoking increased with increasing stressful life events and chronic stress scores. Respondents who scored five or higher on the stressful life events scale were more likely to be current smokers than those who reported having no stressful life events in the previous year (OR=1.69, 95%CI=1.19, 2.40). Similarly, as chronic stress increased so did the odds of being a current smoker (Table 11). In a separate analysis, no clinical factors were found to be significant predictors of current smoking in the pediatric cancer survivors ($p>0.05$).

Table 11: Summary of multivariate logistic regression analysis for variables predicting current smoking in pediatric cancer survivors

Predictor	β	SE	OR	95% CI	Wald Chi^2	p-value	Wald Chi^2	p-value
Intercept	-2.697	0.231			135.888	<0.0001		
Education								
Less than high school	0.796	0.181	2.22	(1.55, 3.16)	19.2545	<0.0001	20.135	<0.0001
High school	0.2801	0.174	1.32	(0.94, 1.86)	2.607	0.1064		
Greater than high school			1.00					
Satisfaction with Life								
5-19 (Dissatisfied)	0.597	0.198	1.82	(1.23, 2.68)	9.081	0.0026	9.651	0.0080
20-28 (Satisfied)	0.446	0.181	1.56	(1.09, 2.23)	6.063	0.0138		
29-35 (More satisfied)			1.00					
Stressful Life Events *								
None			1.00				9.161	0.0102
1-4	0.401	0.179	1.49	(1.05, 2.12)	4.998	0.0254		
5+	0.525	0.179	1.69	(1.19, 2.40)	8.603	0.0034		
Chronic Stress *								
0-5			1.00				17.402	0.0002
6-11	0.471	0.188	1.60	(1.11, 2.31)	6.311	0.012		
12-45	0.814	0.195	2.26	(1.54, 3.31)	17.393	<0.0001		

Model Likelihood ratio=78.7595, df=8, $p<0.0001$
OR=odds ratio; 95% CI=95% confidence interval; SE=standard error.
* Higher score indicates greater stress

Results of the multivariate logistic regression analysis to examine important predictors of current smoking in the control group are presented in Table 12. Ethnicity, education, satisfaction with life, chronic stress, physical health and mental health were all found to be significant predictors of current smoking ($p<0.05$). Controls of non-white ethnicity were significantly less likely to be current smokers than white controls (OR=0.54, 95%CI=0.30, 0.96). The odds of being a current smoker decreased with increasing levels of education. As life satisfaction decreased the odds of being a current smoker increased. The odds of current smoking for participants who were dissatisfied with life were significantly higher than those in the highest satisfaction with life group (OR=1.63, 95%CI=1.14, 2.32). The odds of current smoking increased with increasing chronic stress scores. Respondents who scored highest on the chronic stress inventory were significantly more likely to be current smokers than those who scored in the lowest group (OR=1.59, 95%CI=1.12, 2.26). Respondents with poorer physical health were more likely to be current smokers than those who scored in the highest physical health group. Respondents with the poorest mental health were significantly more likely to be current smokers than those who scored in the highest mental health group (OR=1.72, 95%CI=1.11, 2.67) (Table 12).

Table 12: Summary of multivariate logistic regression analysis for variables predicting current smoking in the control group.

Predictor	β	SE	OR	95% CI	Wald Chi^2	p-value	Wald Chi^2	p-value
Intercept	-2.085	0.240			75.325	<0.0001		
Ethnicity								
White			1.00				7.391	0.0604*
Non-white	-0.613	0.293	0.54	(0.30, 0.96)	4.376	0.0364		
Aboriginal	0.891	0.543	2.44	(0.84, 7.07)	2.693	0.1008		
Mixed	0.054	0.197	1.06	(0.72, 1.55)	0.076	0.7834		
Education								
Less than high school	0.669	0.157	1.95	(1.43, 2.66)	18.149	<0.0001	18.266	0.0001
High school	0.323	0.145	1.38	(1.04, 1.83)	4.970	0.0258		
Greater than high school			1.00					
Physical Health †								
15-48	0.578	0.205	1.78	(1.19, 2.66)	7.967	0.0048	18.070	0.0012
49-53	0.832	0.202	2.30	(1.55, 3.42)	16.939	<0.0001		
54-56	0.434	0.199	1.54	(1.04, 2.28)	4.739	0.0295		
57-58	0.387	0.209	1.47	(0.98, 2.21)	3.437	0.0638		
59-73			1.00					
Mental Health †								
5-39	0.544	0.224	1.72	(1.11, 2.67)	5.914	0.0150	13.790	0.0080
40-48	0.034	0.201	1.03	(0.70, 1.53)	0.028	0.8669		
49-53	-0.036	0.201	0.96	(0.65, 1.43)	0.033	0.8562		
54-56	-0.241	0.213	0.79	(0.52, 1.19)	1.280	0.2580		
57-70			1.00					
Chronic Stress ‡								
0-5			1.00				7.283	0.0262
6-11	0.192	0.168	1.21	(0.87, 1.68)	1.309	0.2526		
12-45	0.465	0.178	1.59	(1.12, 2.26)	6.805	0.0091		
Satisfaction with Life								
5-19 (Dissatisfied)	0.486	0.181	1.63	(1.14, 2.32)	7.227	0.0072	7.233	0.0269
20-28 (Satisfied)	0.232	0.155	1.26	(0.93, 1.71)	2.245	0.1340		
29-35 (More satisfied)			1.00					

Model Likelihood ratio=106.5647, df=17, p<0.0001

*Log likelihood ratio=7.963, df=3, p=0.0468

OR=odds ratio; 95% CI=95% confidence interval; SE=standard error.

† Higher score indicates better health.

‡ Higher score indicates greater stress.

5.3 Alcohol Use

Table 13 shows that in both cancer survivors and the control group the odds of being a current alcohol drinker were significantly higher in all other age groups compared to the youngest one (16-20 years). Female cancer survivors and controls were less likely to be alcohol drinkers than their male counterparts. The odds of being an alcohol drinker increased with increasing income and levels of education in both cancer survivors and controls. Cancer survivors who had a high school education or less or a personal income less than $20,000 were significantly less likely to be alcohol drinkers than those with greater than high school education or a personal income of $20,000 or more. Controls who had less than a high school education or a personal income less than $5,000, were significantly less likely to be alcohol drinkers than those with greater than a high school education or an income greater than $20,000. Cancer survivors who had been in a special education or learning disabled program were significantly less likely to be alcohol drinkers than those who had not (OR=0.54, 95%CI=0.39, 0.74). Cancer survivors and controls that were of a non-white ethnicity were significantly less likely to be alcohol drinkers than white cancer survivors (OR=0.38, 95%CI=0.21, 0.69) and controls (OR=0.28, 95%CI=0.18, 0.44). The odds of being an alcohol drinker increased with increasing chronic stress and stressful life events scores in both cancer survivors and controls where those who reported having stress in the previous year were significantly more likely to be alcohol drinkers than those who reported not having any stress.

The odds of being a current drinker did not differ significantly by mental health, physical health, satisfaction with life, and self-esteem scores for the pediatric cancer survivor group. In the control group respondents that were dissatisfied with life were significantly more likely to be alcohol drinkers than those in the highest satisfaction with life group (OR=1.55, 95%CI=1.12, 2.14). Poor physical and mental health scores were associated with being an alcohol drinker. In the control group being a current alcohol drinker was not associated with self-esteem or having been in a special education or learning disabled program (Table 13).

Table 13: Prevalence, crude odds ratios (ORs) and 95% confidence intervals (95%CIs) for alcohol drinking by demographic, psychosocial and health factors in pediatric cancer survivors and controls.

	Cancer Survivors		Controls	
	Drinker n(%)	OR (95% CI)	Drinker n(%)	OR (95% CI)
Age (years)				
16-20	267 (55.1)	1.00	344 (69.2)	1.00
21-25	265 (77.3)	2.77 (2.04, 3.78) *	307 (79.5)	1.73 (1.26, 2.36) *
26-30	211 (76.4)	2.65 (1.90, 3.69) *	242 (78.6)	1.63 (1.17, 2.27) *
31-37	101 (79.5)	3.17 (1.99, 5.06) *	147 (81.2)	1.92 (1.26, 2.92) *
Gender				
Male	432 (72.7)	1.00	500 (79.6)	1.00
Female	412 (64.7)	0.69 (0.54, 0.87) *	540 (72.6)	0.68 (0.53, 0.87) *
Personal Income				
$0 to $4,999	252 (58.7)	0.33 (0.24, 0.46) *	252 (66.0)	0.44 (0.32, 0.61) *
$5,000 to $19,999	315 (68.5)	0.51 (0.36, 0.71) *	451 (78.3)	0.82 (0.60, 1.13)
$20,000+	277 (81.0)	1.00	337 (81.4)	1.00
Educational Attainment				
Less than high school	187 (55.3)	0.32 (0.23, 0.43) *	224 (68.1)	0.52 (0.38, 0.71) *
High school	313 (67.9)	0.54 (0.40, 0.73) *	348 (75.6)	0.76 (0.57, 1.02)
Greater than high school	344 (79.6)	1.00	468 (80.3)	1.00
Ethnicity				
White	740 (69.9)	1.00	874 (77.8)	1.00
Non-white	21 (46.7)	0.38 (0.21, 0.69) *	45 (50.0)	0.28 (0.18, 0.44) *
Aboriginal	15 (68.2)	0.92 (0.37, 2.29)	11 (73.3)	0.78 (0.25, 2.48)
Mixed	68 (64.8)	0.79 (0.52, 1.21)	110 (76.4)	0.92 (0.61, 1.39)
Special Education/ LD Program				
No	736 (70.8)	1.00	957 (75.9)	1.00
Yes	108 (56.5)	0.54 (0.39, 0.74) *	83 (74.1)	0.91 (0.58, 1.41)
Mental Health Score †				
5-39	182 (73.7)	1.42 (0.98, 2.07)	213 (84.5)	2.36 (1.54, 3.62) *
40-48	156 (66.9)	1.02 (0.71, 1.48)	241 (76.3)	1.39 (0.96, 2.00)
49-53	172 (68.8)	1.12 (0.78, 1.61)	213 (74.0)	1.23 (0.85, 1.77)
54-56	143 (67.1)	1.04 (0.71, 1.51)	181 (75.1)	1.30 (0.88, 1.92)
57-70	191 (66.3)	1.00	192 (69.8)	1.00
Physical Health Score †				
15-48	192 (69.1)	1.05 (0.73, 1.52)	170 (73.3)	0.91 (0.62, 1.35)
49-53	157 (73.7)	1.32 (0.88, 1.98)	206 (83.7)	1.72 (1.12, 2.63) *
54-56	174 (70.7)	1.14 (0.78, 1.66)	237 (75.0)	1.00 (0.70, 1.44)
57-58	147 (61.8)	0.76 (0.53, 1.10)	196 (72.6)	0.88 (0.61, 1.28)
59-73	174 (68.0)	1.00	231 (75.0)	1.00
Satisfaction with life				
5-19 (Dissatisfied)	219 (68.6)	0.99 (0.72, 1.36)	287 (79.5)	1.55 (1.12, 2.14) *
20-28 (Satisfied)	340 (68.3)	0.97 (0.74, 1.29)	417 (77.1)	1.34 (1.01, 1.78) *
29-35 (More satisfied)	285 (68.8)	1.00	336 (71.5)	1.00

Continues

Table 13 continued

Self-Esteem ‡				
6-23	189 (65.6)	0.72 (0.51, 1.02)	221 (74.4)	0.84 (0.89, 1.21)
24-26	175 (68.1)	0.81 (0.56, 1.16)	234 (78.5)	1.06 (0.73, 1.54)
27-29	255 (67.8)	0.80 (0.57, 1.11)	312 (73.4)	0.80 (0.57, 1.11)
30	225 (72.6)	1.00	273 (77.6)	1.00
Chronic Stress Score §				
0-5	238 (57.8)	1.00	248 (63.8)	1.00
6-11	312 (71.6)	1.84 (1.38, 2.45) *	384 (76.9)	1.90 (1.42, 2.55) *
12-45	294 (76.8)	2.41 (1.78, 3.28) *	408 (84.3)	3.05 (2.21, 4.20) *
Stressful Life Events Score §				
None	272 (60.7)	1.00	291 (68.3)	1.00
1-4	266 (67.3)	1.33 (1.01, 1.77) *	378 (77.0)	1.55 (1.16, 2.08) *
5+	306 (78.9)	2.41 (1.77, 3.29) *	371 (81.5)	2.05 (1.50, 2.80) *

* $p<0.05$
† Higher score indicates better health.
‡ Higher score indicates greater self-esteem.
§ Higher score indicates greater stress.

Table 14 shows that the odds of being a current alcohol drinker in pediatric cancer survivors increased with increasing age at diagnosis and that survivors diagnosed with cancer at 0-4 years of age were less likely to be alcohol drinkers. Survivors who had received radiation therapy, radiation and surgery or radiation, chemotherapy and surgery were less likely to be alcohol drinkers compared to those who received chemotherapy only. Survivors of lymphomas, carcinomas and bone tumors were significantly more likely to be alcohol drinkers compared to those who had leukemia. The prevalence of alcohol drinkers was lower in those who had a relapse of their initial cancer but the odds ratio was not statistically significant ($p>0.05$) (Table 14).

Table 14: Prevalence, crude odds ratios (ORs) and 95% confidence intervals (95%CIs) for alcohol drinking by clinical factors in pediatric cancer survivors.

	Drinker n(%)	OR (95% CI)
Age at Diagnosis (years)		
0-4	116 (51.1)	1.00
5-9	208 (63.6)	1.67 (1.18, 2.36) *
10-14	251 (75.4)	2.93 (2.04, 4.20) *
15-19	269 (78.2)	3.43 (2.38, 4.94) *
Type of Cancer Treatment		
Chemotherapy	94 (75.2)	1.00
Radiation	17 (47.2)	0.29 (0.14, 0.64) *
Surgery	156 (75.7)	1.03 (0.61, 1.72)
Chemotherapy & Radiation	163 (66.3)	0.65 (0.40, 1.05)
Chemotherapy & Surgery	152 (73.4)	0.91 (0.55, 1.52)
Radiation & Surgery	97 (63.0)	0.56 (0.33, 0.94) *
Chemotherapy & Radiation & Surgery	152 (64.1)	0.59 (0.36, 0.96) *
No Treatment Reported	13 (65.0)	0.61 (0.22, 1.67)
Cancer Diagnosis		
Leukemia	196 (62.4)	1.00
Hodgkin's Lymphoma	146 (77.3)	2.04 (1.36, 3.08) *
Non-Hodgkin's Lymphoma †	77 (77.8)	2.11 (1.24, 3.57) *
Central Nervous System	127 (58.8)	0.86 (0.60, 1.22)
Renal	36 (58.1)	0.83 (0.48, 1.45)
Bone tumours	57 (77.0)	2.02 (1.12, 3.63) *
Soft Tissue Sarcomas	62 (72.9)	1.62 (0.95, 2.76)
Germ cell/Gonadal	47 (69.1)	1.35 (0.77, 2.37)
Carcinomas	67 (81.7)	2.69 (1.47, 4.92) *
Other ‡	29 (69.1)	1.34 (0.67, 2.68)
Relapse		
No	756 (69.3)	1.00
Yes	88 (62.9)	0.75 (0.52, 1.08)

* $p<0.05$

† Including reticuloendothelial neoplasms and Langerhans cell histiocytosis.

‡ Other cancers include: retinoblastoma, hepatic and sympathetic nervous system.

Table 15 presents the results of the multivariate logistic regression analysis to examine important predictors of current alcohol use in the pediatric cancer survivors. Age, gender, ethnicity, education, special education, chronic stress and stressful life events were all found to be significant predictors of current alcohol use ($p<0.05$). The odds of being an alcohol drinker were significantly higher in all age groups compared to those 16-20 years of age. Females were less likely to be alcohol drinkers than males (OR=0.56, 95%CI=0.43, 0.73) and survivors of a non-white ethnicity were less likely to be alcohol drinkers than white survivors (OR=0.29, 95%CI=0.15, 0.55). The odds of being an alcohol drinker increased with increasing levels of education and were significantly lower in the groups with

high school education or less compared to those with greater than high school education. Similarly, those who had been in a special education program were less likely to be alcohol drinkers than those who had not (OR=0.69, 95%CI=0.48, 0.97). The odds of being an alcohol drinker increased with increasing chronic stress and stressful life events scores. Respondents who scored highest on the stressful life events scale were significantly more likely to be alcohol drinkers than those who reported no stressful life events in the previous year (OR=2.26, 95%CI=1.61, 3.17) (Table15).

Table 15: Summary of multivariate logistic regression analysis for variables predicting alcohol use in pediatric cancer survivors

Predictor	β	SE	OR	95% CI	Wald Chi^2	p-value	Wald Chi^2	p-value
Intercept	0.646	0.229			7.933	0.0049		
Age								
16-20			1.00				13.301	0.0040
21-25	0.600	0.182	1.82	(1.27, 2.61)	10.818	0.0010		
26-30	0.490	0.197	1.63	(1.11, 2.40)	6.219	0.0126		
31-37	0.632	0.266	1.88	(1.12, 3.17)	5.639	0.0176		
Gender								
Male			1.00				18.039	<0.0001
Female	-0.573	0.135	0.56	(0.43, 0.73)	18.039	<0.0001		
Ethnicity								
White			1.00				14.505	0.0023
Non-white	-1.238	0.331	0.29	(0.15, 0.55)	13.991	0.0002		
Aboriginal	-0.053	0.487	0.95	(0.36, 2.46)	0.012	0.9132		
Mixed	-0.221	0.232	0.80	(0.51, 1.26)	0.906	0.3413		
Education								
Less than high school	-0.726	0.206	0.48	(0.32, 0.72)	12.406	0.0004	12.419	0.0020
High school	-0.378	0.177	0.68	(0.48, 0.97)	4.581	0.0323		
Greater than high school			1.00					
Special Education/ LD Program								
Yes	-0.376	0.179	0.69	(0.48, 0.97)	4.428	0.0353	4.428	0.0353
No			1.00					
Stressful Life Events *								
None			1.00				22.697	<0.0001
1-4	0.228	0.154	1.26	(0.93, 1.70)	2.199	0.1381		
5+	0.817	0.173	2.26	(1.61, 3.17)	22.350	<0.0001		
Chronic Stress *								
0-5			1.00				12.916	0.0016
6-11	0.439	0.155	1.55	(1.14, 2.10)	7.977	0.0047		
12-45	0.560	0.172	1.75	(1.25, 2.45)	10.639	0.0011		

Model Likelihood ratio=153.6665, p<0.0001 df=14
OR=odds ratio; 95% CI=95% confidence interval; SE=standard error.
* Higher score indicates greater stress

Table 16 shows the results of an additional multivariate analysis that examined predictors of current alcohol use in pediatric cancer survivors and included demographic, psychosocial, health and clinical factors in the model. Results were similar to those presented in Table 15 however, special education was no longer significant in the model whereas cancer diagnosis and cancer treatment were significant at the α=0.05 level. Cancer survivors who received radiation or radiation in combination with chemotherapy or surgery were significantly less likely to be current alcohol drinkers than those who had received chemotherapy alone. Survivors of a lymphoma were significantly more likely to be alcohol drinkers than survivors of leukemia (Table 16).

