CANCER KNOWLEDGE IN ADOLESCENT AND YOUNG ADULT SURVIVORS

KNOWLEDGE OF DIAGNOSIS, TREATMENT AND LATE EFFECTS IN ADOLESCENT AND YOUNG ADULT SURVIVORS OF CHILDHOOD AND ADOLESCENT CANCER

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A Thesis Submitted to the School of Graduate Studies in Partial Fulfilment of the Requirements for the Degree Master of Science

McMaster University, Hamilton, Ontario - Master of Science in Health Research Methodology (2013)

TITLE: Knowledge of Diagnosis, Treatment and Late effects in Adolescent and Young Adult Survivors of Childhood and Adolescent Cancer

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Number of Pages: xi, 133

Abstract

Purpose: While most children diagnosed with cancer survive their initial disease, the intensive treatments they receive place them at risk for late effects. Long-term follow-up (LTFU) care is recommended for cancer survivors for surveillance and early detection of late effects. Knowledge, or lack thereof, regarding diagnosis, treatment and late effects is an important barrier and/or facilitator for attending LTFU care in adolescent and young adult (AYA) cancer survivors. The purpose of our study was to examine the extent of knowledge in Canadian AYA survivors of childhood and adolescent cancer, and identify factors associated with such knowledge.

Methods: Survivors of childhood and adolescent cancer, between the ages of 15 and 26 years, were recruited from three pediatric oncology centres. Patients were invited to participate in the study through mail and clinic recruitment. A questionnaire booklet, including the Cancer Knowledge Survey that asked questions about cancer, treatment and late effects, was administered to collect necessary information. Clinical data was extracted from hospital records to validate participants' answers.

Results: 250 (response rate= 75.5 percent) out of 331 patients invited to participate completed the questionnaire booklet. 18 (7.2 percent) participants lacked information regarding their type of cancer, whereas 25 (10.3 percent) participants were 'not knowledgeable' of their treatment. Lack of knowledge regarding treatment was associated

with being non-white [odds ratio= 0.3 (0.2-0.6)] compared with white. Also, 83 (33.5 percent) participants were unaware of their late effects. Lack of knowledge regarding late effects was associated with younger age [odds ratio= 1.2 (1.1-1.3)], and having leukemia compared with embryonal tumour [odds ratio= 3.41 (1.10-10.6)].

Conclusion: Results from this study highlights important knowledge deficits, especially in terms of understanding risk of late effects from cancer treatments. Findings from this study can be used to design programs and interventions aimed at increasing cancer knowledge in AYA cancer survivors.

Acknowledgements

Foremost, I would like to express my gratitude to my supervisor Dr. Anne F. Klassen for being a tremendous mentor, and providing guidance throughout the process of my master thesis, especially during writing. I would also like to thank Dr. Ronald Barr and Dr. Lehana Thabane for their continued assistance and expert advice for this research project. Furthermore, I would like to acknowledge Rebecca Wang, Meghna Dua, Leigh-Anne Ward, Marion Nelson and Elena Tsangaris for their help with data collection and entry. Also, I am grateful to the participants of this study who took the time to complete the questionnaire. Lastly, I would like to thank my wonderful parents, sisters and brother-in-law for keeping me harmonious throughout the two years of the master program.

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Figures and Tables

Abbreviations and Symbols

Abbreviations/Symbols	Definition
LTFU	Long-term follow-up care
AYA	Adolescent and young adult
CIHR	Canadian Institute of Health Research
CCSS	Childhood Cancer Survivor Study
HCP	Health care provider
PCP	Primary health care provider
SMART	Social-ecological Model of AYA Readiness for Transition
CNS	Central nervous system
ALL	Acute lymphoblastic leukemia
RCT	Randomized controlled trial
ICC	Intra-class correlation: measure of reliability of ratings.
Kappa	A measure of reliability of ratings.
AML	Acute myeloid leukemia
APML	Acute promyelocytic leukemia
ITR	Intensity of treatment rating
ITR-2	Intensity of treatment rating scale 2.0
REB	Research ethics board
CI	Confidence interval

R^2	Coefficient of determination
POGO	Pediatric Oncology Group of Ontario
CE&B	Department of Clinical Epidemiology and Biostatistics
LMPSU	Laboratory Medicine and Pathobiology Student Union

Declaration of Academic Achievement

I, Iqra Syed, declare that I have written this thesis on my own, without unlawful assistance of anyone else. Sources used for this thesis are perceptibly marked and citations are provided at the end of this document. The work presented in this thesis was not submitted previously to another examination committee or for publication.

Chapter 1: Introduction

This chapter provides an overview of the study 'Knowledge about diagnosis, treatment and late effects in adolescent and young adult (AYA) survivors of childhood and adolescent cancer' by presenting relevant background and a rationale for the goals of the study. To begin, a brief description of cancer care provided in Canada to pediatric populations is given. Following this is a set, list of the varying definitions used to describe AYA survivors globally. The chapter then goes on to describe the potential health-related complications for which survivors of childhood and adolescent cancer are at risk, and the importance of seeking long-term follow-up (LTFU) care in managing the potential late effects. A review of barriers and facilitators to attending LTFU care, with a focus on knowledge of cancer history and late effects, are presented to establish the context in which the goals of the current study are important. Limitations of literature detailing the investigation into patient knowledge about diagnosis, treatment, and late effects, as well as factors associated with knowledge in pediatric cancer survivors are discussed to highlight the importance of the present study. The chapter ends with the rationale, objectives and research questions of the study.

1.1 Survivors of Childhood and Adolescent Cancer

In 2012, an estimated 186,400 new cases of cancer were expected to be diagnosed in Canada, 1,400 (0.75 percent) of which were estimated to be children and adolescents between the ages of 0 and19 years.[1] At a Pan-Canadian Initiative meeting sponsored by

the Canadian Institutes of Health Research (CIHR), pediatric cancer patients were defined as patients under the age of 15 years, whereas adolescents were defined as between the ages 15 and 19 years.[2] In Canada, the upper age limit for admission to one of the 17 pediatric oncology centres is generally before the eighteenth birthday. In addition, some adolescents between the ages of 15 and 17 years, and those over the age of 17 years are treated at an adult facility.

Upon diagnosis, a cancer patient undergoes treatment and remains in active care until treatment is completed. The most common forms of treatment for childhood and adolescent cancer are chemotherapy, radiation therapy, surgery and transplant. These forms of treatment are given alone or in combination depending on the age of the child, type, and severity of their cancer.[3] Upon treatment completion and subsequent entry into remission, the child or adolescent is considered to be 'cured'.

The relative five year survival rate for childhood and adolescent cancer has increased from 75 percent to 82 percent from the years 1990 to 2004.[4] Although survival rates have improved, cancer survivors are at risk for developing various health problems in their adult lives, known as the 'late effects' of cancer treatment. These risks are associated with the type and intensity of the treatments received, which can have an impact on a survivor's physical, social and emotional health in the long-term. The risk of developing late effects as a result of cancer treatment poses new challenges in survivorship care.

1.2 Defining Adolescent and Young Adult (AYA) Survivors

The definition for cancer 'survivor' remains ambiguous. In some of the cancer literature the definition for cancer 'survivor' takes into account both the patient and the family, since the family is also highly impacted by the cancer experience. In other definitions, 'survivor' is focused on the patient, who has received treatment and survived for at least five years.[5] Others define survivor as a person who has completed active treatment of cancer. A view that has become more prominent over the years is that a person becomes a survivor at the time of diagnosis.[6] The definition being used currently to describe cancer survivors and survivorship depends mostly on the purpose (e.g., policy related, epidemiological research) for which the definition may be being used.[5,6]

As mentioned above, a commonly accepted lower and upper age limit for adolescent is 15 to 19 years of age, respectively.[2] The upper limit of what constitutes 'young adult' is highly variable.[7] While the National Cancer Institute in the U.S. defines the upper limit of age for young adults as 39 years,[8] the Canadian Cancer Society defines it to be 29 years.[9] Moreover, Eurocare, which is the largest collaborative research project in Europe, defines the AYA group as having an age range of 15 to 24 years.[10,11] This variability in age of AYA presents a challenge in conducting research specific to these survivors and the general application of survivor research.

1.3 Late Effects and Long-Term Follow-Up (LTFU) Care in Survivors

Research has established that survivors of childhood and adolescent cancer are at risk of developing late effects from their cancer treatments, which can severely impact their

long-term health and quality of life.[12.13,14,15,16,17,19,20,21,22,23,24] Due to the potential long life and productive years ahead of survivors of childhood and adolescent cancer, it is important to investigate potential risks to the long-term health of these survivors after receiving intensive treatments.

The Childhood Cancer Survivor Study (CCSS) is an ongoing initiative that aims to assess the long-term impact of cancer and treatment on the health of survivors. This initiative includes 25 centres across the U.S. and Canada. The CCSS has collected data on almost 15,000 survivors, who had survived their cancer by at least five years, diagnosed before 21 years of age and were diagnosed between the years 1970 and 1986.[18] Questionnaires were sent to survivors to collect demographic and treatment related information, as well as a number of important health outcomes (e.g., pregnancy outcomes, quality of life, psychosocial function).[18] Publications using the full CCSS cohort included reports that adult survivors of childhood cancer were at an increased risk for the following late effects: mortality;[19] second malignancy;[20] various chronic health conditions (e.g., cardiomyopathy, osteoporosis);[15] complications related to pulmonary function;[21] and poor health status.[22]

Other studies have reported similar findings to those of the CCCS,[14,16,23] in addition to risks of cardiotoxcity,[12,24] and growth and kidney problems.[16] The incidence of late effects was shown to vary by type of cancer, type of treatment, and other cancer related factors, such as age at diagnosis. In addition, it was reported in a study of late effects with toxicity grades in young adult survivors of childhood cancer, that as many as two thirds of survivors developed at least one late effect as a result of their cancer treatment.[25]

Since cancer survivors are at an increased risk for long-term health complications, it is imperative that measures be taken to improve health outcomes. To prevent and monitor occurrence of potential late effects from cancer treatments, and provide needed support to AYA survivors of childhood and adolescent cancers, LTFU care is recommended by researchers, health care providers (HCPs) and cancer agencies in Europe, U.S. and Canada.[26,27,28,29]

In Canada, 12 of 17 pediatric centres have a formal program or clinic dedicated to providing specialized survivorship care to pediatric survivors.[29] However, once these survivors turn 18 years of age, only six of the 17 pediatric centres have access to specialized LTFU care for adult survivors of childhood and adolescent cancer, while the remaining 11 centres transfer care to the survivor's primary health care provider (PCP).[29] Survivors between the ages of 15 and 17 years who were initially treated at an adult centre do not have access to any survivorship care.[30]

In Canada, three main models of transition exist to establish transfer of care from pediatric to adult LTFU care. These are set up to ensure childhood cancer survivors continue to receive LTFU care as adults in order to continue the surveillance of potential late effects.[27, 30] The three models of care include: 1) continued care in the pediatric LTFU program as adults; 2) transition to young adult program in an adult setting; and 3) transition to a community physician with continued communication with specialists.[28,29,55] In the continued care program, childhood cancer survivors continue to attend the same pediatric setting with the aim of LTFU care shifting to address issues important to young adults. In the second model of care, survivors move from the pediatric centre to a linked

adult facility. In the third model of care, survivors are transitioned to their family physician after completion of cancer treatment with additional contact maintained between the family physician and an oncologist.[55]

The purpose of providing survivorship care to patients are multifold and include the following: to manage physical, mental and reproductive health of cancer survivors; to monitor and screen for late effects; to provide psychosocial support relevant to developmental needs; to provide survivors with necessary information about their cancer history and late effects; and to provide counsel regarding ways to reduce risk to health.[30,31] Attendance at LTFU care is especially important for AYA cancer survivors because cancer treatment impacts survivors not just biologically (e.g., fertility, sexuality), but also psychosocially (e.g., emotional well-being, memory problems, employment, education progress).[30,32] In addition, survivors potentially have a long life ahead of them, thus it is important to ensure that forthcoming years are productive and that quality of life is not compromised by the cancer experience.

However, it is important to note that not all survivors access LTFU care. Analysis of data from 9,434 participants from the CCSS showed that only 42 percent of patients reported a cancer related visit in two years prior to the data collection. In addition, cancer related visits were lower in patients over the age of 35 years (38 percent), compared with those aged 18 or 19 years (49 percent).[33] This finding suggests that many adult survivors of childhood cancer do not receive cancer specific health care. There may be reasons why transition to LTFU care, which happens about two to five years after cessation of active treatment,[30] does not occur for many survivors. Research that seeks to identify and

understand the key barriers and facilitators associated with seeking cancer related LTFU care in AYA survivors of childhood and adolescent cancer is needed to identify which factors to target with interventions.

1.4 Barriers and Facilitators to LTFU Care: Theoretical Framework

A number of researchers in the U.S. and Canada have identified barriers and facilitators that adolescents and/or adult survivors of childhood cancer face in seeking LTFU care.[28,29,30,31,34] A theoretical framework,[31] combining aspects from three existing models (i.e., Health Belief Model,[35] Health Locus of Control Model,[36] and Behavioural Model of Utilization, [37]) that explain health behaviours in the general population, was adapted to account for barriers and facilitators related to seeking LTFU care in adult survivors of childhood cancer. This theoretical framework includes barriers and facilitators related to the health care system, the HCP and the cancer survivors (see Figure 1).

Barriers and facilitators related to the health care system are categorized into the following three major domains: health insurance (which is less applicable to the survivors in Canada); health care system (e.g., different models of care for LTFU care); and national policies that affect longitudinal health care for cancer survivors.[31] In addition, barriers and facilitators related to the HCP are grouped under the following major categories: the beliefs a HCP has regarding the value of taking preventative measures; the amount of knowledge a HCP has about a patient's risk for late effects; the attitudes of HCP towards survivors; and the organizational structure of the HCP's practice.[31]

Much of the focus in the literature has been towards survivor related barriers and facilitators of LTFU care.[31,34] In the theoretical model discussed here, the survivor related factors are categorized into the following five major domains (each with its own sub-domains and associated barriers and/or facilitators): 1) cancer experience (further described below); 2) health beliefs (i.e., motivation to seek LTFU care, perceived risk and severity of late effects); 3) internal modifiers (e.g., socio-demographic factors such as age and gender); 4) external modifiers (e.g., impact of family and peers on survivor seeking LTFU care); and 5) health locus of control (i.e., survivor's belief regarding the control he or she has in preventing cancer treatment related late effects).[31]

1.4.1 Past Cancer Experience

Past and present experiences of having a chronic health condition such as cancer are important predictors of attending LTFU care. These experiences include psychological factors (e.g., fear, worry) that may act as barriers or facilitators in seeking risk-based survivorship care. In addition, the cancer experience is shaped by knowledge of late effects associated with cancer treatment, which might be initially delivered by the HCP or transferred from parent to the child depending on the age at diagnosis. A study conducted in Japan that investigated factors in order to understand why some childhood cancer survivors stopped attending LTFU care reported that only 31 percent of survivors and 27 percent of guardians received information about possible risks to their future health from cancer treatment to their future health.[38] In addition, when asked about the reasons for not attending specialized risk-based survivorship care, 46 percent believed that they did not need to consult a physician since they were in good health.[38] These findings suggest that

not only did survivors have inadequate information concerning risks of late effects, but they also believed themselves to be in good health and did not realize the potential complications they may experience due to the cancer treatment received. The cancer experience, including psychological factors and knowledge of risks, directly impacts the motivation of seeking LTFU care and the level of perceived seriousness of risks in cancer survivors (see Figure 1).

1.4.2 Barriers and Facilitators to Transition

AYA survivors of childhood and adolescent cancer face additional challenges during the process of transitioning from pediatric to adult LTFU care settings. Many survivors who may attend LTFU care in pediatric setting are lost to follow-up when they turn 18 years of age for various reasons. The Social-ecological Model of AYA Readiness for Transition (SMART) was developed to account for the process of transition readiness in AYA patients with chronic illnesses.

The SMART was developed using literature, expert opinion, and pilot data collected from a sample of survivors describing barriers to transition experienced by childhood cancer survivors.[39] This model includes factors that are pre-existing and less amenable to change, and factors that are modifiable and can be targeted through interventions to improve readiness to transition (see Figure 2). SMART was developed for survivors of all chronic illnesses, but it has particular applicability to the AYA childhood cancer survivors given that the pilot data was collected on childhood cancer survivors.[39] Transition readiness is also particularly important to childhood cancer survivors as they are required to maintain their engagement in prevention and management services. Adult

survivors of childhood cancer are required to continue seeking LTFU care because late effects from cancer treatments often manifest many years after the initial diagnosis. Changing care providers during transition may put this group at risk of being lost to LTFU care.

Pre-existing factors in the SMART include the following: socio-demographic and culture factors (i.e., age, race, socioeconomic status, culture of family, and community); access to insurance (not relevant to the Canadian healthcare system); health status and risks (e.g., late effects); and neuro-cognition status. These pre-existing factors not only affect readiness to transition directly, but also by affecting the modifiable factors, which in turn impact readiness to transition.[39] Modifiable factors that can be targeted through interventions include the following: developmental maturity; skills (i.e., skills related to self-management); beliefs or expectations related to the process of transition and adult LTFU care; goals of the transition process; relationships among patients, parents and HCPs; psychological functioning; and knowledge of disease and risks to health (see Figure 2).[39] Like barriers to LTFU care, knowledge of disease and potential late effects are important factors in the process of transitioning from pediatric to adult LTFU care.

Unlike patients with other chronic childhood conditions, many cancer survivors may feel healthy and therefore may not see the importance of attending LTFU care for surveillance of late effects. A study looking to understand barriers to long-term risk-based follow-up care from the perspective of AYA cancer survivors used a modified Delphi technique and showed that providing knowledge of cancer history and risk of late effects was an important way to motivate survivors to attend LTFU care.[34] Furthermore, it is

important to provide this information to survivors at a young age to ensure they have appropriate time to learn self-management skills and thereby assume responsibility for their ongoing healthcare as adults.

As mentioned above, in Canada, 11 of 17 pediatric centres transition the majority of their cancer survivors to PCP who have taken on their survivorship care. However, given how rare it is for a PCP to care for a childhood cancer patient throughout their cancer trajectory, many may have limited knowledge of the survivor's cancer history and how to monitor for potential late effects.[40] Survivors who lack adequate information about their cancer history and future risks related to their treatment may not have the information they need to advocate for the ongoing surveillance needed to manage their healthcare in the community through a PCP. Moreover, inadequate knowledge of late effects may prevent survivors from ensuring that they engage in health promoting behaviours (e.g., exercise, eating healthy) and avoid risky behaviours (e.g., smoking cigarettes, drinking alcohol).

Since knowledge of disease history and late effects are important factors related to continued attendance in LTFU clinics and successful transition from pediatric to adult care, research is needed that measures survivors' knowledge about their diagnosis, treatment, risks of late effects, and factors that are related to such knowledge. Such information would help to inform the development of targeted interventions that could address knowledge deficits and better prepare survivors to assume disease self-management.

1.5 Knowledge of Cancer History and Late Effects in Survivors: Literature Review

Byrne and colleagues (1989) published a study that measured U.S. childhood cancer survivors' knowledge of diagnosis and treatment as well as factors related to such knowledge. The study included patients diagnosed before the age of 20 years whose first cancer diagnosis was a malignant neoplasm or intracranial tumour. Patients had to be a survivor for at least five years and 21 years of age or older at the time of recruitment.[41] Data was collected on 1,928 survivors using interviews and supplemented by extraction of information from hospital records. During the interviews, survivors were asked if they were informed of their cancer or a benign tumour by their physician, and about the treatments they received.[41] From this study, they identified that 14 percent of participants who were classified as having other types of cancer, were not aware that they ever had cancer. In addition, only a quarter of participants who had a central nervous system (CNS) tumour knew they have had cancer.

In a multivariate analysis, study findings revealed that knowledge deficit with regards to cancer diagnosis was related to the following: being of a non-white race compared to white; being identified from the Connecticut registry compared to others; having a father with low education level (i.e., eighth grade or less); and being a younger age at diagnosis.[41] In a univariate analysis, patients with brain or CNS tumours who received radiation were more likely to know that they have had cancer compared with those who did not receive radiation treatment. Moreover, out of the total number of participants that knew they had cancer, 82 percent of participants with other types of cancer and 86 percent of those with CNS tumours correctly identified the treatments they received.[41]

Bashore (2004) published the first study to report findings on knowledge of childhood and adolescent cancer survivors with regards to their risk of developing late effects and knowledge of diagnosis and treatment. This study included 141 patients in the Life After Cancer Program in Texas, U.S, who were asked six questions pertaining to diagnosis, treatment and late effects.[42] While all participants correctly reported that they had cancer, only 118 (84 percent) correctly reported their cancer type.[42] While 93 percent of participants reported that they had received chemotherapy to treat their cancer, only 50 percent of those patients could name at least one chemotherapy drug received. Furthermore, only 57 percent of patients who received radiation therapy were able to correctly report this fact. For late effects, only 30 percent of participants reported knowing the potential health complications related to their cancer treatment and in this group less than half were able to describe at least two late effects for which they might be at risk.[42] This study highlights that there are important knowledge deficits in childhood cancer survivors. Such deficits may have important implications for survivor's motivation to take care of their health as adults.

