Conclusions of evidence tables surveillance of education and employment outcomes

1.1. What is the risk of poor educational outcomes in survivors of childhood, adolescent and young adult (CAYA) cancers?	
Conclusion single studies	
All types of childhood cancer diagnoses	
Survivors were less likely than controls to report college graduation (44.1% vs. 60.5%, p<0.001). (n=1041 survivors from the St. Jude Lifetime Cohort; Community-based comparison group)	*Hayek et al. 2020*
There were significant differences in educational achievements between survivors and comparisons (p≤0.02). More survivors had no graduation and less had tertiary education. (n=3242 survivors; 0-16 years at diagnosis; 17-49.9 years at study; Matched controls from the general population)	*Ahomäki et al. 2017*
More survivors than comparisons completed school with a delay (7.9% vs. 5.0%; OR=1.63 (95%CI:1.34-2.00). Survivors of CNS tumours (9.7%, lymphomas (9.5%), retinoblastoma (9.3%) and leukaemia (8.8%) were those who most often experienced a delay in passing the ninth-grade exam. (n=1320 survivors; 0-15 years at diagnosis; Comparisons: n=792,012 from general population)	*Andersen et al. 2017*
Survivors are less likely to obtain educational qualifications (OR=0.67, 95%CI:0.40–1.11 for compulsory school; OR=0.81, 95%CI:0.61–1.07 for higher education) than the general population, but differences were not statistically significant. (n=637 Italian survivors; mixed diagnoses; 0-14 years at diagnosis; Controls: general population)	*Maule et al. 2017*
There were significant differences in educational achievements between CAYA cancer survivors and controls (p=0.012): More survivors had only basic education (8% vs. 5%), the same proportion had vocational training (47% vs. 47%), more survivors had upper secondary education (33% vs. 27%), but less survivors had university education (12% vs. 21%). (n=160; Lymphoma>CNS tumor>Leukemia>…; Mean age at study 33.5 years; Controls: n=999 from general population)	*Mader et al. 2017*
A lower proportion of adult survivors of childhood cancer completed intermediate (equivalent to high school) (67 vs. 70%), undergraduate (31 vs. 35%), and graduate (7 vs. 9%) education compared with cancer-free population (p values not provided). (Population-based cohort study, n=2213 survivors and 1,212,623 cancer-free population controls)	*Ghaderi et al. 2016*
There were no significant differences in educational attainment between adolescent and young adult (AYA) cancer survivors and siblings (p=0.09). AYA cancer survivors had higher educational attainment than childhood cancer survivors (College or higher: 54.8% of AYACS vs. 40.6% of CCS; High school or lower: 13.8% of AYACS vs. 20.8% of CCS; p<0.001). (Childhood Cancer Survivor Study (CCSS), n=6192 survivors, 58% were <11 years at diagnosis (childhood cancer survivors), 42% were 11-21 years at diagnosis (AYA cancer survivors); n=390 sibling controls)	*Prasad et al. 2015*
There were no significant differences in level of school completed (p=0.99) and whether or not a school grade was repeated (p=0.159) between childhood cancer survivors and peers. (n=48, median age at diagnosis 11 years, median age at study 16 years)	*Winterling et al. 2015*
Significantly more childhood cancer survivors repeated a class and experienced difficulties in school as compared with controls (repeating a class: 13% vs. 2%, p=0.02; difficulties in school: 51.8% vs. 14.3%, p<0.001) (n=56 survivors, current age 7-18, at least 1 year in remission)	*Yilmaz et al.2014*
Childhood cancer survivors had significantly higher rates of high school graduation (55.5% v 29.9%; p<0.001) and university education (23% v 11.1%, p<0.001) compared to 14-39-year-olds in the general population. (n=201 survivors, median age at study 23 years, median age at diagnosis 10 years)	*Yagci-Kupeli et al. 2013*
Childhood cancer survivors showed different educational achievement compared to the general population (p<0.001). Specifically, more survivors only completing compulsory education (8.7% vs. 5.2%, p<0.001) and fewer achieving a university degree (7.3% vs. 11%, p=0.001), but more survivors than controls achieving upper secondary education (36.1% vs. 24.1%, p<0.001). Among survivors and controls aged	*Kuehni et al. 2012*

27 years or older, there were no significant differences in compulsory education or university degree. (Swiss Childhood Cancer Survivor Study, n=961; mean age at study 27.0 years; mean age at diagnosis 8.1 years)	
