

EDUCATIONAL LATE EFFECTS AMONG SURVIVORS OF CHILDHOOD CANCER

by

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ABSTRACT

Increased survival rates of childhood cancer have meant a growing population of survivors within the education system. Although research suggests that survivors face educational difficulties, methodological shortcomings and lack of consensus have contributed to difficulties interpreting this literature. Moreover, there exists a paucity of literature objectively measuring survivors' educational outcomes, particularly achievement.

In this population-based research, 782 survivors of childhood cancer from the BC cancer registry, and BC school system from 1995-2004, were age and gender-matched with a randomly selected control group of 8386 BC schoolchildren. Objective educational measures including Foundation Skills Assessments (FSAs), Provincial examinations, and special education designations from the BC Ministry of Education were compared between the survivor and control cohorts; potential disease-related risks among survivors were assessed.

Survivors were significantly more likely than controls to have special education or physical disability designations and performed significantly more poorly on several FSAs. Notably, once survivors of central nervous system (CNS) tumours and leukemia were excluded from the analysis, there were no significant achievement differences. Survivors younger at diagnosis (<2 years) had higher educational achievement, despite having more hearing and visual impairments than survivors older at diagnosis (≥ 5 years).

Childhood cancer survivors appear at increased risk for special education utilization. In particular, survivors of leukemia and CNS tumours may be at increased risk for poor educational achievement and special education designations. It is important that potential adverse educational outcomes and associated risk factors be identified such that surveillance and appropriate interventions be provided to ensure survivors a successful educational experience.

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CHAPTER 1: INTRODUCTION AND LITERATURE REVIEW

1.1 Childhood Cancer Survival Rates

In Canada an average of 1289 children aged birth to 19 years were diagnosed with cancer each year from 1999 to 2003 (Canadian Cancer Society/National Cancer Institute of Canada, 2007). In the Canadian province of British Columbia an average 157 children were diagnosed with cancer each year from 1995-2004 (BC Cancer Agency, 2007). Advances in medical treatment have been made within the past 20 years that have resulted in increased survival rates for children diagnosed with cancer (M. Smith & Hare, 2004). By 2003, 5-year survival rates for children (aged 0-14 years) diagnosed with cancer had reached 79.6% (Ries et al., 2007). Thus, as never before, there exists an ever growing population of survivors of childhood cancer who are entering and attending school. Notably, these children outnumber many traditional special education populations within the United States (Peckham, 1991). Within the United Kingdom, approximately 1 in 1000 young adults is a survivor of childhood cancer (Taylor et al., 2004).

1.2 Late Effects

Survival is now a tangible possibility for children diagnosed with cancer, but it has not come without some impact upon the children who survive. Two thirds of all survivors of childhood cancer will experience at least one late effect after surviving cancer (National Cancer Policy Board, 2003). A late effect is considered any complication, disability, or adverse outcome resulting from the cancer itself, the treatment of the cancer, or both, that continues or develops more than five years after t

The most frequently observed late effects of childhood cancer are neurocognitive in nature (National Cancer Policy Board, 2003). Given this, it is not surprising that there exists an abundance of studies that have investigated the neurocognitive late effects of surviving childhood cancer (V. Anderson, Godber, Smibert, Weiskop, & Ekert, 2000; Bleyer et al., 1990; Butler, Hill, Steinherz, Meyers, & Finlay, 1994; D. Hill, Ciesielski, Sethre-Hofstad, Duncan, & Lorenzi, 1997; Kolotas et al., 2001; Rubenstein, Varni, & Katz, 1990; D. Waber, Bernstein, Kammerer, & Tarbell, 1992). Reductions in neuro-cognitive functioning; in particular, decreases in IQ have been reported (Christie, Leiper, Chessells, & Vargha-Khadem, 1995; Fogarty et al., 1988; Moleski, 2000; Robaey et al., 2000), but it has been noted that IQ may not represent the best measure of neurocognitive outcome, given that it is not sensitive enough to identify the deficits or areas that may require accommodation or remediation (C. Armstrong, Gyato, Awadalla, Lustig, & Tochner, 2004). Moreover, although a decrease in measures of intelligence, memory, and other central nervous system functions may have been determined by some studies, there is no decisive demonstration that this is associated with a failure to achieve (Allen, Malpas, & Kingston, 1990).

1.3 Educational Late Effects

Many survivors report that their education has been effected as a result of their childhood cancer (Langeveld, Stam, Grootenhuis, & Last, 2002). In one study, as many as 67% of survivors stated that their education had suffered due to their cancer (Evans & Radford, 1995), and in another study it was found that 45% of survivors felt that their cancer had adversely impacted their educational achievement to a great or very great extent (Dolgin, Somer, Buchvald, & Zaizov, 1999).

1.3.1 Use of Special Education

Special education utilization has been well documented among survivors of childhood cancer (F. Armstrong, Blumberg, & Toledano, 1999; Fogarty et al., 1988; Jenkin, Danjoux, & Greenberg, 1998; Kazak, Christakis, Alderfer, & Coiro, 1994; Kingma, Mooyaart, Kamps, Nieuwenhuizen, & Wilmink, 1993; Mulhern, Wasserman, Friedman, & Fairclough, 1989; Peckham, Meadows, Bartel, & Marrero, 1988; Rubenstein, Varni, & Katz, 1990; D. Waber, Bernstein, Kammerer, & Tarbell, 1992). Reviews report that special education services are often necessary for survivors (D. Anderson et al., 2001) and that increased proportions of survivors require special education (Robaey et al., 2000; Robison et al., 2005) or the use of special education services including tutoring, resource room programs, and special education classes or schools (Stehbens et al., 1991). A review of the literature has indicated that as many as 39-69% of survivors qualify for special education (Coniglio & Blackman, 1995). Studies have found that significantly more survivors than siblings are, or have been, enrolled in special education programs or classes (Kingma, Rammeloo, van Der Does-van den Berg, Rekers-Mombarg, & Postma, 2000; Mitby et al., 2003) and learning disability programs (Haupt et al., 1994).

1.3.2 Grade Retention

An increased rate of grade repetition has been observed among survivors of childhood cancer (I. Moore, Glasser, & Ablin, 1988). Compared to siblings (Haupt et al., 1994) and controls (Buizer, de Sonnevile, van den Heuvel-Eibrink, & Veerman, 2006) survivors are more likely to have repeated a grade. It has been suggested that as many as 26% of survivors will have repeated at least one or more grades during their school career (Coniglio & Blackman, 1995; Mulhern, Wasserman, Friedman, & Fairclough, 1989).

1.3.3 Educational Attainment

The educational attainment or level of education completed by survivors is another educational outcome that has been reported within the literature (Humpl, Fritsche, Bartels, & Gutjahr, 2001; Li, Winston, & Gimbrere, 1984; Syndikus, Tait, Ashley, & Jannoun, 1994). Survivors have been found less likely to graduate high school when compared with siblings (Kelaghan et al., 1988; Nagarajan et al., 2003). As well, some research suggests that those survivors who do graduate from high school are less likely to enter college or continue on to secondary education than siblings (Evans & Radford, 1995; Kelaghan et al., 1988) and to have lower levels of secondary education than their siblings (Kingma, Rammeloo, van Der Does-van den Berg, Rekers-Mombarg, & Postma, 2000; Langeveld, Stam, Grootenhuys, & Last, 2002).

1.3.4 Academic Achievement

Academic difficulties and poor or low academic achievement have been frequently reported within reviews of the literature (D. Anderson et al., 2001; Brown & Madan-Swain, 1993; Cousens, 1997; Patenaude & Kupst, 2005; Robaey et al., 2000; Schwartz, 1999). The most commonly observed measures of academic achievement among studies of survivors are the Wide Range Achievement Test (WRAT) and anecdotal reports of school performance (V. Anderson, Godber, Smibert, & Ekert, 1997; V. Anderson, Smibert, Ekert, & Godber, 1994; V. Anderson, Godber, Smibert, Weiskop, & Ekert, 2000; F. Armstrong & Mulhern, 1999; Copeland et al., 1985; Moehle, Berg, Ch'ien, & Lancaster, 1983; Smibert, Anderson, Godber, & Ekert, 1996). Parents of survivors have reported that their children perform more poorly on everyday cognitive and academic tasks (F. Armstrong & Mulhern, 1999) and have poorer school performances than children without cancer (V. Anderson, Smibert, Ekert, & Godber, 1994). At school, teachers have suggested that survivors express more learning difficulties (Jannoun & Chessells, 1987) and

make slower academic progress compared to other students (Raymond-Speden, Tripp, Lawrence, & Holdaway, 2000). WRAT reading, spelling, and arithmetic scores of survivors have been found to be lower than expected within the general population (Seaver et al., 1994; D. Waber et al., 1990). Furthermore, it has commonly been noted that the greatest or more common deficit exists in arithmetic or mathematic skills (Coniglio & Blackman, 1995; Duffner, 2004; Gamis & Nesbit, 1991; Kaemingk, Carey, Moore, Herzer, & Hutter, 2004; Moleski, 2000; B. Moore, 2005; Mulhern & Palmer, 2003; Peckham, 1991; Peckham, Meadows, Bartel, & Marrero, 1988; Stehbens et al., 1991; Whitt, Wells, Lauria, Wilhelm, & McMillan, 1984).

1.4 Risk Factors

A number of disease-related, personal, and socioeconomic factors are associated with an increased risk of adverse educational late effects among survivors of childhood cancer. These confounding variables include: the cancer diagnosis, treatment modality, therapeutic dose, age at diagnosis or treatment, time elapsed since diagnosis, gender and socioeconomic status (SES).

1.4.1 Cancer Diagnosis

Specific diagnoses including leukemia; in particular, acute lymphoblastic leukemia (ALL), Hodgkin's lymphoma, central nervous system (CNS) tumours, and neuroblastoma have been associated with an increased risk of educational late effects (Barrera, Shaw, Speechley, Maunsell, & Pogany, 2005; Langeveld et al., 2003; Mitby et al., 2003). ALL is the most frequently diagnosed cancer in childhood followed by diagnoses of CNS tumours (National Cancer Policy Board, 2003). Between 1999 and 2003 ALL was diagnosed in 1197 children and CNS tumours in 1068 children in Canada (Canadian Cancer Society/National Cancer Institute of Canada, 2007). ALL is a disease of the blood, and while it is diagnosed in all ages of children, the highest rate of incidence occurs among those aged two to six years (National Cancer Policy

Board, 2003) and peaks dramatically at ages two to three years (M. Smith, Ries, Gurney, & Ross, 1999). The diagnosis of CNS tumours, the majority being brain tumours, is most prevalent between infancy and age seven (National Cancer Policy Board, 2003). The National Cancer Institute reported that U.S. 5-year survival rates from 1996 to 2003 for ALL and CNS tumours diagnosed in children aged 0-14 years were 87.2% and 74.1% respectively (Ries et al., 2007). This suggests that the children with the most common diagnoses, and thus representative of the largest population of survivors, are also the most likely to experience adverse educational late effects and be present within our school systems due to the relatively high survival rates.