Table 16: Summary of multivariate logistic regression analysis for variables predicting alcohol use in pediatric cancer survivors including clinical variables.

Predictor	β	SE	OR	95% CI	Wald Chi^2	p-value	Wald Chi^2	p-value
Intercept	1.122	0.323			12.070	0.0005		
Age (years)								
16-20			1.00				10.706	0.0134
21-25	0.590	0.192	1.80	(1.24, 2.63)	9.415	0.0022		
26-30	0.492	0.219	1.63	(1.06, 2.51)	5.032	0.0249		
31-37	0.627	0.296	1.87	(1.05, 3.34)	4.500	0.0339		
Gender								
Male			1.00				19.238	<0.0001
Female	-0.616	0.140	0.54	(0.41, 0.71)	19.238	<0.0001		
Education								
Less than high school	-0.874	0.210	0.42	(0.28, 0.63)	17.220	<0.0001	17.404	0.002
High school	-0.420	0.181	0.66	(0.46, 0.94)	5.374	0.0204		
Greater than high school			1.00					
Ethnicity								
White			1.00				11.449	0.0095
Non-white	-1.133	0.343	0.32	(0.16, 0.63)	10.910	0.0010		
Aboriginal	0.165	0.505	1.18	(0.44, 3.17)	0.107	0.7436		
Mixed	-0.195	0.242	0.82	(0.51, 1.32)	0.650	0.4200		
Stressful Life Events *								
None			1.00				24.285	<0.0001
1-4	0.235	0.159	1.27	(0.93, 1.73)	2.204	0.1377		
5+	0.865	0.177	2.37	(1.68, 3.36)	23.897	<0.0001		
Chronic Stress *								
0-5			1.00				11.955	0.0025
6-11	0.487	0.159	1.63	(1.19, 2.22)	9.361	0.0022		
12-45	0.497	0.176	1.64	(1.16, 2.32)	7.960	0.0048		

Continues

Table 16 continued

Type of Cancer Treatment								
Chemotherapy			1.00				26.218	0.0005
Radiation	-1.996	0.469	0.14	(0.05, 0.34)	18.068	<0.0001		
Surgery	-0.587	0.371	0.56	(0.27, 1.15)	2.496	0.1141		
Chemotherapy & Radiation	-0.703	0.271	0.49	(0.29, 0.84)	6.738	0.0094		
Chemotherapy & Surgery	-0.609	0.329	0.54	(0.28, 1.04)	3.425	0.0642		
Radiation & Surgery	-1.184	0.373	0.31	(0.15, 0.64)	10.085	0.0015		
Chemo, Radiation & Surgery	-0.975	0.300	0.38	(0.21, 0.68)	10.562	0.0012		
No Treatment Reported	-1.214	0.602	0.30	(0.09, 0.97)	4.070	0.0436		
Cancer Diagnosis								
Leukemia			1.00				18.048	0.0346
Hodgkin's Lymphoma	0.618	0.276	1.86	(1.08, 3.19)	5.028	0.025		
Non-Hodgkin's Lymphoma †	0.677	0.303	1.97	(1.09, 3.56)	4.995	0.025		
Central Nervous System	0.043	0.300	1.04	(0.58, 1.88)	0.020	0.887		
Renal	0.335	0.350	1.40	(0.70, 2.78)	0.912	0.339		
Bone tumours	0.471	0.365	1.60	(0.78, 3.27)	1.666	0.197		
Soft Tissue Sarcomas	0.447	0.319	1.56	(0.84, 2.92)	1.963	0.161		
Germ cell/Gonadal	-0.073	0.368	0.93	(0.45, 1.91)	0.040	0.842		
Carcinomas	0.723	0.423	2.06	(0.90, 4.72)	2.926	0.087		
Other ‡	0.904	0.419	2.47	(1.09, 5.61)	4.653	0.031		

Model Likelihood ratio=197.9322, df=29 p<0.0001

OR=odds ratio; 95% CI=95% confidence interval; SE=standard error; Chemo=chemotherapy.

* Higher score indicates greater stress

† Including reticuloendothelial neoplasms and Langerhans cell histiocytosis.

‡ Other cancers include: retinoblastoma, hepatic and sympathetic nervous system.

Table 17 presents the results of the multivariate logistic regression analysis to examine important predictors of current alcohol use in the control group. Gender, personal income, ethnicity, education, physical health, chronic stress and stressful life events were all found to be significant predictors of current alcohol use ($p<0.05$). Females were significantly less likely to be alcohol drinkers than males (OR=0.59, 95%CI=0.44, 0.78) and respondents of a non-white ethnicity were less likely to be alcohol drinkers than white respondents (OR=0.24, 95%CI=0.15, 0.39). The odds of being an alcohol drinker increased with increasing levels of education and were significantly lower in the group with less than a high school education compared to those with greater than a high school education (OR=0.59, 95%CI=0.41, 0.85). Respondents scoring in the lowest mental health group (5-39) were significantly more likely to be alcohol drinkers compared to those with the highest mental health scores (50-70) (OR=2.14, 95%CI=1.29, 3.55). Respondents scoring in the second lowest physical health group (49-53) were significantly more likely to be alcohol drinkers than those with the highest physical health scores (59-73) (OR=1.82, 95%CI=1.15, 2.89). The odds of being an alcohol drinker increased with increasing chronic stress and

stressful life events scores. Respondents who scored highest on the stressful life events scale were significantly more likely to be alcohol drinkers than those who reported no stressful life events in the previous year (OR=1.64, 95%CI=1.17, 2.31) (Table17).

Table 17: Summary of multivariate logistic regression analysis for variables predicting alcohol use in the control group.

Predictor	β	SE	OR	95% CI	Wald Chi^2	p-value	Wald Chi^2	p-value
Intercept	0.979	0.259			14.308	0.0002		
Gender								
Male			1.00				13.823	0.0002
Female	-0.533	0.143	0.59	(0.44, 0.78)	13.823	0.0002		
Personal Income								
$0 to $4,999	-0.530	0.199	0.59	(0.40, 0.87)	7.090	0.0078	10.069	0.0065
$5,000 to $19,999	-0.068	0.180	0.93	(0.66, 1.33)	0.142	0.7066		
$20,000+			1.00					
Education								
Less than high school	-0.524	0.185	0.59	(0.41, 0.85)	8.004	0.0047	8.187	0.0167
High school	-0.191	0.170	0.83	(0.59, 1.15)	1.259	0.2618		
Greater than high school			1.00					
Ethnicity								
White			1.00				34.316	<0.0001
Non-white	-1.412	0.241	0.24	(0.15, 0.39)	34.195	<0.0001		
Aboriginal	-0.329	0.630	0.72	(0.21, 2.47)	0.274	0.6008		
Mixed	-0.159	0.220	0.85	(0.55, 1.31)	0.521	0.4704		
Mental Health Score *								
5-39	0.761	0.258	2.14	(1.29, 3.55)	8.703	0.0032	9.450	0.0508
40-48	0.257	0.210	1.29	(0.86, 1.95)	1.480	0.2210		
49-53	0.132	0.205	1.14	(0.76, 1.71)	0.412	0.5207		
54-56	0.138	0.214	1.15	(0.75, 1.75)	0.414	0.5197		
57-70			1.00					
Physical Health Score *								
15-48	-0.153	0.220	0.86	(0.56, 1.32)	0.483	0.4870	10.827	0.0286
49-53	0.601	0.235	1.82	(1.15, 2.89)	6.524	0.0106		
54-56	0.123	0.205	1.13	(0.76, 1.69)	0.359	0.5492		
57-58	0.049	0.212	1.05	(0.69, 1.59)	0.054	0.8167		
59-73			1.00					
Stressful Life Events †								
None			1.00				8.699	0.0129
1-4	0.308	0.159	1.36	(0.99, 1.86)	3.719	0.0538		
5+	0.498	0.173	1.64	(1.17, 2.31)	8.257	0.0041		
Chronic Stress †								
1-5			1.00				18.661	<0.0001
6-11	0.405	0.163	1.50	(1.09, 2.06)	6.176	0.0129		
12-45	0.816	0.189	2.26	(1.56, 3.28)	18.545	<0.0001		

Model Likelihood ratio=149.4090, p<0.0001 df=20
OR=odds ratio; 95% CI=95% confidence interval; SE=standard error.
* Higher score indicates better health.
† Higher score indicates greater stress.

5.4 Binge Drinking

Table 18 shows that cancer survivors who were 31-37 years of age were significantly less likely to be binge drinkers than those 16-20 years of age (OR=0.47, 95%CI=0.27, 0.79). In the control group respondents 21 years of age and older were less likely to be binge drinkers than those 16-20 years of age. Females were less likely to be binge drinkers than males in both the cancer survivor and control groups. In the control group the odds of being a binge drinker were significantly higher in those with a personal income less than $19,999 compared to those with a personal income of greater than $20,000. Personal income was not associated with binge drinking in the cancer survivors. In both the cancer survivor and control groups respondents with a high school education or less were significantly more likely to be binge drinkers than those with greater than a high school education. Controls of a non-white ethnicity were less likely to be binge drinkers compared to white controls (OR=0.42, 95%CI=0.24, 0.74). Ethnicity was not associated with binge drinking in the cancer survivors. Having been in a special education or learning disabled program was associated with binge drinking in the control group only (OR=1.62, 95%CI=1.09, 2.41). In the control group respondents who scored in the lowest mental health group were significantly more likely to be binge drinkers than those who scored in the highest mental health group (OR=1.74, 95%CI=1.20, 2.52). As satisfaction with life decreased and chronic stress and stressful life events increased respondents were more likely to be binge drinkers in both the cancer survivor and control groups (Table 18).

Table 18: Prevalence, crude odds ratios (ORs) and 95% confidence intervals (95%CIs) for binge drinking by demographic, psychosocial and health factors in pediatric cancer survivors and controls.

	Cancer Survivors		Controls	
	Binge Drinking n(%)	OR (95% CI)	Binge Drinking n(%)	OR (95% CI)
Age				
16-20	133 (27.4)	1.00	203 (40.8)	1.00
21-25	87 (25.4)	0.90 (0.66, 1.12)	121 (31.3)	0.66 (0.50, 0.87) *
26-30	68 (24.6)	0.86 (0.62, 1.21)	60 (19.5)	0.35 (0.25, 0.49) *
31-37	19 (15.0)	0.47 (0.27, 0.79) *	41 (22.6)	0.42 (0.29, 0.63) *
Gender				
Male	197 (33.2)	1.00	256 (40.8)	1.00
Female	110 (17.3)	0.42 (0.32, 0.55) *	169 (22.7)	0.43 (0.34, 0.54) *
Personal Income				
$0 to $4,999	107 (24.9)	0.97 (0.70, 1.35)	120 (31.4)	1.48 (1.08, 2.02) *
$5,000 to $19,999	113 (24.6)	0.95 (0.69, 1.32)	207 (35.9)	1.81 (1.36, 2.40) *
$20,000+	87 (25.4)	1.00	98 (23.7)	1.00

Continues

Table 18 continued

Educational Attainment				
Less than high school	96 (28.4)	1.74 (1.24, 2.45) *	124 (37.7)	2.09 (1.55, 2.81) *
High school	131 (28.4)	1.75 (1.27, 2.40) *	170 (37.0)	2.02 (1.54, 2.65) *
Greater than high school	80 (18.5)	1.00	131 (22.5)	1.00
Ethnicity				
White	268 (25.3)	1.00	361 (32.1)	1.00
Non-white	9 (20.0)	0.74 (0.35, 1.55)	15 (16.7)	0.42 (0.24, 0.74) *
Aboriginal	7 (31.8)	1.38 (0.56, 3.41)	5 (33.3)	1.05 (0.36, 3.11)
Mixed	23 (21.9)	0.83 (0.51, 1.34)	44 (30.6)	0.93 (0.64, 1.35)
Special Education/ LD Program				
No	252 (24.2)	1.00	379 (30.1)	1.00
Yes	55 (28.8)	1.26 (0.90, 1.78)	46 (41.1)	1.62 (1.09, 2.41) *
Mental Health Score †				
5-39	70 (28.3)	1.33 (0.90, 1.96)	95 (37.7)	1.74 (1.20, 2.52) *
40-48	56 (24.0)	1.06 (0.71, 1.60)	94 (29.7)	1.22 (0.85, 1.75)
49-53	57 (22.8)	0.99 (0.66, 1.49)	98 (34.0)	1.48 (1.03, 2.13) *
54-56	58 (27.2)	1.26 (0.84, 1.89)	67 (27.8)	1.11 (0.75, 1.63)
57-70	66 (22.9)	1.00	71 (25.8)	1.00
Physical Health Score †				
15-48	72 (25.9)	1.09 (0.74, 1.62)	77 (33.2)	1.15 (0.80, 1.66)
49-53	53 (24.9)	1.04 (0.68, 1.58)	82 (33.3)	1.16 (0.81, 1.66)
54-56	61 (24.8)	1.03 (0.69, 1.55)	94 (29.7)	0.98 (0.69, 1.38)
57-58	59 (24.8)	1.03 (0.68, 1.55)	79 (29.3)	0.96 (0.67, 1.37)
59-73	62 (24.2)	1.00	93 (30.2)	1.00
Satisfaction with Life				
5-20 (Dissatisfied)	95 (29.8)	1.98 (1.40, 2.81) *	149 (41.3)	2.36 (1.74, 3.18) *
21-28 (Satisfied)	139 (27.9)	1.81 (1.31, 2.49) *	168 (31.1)	1.51 (1.14, 2.00) *
29-35 (More satisfied)	73 (17.6)	1.00	108 (23.0)	1.00
Self-Esteem ‡				
6-23	72 (25.0)	1.04 (0.72, 1.52)	101 (34.0)	1.13 (0.82, 1.58)
24-26	72 (28.0)	1.22 (0.84, 1.78)	89 (29.9)	0.94 (0.67, 1.31)
27-29	88 (23.4)	0.96 (0.67, 1.36)	125 (29.4)	0.92 (0.67, 1.25)
30	75 (24.2)	1.00	110 (31.2)	1.00
Chronic Stress §				
0-5	83 (20.2)	1.00	98 (25.2)	1.00
6-11	108 (24.8)	1.30 (0.94, 1.80)	154 (30.9)	1.32 (0.98, 1.78)
12-45	116 (30.3)	1.72 (1.24, 2.38) *	173 (35.7)	1.65 (1.23, 2.22) *
Stressful Life Events Score §				
None	78 (17.4)	1.00	107 (25.1)	1.00
1-4	102 (25.8)	1.65 (1.18, 2.30) *	159 (32.4)	1.43 (1.07, 1.91) *
5+	127 (32.7)	2.31 (1.67, 3.19) *	159 (35.0)	1.60 (1.20, 2.14) *

* $p<0.05$

† Higher score indicates better health.

‡ Higher score indicates greater self-esteem.

§ Higher score indicates greater stress

Table 19 shows that survivors diagnosed with cancer at 15-19 years of age were less likely to be binge drinkers than those diagnosed with cancer at 0-4 years of age. The prevalence of binge drinking was highest in those who had only surgery for treatment of their cancer (30.1%) but the odds of binge drinking did not differ significantly between the treatment groups. Survivors of Hodgkin's lymphoma were significantly less likely to be binge drinkers than survivors of leukemia (OR=0.61, 95%CI=0.39, 0.96). Survivors who had a relapse of their initial cancer had a slightly lower prevalence of binge drinking compared to those who did not have a relapse (21.4 vs. 25.4) but the odds of binge drinking were not significantly different between the two groups (OR=0.80, 95%CI=0.52, 1.23) (Table 19).

Table 19: Prevalence, crude odds ratios (ORs) and 95% confidence intervals (95%CIs) for binge drinking by clinical factors in pediatric cancer survivors

	Binge drinking n(%)	OR (95% CI)
Age at Diagnosis (years)		
0-4	62 (27.3)	1.00
5-9	87 (26.6)	0.96 (0.66, 1.41)
10-14	91 (27.3)	1.00 (0.68, 1.46)
15-19	67 (19.5)	0.64 (0.43, 0.96) *
Type of Cancer Treatment		
Chemotherapy	32 (25.6)	1.00
Radiation	4 (11.11)	0.36 (0.12, 1.11)
Surgery	62 (30.1)	1.25 (0.76, 2.06)
Chemotherapy & Radiation	58 (23.6)	0.90 (0.54, 1.47)
Chemotherapy & Surgery	57 (27.5)	1.10 (0.67, 1.83)
Radiation & Surgery	30 (19.5)	0.70 (0.40, 1.23)
Chemotherapy, Radiation & Surgery	62 (26.2)	1.03 (0.63, 1.69)
No Treatment Reported	2 (10.0)	0.32 (0.07, 1.47)
Cancer Diagnosis		
Leukemia	83 (26.4)	1.00
Hodgkin's Lymphoma	34 (18.0)	0.61 (0.39, 0.96) *
Non-Hodgkin's Lymphoma †	21 (21.2)	0.75 (0.43, 1.29)
Central Nervous System	50 (23.1)	0.84 (0.56, 1.25)
Renal	19 (30.6)	1.23 (0.68, 2.23)
Bone tumours	20 (27.0)	1.03 (0.58, 1.82)
Soft Tissue Sarcomas	29 (34.1)	1.44 (0.86, 2.41)
Germ cell/Gonadal	16 (23.5)	0.86 (0.46, 1.58)
Carcinomas	22 (26.8)	1.02 (0.59, 1.77)
Other ‡	13 (30.9)	1.25 (0.62, 2.51)
Relapse		
No	277 (25.4)	1.00
Yes	30 (21.4)	0.80 (0.52, 1.23)

* $p<0.05$

† Including reticuloendothelial neoplasms and Langerhans cell histiocytosis.