Given the elevated risk for cardiac related complications due to the cancer treatment (e.g., anthracycline agents use), Gurney et al. (2007) assessed knowledge of symptoms of heart attack and stroke in adult survivors of childhood acute lymphoblastic leukemia (ALL) in the U.S. Specifically, 70 ALL survivors with no previous history of cardiac event or stroke were recruited from three children's hospitals in Minneapolis/St. Paul area and asked to complete a questionnaire that targeted participants' knowledge of heart attack and stroke symptoms. A population based comparison group of 210 people were

matched to participants on age, sex and body mass index.[43] Both groups were asked to identify the correct symptoms for the two conditions described in the questionnaire. The authors reported that ALL survivors had less accurate knowledge of cardiac and stroke symptoms compared with the comparison group.[43] The authors cannot explain the reason for these findings, but suggested that effective health education needs to be in place to educate survivors of their risks.[43]

More recently, Hess et al. (2011) investigated knowledge of diagnosis, treatment, late effects, and the factors associated with late effects in a study of Norwegian adult survivors of childhood lymphoma. Hospital charts were consulted for clinical information of participants, and a semi-structured interview approach was used to examine survivors' knowledge. The authors included childhood cancer survivors who were currently aged over 18 years and previously diagnosed with malignant lymphoma.[44] Of the 128 participants, 121 (95 percent) correctly reported a diagnosis of lymphoma, and 88 (73 percent) correctly identified the sub-type of lymphoma (i.e., Hodgkin vs. non-Hodgkin). Females were significantly more knowledgeable about their diagnosis (including the sub-type) than males.[45] In addition, 123 (96 percent) of 128 participants correctly reported their treatment modalities, with 93 percent of those that received radiation therapy being aware of the radiation site, though only 28 percent of those that received chemotherapy were able to name at least one of the chemotherapy drugs they had received.[44] To determine their knowledge of late effects, participants were asked if they were made aware of late effects related to their treatment, to which 34 percent said 'yes' and said they could name at least one late effect. The self-reported knowledge of

late effect was higher in patients treated after 1989 and in those treated at a pediatric centre.[44] The significant association between years of treatment and knowledge of late effects is primarily due to the fact that information on cardiac, pulmonary, dental and other late effects has emerged during the last two decades, and was not available to physicians before the 1990s. When asked to comment on the potential risks of late effects informally, gonadal dysfunction was the most cited late effect provided by the participants, with fewer participants reporting the potential risk related to cardiovascular, dental, pulmonary and thyroid function.[44]

As part of the CCSS study described earlier that include 25 centres across the U.S. and Canada, 635 survivors participants were asked to name the type of cancer and treatments they had received. Clinical and demographic information were extracted from hospital records. The research team examined a range of variables as potential predictors of knowledge including the following: type of cancer; gender; income; age at diagnosis; year of diagnosis; age at the time of interview; education level; history of relapse; second malignancy; history of radiation to head or neck; worry about future health problems; receiving summary of diagnosis and treatment; and LTFU care attendance.[45] The authors reported that out of 635 participants, only 454 (72 percent) were able to accurately report the type and sub-type of cancer, whereas 578 (91 percent) participants were able to report type and/or sub-type of cancer. The accuracy of reporting the diagnosis, with or without detail, was highest in participants with bone cancer (98 percent), Hodgkin disease (98 percent), leukemia (94 percent) and Wilms' tumour (98 percent). Knowledge regarding diagnosis was lowest in patients with CNS tumour (75 percent) and neuroblastoma (79

percent).[45] In a logistic regression model, less knowledge of diagnosis with or without sub-type was associated the following variables in an adjusted analysis: male gender; diagnosed between the years 1970 and 1977 compared to 1978 and 1986; and history of CNS tumour or neuroblastoma.[45] Among all the participants, 94 percent were knowledgeable about whether they received chemotherapy or not. In a multivariate analysis in which were included variable that had been found significant in a univariate analysis (i.e., age at diagnosis, year of diagnosis, and cancer type of CNS, non-Hodgkin lymphoma and soft tissue sarcoma) the following patients factors were associated with lack of knowledge about chemotherapy history: having had CNS tumour; diagnosed before the age of five years; and diagnosed between 1970 and1977 compared to 1978 and 1986. [45]

Since anthracyclines (e.g., doxorubicin, daunorubicin), chemotherapeutic agents, can cause cardiotoxcity[24] in cancer patients, a separate descriptive analysis considered patient knowledge of these drugs. Only 33 percent of patients that received doxorubicin and 8 percent that received daunorubicin recalled receiving these specific anthracycline agents.[45] On the other hand, 89 percent of participants who received radiation therapy were knowledgeable about their history of this form of treatment. Those that did not recall receiving radiotherapy were more likely to be younger when diagnosed and at a lower level of education in the multivariate analysis. When patients in the survey were asked whether they believed that serious future health problems could be incurred due to previous treatment, only 35 percent agreed with this.[45]

The CCSS study showed specific knowledge deficits with regards to diagnosis and treatment, and factors related to knowledge deficits in adult survivors of childhood cancer. Specifically, noticeable knowledge deficits were found in patients who received anthracyclines as part of their treatment. Research has shown that survivors of childhood and adolescent cancers who received anthracyclines are two to five times more likely to experience heart failure, pericardial disease, and valvular abnormalities than cancer survivors who did not receive anthracyclines.[46] It is therefore important for adult survivors of childhood cancer who received anthracycline(s) to be aware of their treatment history and associated late effects, as it may motivate them to seek necessary follow-up care, participate in screening for late effects, and avoid high risk behaviours (e.g., physical inactivity, tobacco use) that may put them at increased risk for cardiac related complications later in life.[47]

1.6 Study Rationale, Objectives and Research Questions

1.6.1 Rationale

There is a lack of research looking at knowledge regarding diagnosis, treatment and late effects in Canadian childhood and adolescent cancer survivors. Out of the five studies reviewed above, three were conducted in the U.S.,[41,42,43] one in Norway,[44] and one was conducted in both the U.S. and Canada.[45] The study that included a sub-population of Canadians, only included one Canadian centre out of 25 centres, and did not report results separately for the Canadian cohort.[45] It is important to study knowledge deficits in Canadian childhood cancer survivors as the Canadian society and health care system,

more specifically the way in which LTFU care is organized and delivered, are unique to Canada. Therefore findings from other countries cannot be generalized to Canadian cancer survivors. In addition, there is a scope to examine factors that have not been previously studied, or have been studied less rigorously, but which may help to explain knowledge deficits in childhood cancer survivors (e.g., cancer worry, treatment intensity, parent marital status). Moreover, knowledge of late effects has not been studied in a rigorous fashion; so far, studies have relied on self-report knowledge of late effect in survivors (whether survivors can list some of the late effects) without validation against clinical history. To accurately quantify knowledge deficits, it is important to compare self-report knowledge of late effects, with the actual risk of late effects for each survivor in order to accurately estimate knowledge of late effects in cancer survivors.

1.6.2 Objectives

The primary objectives of this study are as follows:

1) To describe Canadian AYA cancer survivors' knowledge about their diagnosis, treatment and late effects; and
2) To identify factors associated with Canadian AYA cancer survivors' knowledge of their cancer history and potential late effects.

The secondary objectives of this study are as follows:

1) To describe Canadian AYA cancer survivors who received anthracyclines' knowledge about anthracycline specific treatment and late effects; and
2) To identify factors associated with knowledge of treatment and late effects among Canadian AYA cancer survivors who received anthracyclines.

1.6.3 Research Questions

1.6.3.1 For Primary Objectives

1) What is the extent of knowledge of diagnosis, treatment and late effects among Canadian AYA survivors of childhood and adolescent cancer?
2) Among Canadian AYA survivors of childhood and adolescent cancer, what factors are associated with the following:
    a) Knowledge deficits about diagnosis (i.e., type of cancer)?
    b) Knowledge deficits about treatment (i.e., status of chemotherapy, radiation therapy, surgery and transplant)?
    c) Knowledge deficits about late effects (i.e., potential risk of health complications resulting from cancer treatment)?

1.6.3.2 For Secondary Objectives

1) What is the extent of knowledge of treatment and late effects among Canadian AYA survivors of childhood and adolescent cancer, who received anthracycline(s)?
2) Among Canadian AYA survivors of childhood and adolescent cancer who received anthracycline(s), what factors are associated with the following:
    a) Knowledge deficits about treatment (i.e., naming anthracycline(s))?
    b) Knowledge deficits about late effects (i.e., naming complications related to the heart)?

1.7 Chapter Summary

The aim of the study was to identify the extent of knowledge deficiency in a sample of Canadian AYA survivors of childhood and adolescent cancer, and factors related to knowledge. Findings from this study will allow HCPs and researchers to develop and test interventions that target survivors with insufficient knowledge about their cancer history and potential late effects, in order to increase their knowledge accordingly.

This chapter began with a description of childhood and adolescent cancer patients and improvements in their survival rates over the years, followed by different definitions in the literature of AYA survivors. The chapter then discussed the importance of LTFU care in cancer survivors, and outlined a theoretical framework that presents barriers and facilitators to obtaining LTFU care in childhood cancer survivors, as well as a theoretical model to conceptualize the process of transition in AYA patients with chronic conditions, including cancer. A review of literature on knowledge about diagnosis, treatment and late effects in childhood cancer survivors was presented to identify the gaps in the literature providing a rationale for this study.

Chapter 2: Methodology

This chapter provides a description of the study methodology. The chapter begins with a brief description of the rationale for conducting this study, and is followed by the study's hypotheses. Furthermore, a description of the methods, including study design, data collection, data management, analysis, and issues related to research ethics and sample size are provided.

2.1 Declaration of Problem

Over 80 percent of children diagnosed with cancer will survive their initial disease.[4] This high survival rate is widely attributed to intensive treatment; however, more intense treatments have led to the increased risks of developing late effects. Due to the potential risk of health complications in AYA and adult cancer survivors of childhood and adolescent cancer, it is imperative that survivors attend recommended LTFU care for surveillance of potential late effects.[29,30,31,34,40] However, published data has indicated that many survivors stop attending LTFU care as they get older.[33] Many barriers to seeking LTFU care have been identified, with lack of knowledge regarding cancer history and late effects being one of these barriers (see Figures 1 and 2).[31,34,39] Since knowledge deficits regarding diagnosis, treatment and potential late effect can be barriers to attending LTFU care, targeted interventions are needed in order to improve survivors' knowledge about their cancer history and potential risks to their health as a result of the cancer treatment received. However, to be able to design targeted interventions, it is

important to understand the extent of knowledge deficits in this population, and to identify factors associated with inadequate knowledge about diagnosis, treatment and late effects.

Research conducted in other countries has helped to identify important knowledge deficits in childhood cancer survivors.[41,42,43,44,45] In Canada, little is known about how much childhood cancer survivors know about their cancer, treatment and risk of late effects, and about factors associated with these deficits.

2.2 Selecting Independent Variables

The independent variables chosen to address the second question from both the primary and secondary objectives were guided by the theoretical framework of barriers to LTFU care,[31] and the SMART,[39] in addition to previous literature.[41,42,43,44,45] According to the SMART,[39] the pre-existing objective factors, that are less amenable through interventions, affect the modifiable factors (e.g., knowledge related to disease) (see Figure 2). These pre-existing objective factors include socio-demographic and cultural characteristics (e.g., age, race, culture of family), and health status of the patient (e.g., disease history, health risks). In addition, published studies looking to understand factors associated with knowledge of diagnosis, treatment, and late effects described in our review of the literature, also included socio-demographic characteristics and disease history. The following socio-demographic characteristics and disease history factors have been identified in various research studies as significantly associated with a lack of knowledge of diagnosis, treatment and/or late effects: male gender; [44,45] younger age at

diagnosis;[41,45] non-white;[41] lower level of education;[45] lower level of father's education;[41] history of CNS tumours, soft tissue sarcoma or neuroblastoma; [41,45] earlier year of diagnosis;[44,45] treated at a specialized pediatric centre;[44] receiving radiation;[41] and receiving less aggressive treatments.[41] The abovementioned variables that were found to be significantly associated with knowledge deficits for disease history and late effects in previous studies (i.e., gender, age at diagnosis, race, level of education, level of father's education, cancer type, year of diagnosis, treatment type, and treatment intensity) were included as independent variables in the present study. Since all of the participating centres in the study were specialized pediatric centres, we decided to exclude this variable from the list of the independent variables, and instead used it as a control variable. Also, other variables that were included as potential factors associated with cancer knowledge in other studies (i.e., age,[45] mother's education,[41] radiation to head or neck,[45] history of relapse,[45] and worries about health[45]), though not found to be significant were included. In addition, parent marital status was added to the list of potential independent variables to explore its possible association with cancer knowledge. The independent variables selected for this study were grouped into the following categories: 1) patient factors (i.e., gender, current age, race, education level); 2) family factors (i.e., father and mother's education, and parent marital status); 3) cancer factors (i.e., age at diagnosis, cancer type, and year of diagnosis); 4) treatment factors (i.e., treatment type, history of radiation to head or neck, history of relapse, and treatment intensity); and 5) cancer related worries.

Previous studies have investigated whether parameters differ across certain groups by using interaction terms. Byrne et al. (1989) investigated several interaction terms of

which only race by centre approached, but did not reach significance.[41] In addition, Kadan-Lottick et al. (2002) included an interaction term to investigate whether the association between age at diagnosis and knowledge vary by year of diagnosis.[45] However, this term was not found to be significantly associated with knowledge of diagnosis and treatment. We did not include any interaction terms for the purposes of this study, as based on previous studies, we did not presume knowledge to differ across race by centre, and age at diagnosis by year of diagnosis.

2.3 Hypotheses

AYA survivors of childhood and adolescent cancer are expected to be well aware of their diagnosis, treatment and late effects, and are continuously educated about such information during their LTFU appointments. Despite efforts to educate patients, some survivors lack necessary information about their cancer history and late effects. We hypothesized that knowledge deficits would progressively increase in AYA cancer survivors going from diagnosis to treatment, and treatment to late effects. We believed that only patients who knew their diagnosis would recall the treatments they received, which are specific to the type of cancer, and only patients knowledgeable of their treatments would recall its associated long-term risks to health.

We based our hypotheses for the nature of possible associations between independent and dependent variables on previous studies on the topic of cancer knowledge, and our own reasoning. In specific, we hypothesized a greater knowledge deficit regarding diagnosis, treatment and late effects in the following patient groups: 1)

male; 2) younger age at the time of recruitment; 3) non-white; 4) lower level of education; 5) lower level of mother and father's education; 6) parents marital status where the presence of one parent may be limited in a patient's life (i.e., separated, divorced, single, never married, and widowed); 7) history of CNS tumours, soft tissue sarcoma, and neuroblastoma; 8) diagnosed at a younger age; 9) earlier year of diagnosis; 10) received surgery; 11) history of radiation to head or neck; 12) absence of relapse; 13) received less aggressive treatments; and 14) lower levels of cancer worry. We expected that disease related knowledge would progressively get better with increased patient's maturity, and the presence of an educated and nurturing environment. Maturity and presence of an educated and nurturing environment will facilitate an easier transfer of disease related information from HCPs and parents to the patient. Furthermore, we expected patients diagnosed at a younger age, and at the time when information on cancer and potential late effects of treatments was not readily available to lack necessary information about their illness. We also hypothesized that those types of cancer and treatments (e.g., CNS tumours, radiation to head or neck) that can potentially impact patient's acquisition of new information, would lead to a greater disease related knowledge deficits. Moreover, patients treated less aggressively may also lack necessary information regarding their diagnosis, treatment and late effects, as these patients may be less motivated to seek LTFU care. This lack of motivation may stem from the belief that less invasive treatments have a limited impact on their long-term health. Lastly, we expected patients who were less worried about the risks associated with their cancer treatment to lack necessary

cancer knowledge as they may invest less time in learning about their cancer history and risk of late effects.

2.4 Overall Study: Objectives and Epidemiological Approach

The data for this cancer knowledge study was collected as part of a larger program of research that involved two phases, with the overall aim to develop and validate a set of scales to measure specific barriers and facilitators of LTFU care in childhood cancer survivors. The end goal of this program of research was to provide tools which can be used in research and/or in clinical practice to identify survivors who may be at risk of failing to transition from pediatric to adult healthcare. A brief description of the scales developed by the team, as well as the compilation of a set of variables into a questionnaire booklet called the Transition Readiness booklet is provided below.

2.4.1 Transition Readiness Booklet

In the first phase, qualitative interviews were conducted with 38 survivors and the data were used to develop items for the three scales.[48,49] The qualitative interviews led to the development of a Cancer Worry Scale (focused on worry about cancer related issues such as a recurrence and late effects), a Self-Management Scale (focused on skills an adolescent needs to acquire to manage their own health care as an adult), and an Expectations Scale (expectations about the nature of adult LTFU care).

In the second phase, a cross-sectional study design was used to conduct a field-test to collect data for the three developed scales, and to identify the items that represent the best indicators of each scale based on their performance against a standardized set of

psychometric criteria. The three developed scales were included in a questionnaire booklet named the Transition Readiness booklet, which also included a set of items and questions to assess cancer knowledge (i.e., we called this the Cancer Knowledge Survey, which is described in detail below), and questions about lifestyle, child and family characteristics. Questions to assess cancer knowledge and lifestyle characteristics were included in the booklet as these two factors were also found to be important to the transition process in the qualitative interviews (see Appendix A).

2.4.1.1 Cancer Knowledge Survey

As part of the Transition Readiness booklet, a set of items that ask about cancer history and late effects were developed and included. The Cancer Knowledge Survey was divided into two parts. The first part included a series of 13 items with response options that included 'yes', 'no', and 'not sure' (see Appendix A- page 119). The second part of the Cancer Knowledge Survey invited participants to describe their cancer, treatment and late effects via a series of open-ended questions (see Appendix A- pages 122 to 123). More specifically, participants were asked to describe the following: their type of cancer; location of their cancer; their age at diagnosis; their age at treatment completion; the number of times they come to LTFU appointment per year; the names of chemotherapy drugs received; their status of relapse; the late effects they are at risk for (defined as any health problems caused by cancer treatments with examples provided, i.e., heart problems, hearing loss, learning problems); and any learning problems (e.g., trouble with reading, writing or math) they currently have. In addition, participants were asked to check mark the treatments (i.e., chemotherapy, radiation therapy, surgery, and transplant)

they received and to indicate on diagrams of body the location of radiation therapy and surgery, if received.

The goal of the Part One of the Cancer Knowledge Survey was to assess whether or not survivors of childhood and adolescent cancer can accurately report knowing their cancer, treatment and late effects. We wanted to determine whether using a simple yes/no/not sure format is sufficient in determining survivors' knowledge of cancer history and late effects. To determine this, we compared their answers to the information provided in Part Two of the Cancer Knowledge Survey as well as the information from their hospital records. The purpose of Part Two of the Cancer Knowledge Survey and the hospital chart information was therefore to measure the actual knowledge of cancer history and late effects in AYA cancer survivors.

Our team developed our own method for collecting information on patients' knowledge about their cancer history and risks of late effects because there is no standardized or objective instrument available to measure knowledge of disease in childhood cancer survivors. Previous studies assessing knowledge in cancer patients have either used a questionnaire[42,43,44] or conducted interviews [41,45] to collect information regarding patient's knowledge of disease and potential threat to long-term health. We used the questionnaire format because it is a systematic and structured way of collecting data compared to semi-structured interviews, and allows for quantifiable comparisons between participants. In addition, using a questionnaire is also an economical way of targeting a large sample of participants in a short period of time.

Generally, using a questionnaire to collect information presents limitations. One of the main limitations of using a questionnaire that includes items with pre-determined response options is that it provides limited insight into a problem as participants are restricted in what they can and cannot report. However, as mentioned, we also had a series of open-ended questions to obtain the detail that set response options do not allow.

2.4.1.2 Other Information Used from the Transition Readiness Booklet

To collect data on the independent variables to address the second questions of the primary and secondary objectives, we used a number of other variables collected in the Transition Readiness booklet, including cancer worry, and questions concerning patient and family characteristics.

2.4.2 Refinement of the Transition Readiness Booklet

Prior to the field-test, the three scales, Cancer Knowledge Survey, and questions pertaining to lifestyle, patient and family characteristics were presented to 17 experts in the field. These experts included the following: three pediatric oncologists, three parents of childhood cancer survivors, two nurses, two social workers, one childhood cancer survivor, one pediatric neuro-oncologist, one radiation oncologist, one adult oncologist, one psychologist, one neuropsychologist and one pediatrician. Three experts had substantial research expertise on the topic of transition readiness. Experts provided feedback, which was used to revise the Transition Readiness booklet. In addition, interviews were conducted with 7 survivors who ranged in current age (range 16 to 22 years), age at diagnosis (range 4 to 16 years), and gender (5 male, 2 female). Feedback

was sought to identify ambiguities in instructions, response options, item wording and layout.

2.5 Epidemiological Approach: Cross-Sectional Study

A field-test was conducted with survivors aged 15 to 26 years, recruited from three Canadian hospitals between July 2011 and January 2012.[49] Data were collected from 250 childhood cancer survivors. Psychometric analysis showed that the resulting three scales were found to be short, easy to understand, valid and reliable measurement tools.[49]

The field-test was a multi-centered cross-sectional survey study. A cross-sectional study design is useful in estimating prevalence and burden of health problems,[50] as well as for psychometric studies where the aim is to develop a new questionnaire which typically requires a large sample of patients. In addition, this study design was chosen, as it is feasible, quick and the most economical way of collecting information from a large sample of patients in a relatively short period of time. Since there is little known about the experiences of Canadian childhood cancer survivors specifically, the portion of the study that focused on understanding knowledge about cancer, treatments and late effects was considered to be exploratory and, therefore, a cross-sectional study was appropriate.