1.4.2 Treatment Modality

Treatment involving cranial or craniospinal radiation therapy (CRT) and/or intrathecal methotrexate (IT MTX) has consistently been associated with an increased risk of neurocognitive deficits and poorer educational outcomes (Copeland, Dowell, Fletcher, Bordeaux et al., 1988; Kingma et al., 2001; Mitby et al., 2003; Precourt et al., 2002). Survivors treated with CRT are commonly found to have lower WRAT scores than controls or survivors treated with chemotherapy only (V. Anderson, Godber, Smibert, & Ekert, 1997; V. Anderson, Smibert, Ekert, & Godber, 1994; V. Anderson, Godber, Smibert, Weiskop, & Ekert, 2000; Copeland et al., 1985; Raymond-Speden, Tripp, Lawrence, & Holdaway, 2000; Smibert, Anderson, Godber, & Ekert, 1996). As well, survivors who received radiation were found to have lower IQ scores and were more often identified as “learning disabled” in comparison with survivors who received no radiation (von der Weid, 2001). Survivors treated with a combination of CRT and IT MTX have displayed deficits in neuropsychological functioning and poorer performance on school achievement scores (Butler, Hill, Steinherz, Meyers, & Finlay, 1994; J. Hill et al., 1998).

1.4.3 Therapeutic Dosage Level

Not only is the treatment modality a risk factor to be considered, but also the dosage at which the treatment is received. Higher therapeutic doses of CRT and MTX have been correlated with poorer academic achievement and cognitive performance (V. Anderson, Godber, Smibert, & Ekert, 1997; Buizer, de Sonnevile, van den Heuvel-Eibrink, & Veerman, 2006; Kingma, Mooyaart, Kamps, Nieuwenhuizen, & Wilmink, 1993). Specifically, survivors treated with 2400cGy (centigrade) of radiation had lower WRAT scores than those treated with only 1800cGy (Halberg et al., 1992; I. Moore, Kramer, Wara, Halberg, & Ablin, 1991; Smibert, Anderson, Godber, & Ekert, 1996) and lower IQ scores (Halberg et al., 1992; Kingma, Mooyaart, Kamps, Nieuwenhuizen, & Wilmink, 1993). Survivors who received a higher dose of MTX had poorer School Performance Index (SPI) scores for subtests including: total score, mathematics, and language skills than those who received a low dose of MTX (Buizer, de Sonnevile, van den Heuvel-Eibrink, & Veerman, 2006).

1.4.4 Age at Diagnosis or Treatment

Children who are diagnosed at a younger age and/or receive treatment at a younger age are more likely to have cognitive deficits, lower academic achievement, and poorer educational outcomes (Kingma, Mooyaart, Kamps, Nieuwenhuizen, & Wilmink, 1993; Kingma, Rammeloo, van Der Does-van den Berg, Rekers-Mombarg, & Postma, 2000). A greater need for special education, poorer WRAT scores and executive function tasks, lower school levels, and lower IQ scores have all been found to correlate with younger age at diagnosis (V. Anderson, Godber, Smibert, & Ekert, 1997; Copeland et al., 1985; Kingma, Mooyaart, Kamps, Nieuwenhuizen, & Wilmink, 1993; Kingma, Rammeloo, van Der Does-van den Berg, Rekers-Mombarg, & Postma, 2000; Seaver et al., 1994). Those who are less than five years of age at diagnosis or treatment

(especially CRT) appear to be particularly at risk (Jannoun & Chessells, 1987; Smibert, Anderson, Godber, & Ekert, 1996). Moore and colleagues (I. Moore, Kramer, Wara, Halberg, & Ablin, 1991) found that children treated with 2400cGy of radiation before 48 months of age had lower IQ and WRAT scores than those treated after they were 48 months old.

1.4.5 Time Interval since Diagnosis

Reduced cognitive and academic functioning has been associated with longer time intervals since diagnosis or treatment (V. Anderson, Godber, Smibert, & Ekert, 1997; Moehle, Berg, Ch'ien, & Lancaster, 1983; Rubenstein, Varni, & Katz, 1990). IQ scores of survivors have shown a decrease from evaluation at remission or diagnosis to evaluation four or five years later (Ochs et al., 1991; Rubenstein, Varni, & Katz, 1990). As well, significant declines in WRAT reading, spelling, and arithmetic scores have been observed as time off therapy increased (Moehle, Berg, Ch'ien, & Lancaster, 1983; Mulhern, Fairclough, & Ochs, 1991).

1.4.6 Gender

Female survivors of childhood cancer appear more at risk for poorer educational outcomes than males (Eiser, 1991; Haupt et al., 1994; Langeveld et al., 2003). Females are less likely to enter college, and those who do complete one year of college are less likely to complete four years compared to males (Kelaghan et al., 1988). Waber and colleagues (D. Waber, Bernstein, Kammerer, & Tarbell, 1992) found that females were more impaired than males according to a severity rating of 0-5 where 0 represented no services needed and 5 denoted the requirement of a fulltime special education placement. Differences in both Verbal IQ (VIQ) and Performance IQ (PIQ) scores have also been found between males and females. While males did not differ from normative scores regarding any IQ scores (Full Scale, Verbal, or Performance), females had significantly lower PIQ scores than normative data (Brown et al., 1998). In another

study, females more commonly displayed a significant decline (≥ 15 points) in VIQ than their male counterparts (Mulhern, Fairclough, & Ochs, 1991).

1.4.7 Socioeconomic Status (SES)

Lower socioeconomic status has been associated with cognitive performance and educational outcomes among survivors (Butler, Hill, Steinherz, Meyers, & Finlay, 1994; Mulhern & Palmer, 2003). In a review of the literature, it was noted that survivors from families of higher SES had better performance on measures of IQ and other neurocognitive abilities than survivors of families with lower SES (Mulhern & Palmer, 2003). Lower SES has been correlated with more impaired test scores on cognitive (IQ) and academic achievement (WRAT) measures (Butler, Hill, Steinherz, Meyers, & Finlay, 1994). In addition, socioeconomic factors have been considered more powerful correlates of neuropsychological performance among survivors than treatment modality, age at diagnosis, or gender (Whitt, Wells, Lauria, Wilhelm, & McMillan, 1984).

1.5 Large-Scale National Cohort Educational Studies

1.5.1 Canadian Study

A recent publication (Barrera, Shaw, Speechley, Maunsell, & Pogany, 2005) represents one of the few studies to have explored the educational achievements of survivors of childhood cancer using a national population-based cohort. Children who were diagnosed with cancer between 1981 and 1990, surviving more than five years after diagnosis, and still school age (less than 17 years old) at the time of study were identified from pediatric oncology centres and provincial cancer registries across Canada. Of the 1162 eligible survivors, parents or guardians of 800 survivors completed a questionnaire concerning the school experiences of their child. A control group of 1633 age and gender-matched individuals without a history of cancer were

randomly selected from the general population; of which, 923 parents or guardians completed the same questionnaire as the parents of survivors. Items on the questionnaire addressing educational outcomes were selected from the Child Behaviour Checklist (CBCL) and included such questions as: "How would you rank your child's current school performance in the following subjects: English, French, History/Social Science, Mathematics, Science?" and "Has your child ever been in any of the following programs: learning disabled, special education?". Ratings of course performance were categorized as an above-average, average, below-average, or failing grade. Results indicated that survivors were significantly more likely than controls to have poorer educational outcomes. This was determined by the survivors' higher rates of attendance in learning disabled (19% vs. 7%) and special education programs (20% vs. 8%), more often repeating or failing a grade (21% vs. 9%), and more commonly experiencing academic or other school problems (46% vs. 23%) compared to controls. Furthermore, below-average or failing grades were more often obtained by survivors than controls in all areas of study, with the greatest differences noted in mathematics (29% vs. 10%), followed by English (26% vs. 11%), and then science (20% vs. 6%). These results remained significant after controlling for possible confounding variables including: gender, current health problems, stressful events, self-esteem, parental education, and year of study. Parents of all cancer groups were more likely than controls to report poorer educational outcomes with the poorest educational outcomes reported by parents of survivors of CNS tumours, leukemia, and neuroblastoma. In addition, parents of survivors of CNS tumours were most likely to report failing grades in math and English compared to controls.

Data was also extracted from the medical records of the survivor participants so as to investigate possible treatment-related risks. Those who were treated with CRT were more likely

to have reports of repeating a grade, participating in a learning disabled or special education program, and experiencing academic or other school problems compared to survivors who received treatment that did not involve CRT or IT MTX. Survivors whose treatment consisted of both CRT and IT MTX were also more likely to have been a member of a learning disabled class and experienced academic or other school problems than those who received neither treatment. Survivors who had at least two physical health problems were also more likely to report educational difficulties. Survivors who report higher self-esteem and those whose parents had higher postsecondary education were less likely to have academic or school problems. No significant differences in educational outcomes were found according to gender, age at study (6-12 years vs. 13-16 years), or age at diagnosis (<2 years vs. 2-4 years vs. ≥ 5 years).

Barrera and colleagues (Barrera, Shaw, Speechley, Maunsell, & Pogany, 2005) are the first to examine the educational performance, as measured by school achievement, of survivors of childhood cancer and compare them to the general population in a national, large-scale, population-based study. This research adds to the current knowledge regarding the educational late effects of surviving childhood cancer by exploring a concern that had yet to be addressed, that is, how well are these individuals doing at school? Furthermore, this question was considered by investigating the actual academic achievement as measured by the parental rating of the grades attained in the subject areas of English, French, history/social science, math, and science (i.e., failed, below-average, average, above-average grade).

1.5.2 Dutch Study

Langeveld and colleagues (Langeveld et al., 2003) gathered information regarding the highest level of education completed and enrolment in learning disabled programs among a sample of survivors of childhood cancer attending a long-term follow-up clinic established in the

Netherlands. Survivors of the long-term follow-up clinic had successfully completed cancer treatment at least five years earlier. Further inclusion criteria included a cancer diagnosis prior to 19 years of age and at least 16 years of age at the time of study. Comparisons were made with a control group of 1092 individuals with no history of cancer. Results of the author-lead, self-report questionnaire indicated poorer educational achievement of survivors of childhood cancer; specifically, significantly more survivors than controls were unable to participate in regular elementary or secondary school and had to be enrolled in learning disabled programs. Female survivors were less likely to complete high school or attain an advanced graduate degree than male survivors (30% vs. 39%). Survivors of CNS tumours had lower levels of education (i.e., less than high school) compared to survivors of leukemia or non-Hodgkin's lymphoma who were treated without CRT (80% vs. 59%) and survivors of solid tumours (80% vs. 59%). Lower educational levels were also achieved by survivors of leukemia and non-Hodgkin's lymphoma who were treated with CRT than survivors of leukemia and non-Hodgkin's lymphoma who were treated without CRT (78% vs. 59%) and survivors of solid tumours (78% vs. 59%). Furthermore, significant differences were found in the level of education attained with regards to CRT dosage. Survivors who did not receive CRT were less likely to have attained lower educational levels than those who received less than 2500cGy of CRT (59% vs. 82%) and those who received 2600cGy of CRT or more (59% vs. 74%).