‡ Other cancers include: retinoblastoma, hepatic and sympathetic nervous system.

Table 20 shows the results of the multivariate logistic regression analysis to examine important predictors of binge drinking in the pediatric cancer survivors. Gender, education, satisfaction with life and stressful life events were found to be significant predictors of binge drinking ($p<0.05$). Females were significantly less likely to be binge drinkers than males (OR=0.39, 95%CI=0.30, 0.52). Having a high school education or less was associated with being a binge drinker. Survivors who scored in the lowest (OR=1.54, 95%CI=1.07, 2.21) and second lowest categories (OR=1.63, 95%CI=1.17, 2.27) on the satisfaction with life scale were significantly more likely to be binge drinkers than survivors who scored the highest. As reported stressful life events scores increased survivors were more likely to be binge drinkers than those who reported no stressful life events in the past year (Table 20).

Table 20: Summary of multivariate logistic regression analysis for variables predicting binge drinking in pediatric cancer survivors.

Predictor	β	SE	OR	95% CI	Wald Chi^2	p-value	Wald Chi^2	p-value
Intercept	-1.869	0.205			83.188	<0.0001		
Education								
Less than high school	0.529	0.181	1.70	(1.19, 2.42)	8.586	0.0034	11.784	0.0028
High school	0.518	0.167	1.68	(1.21, 2.33)	9.598	0.0018		
Greater than high school			1.00					
Gender								
Male			1.00				43.236	<0.0001
Female	-0.933	0.142	0.39	(0.30, 0.52)	43.236	<0.0001		
Satisfaction with Life								
5-19 (Dissatisfied)	0.429	0.186	1.54	(1.07, 2.21)	5.339	0.0209	9.091	0.0106
20-28 (Satisfied)	0.491	0.169	1.63	(1.17, 2.27)	8.455	0.0036		
29-35 (More satisfied)			1.00					
Stressful Life Events Score*								
0			1.00				31.249	<0.0001
1-4	0.547	0.176	1.73	(1.22, 2.44)	9.689	0.0019		
5+	0.972	0.174	2.64	(1.94, 3.72)	31.248	<0.0001		

Model Likelihood ratio=100.7047, $p<0.0001$ df=7
OR=odds ratio; 95% CI=95% confidence interval; SE=standard error.
* Higher score indicates greater stress.

Table 21 shows the results of an additional multivariate analysis that examined predictors of binge drinking in pediatric cancer survivors including demographic, psychosocial, health and clinical factors in the model. Results were similar to those presented in Table 20; however, cancer diagnosis was found to be an additional predictor of binge drinking. Survivors of Hodgkin's lymphoma were less likely to be binge drinkers than survivors of leukemia and the odds ratio was nearing statistical significance (OR=0.65

95%CI=0.40, 1.05). Survivors of soft tissue sarcomas were more likely to be binge drinkers than survivors of leukemia and the odds ratio was nearing statistical significance (OR=1.64, 95%CI=0.95, 2.82) (Table 21).

Table 21: Summary of multivariate logistic regression analysis for variables predicting binge drinking in pediatric cancer survivors including clinical variables.

Predictor	β	SE	OR	95% CI	Wald Chi^2	p-value	Wald Chi^2	p-value
Intercept	-1.840	0.246			56.087	<0.0001		
Education								
Less than high school	0.511	0.191	1.67	(1.15, 2.42)	7.188	0.0073	9.433	0.0089
High school	0.476	0.173	1.61	(1.15, 2.26)	7.6184	0.0058		
Greater than high school			1.00					
Gender								
Male			1.00				49.693	<0.0001
Female	-1.036	0.147	0.35	(0.27, 0.47)	49.693	<0.0001		
Satisfaction with Life								
5-19 (Dissatisfied)	0.499	0.190	1.65	(1.13, 2.39)	6.898	0.0086	10.275	0.0059
20-28 (Satisfied)	0.511	0.171	1.67	(1.19, 2.33)	8.969	0.0027		
29-30 (More satisfied)			1.00					
Stressful Life Events *								
None			1.00				31.740	<0.0001
1-4	0.575	0.178	1.78	(1.25, 2.52)	10.431	0.0012		
5+	0.991	0.176	2.69	(1.91, 3.80)	31.722	<0.0001		
Cancer Diagnosis								
Leukemia			1.00				18.765	0.0273
Hodgkin's Lymphoma	-0.429	0.243	0.65	(0.40, 1.05)	3.107	0.078		
Non-Hodgkin's lymphoma †	-0.374	0.291	0.69	(0.39, 1.22)	1.654	0.198		
Central Nervous System	-0.203	0.219	0.82	(0.53, 1.25)	0.861	0.354		
Renal	0.361	0.320	1.43	(0.77, 2.69)	1.273	0.259		
Bone tumours	0.375	0.313	1.45	(0.79, 2.69)	1.435	0.231		
Soft Tissue Sarcomas	0.494	0.278	1.64	(0.95, 2.82)	3.155	0.076		
Germ cell/Gonadal	-0.111	0.331	0.89	(0.47, 1.71)	0.113	0.736		
Carcinomas	0.367	0.303	1.44	(0.80, 2.61)	1.468	0.226		
Other ‡	0.475	0.376	1.61	(0.77, 3.36)	1.597	0.206		

Model Likelihood ratio=119.6869, p<0.0001 df=16
OR=odds ratio; 95% CI=95% confidence interval; SE=standard error.
* Higher score indicates greater stress.
† Including reticuloendothelial neoplasms and Langerhans cell histiocytosis.
‡ Other cancers include: retinoblastoma, hepatic and sympathetic nervous system.

Results of the multivariate logistic regression analysis to examine important predictors of binge drinking in the control group are presented in Table 22. Age, gender, personal income, ethnicity, satisfaction with life and stressful life events were found to be significant predictors of binge drinking (p<0.05). Controls over the age of 21 years were less likely to be binge drinkers than those aged 16-20 years. Females were significantly less likely to be binge drinkers than males (OR=0.40, 95%CI=0.31, 0.52). Respondents who had

a personal income between $5,000 and $19,999 were more likely to be binge drinkers than those who had a personal income greater than $20,000, almost reaching statistical significance (OR=1.31, 95%CI=0.94, 1.83). Respondents of a non-white ethnicity were significantly less likely to be binge drinkers than white respondents (OR=0.39, 95%CI= 0.21, 0.70). As life satisfaction scores decreased controls were more likely to be binge drinkers. The odds of being a binge drinker were over two times higher in controls who were dissatisfied with life compared to those who scored highest on the satisfaction with life scale (OR=2.40, 95%CI=1.74, 3.31). The odds of binge drinking increased with increasing stressful life events scores. Controls who reported having stressful life events in the previous year were significantly more likely to be binge drinkers than those who reported no stressful life events (Table 22).

Table 22: Summary of multivariate logistic regression analysis for variables predicting binge drinking in the control group.

Predictor	B	SE	OR	95% CI	Wald Chi^2	p-value	Wald Chi^2	p-value
Intercept	-0.549	0.227			5.844	0.0156		
Age								
16-20			1.00				34.453	<0.0001
21-25	-0.560	0.166	0.57	(0.41, 0.79)	11.433	0.0007		
26-30	-1.130	0.203	0.32	(0.22, 0.48)	30.934	<0.0001		
31-37	-0.947	0.237	0.39	(0.24, 0.62)	16.032	<0.0001		
Gender								
Male			1.00				50.236	<0.0001
Female	-0.911	0.129	0.40	(0.31, 0.52)	50.236	<0.0001		
Personal Income								
$0 to $4,999	-0.119	0.209	0.89	(0.59, 1.34)	0.322	0.5704	7.058	0.0293
$5,000 to $19,999	0.269	0.172	1.31	(0.94, 1.83)	2.458	0.1169		
$20,000+			1.00					
Ethnicity								
White			1.00				9.831	0.0201
Non-white	-0.948	0.303	0.39	(0.21, 0.70)	9.816	0.0017		
Aboriginal	-0.114	0.583	0.89	(0.29, 2.80)	0.038	0.8449		
Mixed	-0.058	0.204	0.94	(0.63, 1.41)	0.081	0.7761		
Satisfaction with life								
5-19 (Dissatisfied)	0.876	0.165	2.40	(1.74, 3.31)	28.309	<0.0001	28.563	<0.0001
20-28 (Satisfied)	0.373	0.151	1.45	(1.08, 1.96)	6.072	0.0137		
29-35 (More satisfied)			1.00					
Stressful life events *								
None			1.00				8.234	0.0163
1-4	0.363	0.156	1.44	(1.06, 1.95)	5.385	0.0203		
5+	0.435	0.161	1.55	(1.13, 2.12)	7.321	0.0068		

Model Likelihood ratio=162.4433, p<0.0001 df=13
OR=odds ratio; 95% CI=95% confidence interval; SE=standard error.
* Higher score indicates greater stress.

5.5 Concurrent Smoking and Alcohol use

The prevalence of concurrent use of alcohol and tobacco was similar across age, gender and personal income groups for both cancer survivors and controls. In both the cancer survivor and control groups respondents who had a high school education or less were significantly more likely to be concurrent users of alcohol and tobacco than those with greater than a high school education. In the control group respondents of a non-white ethnicity were significantly less likely to be concurrent users of alcohol and tobacco than white respondents (OR=52, 95%CI=0.29, 0.92). Cancer survivors who had been in a special education or learning disabled program were significantly more likely to be concurrent users of alcohol and tobacco compared to those who had not (OR=1.48, 95%CI=1.04, 2.12) but in the controls the odds were similar for both groups (OR=1.02, 95%CI= 0.66, 1.57). For both the cancer survivor and control groups respondents scoring in the lowest mental and physical health categories were significantly more likely to be concurrent users of alcohol and tobacco than those scoring highest on the scales. As satisfaction with life and self-esteem scores decreased respondents were more likely to be current smokers than those with high life satisfaction and self-esteem in both the cancer survivor and control groups. As chronic stress and stressful life events scores increased respondents were more likely to be current smokers in both the cancer survivor and control groups (Table 23).

Table 23: Prevalence, crude odds ratios (ORs) and 95% confidence intervals (95%CIs) for concurrent use of alcohol and tobacco by demographic, psychosocial and health factors in pediatric cancer survivors and controls.

	Cancer Survivors		Controls	
	Concurrent use n(%)	OR (95% CI)	Concurrent use n(%)	OR (95% CI)
Age				
16-20	101 (20.8)	1.00	127 (25.5)	1.00
21-25	64 (18.7)	0.87 (0.61, 1.24)	111 (28.8)	1.18 (0.87, 1.58)
26-30	56 (20.3)	0.97 (0.67, 1.40)	83 (27.0)	1.07 (0.78, 1.48)
31-37	30 (23.6)	1.18 (0.74, 1.87)	54 (29.8)	1.24 (0.85, 1.81)
Gender				
Male	125 (21.0)	1.00	169 (26.9)	1.00
Female	126 (19.8)	0.92 (0.70, 1.22)	206 (27.7)	1.04 (0.82, 1.32)
Personal Income				
$0 to $4,999	75 (17.5)	0.84 (0.58, 1.20)	102 (26.7)	1.09 (0.79, 1.49)
$5,000 to $19,999	107 (23.3)	1.20 (0.85, 1.69)	169 (29.3)	1.24 (0.93, 1.65)
$20,000+	69 (20.2)	1.00	104 (25.1)	1.00

Continues

Table 23 continued

Educational Attainment				
Less than high school	92 (27.2)	2.15 (1.50, 3.07) *	115 (34.9)	1.87 (1.39, 2.52) *
High school	95 (20.6)	1.49 (1.05, 2.11) *	130 (28.3)	1.37 (1.04, 1.82) *
Greater than high school	64 (14.8)	1.00	130 (22.3)	1.00
Ethnicity				
White	219 (20.7)	1.00	311 (27.7)	1.00
Non-white	4 (8.9)	0.37 (0.13, 1.06)	15 (16.7)	0.52 (0.29, 0.92) *
Aboriginal	7 (31.8)	1.79 (0.72, 4.44)	7 (46.7)	2.28 (0.82, 6.35)
Mixed	21 (20.0)	0.96 (0.58, 1.58)	42 (29.2)	1.07 (0.73, 1.58)
Special Education/ LD Program				
No	201 (19.3)	1.00	344 (27.3)	1.00
Yes	50 (26.2)	1.48 (1.04, 2.12) *	31 (27.7)	1.02 (0.66, 1.57)
Mental Health Score †				
5-39	71 (28.7)	2.12 (1.40, 3.23) *	98 (38.9)	2.10 (1.44, 3.06) *
40-48	42 (18.0)	1.16 (0.73, 1.83)	90 (28.5)	1.31 (0.91, 1.90)
49-53	49 (19.6)	1.28 (0.82, 2.00)	71 (24.6)	1.08 (0.73, 1.58)
54-56	43 (20.2)	1.33 (0.84, 2.11)	52 (21.6)	0.91 (0.60, 1.37)
57-70	46 (16.0)	1.00	64 (23.3)	1.00
Physical Health Score †				
15-48	75 (27.0)	2.12 (1.37, 3.27) *	79 (34.0)	1.89 (1.27, 2.72) *
49-53	43 (20.2)	1.45 (0.90, 2.35)	89 (36.2)	2.04 (1.40, 2.97) *
54-56	54 (22.0)	1.61 (1.02, 2.55)	77 (24.4)	1.16 (0.80, 1.68)
57-58	41 (17.2)	1.19 (0.74, 1.93)	63 (23.3)	1.09 (0.74, 1.62)
59-73	38 (14.8)	1.00	67 (21.7)	1.00
Satisfaction with Life				
5-20 (Dissatisfied)	88 (27.6)	2.54 (1.74, 3.70) *	138 (38.2)	2.65 (1.94, 3.62) *
21-28 (Satisfied)	109 (21.9)	1.87 (1.31, 2.67) *	148 (27.4)	1.61 (1.20, 2.17) *
29-35 (More satisfied)	54 (13.0)	1.00	89 (18.9)	1.00
Self-Esteem ‡				
6-23	73 (25.3)	1.85 (1.23, 2.78) *	92 (31.0)	1.71 (1.20, 2.45) *
24-26	60 (23.3)	1.66 (1.09, 2.54) *	90 (30.2)	1.65 (1.16, 2.36) *
27-29	70 (18.6)	1.25 (0.83, 1.87)	120 (28.2)	1.50 (1.08, 2.10) *
30	48 (15.5)	1.00	73 (20.7)	1.00
Chronic Stress Score §				
0-5	52 (12.6)	1.00	71 (18.2)	1.00
6-11	89 (20.4)	1.78 (1.22, 2.58) *	137 (27.4)	1.69 (1.23, 2.34) *
12-45	110 (28.7)	2.79 (1.94, 4.02) *	167 (34.5)	2.36 (1.72, 3.24) *
Stressful Life Events Score §				
None	66 (14.7)	1.00	90 (21.1)	1.00
1-4	84 (21.3)	1.56 (1.10, 2.23) *	131 (26.7)	1.36 (1.00, 1.85)
5+	101 (26.0)	2.04 (1.44, 2.88) *	154 (33.8)	1.91 (1.41, 2.59) *

* $p<0.05$

† Higher score indicates better health.

‡ Higher score indicates greater self-esteem.

§ Higher score indicates greater stress

The odds of concurrent alcohol and tobacco use were not significantly different for any of the clinical groups (P>0.05). The prevalence of concurrent alcohol and tobacco use was highest in survivors diagnosed with cancer between 10 and 14 years of age and those who had no treatment reported or were treated with chemotherapy only. Survivors of carcinomas had the highest prevalence of concurrent use of alcohol and tobacco. Survivors who had a relapse of their initial cancer had a lower prevalence of concurrent alcohol and tobacco use than those who did not have a relapse (Table 24).

Table 24: Prevalence, crude odds ratios (ORs) and 95% confidence intervals (95%CIs) for concurrent use of alcohol and tobacco by clinical factors in pediatric cancer survivors.

	Concurrent use n(%)	OR (95% CI)
Age at Diagnosis (years)		
0-4	39 (17.2)	1.00
5-9	68 (20.8)	1.27 (0.82, 1.96)
10-14	74 (22.2)	1.38 (0.89, 2.12)
15-19	70 (20.3)	1.23 (0.80, 1.90)
Type of Cancer Treatment		
Chemotherapy	30 (24.0)	1.00
Radiation	4 (11.1)	0.40 (0.13, 1.21)
Surgery	48 (23.3)	0.96 (0.57, 1.62)
Chemotherapy & Radiation	51 (20.7)	0.83 (0.50, 1.38)
Chemotherapy & Surgery	44 (21.3)	0.85 (0.50, 1.45)
Radiation & Surgery	25 (16.2)	0.61 (0.34, 1.11)
Chemotherapy & Radiation & Surgery	44 (18.6)	0.72 (0.43, 1.22)
No Treatment Reported	5 (25.0)	1.06 (0.35, 3.15)
Cancer Diagnosis		
Leukemia	64 (20.4)	1.00
Hodgkin's Lymphoma	43 (22.8)	1.15 (0.74, 1.78)
Lymphoma and Reticuloendothelial *	20 (20.2)	0.99 (0.56, 1.73)
Central Nervous System	34 (15.7)	0.73 (0.46, 1.15)
Renal	14 (22.6)	1.14 (0.59, 2.19)
Bone tumours	14 (18.9)	0.91 (0.48, 1.73)
Soft Tissue Sarcomas	17 (20.0)	0.98 (0.54, 1.78)
Germ cell/Gonadal	13 (19.1)	0.92 (0.47, 1.79)
Carcinomas	22 (26.8)	1.43 (0.82, 2.51)
Other †	10 (23.8)	1.22 (0.57, 2.61)
Relapse		
No	231 (21.2)	1.00
Yes	20 (14.3)	0.62 (0.38, 1.02)

* Including reticuloendothelial neoplasms and Langerhans cell histiocytosis.
† Other cancers include: retinoblastoma, hepatic and sympathetic nervous system.

Results of the multivariate logistic regression analysis to examine important predictors of concurrent smoking and alcohol use in the pediatric cancer survivors are presented in Table 25. Education, personal income, satisfaction with life, stressful life events and chronic stress were found to be significant predictors of concurrent use ($p<0.05$). The odds of being a concurrent user increased with decreasing levels of education. Survivors who had a high school education or less were significantly more likely to be concurrent users of alcohol and tobacco than those with greater than a high school education. Survivors with a personal income less than $5,000 were significantly less likely to be concurrent smokers and alcohol drinkers than those with a personal income of $20,000 or greater (OR=0.66, 95%CI=0.44, 0.99). As satisfaction with life scores decreased respondents were more likely to be concurrent smokers and alcohol drinkers. As chronic stress and stressful life events scores increased respondents were more likely to be concurrent smokers and alcohol drinkers (Table 25).