Childhood cancer survivors were more likely to repeat a grade than their siblings (33.1% vs. 21.6%, p=0.02). However, the overall rate of repeating a grade was not significantly different between survivors and registry controls. (N=148 survivors; ALL/Lymphoblastic lymphoma>Solid tumor>Hodgkin lymphoma>…; mean age at study 15 years; N=194 siblings and >50,000 health schoolchildren)	*Bonneau et al. 2011*
Adolescent cancer survivors were significantly more likely to attain a high school degree compared to their peers (52.4% vs. 38.3%, p<0.001). No significant differences were found with completion of professional training. The number of persons graduating from university did not differ between survivors and controls. (German Childhood Cancer Registry study, n=820; mean age at study 29.9 years; mean age at diagnosis 15.8 years)	*Dieluweit et al. 2011*
Childhood cancer survivors showed no significant difference in educational attainment compared to siblings (p=0.169). (n=185 survivors, mean age at study 23.1 years; mean age at diagnosis 8.3 years)	*Ishida et al. 2011*
There were no differences in highest attained education between childhood cancer survivors and the general population (basic education 10.8% (survivors) vs. 8.8% (controls); secondary education 54.6% vs. 54.4%; postsecondary education 34.7% vs. 36.8% (no p-values reported)). (n=1716, CNS tumor>Leukemia>Lymphoma>…; mean age at study 31.6 years; n=1,456,089 controls from national registers)	*Boman et al. 2010*
There were no significant differences in the proportion with an academic education (≥4 years) between of childhood low incidence cancer survivors and controls (32% vs. 28%, OR=1.33, p=0.1). ('low incidence cancers' i.e., AML, infratentorial astrocytoma, and Wilms tumor; n=247, mean age at study 23 years; mean age at diagnosis 8 years),	*Johannsdottir et al. 2010*
Childhood cancer survivors had significantly worse educational attainment outcomes across each level of education (ORs=0.77-0.85) compared to the general population. However, when these overall deficits were considered by childhood cancer type, it became apparent that, at all levels, they were restricted exclusively to CNS tumor and leukemia survivors. (British Childhood Cancer Survivor Study, n=10183 survivors; Leukemia>CNS neoplasm>Lymphoma>…; Age range at study: 16-50 years; Controls: n=12,575 from general household survey)	*Lancashire et al. 2010*
There was no significant difference in levels of grade repetitions between childhood cancer survivors and controls (21.5% in survivors vs. 22% in controls). Survivors were more likely to receive special education than controls (OR=3.05; 95%CI:2.6-3.6). (n=782; Leukemia>CNS>Lymphoma>…; Mean age at diagnosis was 4.6 years; Controls n=8386 randomly selected school children)	*Lorenzi et al. 2009*
DCOG 2010[4] No statistically significant difference for level of education of childhood cancer survivors compared to healthy controls.[4] (Childhood Cancer Survivor Study)	*Zeltzer et al. 2008*
DCOG 2010[4] No statistically significant difference for level of education of childhood cancer survivors compared to healthy controls.[4] Childhood cancer survivors were more likely to report repeating a grade than controls.[4]	*Gerhardt et al. 2007*
DCOG 2010[4] Childhood cancer survivors were more likely to report repeating a grade, and attending learning-disability or special-education programs than controls.[4]	*Barrera et al. 2005*

DCOG 2010[4]	No statistically significant difference for level of education of childhood cancer survivors compared to healthy controls.[4]	*Stam et al. 2005*
DCOG 2010[4]	Lower levels of education among childhood cancer survivors as compared to healthy controls[4] Childhood cancer survivors had less frequently entered higher education compared with general population norms.[4]	*Boman et al. 2004*
DCOG 2010[4]	Lower levels of education among childhood cancer survivors as compared to healthy controls[4]	*Koch et al. 2004*
DCOG 2010[4]	Lower levels of education among childhood cancer survivors as compared to healthy controls[4] Childhood cancer survivors were more likely to report attending learning-disability or special-education programs.[4]	*Langeveld et al. 2003*
DCOG 2010[4]	No statistically significant difference for repeating a grade when comparing childhood cancer survivors to controls.[4] Childhood cancer survivors started school later than controls[4]	*Lahteenmaki et al. 2002*
DCOG 2010[4]	No statistically significant difference for level of education of childhood cancer survivors compared to healthy controls.[4]	*Hays et al. 1992*
DCOG 2010[4]	No statistically significant difference for level of education of childhood cancer survivors compared to healthy controls.[4]	*Meadows et al. 1998*
Leukemia and Lymphoma		