1.5.3 U.S. Study

Mitby and colleagues (Mitby et al., 2003), similar to the Canadian study (Barrera, Shaw, Speechley, Maunsell, & Pogany, 2005), employed a questionnaire to investigate the use of special education services and the level of education attained by cancer survivors. From Childhood Cancer Survivor Study (CCSS) centres across Canada and the United States 20 276 5-

year survivors of cancer, diagnosed before 21 years of age between 1970 and 1986 were identified as potential participants. Of those eligible, 12 431 completed questionnaires along with 3528 siblings from a potential 5800 who had been acknowledged. Questionnaire items pertaining to education included the highest grade or level of schooling completed and the type of high school diploma received: standard, as compared to general educational development credit (GED) which is an alternative method of completing high school through an equivalency test (Mitby et al., 2003). Participation in special education or learning disabled services was also examined, and for those who indicated that they had received these services the reason for these services and the grade levels in which they were received were sought. Results indicated that survivors of cancer were overall more likely to be enrolled in special education than their siblings (23% vs. 8%), with the greatest differences observed between females and same-gender siblings than males and same-gender siblings (e.g., female survivors of leukemia diagnosed at 0-5 years were 7.6 times more likely vs. males with the same diagnosis and age group who were 2.9 times more likely). Survivors diagnosed before the age of six years were most likely to have received special education, especially survivors of CNS tumours (OR: 18.8; 95% CI: 15.01-23.49), leukemia (OR: 4.4, 95% CI: 3.75-5.16) and Hodgkin's lymphoma (OR: 4.4, 95% CI: 2.64-7.24). Special education use was also significantly different by treatment era (overall rates were 17%, 22%, and 25% for those diagnosed during 1970-1975, 1976-1980, and 1981-1986 respectively) and by all three treatment categories: IT MTX only (OR: 1.3, 95% CI: 1.09-1.78), CRT only (OR: 7.2, 95% CI: 6.14-8.39), and CRT plus IT MTX (OR: 2.6, 95% CI: 2.30-2.95). The risk of using special education also increased significantly as the dose of CRT increased. Survivors, compared with siblings, received special education at an increased rate due to school missed; most notably, survivors of bone tumours (OR: 7.4, 95% CI: 3.95-13.92) and soft tissue

sarcoma (OR: 6.2, 95% CI: 3.34-11.33). Those treated with CRT alone or CRT plus IT MTX most often reported low test scores and problems learning and concentrating as the reasons for receiving special education. Those diagnosed with leukemia, CNS tumours, non-Hodgkin's lymphoma, kidney cancer, and neuroblastoma were mostly likely to report the reason for special education as low test scores (53.4%, 50.8%, 40.0%, 48.5%, and 56.5% respectively). With respect to the duration of special education services rendered, those who received high-dose CRT required services for a significantly longer time (mean of 5.7 years) than survivors who never had CRT (mean of 4.7 years). Survivors of leukemia, CNS tumours, non-Hodgkin's lymphoma, and neuroblastoma were significantly less likely than siblings to complete high school; whereas there was no significant difference between the other diagnosis groups and siblings. A similar pattern was identified regarding college completion. No significant results were found for treatment modality and high school completion, but survivors who participated in special education and received CRT were 1.9 times more likely not to complete college than siblings. Lastly, results suggested that children diagnosed with neuroblastoma were at risk for educational deficits, a finding that had not been previously documented, but has since been supported by the Canadian study (Barrera, Shaw, Speechley, Maunsell, & Pogany, 2005).

1.5.4 Danish Study

In Denmark 2384 children who had been diagnosed with cancer before the age of 20 between 1960 and 1996 were identified from the Danish Cancer Register (Koch, Kejs, Engholm, Johansen, & Schmiegelow, 2004). Survivor participants were born within 1960 to 1980 to allow adequate follow-up time, and were at least 13 years of age at the start of follow-up. A random sample of 53 143 age and gender matched controls were selected from the Register of Population Statistics. Information pertaining to educational attainment was collected from education records

obtained from Statistics Denmark. It was discovered that overall, similar proportions of survivors of childhood cancer and controls were reaching some level of higher education (17% vs. 18%). However, while male survivors attained levels of higher education equally well as, if not slightly better than male controls (RR: 1.13, 95% CI: 0.97-1.32), female survivors had a reduced chance (RR: 0.75, 95% CI: 0.62-0.90). Survivors of non-CNS tumours attained similar higher education levels overall compared to controls (34% vs. 34% for males and 18% vs. 21% for females). On the other hand, survivors of CNS tumours had reduced chances of attaining education at most levels compared with controls (e.g., attaining higher education overall, RR: 0.77, 95% CI: 0.55-1.07 for males and RR: 0.55, CI: 0.37-0.82 for females). Overall, a significant trend was found for attaining youth education (upper secondary school) with increasing age at diagnosis (non-CNS tumours, RR per year: 1.02, 95% CI: 1.01-1.04; CNS tumours, RR per year: 1.06, 95% CI: 1.03-1.10), but not for higher education. Educational outcomes did not appear to be influenced by treatment era or time since diagnosis. Survivors of CNS tumours were more likely to finish vocational training if their parents had higher education than lower education levels (RR: 2.12, 95% CI: 1.36-3.31), yet male survivors of CNS tumours whose parents had higher education were less likely to attain higher education (RR: 0.37, 95% CI: 0.18-0.78).

1.5.5 Finnish Studies

Finnish population-based studies investigated 300 individuals with brain tumours (Lahteenmaki et al., 2007) and 371 individuals diagnosed with leukemia (Harila-Saari et al., 2007) and compared them with population controls matched by age, gender and region of residence. These are the only studies to have utilized record linkage and data of standardized reporting to investigate scholastic achievement. Both studies identified patients born between 1974 and 1986 who were diagnosed before 16 years of age and alive on their 16th birthdays. The

age 16 was used as this is the common age of individuals in grade 9, the year for which data was collected. Demographic and clinical data were collected from the Finnish Cancer Registry and scholastic achievement data based upon grade 9 (which is the last year of comprehensive schooling) school reports collected since 1990 by Statistics Finland. National annual testing of core grade 9 school subjects provides uniform grading. Findings indicated that those with brain tumours had lower overall averages and specific course averages than controls irrespective of treatment, but that females treated with cranial radiation were most at risk for poor scholastic achievement (Lahteenmaki et al., 2007). Individuals diagnosed with leukemia and treated with cranial radiation had both lower overall and lower course averages; of those treated with chemotherapy, only females treated before 7 years of age were at risk for lower school marks than their controls (Harila-Saari et al., 2007). Interestingly, both studies noted greatest discrepancies in marks for foreign language course; both studies suggest this represents impairment in verbal performance.

1.6 Methodological Shortcomings of Previous Research

Findings regarding long-term educational outcomes among survivors of childhood cancer have not been consistent (Dolgin, Somer, Buchvald, & Zaizov, 1999; Haupt et al., 1994; Hays et al., 1992); this lack of consensus may be due to methodological shortcomings (Moleski, 2000). There exists a general lack of consideration of confounding variables that may affect school performance; specifically, SES (Bader-Meunier, Tchernia, & Dommergues, 1996) and physical health or physical impairments (F. Daniel Armstrong & Horn, 1995). As well, studies have been criticized for employing inappropriate comparison groups or no comparison group (Madan-Swain & Brown, 1991; Moleski, 2000) and for the use of small sample sizes (Patenaude & Kupst, 2005). Moreover, objective outcome measures are necessary to investigate educational

achievement (Brown & Madan-Swain, 1993). Recent studies have commonly employed self-reported or proxy-reported data in exploring educational outcomes among survivors (Barrera, Shaw, Speechley, Maunsell, & Pogany, 2005; Langeveld et al., 2003; Mitby et al., 2003). It is crucial that any possible areas of academic deficit be identified that may obstruct school success which may be addressed by early identification and appropriate educational intervention (Peckham, 1991).

1.7 Gaps within the Literature

Moreover, while researchers have considered the school experiences of survivors of childhood cancer with respect to special education utilization, level of education attained, grade retention, and school achievement based on anecdotal reports or academic achievement tests, namely the WRAT, rarely has the actual educational achievement within school or school performance been examined. Only two studies (Harila-Saari et al., 2007; Lahteenmaki et al., 2007) to date employ school achievement data of standardized reporting and these studies investigated only two specific cancer diagnoses: leukemia and brain tumours. As well, published work has often focused on IQ rather than actual learning difficulties, yet it is these learning difficulties that have been reported to cause the most angst for teachers and parents (Eiser, 1998) and likely the survivors themselves. Furthermore, numerous studies have considered the immediate or acute effects of surviving childhood cancer on education (Brown et al., 1992; Copeland, Dowell, Fletcher, Sullivan et al., 1988; Eiser, 1980; Precourt et al., 2002), but there exists a paucity of research concerning the educational late effects (Eiser, 1998). "Although a growing number of studies have documented the considerable impact of cancer diagnosis and treatment in quality of life in short-term survivors, less attention has focused on quality of life in long-term young adult survivors, partly because the rise in survival rates is relatively

recent”(Langeveld et al., 2002, p. 580). Awareness and understanding of the distinct learning needs of survivors of childhood cancer, as an at risk population, must be addressed and raised among educators. In doing so, early identification of learning difficulties can be made so as to effectively plan special education interventions (Robison, 2005) and preventions that will improve the educational experiences and quality of life for survivors of childhood cancer.

1.8 Objectives and Hypotheses

This research project endeavours to explore the educational outcomes, specifically academic achievement and special education utilization, of survivors of childhood cancer and draw comparisons with the general population. As well, disease-related effects and other possible modifiers including demographic, socioeconomic, and school system variables will be investigated. Specifically, this project intends to:

1. Describe the level of educational achievement in a cohort of 5-year survivors of childhood cancer compared to a control group representative of the general population.

Hypothesis: Survivors of childhood cancer will have poorer educational achievement than population controls.

2. Describe the use of special education services among the survivor cohort compared to a control group representative of the general population.

Hypothesis: Survivors of childhood cancer will have increased special education utilization compared to population controls.

3. Examine the relationship between potentially modifying risk factors and educational outcomes (including achievement and special education) among survivors.

Hypothesis: Survivors of leukemia and CNS tumours, female gender, those treated with radiation or cranial radiation, and those younger in age at diagnosis will be at increased risk for poor educational outcomes compared to other survivors.

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CHAPTER 2: EDUCATIONAL LATE EFFECTS AMONG SURVIVORS OF CHILDHOOD CANCER IN BRITISH COLUMBIA¹

2.1 Background

Advances in medical treatment have been made within the past 20 years that have resulted in dramatically increased survival rates for children diagnosed with cancer (Smith & Hare, 2004). The five-year survival rate of childhood cancer has increased substantially since 1970 (Canadian Cancer Society/National Cancer Institute of Canada, 2007), recently reaching almost 80% (Ries et al., 2007). This has led to a growing population of children within our education systems that did not previously exist, and of whom relatively little is known regarding long term educational achievement. Within the United States, survivors of childhood cancer outnumber traditional special education populations such as those with hearing impairments, deafness, visual impairments, and severe intellectual disabilities (Peckham, 1991).