Table 25: Summary of multivariate logistic regression analysis for variables predicting concurrent alcohol and tobacco use in pediatric cancer survivors.

Predictor	B	SEB	OR	95% CI	Wald Chi^2	p-value	Wald Chi^2	p-value
Intercept	-2.822	0.262			115.744	<0.0001		
Education								
Less than high school	0.989	0.201	2.69	(1.81, 3.99)	24.223	<0.0001	24.453	<0.0001
High school	0.466	0.187	1.59	(1.10, 2.30)	6.176	0.0129		
Greater than high school			1.00					
Personal income								
$0 to $4,999	-0.414	0.206	0.66	(0.44, 0.99)	4.040	0.0444	6.035	0.0489
$5,000 to $19,999	-0.004	0.186	1.00	(0.69, 1.43)	0.0004	0.9844		
$20,000+			1.00					
Satisfaction with Life								
5-19 (Dissatisfied)	0.544	0.208	1.72	(1.15, 2.59)	6.858	0.0088	7.639	0.0219
20-28 (Satisfied)	0.440	0.189	1.55	(1.07, 2.25)	5.399	0.0201		
29-35 (More satisfied)			1.00					
Stressful Life Events *								
None			1.00				8.719	0.0128
1-4	0.442	0.188	1.56	(1.08, 2.25)	5.525	0.0187		
5+	0.523	0.187	1.69	(1.17, 2.43)	7.808	0.0052		
Chronic stress *								
0-5			1.00				13.262	0.00013
6-11	0.496	0.198	1.64	(1.11, 2.42)	6.286	0.0122		
12-45	0.752	0.207	2.12	(1.41, 3.18)	13.192	0.0003		

Model Likelihood ratio=78.0930, $p<0.0001$ df=10
OR=odds ratio; 95% CI=95% confidence interval; SE=standard error.
* Higher score indicates greater stress.

Table 26 shows the results of an additional multivariate analysis that examined predictors of concurrent use of alcohol and tobacco in pediatric cancer survivors that included demographic, psychosocial, health and clinical factors in the model. Results were similar to those presented in Table 25 however, relapse of cancer was found to be an additional predictor of concurrent use of alcohol and tobacco at the 0.05 level of significance. Cancer survivors who had a relapse of their initial cancer were significantly less likely to be concurrent alcohol and tobacco users than survivors who had not (OR=0.57, 95%CI=0.34, 0.95) (Table 26).

Table 26: Summary of multivariate logistic regression analysis for variables predicting concurrent alcohol and tobacco use in pediatric cancer survivors including clinical variables.

Predictor	B	SEB	OR	95% CI	Wald Chi^2	p-value	Wald Chi^2	p-value
Intercept	-2.771	0.263			110.846	<0.0001		
Education								
Less than high school	1.006	0.202	2.73	(1.84, 4.06)	24.885	<0.0001	25.060	<0.0001
High school	0.485	0.188	1.62	(1.12, 2.35)	6.639	0.0100		
Greater than high school			1.00					
Personal income								
$0 to $4,999	-0.444	0.207	0.64	(0.43, 0.96)	4.615	0.0317	6.408	0.0406
$5,000 to $19,999	-0.031	0.186	0.97	(0.67, 1.40)	0.028	0.8678		
$20,000+			1.00					
Satisfaction with Life								
5-19 (Dissatisfied)	0.567	0.208	1.76	(1.17, 2.65)	7.425	0.0064	8.200	0.0166
20-28 (Satisfied)	0.453	0.190	1.57	(1.09, 2.28)	5.703	0.0169		
29-35 (More satisfied)			1.00					
Stressful Life Events *								
None	0.448	0.188	1.57	(1.08, 2.26)	5.703	0.0169	8.532	0.0140
1-4	0.512	0.187	1.67	(1.16, 2.41)	7.470	0.0063		
5+			1.00					
Chronic stress *								
0-5	0.504	0.198	1.65	(1.12, 2.44)	6.451	0.0111	13.256	0.0013
6-11	0.753	0.207	2.12	(1.41, 3.19)	13.160	0.0003		
12-45			1.00					
Relapse								
No			1.00				4.610	0.0318
Yes	-0.559	0.261	0.57	(0.34, 0.95)	4.610	0.0318		

Model Likelihood ratio=83.1612, p<0.0001 df=11
OR=odds ratio; 95% CI=95% confidence interval; SE=standard error.
* Higher score indicates greater stress.

Results of the multivariate logistic regression analysis to examine important predictors of concurrent smoking and alcohol use in the control group are presented in Table 27. Education, satisfaction with life, stressful life events, chronic stress and physical health were found to be significant predictors of concurrent use (p<0.05). The odds of being a

concurrent user increased with decreasing levels of education. Respondents with a high school education or less were significantly more likely to be concurrent users of alcohol and tobacco compared to those with greater than a high school education. The odds of being a concurrent user increased with decreasing satisfaction with life. Respondents who scored lowest on the satisfaction with life scale were significantly more likely to be concurrent users of alcohol and tobacco than the group that scored the highest (OR=1.88, 95%CI=1.33, 2.66). The odds of concurrent use increased with increasing stressful life events and chronic stress scores. Respondents who scored in the highest stressful life events category were significantly more likely to be concurrent users than those who reported no stressful life events in the past year (OR=1.59, 95%CI=1.16, 2.19). Respondents who scored in the lowest two categories on the physical health scale were more likely to be concurrent smokers and alcohol drinkers than those who scored highest on this the scale (Table 27).

Table 27: Summary of multivariate logistic regression analysis for variables predicting concurrent alcohol and tobacco use in the control group.

Predictor	B	SEB	OR	95% CI	Wald Chi^2	p-value	Wald Chi^2	p-value
Intercept	-2.463	0.236			108.801	<0.0001		
Education								
Less than high school	0.631	0.160	1.88	(1.37, 2.57)	15.549	<0.0001	15.672	0.0004
High school	0.310	0.148	1.36	(1.02, 1.82)	4.379	0.0364		
Greater than high school			1.00					
Satisfaction with Life								
5-19 (Dissatisfied)	0.632	0.176	1.88	(1.33, 2.66)	12.830	0.0003	12.914	0.0016
20-28 (Satisfied)	0.298	0.159	1.35	(0.99, 1.84)	3.518	0.0607		
29-30 (More satisfied)			1.00					
Stressful Life Events *								
None			1.00				8.292	0.0158
1-4	0.233	0.161	1.26	(0.92, 1.73)	2.083	0.1490		
5+	0.465	0.162	1.59	(1.16, 2.19)	8.223	0.0041		
Chronic Stress *								
0-5			1.00					
6-11	0.346	0.173	1.41	(1.01, 1.98)	3.999	0.0455	9.854	0.0072
12-45	0.569	0.181	1.77	(1.24, 2.52)	9.850	0.0017		
Physical Health †								
15-48	0.439	0.202	1.55	(1.04, 2.31)	4.728	0.0297	15.082	0.0045
49-53	0.721	0.198	2.06	(1.40, 3.03)	13.310	0.0003		
54-56	0.208	0.195	1.23	(0.84, 1.81)	1.136	0.2865		
57-58	0.270	0.207	1.31	(0.87, 1.96)	1.711	0.1908		
59-73			1.00					

Model Likelihood ratio=90.2186, p<0.0001 df=12
OR=odds ratio; 95% CI=95% confidence interval; SE=standard error.
* Higher score indicates greater stress
† Higher score indicates better health.

5.6 Structural Equation Modeling

Correlations among variables included in the structural equation model are shown in Table 28 for both cancer survivors (below diagonal) and the control group (above diagonal). The correlations between the stress variables and mental health were moderate as well as between self-esteem and mental health. Satisfaction with life was moderately correlated with mental health, physical health, chronic stress and self-esteem. Chronic stress and stressful life events measures were moderately correlated. Correlations were similar between cancer survivors and controls although the correlation between physical health and mental health was much lower in the cancer survivors compared to the control group. Concurrent use of alcohol and tobacco was most strongly correlated with education and chronic stress in cancer survivors and with education, chronic stress and life satisfaction in the control group.

Table 28: Correlations for variables included in the structural equation model in cancer survivors (Below diagonal n=1231) and the control group (Above diagonal n=1372).

	1	2	3	4	5	6	7	8
1. Concurrent Use	-	-0.141	-0.077	0.162	0.117	-0.177	-0.167	-0.077
2. Mental Health	-0.082	-	-0.151	-0.393	-0.228	0.458	0.010	0.440
3. Physical Health	-0.081	-0.009	-	-0.140	-0.058	0.114	0.040	0.133
4. Chronic Stress	0.156	-0.427	-0.177	-	0.287	-0.456	0.056	-0.245
5. Stressful Life Events	0.105	-0.258	-0.143	0.349	-	-0.207	0.020	-0.101
6. Satisfaction with life	-0.121	0.506	0.257	-0.374	-0.163	-	0.076	0.479
7. Education	-0.191	-0.010	0.055	0.082	0.028	0.098	-	0.107
8. Self-esteem	-0.076	0.497	0.151	-0.270	-0.067	0.574	0.112	-

Note: Correlations between continuous variables (mental health, physical health, chronic stress, stressful life events, satisfaction with life and self-esteem) are Pearson product-moment correlations. Correlations between categorical variables (education and concurrent use) are polychoric. Correlations between continuous variables and dichotomous (concurrent use) are point biserial. Correlations between continuous variables and ordered categorical (education) are Kendall's tau-b.

Results from the multiple group CFA in cancer survivors and controls are shown in Table 29. All items on the self-esteem and satisfaction with life scales loaded significantly onto their latent construct. Item six on the self-esteem scale and item five on the satisfaction with life scale had the weakest factor loadings for their respective latent constructs. Model fit was acceptable with a CFI=0.985, a TLI=0.991 and RMSEA=0.054. The chi-square value was significant (χ^2=246.183, df=51, p<0.001), which could be expected due to the large sample size. The variances and covariances for the latent constructs were similar in the cancer survivor and control groups. The variance was higher for the satisfaction with life construct compared to the self-esteem construct.

Table 29: Multiple group confirmatory factor analysis results with two latent constructs (satisfaction with life and self-esteem).

Latent Construct	Cancer Survivors			Control Group		
	Parameter Estimate	Standard Error	Standardized Estimate	Parameter Estimate	Standard Error	Standardized Estimate
Self-Esteem						
Item 1	1.000	0.000	0.780	1.000	0.000	0.786
Item 2	0.892	0.102	0.743	0.804	0.101	0.715
Item 3	0.989	0.117	0.777	0.805	0.099	0.715
Item 4	1.275	0.146	0.846	1.419	0.163	0.875
Item 5	2.254	0.375	0.942	2.220	0.353	0.943
Item 6	0.726	0.094	0.671	0.773	0.091	0.701
Satisfaction with Life						
Item 1	1.000	0.000	0.895	1.000	0.000	0.891
Item 2	1.161	0.096	0.919	1.116	0.095	0.909
Item 3	1.754	0.191	0.962	1.895	0.211	0.966
Item 4	0.760	0.062	0.836	0.778	0.063	0.836
Item 5	0.551	0.048	0.741	0.636	0.053	0.780
Variance SWLS	4.013	0.503	1.00	3.831	0.492	1.00
Variance Self-Esteem	1.554	0.317	1.00	1.618	0.326	1.00
Covariance	1.748	0.226	0.700	1.567	0.209	0.630

Note: Residual variances of the factor loadings are fixed at one and the means of the latent constructs are fixed at zero so that the model will be identified.
*$p<0.05$
$\chi^2=246.183$, df=51, $p<0.001$; CFI=0.985; TLI=0.991; RMSEA=0.054

Results for the test of measurement invariance for the self-esteem and satisfaction with life scales in cancer survivors and controls are shown in Table 30. The baseline model where factor loadings and thresholds for each latent construct were freely estimated across groups was compared to a more restrictive model where the factor loadings and thresholds were constrained to be equal. The chi-square difference test showed that the constrained model was not significantly different from the baseline model suggesting that there was measurement invariance ($\Delta\chi^2=0.220$, Δdf=6, $p=0.9998$). The change in the CFI was also less than –0.01 providing additional support for measurement invariance.

Table 30: Goodness-of-fit statistics for tests of measurement invariance of the self-esteem and satisfaction with life scales across the cancer survivor and control groups.

Model Description	χ^2	df	Comparative Model	$\Delta\chi^2$	Δdf	P-value	CFI	ΔCFI
1. Baseline model *	246.183	51	-	-	-	-	0.985	-
2. Factor loadings & thresholds for SE & SWL constrained equal †	265.010	54	Model 1	0.220	6	0.9998	0.984	-0.001

* Factor loadings and thresholds free across groups; residual variances fixed to one in all groups; factor means fixed to zero in all groups.
† Residual variances fixed in the control group and free in survivors; factor means fixed to zero in controls and free in survivors (Mplus default).

Results from the multiple group structural equation modeling analysis are shown in Table 31. Model fit was acceptable with a CFI=0.973, TLI=0.975, and RMSEA=0.041. The chi-square test was significant but could be expected due to the large sample size (χ^2=387.815, df=121, p<0.001). In the cancer survivors, only the paths between education and concurrent use of alcohol and tobacco and chronic stress and concurrent use of alcohol and tobacco were significant. Cancer survivors with a high school education or less were significantly more likely to be concurrent users of alcohol and tobacco than those with greater than a high school education. Survivors who reported higher levels of chronic stress were more likely to be concurrent users of alcohol and tobacco. The R^2 was 0.087, which represents the standard deviation change in the underlying latent construct for a one unit change in the exogenous variables.

In the control group all paths to concurrent use of alcohol and tobacco were significant. For the education variable two dummy variables were created and the path from high school education to concurrent use of alcohol and tobacco was not significant (β=0.180, p>0.05) while the path from less than high school education to concurrent use of alcohol and tobacco was significant (β=0.380, p<0.05).

The relationship between less than high school education and concurrent use of alcohol and tobacco was the strongest. Respondents in the control group who had less than a high school education were more likely to be concurrent users of alcohol and tobacco than those with greater than a high school education. As chronic stress and stressful life events increased, respondents were more likely to be concurrent users of alcohol and tobacco. As satisfaction with life, mental health and physical health decreased, respondents were more likely to be concurrent users of alcohol and tobacco. As self-esteem increased, respondents were more likely to use alcohol and tobacco. The R^2 was 0.115, which represents the standard deviation change in the underlying latent construct for a one unit change in the exogenous variables.

None of the paths to satisfaction with life were significant in the cancer survivors. In the control group the paths from less than high school education, chronic stress, mental health and self-esteem to satisfaction with life were significant. Respondents with less than a high school education had a lower life satisfaction than respondents with greater than a high school education. As chronic stress increased satisfaction with life decreased. As mental

health and self-esteem scores increased satisfaction with life increased. The R^2 values suggest that the exogenous variables explain 54% of the variance in the satisfaction with life construct in the cancer survivors and 45% in the control group.

The pathways from education, physical health and mental health to self-esteem were all significant in both the cancer survivors and the control group. Having a high school education or less was associated with a lower self-esteem compared to respondents with greater than a high school education. As physical and mental health increased, so did self-esteem. The R^2 values suggest that the exogenous variables explain 30% of the variance in the satisfaction with life construct in the cancer survivors and 24% in the control group.

Table 31: Unstandardized parameter estimates from the multiple group structural equation modeling analysis in cancer survivors and the control group.

Concurrent use of alcohol and tobacco				
	Cancer survivors		Control group	
Predictor	Estimate	Standard error	Estimate	Standard error
R-square value	R^2=0.087		R^2=0.115	
Less than high school †	0.454*	0.109	0.380*	0.097
High school †	0.222*	0.101	0.180	0.090
Chronic stress	0.025*	0.007	0.012*	0.007
Stressful life events	0.017	0.009	0.019*	0.009
Mental Health	0.001	0.005	-0.012*	0.005
Physical Health	-0.005	0.005	-0.013*	0.006
Self-Esteem	0.009	0.083	0.122*	0.054
Satisfaction with life	-0.032	0.042	-0.108*	0.035
Satisfaction with Life				
Predictor	Estimate	Standard error	Estimate	Standard error
R-square value	R^2=0.544		R^2=0.451	
Less than high school †	-0.573	0.351	-0.389*	0.139
High school [a]	-0.253	0.206	-0.131	0.121
Chronic stress	-0.058	0.033	-0.085*	0.010
Stressful life events	0.023	0.018	-0.019	0.012
Mental Health	0.043	0.025	0.028*	0.007
Physical Health	0.040	0.023	0.010	0.007
Self-Esteem	1.041	0.622	0.605*	0.097
Self-esteem				
Predictor	Estimate	Standard error	Estimate	Standard error
R-square value	R^2=0.299		R^2=0.239	
Less than high school †	-0.278*	0.121	-0.382*	0.119
High school †	-0.226*	0.107	-0.227*	0.105
Mental Health	0.050*	0.014	0.058*	0.008
Physical Health	0.019*	0.007	0.032*	0.007

*p<0.05

† Greater than high school education is reference group

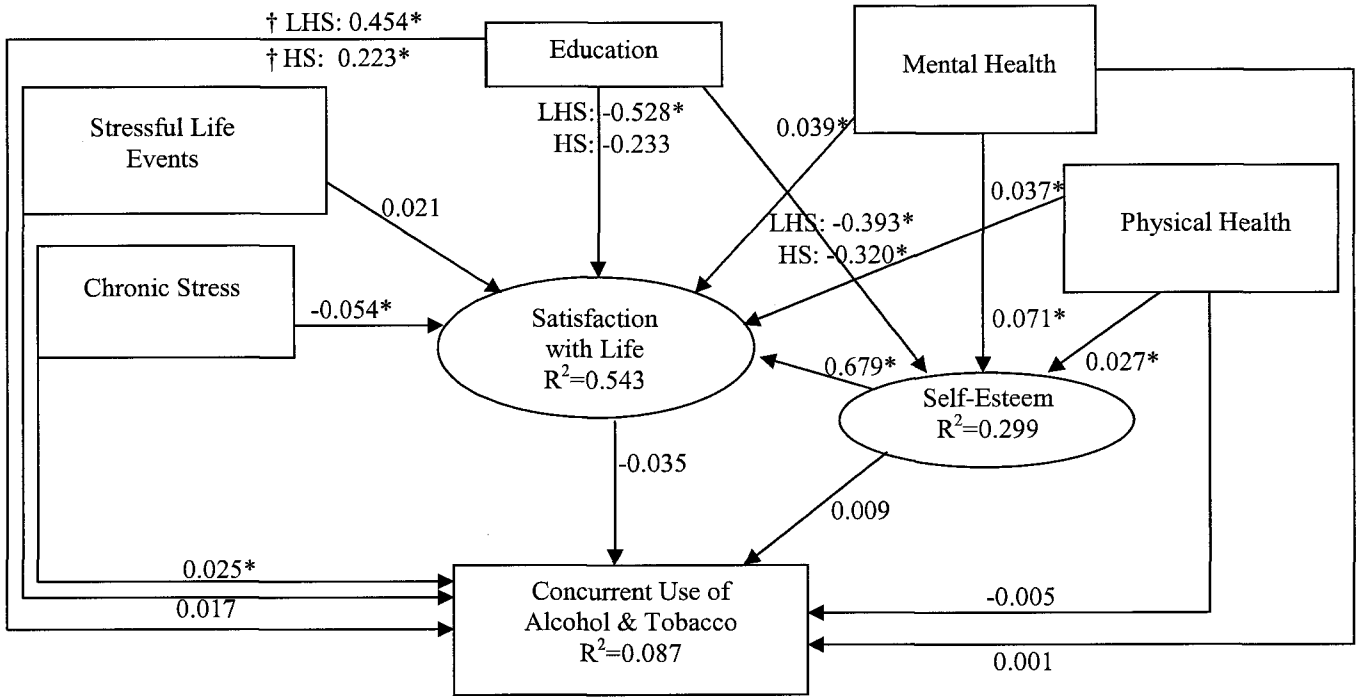
χ^2=387.815, df=121, p<0.001; CFI=0.973; TLI=0.975; RMSEA=0.041

In the multiple group analysis there were many paths that were significant in the control group that were non-significant in the cancer survivors suggestive of structural invariance. Models were therefore run separately in the cancer survivor and control groups. Figure 4 shows the results from the single group SEM analysis in the cancer survivors. Model fit was acceptable with a CFI=0.951, TLI=0.958 and RMSEA=0.051. The chi-square was significant but could be expected due to the large sample size (χ^2=265.327, df=64, p<0.001). Unstandardized structural parameter estimates, standard errors and 95% confidence intervals can be found in Appendix 7.