Survivors were more likely to repeat a grade than siblings (28.5% vs. 21.9%; OR=1.87 (95%CI:1.48-2.35; p<0.001)). (LEA cohort; n=855 ALL & AML survivors; mean 16.2 years at study; Controls: n=1304 siblings mean 18.5 years at study)		*Bonneau et al. 2019*
Survivors were more likely to attend a learning disability program than siblings (34% vs. 14%; OR=3.0 (95%CI:1.0-9.2; p=0.05)). There were no significant differences in education (≥20 years) between survivors and siblings (77% vs. 65%; OR=1.7 (95%CI:0.2-16), p>0.05)). (NOPHO-AML cohort; n=95 AML/AlloHSCT survivors; median 22 years at study; Controls: n=35 siblings)		*Wilhelmsson et al. 2019*
Childhood survivors of non-hodgkin lymphoma had no significant differences in educational attainment (≥ college graduate vs. < college graduate) compared to comparisons (p = 0.08). (St. Jude Lifetime Cohort Study; n=187, median age at diagnosis 10.4 years, median 25.5 years from diagnosis)		*Ehrhardt et al. 2018*
Survivors of lymphohaemopoetic system tumors were less likely to obtain educational qualifications (OR=0.71, 95%CI:0.33–1.54 for compulsory school; OR=0.73, 95%CI:0.48–1.09 for higher education) than the general population, but differences were not statistically significant. (n=637 Italian survivors; mixed diagnoses; 0-14 years at diagnosis; Controls: general population)		*Maule et al. 2017*

	There were no significant differences in education attainment between childhood ALL survivors and siblings: 45% of survivors and siblings had graduated college and 55% of survivors and siblings had less than a college education (p=0.76). (CCSS, n=556, age at diagnosis 1-9.9 years; median current age 27.8 years; n=2232 sibling controls)	*Essig et al. 2014*
	There were no significant differences in educational levels between childhood leukemia survivors and the healthy population. (n=141 leukemia survivors; 21-49 years at time of study; median age at diagnosis 4.8 years)	*Pillon et al. 2013*
	Childhood leukemia survivors had significantly higher graduation ratios compared to the general population (graduation from high school in 48.6% (female patients) vs. 38.0% (female controls) and 52.6% (male patients) vs. 35.8% (male controls); p<0.001). (n=1476, mean age at study 25.7 years, mean 18 years of follow-up)	*Zynda et al. 2012*
	Childhood acute myeloid leukemia (AML) survivors were not significantly different from their siblings in attending learning-disability programs in elementary school (29% vs. 20%; OR=2.2, 95%CI:0.9-5.3, p=0.1) or having completed an academic education or vocational training of three years (Controls (Ref. siblings) OR=1.2, 95%CI:0.2-6.8, p=0.8). More survivors than siblings (≥20 years of age) were full time students (33% vs. 15%, p=0.07). (n=102, median age at study 16.2 years, median years after diagnosis 10.6 years)	*Molgaard-Hansen et al. 2011*
	Childhood ALL survivors completed secondary school to the same extent as controls, but graduated from high school less often than controls (78.8% vs. 84.5%, p=0.042). Survivors were older at completion of secondary school (16.07 vs. 16.00 years, p<0.001) and at age at graduation from high school (19.16 vs. 18.98 years, p=0.005). (n=167 survivors, 61.6%<30 years at study) and n=8350 matched controls from population registry	*Holmqvist et al. 2010*
	Childhood ALL survivors who had received RT had significantly worse educational attainment outcomes across each level of education (i.e., University degree, A' Levels, O' Levels or teaching qualification) (ORs=0.60-0.77) compared to the general population. There were insufficient leukemia survivors known to have been unexposed to cranial irradiation for separate assessment. (British Childhood Cancer Survivor Study, n=10183 survivors; Leukemia>CNS neoplasm>Lymphoma>…; Age range at study: 16-50 years; Controls: n=12,575 from general household survey)	*Lancashire et al. 2010*
DCOG 2010[4]	Survivors of childhood leukemia have a lower level of education than healthy controls[4] (Childhood Cancer Survivor Study)	*Mody et al. 2008*
DCOG 2010[4]	Survivors of childhood leukemia have a lower level of education than healthy controls[4] (Childhood Cancer Survivor Study)	*Mulrooney et al. 2008*
DCOG 2010[4]	Survivors of childhood leukemia had poorer school performance and more often repeated a grade than controls[4]	*Buizer et al. 2006*
DCOG 2010[4]	Survivors of childhood leukemia have a lower level of education than healthy controls[4]	*Link et al. 2006*
DCOG 2010[4]	Survivors of childhood leukemia have a lower level of education than healthy controls[4] Survivors of childhood lymphoma did not have significantly different levels of education as compared to healthy controls[4] (Childhood Cancer Survivor Study)	*Mitby et al. 2003*