Only two studies (Harila-Saari et al., 2007; Lahteenmaki et al., 2007), recently published, have investigated educational achievement using standardized data of school marks. Although there is a paucity of literature regarding objective educational achievements of survivors of childhood cancer, educational difficulties have been reported by survivors, parents and teachers (Dolgin, Somer, Buchvald, & Zaizov, 1999; Jannoun & Chessells, 1987; Raymond-Speden, Tripp, Lawrence, & Holdaway, 2000). As well, it has been found that survivors of childhood cancer attain lower levels of education (Koch, Kejs, Engholm, Johansen, & Schmiegelow, 2004; Link et al., 2006; Nagarajan et al., 2003; Zebrack et al., 2007), have an increased use of special education services compared to both peers and siblings (Barrera, Shaw, Speechley, Maunsell, & Pogany, 2005; Kingma, Rammeloo, van Der Does-van den Berg, Rekers-Mombarg, & Postma,

¹ A version of this chapter will be submitted for publication.

2000; Mitby et al., 2003; Robison et al., 2005), and have a greater likelihood of grade repetition (Barrera, Shaw, Speechley, Maunsell, & Pogany, 2005; Buizer, de Sonnevile, van den Heuvel-Eibrink, & Veerman, 2006). There is no lack of evidence within the literature of adverse neurocognitive late effects (Campbell et al., 2007; Dickerman, 2007; Mulhern & Palmer, 2003; National Cancer Policy Board, 2003) or long-term neuropsychological deficits (Link et al., 2006) among survivors of childhood cancer which may inhibit educational performance; specifically, lower intelligence quotient (IQ) scores compared to normative or sibling data (Christie, Leiper, Chessells, & Vargha-Khadem, 1995; Moleski, 2000).

Several clinical factors are associated with an increased risk of adverse educational outcomes. These include younger age at diagnosis and/or treatment (V. Anderson, Godber, Smibert, & Ekert, 1997; Jannoun & Chessells, 1987; Kingma, Rammeloo, van Der Does-van den Berg, Rekers-Mombarg, & Postma, 2000; Seaver et al., 1994), treatment involving cranial or craniospinal radiation therapy (CRT) and/or intrathecal methotrexate (IT MTX) (V. Anderson, Godber, Smibert, & Ekert, 1997; V. Anderson, Godber, Smibert, Weiskop, & Ekert, 2000; Dolgin, Somer, Buchvald, & Zaizov, 1999; Hill et al., 1998; Kingma et al., 2001; Mitby et al., 2003; Smibert, Anderson, Godber, & Ekert, 1996), higher therapeutic doses of CRT or IT MTX (V. Anderson, Godber, Smibert, & Ekert, 1997; Buizer, de Sonnevile, van den Heuvel-Eibrink, & Veerman, 2006; Halberg et al., 1992; Kingma, Mooyaart, Kamps, Nieuwenhuizen, & Wilmink, 1993; I. Moore, Kramer, Wara, Halberg, & Ablin, 1991; Smibert, Anderson, Godber, & Ekert, 1996), and a diagnosis of leukemia (in particular, acute lymphoblastic leukemia: ALL), Hodgkin's lymphoma, central nervous system (CNS) tumours, or neuroblastoma (Barrera, Shaw, Speechley, Maunsell, & Pogany, 2005; Langeveld et al., 2003; Mitby et al., 2003). Other demographic, socioeconomic and temporal variables have been associated with an increased risk

of poorer educational outcomes among survivors of childhood cancer such as female gender (Brown et al., 1998; Eiser, 1991; Haupt et al., 1994; Kelaghan et al., 1988; Langeveld et al., 2003; Mulhern, Fairclough, & Ochs, 1991; Waber, Bernstein, Kammerer, & Tarbell, 1992), lower socioeconomic status (SES) (Butler, Hill, Steinherz, Meyers, & Finlay, 1994; Mulhern & Palmer, 2003; Whitt, Wells, Lauria, Wilhelm, & McMillan, 1984), and longer time interval since diagnosis (V. Anderson, Godber, Smibert, & Ekert, 1997; Moehle, Berg, Ch'ien, & Lancaster, 1983; Mulhern, Fairclough, & Ochs, 1991; Rubenstein, Varni, & Katz, 1990).

Unfortunately, past research has lacked consensus regarding the long term educational outcomes of survivors of childhood cancer (Dolgin, Somer, Buchvald, & Zaizov, 1999; Haupt et al., 1994). Inconsistencies within the literature may be due in part to methodological shortcomings (Moleski, 2000). The methodological shortcomings of prior research, as mentioned earlier, include a lack of control for potential confounding variables, small sample sizes, inappropriate or no control group(s), and subjective educational measures must be addressed.

This study addresses the need for objective measures of long term school achievement among survivors of childhood cancer while considering the methodological limitations of previous research in this field. New data is provided on the overall educational achievement among survivors of childhood cancer and the disease-related impact on educational outcomes. These findings will further the understanding of how various clinical variables such as: diagnosis group, age at diagnosis, and treatment modality may be associated with long term educational performance.

By identifying those survivors who may be at risk for poorer educational outcomes, educational interventions can be developed, including preventative and rehabilitative programs, that will improve the educational experiences and learning opportunities for the growing

population of children who have survived cancer. Although evidence exists that survivors of childhood cancer are at risk for learning problems, very little connection has been made, or work done, regarding possible intervention or rehabilitation opportunities for these children (Eiser, 2004). In addition, it is hoped that this study will elicit and inform future research that will more profoundly explore the educational achievements of these individuals and continue to address their unique and specific educational needs.

2.2 Materials and Methods

The study cohort included all individuals with a primary diagnosis of cancer included in the International Classification of Childhood Cancer (ICCC) (Kramarova & Stiller, 1996) between 1975 and 1995 and resident in the province of British Columbia (BC) at the time of diagnosis, identified from the BC Cancer Registry. Individuals were considered survivors of childhood cancer if they were diagnosed with a primary cancer before 15 years of age and had survived five years or more since diagnosis. Our original cohort included only those individuals who were identified within the BC Kindergarten to Grade 12 (secondary school graduation year) school system between the years 1990 and 2004 (including the 2004/2005 school year), but due to a lack of educational data (i.e., some key outcome measures) for the earlier years, we restricted our survivor cohort (and control group) to those found in the system between the 1995/1996 and 2004/2005 school year. Only data occurring post-survivorship (at least 5 years since diagnosis), with the inclusion of the school year in which survivorship was attained, was included.

A comparison group was provided by the BC Ministry of Education (MOE). This cohort initially consisted of randomly selected age and gender frequency matched individuals enrolled within the BC school system between the years 1990 and 2004, but as stated above, was

eventually restricted to those in the system between 1995 and 2004.

The BC MOE requires that records be kept of all students enrolled in the BC K-12 school system through Edudata Canada, a repository of MOE datasets for research use, based at the University of BC. Educational data included: a) standardized scores and percentages of Foundation Skills Assessments (FSAs) written in Grades 4, 7, and 10 in the subject areas of reading, writing and numeracy; b) Grade 12 provincial examination scores in English, Mathematics (Math), Biology, History, and Communications; and c) special education utilization, including particular special education designations such as: learning disability, gifted, deaf/blind, hearing impairment, visual impairment, and physical disability/chronic health impairment. FSAs are province-wide, standardized tests employed by BC's MOE to assess annually student performance with respect to basic academic skills. FSAs are scored on a 5-point scale defined as: 1) exceeds expectations, 2) borderline between meets and exceeds expectations, 3) meets expectations, 4) borderline between meets and does not meet expectations, and 5) does not meet expectations. Achievement on FSAs was investigated using a cut-point of meets expectations. FSA data was available for Grades 4 and 7 for the 1999/2000 to 2004/2005 school years and for Grade 10 from 1999/2000 to 2002/2003 school years. The Grade 12 provincial exams are also a standardized measure for which percent scores are given. A letter grade mark of C, which is equal to 60%, was employed as an achievement cut-point for the Grade 12 provincial exams; a mark of C is considered satisfactory performance with respect to standard learning objectives (BC Ministry of Education, 2006). FSA participation was calculated as having FSA test data (i.e., possessing a scaled-score) and being in the appropriate grade for the corresponding FSA (i.e., in Grade 4 and wrote a Grade 4 FSA). For Grade 12 courses, participation was determined as those ever having a school mark (score assigned for the course by the school) or

provincial exam mark and had reached Grade 12 or graduated. Special education designations refer to the special education services/program the student requires for a disability of an intellectual, physical, sensory, emotional or behavioural nature, a learning disability or special gifts or talents (*Policy Document: Special Education*, 2006). FSA and Grade 12 provincial exam measures were considered educational achievement, while educational outcome included both educational achievement (i.e., FSA and Grade 12 provincial exams) and special education data. Only data occurring post-survivorship (at least 5 years since diagnosis), with the inclusion of the school year in which survivorship was attained, was included.

Sociodemographic measures (neighborhood SES quintile and rural/urban status) were derived by Edudata who employed Statistics Canada postal code conversion software (Wilkins, 2002) which linked the individual's postal code to the appropriate census enumeration area. In cases where an individual had more than one postal code, the earliest available postal code (i.e., closest to the 5-year survivor date) was used.

Clinical data for the survivor cohort was provided by chart abstraction from individual health records to supply specific details pertaining to the diagnosis and treatment. This data included: a) diagnosis group (classified according to the ICCC), b) age at diagnosis and c) treatment for primary cancer diagnoses. At the time of this study, treatment data was available for leukemia, lymphoma, and CNS cancer diagnoses and treatment modality. Treatment was categorized as: 1) ever having received chemotherapy, 2) ever having received radiation, and 3) ever having received CRT; these categories are not mutually exclusive, thus it is possible for a survivor to have received more than one type of treatment. Age at diagnosis was classified into three categories: <2 years, 2 to <5 years, and ≥ 5 years.

2.2.1 Statistical Analysis

Demographic and socioeconomic characteristics of both the survivor and control cohorts and clinical characteristics of the survivors were investigated through crosstabulations and chi-square test. Participation rates of survivors as a whole and specific diagnosis groups compared with controls for the FSAs and Grade 12 courses were computed using independent-samples t-tests. Logistic regression analyses were employed to compare the educational outcomes of the survivor cohort with the control group and the relationship between potential modifiers (gender, diagnosis group, age at diagnosis, and treatment modality) and educational outcomes among the survivor cohort. Odds ratios (OR), adjusted odds ratios (OR_{adj}), 95% confidence intervals (95%CI), and p values are reported. All statistical analyses were calculated using the *Statistical Package for the Social Science* (SPSS, Inc., 2001).

2.3 Results

2.3.1 Sociodemographic and Clinical Characteristics of Survivors and Controls

Sociodemographic characteristics were, in general, comparable between survivors and controls (Table 1). More than 50% of both survivors and controls were male and both groups had reached similar levels of education within the K-12 system. A greater proportion of survivors than controls had physical disabilities (19.2% vs. 1.1%, $p < 0.001$).

As expected, leukemia was the most common diagnosis among survivors, followed by CNS tumours (Table 2). Survivors were a mean age of 4.6 years at diagnosis. Among those survivors where treatment data was available (diagnoses of leukemia, lymphoma, and CNS cancer) chemotherapy (75.8%) was the most common treatment received, followed by radiation (30.3%).