2.5.1 Strength and Limitations of a Cross-Sectional Study Designs Compared to Other Research Study Designs

One of the main limitations of a cross-sectional design is that there is temporal ambiguity and hence it cannot be determined whether the factors under study precede patient outcomes. Nevertheless, the purpose our study was to measure associations, not

causality, between factors and knowledge of disease, treatment and late effects in order to better understand cancer knowledge deficits. One of the major strengths of observational research (with the exception of cross-sectional study design) is that causality bias is avoided because of their longitudinal nature. However, these study designs can be expensive and time-consuming, therefore limiting their feasibility. Given that treatment (e.g., treatment intensity), cancer (e.g., type of cancer) and some of patient factors (e.g., gender, race) precedes the outcome of interest (i.e., knowledge of diagnosis, treatment and late effects), we can be sure that temporal ambiguity is not a limiting factor. Recruitment of survivors that have already undergone treatment means that if we found a significant association between the factors mentioned above and knowledge, we can presume that the factors are predictors, as they precede the outcome. Furthermore, a randomized controlled trial (RCT) was not warranted since there is limited research available on the nature of the association between knowledge and modifiable factors; generally, an extensive understanding and research is needed before an RCT can be conducted.

2.6 Hospital Chart Information

In addition to the data collected using the Transition Readiness booklet, we extracted information on cancer and treatment related independent variables from hospital charts. Information extracted from hospital records also aided in determining of participants' knowledge of type of cancer, treatment and late effects. Hospital records were located and extracted for all 250 of the respondents at the three participating centre. In addition,

hospital records were also extracted for all of the non-respondents to collect information on their age, gender, age at diagnosis, and cancer type; this was done to determine if respondents and non-respondents differed.

To ensure accuracy of data extracted from the hospital records, one research assistant collected the information, and a second research assistant checked the recorded information on all variables. In the case the two research assistants differed in their extraction, a third research assistant or a graduate student checked the hospital records and corrected the information. To establish inter-rater reliability between the chart extraction data, Intra-Class Correlation (ICC) for continuous and kappa statistic for categorical variables were calculated. An ICC coefficient of greater than 0.4 [ICC= 0.4-0.75 (fair to good reproducibility); ICC> 0.75 (excellent reproducibility)][51] and a kappa statistic of greater than 0.60 [kappa= 0.41-0.60 (moderate agreement); kappa= 0.61-0.80 (substantial agreement); kappa= 0.81-0.99 (almost perfect agreement)] [48] were considered acceptable.

2.7 Variables

The level of measurement for independent and dependent variables included in this study are presented in Table 1.

2.7.1 Dependent Variables

The dependent variables described below were used as outcomes to answer questions one and two for both the primary and secondary objectives.

1) Knowledge of Diagnosis

Knowledge of diagnosis was determined from the question included in the Cancer Knowledge Survey that asked participants to write down the type of cancer they had (i.e., What type of cancer did you have?) (see Appendix A- page 123). The answer was left open-ended to allow participants to write the appropriate answer in as much detail as they could recall. Answers provided by the participants were compared to the information on the type of cancer available in their hospital records. Two categories were created to determine the knowledge of diagnosis, 'knowledgeable' and 'not knowledgeable' (nominal). The participant was 'knowledgeable' about their diagnosis if he or she put the correct major type of cancer (e.g., leukemia, lymphoma, sarcoma), or correct sub-type of cancer (e.g., ALL, non-Hodgkin lymphoma, osteosarcoma). In addition, patients with CNS tumours were considered to be 'knowledgeable' if they put their specific cancer type (e.g., astrocytoma), 'brain cancer' or 'brain tumour'. However, if the participant put the correct major type of cancer (e.g., leukemia) in addition to putting the incorrect sub-type of cancer (e.g., acute myelogenous leukemia instead of ALL), or if the participant only put the incorrect sub-type of cancer, then they were considered to be 'not knowledgeable'. This was considered 'not knowledgeable' because many sub-types of cancers have very different type and intensity of treatments.[54] If a survivor has incorrect beliefs about their type of cancer, it may lead to problems when trying to understand the late effects related to their cancer. In addition, if the participant left the question blank, put 'cancer' or 'tumour', or put

the location of cancer instead of type of cancer, they were considered to be 'not knowledgeable'.

The 'knowledgeable' category was further classified into two sub-groups; i.e., 'detailed' or 'not detailed' (nominal). The answers were considered 'detailed' if the participants provided the sub-type of cancer. The following types of cancer were 'detailed' and no other sub-type for these cancers were needed: neuroblastoma, hepatoblastoma, Wilms' tumour, and germ cell tumour. Other than the abovementioned types of cancer, the answers were considered to be 'not detailed' when only the correct major type of cancer was written, without the sub-type. Expert opinion was sought for any cancer types the graduate student was unsure about.

2) Knowledge of Treatment

A question in the Cancer Knowledge Survey asked participants to mark the appropriate response to indicate whether or not they had received any of the four cancer treatments (i.e., chemotherapy, radiation therapy, surgery, bone marrow or stem cell transplant) (see Appendix A- page 123). The possible range of answers for each treatment were as follows: 'Yes', 'No', and 'Not sure'. The answers provided by participants for each of the four treatments were compared to the data from the hospital records. For each treatment the answer was categorized as 'correct' or 'incorrect' depending on if participant's response matched the information from hospital records. Answers for participants who said 'Not sure' to any of the treatment questions, were considered 'incorrect'.

A new variable, 'level of knowledge about treatments' was created to assess the extent of knowledge in AYA survivors of childhood and adolescent cancer about their treatments (ordinal). The possible categories for this variable were as follows: none correct; one correct out of four; two correct out of four; three correct out of four; and all correct. Participants were considered to be 'knowledgeable' if they knew all of the four types of treatment, 'not knowledgeable' if they did not know their status of having received any, one, or two of the four treatments. In addition, participants were 'partially knowledgeable' if they got the status of three out of four treatments correct. The categories, 'knowledgeable', 'not knowledgeable' and 'partially knowledgeable' were categorized based on the number of correct responses in each of the five categories, 'none correct', 'one correct out of four', 'two correct out of four', 'three correct out of four', and 'all correct'.

3) Knowledge of Late Effects

The Cancer Knowledge survey asked participants to list the late effects that they believed they were at risk for based on their cancer treatments (see Appendix A- page 123). Space was provided for participants to write as many late effects as they could recall.

The study co-principal investigator, who is a leading expert in childhood cancer late effects, was asked to determine the late effects for each participant based on their treatment information available in the hospital records. An Excel file was compiled that included detailed information for each participant using data from their hospital records. Specifically, in addition to the participants' answer to the question for late

effects from the Cancer Knowledge Survey, the expert was provided with the following information: age at diagnosis; cancer type and sub-type; location of primary cancer; relapse status; surgery; chemotherapy (including cumulative doses where important); radiation dose and field; and hematopoietic stem cell transplantation. For two participants, adequate information on the dose of chemotherapy drugs was not available in their hospital records to inform the assessment of knowledge of late effects. Responses were classified as: 1) incorrect, 2) correct, or 3) mixed (ordinal). Participants at risk for late effects, but who failed to describe any in the cancer survey, and patients who described late effects for which they were not at risk, were placed in the 'incorrect' category and were considered to be 'not knowledgeable' about late effects. Participants who correctly identified that they were not at risk for any late effects and those who identified one or more late effects for which they were actually at risk for were placed in the 'correct' category, and were considered 'knowledgeable'. It was not necessary to identify all potential late effects in order to be classified as 'correct'. Participants who identified one or more late effects correctly, but also listed at least one late effect for which they were not at risk for were placed in the 'mixed' category, and hence were 'partially knowledgeable'.

4) Knowledge of Anthracyclines

One of the questions in the Cancer Knowledge Survey asked participants to list the names of any chemotherapy drugs they were given during cancer treatment (see Appendix A- page 123). A space was provided to allow survivors to write the names of as many chemotherapy drugs as they could remember. Participants who received an

anthracycline agent (e.g., doxorubicin, daunorubicin) were expected to know name of at least one of the anthracycline agents, or to write 'anthracycline'. Participants who reported at least one of the anthracycline agents were considered to be 'knowledgeable' about their treatment of anthracycline, whereas those who received an anthracycline, but did not list the name of at least one anthracycline were considered to be 'not knowledgeable' (nominal).

5) Knowledge of Anthracycline Specific Late Effects

Participants who received anthracycline agents were expected to write down late effects associated with it when asked to list the late effects in The Cancer Knowledge survey (see Appendix A- page 123). Participants who received anthracyclines and wrote anything related to the heart, were considered to be 'knowledgeable' about anthracycline specific late effects. However, if no mention of anthracycline related late effects was made, then participants were considered to be 'not knowledgeable' of their late effects associated with anthracyclines.

2.7.2 Independent Variables

The variables described below were used as independent variables to answer the second question for both the primary and secondary objectives. For information extracted from the hospital records, the level of agreement is reported.

1) Patient Factors

a. Age, and **b.** Gender

Participants were asked to provide their age in years (ratio), and gender as 'Male' or 'Female' (nominal) at the time of filling out the Transition Readiness booklet (see Appendix A- Page126).

c. Race

The patient and family related questions in the questionnaire booklet asked participants to report their mother and father's race or ethnic background (see Appendix A- Page126). The answers were left open-ended to allow participants to report answers that they find most appropriate. A variable was created called 'child's race' (nominal) and the possible options were 'white' or 'non-white'. Participants that reported the mother and father's race as at least one of the following were placed in the 'white' category; all other participants were placed in 'non-white' category: Canadian; Caucasian; white; Serbian; Italian; Dutch; European; German; Irish; Greek; English; Russian; British; French; Scottish; Danish; Welsh; and Ukrainian.

d. Education Level

Participants were asked to indicate their current level of education from the following options in the Transition Readiness booklet (ordinal): 'I am a High School student'; 'I have completed High School'; 'I am a College or University student'; and 'I have completed College or University' (see Appendix A- Page126).

2) Family Factors

a. Father's, and **b.** Mother's Education Level

Participants were asked to indicate one of the following options for their mother and father's highest level of completed education (ordinal) in the questionnaire booklet:

'Did not finish High School'; 'Finished High School'; and 'Finished College or University' (see Appendix A- Page126).

c. Parent Marital Status

Participants were asked to choose one of the following categories that best describes their parent marital status in the questionnaire booklet (nominal): 'Married/Common-law'; 'Widowed'; 'Separated'; 'Divorced'; and 'Single/Never married' (see Appendix A- Page126).

3) Cancer Factors

a. Age, and **b.** Year of Diagnosis

The date of diagnosis extracted from hospital records (ICC=0.50) was used in the analysis. Using date of diagnosis and date of birth, age at diagnosis was calculated in years (ratio) with two decimal places. The year of the date of diagnosis (ratio) was dichotomized into the following two categories for the analysis to balance the number of participants while maintaining equal number of years in each group: 1986 to 1998; and 1999 to 2011.

c. Cancer Type

Type of cancer from the hospital records included the major and sub-type of cancer (kappa= 0.99). The cancer types were classified into the following six types of cancer according to the International Classification of Childhood Cancer[53] (nominal): 'Leukemia'; 'Lymphoma'; 'CNS tumours'; 'Embryonal tumours'; 'Renal tumours'; and 'Sarcomas'. Each of the six categories included many sub-type of cancers; 'Leukemia' included ALL, acute myeloid leukemia (AML), and acute promyelocytic

leukemia (APML), and 'Lymphoma' included both Hodgkin and non-Hodgkin lymphomas. The category of 'CNS tumours' included astrocytoma, brain tumours, brainstem glioma, germinoma, brainstem glioblastoma, medulloblastoma, optix complex glioma, clival chordoma, and nasopharyngeal carcinoma. In addition, the following cancer types were included in the category 'Embryonal tumours': neuroblastoma, ganglioneuroblastoma, hepatoblastoma, germ cell and yolk sac tumour. 'Renal tumours' included Wilms' tumours, and 'Sarcomas' included both, bone and soft tissue sarcomas, including rhabdomyosarcoma, clear cell sarcoma, Ewing's, and osteosarcoma.

4) Treatment Factors

a. Treatment Types (i.e., Chemotherapy, radiation therapy, surgery to remove cancer, and stem cell transplant or bone marrow transplant)

Types of treatment received by participants according to hospital records was extracted using a yes/no option to indicate if the patients had the treatment or not (nominal): chemotherapy (kappa= 0.93), radiation therapy (kappa= 0.62), surgery (kappa= 0.86); and transplant (kappa= 0.69).

b. History of Radiation to Head or Neck, and **c.** History of Relapse

Information on the field of radiation (kappa= 0.98) and status of relapse (kappa= 0.86) was collected from the hospital records for all the participants. If the field of radiation included at least one of the following, participants were considered to have received radiation to the head or neck (nominal): cranium; whole brain; total body irradiation; spine; posterior fossa; head, neck; mantle; maxillary sinus; ventricular;

ear; and periauricular region. In addition, if the charts indicated that the patient had relapsed at least once, the participant was considered to have a 'history of relapse', otherwise 'no relapse' (nominal).

d. Treatment Intensity

An improved version of the intensity of treatment rating (ITR) called the intensity of treatment rating scale 2.0 (ITR-2) was used to classify the treatment intensity (ordinal).[54] This has shown to evidence validity (content validity: r= 0.95, range 0.71-0.91) and reliability (inter-rater reliability: r= 0.87) in a study aimed at modifying and validating this new treatment intensity scale.[54] To compute this score, we extracted information on type of treatments, relapse status and type of cancer, including stage/risk. Intensity of treatment was classified into the following categories: Level 1: Least Intensive Treatments; Level 2: Moderately Intensive Treatments; Level 3: Very Intensive Treatments; and Level 4: Most Intensive Treatments. The 'Least Intensive Treatments' category included patients who were diagnosed and treated in the following manner: germ cell tumour- surgery only; neuroblastoma- surgery only; retinoblastoma- without chemotherapy; Wilms' tumour stage 1 and 2; and patients who received only surgery for their treatment (excluding brain tumour patients). On the contrary, the 'Most Intensive Treatments' category included the following patients: relapsed (with the exception of patients who had Hodgkin lymphoma or who only relapsed once of Wilms' tumour); received stem cell transplant; and diagnosed with AML.[54] In addition, if there was any confusion or disagreement surrounding the classification system, an expert opinion was sought to appropriately classify the

treatment intensity for a participant. One of the patients was diagnosed with hepatoblastoma, treated with a liver transplant and chemotherapy. According to the ITR-2, this patient would have been placed in the 'Level 3' category. However, upon discussion with the expert in the field of oncology and late effects, 'Level 4' was deemed more appropriate as patient had received a cadaveric liver transplant.

5) Cancer Worry

The research team's new 6-item Cancer Worry scale was used as a measure of participants thoughts and feelings related to their cancer history and late effects.[49] This scale was found to be reliable in the field-test sample, with a Person Separation Index= 0.82, Cronbach's alpha= 0.85, and test re-rest= 0.85. Further information on this scale's development is provided elsewhere.[49] For each of the six items, the following four response options are provided: 'Strongly Agree'; 'Agree'; 'Disagree'; and 'Strongly Disagree'. The total score for the Cancer Worry scale ranged from 0 to 100, with higher scores indicating less worry (interval).

2.7.3 Control Variables

The control variables described below were used in the multivariable model conducted to address the second question for both the primary and secondary objectives.

1) Centre and **2) Method of Recruitment**

The hospital and method of recruitment were recorded at the time of recruitment. The three centres included centre A, centre B, and centre C (nominal), and the two methods of recruitment were clinic and mail recruitment (nominal).

2.8 Ethics

Research Ethics Board (REB) approval was obtained at each center prior to recruiting patients into the study. The sample of patients invited to participate were provided a consent letter that complied with Hamilton Health Sciences REB in its outline of the study purpose, process, benefits, contacts of team members, and information on confidentiality, roles and rights. The consent letter outlined that participation in the study was voluntary and that participants have the option of declining at any stage of the study, with no effect on their medical care. Each participant was assigned an identifying number, which was matched to his or her personal information (e.g., name, date of birth). All files were kept confidential and password protected. Consent letters were kept in a locked file cabinet in the principal investigator office. Study participants were informed of the minimal harm or threats (e.g., anxiety related to remembering cancer experience) if they chose to participate. The parents of patients less than or equal to 15 years of age were approached to obtain assent (see Appendix B) while patients over 15 were asked to sign for themselves (see Appendix C). Each patient invited to participate in the study received a five-dollar gift card as a thank-you for considering participating in the study.

2.9 Subjects

2.9.1 Definition of AYA Survivors of Childhood and Adolescent Cancer

For the purposes of this study, survivors were defined as patients that had completed treatment and were currently attending an off-treatment or LTFU care clinic. We included

all participants regardless of length of time off treatment in order to ensure an adequate sample size was achieved for the psychometric analysis.

The upper age limit for sample was set at 26 years. This upper age limit was chosen because of the goal of the project to better understand the transition process and develop scales that measure factors related to successful and unsuccessful transition from pediatric to adult LTFU care. The study investigators determined that setting the upper age limit at 26 years allows for adequate time to establish whether or not a childhood cancer survivor has successfully transitioned to adult LTFU care. For this study, adolescents and young adults were defined as participants between the ages of 15 and 19 years, and 20 and 26 years, respectively. Since commonly accepted upper age limit can be highly variable for young adults, ranging from 24[10,11] to 39,[8] the selected upper age limit of 26 years for our study was acceptable.

2.9.2 Selection Criteria: Inclusion and Exclusion Criteria

The inclusion criteria for this study were as follows: 1) survivors of childhood or adolescent cancer; 2) current age between 15 and 26 years; and 3) attending off-treatment or LTFU clinics at one of the three participating cancer centres.

Patients with a neuro-cognitive disability that could prevent independent completion of the questionnaire booklet (e.g., Down syndrome) were not included.

2.9.3 Sampling Design

A multi-stage sampling approach was used to recruit patients for this study, with hospital being the primary unit, and persons second. The study involved the centres of the two co-principal investigators, with each centre following a different model of care for

transition. A third centre was invited to participate in the study in order to increase sample size and provide an additional model of care for transition. The three models of care for transition employed by each centre were, continued care in the pediatric LTFU program as adults, transition to young adult program in an adult setting, and transition to community physician with continued communication with specialists.

At two of the three centres a database of patients was extracted from hospital records, including their expected date of attendance at off-treatment or LTFU clinic appointment. This was done to determine which patients met the inclusion criteria of the study and their approximate date of clinic appointment. At the third centre, the charge nurse of the LTFU clinic determined whether a patient met the inclusion criteria of the study or not and approached potential participants directly.

Two separate methods of recruitment (i.e., clinic and mail recruitment) were used to recruit patients based on the inclusion criteria. In the clinic recruitment period, extending from July 2011 to January 2012, patients in all three hospitals were approached before their appointment and asked to complete the questionnaire booklet during their clinic visit. Since most survivors attend LTFU clinic only once a year, mail recruitment at two of the centres was also used to reach out to the maximal number of patients. Recruitment by mail was conducted for participants not expected to come into the LTFU appointment during the clinic recruitment period. The mail survey was conducted according to 'the tailored design method' by Dillman,[56] which highlights five required elements for high response rate; these include: 1) respondent friendly questionnaire by using readable font size and easy to follow layout; 2) up to three reminders to increase response rate; 3)

inclusion of a stamped return envelope to encourage people to reply without financial input; 4) personalized correspondence by including hand written addresses and cover letter with contact information of principal and co-investigators; and 5) financial incentive, which for us included a five dollar gift card as a thank-you gesture. If the mailed questionnaire was returned due to address change, hospital records were re-checked to obtain the updated contact information. However, if no updated information was available in the hospital records, those participants were excluded from the sample.

Patients with neuro-cognitive disability that would prevent independent completion of the questionnaire were excluded from the study. The charge nurse of the off-treatment or LTFU clinics assessed the neuro-cognitive disability during clinic recruitment. Charge nurses are often well aware of the patients' cancer history, which is why they were approached by the graduate student or research assistant to assess the suitability of the patient prior to approaching the patient. For mail recruitment, the principal investigator was responsible for judging the neuro-cognitive status of participants. However, not all patients with neuro-cognitive disability were screened out pre-emptively. Notes and phone calls were received from parents by the principal investigator, to inform that their child was not capable of completing the questionnaire independently; these patients were excluded from the study.

2.10 Data Management

Information on the respondents and non-respondents (e.g., method of recruitment, centre of recruitment, date of recruitment, and date of reminders for the mail-outs) were

tracked in an excel document. Upon return of completed questionnaires, information required from the patient's hospital record was extracted. All data were entered by study research assistants into Microsoft Excel using a specified coding scheme. A second research assistant checked the entered data. Any discrepancies were reviewed by the study principal investigator and/or graduate student. Information on non-respondents was also entered and checked by research assistants, in a similar manner.

2.11 Data Analyses

SPSS Statistics 20 software was used to conduct the analysis for this study with two-tailed statistical tests at 0.05 level of significance. P-values and 95 percent confidence intervals (CI) are reported wherever necessary. Ordinal and nominal data were converted to a categorical scale of measurement. Ratio and interval data were converted to continuous variables, with the exception of 'Year of diagnosis', which was converted to a categorical variable.