The only significant pathways to concurrent use of alcohol and tobacco were from chronic stress and education. Respondents with a high school education or less were more likely to be concurrent users of alcohol and tobacco than those with greater than a high school education. As chronic stress increased respondents were also more likely to be concurrent users of alcohol and tobacco. Having less than a high school education was most strongly associated with concurrent use of alcohol and tobacco in cancer survivors (standardized probit coefficient=0.194).

Those with less than a high school education were also more likely to have lower life satisfaction than those with greater than a high school education. As chronic stress decreased, physical and mental health improved and self-esteem increased survivors had greater life satisfaction. Self-esteem was most strongly associated with life satisfaction (standardized coefficient=0.487).

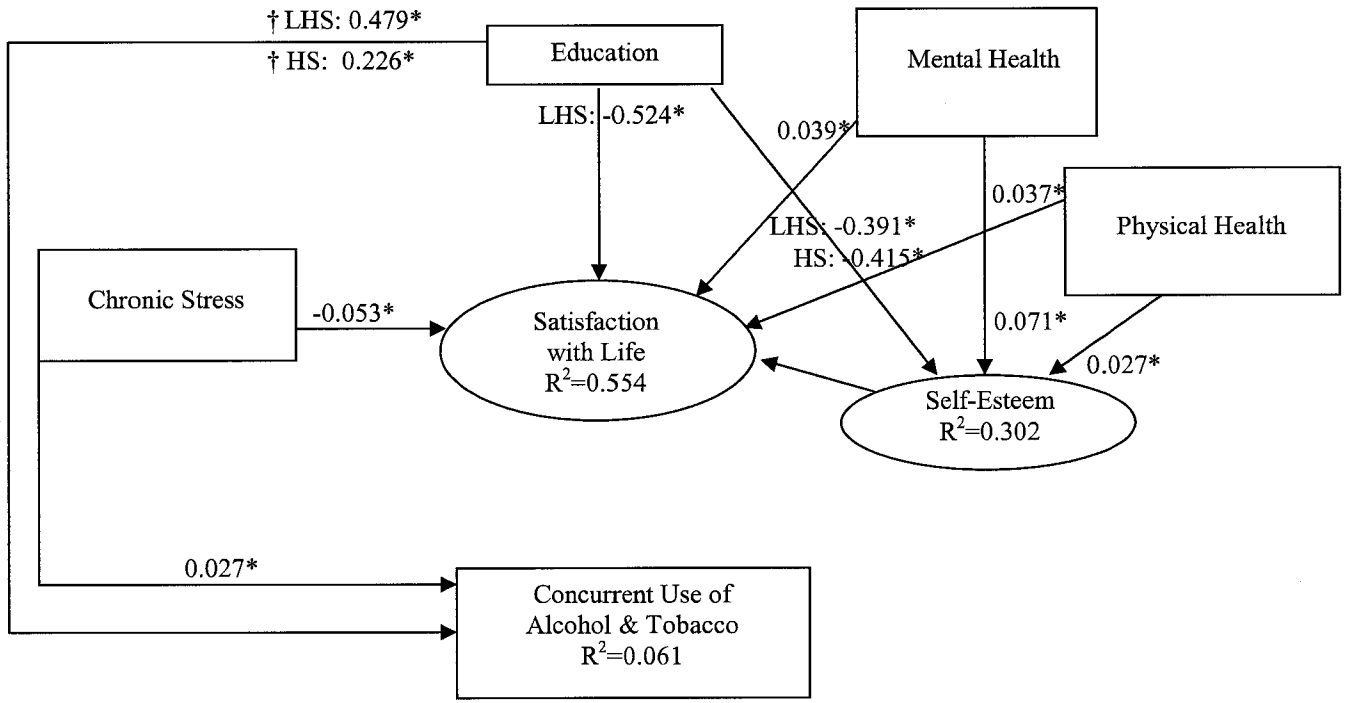
There were significant paths from education, physical and mental health to self-esteem. Those with a high school education or less had lower self-esteem than those with greater than a high school education. As physical and mental health increased, self-esteem increased. Mental health was most strongly associated with self-esteem (standardized coefficient=0.511).



* p<0.05
†Greater than high school education is reference group
χ^2=265.327, df=64, p<0.0001; CFI=0.951; TLI=0.958; RMSEA=0.051

Figure 4: Results from the single group SEM analysis in cancer survivors; standardized structural parameter estimates

Non-significant paths were removed sequentially from the model and results for the reduced model in cancer survivors are presented in Figure 5. Model fit was improved slightly with CFI=0.958, TLI=0.963 and RMSEA=0.047, however, the chi-square difference test was non-significant suggesting that the reduced model explains the data just as well as the full model (χ^2_{Diff}=9.653, df=6, p=0.1399). The pseudo R^2 value for concurrent use of alcohol and tobacco was 0.06, which represents the standard deviation change in the underlying latent construct for a one unit change in the exogenous variables. The exogenous variables explained 55% and 30% of the variance in the satisfaction with life and self-esteem constructs respectively (Figure 5). Unstandardized structural parameter estimates, standard errors and 95% confidence intervals can be found in Appendix 8.



* $p<0.05$
† Greater than high school education is reference group
χ^2=237.246, df=63, $p<0.001$; CFI=0.958; TLI=0.963; RMSEA=0.047; χ^2Diff=9.653, df=6, p=0.1399

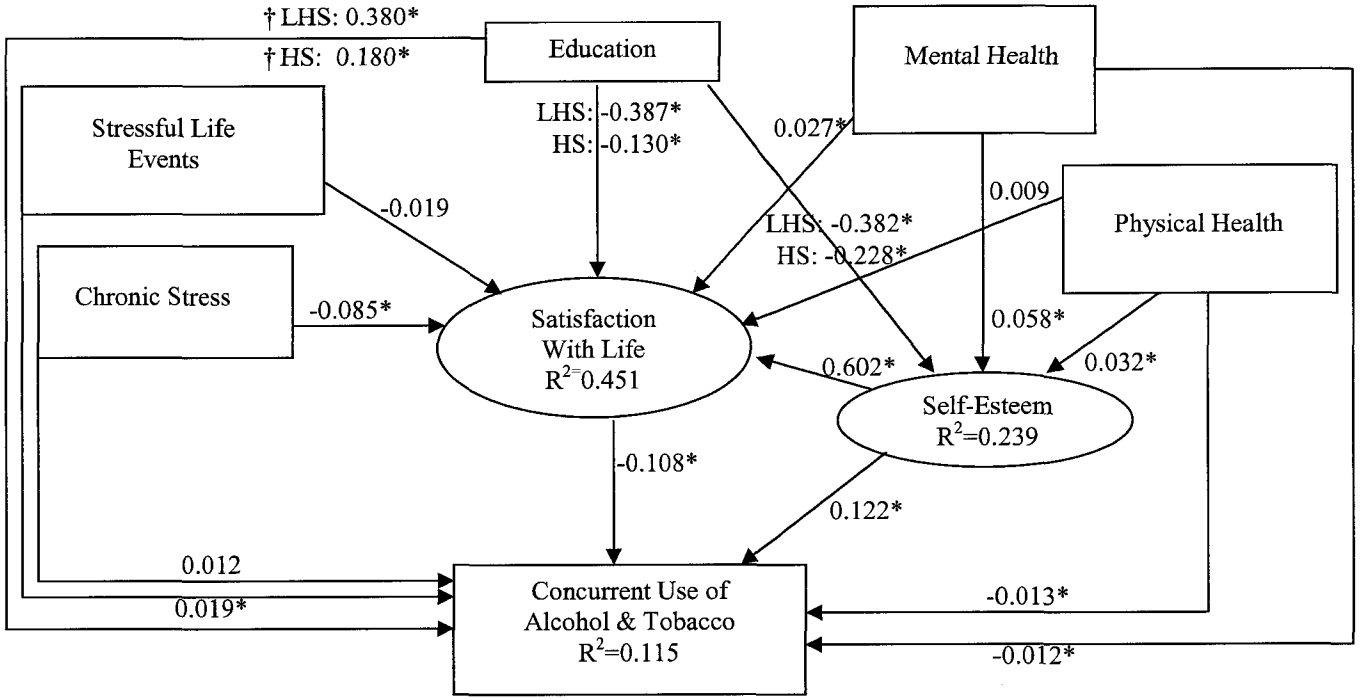
Figure 5: Results from the single group SEM analysis in cancer survivors with non-significant paths removed; standardized structural parameter estimates

Figure 6 shows the results from the single group SEM analysis in the control group. Model fit was acceptable with CFI=0.984; TLI=0.986; RMSEA=0.033. The chi-square was significant but could be expected due to the large sample size (χ^2=152.472, df=62, p<0.001). Unstandardized structural parameter estimates, standard errors and 95% confidence intervals can be found in Appendix 9.

The only non-significant path to concurrent use of alcohol and tobacco was from chronic stress. Respondents with a high school education or less were more likely to be concurrent users of alcohol and tobacco than those with greater than a high school education. As stressful life events and self-esteem increased respondents were also more likely to be concurrent users of alcohol and tobacco. As mental health, physical health and satisfaction with life decreased respondents were more likely to be concurrent users of alcohol and tobacco. Satisfaction with life was most strongly associated with concurrent use of alcohol and tobacco (standardized probit coefficient= -0.194).

Those with less than a high school education were also more likely to have lower life satisfaction than those with greater than a high school education. As chronic stress decreased, mental health improved and self-esteem increased survivors had greater life satisfaction. Self-esteem was most strongly associated with life satisfaction (standardized coefficient=0.410).

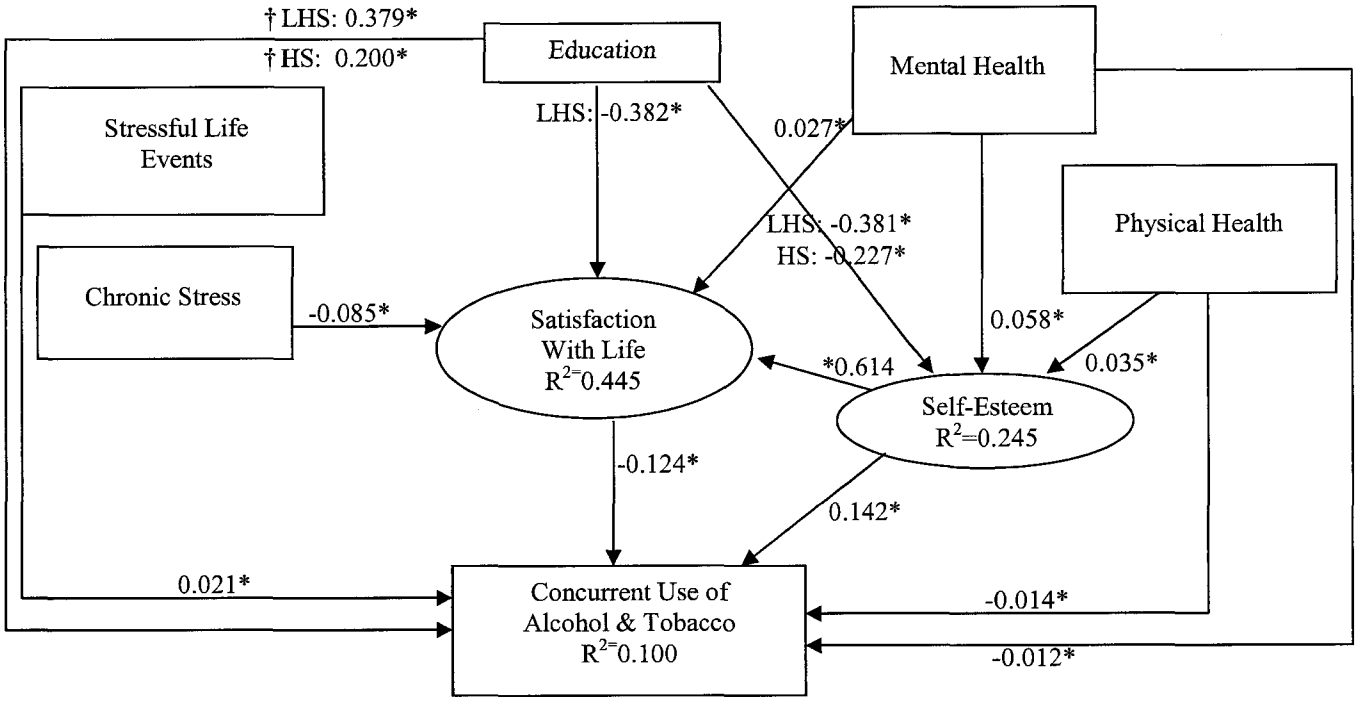
There were significant paths from education, physical and mental health to self-esteem. Those with a high school education or less had lower self-esteem than those with greater than a high school education. As physical and mental health increased, self-esteem increased. Mental health was most strongly associated with self-esteem (standardized coefficient=0.46).



* $p<0.05$
†Greater than high school education is reference group
χ^2=387.815, df=121; CFI=0.973; TLI=0.975; RMSEA=0.041

Figure 6: Results from the single group SEM analysis in the control group; standardized structural parameter estimates

Non-significant paths were removed sequentially from the model and results for the reduced model in the control group are presented in Figure 7. Model fit was improved slightly with a CFI=0.985; TLI=0.986; RMSEA=0.032; however, the chi-square difference test was non-significant suggesting that the reduced model explains the data just as well as the full model (χ^2Diff=7.739, df=4, p=0.1013). The pseudo R^2 value for concurrent use of alcohol and tobacco was 0.100, which represents the standard deviation change in the underlying latent construct for a one unit change in the exogenous variables. The exogenous variables explained 44% and 24% of the variance in the satisfaction with life and self-esteem constructs respectively (Figure 7). Unstandardized structural parameter estimates, standard errors and 95% confidence intervals can be found in Appendix 10.



*p<0.05
† Greater than high school education is reference group
χ^2=144.283, df=60, p<0.001; CFI=0.985; TLI=0.986; RMSEA=0.032;
χ^2 Diff=7.739, df=4, p=0.1013.

Figure 7: Results from the single group SEM analysis in the control group with non-significant paths removed; standardized structural parameter estimates

Results from the test for mediation of the satisfaction with life latent construct are presented in Table 32. Satisfaction with life was not likely to be a mediator in the model for cancer survivors as the path between satisfaction with life and concurrent use of alcohol and tobacco was non-significant ($p>0.05$). In the control group satisfaction with life was found to be a significant mediator in the relationships of: self-esteem, mental health, chronic stress and education with concurrent use of alcohol and tobacco ($p<0.05$). There were negative indirect effects for self-esteem ($\alpha\beta$=-0.076, 95%CI=-0.122, -0.016) and mental health ($\alpha\beta$=-0.003, 95%CI=-0.006, -0.001) meaning that respondents with low self-esteem or low mental health were more likely to be concurrent users of alcohol and tobacco through decreased life satisfaction. There was a positive indirect effect for chronic stress ($\alpha\beta$=0.011, 95%CI=0.003, 0.018) meaning that respondents with higher reported levels of chronic stress were more likely to be concurrent users of alcohol and tobacco through decreased satisfaction with life. There was also a positive indirect effect for education ($\alpha\beta$=0.047, 95%CI=0.007, 0.088) where those with less than high school education were more likely to be dissatisfied with life than those with greater than a high school education and in turn were more likely to be concurrent users of alcohol and tobacco (Table 32).

There was full mediation for the path from chronic stress to concurrent use of alcohol and tobacco through satisfaction with life as this indirect path was significant and the direct path from chronic stress to concurrent use of alcohol and tobacco was non-significant (Figure 6, Table 32). There was partial mediation for the paths from mental health, education and self-esteem to concurrent use of alcohol and tobacco through life satisfaction as the direct paths to concurrent use of alcohol and tobacco were also significant (Figure 6, Table 32). There was a suppression effect for self-esteem as the direct effect from self-esteem to concurrent use of alcohol and tobacco had a significant positive coefficient (0.142, $p<0.05$) and the indirect effect and a significant negative coefficient (-0.076, $p<0.05$).

Table 32: Indirect effects of exogenous variables on concurrent use of alcohol and tobacco through satisfaction with life.