DCOG 2010[4]	Survivors of childhood lymphoma did not have significantly different levels of education as compared to healthy controls[4]	*Wassermann et al. 2003*
DCOG 2010[4]	Survivors of childhood leukemia have a lower level of education than healthy controls[4] Survivors of childhood leukemia who all had been treated with cranial radiotherapy were more often placed in special education programs than their siblings[4]	*Kingma et al. 2000*
DCOG 2010[4]	No statistically significant differences in level of education between survivors of childhood leukemia and controls. The results may have been biased by cranial radiotherapy as in the studies that showed an effect cranial radiotherapy was given to the leukemia patients, whereas in the two studies that did not find an effect patients were not treated with cranial radiotherapy.[4]	*Ness et al. 2000*
DCOG 2010[4]	No statistically significant differences in level of education between survivors of childhood leukemia and controls. The results may have been biased by cranial radiotherapy as in the studies that showed an effect cranial radiotherapy was given to the leukemia patients, whereas in the two studies that did not find an effect patients were not treated with cranial radiotherapy.[4]	*Moe et al. 1997*
Bone Tumors		
Survivors and controls had similar percentages for college attendance (63.6 vs. 68.5 %, p=0.06). (n=206 bone/soft tissue sarcoma (STS) survivors from the SJLIFE cohort; median age at study 38.2/33.4 yrs (bone/STS); mean age at diagnosis 13.7/12.0 yrs (bone/STS); n=206 controls from among family/friends)		*Fernandez-Pineda et al. 2017*
Childhood osteosarcoma survivors had either the same (49%) or higher (42%) level of education as their siblings, with 82% having education beyond high school (no percentage given for siblings). Educational level was found to be higher than published data from the general population. (n=38, mean age at study 37.9 years, mean age at diagnosis 13.2 years).		*Ottaviani et al. 2013*
DCOG 2010[4]	Survivors of osteosarcoma more often went to university than controls, but the results were not statistically significant.[4]	*Yonemoto et al. 2007*
DCOG 2010[4]	No statistically significant difference for level of education of childhood bone tumor survivors compared to healthy controls.[4] (Childhood Cancer Survivor Study)	*Mitby et al. 2003*
DCOG 2010[4]	Survivors of osteosarcoma aged older than 12 years at time of amputation had a lower level of education than controls.[4] (Childhood Cancer Survivor Study)	*Nagarajan et al. 2003*
DCOG 2010[4]	No statistically significant difference for level of education of childhood bone tumor survivors compared to healthy controls.[4]	*Felder et al. 1998*
DCOG 2010[4]	No statistically significant difference for level of education of childhood bone tumor survivors compared to healthy controls.[4]	*Novakovic et al. 1997*
Stem cell transplant		

There was a significantly higher average academic delay at start of year 10 and 13 (final year secondary school) in childhood acute lymphoblastic leukemia (ALL) survivors treated with allogeneic stem cell transplant as compared with the general population (average academic delay year 10: 0.98 yr vs. 0.34 yr years, p<0.001; average academic delay year 13: 1.32 yr vs. 0.51 yr, p<0.002). Overall, cancer survivors received secondary school diplomas at similar rates to the general population (15.3% of survivors received no diploma vs. 13.8% general population, p>0.05). (n=59 survivors, median age at a-HSCT 10.5 years, current median age 23 years)	*Freycon et al. 2014*
Significantly more childhood hematopoietic stem cell transplant survivors were attending secondary school compared with healthy controls (79% vs. 54%, p<0.0001). Twelve patients (21%) graduated, compared with 45% of controls (p>0.05). 13 survivors were still enrolled at a university, whereas the majority of the controls had graduated. (n=55; median age at study 25 years; median age at diagnosis 5.2 years)	*Uderzo et al. 2012*
Wilms tumor	
Among childhood Wilms tumor survivors there was a significantly lower proportion that graduated from college as compared to siblings (45.0% of survivors vs. 51.4% of siblings, p=0.045). (CCSS, n=645, age at diagnosis 0-18 yr, attained age 5->50 yr)	*Termuhlen et al. 2011*
Retinoblastoma	
Childhood retinoblastoma survivors had significantly lower levels of education than the general population (low education 47% of survivors vs. 35% of controls; intermediate education 38% vs. 43%; high education 15% vs. 22%; p<0.01). Non-attendance of mainstream education was significantly higher in survivors than controls (37% vs. 3.6%, p<0.01). (n=156; mean age at study 20.8 years; Controls were norms from the general population)	*Van Dijk et al. 2010*