2.11.1 Analytic Approach

2.11.1.1 Descriptive Analyses

Descriptive analysis was conducted first to explore the data and distributions of variables by computing frequency tables. The frequency tables allowed the graduate student to make decisions on collapsing categories for univariable and multivariable analysis and to present information on variables used in the study. The percent of participants who reported knowledge for their diagnosis, and late effects in Part One of

the Cancer Knowledge Survey, and were actually knowledgeable (based on Part Two of the Cancer Knowledge survey), is reported to provide a descriptive overview.

To address the second question for the primary and secondary objectives, the extent of knowledge deficits with regards to the diagnosis, treatment, and late effects, and knowledge of anthracycline specific treatment and late effects, was determined by reporting percentages of participants who were 'knowledgeable' and 'not knowledgeable'.

2.11.1.2 Univariable Analyses

A univariable analysis was conducted to screen for potential associations between the outcomes and independent variables. Since the 'knowledge of diagnosis' did not have sufficient cases, no further analysis were conducted. For the other outcomes, all of the abovementioned independent variables were looked at individually to assess the associations with the outcome variables to answer the second question of the primary and secondary objectives.

To determine associations, ordinal logistic or binary logistic regressions were conducted with one independent variable at a time. This was because the dependent variables were all categorical scales of measurement, and to assess association between a categorical outcome and a continuous or categorical independent variable, logistic regression is preferred.

Due to small sample sizes, the following categories were collapsed into one category for each of the following independent variables: Education- 'Completed high school' and 'In college or university'; Parent's marital status- 'Widowed' and 'Single/never married',

and ‘Divorced’ and ‘Separated’; and Treatment type- ‘Surgery’ and ‘Transplant’. In addition, for the dependent variable knowledge of treatment, the categories were collapsed to the following final categories: ‘0, 1, or 2 correct’; ‘3 correct’; and ‘All correct’.

For categorical variables with more than one response options, dummy coding was used with the referent category being the category with the largest number of participants. However, in the case of an ordinal response option, the highest or lowest category with the largest sample size was assigned as referent category.

2.11.1.3 Multivariable Analyses

A multivariable analysis was conducted to answer the second question for the primary and secondary objectives. Variable(s) found to be significantly associated with the dependent variable in the univariable analysis were included in the multivariable binary or ordinal logistic regression with the control variables. A regression model for the primary objectives was only constructed if the outcome had at least 25 cases, and allowed for the inclusion of all the variables found significant in the univariate analysis, following the 10 cases per predictor rule. Based on the multivariable analysis parameters estimates, odds ratio was calculated and reported, along with R^2 for strength of association.

Regression models were also tested for fit and assumptions. For ordinal logistic regression, assumption of proportional odds (i.e., the relationship between the independent variables and logits are the same for all logits) was tested by conducting a test of parallel lines; if the test was found to be non-significant, the null hypothesis (i.e., parameters are the same for all response categories) was not rejected. However, if the null

hypothesis was rejected, a multinomial logistic regression was supposed to be conducted instead of an ordinal logistic regression. In addition, Pearson's goodness-of-fit measure was used to assess model fit; if Pearson's goodness-of-fit was found to be significant, the null hypothesis (i.e., the model fits) was rejected,. Overall model fit was tested for ordinal logistic regression by looking at the change in -2 log likelihood between the final and intercept only model. If the change was found to be significant, the model with independent variables was considered to be a better model fit than the intercept only model, and hence the overall model was accepted. Model fit for the binary logistic regression was assessed by conducting Hosmer-Lameshow test; if the test was found to be non-significant, then the null hypothesis (i.e., the model has a good fit) was not rejected.

2.11.2 Missing Data

Multiple imputation[67] was used as a method of dealing with missing data during the univariable and multivariable analysis. Missing data was present for the following independent variables (percent missing cases out of 250 reported in brackets): race (1.6 percent); education level (0.8 percent); mother's education (2.0 percent); father's education (4.8 percent); parent marital status (2.0 percent); year of diagnosis (0.8 percent); history of radiation to head or neck (2.0 percent); treatment intensity (6.0 percent); and cancer worry (0.4 percent).

2.12 Sample Size

The sample size for this study was determined by the sample size requirements of the Rasch model, as this was the psychometric method used for scales development. The sample size for the field-test was set to at least 243 participants as it gave a 99 percent confidence level that the item estimates would fall within the 0.5 logits, which according to Wright and Douglas would present measures free of bias.[57] Since the Cancer Knowledge Survey information was descriptive, sample size requirements are based on the statistical analysis for which the data were used to address question two of the primary objective of the study.

Very few books have discussed the sample size requirements for logistic regressions, especially for ordinal logistic regressions. However, in 1996, Peduzzi et al. published their findings from a Monte Carlo study which discussed the number of events or cases needed per variable in a logistic regression.[58] This simulation study showed that a minimum of 10 events or cases are required per variable in order to avoid over and under estimating of the variances of the regression coefficients.[58] Many other authors have also suggested using this approach,[59,60] i.e., 10 events or cases per variable in the logistic model, and hence we chose this approach to determine the adequacy of the sample size in conducing logistic models. A univariable analysis was proposed to explore the associations between independent variables and the two outcomes, knowledge of treatment and knowledge of late effects. Variables found significant in the univariable analysis were included in the multivariable logistic regressions, in addition to control variables. The following 31 variables used to determine the maximum number of participants needed to conduct a multivariable analysis, potentially including all of these

variables: Recruitment- mail recruitment; Centre- centre B and centre C; Age during recruitment; Gender- female; Race- non-white; Education level- completed high school or in college/university, and completed college/university; Mother's education- no high school, and completed high school; Father's education- no high school, and completed high school; Parents marital status- married/common-law, separated/ divorced, and single/never married/ widowed; Age at diagnosis; Cancer type- lymphoma, CNS tumours, embryonal tumours, renal tumours, and sarcoma; Diagnosed during 1986-1998; Did not have chemotherapy; Did not have radiation therapy; Had surgery and/or transplant; History of radiation to head or neck; History of relapse; Treatment intensity- level 1, 2, and 3; Cancer worry. Following the 10 cases per variable rule, we needed a maximum sample size of 310 participants in order to allow for inclusion of all independent and control variables in the multivariable analysis, accounting for dummy coding.

2.13 Chapter Summary

This chapter summarizes the methods used to achieve the goals of the study. The chapter began with a brief description of the research problem and limitations of previous research to date. The chapter then outlined the procedure of choosing independent variables for the planned analyses. A methodological approach with distinct strength and limitations were provided to support the use of cross-sectional study design. A thorough description of data collection, sampling approach, data management, ethics, and analyses was also provided to outline the methods by which the study was conducted.

Chapter 3: Results

This chapter describes the results of the cancer knowledge study and thereby addresses both the primary and secondary objectives of the study. The chapter begins with findings for the response rates and demographic characteristics of the sample, including differences between the respondents and non-respondents. This is followed by presentation of the descriptive results that address the first question for both the primary and secondary objectives. Results from the univariable and multivariable analyses are then described to address the second question of the primary and secondary objectives.

3.1 Study Overview: Response Rate, Non-Respondent Analysis, and Demographics

A total of 331 AYA survivors of childhood and adolescent cancer were approached, of which 250 (response rate= 75.5 percent) participated in the study and completed the Transition Readiness questionnaire. The response rate for clinic recruitment (96.6 percent) was significantly higher on the chi-square test ($p<0.01$) than mail recruitment (63.8 percent). Table 2 shows the number of participants recruited at each centre by using the two methods of recruitment. The non-respondents were significantly younger in age with a mean of 17.2 versus 18 years ($p<0.01$ on t-test). No differences were found between respondents and non-respondents in terms of gender, age at diagnosis, and type of cancer.

Table 3 shows the characteristics of the sample under study and also the distribution of variables used for this study. This table presents the numbers and proportions before

collapsing across variable categories to ready the data for the planned data analyses (due to small sub-group sample size). The sample had 135 (54.0 percent) males and an average age of 18.1 years, with the majority of participants between the ages of 15 and 17 years (53.6 percent). The majority of participants were Caucasian (73.6 percent), diagnosed between the ages 0 and 5 years (50.4 percent), and treated with chemotherapy (96.4 percent).

3.2 Descriptive Analyses

3.2.1 Self-Report Knowledge

In the first part of the Cancer Knowledge Survey, 240 (96.4 percent) participants indicated 'yes' and 9 (3.6 percent) said 'no' to 'I know the type of cancer I had' (see Appendix A- page 119). Out of the 240 participants who indicated that they know the type of cancer they had, 226 (94.2 percent) wrote the correct type of cancer in Part Two of the Cancer Knowledge Survey. Of the nine participants that indicated 'no' to knowing the type of cancer in Part One, five (55.5 percent) wrote the correct cancer type in Part Two of the Cancer Knowledge Survey. Overall, 19 (7.6 percent) participants out of a total of 249 were unable to indicate their true knowledge of diagnosis, or lack thereof.

195 (79.3 percent) participants said 'yes' and 51 (20.7 percent) said 'no' to the item 'I know some or all of the late effects that can be caused by my cancer treatment' (see Appendix A- page 119). Out of those that said 'yes', 149 (76.4 percent) wrote at least one late effects they were at risk for. Out of those that said 'no', 15 (29.4 percent) wrote at least one of the late effects they were at risk for. Overall, 61 (26.0 percent) participants

out of a total of 246 were unable to indicate their true knowledge of their risk of late effects, or lack thereof.

3.2.2 Primary Objective

Table 4 summarizes the findings of the descriptive analysis for the primary objective of this study.

3.2.2.1 Knowledge of Diagnosis

Out of 250 participants in the sample, 232 (92.8 percent) were 'knowledgeable' about their cancer-type with 183 (78.9 percent) out of 232 who also provided sub-type of their cancer.

3.2.2.2 Knowledge of Treatment

When asked to indicate whether or not they had received chemotherapy, radiation therapy, surgery, or a transplant as part of their treatment, the following number of participants were 'correct' about their status: chemotherapy - 240 (96.0 percent) out of 250; radiation therapy- 217 (87.5 percent) out of 248; surgery- 213 (85.5 percent) out of 249; and transplant- 206 (82.7 percent) out of 249. In addition, out of the 244 participants that had indicated their status on the questionnaire for all four treatments, only 2 (0.8 percent) were incorrect about the status for any of the four treatments received, while 8 (3.3 percent) had one treatment right, 15 (6.1 percent) had two treatments correct, 54 (22.1 percent) had three treatments correct, and 165 (67.6 percent) got all the four treatments' status correct. All in all, 25 (10.3 percent) participants were 'not knowledgeable', 54 (22.1 percent) were 'partially knowledgeable', and 165 (67.6 percent) were deemed 'knowledgeable' about their treatment.

3.2.2.3 Knowledge of Late effects

From the 248 participants who had sufficient information in their charts to deduce potential late effects, 83 (33.5 percent) failed to identify any late effects they were at risk for or provided incorrect late effects; these patients were classified as 'not knowledgeable' about their late effects. In addition, 31 (12.5 percent) patients were 'partially knowledgeable' as they provided some late effects that were correct and some that were incorrect. Finally, 134 (54.0 percent) were 'knowledgeable' of their potential late effects.

3.2.2.4 Overview of Knowledge of Diagnosis, Treatment and Late effects

Figure 3 presents an overview of the outcomes described above. More specifically, it presents data on the number of participants who were 'knowledgeable' of all three outcomes, diagnosis, treatment and late effects. Out of a total of 242 participants who had information available for all three outcomes, 225 (93.0 percent) were 'knowledgeable' about their diagnosis. In addition, out of the participants who were 'knowledgeable' of their diagnosis, 156 (69.3 percent) and 50 (22.2 percent) participants were 'knowledgeable' and 'partially knowledgeable' of their treatments, respectively. Furthermore, of those who were found to be aware of their diagnosis and treatments, 94 (60.3 percent) participants were found to be 'knowledgeable' of their late effects. Overall, 94 (38.8 percent) participants out of a total of 242 participants were aware of all the three outcomes: diagnosis, treatment and late effects (see Figure 3).

3.2.3 Secondary Objective

Table 4 includes the findings of the descriptive analyses for the secondary objective of this study.

3.2.3.1 Knowledge of Anthracyclines

According to the hospital records, 191 participants received anthracyclines. From this subset, 47 (24.6 percent) were 'knowledgeable' about receiving anthracycline(s) for their cancer treatment.

3.2.3.2 Knowledge of Anthracycline Related Late Effects

Out of the participants who received anthracycline(s), 95 (49.7 percent) were able to name late effects associated with the heart. Sixty four (44%) of all the participants who were unaware of the names of anthracyclines reported late effects associated with the heart, versus 31 (66.0%) of all participants that successfully named at least one of the anthracyclines they received.

3.3 Univariable Analyses

3.3.1 Primary Objective

In the univariable analysis looking at factors associated with knowledge of treatment, the following variables were found to be significantly associated with lower level of knowledge of treatment: non-white [odds ratio= 0.38 (95 percent CI= 0.21-0.66)] versus white; younger age at diagnosis [odds ratio= 1.08 (95 percent CI= 1.03-1.14)]; and diagnosed between the years 1986 and 1998 [odds ratio= 0.46 (95 percent CI= 0.27-0.77)] versus 1999 and 2011 (Table 5).

In univariable analysis looking at the relationship between several independent variables and knowledge of late effects, the following variables were found to be significantly associated with higher level of knowledge of late effects: older age at the time of recruitment [odds ratio= 1.12 (95 percent CI= 1.03-1.23)]; and having sarcoma [odds ratio= 2.66 (96 percent CI= 1.18-5.90)] and embryonal tumours [odds ratio= 3.27 (95 percent CI= 1.08-9.96)] compared to leukemia (Table 5).

3.3.2 Secondary Objective

The first simple binary logistic regression looked at all the independent variables under study to assess their association with knowledge of anthracyclines. The following independent variables were found to be significantly associated with a lack of knowledge of anthracyclines: younger age at diagnosis [odds ratio=1.11 (95 percent CI= 1.04-1.19)]; and having leukemia compared to sarcoma [odds ratio= 5.03 (95 percent CI= 1.97-12.85)].

Post-hoc analysis revealed that patients who received higher cumulative dose of anthracyclines were significantly more knowledgeable about anthracyclines, than patients with lower dose of anthracyclines (mean dose of 260 mg/m^2 versus 215mg/m^2; p=0.03 on t-test). Furthermore, patients with a history of sarcoma, also received significantly higher cumulative dose of anthracyclines than patients with other cancer types (mean dose of 343 mg/m^2 versus 207 mg/m^2, p<0.001 on t-test), and more specifically with a history of leukemia (mean difference of 139 mg/m^2; p<0.001 on ANOVA).

In addition, the following variables were found to be significantly associated with a lack of knowledge of anthracycline related late effects: non-white [odds ratio= 0.48 (95

percent CI= 0.25-0.94)] compared to white; mother [odds ratio= 0.28 (95 percent CI= 0.09-0.91)] and father [odds ratio= 0.34 (95 percent CI= 0.14-0.84)] not completing high school, compared to completing college or university; and having leukemia compared to an embryonal tumour (odds ratio= 5.31 (95 percent CI= 1.36-20.78)] (Table 6).

3.4 Multivariable Analyses

3.4.1 Primary Objective

3.4.1.1 Knowledge of Treatment

Ordinal logistic regression conducted to assess the association between knowledge of treatment, and race, age at diagnosis and year of diagnosis, controlling for centre and method of recruitment, showed a significant -2 Log Likelihood ($p<0.001$), and a non-significant Pearson's goodness of fit ($p=0.778$) and test of parallel lines ($p=0.186$). These values indicated a good model fit and also showed that assumption of proportional odds was valid. According to the Nagelkerke R^2 value, 12.2 percent of variance in the outcome (knowledge of treatment) was accounted for by the variables race, age at diagnosis, year of diagnosis, centre and method of recruitment. In the multivariable model, being non-white [odds ratio= 0.35 (95 percent CI= 0.19-0.64)] was significantly associated with lower knowledge of treatment, compared to white (Table 5).

Out of a total 63 non-white participants who provided an answer for all of the four treatment questions, 12 (19.0 percent) were 'not knowledgeable', 19 (30.2 percent) were partially knowledgeable, and 32 (50.8 percent) were 'knowledgeable' of their treatment. Whereas of the 178 white participants who provided an answer for all of the four

treatment questions, 12 (6.7 percent) were 'not knowledgeable', 35 (19.7 percent) were 'partially knowledgeable' and 131 (73.6 percent) were 'knowledgeable' of their treatment.

3.4.1.2 Knowledge of Late Effects

The model looking at knowledge of late effects with age and type of cancer as independent variables, and controlling for centre and method recruitment, showed a significant model fit compared to intercept only model ($p<0.001$), and a non-significant Pearson's goodness of fit test ($p=0.217$) and test of parallel lines ($p=0.402$). These values indicated a good model fit and a valid assumption of proportional odds. In addition, according to the Nagelkerke R^2 value, 13.9 percent of variance in the outcome (knowledge of late effects) was accounted for by the variables age during recruitment, type of cancer, centre and method of recruitment. The independent variables found to be significantly associated with a lower level of knowledge of late effects were as follows: younger age at the time of recruitment [odds ratio= 1.20 (95 percent CI= 1.07-1.34)]; and having leukemia as opposed to an embryonal tumour [odds ratio= 3.41 (95 percent CI= 1.10-10.58)].

The mean age for patients 'not knowledgeable' of their late effects was 17.36 years. Whereas the mean age for 'partially knowledgeable' and 'knowledgeable' participants 18.39 years and 18.41 years respectively. Moreover, out of 100 survivors of leukemia, 38 (38.0 percent) were 'not knowledgeable', 16 (16.0 percent) were 'partially knowledgeable' and 46 (46.0 percent) were 'knowledgeable' of their late effects. Among the 19 survivors of embryonal tumours who indicated their knowledge of late effects, 2

(10.5 percent) were ‘not knowledgeable’, 3 (15.8 percent) were ‘partially knowledgeable’ and 14 (73.7 percent) were ‘knowledgeable’. Centre C [odds ratio= 4.97 (95 percent CI= 1.78-13.9)] was also found to be significantly associated with a higher level of knowledge of late effects, compared with centre A (Table 5).

3.4.2 Secondary Objective

3.4.2.1 Knowledge of Anthracyclines

The multivariable logistic regression conducted to determine factors associated with knowledge of anthracyclines showed a good model fit with a non-significant Hosmer-Lameshow test (p=0.545). Also, according to the Nagelkerke R^2 value, 18.1 percent of variance in the outcome (knowledge of anthracycline use) was accounted for by the variables age at diagnosis, cancer type, centre and method of recruitment. In the multivariable analysis looking at the association between independent variables found significant in univariable analysis and knowledge of anthracyclines, the following independent variables were found to be significantly associated with a lack of knowledge of anthracyclines: younger age at diagnosis [odds ratio= 1.14 (95 percent CI= 1.04-1.25)]; and having had leukemia compared to sarcoma [(odds ratio= 4.30 (95 percent CI= 1.52-12.13)] (Table 6).

The mean age at diagnosis for participants ‘not knowledgeable’ and ‘knowledgeable’ of anthracyclines was 6.5 years 9.2 years respectively. Moreover, out of 83 survivors of leukemia who had received anthracyclines, 70 (84.3 percent) were ‘not knowledgeable’ and 13 (15.7 percent) were ‘knowledgeable’ of anthracyclines. In addition, out of 29

survivors of sarcoma who had received anthracyclines, 15 (51.7 percent) were ‘not knowledgeable’ and 14 (48.3 percent) were ‘knowledgeable’ of anthracyclines.

3.4.2.2 Knowledge of Anthracycline Related Late Effects

The multivariable logistic model conducted to determine factors associated with knowledge of anthracycline related late effects showed a good model fit with a non-significant Hosmer-Lameshow test (p=0.71). In addition, 24.0 percent of variance in the outcome (knowledge of anthracycline related late effects) was accounted for by the variables race, mother and father’s level of education, cancer type, centre, and method of recruitment. In the binary logistic model, the following factors were significantly associated with a lack of knowledge of anthracycline related late effects: being non-white [odds ratio= 0.33 (95 percent CI= 0.14-0.76)] compared to white; and cancer type leukemia compared to embryonal tumour [odds ratio= 5.08 (95 percent CI= 1.19-21.77)].

Out of 51 non-white participants who had received anthracyclines, 32 (62.7 percent) were ‘not knowledgeable’ and 19 (37.3 percent) were ‘knowledgeable’ of the late effects associated with the heart. Whereas, out of 138 white participants who had received anthracyclines, 62 (44.9 percent) were ‘not knowledgeable’ and 76 (55.1 percent) were ‘knowledgeable’ of the late effects associated with the heart. Moreover, out of 83 survivors of leukemia who had received anthracyclines, 51 (61.4 percent) were ‘not knowledgeable’ and 32 (38.6 percent) were ‘knowledgeable’ of anthracycline related late effects. In addition, out of 13 survivors of embryonal tumours who had received anthracyclines, 3 (23.1 percent) were ‘not knowledgeable’ and 10 (76.9 percent) were ‘knowledgeable’ of anthracycline related late effects. Centre B [odds ratio= 3.0 (95

percent CI= 1.3-7.0)] was also significantly associated with knowledge of anthracycline related late effects compared to centre A (Table 6).