Table 2.1 Sociodemographic Characteristics of Survivors and Controls

Characteristic	Survivors (n=782)		Controls (n=8386)		<i>P</i> value
	No.	%	No.	%	
Gender					
Male	431	55.1	4529	54.0	
Female	351	44.9	3857	46.0	
Highest Grade					
Home School	2	0.3	16	0.2	
Elementary	1	0.1	11	0.1	
Kindergarten	0	0	19	0.2	
Grade 1	2	0.3	32	0.4	
Grade 2	2	0.3	31	0.4	
Grade 3	3	0.4	51	0.6	
Grade 4	11	1.4	117	1.4	
Grade 5	19	2.4	197	2.3	
Grade 6	25	3.2	283	3.4	
Grade 7	25	3.2	248	3.0	
Grade 8	66	8.4	635	7.6	
Grade 9 ⁱ	40	5.1	420	5.0	
Grade 10	49	6.3	591	7.0	
Grade 11	76	9.7	905	10.8	
Grade 12	461	59.0	4830	57.6	
Physical Disability ^a					
Yes	150	19.2	94	1.1	<0.001
No	632	80.8	8263	98.9	
SES Quintile ^a					
1 (lowest)	102	14.2	1358	17.8	
2	154	21.5	1433	18.7	
3	142	19.8	1569	20.5	
4	156	21.8	1608	21.0	
5 (highest)	162	22.6	1676	21.9	
Residence Status ^a					
Rural	126	17.5	1426	18.6	0.003
Small Community	116	16.1	1050	13.7	
Large Community	129	17.9	1080	14.1	
Metropolitan	348	48.4	4126	53.7	

^aData were missing from Edudata on physical disability for 29 controls. SES quintile was missing for 66 survivors and 742 controls, and urban/rural status for 63 survivors and 704 controls as SES and urban/rural status were derived from postal codes which in some cases were missing in Edudata and in other cases were not able to be linked by the Statistics Canada software.

Table 2.2 Clinical Characteristics of Survivors

Characteristic	Survivors (n=782)	
	No.	%
Diagnosis		
Leukemia	270	34.5
Lymphoma	58	7.4
CNS Tumours	166	21.2
Neuroblastoma	48	6.1
Other	240	30.7
Age at Diagnosis		
<2yrs	225	28.8
2 - <5yrs	279	35.7
≥5 yrs	278	35.5
Treatment ^a		
Chemotherapy	361	75.8
Radiation	144	30.3
CRT	136	28.6

CRT: cranial radiation therapy

^aTreatment data was only available for leukemia, lymphoma, and CNS tumours (n=476) and referred only to treatment for primary cancers; categories were not mutually exclusive.

2.3.2 Educational Outcomes of Survivors and Controls

In general, controls performed at higher levels than survivors on all FSAs; specifically, controls were significantly more likely than survivors to meet or exceed expectations on Numeracy Grades 4 and 7, and Reading Grades 7 and 10. There were no significant differences in achievement between the controls and survivors on any of the Grade 12 provincial examinations (Table 3). There were no significant differences in FSA participation rates between survivors and controls; survivor participation rates were at least 95.3%. A significantly higher percentage of controls than survivors were enrolled in English 12, Math 12, and History 12 (75.9% vs. 66.6%, $p<0.001$; 37.6% vs. 25.4%, $p<0.001$; and 20.0% vs. 16.1%, $p=0.028$ respectively).

With respect to special education, survivors had significantly increased special education designations than controls. In particular, survivors were significantly more likely than controls to have a physical disability, visual disability, and/or hearing disability designation (Table 3). There were no significant differences regarding grade repetition (ever having repeated a school grade), learning disability or gifted designation between the two cohorts.

Male and female survivors compared with male and female controls differed on some educational achievement measures and special education designations. Although male survivors were significantly less likely than male controls to meet or exceed expectations on FSA Numeracy Grades 4 and 7 and Reading Grade 7, female survivors were significantly less likely than female controls to meet or exceed expectations on FSA Numeracy Grades 7 and 10, Reading Grade 10, and Writing Grade 7, and to have a mark of at least 60% on the Communications 12 provincial exam. Regarding special education, both male and female survivors compared with their control counterpart were significantly more at risk to have special

education, physical disability, hearing disability and visual disability designations. In addition, female survivors were also significantly more likely to have a learning disability than female controls whereas male survivors were no more likely than male controls to have a learning disability (Table 4). There were significantly less female controls with a learning disability than male controls (OR, 0.298, $p < 0.001$); in contrast, there was no significant difference in the number with a learning disability designation between female and male survivors (OR, 0.563, $p = 0.149$).

Table 2.3 Educational Outcomes of Survivors and Controls

Controls							
Outcome	(n=8386)		Survivors (n=782)		OR _{adj} ^a	95% CI	p value
	No.	%	No.	%			
5-Pt FSA meets expectations ^b							
Numeracy Gr 4	836	68.2	72	53.3	0.51	0.4-0.8	0.001
Numeracy Gr 7	1255	66.1	107	53.8	0.76	0.4-0.8	0.001
Numeracy Gr 10	1024	52.6	89	46.8	0.79	0.6-1.1	
Reading Gr 4	799	65.2	77	57.0	0.74	0.5-1.1	
Reading Gr 7	1233	64.9	107	53.8	0.63	0.5-0.9	0.003
Reading Gr 10	1029	52.8	85	44.7	0.73	0.5-1.0	0.043
Writing Gr 4	1006	82.1	102	75.6	0.72	0.5-1.1	
Writing Gr 7	1419	74.7	135	67.8	0.73	0.5-1.0	
Writing Gr 10	1212	62.2	117	61.6	0.97	0.7-1.3	
Gr 12 Provincial Exam C (60%) or above ^c							
English	2825	77.1	239	77.9	1.12	0.8-1.5	
Math	1296	71.3	77	65.8	0.81	0.5-1.3	
History	695	71.9	56	75.7	1.20	0.7-2.1	
Biology	929	61.1	85	61.6	0.97	0.7-1.4	
Communications	472	74.7	57	69.5	0.87	0.5-1.5	
Special education	1176	14.1	254	32.5	3.05	2.6-3.6	<0.001
Physical disability	94	1.1	150	19.2	21.47	16-28	<0.001
Visual disability	31	0.4	43	5.5	16.18	10-26	<0.001
Hearing disability	24	0.3	21	2.7	9.69	5.4-18	<0.001

95% CI: 95% confidence interval; OR_{adj}: adjusted OR

No.: number of individuals who meet the outcome criteria.

^aAdjusting for: gender, urban/rural status, SES, hearing disability and visual disability; except special education, physical disability, hearing disability, and visual disability outcomes which were not adjusted for visual or hearing disability.

^bCompared with does not meet expectations and those who did not write.

^cCompared with a percent mark below a letter grade of C (60%) and those who did not write.

Table 2.4 Educational Outcomes of Males and Females

Outcome	Male Controls* (n=4529)		Male Survivors (n=431)		OR _{adj} ^a p value		Female Controls* (n=3857)		Female Survivors (n=351)		OR _{adj} ^a p value	
	No.	%	No.	%			No.	%	No.	%		
5-Point FSA score meets expectations ^b												
Numeracy Grade 4	450	69.0	33	47.1	0.41	0.001	386	67.4	39	60.0	0.68	
Numeracy Grade 7	675	66.7	60	54.5	0.60	0.016	580	65.4	47	52.8	0.55	0.013
Numeracy Grade 10	555	52.8	54	52.9	0.97		469	52.3	35	39.8	0.63	0.048
Reading Grade 4	413	63.3	35	50.0	0.64		386	67.4	42	64.6	0.84	
Reading Grade 7	617	61.0	53	48.2	0.62	0.024	616	69.4	54	60.7	0.66	
Reading Grade 10	494	47.0	47	46.1	0.93		535	59.6	38	43.2	0.56	0.013
Writing Grade 4	511	78.4	50	71.4	0.74		495	86.4	52	80.0	0.69	
Writing Grade 7	695	68.7	70	63.6	0.85		724	81.6	65	73.0	0.57	0.034
Writing Grade 10	582	55.4	61	59.8	1.13		630	70.2	56	63.6	0.75	
Gr 12 Provincial Exam C (60%) or above ^c												
English	1277	71.6	115	70.6	0.94		1548	82.3	124	86.1	1.53	
Math	672	68.7	41	62.1	0.72		624	74.3	36	70.6	0.97	
History	355	72.6	37	77.1	1.29		340	71.1	19	73.1	1.07	
Biology	311	58.5	34	59.6	0.96		618	62.5	35	63.0	0.98	
Communications	317	73.2	38	73.1	1.25		155	77.9	19	63.3	0.41	0.045
Special education	715	15.8	147	34.1	2.89	<0.001	461	12.0	107	30.5	3.32	<0.001
Learning disability	179	4.0	20	4.6	1.22		48	1.2	10	2.8	2.42	0.013
Physical disability	57	1.3	81	18.8	18.69	<0.001	37	1.0	69	19.7	26.53	<0.001
Visual disability	17	0.4	21	4.9	14.20	<0.001	14	0.4	22	6.3	19.13	<0.001
Hearing disability	12	0.3	10	2.3	9.11	<0.001	12	0.3	11	3.1	10.35	<0.001

*Reference group

OR: odds ratio; 95% CI: 95% confidence interval; OR_{adj}: adjusted OR

No. Enrolled: number of individuals ever in the corresponding grade for the FSA's and ever having a school score or a provincial exam score in the corresponding course for the grade 12 outcomes

No.: number of individuals who meet the outcome criteria

^aAdjusting for: gender, urban/rural status, SES, hearing disability and visual disability; except special education, physical disability, visual disability, and hearing disability outcomes which were not adjusted for hearing or visual disability

^bCompared with does not meet expectations and those who did not write.

^cCompared with a percent mark below a letter grade of C (60%) and those who did not write.

2.3.3 Educational Outcomes by Diagnosis

Two diagnosis groups appeared most at risk for poor educational outcomes: CNS tumours and leukemia. Survivors of CNS tumours compared with controls were significantly less likely to meet or exceed expectations on all FSAs: Numeracy Grades 4, 7 and 10; Reading Grades 4, 7 and 10; and Writing Grades 4, 7 and 10 and significantly more likely to have a Communications Grade 12 provincial exam mark below 60%. Survivors of CNS tumours had

significantly more special education, physical disability, visual disability, and hearing disability designations than controls. Survivors of leukemia were significantly less likely to meet or exceed expectations than controls on FSA Numeracy Grades 4 and 7 and Reading Grade 7, and had significantly increased special education, learning disability, physical disability and visual disability designations compared with controls. Once survivors of CNS tumours and leukemia were excluded from the analysis of survivors compared with controls, educational achievement measures (i.e., FSAs and Grade 12 provincial exams) no longer exhibited any significant differences between survivors and controls, while special education designations which were previously significant remained so (Table 5). As well, with the exclusion of survivors of both CNS tumours and leukemia, only Math 12 continued to have a significantly higher enrolment rate among controls than survivors (37.6% vs. 29.9%, $p=0.019$) while all other grade 12 course enrolment rates remained insignificantly different between survivors and controls.