Variable	Estimate	Standard Error	95%CI
Self-esteem	-0.076*	0.024	(-0.122, -0.016)
Mental Health	-0.003*	0.001	(-0.006, -0.001)
Chronic stress	0.011*	0.003	(0.005, 0.016)
Less than H.S. Education †	0.047*	0.021	(0.007, 0.088)

* $p<0.05$

† H.S.=high school; reference group is greater than high school education.

6.0 DISCUSSION

This was the first known national study of smoking and alcohol use in Canadian pediatric cancer survivors. It identifies the prevalence and important demographic, psychosocial and health related risk factors for smoking, binge drinking, alcohol use and concurrent use of alcohol and tobacco in pediatric cancer survivors. This is of importance as cancer survivors are at increased risk for developing health conditions related to their cancer treatment and smoking and heavy alcohol use may amplify this risk. Additionally, many of the psychosocial risk factors identified in this study have not been studied extensively in pediatric cancer survivors.

Overall, results from the current study showed that a substantial proportion of pediatric cancer survivors were engaging in health risk behaviours. Important factors associated with smoking and alcohol use in the cancer survivors were low education, poor life satisfaction and high stress. Male gender was also identified as an important risk factor for binge drinking. When taking into account more complex relationships in a theoretical model high stress and low education remained the most important predictors.

Prevalence of Smoking and Alcohol use

Consistent with findings from recent studies, pediatric cancer survivors were significantly less likely to be current smokers, alcohol drinkers, binge drinkers and concurrent users of tobacco and alcohol than the control group [6, 7, 51, 61]. The prevalence of smoking in Canadian pediatric cancer survivors who were age 16 to 37 at the time of the current study was 22.8%. Recent studies of pediatric cancer survivors over age eighteen in the United States, Australia and the United Kingdom reported the prevalence of current smoking ranging from 14% to 29% [6-8, 58, 60, 61]. Differences in the definitions of smoking, years of diagnosis and the age of the cohorts make it difficult to consider regional differences in the prevalence of smoking. The prevalence of current smoking in the general Canadian population aged 15 to 44 years from the Canadian Community Health Survey (2000-2001) was 30.7%, which is comparable of the control group (30.2%) in the current study and higher than that of the pediatric cancer survivors (22.8%) [196]. Smoking behaviours of cancer survivors in the current study were comparable to previous studies of pediatric cancer survivors and controls were similar to the general population.

Alcohol drinking behaviours reported by cancer survivors in this study were comparable to those reported from other studies of pediatric cancer survivors. The prevalence of alcohol drinkers, moderate to heavy drinkers and binge drinkers for the pediatric cancer survivors was 68.6%, 26.8% and 24.9% respectively. Recent studies of pediatric cancer survivors over age eighteen in the United States, Australia and the United Kingdom reported the prevalence of alcohol drinking ranging from 54% to 90% and the prevalence of binge drinking ranging from 12.5% to 53%. Some of the studies found that pediatric cancer survivors were significantly less likely to be alcohol and binge drinkers than the control groups while others did not [6, 58, 59, 61]. Cancer survivors in the current study were less likely to be alcohol and binge drinkers than the control group.

Age was found to be an effect modifier of the relationship between binge drinking and cancer survivor status. The adjusted odds of being a binge drinker were significantly lower in cancer survivors compared to the controls in all age groups except for the 26-30 year olds. The prevalence of binge drinking was 24.6% in survivors aged 26-30 years and in the control group was 19.5%. In the control group aged 26-30 years this prevalence was lower than expected. Results from the Canadian Community Health Survey in 2003 showed that in a representative sample of the Canadian population approximately 29.6% of participants aged 25 to 34 were binge drinkers [197]. The participants' age 26-30 years old included in the current study may not be representative of the general population of the same age. Therefore, the non-stratum specific odds ratios may better represent the relationship between binge drinking and cancer survivors and controls where pediatric cancer survivors are significantly less likely to be binge drinkers than the controls regardless of their age.

Previous research has not directly studied the concurrent use of alcohol and tobacco in pediatric cancer survivors. The prevalence of concurrent use of alcohol and tobacco was 20.4% for pediatric cancer survivors in the current study. Findings from studies of the general population have consistently found that there is a moderate to strong association between smoking and alcohol drinking where those who consume alcohol are more likely to smoke cigarettes than those who do not, and vice versa. This suggests that there may be common factors that predispose someone to engage in these health risk behaviours [11]. Future research is needed in this area as engaging in both health risk behaviours may increase the

risk for negative health outcomes either additively or synergistically as is suspected with pancreatitis [198].

Predictors of Smoking and Alcohol use

The current study examined important demographic, psychosocial and clinical predictors of smoking and alcohol use in pediatric cancer survivors and the control group separately.

Age

Age was found to be an important predictor of alcohol use and binge drinking in both the pediatric cancer survivor and control groups. There have been few studies on alcohol use in pediatric cancer survivors and among the studies conducted the prevalence of alcohol use was lower in survivors under the age of 18 years compared to those over the age of 18 years, which is consistent with findings from the current study [57, 61]. Participants over the age of 20 years were significantly more likely to drink alcohol than those aged 16 to 20 years in both the cancer survivor and control groups. In the multivariate analysis age was only a significant predictor of alcohol drinking for the cancer survivors. Results from multivariate analyses also showed that age was a significant predictor of binge drinking in the control group only, where those aged 16 to 20 years had higher odds of being a binge drinker than those over the age of 20 years. These findings suggest that cancer survivors aged 16 to 20 years are engaging in alcohol use less than older survivors and less than the control group of the same age. In survivors over the age of 20 years the prevalence of alcohol use was similar to the control group. This may indicate that as survivors grow older and have a longer time since treatment they begin to consume alcohol at a similar rate as their peers. It may also suggest that older survivors in the current study received less education about the risks of heavy alcohol use or about the health risks associated with their cancer treatment.

Age was not found to be an important predictor of current smoking or concurrent use of alcohol and tobacco in either the cancer survivors or the control group in this study. In previous studies of pediatric cancer survivors, age was found to be an important predictor of smoking where older survivors were significantly more likely to be smokers [7, 8, 69]. Reasons for the discrepancy may be differences in the age of participants included in the studies, birth

cohort effects in studies that included participants born in earlier years when smoking was more socially desirable and different categorizations of the age variable. It is also possible that older participants in the current study have quit smoking, resulting in a similar prevalence to younger survivors or that younger survivors are smoking more.

Gender

Younger age and being male may be risk factors for alcohol use and binge drinking in cancer survivors. Some previous studies found that male gender was an important predictor of smoking, binge drinking and health risk behaviours in pediatric cancer survivors, while others did not [3, 6, 7]. The current study found that male gender was an important predictor of alcohol use and binge drinking in both pediatric cancer survivors and the control group but was not a predictor of smoking or the concurrent use of alcohol and tobacco in either group. These findings are consistent with a study by Allison et al. [87] of the Canadian National Population Health survey that found that males were significantly more likely to be heavy drinkers than females but that gender was not a significant predictor of smoking. A literature review on the psychosocial factors related to smoking reported that in North America males had a higher prevalence of smoking than females in the past; in more recent years the prevalence of smoking was approximately equal in the two groups and sometimes higher for female adolescents than males [118]. Interventions and education about the risks of heavy alcohol use in the general population or targeted to cancer survivors should consider gender differences in their design. This study supports that males are a high-risk group for engaging in alcohol use and binge drinking.

Education

Education was one of the most consistent predictors of smoking and alcohol use in both the cancer survivors and control group in the current study, where those with a high school education or less were more likely to engage in smoking, binge drinking and concurrent use of alcohol and tobacco but less likely to be alcohol drinkers than those with greater than a high school education. Previous research has found low education to be an important predictor of smoking and health risk behaviours in pediatric cancer survivors and to have a strong independent relationship with smoking in the general population even after

adjusting for other factors related to socioeconomic status [3, 7, 8, 8, 71, 77, 84]. Pediatric cancer survivors and controls with greater than a high school education in the current study were more likely to be alcohol drinkers and may reflect the socialization of alcohol use in this group or greater disposable income to spend on alcohol. Although participants with a higher level of education were more likely to be alcohol drinkers they were significantly less likely to engage in risky behaviours such as smoking, binge drinking and concurrent use of alcohol and tobacco.

Special Education/Learning Disabled Program

Cancer survivors in the current study had an overall lower educational attainment than their peers and in addition were more likely to have been in a special education or learning disabled program. This is consistent with previous studies that found that cancer survivors were significantly more likely to have learning disabilities and require special education services than their siblings [199, 200]. Previous research has suggested that intensive cancer treatment, cranial radiation and central nervous system tumours may increase the risk for cognitive late effects and the need for special education services [200]. Studies have also suggested that cognitive late effects may result in poor decision-making abilities increasing the risk for engaging in smoking and health risk behaviours [63, 64, 75, 77].

The prevalence of current smokers and concurrent users of alcohol and tobacco were higher in pediatric cancer survivors who had been in a special education or learning disabled program. Studies of adolescents in the general population have found that adolescents with learning disabilities may be at increased risk for substance abuse [85, 86]. However, the relationship between smoking and special education was not observed in the control group or in the multivariate analyses in pediatric cancer survivors. The reason for this may be that the relationship between smoking and special education was adjusted for educational attainment in the multivariate model. Cancer survivors in a special education program may have an overall lower educational attainment and low education has been strongly associated with smoking [3, 7, 8, 8, 71, 77, 84].

Unlike smoking, cancer survivors who had been in a special education or learning disabled program were less likely to be alcohol drinkers. Having been a cancer survivor in a special education or learning disabled program may be protective against being an alcohol

drinker. However, this relationship may again reflect a lower level of educational attainment. The current study found that lower educational attainment was associated with reduced odds of being an alcohol drinker compared to those with greater than a high school education. This may reflect the socialization of alcohol use in those with higher education or having greater income to spend on alcohol.

Personal Income

Personal income was found to be a significant predictor of alcohol use in the control group and of concurrent use of alcohol and tobacco in the cancer survivors. In the control group participants with the lowest personal income (less than $5,000) had significantly lower prevalence of alcohol drinkers compared to those with an income greater than $20,000. In the cancer survivors, participants in the lowest income group (less than $5,000) were significantly less likely to be concurrent users of alcohol and tobacco than the high-income group (greater than $20,000). These results may suggest that having a lesser amount of disposable income is protective from alcohol drinking and concurrent use of alcohol and tobacco. Among adolescents it has been found that a higher personal income is associated with smoking presumably because they have more disposable income to spend on tobacco products, independent of their parents [118]. Differences in the relationship between personal income and alcohol use and concurrent use with tobacco between cases and controls may be due to the statistically significant difference in the frequency distribution of income between the two groups. Ideally, household income would have been used in the current study as a measure of socioeconomic status for all survivors as personal income varies greatly with age and may have a different relationship with health risk behaviours for adults and adolescents.

Ethnicity

Ethnicity may be an important risk factor for engaging in health risk behaviours. The prevalence of current smoking was higher for respondents whose parents' ancestors were Aboriginal in both the cancer survivor and control groups. In the multivariate analyses ethnicity was only found to be a significant predictor of current smoking and binge drinking in the control group where the odds of smoking were significantly lower for respondents whose parents' ancestors were non-white. The inconsistent findings for cancer survivors and

controls are most likely due to small samples sizes. Approximately 86% of cancer survivors and 82% of controls reported having white ancestors. Although statistical significance was not met, the observed trends were expected. Previous research of the general population has found that Aboriginals were significantly more likely to be smokers, followed by whites, with most non-white ethnicities being significantly less likely to be smokers [89, 118]. Ethnicity was found to be a significant predictor of smoking initiation, smoking and binge drinking in previous studies of pediatric cancer survivors where non-black participants were more likely to engage in health risk behaviour [8, 201]. Cultural differences in the socialization of smoking may explain differences in the prevalence of smoking. Acculturation may also influence the prevalence of smoking within a cultural group [79, 118].

Self-Esteem

Self-esteem was inconsistently related to health risk behaviours. The prevalence of current smoking and concurrent use of alcohol and tobacco was higher in respondents with low self-esteem. However, in the multivariate analyses self-esteem was not found to be an important predictor of smoking or alcohol use in the cancer survivors or the control group. Similar to the current study, Tao et al. [7] found that self-concept was not related to smoking in childhood cancer survivors. Some studies from the general population suggested that low self-esteem was an important predictor of smoking [67, 118]. However, similar to results found here an analysis of the National Population Health Survey in Canada found that self-esteem was not a predictor of health risk behaviours in adults aged 20-24 years [87]. One explanation for the discrepancy may be that low self-esteem is an important predictor of smoking initiation but not the maintenance of smoking behaviours. Persons with low self-esteem may be more susceptible to peer pressure and thus begin smoking but may not continue to smoke because of low self-esteem. Other factors such as high stress may be associated with the continuation of smoking behaviours. Self-esteem has also been shown to be an important predictor and to have high correlations with satisfaction with life, which was included in the multivariate models. Satisfaction with life may therefore, be an important mediator of the relationship between self-esteem and smoking or alcohol use [117].

Life Satisfaction

Satisfaction with life was a significant predictor of smoking, binge drinking and concurrent use of alcohol and tobacco in pediatric cancer survivors and the control group. Participants who had greater dissatisfaction with life were more likely to be current smokers, binge drinkers and concurrent users of alcohol and tobacco. One previous study of adolescents in the general population examined the relationship between life satisfaction and substance use. Zullig et al. [116] found that reduced life satisfaction was significantly associated with cigarette smoking, regular alcohol use, binge drinking, and other substance use. Life satisfaction was not found to be a significant predictor of being an alcohol drinker in the current study, suggesting that it may only be an important predictor of high-risk behaviours. For future studies, dichotomizing alcohol use into abstain/light and moderate/heavy may better represent high and low risk alcohol use for negative health outcomes.

Physical and Mental Health

The relationship between health status and smoking and alcohol use differed in cancer survivor and control groups in the current study. The prevalence of current smokers and concurrent users of alcohol and tobacco was higher in cancer survivors and controls that had low physical and mental health scores. However, multivariate analyses showed that poor physical and mental health were associated with current smoking and current alcohol drinking for the control group only. In the control group there was a trend in the odds ratios where the odds of being a smoker or alcohol drinker decreased with improved physical and mental health. This trend was not observed in the cancer survivors and may be explained by the possibility that their physical and mental health was more strongly associated with their cancer treatment than their smoking status. Differences between the univariate and multivariate analyses in the cancer survivors suggest that it is also possible that other factors included in the model were confounding the relationship between health status and tobacco or alcohol use, such as chronic stress or satisfaction with life in the cancer survivors. These factors may also act as mediators in the relationship between physical and mental health and health behaviours

Previous studies partially support the results from the current study. The finding that smoking and alcohol use were related to poor health in the control group is similar to findings from studies of the general population. Current smoking and binge drinking in the general population were associated with poor physical and mental health scores on the SF-36 scale [124-126]. Previous studies of pediatric cancer survivors have had provided inconsistent results on the relationship between mental health and health risk behaviours. One study of pediatric cancer survivors found that increased depression was associated with engaging in health risk behaviours [66] and another found that more severe symptoms of depression, anxiety and somatic symptoms were associated with current smoking and dependence on tobacco [71]. However, two other studies did not find that mood was associated with smoking and health risk behaviour [7, 77].

Due to the cross-sectional nature of the current study causal relationships cannot be determined. Poor physical and mental health may be risk factors for smoking or smoking may cause poor physical and mental health. It has been hypothesized that poor physical health would be a protective factor for engaging in health risk behaviours in pediatric cancer survivors as they would perceive themselves to be more vulnerable to health consequences [92]. This was not observed as the univariate analysis found that pediatric cancer survivors in the lowest physical health groups had significantly higher odds of being a current smoker. However, the poor physical health reported by these survivors may be a result of smoking rather than a risk factor.

Stress

Chronic stress was found to be a significant predictor of smoking, alcohol drinking and concurrent use of tobacco and alcohol in both pediatric cancer survivors and the control group. Higher scores on the chronic stress scale were associated with increased odds of being a current smoker, alcohol drinker and concurrent user of alcohol and tobacco. As in the current study, Allison et al. [87] found that chronic stress was one of the most consistent predictors of health risk behaviour in a study of the Canadian National Population Health Survey and significantly predicted daily smoking and heavy alcohol use.

The current study found that a higher stressful life events score but not chronic stress was associated with binge drinking. Stressful life events are considered to be more acute in

nature, with the stress terminating after a shorter period of time [146]. Binge drinking is also considered to be acute in nature, with greater than five drinks being consumed at one occasion. Acute stressors may be a risk factor for engaging in acute health risk behaviours while more chronic stressors are associated with engaging in health risk behaviour over a longer time period.

Chronic life stress and traumatic life events have been associated with both alcohol and tobacco use in the general population [88]. It has been suggested that when under stress persons may engage in tobacco and alcohol use as a coping function. Alcohol is a known depressant that may reduce physiological stress responses and provide distraction from stressors. Contrary to this smoking is a stimulant that increases attention and concentration. Smoking could be a contributor to stress, as withdrawal symptoms create anxiety and increased stress. However, smokers also report that smoking is relaxing suggesting that the relationship between smoking and stress is complex [88, 89, 118].

Higher scores on the stressful life events scale were associated with smoking in pediatric cancer survivors and with alcohol use, binge drinking and concurrent use of tobacco and alcohol in both the survivor and control groups. Higher severity scores on the stressful life events scale were associated with increased odds of being a current smoker, alcohol drinker, binge drinker and concurrent user of tobacco and alcohol. In the control group stressful life events were not found to be a significant predictor of current smoking as it was in the cancer survivors in the multivariate analyses. There was a stronger relationship between high scores on the stressful life events scale and current smoking in the cancer survivors compared to the control group. It is possible that because cancer survivors have already had a significant life event (having cancer) additional stressful life events exceed their coping abilities putting them at risk for engaging in smoking.

Clinical Factors

None of the clinical factors were associated with current smoking or concurrent use of alcohol and tobacco. Previous studies of childhood cancer survivors also did not find any association between clinical factors and current smoking [4, 56, 57, 61, 69]. However, one study by Emmons et al. [8] found an association between clinical factors and smoking initiation where an older age at diagnosis, not having had pulmonary-related cancer treatment or brain

radiation were associated with initiation of smoking. Clinical factors may be important predictors of whether a cancer survivor begins smoking, but once they have started are not associated with maintenance of smoking behaviours. This may suggest that educational programs to prevent smoking initiation should utilize clinical information to improve survivors' knowledge about late effects and perceived vulnerability to negative health outcomes but that additional factors should be considered for smoking cessation programs.