Neuroblastoma	
Survivors were more likely than comparisons to report less than college graduation (37.5% vs. 19.5%), but differences were not statistically significant (PR=1.2; 95%CI:0.8-1.8; p=0.31). (n=136 neuroblastoma survivors from the St. Jude Lifetime Cohort; Median 31.9 years at study; Community-based comparison group n=272)	*Wilson et al. 2020*
Survivors were more likely to use special education services (OR=2.25; 95%CI:1.8-2.7; p<0.001) and to have less than college education (OR=1.71; 95%CI:1.2-2.5; p=0.007) as compared to siblings. (n=859 neuroblastoma survivors from the Childhood Cancer Survivor Study; n=872 siblings)	*Zheng et al. 2018*
Central nervous system (CNS) Tumors	
Pediatric brain tumor survivors were less likely than controls to qualify for school years 10-12 (equivalent to high school; 77.3% vs. 90.6%; OR=2.8 (95%CI:2.2-3.7), p<0.001). They were also more likely than controls to graduate with a delay (11.4% vs. 2.3%; OR=5.4 (95%CI:3.6-8.0), p<0.001). (n=475 pediatric brain tumor survivors; n=2197 controls from Statistics Sweden)	*Lönnerblad et al. 2020*
Pediatric astrocytoma survivors were less likely than siblings to earn a college degree or higher (40% vs. 55%; RR=0.77 (95%CI:0.70-0.84)). (n=1182 astrocytoma survivors from the Childhood Cancer Survivor Study; n=4023 siblings)	*Effinger et al. 2019*
Survivors of medulloblastoma were less likely than siblings to earn a college degree (relative risk [RR]: 0.49, 95% CI: 0.39–0.60). (CCSS, n=389; Median age at study = 30 years; Controls = 4031 siblings)	*King et al. 2017*
Survivors of CNS tumors were less likely to obtain educational qualifications (OR=0.44, 95%CI:0.19–1.02 for compulsory school; OR=0.56, 95%CI:0.31–1.01 for higher education) than the general population, but differences were not statistically significant. (n=637 Italian survivors; mixed diagnoses; 0-14 years at diagnosis; Controls: general population)	*Maule et al. 2017*
Childhood CNS neoplasm survivors had significantly worse educational attainment outcomes across each level of education (ORs=0.31-0.46) for those who had received radiotherapy (ORs+0.31-0.46) and for those who had not received radiotherapy (ORs=0.58-0.72) compared to the general population.	*Lancashire et al. 2010*

(British Childhood Cancer Survivor Study, n=10,183 survivors; Leukemia>CNS neoplasm>Lymphoma>…; Age range at study: 16-50 years; Controls: n=12,575 from general household survey)		
Childhood central nervous system malignancy survivors were significantly less likely to report college graduation as compared to sibling controls (RR siblings vs. survivors=1.4, 95%CI:1.3-1.5). (CCSS; b=1877; CNS tumor survivors; 56.8% <25 years at study; Controls: n=3899 siblings)		*Armstrong et al. 2009*
DCOG 2010[4]	A low number of survivors of medulloblastoma participated in normal education[4]	*Maddrey et al. 2005*
DCOG 2010[4]	Childhood brain tumor survivors had lower levels of education than healthy siblings[4] (Childhood Cancer Survivor Study)	*Zebrack et al. 2004*
DCOG 2010[4]	Survivors of childhood CNS tumors more often did not finish high-school or college as compared to healthy sibling[4] (Childhood Cancer Survivor Study)	*Mitby et al. 2003*
Overall Conclusion		
Across all types of childhood cancer diagnoses including studies focusing on all types of tumors and studies focusing on specific tumor types		
Some evidence suggests that survivors of CAYA cancers are at risk for lower educational achievement than controls.		46 studies (37 samples) Level C[7-52]
Some evidence suggests that fewer survivors of CAYA cancers have a university/college education compared to controls.		23 studies (13 samples) Level B[7,8,11,12,14-17,19,21,25-27,37,39,48,53-59]
There is evidence that there is a delay in completing their education in CAYA cancer survivors compared to controls.		8 studies Level A[19,21,22,24,49,60-62]
Evidence suggests that survivors of CAYA cancers are more likely to repeat a grade compared to controls		9 studies Level B[10,28,60,63-68]
Evidence suggests that survivors of CAYA cancers are less likely to attend mainstream education than controls.		9 studies (8 samples) Level B[21,26,40,41,50,56,65,67,69]
In CNS tumor survivors		
Evidence suggests that survivors of CAYA CNS tumors are at risk for lower educational achievement (Level B), not getting a university/college degree (Level B), or for completing their education with a delay (Level C) compared to controls.		8 studies (4 samples) Level B-C[16,27,47-49,52,55,58]