3.5 Chapter Summary

This chapter gave an overview of the study with response rates, non-respondent analysis, and sample characteristics to provide information on the sample. The chapter then provided descriptive analyses of the outcomes to address the first question of the primary and secondary objectives, by providing the extent of knowledge deficits in the sample. Variables found significant in the univariable analysis were identified for both primary and secondary objectives. The chapter also presented the odds ratios and CI of independent variables found significant in the analyses, and reported values for tests that determined the adequacy of the model fit.

Chapter 4: Discussion

This chapter summarizes the main findings, contextualizing it to the objectives set out for this study. Plausible explanations for the observed associations are also presented. The results from this study are discussed in this chapter from the perspective of both statistical and clinical significance.

The chapter begins with an overview of the rationale for conducting this study and a summary of results. The chapter addresses the importance of using detailed questions to ascertain knowledge in cancer survivors, instead of using self-report measures. The chapter then discusses results obtained to achieve primary and secondary objectives of this study and how they compare to findings from previous studies. To end the chapter, a summary of approaches that can be used to educate survivors of their diagnosis, treatment and late effects is presented.

4.1 Assessing Knowledge in AYA Survivors of Childhood and Adolescent Cancer

To the best of our knowledge, this study is the first to examine the extent of knowledge deficits regarding diagnosis, treatment and late effects specifically in a sample of Canadian AYA survivors of childhood and adolescent cancer. Previous studies have reported the importance of adequate disease related knowledge in motivating survivors to attend LTFU care, as well as living a healthy lifestyle.[31,34,38,61] Furthermore, knowledge of cancer history and risks associated with the treatments have also been shown to be important facilitators in successful transition from pediatric to adult LTFU care.[39,48]

The goal of this study was to look at the extent of knowledge related to diagnosis, treatment and late effects, and identify factors associated with such knowledge in AYA survivors of childhood and adolescent cancer. Through findings from this study, we wanted to provide research evidence about any patient, family, cancer and treatment factors, including cancer worry that could be targeted and studied further to see if cancer knowledge can be improved in the future. In addition, findings from this study could also be used to inform the HCPs and researchers working in the field of LTFU care, where more education is required, as well as to initiate a discussion about the approaches used to tackle these issues.

Unlike some of the previous studies reporting knowledge deficits with regards to diagnosis, our study showed that a high proportion of participants were aware of their diagnosis of cancer and the type of cancer. However, the study findings exhibited important knowledge deficits with regards to treatment and late effects. Knowledge deficiency regarding treatment in all AYA cancer survivors was more pronounced in non-Caucasian compared to Caucasian patients. In patients who received anthracycline agents, knowledge deficits regarding treatment of anthracyclines was associated with being diagnosed at a younger age, and to having leukemia compared to sarcoma. In addition, less knowledge regarding late effects in all AYA cancer survivors was associated with younger age at the time of recruitment and having had leukemia, compared to embryonal tumours. Moreover, knowledge deficits regarding late effects associated with anthracyclines was also associated with being non-Caucasian versus Caucasian, and having had leukemia instead of embryonal tumour.

4.2 Self-Reported Knowledge of Diagnosis and Late Effects

Our results showed that future research looking to assess disease knowledge, specifically of diagnosis and late effects in survivors of childhood and adolescent cancer, should not be determined from a set of 'yes/no/not sure' format questions. The inadequacy of 'yes/no/not sure' format questions was established from the findings of our study, which indicated that patients did not provide accurate information using this format. Our findings are similar to those of Bashore (2004) who showed that although all of the survivors or parents reported knowing the type of cancer the patient had in the self-report part of the interview, only 84 percent were actually able to list their diagnosis.[42]

Part of the findings of the current study on self-report knowledge can be explained by what has been reported in the literature concerning social desirability bias in self-report inventories. It has been reported that social desirability of certain responses play a critical role in participants' reporting, where participants either believe in the inaccurate information they provide (self-deception) or provide responses to conform to socially acceptable, approved or appreciated values.[62,63,64] Specific to our study, being more knowledgeable about cancer history and late effects may be viewed as socially desirable, compared to not being aware of such information. This bias may explain why we observed 14 participants who had initially reported knowing their diagnosis, who then failed to write their diagnosis in Part Two of the Cancer Knowledge Survey, compared to only 5 participants who initially reported not being aware of their diagnosis, but then correctly reporting the type of cancer they had. Similarly, 46 participants who had

initially reported being knowledgeable of late effects failed to provide at least one late effect they were at risk for, compared to only 15 who indicated not knowing their late effects in Part One of the Cancer Knowledge Survey, but correctly identified at least one late effect in Part Two of the survey.

Although social desirability bias may explain why some participants in our study reported knowing their diagnosis and late effects in the self-report part of the Cancer Knowledge Survey, even though they lack true knowledge, it does not explain why some participants reported being unaware of their diagnosis and late effects, but in fact wrote the correct information in Part Two of the Cancer Knowledge Survey. One plausible explanation for this result maybe that these patients are unsure about their diagnosis and/or late effects and hence, lack confidence in the information they recall. Therefore, when asked to write down the detailed answer, participants provided answer to the best of their ability, with perhaps an equal chance of getting the question right as wrong. Because of the inaccuracies and inconsistencies in self-report knowledge of diagnosis and late effects, future research that examines knowledge of cancer history and late effects in survivors of childhood and adolescent cancer should avoid relying solely on the use of self-report surveys.

4.3 Knowledge of Diagnosis, Treatment and Late Effects

Knowledge of diagnosis is the bare minimum of what is required of the patients; a patient cannot be expected to know the type of treatments and associated late effects if they are unaware of their diagnosis. Further knowledge of treatment and its associated late effects can be learned once the diagnosis is accurately understood. For the purposes of this study, we hypothesized that AYA survivors would have a progressively higher amount of knowledge deficiencies moving from knowledge of diagnosis, to treatment, to late effects. Our results supported this hypothesis by showing increasing knowledge deficiencies. As reported in the Results chapter, findings showed that 18 (7 percent) participants were 'not knowledgeable' about their diagnosis, compared to 25 (10 percent) participants being unaware of at least two of the treatments they received, and 83 (34 percent) 'not knowledgeable' of their late effects. In addition, 8 percent of participants who knew their diagnosis were 'not knowledgeable' of their treatments, whereas 29 percent of participants who knew their status of all the four treatments were unaware of any of the late effects. This shows a progressive decline in disease knowledge. These findings of increasing knowledge deficits by category of information indicate a need for education of survivors to ensure that they know their diagnosis, and once that is accomplished, to add in knowledge of treatments and associated late effects.

Knowledge of risks associated with the cancer treatment has been shown to be an important factor impacting survivors' core health beliefs in seeking LTFU care, including their motivation to seek such care, perceived susceptibility and seriousness of late effects.[31] These core health beliefs then impact survivor attending the longitudinal risk-based care.[31] According to the theoretical framework, presenting barriers and facilitators

to longitudinal risk-based care in adult cancer survivors, adequate knowledge may motivate survivors to seek LTFU care, facilitating the process (see figure 1). In addition, according to SMART, knowledge of cancer history and late effects may also facilitate the process of transition and eventual transfer to adult care (see figure 2). However, inadequate knowledge of late effects in survivors of childhood and adolescent cancer, main finding of this study, may present a barrier to survivors' attendance to LTFU care in general, and to the process of transitioning in specific.[39] Needless to say, knowledge of late effects is critical in patients managing their health care and modifying their lifestyle.[31,61]

Since a large portion of our sample came from survivors attending LTFU care who were recruited during clinic appointments, we expected to see greater knowledge regarding diagnosis, treatments and late effects in patients who were older. This was based on an assumption that patients attending LTFU care are frequently made aware of their cancer history and risks associated with their treatments, as this is one of the goals of LTFU care. It was then expected that with increasing age, more relevant information would be delivered by the HCP to the patient during LTFU care appointments. However, we did not see a consistent association between age and all of the outcomes considered in this study. This is concerning to us since we expected that LTFU care would progressively educate survivors of their cancer history and late effects as they get older, especially before transition. In addition, we also expected to find significant knowledge deficits with regards to diagnosis, treatment, and late effects in patients diagnosed at an earlier age. This is because patients diagnosed at a younger age may not recall their

cancer experience and treatment process. If age at diagnosis was in fact found to be significant, it would have pointed to the need of better transfer of information related to cancer and late effects from HCPs and parents to patient.

4.3.1 Knowledge of Diagnosis

The descriptive analysis concerning knowledge of diagnosis showed that 232 (93 percent) participants were able to write the correct cancer type when asked to provide this information. A similar level (i.e., over 84 percent) of knowledge of type of cancer has been reported in two studies of predominantly U.S. childhood cancer survivors over the age of 16 years.[42,45] Similar findings have been reported in adult survivors of childhood lymphoma. Findings published by Hess et al. (2011), who examined cancer knowledge specifically in adult survivors of childhood lymphoma, reported that 95 percent of a sample of 128 participants was aware of having been diagnosed with lymphoma. On the other hand, Bryne et al. (1989) reported a knowledge deficit with 14 percent of patients with other cancer types, and 75.3 percent of patients with CNS tumours were unaware of having been diagnosed with cancer. This study did not look at whether survivors knew of their cancer type, but rather the knowledge of ever been diagnosed with cancer. It is important to note that the Bryne study was conducted 24 years ago and continued improvement has since occurred in delivering LTFU care over the years, where part of the focus is to educate survivors of their cancer history; this may account for better cancer knowledge in our study.

According to the findings from our study, the majority of the participants who knew their type of cancer were able to provide the sub-type of their cancer (79 percent).

Previous studies that specifically asked for detailed answers regarding cancer diagnosis showed a similar proportion of participants being aware of their cancer sub-type as our study. A study conducted by Kadan-Lottick et al. (2002) showed that 72 percent of childhood cancer survivors were accurate in reporting their cancer sub-type, after additional prompting, which was similar to the proportion found in our study, without prompting. In addition, findings reported by Hess and colleagues (2011), looking at knowledge in 128 adult survivors of childhood lymphoma, showed that 73 percent of participants could provide their sub-type of lymphoma. Although we were unable to look at the factors associated with knowledge of diagnosis, a primary objective of our study, due to limited sample size, previous studies have reported a lack of knowledge regarding type of cancer in males,[44,45] survivors of CNS tumours and neuroblastoma,[45] those diagnosed at a younger age,[44] and an earlier era of treatment.[45] Since the proportion of participants in our study who were unaware of their diagnosis was relatively small, very large sample sizes may be required in future studies to look at factors associated with knowledge of diagnosis.

Findings from our study further confirm the high level of knowledge of diagnosis in childhood cancer survivors. This is an important finding as it reveals the high level of knowledge regarding type of cancer in childhood cancer survivors. The existing knowledge of diagnosis can form the base upon which HCPs can further educate survivors of their treatments and late effects.

4.3.2 Knowledge of Treatment

Important knowledge deficits regarding treatment were identified in our study. When asked to indicate whether or not they had received chemotherapy, radiation therapy, surgery and transplant, almost all (96 percent) of participants accurately indicated their status for chemotherapy compared with 88 percent for radiation therapy. Higher knowledge deficiency with regards to radiation therapy compared to chemotherapy found in our study, is consistent with findings of previous studies.[42,45] Bashore (2004) reported a greater knowledge deficit with regards to status of receiving radiation therapy (43 percent) in a sample of 141 childhood and adolescent cancer survivors compared to our study.[42] However, in the study published by Bashore (2004), the proportion of participants knowledgeable of their treatment of chemotherapy (93 percent) were similar to our study findings.[42] Also, Kadan-Lottick et al. (2002) showed similar findings as those in our study, with lower knowledge level about radiation therapy (89 percent) than for chemotherapy (94 percent).[45]

None of the five studies in our literature review looked specifically at transplant. In our study, we found the lowest level of knowledge for this form of treatment; 83 percent of participants were able to correctly report whether or not they had a transplant as part of their treatment or not. Contrary to this finding, we had expected relatively low inaccurate responses concerning the status of receiving a transplant as this is the most intensive form of treatment. We had expected those who received a transplant to remember receiving it, and those who did not receive it to know they had not. All of the participants who received a transplant in our sample were aware of receiving this form of treatment. However, of those who were inaccurate in reporting whether or not they had received

transplant as part of their treatment, 42 percent reported being 'not sure' of their status of transplant. Because transplant is an uncommon cancer treatment, cancer survivors may lack general information regarding this form of treatment. This lack of general information regarding transplant may be the reason why patients who did not receive this treatment reported being unsure of whether or not they had received transplant.

This study is the first to look at the level of knowledge of treatment and examine factors associated with this knowledge. Previous studies have looked at treatments separately in order to examine knowledge deficits and factors associated with it, with a particular focus on chemotherapy and radiation therapy.[42,44,45] We decided to look at all four treatments, given that they all have implications for late effects. Although we saw a significant association between age at diagnosis, year of diagnosis, and level of knowledge of treatment in the univariable analysis, this effect diminished in multivariable analysis. Only race was found to be significantly associated with the outcome, knowledge of treatment, in the multivariable analysis, with non-white participants being significantly less knowledgeable of their treatment. Most of the non-white participants in our sample were South Asians and people who reported mixed ethnicity. We found that among non-white participants, as compared with white participants, the odds of the combined 'knowledgeable' and 'partially knowledgeable' categories versus 'not knowledgeable' were 0.35 times lower. This association persisted even after controlling for socio-economic factors such as a patient's education, and mother and father's level of education. It is difficult to say whether these differences are due to differential treatment of white compared to non-white patients by the healthcare system in general, and HCPs in

particular, or if it is related to cultural differences in the way cancer related information is treated between white and non-white patients. Since the majority of the non-white participants in our sample reported mixed ethnicity, we do not believe that language barrier can explain the differences in knowledge of treatment between white and non-white participants. Similar to our findings, the study by Bryne and colleagues (1989) reported a significant association between non-white participants and lack of knowledge regarding diagnosis, which was apparent after adjusting for socio-economic factors.[41]

To achieve one of the secondary objectives of the study, knowledge of anthracyclines and its potential predictors were examined. Results showed that three quarters of participants failed to name at least one of the anthracycline agents they had received during their treatment. This finding was similar to that of Kadan-Lottick et al. (2002) who found that 75 percent of 266 participants in their study of 635 childhood cancer survivors who received either doxorubicin or daunorubicin, were unaware of this treatment.[45]

The multivariable analysis revealed a strong positive association between knowledge of anthracyclines and age at diagnosis; i.e., with every one year increase in age at diagnosis, the odds of being 'knowledgeable' versus 'not knowledgeable' was 1.14 times greater. The narrow 95 percent CI may limit the clinical significance of this finding; however, the estimates are for every one year increase in age at diagnosis that may be stronger over a few years. Although other studies have also found strong positive associations between age at diagnosis and cancer knowledge, those findings were specific to either knowledge of diagnosis[41] or radiation therapy.[45] It is plausible that patients diagnosed at a younger age are perhaps too young to remember general information about

their cancer, let alone specifically anthracyclines. Hence, that is a potential reason why less knowledge about anthracyclines was reported. Lack of transfer of detailed anthracycline related information from the HCP and/or parent to patient may also explain this relationship.

In addition, an association was also observed between patients with a history of sarcoma and knowledge of anthracyclines; in patients with a history of sarcoma, the odds of being 'knowledgeable' versus 'not knowledgeable' were 4.3 times greater, compared to patients with a history of leukemia. The intensity of treatment may explain why patients with a history of sarcoma were more knowledgeable about anthracyclines than patients with leukemia. It has also been reported that in cancer survivors diagnosed before the age of 18, a cumulative dose of equal to or greater than 300 mg/m^2 is associated with a higher risk of anthracycline related late effects (e.g., cardiomyopathy).[27,47,66] The patients with a history of sarcoma in our sample (mean cumulative dose of anthracycline= 343 mg/m^2) are at increased risk of such late effects.

Knowledge deficiencies regarding cancer treatment in general, and anthracyclines in particular have several implications for knowledge of late effects. As stated previously, patients should first be aware of their diagnosis, then learn about treatments, and subsequently, learn the late effects associated with their treatments. Patients cannot be expected to understand and remember the late effects associated with cancer treatments, especially anthracyclines, if they do not even know that they have had such treatments. Knowledge deficits regarding cancer treatments found in our study points to the importance of educating survivors of their treatments, specifically if they received

anthracyclines, given its association with several cardiac related complications later in life.[47]

4.3.3 Knowledge of Late Effects

The results of this study showed knowledge deficits with regards to late effects. One-third of the participants in this study were unable to name at least one of the late effects for which they were at risk. In addition, almost half of the participants either did not report any late effects, or reported some correct and some incorrect late effects. The proportion of participants knowledgeable of their late effects in our study was higher than that reported in previous studies looking at knowledge of late effects in childhood cancer survivors. According to Bashore (2004), 30 percent of patients in her sample of 141 childhood cancer survivors reported being able to provide their late effects of their cancer treatments. However, only half of the 30 percent actually provided at least two late effects.[42] Unlike our study, the late effects that participants provided were not checked against the hospital information; if participants' answers were compared against the late effects they were actually at risk for, the reported proportion of participants knowledgeable about their late effects would have reduced. Kadan-Lottick et al. (2002) reported results similar to Bashore, with 35 percent of participants believing that the cancer treatments they had received can cause serious health problems later on in life.[45] Another study, looking at knowledge of late effects in adult survivors of lymphoma, showed that 34 percent of participants indicated that they knew at least one of the late effects, which was significantly related to the treatment period.[44] It is possible that the higher proportion of participants being aware of their late effects in our study, compared

to previously published studies almost a decade ago, could be attributed to recent efforts of establishing and implementing guidelines for LTFU care, which focuses on prevention, detection and intervention of complications related to cancer treatments.[65]

In terms of factors that can explain knowledge of late effects, we found a significant association with age; with every one year increase in age, the odds of being 'knowledgeable' versus the combined 'partially knowledgeable' and 'not knowledgeable' categories were 1.20 times greater. The clinical relevance of this finding might be doubtful at first as the 95 percent CI indicates that there is 95 percent certainty that the true effect lies within the odds ratio of 1.07 and 1.34, both of which are very close to the no difference point of one. However, it is important to note here that these values are for every one year increase in age, and that the effect would be larger over years.

That age can explain knowledge of late effects supports the idea of starting to educate survivors about their cancer and late effects at a young age in order to prepare them for the eventual transition to adult healthcare. By starting the education process early, survivors will have adequate time before the process of transition to learn their late effects, which may in turn motivate them to continue seeking LTFU care as adults. According to the transition framework for pediatric patients with chronic diseases, developed by the Western Australian Child and Youth Health Network's Pediatric and Adolescent Chronic Diseases Transitional Care Working Party, active preparation for transition to adult care should begin at the age of 12 years.[68] Educating survivors of their cancer history and potential long-term health complications due to their cancer treatment

at the age of 12 years will allow for sufficient time to address any knowledge deficits before transition to adult care occurs.

We also found a significant association between knowledge of late effects and embryonal tumours, which became stronger from univariable to multivariable analysis; in patients with embryonal tumours, the odds of being 'knowledgeable' versus combined 'partially knowledgeable' and 'not knowledgeable' were 3.41 times greater compared to patients with leukemia. This finding was opposite to that reported by Kadan-Lottick et al. (2002), who found that patients with neuroblastoma lacked knowledge about their diagnosis and radiation therapy.[45] Ten out of 20 participants of our study in the embryonal tumours category had neuroblastoma, most of which were at stage three or four, placing them in the intensity level three, out of four.[54] It is possible that due to the high treatment intensity associated with having a higher stage of neuroblastoma, more patients were aware of their associated late effects. In addition, we had also hypothesized a significant association between knowledge of late effects and year of diagnosis because of the emergence of new information on late effects over the past decade, which is now available to the survivors of childhood and adolescent cancer. However, we did not observe this association in our univariable or multivariable analyses.

Findings from this study also showed knowledge deficits with regards to late effects associated with anthracyclines, with less than half of the sample at risk for cardiac related late effects aware of such long-term complications. This knowledge deficit was more pronounced in patients who failed to write the names of at least one of the anthracycline agents, compared to those who mentioned receiving anthracycline(s). This finding further

confirms the idea proposed above that patients should be educated about their treatment, prior to educating them about its associated late effects.

Although a mother and father's education were both found to be significantly associated to knowledge about anthracycline related late effects in the univariable analysis, this significance diminished in multivariable model. However, significance of association between non-white and embryonal tumours with the outcome knowledge of anthracycline related late effects persisted after accounting for other independent variables found significant in univariable analysis. In non-white participants, the odds of being 'knowledgeable' versus 'not knowledgeable' were 0.33 times lower, compared to white participants. In addition, in patients with embryonal tumours, the odds of being 'knowledgeable' versus 'not knowledgeable' was 5.31 times higher than in patients with a history of leukemia. The odds ratio, however, was lower for non-white participants in the multivariable model compared to univariable. It is perhaps possible that socio-economic variables such as mother and father's education confounded association between race and knowledge of anthracycline related late effects. The negative association between non-white participants and knowledge of late effects associated with anthracyclines is probably for the same reason as the observed negative association between being non-white and knowledge of treatments (discussed above). Moreover, similar to what was mentioned above, most of the embryonal tumour patients in the sub-group of patients that received anthracyclines, had either stage three or stage four neuroblastoma. This may explain why we observed a positive association between embryonal tumours and knowledge of anthracycline related late effects. Thus, it is

important for HCPs to educate non-white survivors to ensure adequate knowledge is attained. Knowledge of risks may motivate these survivors to engage in health promoting behaviours (e.g., exercising) and not in health behaviours that are risky to one's health (e.g., tobacco use), as this is shown to prevent cardiotoxicity related to anthracycline.[47]

We had not expected to find a significant association between centres and knowledge of cancer and late effects. However, for knowledge of late effects, including knowledge of anthracycline related late effects, centres B and C were significantly associated with increased knowledge, compared to centre A. This, however, may be misleading since there was a discrepancy between the centres in the number of participants recruited, which may have influenced these estimates.