Survivors of neuroblastoma compared with controls showed no significant differences on any educational achievement measure, but were significantly more likely to have special education (OR, 2.3, $p=0.010$) and physical disability (OR, 9.6, $p<0.001$) designations than controls. There were no significant differences between survivors of lymphoma and controls on any educational achievement measures or special education designation. Other diagnosis groups were numerically too small to perform meaningful comparisons.

Table 2.5 Educational Outcomes by Diagnosis

Outcome	Controls* (n=8386)		Survivors excluding CNS tumours and Leukemia (n=346)				Leukemias (n=270)				CNS Tumours (n=166)			
	No.	%	No.	%	OR _{adj} ^a	P value	No.	%	OR _{adj} ^a	P value	No.	%	OR _{adj} ^a	P value
5-pt FSA meets expectations ^b														
Numeracy Gr 4	836	68.2	41	59.4	0.69		26	53.1	0.48	0.016	5	29.4	0.16	0.001
Numeracy Gr 7	1255	66.1	53	58.9	0.70		41	54.7	0.60	0.033	13	38.2	0.29	0.001
Numeracy Gr 10	1024	52.6	50	58.8	1.33		30	43.5	0.67		9	25.0	0.30	0.002
Reading Gr 4	799	65.2	45	65.2	1.14		27	55.1	0.64		5	29.4	0.20	0.003
Reading Gr 7	1233	64.9	54	60.0	0.79		40	53.3	0.61	0.042	13	38.2	0.34	0.003
Reading Gr 10	1029	52.8	42	49.4	0.94		32	46.4	0.74		11	30.6	0.37	0.008
Writing Gr 4	1006	82.1	53	76.8	0.79		40	81.6	1.00		9	52.9	0.20	0.002
Writing Gr 7	1419	74.7	65	72.2	0.87		52	69.3	0.76		18	52.9	0.39	0.010
Writing Gr 10	1212	62.2	54	63.5	1.14		47	68.1	1.25		16	44.4	0.41	0.012
Gr 12 Prov. Exam C (60%) or above ^c														
English	2825	77.1	115	79.3	1.33		83	76.9	0.97		41	75.9	1.04	
Math	1296	71.3	38	63.3	0.72		28	71.8	0.96		11	61.1	0.90	
History	695	71.9	25	80.6	1.83		26	76.5	1.21		5	55.6	0.46	
Biology	929	61.1	38	61.3	1.08		32	61.5	0.98		15	62.5	0.69	
Communications	472	74.7	25	73.5	1.05		20	83.3	1.81		12	50.0	0.38	0.037
Special education	1176	14.1	87	25.1	2.09	<0.001	89	33.0	3.05	<0.001	78	47.0	6.13	<0.001
Learning disability	227	2.7	12	3.5	1.25		15	5.6	2.11	0.007	3	1.8	0.70	
Physical disability	94	1.1	48	13.9	14.43	<0.001	40	14.8	15.50	<0.001	62	37.3	57.65	<0.001
Visual disability	31	0.4	22	6.4	19.06	<0.001	4	1.5	4.07	0.009	17	10.2	32.79	<0.001
Hearing disability	24	0.3	14	4.0	15.24	<0.001	0	0	-		7	4.2	16.05	<0.001

*Reference group

OR_{adj}: adjusted OR

No.: number of individuals who meet the outcome criteria.

^aAdjusting for: gender, urban/rural status, SES, hearing disability and visual disability; except special education, physical disability, visual disability, and hearing disability outcomes which were not adjusted for hearing or visual disability.^bCompared with does not meet expectations and those who did not write.^cCompared with a percent mark below a letter grade of C (60%) and those who did not write.**2.3.4 Clinical Factors Related to Educational Outcomes among Survivors**

An investigation of the treatment modality for the primary cancer indicated that survivors who received radiation were significantly less likely than survivors who received no radiation to meet expectations on FSA Numeracy Grades 7 and 10 and Writing Grade 7 and to have a Communications 12 provincial exam letter grade of at least C (60%). As well, survivors who received radiation were more likely to have physical and visual disabilities than those survivors never having had radiation. The findings were similar among the survivors who received CRT compared to those who had no CRT. Survivors who ever received chemotherapy compared with survivors never receiving chemotherapy were significantly more likely to meet expectations on

FSA Writing Grade 10 and less likely to have a physical disability (Table 6).

With respect to the age at diagnosis, survivors who were less than 2 years of age at diagnosis were significantly more likely to meet expectations on FSA Numeracy Grade 7 and Writing Grade 7, despite having significantly more visual and hearing disabilities than those who were 5 years of age or older at diagnosis (Table 6).

Table 2.6 Clinical Factors Related to Selected Educational Outcomes among Survivors

Factors	FSA Numeracy Gr 7 meets expectations ^b		FSA Numeracy Gr 10 meets expectations ^b		FSA Writing Gr 7 meets expectations ^b		FSA Writing Gr 10 meets expectations ^b		Communications Gr 12 Exam of C (60%) or above ^c		Physical Disability Designation		Visual Disability Designation		Hearing Disability Designation	
	OR _{adj} ^a	p value	OR _{adj} ^a	p value	OR _{adj} ^a	p value	OR _{adj} ^a	p value	OR _{adj} ^a	p value	OR _{adj} ^a	p value	OR _{adj} ^a	p value	OR _{adj} ^a	p value
Treatment																
No Radiation ^d	1.00															
Radiation	0.26	0.027	0.33	0.040	0.29	0.035	0.68		0.01	0.011	2.29	0.001	3.79	0.006	-	
No CRT ^d	1.00															
CRT	0.26	0.027	0.20	0.008	0.29	0.035	0.56		0.01	0.011	2.50	<0.001	3.52	0.009	-	
No Chemotherapy ^d	1.00															
Chemotherapy	1.38		1.56		0.98		2.51	0.050	3.68		0.56	0.021	0.56		0.80	
Age at Diagnosis																
<2 years ^d	1.00															
2 to <5 years	0.63		0.66		0.49	0.049	1.14		0.52		1.02		0.80		0.72	
≥5 years	0.30	0.013	0.85		0.35	0.033	0.80		0.97		0.85		0.28	0.008	0.17	0.023

OR_{adj}: adjusted OR

^aAdjusting for: gender, urban/rural status, SES, hearing disability and visual disability; except special education, physical disability, visual disability, and hearing disability outcomes which were not adjusted for hearing or visual disability.

^bCompared with does not meet expectations and those who did not write.

^cCompared with a percent mark below a letter grade of C (60%) and those who did not write.

^dReference group.

2.4 Conclusions

This is the first Canadian, population-based cohort study to examine the educational late effects of survivors of childhood cancer using standardized data. Based upon data collected by the BC Ministry of Education on FSA and provincial exams, survivors were at increased risk for poor educational achievement compared to population controls, although this excess risk was generally confined to survivors of CNS tumours and leukemia. As well, consistent with earlier research (Kingma, Rammeloo, van der Does-van den Berg, Rekers-Mombarg, & Postma, 2000; Langeveld et al., 2003; Mitby et al., 2003; Robison et al., 2005), survivors were more likely than population controls to require special education services. In particular, survivors were at increased risk to have a physical disability, visual disability, and/or hearing disability. Unlike some studies (Buizer, de Sonnevile, van den Heuvel-Eibrink, & Veerman, 2006; Haupt et al., 1994; I. Moore, Glasser, & Ablin, 1988), survivors were no more likely than population controls to have repeated a grade in school.

Consistent with the literature (Barrera, Shaw, Speechley, Maunsell, & Pogany, 2005; Haupt et al., 1994; Koch, Kejs, Engholm, Johansen, & Schmiegelow, 2004; Mitby et al., 2003; Peckham, Meadows, Bartel, & Marrero, 1988) survivors of CNS tumours and survivors of leukemia appeared most at risk for poor educational outcomes, as demonstrated by an increased likelihood of poor achievement and greater special education utilization compared with population controls. Survivors of CNS tumours were also more likely to have physical disability designations, including increased visual and/or hearing disabilities than population controls. Visual and hearing disabilities have previously been observed among survivors of CNS tumours (Aarsen et al., 2006; F. D. Armstrong & Mulhern, 1999; Hoppe-Hirsch et al., 1995; Jenkin, Danjoux, & Greenberg, 1998; Packer et al., 2003). Similar to Mulhern and colleagues (Mulhern,

Wasserman, Friedman, & Fairclough, 1989), survivors of leukemia were more likely to have visual disabilities than population controls and consistent with several studies (Haupt et al., 1994; Madan-Swain & Brown, 1991; Stehbens et al., 1991), survivors of leukemia also had significantly more learning disability designations than the control group. Unlike Barrera et al. (Barrera, Shaw, Speechley, Maunsell, & Pogany, 2005), survivors of neuroblastoma were not more likely to have academic school problems than the comparison population based upon achievement on FSA or provincial exams; however, in agreement with Mitby and colleagues (Mitby et al., 2003), survivors of neuroblastoma were at increased risk for special education compared to population controls.

Notably, survivors of childhood cancer other than survivors of both leukemia and CNS tumours displayed no performance differences in comparison with the general population controls on any educational achievement measure (FSA or provincial exam). This finding suggests that cancer survivors, excluding those of leukemia and CNS tumours, are achieving similarly within school to their peers. In addition, when comparing the remaining survivor group - CNS tumours and leukemia excluded - with the comparison population there were no significant differences in FSA participation rates or Grade 12 course enrolment rates, except in Math 12. Both survivors of CNS tumours and leukemia displayed significantly reduced enrolment in Math 12 compared to population controls. It is possible that the decreased enrolment in Math 12 may reflect a decision not to partake in this course due to a deficit in mathematic skills; deficits in this area and poor arithmetic achievement have been commonly reported among survivors of childhood cancer (Coniglio & Blackman, 1995; Duffner, 2004; Gamis & Nesbit, 1991; Kaemingk, Carey, Moore, Herzer, & Hutter, 2004; Moleski, 2000; B. Moore, 2005; Mulhern & Palmer, 2003; Peckham, 1991; Peckham, Meadows, Bartel, &

Marrero, 1988; Stehbens et al., 1991; Whitt, Wells, Lauria, Wilhelm, & McMillan, 1984).

Among survivors for whom treatment data was available, survivors whose treatment involved radiation, or more specifically cranial radiation, had poorer achievement and more physical disabilities, including increased visual disability designations, than those survivors who did not receive these treatments. Radiation, especially cranial radiation, is frequently noted as a risk factor for poor educational outcomes among survivors of childhood cancer (V. Anderson, Godber, Smibert, & Ekert, 1997; V. Anderson, Smibert, Ekert, & Godber, 1994; V. Anderson, Godber, Smibert, Weiskop, & Ekert, 2000; Copeland et al., 1985; Hill et al., 1998; Smibert, Anderson, Godber, & Ekert, 1996) and visual impairments are often reported among those who receive radiation treatment (F. Armstrong & Mulhern, 1999; Jenkin, Danjoux, & Greenberg, 1998; Mulhern, Wasserman, Friedman, & Fairclough, 1989; Ober, Beaverson, & Abramson, 2004; Syndikus, Tait, Ashley, & Jannoun, 1994).