1.2 What is the risk of poor employment outcomes in CAYA cancer survivors?	
Conclusion single studies	
All types of childhood cancer diagnoses	
Survivors were less likely than controls to report employment (77.4% vs. 84.6%, p<0.001). (n=1041 survivors from the St. Jude Lifetime Cohort; Community-based comparison group)	*Hayek et al. 2020*
Survivors were less likely to be "full-time student, not working" (17 vs. 21%), "student and part-time work" (22 vs. 29%), and "full-time work only" (43 vs. 50%), and more likely to be "student and full-time work" (4 vs. 0%) and "part-time work only" (13 vs. 0%) as compared to comparisons. Differences were not statistically tested. (n=23, multiple diagnoses, Mean age at study 23.8 years; Controls: n = 14 referred by survivor)	*Nugent et al. 2018*
Survivors were equally likely than comparisons to be unemployed (p>0.05), but more likely to be retired early (p<0.001). (n=3242 survivors; 0-16 years at diagnosis; 17-49.9 years at study; Matched controls from the general population)	*Ahomäki et al. 2017*
Compared to the general population, survivors were less likely to be employed (OR=0.89, 99%CI:0.81-0.98) or caring for home/family (OR=0.63, 99%CI:0.53-0.74). Survivors were more likely to be unable to work due to illness/disability (OR=4.99, 99%CI:4.06-6.13). There was no significant difference from the general population for being a student (OR=1.13, 99%CI:0.97-1.32) or unemployed and looking for work (OR=0.89, 99%CI:0.72-1.09). (n=10,257; British Childhood Cancer Survivor Study; Controls from general population study)	*Frobisher et al. 2017*
Survivors were less likely to gain employment (i.e., having had at least one paid occupation) than the general population (OR=0.66, 95%CI:0.45-0.98). (n=637 Italian survivors; mixed diagnoses; 0-14 years at diagnosis; Controls: general population)	*Maule et al. 2017*
Survivors had a 34% increased risk of not being employed (HR, 1.3; 95% CI, 1.2-1.5) compared with those in the noncancer group. (n=5440 Norwegian survivors; <25 years at diagnosis; n=595,089 non-cancer controls)	*Gunnes et al. 2016*
Adult survivors of childhood cancers were less likely to be employed (54.3% vs 69.6%; P<0.001) and more likely to report being unable to work because of health (18.7% vs 7.1%; P<0.001) during the past year. (n=239; Multiple diagnoses at age 0-14; Current age 18+; Controls: n=304,265 from National Health Interview Survey)	*Guy et al. 2016*
There were no significant differences in employment status between childhood cancer survivors and controls (unemployment rate: 9% vs. 11%; employment rate: 91% vs. 90%; p=0.515) (n=160; Lymphoma>CNS tumor>Leukemia>…; Mean age at study 33.5 years; Controls: n=999 from general population)	*Mader et al. 2017*
Compared to siblings, survivors diagnosed during AeYA had statistically significant differences in employment outcomes (p<0.001). Unemployment (10.6% vs. 11.3%) and working full time (70.1% vs. 70.0%) was similar between survivors and controls, but survivors were more likely to be unable to work (7.8% vs. 1.5%), and less likely to be students (1.0% vs. 3.9%) or working part-time (9.4% vs. 13.1%) as compared to siblings. Of note, age was not accounted for and siblings were younger than AeYA cancer survivors. (CCSS, n=6192 survivors, , 42% were 11-21 years at diagnosis (AeYA cancer survivors); n=390 sibling controls)	*Prasad et al. 2015*
The unemployment rate in childhood cancer survivors was significantly higher than the unemployment rate in the general population (36.8% vs. 10.3-11.7%, p<0.001). (n=201 survivors, median age at study 23 years, median age at diagnosis 10 years)	*Yagci-Kupeli et al. 2013*
Adolescent cancer survivors were more likely to be employed at the time of study compared to controls (79.6% vs. 64.2%) but not after controlling for gender, age, high school graduation and college/university degree. Survivors were significantly older when starting their first occupation than controls (OR=1.90, 95%CI:1.67-2.17, p<0.001). (German Childhood Cancer Registry study, n=820; mean age at study 29.9 years; mean age at diagnosis 15.8 years)	*Dieluweit et al. 2011*
There was no significant difference in working ability or annual income between childhood cancer survivors and siblings (p>0.4). (n=185 Japanese survivors, mean age 23.1 years; mean age at diagnosis 8.3 years)	*Ishida et al. 2011*

There were significantly more childhood cancer survivors unemployed as compared to siblings (27% vs. 19%, p<0.001). Multivariable regression comparing currently employed survivors and siblings showed that survivors were less likely to hold "Managerial/Professional" jobs (RR=0.93; 95%CI:0.89-0.98) and more likely to be employed in "Nonphysical Service" jobs (RR=1.15; 95%CI:1.07-1.24) than siblings. (CCSS, n=6671; 57% 25-34 years at study)	*Kirchhoff et al. 2011b*
A slightly larger proportion of childhood cancer survivors was employed as compared to the general population (84.0% vs. 77.0% of controls; no p-value reported). (n=1716, CNS tumor>Leukemia>Lymphoma>…; mean age at study 31.6 years; n=1,456,089 controls (national register))	*Boman et al. 2010*