4.4 Attending to the Problems of Knowledge Deficits

All in all, we only had 94 (40 percent) participants who knew their type of cancer, all four treatments, and some or all of the late effects associated with their treatments. Since the majority of our sample was unaware of their diagnosis, treatment and/or late effects, this shows that knowledge deficiency in some survivors needs to be addressed by HCPs. Possible approaches to address knowledge deficits include providing survivors with a comprehensive, but concise, written summary of their diagnosis, treatment and late effects for which they are at risk, in addition to lifestyle choices that will mitigate any risks for particular late effects. In addition, patients attending LTFU care should be quizzed periodically to determine their level of knowledge in order to identify gaps in knowledge. These gaps can then be targeted to ensure that survivors acquire the

knowledge they need to manage their health and healthcare. The regular evaluation of knowledge by HCPs will also allow them to ascertain whether survivors have adequate information related to their cancer history and a satisfactory understanding of how their behaviours may impact their long-term health. Furthermore, we suggest that the process of educating survivors should start early in the LTFU care (at recommended age of 12 years) so that patients have sufficient time to learn pertinent information regarding their chronic condition, allowing them to take responsibility for their care when they transition to either an adult LTFU care program or to PCP.

4.5 Chapter Summary

This chapter provided in-depth discussion of the results obtained for the primary and secondary objectives of the study. Inferences from previous findings are also drawn to provide a context and importance of our findings compared to results reported by previous studies looking at knowledge of diagnosis, treatment and late effects. At the end of the chapter, a discussion of approaches to address knowledge deficits is provided to provide a brief overview of the implications of our findings.

Chapter 5: Strengths, Limitations, Implications, Future Research, Dissemination of Findings and Conclusion

This chapter provides a summary of the strengths and limitations of the study. Furthermore, the implications of the study findings are provided along with future research that may be required to further understand the gaps in knowledge of cancer history, late effects, and survivorship care. Plan of dissemination of study findings are then discussed, after which a brief conclusion of the overall study findings is presented.

5.1 Strengths and Limitations of the Study

According to the literature review presented in the Introduction chapter, few studies published in the last decade exist that look at the extent of knowledge of cancer history and late effects in childhood and adolescent cancer survivors. To the best of our knowledge, the latest publication that examined knowledge deficits with regards to diagnosis, treatment and late effects in survivors of all cancer types was published in the year 2004.[42] Since much new information has emerged on the risks to physical and psycho-social health as a result of cancer and treatments in the last decade,[13,14,15,17,19,22,23,24] new research is needed to evaluate the current knowledge of childhood and adolescent cancer survivors with regards to their cancer history and late effects. Furthermore, research is needed to understand the extent of knowledge specific to Canadian AYA survivors of childhood and adolescent cancer. The present study was an attempt to fill this gap in the literature by looking at current knowledge regarding

diagnosis, treatment and late effects in Canadian AYA survivors of childhood and adolescent cancer.

One of the strengths of this study, compared to studies described in our review of the literature, was that we used more than one source of data to ensure rigor in the results, including self-report knowledge regarding diagnosis, and late effects and information extracted from hospital records. The only study published to date that looked at knowledge of late effects in childhood survivors of all types of cancers, used only self-report knowledge of late effects.[42] However, we were able to determine that self-report information is not an adequate means of determining the knowledge of cancer survivors, because some survivors cannot accurately report their knowledge. We also determined the late effects for each participant in our study based on their treatment history. One oncologist expert in LTFU care ascertained late effects based on the diagnosis and treatment information extracted from hospital records. Thus, we were able to look at the accuracy of reported late effects by comparing the answers provided by participants with the ascertained late effects, according to which, participants were deemed 'knowledgeable', 'partially knowledgeable' or 'not knowledgeable'. Moreover, we ensured we collected the full range of variables to create composite variables such as for late effects (as just described) and treatment intensity. One of the previous studies looking to evaluate the strength of association between treatment intensity and cancer related knowledge, for example, only used types of treatments received to categorize intensity of treatment.[41]

This study had several limitations that must be recognized. The external validity of this study was impacted by several factors. First, LTFU care varies throughout the 17 pediatric oncology centres in Canada; therefore, given that participants for this study were only recruited from three of the 17 centres, findings from this study cannot be extended to all Canadian AYA survivors. Second, although we included three centres, employing three different models of care for transition, we only recruited transitioned adult patients from one of the three pediatric oncology hospitals (i.e., with the joint pediatric-adult LTFU clinic). This is to say that we did not include participants that have been transitioned from pediatric centre to the linked adult facility, and to community or PCP. This limits the external validity of our study as adult patients that attend, or are expected to attend LTFU care at a specialized centre may differ in their knowledge of their diagnosis, treatment and late effects, compared to those who have been transitioned to a non-specialized LTFU care facility. Third, one of the participating centres was included later in the recruitment period and provided smaller number of participants compared to the other two centres. Because of the relatively small sample size from one of the participating centres, there was a clear discrepancy between the size of the centres and the number of participants recruited from each centre. Fourth, although CNS tumours are the second largest childhood cancer type, our sample is not representative of the population as we excluded participants with neuro-cognitive disability if it meant they were not able to independently complete the questionnaire booklet.

Several limitations also impacted the internal validity of this study. As stated above, the response rate for clinic recruitment was significantly higher than mail recruitment,

which introduced a non-respondent bias, leading to selection bias. Another limitation related to using mail as a method of recruitment was that although the information mailed to potential participants stressed the importance of completing the questionnaire independently, without external resources or aid, there was no way of ensuring that instructions were strictly followed by the participants. Because methods of recruitment may be a confounder, we included this variable as a control variable in the analyses.

This study was also impacted by non-respondent bias, where non-respondents were found to be significantly younger in age than respondents, impacting the internal validity of the study. However, an assumption can be made that had these respondents been part of our study, the knowledge deficits might have been more pronounced since age was positively related to the outcome, knowledge of late effects, in multivariable analysis. Also, the non-respondents may have differed from respondents in factors other than what we accounted for in our non-respondent analysis (i.e., age, gender, age at diagnosis, and type of cancer), introducing participating bias.

The multivariable ordinal logistic regression model that we conducted to examine the association between knowledge of treatment and factors found significant in the univariable analysis, controlling for centre and method of recruitment, included six variables in the model. Since we had a total of 165 participants who were 'knowledgeable' of their treatment, we had an adequate number of cases to conduct the multivariable logistic regression model. In addition, the multivariable model conducted to examine the association between variables found significant in the univariable analysis and knowledge of late effects required a minimum of 90 cases since there were nine

variables included in the model. The model was adequate to conduct the multivariable analysis as there were a total of 134 participants who were 'knowledgeable' about their risks of late effects. However, although the sample size was adequate and allowed for inclusion of variables found significant in the univariable analysis in multivariable analysis, there was small number of participants in some of the categories for certain variables. We had a total sample size of 250, with only 18 (7.2 percent) participants 'not knowledgeable' of their diagnosis, which limited our ability to conduct the multivariable analysis to examine factors related to knowledge of diagnosis. Furthermore, there were also a small number of participants in some of the categories of the independent variables. Although many small categories were amalgamated in an attempt to provide sufficient power to detect differences between groups, in some cases amalgamation was not possible due to lack of theoretical reasoning for collapsing categories. However, given the lack of research available to understand factors related with cancer knowledge, and the exploratory nature of our study, future research can further study variables included in our study with an adequate sample size.

One of the limitations of the Cancer Knowledge survey was that Part Two of the survey did not probe for sub-type of cancer. In our results, we reported that 183 (73 percent) out of 250 participants provided the sub-type of their cancer without probing for such information. The proportion of participants who knew about their sub-type of cancer may have been higher had we specifically asked participants to provide the sub-type of their cancer.

5.2 Implications of Study Findings

Findings from this study provide information about the extent of knowledge of AYA survivors of childhood and adolescent cancer, concerning their diagnosis, treatment and late effects, specific to a sample of Canadians. The findings from this study can help HCPs, specifically those that work with survivors in LTFU clinics (e.g., oncologists, nurses), to determine areas where more focus is needed to educate survivors. In addition, results from this study could be used to educate HCPs about factors that are associated with knowledge deficits to identify AYA cancer survivors who may lack necessary information about their diagnosis, treatments and, most importantly, late effects as a result of cancer treatments they received. Furthermore, results from this study may also help in the development of programs and targeted interventions that aim to educate AYA cancer survivors regarding their cancer history and late effects. Health care decision makers, planners and policy makers can use pertinent information from this study to guide the development of new programs that aim to better prepare AYA survivors in taking care of their own health.

5.3 Future Research

As discussed above, this study had several strengths which set it apart from previously published studies. But it is important to keep in mind the limitations that impacted the external validity. Future research can aim to improve on these limitations by recruiting a comprehensive sample of Canadian AYA survivors of childhood and adolescent cancer from the 17 pediatric oncology centres. In addition, future research that

focuses on evaluating the extent of knowledge in AYA cancer survivors attending LTFU care at an adult facility or through a PCP is warranted. Such research may help to determine whether this sub-group of AYA survivors of childhood and adolescent cancer differ in any way with regards to their knowledge of cancer history and late effects from those attending pediatric centres for LTFU care. Future research should also focus on exploring additional variables that may be associated with knowledge of diagnosis, treatment and late effects given that the variables we investigated only accounted for small percent variance in the outcomes. The small percentage of variance yielded from the multivariable analysis shows that there is room to explore other variables that may explain remaining variance in the outcomes, knowledge of treatment and late effects.

The amount of knowledge a HCP has about a patient's risk for late effects has also been found to be an important barrier/facilitator to LTFU care.[31] Future research should also look to asses HCPs' knowledge of late effects in order to ensure that barriers related to the HCP are tackled along with survivors related barrier in an appropriate manner. It will be important to know whether knowledge deficits exist in HCPs to design interventions to educate HCPs, prior to targeting survivors, as in most cases, HCPs are responsible for educating survivors and answering questions pertaining to late effects.

The findings from this study suggest important knowledge deficits exist in a sample of AYA survivors of childhood and adolescent cancer. Based on these findings, a program of research should be initiated to improve these knowledge deficits related to treatment and late effects. A longitudinal study is needed to identify approaches that may successfully increase knowledge in survivors over a period of time.

5.4 Dissemination of Findings

The preliminary results of this study have been presented at a number of national and local conferences. More specifically, the following presentations have been made: a poster presentation at Pediatric Oncology Group of Ontario (POGO) multi-disciplinary symposium in November of 2011 and 2012; a poster presentation at the Faculty of Health Sciences Research Plenary at McMaster University in May 2013; a poster presentation at McMaster University Clinical Epidemiology and Biostatistics (CE&B) 9th and 10th Annual Research Day in March 2012 and 2013; an oral presentations at the 9th Annual Oncology Student Research Day at Juravinski Cancer Centre in June 2012; and an oral presentation at the Laboratory Medicine and Pathobiology Student Union (LMPSU) Undergraduate Conference on Cancer at University of Toronto in January 2013.

Abstracts will be submitted for oral and/or poster presentations at other conferences to disseminate final results of the study, including the POGO multi-disciplinary symposium, and Congress of the International Society of Pediatric Oncology in Toronto. Manuscripts will also be prepared, featuring findings from this study, for publication in peer-reviewed journals.

5.5 Conclusion

This study revealed important knowledge deficits with regards to treatment and late effects, which point to a need of programs and interventions designed to educate survivors of this pertinent information. The factors identified in this study to be significantly associated with knowledge deficits about treatments and late effects will

help inform future researchers to design and evaluate any educational programs and/or interventions, in order to specifically target those at risk of inadequate knowledge.

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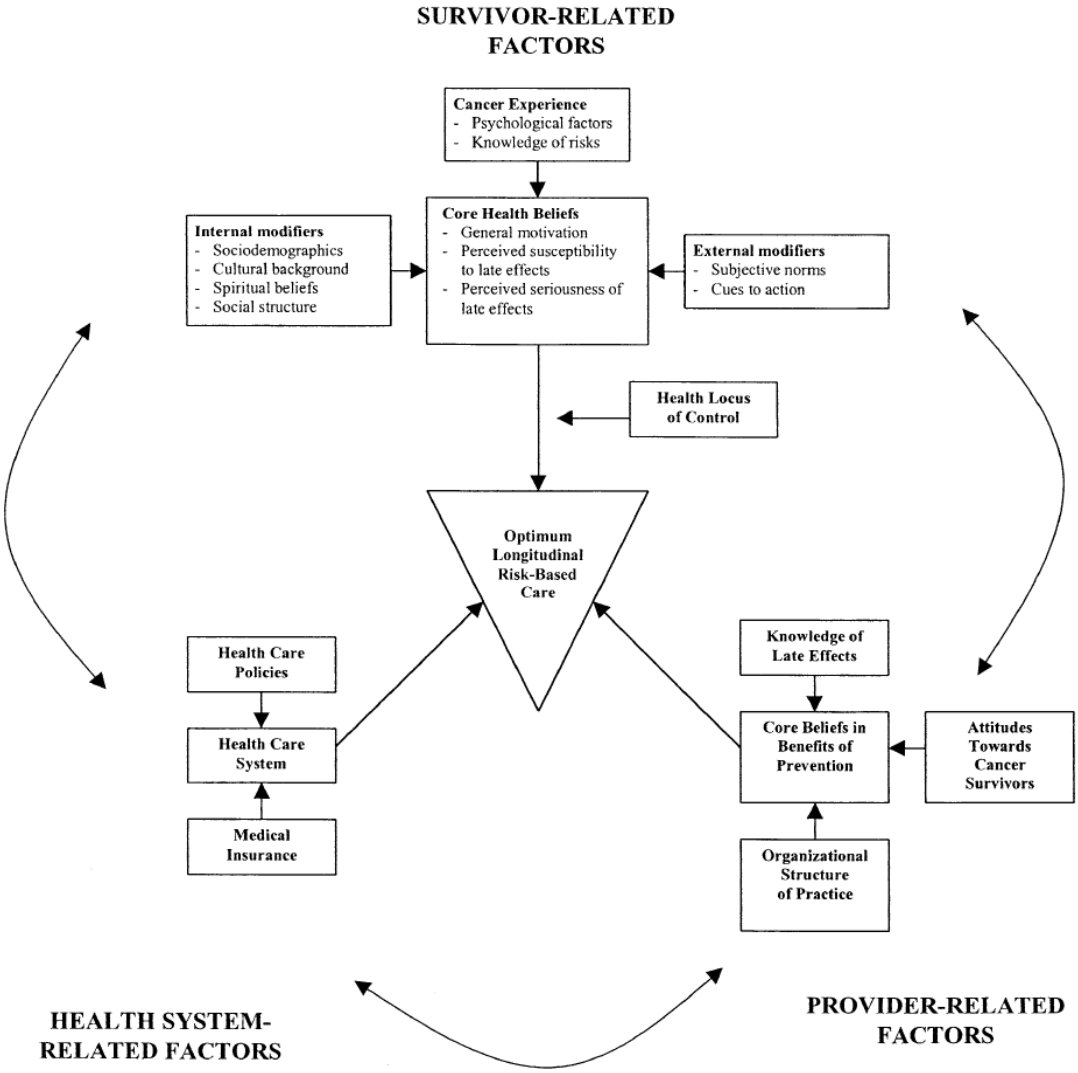


Figure 1: Theoretical framework of potential barriers and facilitators to the longitudinal cancer-related health care of adult survivors of childhood cancer.[31]

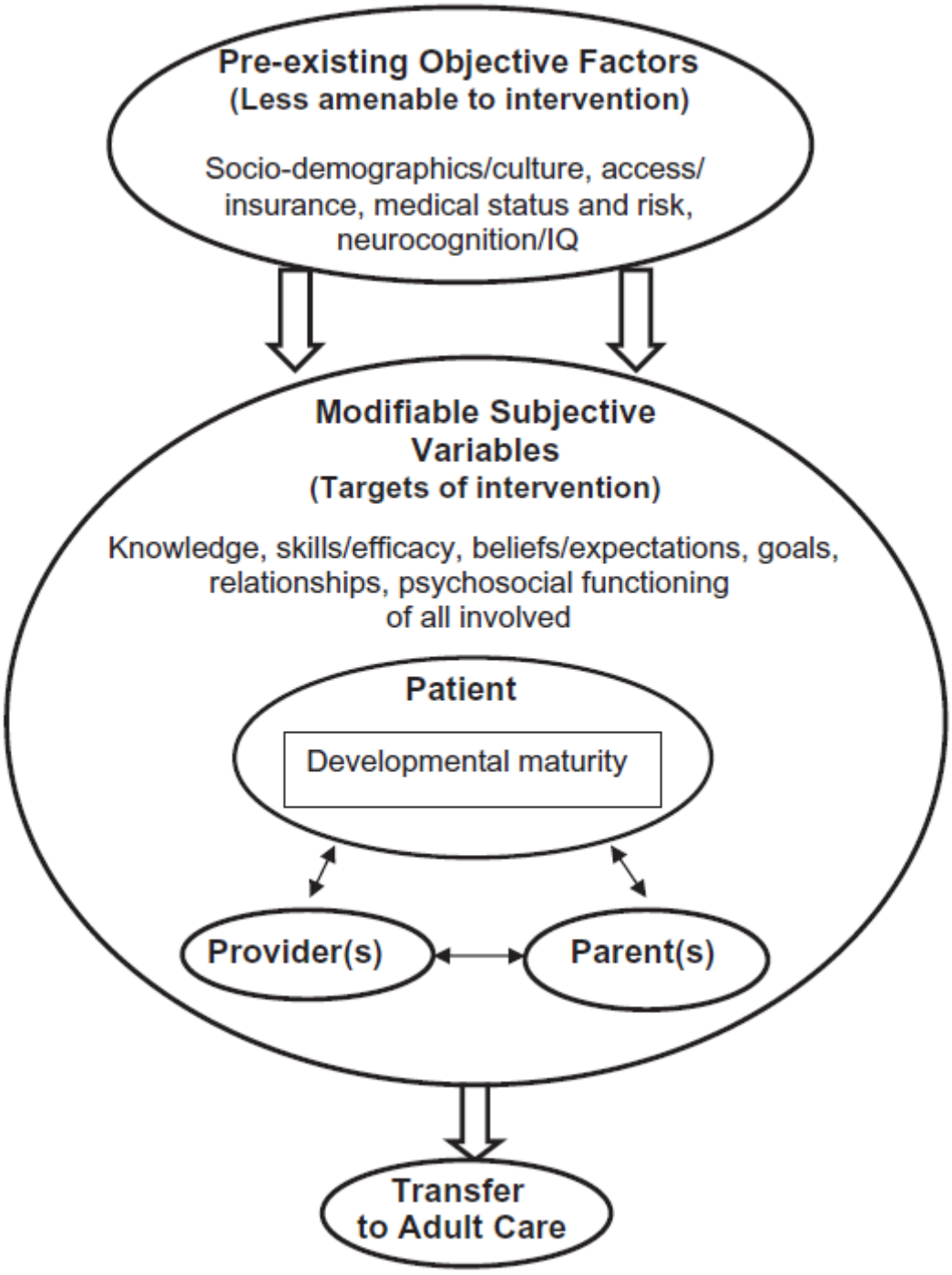


Figure 2: Social-Ecological Model of Adolescent and Young Adult Readiness for Transition (SMART).[39]

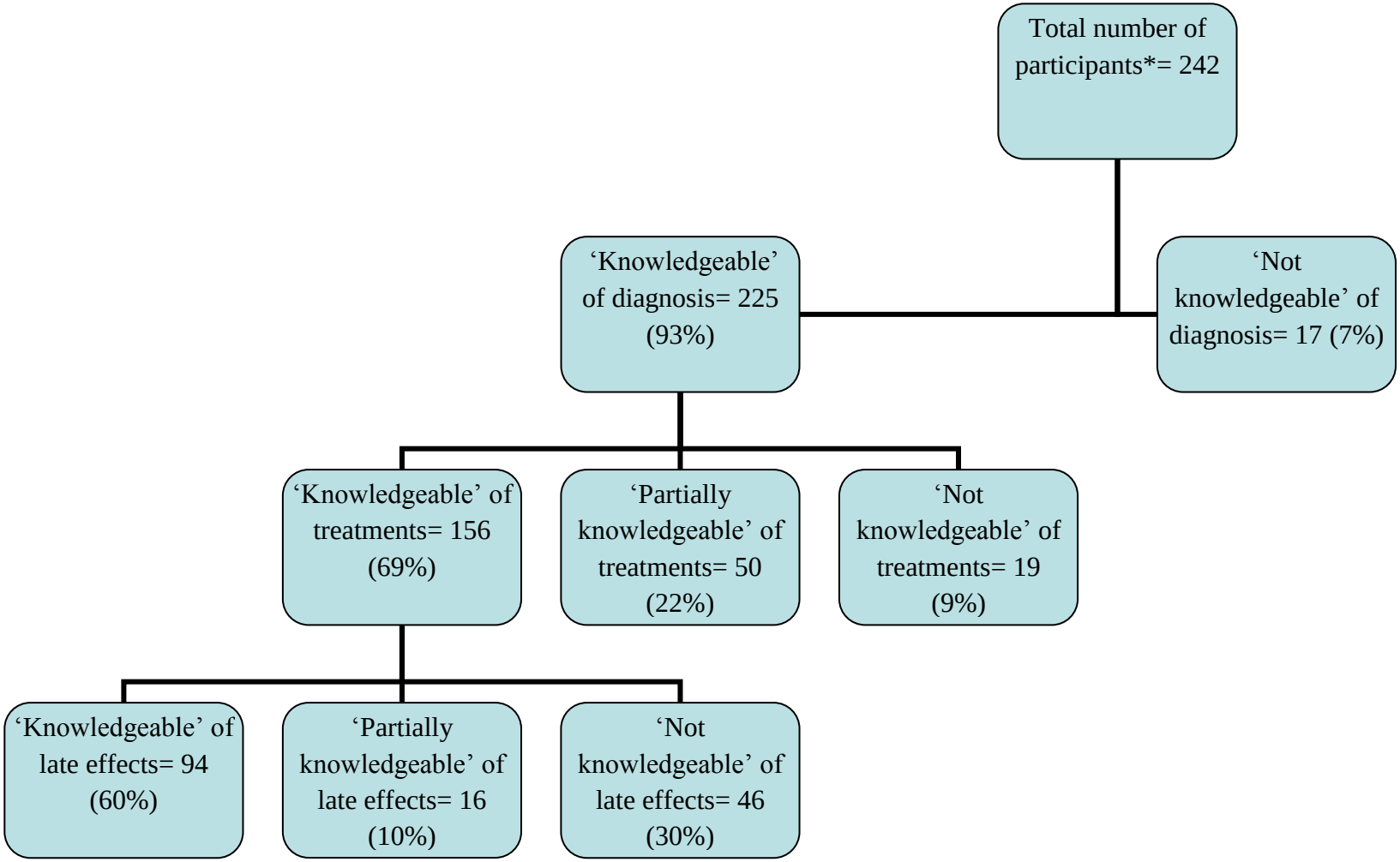


Figure 3: Number of participants knowledgeable about their diagnosis, treatment and late effects (*total number of participants with information on all three outcomes).