Age at diagnosis, cancer diagnosis and treatment modalities were associated with alcohol drinking in the cancer survivors. Univariate analyses showed that survivors diagnosed with cancer at zero to four years of age were significantly less likely to be current alcohol drinkers, probably reflecting a lower age at the time of the study and being below the legal drinking age. Survivors of lymphomas, carcinomas and bone tumours were more likely to be alcohol drinkers than survivors of leukemia. Results from the multivariate analyses showed the odds of being an alcohol drinker were not significantly different for survivors of bone tumours and leukemia. In the Late Effects Study the mean age at the time of the study was higher for survivors of lymphomas, carcinomas and bone tumours than survivors of Leukemia (data not shown). Alcohol drinking was probably higher in survivors diagnosed with these types of cancer, as they were more likely to be of legal drinking age. Survivors who received radiation therapy or radiation in combination with other therapies were significantly less likely to be alcohol drinkers than survivors who received chemotherapy. Future studies are needed to examine specific sites of radiation to try to explain why survivors treated with radiation are less likely to be alcohol drinkers than those receiving chemotherapy.

Age at diagnosis and cancer diagnosis were associated with alcohol drinking as well as binge drinking in the current study. Survivors diagnosed with cancer between 15 and 19 years age were significantly less likely to be binge drinkers than survivors diagnosed with cancer between zero and four years of age. Again, this likely reflects an older age at the time of study and a decrease in the prevalence of binge drinking at older ages. Survivors of Hodgkin's disease had 35% lower odds of being a binge drinker, than survivors of leukemia and the odds ratio was nearing statistical significance. This finding could be expected as survivors of Hodgkin's are at greater risk for late effects associated with their treatment and may be avoiding health risk behaviours [17, 25, 28, 202].

Results on the relationships between clinical factors and health behaviours must be interpreted with caution, as the sample sizes for some of the clinical groups were small. Future studies should look at measures of treatment intensities, and specific late effects if the information is available and with a sufficient sample size.

Public Health Implications

Although cancer survivors were smoking and drinking alcohol less than their peers, approximately one-fifth to one-quarter of survivors were engaging in these behaviours. This is of concern because of the late effects associated with cancer treatment and the increased risk for negative health outcomes. These findings suggest a need for greater emphasis on preventive education for smoking and heavy alcohol use in cancer survivors.

Interventions, education and health promotion programs may target high-risk groups and consider factors that may act as impediments to changing health risk behaviours. Male gender was found to be a risk factor for alcohol use and binge drinking. Factors associated with smoking and alcohol use in the pediatric cancer survivor and control groups were similar with low education, high stress and poor life satisfaction being the most consistent predictors.

Population-based interventions and health policies should be influential in changing pediatric cancer survivors' health behaviours because similar demographic and psychosocial factors as the general population were found to be associated with smoking and alcohol use. However, differences between cancer survivors and the general population also allow for targeted interventions. Previous intervention studies have focused on changing survivors' perceptions about their vulnerability to negative health outcomes or to improve their knowledge about their treatments, late effects and risks associated with health behaviours [103, 105, 106]. The interventions were found to be moderately effective and may be more effective if they consider demographic and psychosocial impediments such as low education and high chronic stress.

6.1 SEM Discussion

Following the logistic regression analyses a structural equation model was developed and tested to try to explain the complex relationships between the psychosocial variables and why pediatric cancer survivors would engage in concurrent use of alcohol and tobacco. Satisfaction with life was specified as a mediator in the model. It was hypothesized that physical health, mental health, self-esteem, education and stress would predict ones satisfaction with life which would in turn predict alcohol and tobacco use. It was hypothesized that satisfaction with life would only be a partial mediator and that there would still be significant direct effects from the psychosocial variables to concurrent use of alcohol and tobacco. It was also hypothesized that physical health, mental health and education would predict respondents' self-esteem. The model fit was adequate in both the cancer survivor and control groups; however, many of the paths were non-significant in the cancer survivors not supporting the specific hypotheses.

First a measurement model was specified and a multiple group confirmatory factor analysis was conducted to test for significance of factor loadings on the self-esteem and satisfaction with life latent constructs as well as for measurement invariance of the psychological scales across the cancer survivor and control groups. Results showed measurement invariance for the satisfaction with life and self-esteem scales providing support that items on the scales were measuring the same latent constructs in both cancer survivors and the control group. Once measurement invariance was determined the full structural model was tested in a multiple group structural equation modeling analysis. Results from this analysis showed that there were quite a few paths that were significant in the control group that were non-significant in the cancer survivors which suggested structural invariance. The models were then run separately in the cancer survivor and control groups.

When the structural model was tested in cancer survivors the model fit the data adequately. Still, there were a number of non-significant paths so the model was trimmed by sequentially removing non-significant paths beginning with the least significant. This resulted in a more parsimonious model that fit the data as well as the more complex model. Although the reduced model fit the data well in this sample it would need to be tested in other populations before results could be generalized to other samples and to the population of pediatric cancer survivors as a whole as the modifications were based on the data for the

current study sample only. Future research would need to be conducted to determine the plausibility of the model in other samples [203].

Results from the SEM analysis in cancer survivors showed that only the paths from chronic stress and education to concurrent use of alcohol and tobacco were significant. Having a high school education or less was associated with a greater likelihood of being a concurrent user of alcohol and tobacco compared to respondents with greater than a high school education. As chronic stress increased so did the probability of being a concurrent user of alcohol and tobacco. As discussed earlier high chronic stress and low education have been found to be strongly associated with substance use in the general population [84]. A study by Allison et al. [87] of young adults in Canada found that chronic stress and education were the most important predictors of daily smoking. Low education has also been associated with smoking and alcohol use in cancer survivors [3, 7, 8, 71]. In the logistic regression analysis low education and high chronic stress were also significantly associated with concurrent use of alcohol and tobacco in the cancer survivors. In both the SEM and logistic regression analyses education was more strongly associated with concurrent use of alcohol and tobacco than chronic stress for the cancer survivor and control groups.

Satisfaction with life was not a significant mediator or significantly associated with concurrent use of alcohol and tobacco in the SEM analysis in cancer survivors. This result was unexpected as the multivariate logistic regression analysis found satisfaction with life to be significantly associated with concurrent use of alcohol and tobacco in both the cancer survivor and the control groups. In the logistic regression analyses the sum scores from the satisfaction with life scale were categorized to create the variable and was assumed to have zero measurement error. In the SEM analysis the scale items were used as indicators of the latent construct in order to account for measurement error. It is known from previous research that assuming zero measurement error tends to attenuate the relationship between the exogenous variable and the dependent variable where one would be more likely to find a significant relationship when there truly wasn't one [204].

It is possible that even though cancer survivors were found to be equally dissatisfied with life as the control group, they were using alcohol and tobacco for other reasons not included in this model. The cancer survivors may have a greater desire to fit in with their peer groups after having been differentiated by their cancer experience. A qualitative study

found that among fourteen pediatric cancer survivors some survivors reported that they did not want to be viewed differently than the general population and among survivors who smoked it was commonly reported that they would rather enjoy life now and not worry about the future [205]. Future research should examine whether cancer survivor's peers and family members smoke and whether a reason for smoking is to be alike their peers.

Results from the final multivariate logistic regression analyses found that chronic stress and education were the strongest predictors of concurrent use of alcohol and tobacco in the cancer survivors. In the control group life satisfaction and education were the strongest predictors of concurrent use of alcohol and tobacco. These results are consistent with findings from the SEM analysis.

The path between satisfaction with life and concurrent use of alcohol and tobacco remained significant in the control group model. The structural equation model suggests that cancer survivors are truly different from the control group in predictors of concurrent alcohol and tobacco use after taking in to account the complex relationships between predictor variables. For the cancer survivors the paths from chronic stress and education to concurrent use of alcohol and tobacco were statistically significant and of greater magnitude than those in the control group. In the control group the direct path from chronic stress to concurrent use of alcohol and tobacco was non-significant. The cancer survivors had significantly lower education than the control group and reported lower levels of chronic stress.

A previous study of adolescents in the general population showed life satisfaction to be associated with substance use [116]. The SEM analysis in the control group found satisfaction with life to be significantly associated with concurrent use of alcohol and tobacco. It was also found to be a significant mediator where lower self-esteem, education, mental health and higher chronic stress predicted decreased life satisfaction, which in turn predicted concurrent use of alcohol and tobacco. The proposed model fit the control group data better and results were more consistent with the hypotheses. There was full mediation for the path from chronic stress to concurrent use of alcohol and tobacco through satisfaction with life. This suggests that chronic stress is related to concurrent use of alcohol and tobacco through life satisfaction. There was partial mediation for the paths from mental health, education and self-esteem to concurrent use of alcohol and tobacco through life satisfaction as the direct paths to concurrent use of alcohol and tobacco were also significant. This

suggests that there was a significant relationship between mental health, education and self-esteem that is not explained by life satisfaction.

The partial mediation observed for the self-esteem variable was unexpectedly found to be a suppression effect. The path between self-esteem and concurrent use of alcohol and tobacco was statistically significant and positive (standardized β=0.142, $p<0.05$). The indirect path from self-esteem to concurrent use of alcohol and tobacco through self-esteem was negative and statistically significant ($\alpha\beta$=-0.076, $p<0.05$). The indirect path suggests that as self-esteem decreases the likelihood of being a current smoker increases through decreased life satisfaction. The positive path from self-esteem to concurrent use of alcohol and tobacco suggests suppression may be occurring. Suppression occurs when the direct and mediated effects of an independent variable on a dependent variable have opposite signs. This is also called inconsistent mediation [189]. Here the indirect and direct effects have opposite signs (indirect effect=-0.076, direct effect=0.142) and the direct path is statistically significant. In this model inconsistent mediation suggests that if life satisfaction were held constant at its mean value self-esteem (adjusted for mental health, education and physical health) would be positively associated with concurrent alcohol and tobacco use. Suppression effects are expected to be spurious approximately half of the time due to sampling fluctuations but are not likely to be statistically significant. Here the suppression effect was statistically significant and should be interpreted with caution. It is possible that an alternative model that is not additive would better explain the relationship [114, 115].

In the control group, other than the path from self-esteem to concurrent use of alcohol and tobacco the direction of relationships were as hypothesized. Model fit was adequate and only a few paths were non-significant. Stressful life events and physical health were not found to be significantly associated with life satisfaction and chronic stress was not significantly associated with concurrent use of alcohol and tobacco. The stressful life events variable was not found to be associated with life satisfaction in the cancer survivors or the control group and may be due to the timing of administration of the questionnaire. Stressful life events tend to occur over shorter periods of time and may therefore not affect ones life satisfaction as much as an ongoing chronic stressor, or may not have occurred near the time that the respondents completed the questionnaire, affecting their recall [148]. Physical health was associated with life satisfaction in the cancer survivors and not the control group and

may be because the cancer survivors had significantly more respondents scoring lower on the physical health scale (Table 5). This finding has important implications as it suggests that pediatric cancer survivors have poorer physical health, likely related to their cancer treatment, and this is negatively impacting their life satisfaction.

Based on SEM results from this study, although largely exploratory, it appears that psychosocial predictors of concurrent smoking and alcohol use and their interrelationships were different in pediatric cancer survivors compared to the control group. The proposed model fit the data well in pediatric cancer survivors but a number of the hypothesized interrelationships were non-significant. Physical health, mental health, self-esteem, satisfaction with life and stressful life events were not significantly associated with concurrent alcohol and tobacco use either directly or indirectly through life satisfaction.

Public Health Implications

This exploratory model suggests that health policy and interventions should be focused on improving education in pediatric cancer survivors in order to improve their health behaviours as low educational attainment was strongly associated with smoking and alcohol use. Results from this study and previous research have shown that educational attainment is lower in pediatric cancer survivors compared to their peers and that they are more likely to have learning disabilities and require special education services [120, 199, 200]. During cancer treatment children and adolescents often miss a lot of school and may have difficulty adjusting when they return to the classroom. Additionally cognitive late effects associated with cancer treatment; especially for CNS cancers and brain tumours may hinder their academic success [120, 206, 207].

Reported chronic stress was significantly lower in cancer survivors compared to the control group in the current study but had a stronger association with concurrent use of alcohol and tobacco. It is possible that cancer survivors are not coping well with chronic life stressors and are engaging in substance use as a coping function [88, 89, 118]. Mackie et al. [208] found that pediatric cancer survivors may have more deficits in daily coping than their peers. Deficits in daily coping were associated with lower intelligence suggesting that cognitive late effects associated with treatment may affect coping abilities. Individuals with low self-esteem may also have low self-efficacy and poor coping abilities increasing their risk for

engaging in health risk behaviours [119]. Interventions and programs to help survivors deal with chronic life stress may help to reduce substance use in this population. Results from the SEM analysis showed that improving education and reducing chronic stress in pediatric cancer survivors may have the additional benefit of improving their life satisfaction and self-esteem.

6.2 Strengths, Limitations and Potential Biases

Strengths of this study were that it was a large national study of pediatric cancer survivors in Canada and it included a frequency matched control group from the general population, which most previous research lacked. The study examined important psychosocial predictors of smoking and alcohol use and the concurrent use of tobacco and alcohol, which have not been previously studied in pediatric cancer survivors. Statistical methods took into account the categorical nature of outcome variables and structural equation modeling allowed for the analysis of complex relationships between predictor and outcome variables.

Although the overall study had a large sample size, most of the participants were white making it difficult to assess the association between ethnicity and smoking and alcohol use, which has been shown to have a significant association in studies of the general population. It was also difficult to assess the association between clinical factors and health risk behaviours as some clinical groups had small sample sizes. However, the sample of pediatric cancer survivors included in the current study were representative of pediatric cancer survivors in Canada [128].

A limitation of this study is that the use of cross sectional data does not allow for conclusions about temporal relationships even with structural equation modeling. Structural equation models, although once termed "causal models", like other statistical methods cannot determine causality. Similarly, tests of mediation may be biased with cross-sectional data, as you cannot know which factor actually preceded another [209].

A potential limitation of this study was that data was collected from self-report questionnaires that required respondents to recall past health risk behaviours. This could lead to recall bias if participants could not accurately recall their past behaviours and potential underreporting or over reporting of health risk behaviours if the respondent

perceived the behaviour to be socially undesirable or desirable by society. However, Williams et al.[210] found that adolescents accurately reported smoking behaviours, as verified by plasma cotinine levels, as long as participants were assured that their reports would remain confidential. The Late Effects Study researchers mailed questionnaires to participants and ensured confidentiality.

Another potential bias may occur if childhood cancer survivors were less likely to report their health risk behaviours because they were aware that they are at increased risk for negative health outcomes due to their treatment. Underreporting may then be more likely to occur in childhood cancer survivors compared to the controls. However, Bashore [93] and Kadan-Lottick, et al.[94] found that childhood cancer survivors lacked knowledge about their cancer diagnosis, treatment and the late health complications associated with their treatment and therefore would not likely underreport their behaviours.

Misclassification of participants may have also occurred for some of the covariates that had missing data due to single imputation of missing values. However, the percentage of missing data for each covariate was small and would not likely have introduced a large amount of bias. Cases deleted from the study had similar demographic characteristics of included cases.

Selection bias is another bias that could affect the current study, as response rates were low. However, Shaw et al. [128] examined the late effects data and determined that cancer survivor respondents were a good representation of childhood cancer survivors in Canada and controls good representatives of age matched Canadians who had never had cancer. Among childhood cancer survivors there were slightly fewer survivors of germ cell tumours, carcinomas and intense or multiple series of treatments. Controls had slightly higher level of education and income based on census data but otherwise were similar to the general population [128]. The current study also identified that the control group aged 26 to 30 had a lower prevalence of binge drinking than in the general population.

A limitation of structural equation modeling is that there may be many alternative models that would fit the model as well or better than the specified model. All models that one could specify cannot be expected to exactly fit the data and will be somewhat incorrect but may be a close approximation of the data [170]. Even if a model has good fit important variables omitted from the model can result in biased parameter estimates and inaccurate

standard errors [209]. The Late Effects Study did not collect information on smoking and alcohol use in peers and family members. Future studies including this information would be important as having family or friends that smoke has been identified as an important predictor of smoking and alcohol use in adolescents from the general population [89-91]. As well, the current study did not collect data on the household income of all participants and future studies should include this variable as it has been associated with substance use in pediatric cancer survivors and would be a better measure of socioeconomic status than personal income [7, 8]. Only single measures were available for some of the important constructs included in the structural equation model. Having multiple indicators of each construct is important to reduce bias created by measurement error.

The generalizability of the study findings is limited by the age of the cohort and the country where the study was conducted. The Late Effects Study included a cohort of cancer survivors diagnosed with cancer in Canada between 1981 and 1990. Results may not be generalizable to cancer survivors in other countries, as substance use is known to differ by geographical region.

6.3 Conclusions

This was the first known national study of smoking and alcohol use in Canadian pediatric cancer survivors. A substantial proportion of survivors were smoking, drinking alcohol, binge drinking and using both tobacco and alcohol in the current study. Engaging in a healthy lifestyle may be one of the only measures survivors can take to prevent health complications related to cancer treatments they received. This signifies a need for greater emphasis on preventive education on the risks of smoking and heavy alcohol use.

This study also identified important risk factors for smoking and alcohol use including low education, high stress and poor life satisfaction. Male gender was also an important risk factor for alcohol use and binge drinking. Interventions, preventive education and health promotion programs may target high-risk groups and consider factors that may act as impediments to changing health risk behaviours. Low education and high stress were identified as the strongest predictors of smoking and alcohol use in the cancer survivors. Interventions may target survivors' ability to cope with stress, as it is a modifiable factor associated with substance use. Interventions and programs to help improve survivors

educational attainment and ability to cope with chronic life stress may help to reduce substance use in this population and have the additional benefit of improving their life satisfaction and self-esteem.

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APPENDICES

Appendix 1: Means, standard deviations, skewness, kurtosis and Cronbach alpha statistics for each psychological scale by group.