There were significantly fewer childhood cancer survivors employed than controls (59% vs. 77%, OR=0.45, p<0.01). Significantly more survivors than controls were recipients of social benefits (6.7% vs. 3.1%, OR=2.31, p<0.01). ('low incidence cancers' i.e., AML, infratentorial astrocytoma, and Wilms tumor; n=247, mean age at study 23 years; mean age at diagnosis 8 years),	*Johannsdottir et al. 2010*
Significantly more childhood cancer survivors than sibling controls reported health-related unemployment (10.4% vs. 1.8%, p<0.001). Survivors were significantly more likely to be unemployed but seeking work (5.7% vs. 2.7% of siblings, p<0.001). In multivariable comparisons adjusted for age, sex, and race, survivors were more likely to report health-related unemployment than siblings (RR=6.07; 95%CI:10.42-21.14) and to be unemployed but seeking work vs. siblings (RR=1.90; 95%CI:1.43-2.54). (n=6339 survivors; CCSS; Leukemia>Lymphoma>CNS malignancies>…; mean age 34.2 years at study; n=1967 sibling controls (mean age 36.1 years at study))	*Kirchhoff et al. 2010*
DCOG 2010[4] Young adult survivors of childhood cancer are at increased risk of being unemployed as compared to healthy controls (odds ratio (OR) 1.85, 95% confidence interval (95% CI) 1.27-2.69). Furthermore, survivors in the US had an overall higher risk (OR 3.24, 95% CI 2.16-4.86) of becoming unemployed, whereas no such risk was found for European survivors (OR 1.00, 95% CI 0.58-1.70).[4]	*De Boer et al. 2006*
Leukemia and Lymphoma	
There were no significant differences in employment "working full-time" (≥20 years) between survivors and siblings (40% vs. 65%; OR=0.7 (95%CI:0.1-4.2), p>0.05)). (NOPHO-AML cohort; n=95 AML/AlloHSCT survivors; median 22 years at study; Controls: n=35 siblings)	*Wilhelmsson et al. 2019*
Childhood survivor of non-hodgkin lymphoma had no significant differences in employment (full-time vs. part-time) compared to comparisons (p=0.44). (St. Jude Lifetime Cohort Study; n=187, median age at diagnosis 10.4 years, median 25.5 years from diagnosis)	*Ehrhardt et al. 2018*
Survivors of lymphohaemopoietic system tumors were equally likely to gain employment (i.e., having had at least one paid occupation) than the general population (OR=1.16; 95%CI:0.60–2.23). (n=637 Italian survivors; mixed diagnoses; 0-14 years at diagnosis; Controls: general population)	*Maule et al. 2017*
More survivors than expected were currently employed and the number of survivors seeking a job was significantly lower than expected compared with the general French population (p≤0.04). (n=845 leukemia survivors; <18 years at diagnosis; mean 22.3 years at study; Controls: general French population)	*Berbis et al. 2016*
There was no significant difference in job distribution in childhood ALL survivors treated with allogeneic stem cell transplant as compared with the general population, except more female survivors were employed in intermediate-level professional positions than the number expected in the general population (observed/expected=2.4, 95%CI:1.2-4.2). (n=59 survivors, median age at a-HSCT 10.5 years, current median age 23 years)	*Freycon et al. 2014*
There was no significant difference in employment rates between childhood leukemia survivors and healthy controls. (n=141 survivors; 21-49 years at time of study; median age at diagnosis 4.8 years)	*Pillon et al. 2013*
There were significantly fewer adult survivors of childhood AML working full-time as compared to siblings (39% vs. 62%; OR=11.0, 95%CI:1.3-91.7, p=0.03). However, slightly more AML survivors were full time students as compared to siblings (33% vs. 15%, p=0.07). There were no significant differences between survivors and siblings in	*Molgaard-Hansen et al. 2011*

	not being able to work due to illness or disability (6% vs. 8%, p=0.2) or being turned down when applying for jobs (8% vs. 12%, p>0.05). (n=102, median age at study 16.2 years, median years after diagnosis 10.6 years)	
	There were no significant differences in employment at 25 years between childhood ALL survivors and controls (67.3% vs. 67.8% employed, p=0.909). Compared to controls, a significantly lower proportion of childhood ALL survivors was employed at the age of 30 (69.8% vs. 82.3%, p=0.011). (N=167 survivors, 61.6%<30 years at study) and the population register (N=8350 matched controls)	*Holmqvist et al. 2010*
DCOG 2010[4]	Higher risk of being unemployed in female survivors of childhood leukemia but not in males.[4] (Childhood Cancer Survivors Study)	*Mody et al. 2008*
DCOG 2010[4]	No statistically significant difference in employment status among survivors of childhood leukemia and lymphoma compared to healthy controls.[4] (Childhood Cancer Survivors Study)	*Mulrooney et al. 2008*
DCOG 2010[4]	No statistically significant difference in employment status among survivors of childhood leukemia and lymphoma compared to healthy controls.[4]	*Servitzoglou et al. 2008*
DCOG 2010[4]	Higher risks for being unemployed in irradiated and non-irradiated survivors of hematological malignancies.[4]	*Crom et al. 2007*