Table 1: Level of measurement of dependent, independent, and control variables.

	Ratio	Interval	Nominal	Ordinal
Dependent Variables				
Knowledge of Diagnosis			**O**	
Knowledge of Treatment				**O**
Knowledge of Late effects				**O**
Knowledge of Anthracyclines			**O**	
Knowledge of Late Effects Related to Anthracyclines			**O**	
Independent Variables				
Age	**O**			
Gender			**O**	
Race			**O**	
Education Level				**O**
Father's Education Level				**O**
Mother's Education Level				**O**
Parent Marital Status			**O**	
Age at Diagnosis	**O**			
Cancer Type			**O**	
Year of Diagnosis	**O**			
Treatment Type			**O**	

Radiation to Head or Neck			**O**	
History of Relapse			**O**	
Treatment Intensity				**O**
Cancer Worry		**O**		
Control Variables				
Centre			**O**	
Method of Recruitment			**O**	

Table 2: Number of potential and actual participants by centre and method of recruitment.

		A	**B**	**C**	**Response Rate**
Mail	**Participated**	66	70	0	63.8%
	Approached	93	120	0	
Clinic	**Participated**	68	17	29	96.6%
	Approached	70	19	29	
Response Rate		82.2%	62.6%	100%	75.5%

Table 3: Sample characteristics and distribution of other variables: (N=250).

	n (%)	Mean (SD)
Gender: n= 250		
Male	135 (54.0)	
Female	115 (46.0)	
Age (years): n= 250		18.06 (2.80)
15-17	134 (53.6)	
18-20	62 (24.8)	
21-23	42 (16.8)	
24-26	12 (4.8)	
Race*: n= 246		
White	181 (73.6)	
Non-white	65 (26.4)	
Education*: n= 248		
In high school	148 (59.7)	
Completed high school	19 (7.7)	
In university or college	50 (20.1)	
Completed college or university	31 (12.5)	
Mother's Education*: n= 245		
Did not complete high school	24 (9.8)	
Completed high school	73 (29.8)	
Completed college or university	148 (60.4)	

Father's Education*: n= 238		
Did not complete high school	38 (16.0)	
Completed high school	78 (32.8)	
Completed college or university	122 (51.2)	
Parent's Marital Status*: n= 245		
Married/Common-law	176 (71.8)	
Widowed	6 (2.5)	
Divorced	32 (13.1)	
Separated	17 (6.9)	
Single/Never married	14 (5.7)	
Age at diagnosis (years): n= 250		7.13 (5.06)
0- 5	126 (50.4)	
6-11	66 (26.4)	
12-17	58 (23.2)	
Year of Diagnosis*: n= 248		
1986-1998	97 (39.1)	
1999-2011	151 (60.9)	
Cancer: n= 250		
Leukemia	100 (40.0)	
Lymphoma	55 (22.0)	
CNS tumour	15 (6.0)	
Embryonal tumour	20 (8.0)	

Renal tumour	26 (10.4)	
Sarcoma	34 (13.6)	
Treatment Type		
Chemotherapy: n= 250	241 (96.4)	
Radiation Therapy: n= 250	116 (46.4)	
Surgery: n= 250	92 (36.8)	
Transplant: n= 250	20 (8.0)	
History of Radiation to Head or Neck*: n= 245	74 (30.2)	
History of Relapse: n= 250	18 (7.2)	
Treatment Intensity*: n= 235		
Least	15 (6.4)	
Moderate	89 (37.8)	
Very	97 (41.3)	
Most	34 (14.5)	
Cancer Worry*: n= 249		57.78 (19.4)

*** had missing data for some cases**

SD: standard deviation

Table 4: Descriptive analysis of knowledge of diagnosis, treatment and late effects, and anthracyclines and its related late effects.

Knowledge		**n (%)**
Diagnosis: n= 250		
Not knowledgeable		18 (7.2)
Knowledgeable		232 (92.8)
Treatment (i.e., chemotherapy, radiation therapy, surgery, and transplant)*: n= 244		
0 correct	Not Knowledgeable	2 (0.8)
1 correct		8 (3.3)
2 correct		15 (6.2)
3 correct	Partially knowledgeable	54 (22.1)
All correct	Knowledgeable	165 (67.6)
Late effect*: n= 248		
Not knowledgeable		83 (33.5)
Partially knowledgeable		31 (12.5)
Knowledgeable		134 (54.0)
Anthracyclines: n= 191		
Not knowledgeable		144 (75.4)
Knowledgeable		47 (24.6)
Anthracyclines related late effects: n= 191		
Not knowledgeable		96 (50.3)

Knowledgeable	95 (49.7)

*** had missing data for some cases**

Table 5: Unadjusted and adjusted analysis of knowledge of treatment, and late effects (primary objective).

	Odds ratio (95% CI)			
	Treatment		Late effects	
	Unadjusted	Adjusted	Unadjusted	Adjusted
Mail Recruitment	-	0.8 (0.4-1.4)	-	0.6 (0.4-1.1)
Centre	-		-	
A*		1.0		1.0
B		1.2 (0.6-2.5)		1.7 (0.9-2.7)
C		1.2 (0.5-3.0)		4.9 (1.7-13.8)**
Age (years)	1.0 (0.9-1.1)		1.1 (1.03-1.2)**	1.2 (1.1-1.3)**
Female	1.4 (0.8-2.4)		1.0 (0.6-1.6)	
Non-white	0.3 (0.2-0.6)**	0.3 (0.2-0.6)**	0.7 (0.4-1.3)	
Education				
In high school*	1.0		1.0	
Completed high school or in	0.8 (0.4-1.4)		1.4 (0.8-2.4)	

college/university				
Completed college/university	0.9 (0.4-2.0)		2.2 (1.0-4.9)	
Mother's education				
Did not complete high school	0.7 (0.2-1.8)		0.7 (0.3-1.6)	
Completed high school	1.1 (0.6-2.0)		0.9 (0.5-1.6)	
Completed college/university*	1.0		1.0	
Father's education				
Did not complete high school	1.0 (0.5-2.3)		1.1 (0.5-2.2)	
Completed high school	1.5 (0.8-2.8)		1.0 (0.6-1.8)	
Completed college/university*	1.0		1.0	
Parent marital status				
Married/common-law*	1.0		1.0	
Separated/Divorced	0.6 (0.3-1.2)		0.6 (0.3-1.1)	
Single/Never married/widowed	0.5 (0.2-1.3)		0.8 (0.3-2.4)	
Age at diagnosis (years)	1.1 (1.0-1.1)**	1.1 (1.0-1.1)	1.0 (1.0-1.1)	

Cancer type				
Leukemia*	1.0		1.0	1.0
Lymphoma	0.8 (0.4-1.7)		1.3 (0.7-2.5)	1.4 (0.7-2.7)
CNS tumours	1.5 (0.4-4.7)		1.4 (0.8-2.3)	1.8 (0.6-5.4)
Embryonal	1.8 (0.6-5.2)		3.27 (1.1-10.0)**	3.41 (1.10-10.6)**
Renal tumours	2.3 (0.8-6.6)		0.8 (0.5-1.2)	0.7 (0.3-1.7)
Sarcoma	1.6 (0.7-3.7)		2.6 (1.2-5.9)**	2.3 (1.0-5.3)
Diagnosed during 1986-1998	0.5 (0.3-0.8)**	0.6 (0.3-1.4)	1.0 (0.6-1.7)	
Did not have chemotherapy	1.0 (0.2-4.0)		1.2 (0.3-5.1)	
Did not have radiation	0.7 (0.4-1.2)		0.6 (0.4-1.1)	
Had surgery and/or transplant	1.3 (0.8-2.3)		1.5 (0.9-2.5)	
History of radiation to head or neck	0.9 (0.5-1.6)		1.5 (0.9-2.5)	
History of relapse	0.6 (0.2-1.5)		0.9 (0.4-2.4)	
Treatment intensity				

Level 1	1.0 (0.3-3.5)		0.8 (0.2-2.8)	
Level 2	0.8 (0.3-2.1)		1.3 (0.6-2.7)	
Level 3	1.2 (0.5-2.9)		1.5 (0.7-3.2)	
Level 4*	1.0		1.0	
Cancer worry	1.0 (1.0-1.0)		1.0 (0.98-1.0)	

*** reference category**

**** significant at alpha= 0.05**

Table 6: Unadjusted and adjusted analysis of knowledge of treatment and late effects associated with anthracyclines (secondary objective).

	Odds ratio (95% CI)			
	Treatment		Late effects	
	Unadjusted	Adjusted	Unadjusted	Adjusted
Mail Recruitment	-	2.0 (0.8-4.7)	-	1.3 (0.6-2.8)
Centre	-		-	
A*		1.0		1.0
B		0.8 (0.3-1.9)		3.0 (1.3-7.0)**
C		0.4 (0.1-1.7)		1.8 (0.6-5.0)
Age (years)	1.0 (0.9-1.1)		1.0 (0.9-1.1)	
Female	1.1 (0.6-2.1)		1.1 (0.6-2.0)	
Non-white	0.9 (0.4-1.9)		0.5 (0.2-0.9)**	0.3 (0.1-0.7)**
Education				
In high school*	1.0		1.0	

Completed high school or in college/university	1.0 (0.5-2.0)		0.8 (0.4-1.5)	
Completed college/university	0.8 (0.3-2.1)		1.1 (0.5-2.5)	
Mother's education				
Did not complete high school	0.2 (0.02-1.3)		0.3 (0.1-0.9)**	0.2 (0.04-1.1)
Completed high school	0.9 (0.5-1.9)		1.0 (0.5-1.8)	1.0 (0.5-2.0)
Completed college/university*	1.0		1.0	1.0
Father's education				
Did not complete high school	0.4 (0.1-1.3)		0.3 (0.1-0.8)**	0.3 (0.1-1.0)
Completed HS	1.6 (0.8-3.3)		1.1 (0.6-2.0)	0.9 (0.4-1.9)
Completed college/university*	1.0		1.0	1.0
Parent's marital status				
Married/common-law*	1.0		1.0	
Separated/Divorced	0.8 (0.3-1.9)		0.6 (0.3-1.2)	
Single/Never married/widowed	1.1 (0.3-3.7)		0.7 (0.3-2.2)	

Age at diagnosis (years)	1.1 (1.04-1.2)**	1.1 (1.04-1.2)**	1.0 (0.9-1.0)	
Cancer type				
Leukemia*	1.0	1.0	1.0	1.0
Lymphoma	1.9 (0.8-4.6)	1.1 (0.4-2.9)	1.8 (0.9-3.7)	1.7 (0.8-3.7)
CNS tumours	-	-	-	-
Embryonal	1.6 (0.4-6.7)	2.7 (0.6-12.2)	5.3 (1.4-20.8)**	5.1 (1.2-21.8)*
Renal tumours	1.7 (0.5-5.9)	2.1 (0.6-8.2)	2.9 (1.0-8.7)	2.5 (0.8-8.5)
Sarcoma	5.0 (2.0-12.8)**	4.3 (1.5-12.1)**	2.0 (0.80-4.6)	1.9 (0.7-5.2)
Diagnosed during 1986-1998	0.5 (0.2-1.1)		1.5 (0.8-2.7)	
Did not have chemotherapy	-		-	
Did not have radiation	0.9 (0.5-1.7)		0.9 (.5-1.6)	
Had surgery and/or transplant	1.6 (0.8-3.0)		1.3 (0.7-2.4)	
History of radiation to head or neck	0.7 (0.4-1.5)		0.8 (0.4-1.5)	
History of relapse	2.2 (0.7-6.5)		0.6 (0.2-1.9)	

Treatment intensity				
Level 1	0.3 (.04-2.8)		0.7 (0.2-2.7)	
Level 2	0.6 (0.2-1.6)		1.1 (0.5-2.8)	
Level 3	1.1 (0.4-2.6)		1.2 (0.5-3.0)	
Level 4*	1.0		1.0	
Cancer worry	0.99 (0.97- 1.00)		1.0 (0.98-1.0)	

*** reference category**

**** significant at alpha= 0.05**

APPENDIX A- TRANSITION READINESS QUESTIONNAIRE

Study # _____

Clinic: _____

Improving Transition to Follow-up Care in Childhood Cancer Survivors: Development of a Questionnaire to Measure ***Transition Readiness***

We would like to understand what it is like to be a young person who has had cancer. We would like to know if we are doing a good job helping you get ready to move to adult healthcare.

Please complete this questionnaire booklet on your own.

Thanks for agreeing to answer these questions for us!

Today's date is: __ __ Day __ __ Month __ __ __ __ Year

PLEASE READ THESE INSTRUCTIONS BEFORE STARTING

We would like to understand the experiences of youth who have had cancer. These questions are about **lifestyle choices that can influence the health of childhood cancer survivors.** There are no right or wrong answers. If you are unsure about an item, please circle your best answer. Think about how often you have done these things in the **PAST MONTH**. For each question, please circle **only 1 answer**.

IN THE PAST MONTH...	NEVER did this	SOMETIMES did this	OFTEN did this	ALWAYS did this
1. I ate breakfast.	0	1	2	3
2. I ate a healthy diet (i.e., veggies, fruits, grains, dairy products and proteins).	0	1	2	3
3. I had food or drinks that were high in sugar (e.g., candy, pop).	0	1	2	3
4. I took vitamins to keep healthy.	0	1	2	3
5. I took health food supplements to build my body (e.g., protein powder, meal replacements).	0	1	2	3
6. I used sunscreen when I was in the sun.	0	1	2	3
7. I tried to maintain a healthy weight by eating healthy food and being active.	0	1	2	3
8. I did physical activity for at least 1 hour a day (e.g., walk, run, ride a bike).	0	1	2	3
9. I got at least 8 hours of sleep a night.	0	1	2	3
10. I smoked cigarettes.	0	1	2	3
11. I drank alcohol.	0	1	2	3
12. I used marijuana or other drugs.	0	1	2	3
13. I followed the advice of my doctor(s).	0	1	2	3
14. I reduced my risk of getting injured (e.g., wore a seatbelt or bike helmet).	0	1	2	3
15. I was responsible for my sexual health (e.g., practiced safe sex, used birth control).	0	1	2	3
16. I took time each day to relax.	0	1	2	3

PLEASE READ THESE INSTRUCTIONS BEFORE STARTING

These statements are about **your cancer and treatment**. Near the end of the questionnaire, we will ask you some specific questions about your cancer and treatment. For the scale below, we would like to find out how much you remember about your cancer experience. For each question, please circle **only 1 answer**.

	YES	NO	
1. I know the type of cancer I had.	0	1	
2. I know how old I was when my cancer was diagnosed.	0	1	
3. I know how old I was when I finished my cancer treatment.	0	1	
4. I know where in my body the cancer was located.	0	1	
5. I know some or all of the late effects that can be caused by my cancer treatment. (Note: late effects are health problems caused by cancer treatments, e.g., heart problems, hearing loss, learning problems).	0	1	
6. I know how often I need to come for cancer follow-up appointments.	0	1	
7. I relapsed at least once (i.e., my cancer came back).	0	1	NOT SURE
8. I had a bone marrow or stem cell transplant.	0	1	NOT SURE
9. I had surgery to remove my cancer.	0	1	NOT SURE
10. I had chemotherapy.	0	1	NOT SURE
11. I had radiation therapy.	0	1	NOT SURE
If you did not have chemotherapy, you can skip to question 13. If you had chemotherapy, please answer question 12.			
12. I know the names of some or all of the chemotherapy drugs I had that can cause late effects.	0	1	
If you did not have radiation therapy, you can continue on the next page. If you had radiation therapy, please answer question 13.			
13. I know which parts of my body received radiation therapy.	0	1	

PLEASE READ THESE INSTRUCTIONS BEFORE STARTING

These questions are about **being in charge of your health**. For each question, please circle **only 1 answer**.

	STRONGLY AGREE	AGREE	DISAGREE	STRONGLY DISAGREE
1. I depend on my parent(s) to help me with my health care.	0	1	2	3
2. I need my parent(s) to explain what the doctor or nurse says.	0	1	2	3
3. I prefer it when a doctor speaks to me instead of my parent(s).	0	1	2	3
4. I answer a doctor's or nurse's questions.	0	1	2	3
5. I talk about my medical condition to people when I need to.	0	1	2	3
6. I prefer to see a doctor or nurse without my parent(s) with me.	0	1	2	3
7. I ask the doctor or nurse questions.	0	1	2	3
8. I talk to a doctor or nurse when I have health concerns.	0	1	2	3
9. If I have questions about late effects, I make sure I ask a doctor or nurse. (Note: late effects are health problems caused by cancer treatments, e.g., heart problems, hearing loss, learning problems).	0	1	2	3
10. I can briefly describe my medical history when asked.	0	1	2	3
11. I make sure I go to all my doctor's appointments.	0	1	2	3
12. My parent(s) sits in the waiting room when I see a doctor or nurse.	0	1	2	3
13. I participate in making decisions about my health.	0	1	2	3
14. I know how to contact a doctor if I need to.	0	1	2	3
15. I book my own doctor's appointments.	0	1	2	3
16. I know how to get medical care when I am sick (e.g., go to family doctor or walk-in clinic).	0	1	2	3
17. I am in charge of taking any medicine that I need.	0	1	2	3
18. I know all that I need to know about my medical condition.	0	1	2	3
19. I have a written summary of my medical history (e.g., health passport).	0	1	2	3
20. I know how to access medical care when I travel.	0	1	2	3
21. I travel on my own to a doctor's appointment.	0	1	2	3
22. I fill my own prescriptions when I need medicine.	0	1	2	3
23. I know the type of medical insurance I have (Note: medical insurance pays for things not paid for by the healthcare system).	0	1	2	3
24. I am ready to transfer to adult healthcare.	0	1	2	3

PLEASE READ THESE INSTRUCTIONS BEFORE STARTING

Childhood cancer patients who receive treatment and follow-up in a children's hospital eventually need to **transfer** to a new hospital or to a family doctor for long-term follow-up care as an adult. Imagine that you are about to go for your first adult follow-up appointment. What do **you expect** this appointment will be like? For each question, please circle **only 1 answer**.

When I transfer to adult care....	STRONGLY AGREE	AGREE	DISAGREE	STRONGLY DISAGREE
1. ...I expect to be able to choose the date of my appointment.	0	1	2	3
2. ...I expect to get a reminder call before my appointment.	0	1	2	3
3. ...I expect my appointment will start on time.	0	1	2	3
4. ...I expect the doctor's office will be well organized.	0	1	2	3
5. ...I expect my parent(s) will be able to see the doctor with me.	0	1	2	3
6. ...I expect other appointments related to my cancer will be booked for the same day.	0	1	2	3
7. ...I expect to be seen by the same doctor each time I visit.	0	1	2	3
8. ...I expect the doctor to know my cancer history.	0	1	2	3
9. ...I expect to have enough time to ask the doctor questions.	0	1	2	3
10. ...I expect the doctor will spend a lot of time with me.	0	1	2	3
11. ...I expect to be able to call the doctor any time I need to (e.g., if I have questions about late effects).	0	1	2	3
12. ...I expect the doctor will become like a friend.	0	1	2	3
13. ...I expect the doctor will look after all my health care needs.	0	1	2	3
14. ...I expect to be called if I miss my appointment.	0	1	2	3
15. ...I expect to like going to cancer follow-up appointments.	0	1	2	3
16. ...I expect I will go to cancer follow-up appointments for as long as the doctor wants me to.	0	1	2	3

PLEASE READ THESE INSTRUCTIONS BEFORE STARTING

These statements are about **thoughts and feelings you may have as a cancer survivor.** For each question, please circle **only 1 answer**.