Cancer Survivors					
Scale	Mean	SD	Skewness	Kurtosis	Cronbach Alpha
Satisfaction With Life	23.93	7.46	-0.69	- 0.30	0.898
Self-esteem	26.00	4.27	-1.37	1.91	0.835
Chronic Stress	9.46	7.03	1.15	1.60	0.829
Stressful Life Events	3.93	4.59	1.54	2.79	0.529
Physical health (SF-36)	52.64	8.43	-1.42	2.12	0.773
Mental health (SF-36)	48.36	10.64	-1.05	0.59	0.823
Control Group					
Scale	Mean	SD	Skewness	Kurtosis	Cronbach Alpha
Satisfaction With Life	24.12	7.29	-0.61	-0.49	0.906
Self-esteem	26.13	4.13	-1.40	2.06	0.852
Chronic Stress	10.07	6.79	0.89	0.73	0.808
Stressful Life Events	4.01	4.20	1.62	2.11	0.425
Physical health (SF-36)	53.86	7.14	-1.46	3.14	0.709
Mental health (SF-36)	48.15	10.24	-1.13	1.07	0.806

SD=Standard Deviation

Appendix 2: Results from the tolerance and variance inflation factor tests for collinearity among independent variables

Variable	TOL *	VIF †
Age	0.341	2.93
Gender	0.896	1.11
Education	0.688	1.45
Ethnicity	0.977	1.02
Personal Income	0.682	1.47
Special Education/LD Program	0.901	1.09
Physical Health	0.867	1.15
Mental Health	0.636	1.57
Satisfaction with life	0.627	1.59
Self-esteem	0.666	1.50
Chronic stress	0.736	1.36
Stressful life events	0.891	1.12
Age diagnosis	0.364	2.75
Type cancer	0.937	1.07
Type treatment	0.931	1.07
Relapse	0.947	1.06

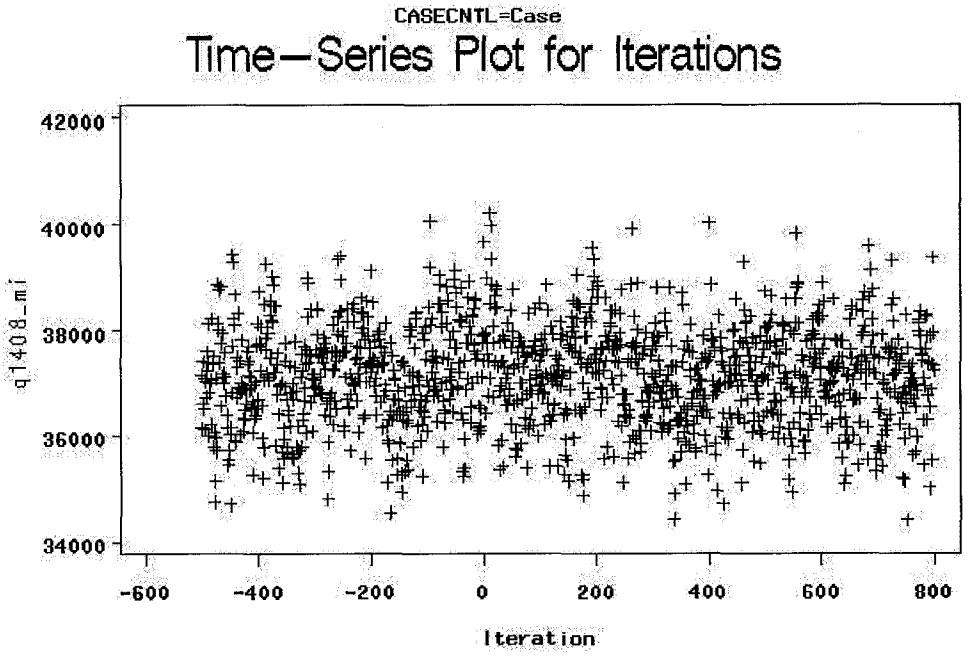
* Tolerance statistic: if less than 0.20, may be concerned about collinearity and if less than 0.10 indicates serious collinearity [167].

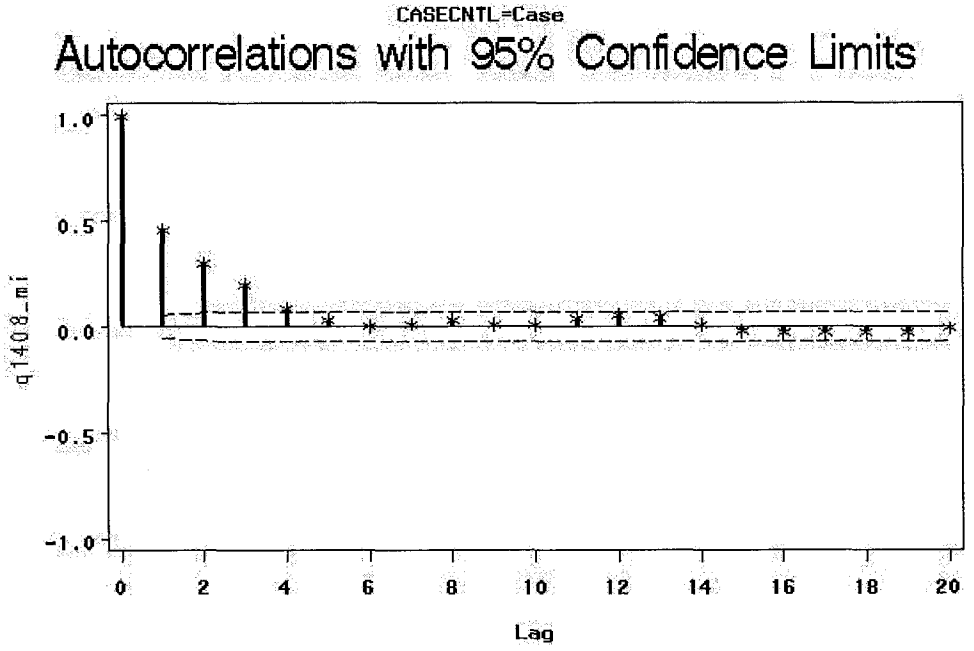
† Variance Inflation Factor: no criteria but a value of 2.5 to 10 may indicate collinearity.

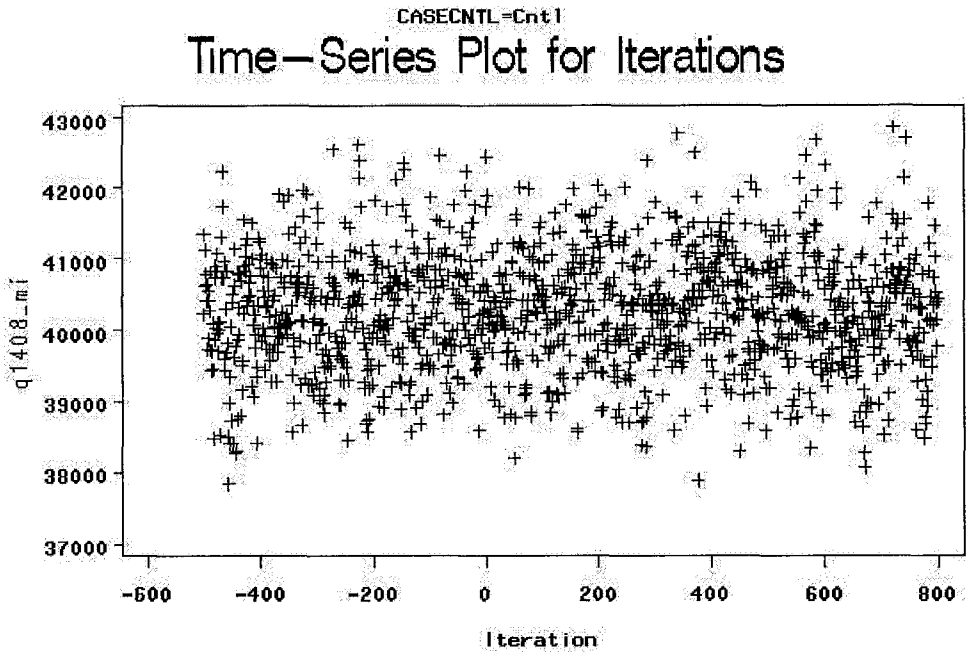
Appendix 3: Quantity and percentage of missing data by variable and missing data treatment.

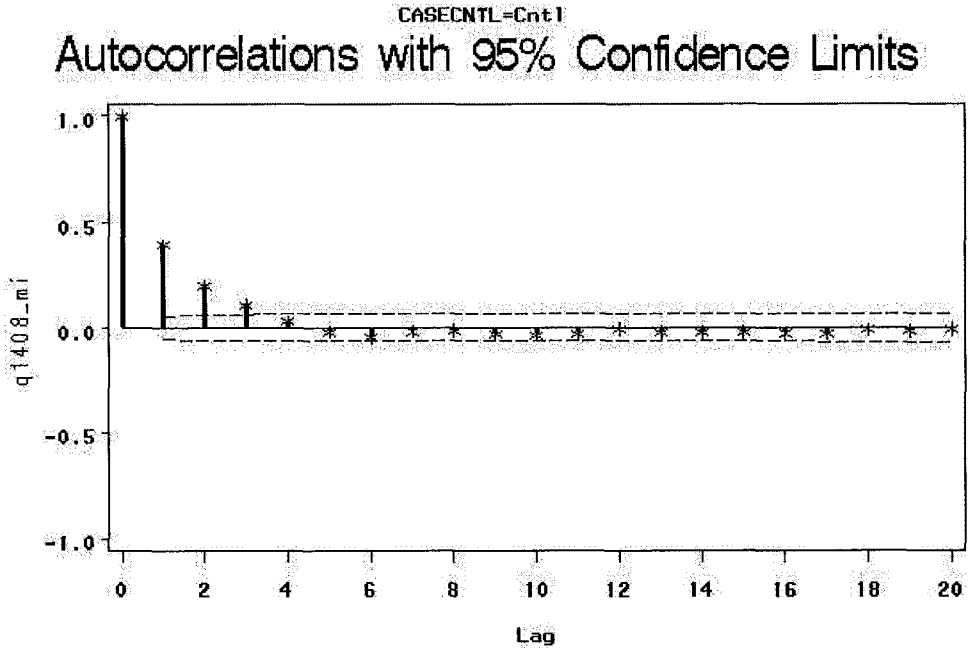
Variable	Missing data (n)	%	Cases (n)	Controls (n)	Type of Variable	Missing Data Treatment
N=2811			1334	1477		
Smoking	15	0.53	8	7	Categorical	Listwise Deletion & assume that 11 other cases who had smoked at least 100 cigarettes in life were current smokers
Alcohol use	118	4.20	57	61	Categorical	Listwise Deletion of those that could not be categorized as abstainers, light or moderate to heavy drinkers.
Total Deleted	*133*	*4.73*	*65*	*68*		
N=2678			1269	1409		
Mental Health	47 (after imputation)	1.75	26	21	Likert Scale	Mean imputation by person for >50% of data present, followed by listwise deletion
Physical Health	47 (after imputation)	1.75	26	21	Likert Scale	Mean imputation by person for >50% of data present, followed by listwise deletion
Self-Esteem	19 (after imputation)	0.71	9	10	Likert Scale	Mean imputation by person for >50% of data present, followed by listwise deletion
Satisfaction With Life	15 (after imputation)	0.56	4	11	Likert Scale	Mean imputation by person for >50% of data present, followed by listwise deletion
Total deleted	*208*	*7.4*	*103*	*105*		
N=2603			1231	1372		
Age	0	0	0	0	Categorical	None
Gender	0	0	0	0	Dichotomous	None
Ethnicity	69	2.65	25	44	Categorical	Recode unknown group as white as ~84% of population is white.
Personal Income	358	13.75	164	194	Categorical	Recode unknown group as median category.
Education	49	1.88	28	21	Categorical	Recode unknown group as less than high school to be more conservative.
Stressful Life Events	46	1.77	27	19	Likert Scale	Assume that those who left questions blank had no stress.
Chronic Stress	133	5.11	71	62	Likert Scale	Assume that those who left questions blank had no stress.
Special Ed/LD	162	6.22	86	76	Dichotomous	Recode missing group as "no"

Appendix 4: Autocorrelations and time series plots for cancer survivors (cases) and the control group for the household income variable (q1408_mi).









Appendix 5: Items from Rosenberg's Self-Esteem Scale that were included in the Late Effects Study Questionnaire [144].

The following statements also describe the ways people sometimes feel about themselves. For each statement, check the box that indicates how strongly you agree or disagree.	
Scale Items	Possible Answers
a) I feel that I have a number of good qualities. b) I feel that I'm a person of worth at least equal to others. c) I am able to do things as well as most other people. d) I take a positive attitude toward myself. e) On the whole I am satisfied with myself. f) All in all, I'm inclined to feel that I'm a failure.	Strongly disagree, mildly disagree, neither agree nor disagree, mildly agree, strongly agree.

Appendix 6: Items from Diener's Satisfaction With Life Scale that were included in the Late Effects Study Questionnaire [142].

Please indicate how strongly you agree with each of the following statements.	
Scale Items	Possible Answers
a) In most ways my life is close to my ideal. b) The conditions of my life are excellent. c) I am satisfied with my life. d) So far I have gotten the important things I want in life. e) If I could live my life over, I would change almost nothing.	Strongly disagree, disagree, slightly disagree, neither agree nor disagree, slightly agree, agree, strongly agree.

Appendix 7: Unstandardized structural parameter estimates, standard errors and 95% confidence intervals from the single group SEM analysis in cancer survivors.

Concurrent use of alcohol and tobacco			
Predictor	Estimate	95%CI	Standard error
Less than high school †	0.454*	0.242, 0.667	0.109
High school †	0.223*	0.024, 0.421	0.101
Chronic stress	0.025*	0.012, 0.039	0.007
Stressful life events	0.017	-0.002, 0.035	0.009
Mental Health	0.001	-0.009, 0.011	0.005
Physical Health	-0.005	-0.015, 0.005	0.005
Self-Esteem	0.007	-0.109, 0.122	0.059
Satisfaction with life	-0.035	-0.116, -0.047	0.042
Satisfaction with life			
Predictor	Estimate	95%CI	Standard error
Less than high school †	-0.528*	-0.831, -0.224	0.155
High school †	-0.233	-0.510, 0.044	0.141
Chronic stress	-0.054*	-0.073, -0.034	0.010
Stressful life events	0.021	-0.004, 0.046	0.013
Mental Health	0.039*	0.024, 0.055	0.008
Physical Health	0.037*	0.023, 0.051	0.007
Self-Esteem	0.679*	0.452, 0.905	0.116
Self-esteem			
Predictor	Estimate	95%CI	Standard error
Less than high school †	-0.393*	-0.681, -0.105	0.147
High school †	-0.320*	-0.581, -0.059	0.133
Mental Health	0.071*	0.051, 0.091	0.010
Physical Health	0.027*	0.014, 0.040	0.007

*$p<0.05$

† Greater than high school education is reference group

Appendix 8: Unstandardized structural parameter estimates, standard errors and 95% confidence intervals from the single group SEM analysis in cancer survivors with non-significant paths removed.

Concurrent use of alcohol and tobacco			
Predictor	Estimate	95%CI	Standard error
Less than high school †	0.479*	0.271, 0.686	0.106
High school †	0.226*	0.039, 0.432	0.100
Chronic stress	0.027*	0.014, 0.040	0.007
Satisfaction with life			
Predictor	Estimate	95%CI	Standard error
Less than high school †	-0.524*	-0.826, -0.222	0.154
Chronic stress	-0.053*	-0.073, -0.034	0.010
Mental Health	0.039*	0.024, 0.054	0.008
Physical Health	0.037*	0.022, 0.051	0.007
Self-Esteem	0.686*	0.458, 0.914	0.116
Self-esteem			
Predictor	Estimate	95%CI	Standard error
Less than high school †	-0.391*	-0.679, -0.104	0.147
High school †	-0.415*	-0.678, -0.153	0.134
Mental Health	0.071*	0.051, 0.091	0.010
Physical Health	0.027*	0.014, 0.040	0.007

*p<0.05

† Greater than high school education is reference group

Appendix 9: Unstandardized structural parameter estimates, standard errors and 95% confidence intervals from the single group SEM analysis in the control group.

Concurrent use of alcohol and tobacco			
Predictor	Estimate	95%CI	Standard error
Less than high school †	0.380*	0.190, 0.569	0.097
High school †	0.180*	0.004, 0.355	0.090
Chronic stress	0.012	-0.001, 0.012	0.007
Stressful life events	0.019*	0.001, 0.037	0.009
Mental Health	-0.012*	-0.024, -0.002	0.005
Physical Health	-0.013*	-0.022, -0.003	0.006
Self-Esteem	0.122*	0.015, 0.229	0.055
Satisfaction with life	-0.108*	-0.178, -0.039	0.035
Satisfaction with life			
Predictor	Estimate	95%CI	Standard error
Less than high school †	-0.387*	-0.658, -0.116	0.138
High school †	-0.130	-0.366, -0.130	0.120
Chronic stress	-0.085*	-0.104, -0.065	0.010
Stressful life events	-0.019	-0.043, 0.006	0.012
Mental Health	0.027*	0.014, 0.041	0.007
Physical Health	0.009	-0.005, 0.024	0.007
Self-Esteem	0.602*	0.412, 0.791	0.097
Self-esteem			
Predictor	Estimate	95%CI	Standard error
Less than high school †	-0.382*	-0.616, -0.149	0.119
High school †	-0.228*	-0.435, -0.021	0.106
Mental Health	0.058*	0.043, 0.074	0.008
Physical Health	0.032*	0.019, 0.046	0.007

*$p<0.05$

†Greater than high school education is reference group

Appendix 10: Unstandardized structural parameter estimates, standard errors and 95% confidence intervals from the single group SEM analysis in the control group with non-significant paths removed.

Concurrent use of alcohol and tobacco			
Predictor	Estimate	95%CI	Standard error
Less than high school †	0.379	0.189, 0.570	0.097
High school †	0.200	0.023, 0.377	0.090
Stressful life events	0.021	0.003, 0.039	0.009
Mental Health	-0.012	-0.022, -0.003	0.005
Physical Health	-0.014	-0.025, -0.003	0.006
Self-Esteem	0.142	0.034, 0.249	0.055
Satisfaction with life	-0.124	-0.190, -0.058	0.034
Satisfaction with life			
Predictor	Estimate	95%CI	Standard error
Less than high school †	-0.382	-0.652, -0.111	0.138
Chronic stress	-0.085	-0.104, -0.066	0.010
Mental Health	0.027	0.014, 0.040	0.007
Self-Esteem	0.614	0.425, 0.803	0.096
Self-esteem			
Predictor	Estimate	95%CI	Standard error
Less than high school †	-0.381	-0.615, -0.148	0.119
High school †	-0.277	-0.486, -0.068	0.107
Mental Health	0.058	0.043, 0.074	0.008
Physical Health	0.035	0.022, 0.049	0.007

*$p<0.05$

† Greater than high school education is reference group