Contrary to previous findings (V. Anderson, Godber, Smibert, & Ekert, 1997; Copeland et al., 1985; Jannoun & Chessells, 1987; Kingma, Mooyaart, Kamps, Nieuwenhuizen, & Wilmink, 1993; Kingma, Rammeloo, van der Does-van den Berg, Rekers-Mombarg, & Postma, 2000; I. Moore, Kramer, Wara, Halberg, & Ablin, 1991; Seaver et al., 1994; Smibert, Anderson, Godber, & Ekert, 1996), survivors who were younger in age at diagnosis (<2 years) were less at risk for poor educational achievement than survivors who were older in age at diagnosis (≥ 5 years). Furthermore, this was despite survivors younger in age at diagnosis being more likely to have hearing and/or visual disabilities than survivors older in age at diagnosis. It is possible that the accommodations provided for these disabilities may have helped compensate with respect to achievement.

Gender differences within the survivor group were similar to past research (Brown et al., 1998; Eiser, 1991; Haupt et al., 1994; Kelaghan et al., 1988; Langeveld et al., 2003; Mulhern, Fairclough, & Ochs, 1991; Waber, Bernstein, Kammerer, & Tarbell, 1992); females were more at risk for poorer educational outcomes than males with respect to both achievement and special education designations. Although both female and male survivors were more likely to have special education designations and physical, hearing and/or visual disabilities than their control counterparts, female survivors also had increased learning disability designations than female controls whereas there were no differences in learning disability designations between male survivors and controls. There were no significant differences between male and female survivors with respect to learning disability designations and within controls, males were significantly more likely than females to have a learning disability. Interestingly, female gender also appears to be a risk factor among disorders such as autism and attention deficit hyperactivity disorder (ADHD); while these disorders are more prevalent among males, females with these disorders are more severely impaired (DuPaul et al., 2006; Eme, 1992; Madan-Swain & Brown, 1991; Rucklidge & Tannock, 2001), including more impaired intellectual functioning (Gaub & Carlson, 1997; Gershon, 2002; Volkmar & Szatmari, 1993).

This study addresses past methodological shortcomings, particularly in using standardized educational data to investigate long-term educational achievement. Commonly employed questionnaire-based survivor cohort studies (Barrera, Shaw, Speechley, Maunsell, & Pogany, 2005; Kadan-Lottick et al., 2002; Langeveld et al., 2003; Taylor et al., 2004) that use self- or proxy-reported data are less reliable than primary sources of outcome data, and limited to outcome information that is identified prior to the study and what can be reasonably and reliably recalled. Only two recent studies (Harila-Saari et al., 2007; Lahteenmaki et al., 2007) have

employed outcome data with standardized reporting to investigate educational achievement and these studies involved only leukemia and brain tumours. As well, the use of a population-based cohort ascertains information on a complete survivor group and relieves concerns of small sample sizes.(Patenaude & Kupst, 2005) Earlier studies have typically been small institution-based case series or cooperative group studies focused on specific diagnostic groups with short follow-up.

In addition to addressing methodological issues of earlier research, this study fills a gap in the literature on late effects of survivors of childhood cancer by examining standardized educational achievement from an objective data source. Although previous studies have investigated educational attainment, special education utilization, and reported educational difficulties, until now, there have been no reports on how survivors, as a population, are actually performing in school long-term. It has been consistently suggested that survivors experience adverse neurocognitive late effects (Campbell et al., 2007; Dickerman, 2007; Mulhern & Palmer, 2003; National Cancer Policy Board, 2003; Spencer, 2006), but this has yet to be clearly linked with poor achievement in school.

Knowing that survivors of leukemia and CNS tumours appeared at risk for poor educational achievement, while the remainder of survivors were essentially achieving similarly to their peers, has important implications for educators. This remaining group of survivors did exhibit an increased use of special education programs, suggesting that surveillance may be necessary to address possible special education needs, but intense and time consuming assessment may not be required. Survivors of leukemia and CNS tumours, given their susceptibility as a high risk group for both poor achievement and special education utilization, should be more thoroughly monitored and assessed to ensure that the necessary interventions are

developed and implemented. In addition, regular monitoring of progress over time (F. Armstrong, Blumberg, & Toledano, 1999; F. Armstrong & Horn, 1995) and early identification (Coniglio & Blackman, 1995; Robison et al., 2005; Spencer, 2006) are essential in providing appropriate special education services or approaches to learning. Educational practitioners need to be aware of potential educational difficulties and associated risk factors, particularly who is most at risk, among survivors of childhood cancer so as to meet the educational needs of this population as their numbers continue to increase (Dickerman, 2007). Furthermore, dissemination of information between medical and school personnel is fundamental (Coniglio & Blackman, 1995) towards improving the educational experiences of survivors.

2.5 References

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CHAPTER 3: DISCUSSION

3.1 Conclusions

Survivors of childhood cancer as a whole may not necessarily be at risk for poor educational outcomes with respect to school achievement. However, survivors of CNS tumours, followed by survivors of leukemia, were found most at risk for both poor achievement (according to provincial exams and FSAs) and increased special education utilization (overall and with respect to several specific special education designations). Once survivors of these diagnoses were excluded from analyses, remaining survivors performed similarly on all FSAs and provincial exams to population controls. These remaining survivors were still more likely to have a special education designation; specifically, to have a physical disability, a hearing disability, or a visual disability compared to population controls and as such survivors of childhood cancer as a whole may require some unique consideration within the education system. These might include surveillance or extra vigilance and the provision of accommodations on the part of educators and school personnel.

As was noted earlier, survivors of childhood CNS tumours and leukemia are particularly at risk for poor educational outcomes. Survivors of CNS tumours are clearly the most at risk group for poor achievement, performing more poorly on all FSAs and the Communications 12 provincial exam than population controls. Survivors of leukemia, on the other hand, performed more poorly on three of the nine FSAs than the population control group, but similarly on all five provincial exams investigated. With respect to special education, both survivors of CNS tumours and leukemia were more likely, overall, to have a special education designation, and specifically, a general physical disability or a visual disability than the population control group. Survivors of CNS tumours were also more likely to have a hearing disability and survivors of leukemia a

learning disability compared to controls. Survivors of neuroblastoma were the only other diagnosis group to show any specific at risk tendencies, being more likely to have a special education designation or physical disability than population controls. Survivors of CNS tumours (most obviously) and survivors of leukemia are most in need of early educational intervention given their propensity towards both poor achievement and increased special education. Survivors of neuroblastoma still require additional support from educators due their likelihood of increased special education designations.

Several other at risk groups emerged among survivors that may also require educational interventions; these include female survivors and survivors who received radiation or CRT. First, female survivors may be more likely to have poor achievement as they performed more poorly than their control counterparts on more FSA and provincial exams than males survivors compared to their control counterparts. As well, female survivors were more likely to have a learning disability than female controls, while there was no difference between male survivors and male controls with respect to learning disabilities. Secondly, although treatment data was limited, among survivors of leukemia, lymphoma, and CNS tumours it was found that those treated with radiation or CRT were more at risk for poor achievement and physical and visual disabilities than those not receiving radiation or CRT. Age at diagnosis was also explored; survivors younger in age at diagnosis (<2 years) were less likely than survivors older in age at diagnosis (5 years or older) to have poor educational achievement (although the difference existed on only two outcome measures), but more likely to have hearing and visual disabilities. It may be more informative to examine the effects of age at treatment rather than age at diagnosis as some studies have suggested that an interaction between age and radiation exists in that individuals who are younger in age at treatment are more vulnerable to the effects of radiation,

particularly CRT, and as such are more likely to experience educational deficits (Moore, Kramer, Wara, Halberg, & Ablin, 1991; Smibert, Anderson, Godber, & Ekert, 1996); literature reviews have reported similarly (F. D. Armstrong & Mulhern, 1999; Eiser, 1998; Mulhern & Palmer, 2003).

In general these findings are consistent with the current survivorship literature on long-term educational outcomes. Survivors of CNS cancer and survivors of leukemia are commonly identified as likely to experience educational difficulties (Barrera, Shaw, Speechley, Maunsell, & Pogany, 2005; Langeveld et al., 2003; Mitby et al., 2003). However, survivors of Hodgkin's and non-Hodgkin's lymphoma were not found at increased risk for poor educational outcome as was reported previously (Mitby et al., 2003) and nor were survivors of neuroblastoma more likely to have poor scholastic achievement (Barrera, Shaw, Speechley, Maunsell, & Pogany, 2005), although they were more vulnerable towards special education designations than population controls. Also in agreement with past findings, treatment including radiation or CRT was related to increased educational deficits among survivors (Kingma et al., 2001; Mitby et al., 2003; Precourt et al., 2002; von der Weid, 2001). Female gender among survivors as a risk modifier for increased likelihood of poor educational outcomes (Eiser, 1991; Haupt et al., 1994; Langeveld et al., 2003) was also supported by this research. And lastly, conversely to prior results, younger age at diagnosis (<2 years) was not associated with poorer educational achievement (Anderson, Godber, Smibert, & Ekert, 1997; Copeland et al., 1985; Jannoun & Chessells, 1987; Kingma, Mooyaart, Kamps, Nieuwenhuizen, & Wilmink, 1993; Kingma, Rammeloo, van Der Does-van den Berg, Rekers-Mombarg, & Postma, 2000; Moore, Kramer, Wara, Halberg, & Ablin, 1991; Seaver et al., 1994; Smibert, Anderson, Godber, & Ekert, 1996).

3.2 Strengths and Limitations

Potential limitations of this study include the heterogeneity of the survivor group, small sample sizes within survivor subgroups, the comparison group used, and the consideration of possible confounding variables. Every effort was made to address or make adjustments for these potential shortcomings and one of the major strengths of this project is that it addresses methodological criticisms of previous research. Furthermore, this project has considerable value in its use of a population-based survivor cohort and use of objective education data that was collected and reported in a standardized manner.

The heterogeneous nature of the survivor cohort, given that this was a population-based cohort study, was unavoidable; no one survivor will have the exact same experience as another. In an attempt to attend to this concern, in addition to examining the survivor cohort in its entirety, analyses of specific diagnosis groups and clinical-related modifiers (e.g., treatment modality and age at diagnosis) were considered in relation to educational outcome. This assists in improving the homogeneity of the study cohort by limiting the group to only specific diagnosis or diagnoses groups, those who received particular treatment regimens, and certain age at diagnosis groups. However, the impact of the cancer itself and its treatment may vary even within a group who have the same diagnosis and treatment (F. Daniel Armstrong & Horn, 1995).

In creating more homogeneous groups, through the study of particular subgroups within the survivor cohort (e.g., specific diagnosis groups and treatment modality), sample size was at times compromised. Some of the specific cancer diagnoses and potential modifiers intended for study elicited relatively small subgroups which limited, and in some cases, even eliminated probable statistical analyses. Small sample sizes have commonly been noted as a methodological shortcoming among studies of survivors of cancer (Brown & Madan-Swain, 1993; Patenaude &

Kupst, 2005). Conversely, the fact that this was a population-based cohort was a significant strength as the survivor cohort was more than ample in numbers and findings are representative of a complete populace of survivors for a geographical region (an entire Canadian province). Earlier studies have often been small institution-based case series or cooperative group studies focused on specific diagnostic groups limited in both length and nature of follow-up.