	STRONGLY AGREE	AGREE	DISAGREE	STRONGLY DISAGREE
1. I worry about my cancer every day.	0	1	2	3
2. Cancer is always at the back of my mind.	0	1	2	3
3. I worry my cancer will come back (i.e., relapse).	0	1	2	3
4. I worry about getting a new type of cancer.	0	1	2	3
5. I worry about late effects that might happen to me. (Note: late effects are health problems caused by cancer treatments, e.g., heart problems, hearing loss, learning problems).	0	1	2	3
6. I worry it might be difficult to have children in the future.	0	1	2	3
7. I hide the fact that I had cancer from others.	0	1	2	3
8. I do not like being reminded about my cancer.	0	1	2	3
9. I try not to think about my cancer.	0	1	2	3
10. I sometimes forget that I had cancer.	0	1	2	3
11. I hardly ever think about my cancer.	0	1	2	3
12. I believe my cancer is over and done with.	0	1	2	3
13. I have moved on with my life.	0	1	2	3

Next are some questions for us to learn more about your **cancer and treatment**. If you do not know the answer to a question, please skip and continue with the next question.

1. What **type of cancer** did you have? _____

2. **How old were you** when you were diagnosed with cancer? _____ years old

3. How old were you when you **finished treatment**? _____ years old

4. **How often** do you need to come for cancer follow-up appointments?

O 1 visit every 2 years O 1 visit a year O 2 or more visits a year O Not sure

5. Where in your body was the cancer located? _____

6. Has your cancer ever come back after treatment was finished (**relapsed**)? O Yes O No

7. What **cancer treatments** did you have? (Mark all that apply)

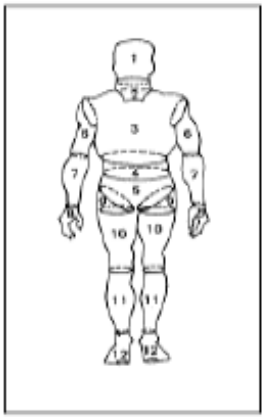
	Yes	No	Not sure
Chemotherapy	O	O	O
Radiation	O	O	O
Surgery to remove cancer	O	O	O
Bone marrow or stem cell transplant	O	O	O

8. Please list the **names** of any **chemotherapy drugs** you were given.

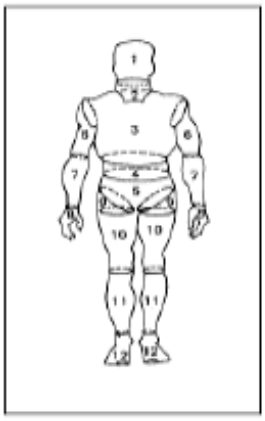
_____

_____

9. If you had **radiation therapy**, please circle the number(s) to show the part(s) of your body that received radiation.



10. If you had **surgery to remove cancer**, please circle the number(s) to show the part(s) of your body that was operated on.



11. Please list the **late effects** that you know can happen as a result of your cancer treatment. By late effects, we mean any health problems caused by cancer treatments, e.g., heart problems, hearing loss, learning problems.

_____

_____

12. Do you have any type of learning problem (e.g., trouble with reading, writing or math)? If yes, please describe these here.

_____

These are more questions about **being in charge of your health**. For each question, please circle **only 1 answer**.	STRONGLY AGREE	AGREE	NEITHER DISAGREE NOR AGREE	DISAGREE	STRONGLY DISAGREE
1. I can describe my condition and explain my special health care needs to others.	0	1	2	3	4
2. I know what my health may bring in the future.	0	1	2	3	4
3. I have a family doctor that I like and will continue to see as an adult.	0	1	2	3	4
4. I know the types of doctors I will need to see as an adult.	0	1	2	3	4
5. I know I have the right information about myself and my health.	0	1	2	3	4
6. I have a person who will help me with my health if my family cannot.	0	1	2	3	4
7. I plan how to take care of my own health needs.	0	1	2	3	4
8. I take part in health care discussions about me.	0	1	2	3	4
9. I know what kinds of medical insurance I have.	0	1	2	3	4
10. I know the names of my medications, what they do and how to buy them.	0	1	2	3	4
11. I prepare/take my own medications/treatments as required.	0	1	2	3	4
12. I keep track of my health care visits, treatment plan and medications.	0	1	2	3	4
13. I know how to schedule an appointment.	0	1	2	3	4
14. I can get myself to medical appointments.	0	1	2	3	4
15. I spend time alone and/or speak for myself with my health care provider at each visit.	0	1	2	3	4
16. I know who to call in case of emergency.	0	1	2	3	4
17. I understand how my condition will affect the way I develop through puberty.	0	1	2	3	4
18. I have discussed my sexuality issues with my health care provider.	0	1	2	3	4
19. I know how to get birth control and protection from sexually transmitted infections.	0	1	2	3	4
20. My family are a support to me in managing my condition.	0	1	2	3	4
21. I have discussed the use of tobacco, alcohol and drugs with my health care provider.	0	1	2	3	4

PLEASE READ THESE INSTRUCTIONS BEFORE STARTING

Please read every question carefully. What answer comes to your mind first? Please check the circle that best describes your answer. It is important that you answer all the questions and also that we can see your checks clearly. When you think of your answer please try to remember the last week.

In general, how would you say your health is?

1.	○ Excellent	○ Very Good	○ Good	○ Fair	○ Poor

Thinking about the last week...

2.	Have you physically felt fit and well?	not at all ○	slightly ○	moderately ○	very ○	extremely ○
3.	Have you been physically active (e. g. running, climbing, biking)?	not at all ○	slightly ○	moderately ○	very ○	extremely ○
4.	Have you been able to run well?	not at all ○	slightly ○	moderately ○	very ○	extremely ○
5.	Have you felt full of energy?	never ○	almost never ○	sometimes ○	almost always ○	always ○

Thinking about the last week...

6.	Has your life been enjoyable?	not at all ○	slightly ○	moderately ○	very ○	extremely ○
7.	Have you been in a good mood?	never ○	almost never ○	sometimes ○	almost always ○	always ○
8.	Have you had fun?	never ○	almost never ○	sometimes ○	almost always ○	always ○
9.	Have you felt sad?	never ○	almost never ○	sometimes ○	almost always ○	always ○
10.	Have you felt so bad that you didn't want to do anything?	never ○	almost never ○	sometimes ○	almost always ○	always ○
11.	Have you felt lonely?	never ○	almost never ○	sometimes ○	almost always ○	always ○
12.	Have you been happy with the way you are?	never ○	almost never ○	sometimes ○	almost always ○	always ○

PLEASE CONTINUE ON THE BACK PAGE ⇨

FEW FINAL QUESTIONS ABOUT YOU

1. Are you? O Male O Female

2. How old are you? _____ years old

3. What is your parent's **ethnic background** (e.g., South Asian, Chinese, Caucasian)?

   Mother: _____ Father: _____

4. What is the **highest level of education that you have completed**?

   O I am a High School student (I have completed _____ grade)
   O I have completed High School
   O I am a College or University student
   O I have completed College or University

5. Which of the following categories describes your **parents' current marital status**?

O	O	O	O	O
Married/ Common-law	Widowed	Separated	Divorced	Single/ Never married

6. What is the **highest level of education** your mother and father have completed? (Choose only one answer for each parent)

	Mother		**Father**
O	Did not finish High School	O	Did not finish High School
O	Finished High School	O	Finished High School
O	Finished College or University	O	Finished College or University

7. Is your **mother** currently working? Is your **father** currently working?

   O Yes O No O Yes O No

8. What job does your **mother** do for a living? What job does your **father** do for a living?

   _____ _____

APPENDIX B- ASSENT FORM

McMaster University HEALTH SCIENCES

McMaster Children's Hospital

Improving Transition to Follow-up Care in Childhood Cancer Survivors:
Development of a Questionnaire to Measure Transition Readiness (Phase II)

Subject Information and Assent Form

Principal Investigators: Dr Ronald Barr, Division of Hematology/Oncology, McMaster Children's Hospital, Hamilton, Ontario (905) 521-2100 x 73464

Anne Klassen, Associate Professor, Department of Pediatrics
McMaster Children's Hospital, Hamilton, Ontario
(905) 521-2100 x 73775

Co-Investigators:
Dr Paul Nathan *Division of Hematology/Oncology, The Hospital for Sick Children, Toronto, Ontario*
Dr. Mark Greenberg *Division of Hematology/Oncology, The Hospital for Sick Children, Toronto, Ontario*
Dr. Katherine Boydell *Department of Psychology, The Hospital for Sick Children, Toronto, Ontario*
Dr. Norma D'Agostino *Department of Psychosocial Oncology, Princess Margaret Hospital, Toronto*
Dr Elizabeth Dettmer *Division of Adolescent Medicine, The Hospital for Sick Children, Toronto*

Sponsor: AHSC AFP Innovation Fund 2008-2009

Introduction
Your child is being invited to take part in this research study because he/she is a childhood cancer survivor aged 15 years. This letter is to help you decide if you would like him/her to take part in our study.

Why is this study being done?
Survivors of childhood cancer are at risk of future health problems because of the treatment they had for their cancer. In Toronto and Hamilton there are long-term follow-up clinics at the hospital where adult survivors of childhood cancer (anyone aged 18 or older) are seen by doctors. The problem is that many survivors do not see the benefits of going to one of these clinics. We hope to change that. We have developed a questionnaire that will help us to identify what makes going to an adult hospital easier and/or harder.

How many people will take part in this study?
A total of 200 childhood cancer survivors aged 15 to 26 years are being asked to complete our newly developed questionnaire. We are recruiting individuals from McMaster Children's Hospital (Hamilton), The Hospital for Sick Children (Toronto) and the Princess Margaret Hospital (Toronto).

Is there any remuneration/compensation?
You will receive a gift certificate worth $5.

What is involved in participating in this study?
If your child agrees to be in this study, he/she will be asked to complete our questionnaire, which will take approximately 15 minutes of his/her time. Once completed, they will return the questionnaire to us using the prepaid envelope we have provided. After completing the questionnaire, your child will have finished the study.

DEPARTMENT OF PEDIATRICS
HSC 3N27 – 1200 Main Street West, Hamilton, ON Canada L8S 4J9
905-521-2100 Ext. 73464, Fax 905-521-1703

Version 5 for ages 15 to 26 years: 26 May 2011

What happens to the interview data that you provide?
If your child agrees to participate, his/her privacy will be respected. Information about him/her will not be given out without your permission unless required by law or regulation. No one in the cancer clinic he/she attends will be told he/she is part of this study. Information collected will be used for research purposes only. All personal information such as names, email addresses and phone numbers will be removed from the interview data. It will be replaced with a number. A list linking the number with your child's name will be kept in a secure place, separate from the interview data. The interview recordings and all typed data will be kept in a locked filing cabinet and on a password-protected computer. If the results of the study are published, no names will be used. Only the researchers in charge and their research assistants will have access to your child's personal information. You have the right to review the tapes. At the end of the study, the tapes will be erased.

What are the risks of the study?
We believe there are minimal risks involved in being in this study. However, sometimes when people complete a questionnaire that asks about their experiences they may find that they then want a chance to talk to someone for support. If this happens, you can call Dr Anne Klassen, at 905 521-2100 ext. 73775, and she will help you find someone to talk to who will be able to help.

Are there benefits to taking part in the study?
There is no direct benefit to taking part in this study. However, the information your child provides may be used to help plan oncology services for other childhood cancer survivors.

What are your rights as a participant?
Your child's participation is entirely voluntary. This means that he/she does not have to participate if he/she doesn't want to. If your child does participate, he/she may refuse to answer any question that they do not want to answer. Your child can agree to participate now, and then change his/her mind at any time and have their information removed from the study. If your child chooses to not take part, or if he/she decides to drop out from the study, his/her care will not be affected and there will be no consequences.

Who do you call if you have questions about the study?
For more information concerning the research, you may call Dr Anne Klassen 905-521-2100 ext. 73775.

Who do you call if you have questions or about your rights as a research participant?
If you have any questions regarding your child's rights as a research participant you may contact the Office of the Chair of the Hamilton Health Sciences/Faculty of Health Sciences Research Ethics Board at 905-521-2100 ext. 42013.

What is the next step?
We hope that you will decide to complete our questionnaire. Either way, we would like to know your decision. Next week our Project Coordinator will call you at home to find out your decision. In the meantime, we would be very grateful if you would complete and return the questionnaire booklet to us using the prepaid envelope provided.

Where can I get more information about childhood cancer?
I may call The Canadian Cancer Society: 1-888-939-3333
I may visit the Canadian Cancer Society Web site: http://www.cancer.ca
I may visit the National Cancer Institute website: http://cancernet.nci.nih.gov.

DEPARTMENT OF PEDIATRICS
HSC 3N27 – 1200 Main Street West, Hamilton, ON Canada L8S 4J9
905-521-2100 Ext. 73464, Fax 905-521-1703

Version 5 for ages 15 to 26 years: 26 May 2011

I have read the above information carefully. I agree to participate in this study. By completing and returning the questionnaire, I am agreeing to participate in this study.

How else can you help with our research?
Our questionnaire is still being developed, which means we are not quite finished. We would be really grateful if your child would help us with two additional tasks.

1) We need 100 participants to complete a second copy of our questionnaire booklet shortly after completing the first copy. This will help us to see if our questionnaire booklet is reliable, which means that if a person completed our questionnaire two times, they should answer the questions very similarly if nothing has changed in their life. If your child is willing to help us in this way, please tick "Yes" below and we will mail you another questionnaire booklet to complete.

   O Yes O No

2) We are going to use our findings to develop a much shorter questionnaire that includes only the best questions from the longer version. When we have finished developing our short questionnaire (about one year from now), would your child be willing to fill this out for us?

   O Yes O No

3) Our team feels that there is a great deal to learn about transitioning from child to adult care. We may therefore, want to contact you in 3-5 years to follow-up on your transition experience. Specifically, we want to determine whether our questionnaire is useful in identifying adolescents who are at risk of not continuing with follow-up care when they become adults. We would like to know if you would be okay with us contacting your child in the future.

   O Yes O No

I have read the above information carefully. I have had the chance to ask questions. All of my questions have been answered to my satisfaction. I understand that I will receive a signed copy of this form. I agree to allow the research team to contact my child in the future for a related study on transition.

Participant (sign)	Date	Name printed
Person Obtaining Consent (sign)	Date	Name printed
Researcher (sign)	Date	Name printed

DEPARTMENT OF PEDIATRICS
HSC 3N27 – 1200 Main Street West, Hamilton, ON Canada L8S 4J9
905-521-2100 Ext. 73464, Fax 905-521-1703

APPENDIX C- CONSENT FORM

McMaster University HEALTH SCIENCES

McMaster Children's Hospital

Improving Transition to Follow-up Care in Childhood Cancer Survivors:
Development of a Questionnaire to Measure Transition Readiness (Phase II)

Subject Information and Consent Form

Principal Investigators: Dr Ronald Barr, Division of Hematology/Oncology, McMaster Children's Hospital, Hamilton, Ontario (905) 521-2100 x 73464

Anne Klassen, Associate Professor, Department of Pediatrics
McMaster Children's Hospital, Hamilton, Ontario
(905) 521-2100 x 73775

Co-Investigators:
Dr Paul Nathan *Division of Hematology/Oncology, The Hospital for Sick Children, Toronto, Ontario*
Dr. Mark Greenberg *Division of Hematology/Oncology, The Hospital for Sick Children, Toronto, Ontario*
Dr. Katherine Boydell *Department of Psychology, The Hospital for Sick Children, Toronto, Ontario*
Dr. Norma D'Agostino *Department of Psychosocial Oncology, Princess Margaret Hospital, Toronto*
Dr Elizabeth Dettmer *Division of Adolescent Medicine, The Hospital for Sick Children, Toronto*

Sponsor: AHSC AFP Innovation Fund 2008-2009

Introduction
You are being asked to complete our questionnaire because you are a childhood cancer survivor aged 15 to 26 years. This letter is to help you decide if you would like to take part in our study.

Why is this study being done?
Survivors of childhood cancer are at risk of future health problems because of the treatment they had for their cancer. In Toronto and Hamilton there are long-term follow-up clinics at the hospital where adult survivors of childhood cancer (anyone aged 18 or older) are seen by doctors. The problem is that many survivors do not see the benefits of going to one of these clinics. We hope to change that. We have developed a questionnaire that will help us to identify what makes going to an adult hospital easier and/or harder.

How many people will take part in this study?
A total of 200 childhood cancer survivors aged 15 to 26 years are being asked to complete our newly developed questionnaire. We are recruiting individuals from McMaster Children's Hospital (Hamilton), The Hospital for Sick Children (Toronto) and the Princess Margaret Hospital (Toronto).

Is there any remuneration/compensation?
You will receive a gift certificate worth $5.

What is involved in participating in this study?
If you agree to be in this study, we simply ask you to complete our questionnaire, which will take approximately 15 minutes of your time. Once you are done, please return the questionnaire to us using the prepaid stamped envelope we have provided. After you complete the questionnaire, you will have finished the study.

DEPARTMENT OF PEDIATRICS
HSC 3N27 – 1200 Main Street West, Hamilton, ON Canada L8S 4J9
905-521-2100 Ext. 73464, Fax 905-521-1703

What happens to the interview data that you provide?
If you agree to participate, your privacy will be respected. Information about you will not be given out without your permission unless required by law or regulation. No one in the cancer clinic you attend(ed) will be told you are part of this study. Your information will be used for research purposes only. All personal information such as your name, address and phone number will be kept separate from the questionnaire data. It will be replaced with a number. A list linking the number with your name will be kept in a secure place, separate from the interview data. The questionnaires will be kept in a locked filing cabinet and on a password-protected computer. If the results of the study are published, your name will not be used. Only the researchers in charge and their research assistants will have access to your personal information. At the end of the study, the questionnaires will be destroyed.

What are the risks of the study?
We believe there are minimal risks involved in being in this study. However, sometimes when people complete a questionnaire that asks about their experiences they may find that they then want a chance to talk to someone for support. If this happens, you can call Dr Anne Klassen, at 905 521-2100 ext. 73775, and she will help you find someone to talk to who will be able to help.

Are there benefits to taking part in the study?
There is no direct benefit to you for taking part in this study. However, the information you provide may be used to help plan oncology services for other childhood cancer survivors.

What are your rights as a participant?
Your participation is entirely voluntary. This means that you don't have to participate if you don't want to. If you do participate, you may refuse to answer any question that you don't want to answer. You can agree to participate now, and then change your mind at any time and have your information removed from the study. If you chose to not take part, or if you decide to drop out from the study, your care will not be affected and there will be no consequences.

Who do you call if you have questions about the study?
For more information concerning the research, you may call Dr Anne Klassen 905-521-2100 ext. 73775.

Who do you call if you have questions or about your rights as a research participant?
If you have any questions regarding your rights as a research participant you may contact the Office of the Chair of the Hamilton Health Sciences/Faculty of Health Sciences Research Ethics Board at 905-521-2100 ext. 42013.

What is the next step?
We hope that you will decide to complete our questionnaire. Either way, we would like to know your decision. Next week our Project Coordinator will call you at home to find out your decision. In the meantime, we would be very grateful if you would complete and return the questionnaire booklet to us using the prepaid envelope provided.

Where can I get more information about childhood cancer?
I may call The Canadian Cancer Society: 1-888-939-3333
I may visit the Canadian Cancer Society Web site: http://www.cancer.ca
I may visit the National Cancer Institute website: http://cancernet.nci.nih.gov.

I have read the above information carefully. I agree to participate in this study. By completing and returning the questionnaire, I am agreeing to participate in this study.

DEPARTMENT OF PEDIATRICS
HSC 3N27 – 1200 Main Street West, Hamilton, ON Canada L8S 4J9
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How else can you help with our research?
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1) We need 100 participants to complete a second copy of our questionnaire booklet shortly after completing the first copy. This will help us to see if our questionnaire booklet is reliable, which means that if a person completed our questionnaire two times, they should answer the questions very similarly if nothing has changed in their life. If you are willing to help us in this way, please tick "Yes" below and we will give you another questionnaire booklet to complete.

   ○ Yes ○ No

2) We are going to use our findings to develop a much shorter questionnaire that includes only the best questions from the longer version. When we have finished developing our short questionnaire (about one year from now), would you be willing to fill this out for us?

   ○ Yes ○ No

3) Our team feels that there is a great deal to learn about transitioning from child to adult care. We may therefore, want to contact you in 3-5 years to follow-up on your transition experience. Specifically, we want to determine whether our questionnaire is useful in identifying adolescents who are at risk of not continuing with follow-up care when they become adults. We would like to know if you would be okay with us contacting you in the future.

   ○ Yes ○ No

I have read the above information carefully. I have had the chance to ask questions. All of my questions have been answered to my satisfaction. I understand that I will receive a signed copy of this form. I agree to allow the research team to contact me in the future for a related study on transition.

Participant (sign)	Date	Name printed
Person Obtaining Consent (sign)	Date	Name printed
Researcher (sign)	Date	Name printed

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