Some would consider the sole use of a population control group for comparison purposes inadequate; however, the use of healthy population controls matched by gender, age, and SES have been noted as more appropriate controls than normative data (Campbell et al., 2007). Some studies have employed or suggested that sibling control groups (Buizer, de Sonnevile, van den Heuvel-Eibrink, & Veerman, 2006; Haupt et al., 1994; Mitby et al., 2003), samples of individuals with a chronic illness (Raymond-Speden, Tripp, Lawrence, & Holdaway, 2000), or even groups of other survivors of cancer with different diagnoses or treatments (Madan-Swain & Brown, 1991) provide the best comparison groups. There does not appear to be consensus within the literature as to what entails the most appropriate comparison group for survivors of childhood cancer research. The omission of a control group is obviously of concern, and in some cases, past studies have lacked a control group all together (Brown et al., 1998; Fogarty et al., 1988; Humpl, Fritsche, Bartels, & Gutjahr, 2001; Rubenstein, Varni, & Katz, 1990; Syndikus, Tait, Ashley, & Jannoun, 1994). With respect to the present project, the identification of a sibling control group had been intended for comparison purposes; unfortunately, this was not possible as approval from the BC Ministry of Education was not granted for the release of sibling education data at the time of the initial data request. This research did however employ gender- and age-matched population controls, as well as performed analyses within the survivor cohort comparing different treatment modality groups and age at diagnosis groups; thus, in effect, comparing

different survivor groups with each other.

Although many possible confounding variables have been taken into consideration, school missed is one factor that could not be directly controlled for given that school records providing this information could not be acquired. A criticism of previous studies is their lack of control for school attendance (Brown & Madan-Swain, 1993). Although it should be noted that school attendance may be of concern during treatment, attendance does improve after therapy completion (Eiser & Vance, 2002; Jannoun & Chessells, 1987) and thus would not appear to be a problem for 5-year survivors, as is the case in this research project. As an indicator of school attendance, the full-time course enrolment status of both cohorts was explored and found not to differ between survivors and population controls (not reported). With respect to other potential confounding factors raised within the literature such as SES (Bader-Meunier, Tchernia, & Dommergues, 1996) and health or physical impairments, (F. Daniel Armstrong & Horn, 1995) these were all considered in the analysis model of all educational outcomes (achievement measures and special education designations).

One of the most important aspects of this research was the type of data and data collection method employed. To date, very few studies have investigated school performance through actual school marks (Harila-Saari et al., 2007; Lahteenmaki et al., 2007) and the use of self- or proxy-reported data has been common among recent survivor population studies in this field (Barrera, Shaw, Speechley, Maunsell, & Pogany, 2005; Langeveld et al., 2003; Mitby et al., 2003). Self- or proxy-reported data relies on an individual's ability to recall accurately past information and can often be biased. The use of objective data that has been collected and reported in a standardized format, as is the case in this project, provides higher quality and substantially more accurate data and thus more credible results upon which to base

interpretations and recommendations.

Unfortunately, there were several limitations of the data which reduced potential analyses or posed possible shortcomings within this project. First, clinical data with respect to treatment was only available, at the time of analysis, for diagnoses of leukemia, lymphoma, and CNS tumours. Fortunately, these diagnosis groups were the predominant cancer diagnoses within the survivor cohort, but interpretation of the effects of treatment should still only consider those cancer diagnoses for which treatment information was available. As well, only basic treatment modality (chemotherapy, radiation, CRT, and surgery) data existed and more specific information pertaining to radiation dosage and chemotherapy drug and dosage were unavailable at the time of study. Although treatment data was incomplete valuable preliminary results were still established. Moreover, many studies lack treatment data entirely, such as the Danish population study (Koch, Kejs, Engholm, Johansen, & Schmiegelow, 2004).

Lastly, the potential exists that these findings may not generalize to other populations of survivors of childhood cancer. Although a major strength of research is the fact that it is a population-based cohort, not a sample group, and thus better representative of the study population, it is still the population of a specific geographical region within a specific country. Other geographical regions, due to any number of potential differences within the population such as their cancer treatment protocols, education system, and so on, may therefore find alternative outcomes among survivors of childhood cancer.

3.3 Significance

This research provides long-term objective data on overall and disease-related educational outcomes of survivors of childhood cancer. This is the first Canadian population cohort study to investigate educational late effects by means of standardized educational data

including school marks. Only two recently published studies (Harila-Saari et al., 2007; Lahteenmaki et al., 2007) have utilized standardized school marks to investigate the educational achievements of a population of individuals diagnosed with cancer. What these two studies lack is a complete survivor population as one of these studies focused solely on childhood leukemia (Harila-Saari et al., 2007) and the other on childhood brain tumours (Lahteenmaki et al., 2007). The only other Canadian population-based research of survivors' educational outcomes employed proxy-reported data (Barrera, Shaw, Speechley, Maunsell, & Pogany, 2005). As was noted earlier, employing actual school data that is collected and reported in a standardized fashion improves the quality of data, particularly in comparison with self- or proxy-reported data which has been previously utilized within other population studies (Langeveld et al., 2003; Mitby et al., 2003). This project is clearly unique, and therefore fills a gap within the literature, in its use of standardized education achievement (school marks) data through administrative records to investigate the long-term educational outcomes of a population of survivors of childhood cancer. As well, as was mentioned within the previous section discussing the limitations and strengths, this research addresses the methodological shortcomings of previous work in this field of study; taking into consideration the criticisms of prior studies and improving upon earlier work. The distinctiveness of this research in its methodologies (survivor population and data utilized) and ability to attend to previous concerns within this area of the survivorship literature provide significant impact.

The findings of this project will add to our understanding of the effects of diagnosis on the long-term educational achievement and special education utilization of survivors of childhood cancer. These findings clearly indicate which diagnosis groups are most at risk for poor educational achievement and special education designations and thus suggests where

resources may most be needed with respect to monitoring and intervention within the education system. A significant and optimistic finding to come out of this research was that while survivors of childhood leukemia and CNS tumours are the most at risk diagnosis groups for poor educational outcomes (including both exam/test achievement and special education designations), excluding these survivors from analyses indicates that the remainder of survivors are achieving similarly (according to standardized test/exam marks) to population controls. Moreover, this result is one not commonly reported, in fact, just the opposite was recently suggested in a survivor population within Canada (Barrera, Shaw, Speechley, Maunsell, & Pogany, 2005).

The results of this research support the current understanding of how cancer treatment impacts long-term educational outcomes. Although treatment data was only available for survivors of leukemia, lymphoma, and CNS tumours (approximately half the study population), findings are in keeping with previous studies. Survivors who receive radiation therapy or CRT are more at risk for poor educational outcomes (both achievement and special education) than those not receiving these therapies. In addition, findings regarding gender are in keeping with current survivorship literature; female survivors of childhood cancer are more at risk for poor educational outcomes (achievement and special education, especially learning disabilities) than male survivors. These effects of treatment and gender among survivors indicate that these are also potential at risk groups within the education system who may therefore require appropriate monitoring and intervention on behalf of educators.

It is hoped that this work will elicit an increased awareness among educators that survivors of childhood cancer are a potential at risk population within the school system who may require monitoring and intervention. Moreover, in providing information that increases the

understanding of which subgroups of survivors may be at increased risk of poor educational outcomes informs educational practice in aiding educators in the decision making process of who might be more in need of monitoring and intervention, and thus where to focus resources (e.g., time and money). These findings will help guide the development of appropriate educational interventions, including preventive and rehabilitative programs within schools. Overall, this project is intended to assist in providing successful educational experiences for survivors and improve the quality of life of survivors.

3.4 Future Research

It is important to note that the number of survivors of childhood cancer will only continue to increase (Dickerman, 2007) and thus so will the number of survivors within our education systems. A continuation of research regarding the long term educational outcomes and experiences of survivors of childhood cancer is necessary to support current understandings, but also to continue to investigate the clinically-related effects; particularly as time passes and treatment regimens change due to medical improvements. As well, to better understand why it is that certain diagnosis groups are more at risk for poor educational outcomes than others; is it the diagnosis itself, the treatment received, or a combination of both? Clearly, more work is needed with respect to more detailed treatment-related influences on long-term educational outcome such as mode of chemotherapy (intravenous, intrathecal, etc.), chemotherapy drug, dose of chemotherapy, and radiation or CRT dose. Obviously, the more knowledge that exists pertaining to which survivors are possibly more likely to experience poor educational outcomes, the more informative this is to educational practice and decision-making. Education personnel will be capable of more readily allocating resources and designing interventions that meet both the needs of educators and most importantly, survivors of childhood cancer.

With respect to appropriate educational intervention, further research is much needed identify where and what intervention is required. Presently, there exists a void as to which areas of learning within school, outside of standardized educational assessments, may pose the greatest difficulties for survivors and what type of intervention(s) may most meet their individual needs in providing success at school. Intervention design is challenging when little is known regarding which scholastic areas are likely to present problems among survivors (and certainly these may differ among survivor subgroups according diagnosis, treatment and so forth) and which particular interventions may most address these deficits within this population. The study of educational intervention effectiveness among survivors is even more lacking than that of the specific learning deficits. There exists almost no research on which intervention methods are best suited for these at risk individuals.

Knowledge dissemination and transfer is another area where additional research would have a profound impact in the field of educational outcomes of survivors. More is needed to be done to increase the awareness among educators that survivors, notably particular subgroups of survivors, are potentially at risk for poor educational achievement and increased special education utilization. Educators have many students to be concerned with and may have few resources at hand (including their time) to already deal with the demanding responsibilities at hand; thus, the more information that can be provided them that informs decision-making and practice will only assist both educators and survivors. Communication between medical and educational personnel is key, but first it is necessary to answer questions such as how this might be facilitated? Whether directly or indirectly, it is necessary for educators to be given specific information about the students they work with who are survivors of childhood cancer. It is all well to have educators aware of potential at risk groups among survivors, but this serves little

purpose if they do not know if their student falls into any of these subgroups. Whose responsibility is it to provide information to the schools? It may not be practical or feasible (or even legal) for medical practitioners to have direct contact with educators regarding specific cases, so are parents expected to relay and explain all medical information to their child's school or teacher? What methods and processes are in place to educate parents and educators? One study found that teachers provided with a web-based cancer education program demonstrated significant growth in their knowledge of cancer from pre- to post-test and most (87.8%) indicated that they would recommend the training to a colleague (Dubowy et al., 2006); unfortunately, few similar studies exist. Survivors themselves are not always able to provide accurate information with respect to their diagnosis or treatment (Kadan-Lottick et al., 2002) and of substantial concern is the fact that some survivors and their families even claim they were never made aware of potential late effects or the need for follow-up (National Cancer Policy Board, 2003). The goal of future survivorship research in the field of educational late effects should be how do we best ameliorate the educational experiences of survivors? This is a demanding goal, but one that is essential to improving the quality of life of survivors.

3.5 References

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