DCOG 2010[4]	No statistically significant difference in employment status among survivors of childhood leukemia and lymphoma compared to healthy controls.[4]	*Gerhardt et al. 2007*
DCOG 2010[4]	No statistically significant difference in employment status among survivors of childhood leukemia and lymphoma compared to healthy controls.[4]	*Johannesen et al. 2007*
DCOG 2010[4]	Adult survivors of childhood leukemia, Hodgkin and non-Hodgkin lymphoma had a significantly increased risk of never being employed as compared to healthy siblings.[4] (Childhood Cancer Survivors Study)	*Pang et al. 2008*
DCOG 2010[4]	Adult survivors of hematological malignancies were more likely to become unemployed than the controls, but the result was not statistically significant (OR 1.42, 95% CI 0.79-2.55).[4]	*De Boer et al. 2006*
Bone Tumors		
	Survivors and controls had similar percentages for employment (70.9 vs. 75.7 %, p=0.14). (n=206 bone/soft tissue sarcoma (STS) survivors from the SJLIFE cohort; median age at study 38.2/33.4 yrs (bone/STS); mean age at diagnosis 13.7/12.0 yrs (bone/STS); n=206 controls from among family/friends)	*Fernandez-Pineda et al. 2017*
	There was no significant difference in employment status between childhood osteosarcoma survivors and siblings. (n=38, mean age at study 37.9 years, mean age at diagnosis 13.2 years)	*Ottaviani et al. 2013*

DCOG 2010[4]	Adult survivors of childhood bone tumors had a significantly increased risk of never being employed as compared to healthy siblings[4] (Childhood Cancer Survivors Study)	*Pang et al. 2008*
DCOG 2010[4]	Adult survivors of childhood bone tumors were more likely to become unemployed than the controls, but the result was not statistically significant (OR 1.97, 95% CI 0.88-4.40)[4]	*De Boer et al. 2006*
Stem Cell Transplant		
Slightly more childhood hematopoietic stem cell transplantation survivors had problems keeping a job than controls (44% vs. 33%), but the difference was not statistically significant. (n=55; median age at study 25 years; median age at diagnosis 5.2 years)		*Uderzo et al. 2012*
Wilms Tumor		
Among childhood Wilms tumor survivors there was a significantly lower proportion that had ever been employed as compared to siblings (96.6% vs. 99.6%, p=0.046). (CCSS, n=645, age at diagnosis 0-18 yr, attained age 5->50 yr)		*Termuhlen et al. 2011*
Retinoblastoma		
There were no significant differences in employment rates between childhood retinoblastoma survivors and the general population. (N=156; mean age at study 20.8 years; Controls were general population norms)		*Van Dijk et al. 2010*
Neuroblastoma		
Survivors were more likely than comparisons to report “not currently working” (23.5% vs. 16.0%), but differences were not statistically significant (PR=1.3 (95%CI:0.8-2.1, p=0.26)). (n=136 neuroblastoma survivors from the St. Jude Lifetime Cohort; Median 31.9 years at study; Community-based comparison group n=272)		*Wilson et al. 2020*
There were no statistically significant differences in unemployment in last 12 months (OR=1.42; 95%CI:0.8-2.5; p=0.24) in survivors compared to siblings. (n=859 neuroblastoma survivors from the Childhood Cancer Survivor Study; n=872 siblings)		*Zheng et al. 2018*
Central Nervous System (CNS) Tumors		
Pediatric astrocytoma survivors were less likely than siblings to be employed (63% vs. 84%; RR=0.80 (95%CI:0.77-0.84)). (n=1182 astrocytoma survivors from the Childhood Cancer Survivor Study; n=4023 siblings)		*Effinger et al. 2019*
Survivors were more likely to be currently unemployed (31.6%; 95%CI:18-49%) as compared to comparisons (7.2%). (n=38 brain tumour survivors; median age at study 27 years; n=4091 population-based controls)		*Sato et al. 2018*
Survivors of medulloblastoma were less likely than siblings to be employed ≥30 hours/week (RR: 0.59, 95% CI: 0.50–0.69). (CCSS, n=389; Median age at study = 30 years; Controls = 4031 siblings)		*King et al. 2017*
Survivors of CNS tumors were less likely to gain employment (i.e., having had at least one paid occupation) than the general population (OR=0.28; 95%CI:0.13–0.58). (n=637 Italian survivors; mixed diagnoses; 0-14 years at diagnosis; Controls: general population)		*Maule et al. 2017*
Childhood central nervous system malignancy survivors were significantly less likely to report current employment as compared to controls (RR siblings vs. survivors=1.4, 95%CI:1.3-1.5). (CCSS; N=1877; CNS tumor survivors; 56.8% <25 years at study; Controls: N=3899 siblings)		*Armstrong et al. 2009*
DCOG 2010[4]	Survivors of childhood CNS tumors had higher rates of being unemployed than same-aged peers in the general population[4]	*Johannesen et al. 2007*

DCOG 2010[4]	Adult survivors of childhood CNS tumors had a significantly increased risk of never being employed as compared to healthy siblings[4] (Childhood Cancer Survivors Study)	*Pang et al. 2008*
DCOG 2010[4]	Adult survivors of CNS tumors were more likely to be unemployed as compared to healthy controls (OR 4.74, 95% CI 1.21-18.65).[4]	*De Boer et al. 2006*
Rhabdomyosarcoma		
DCOG 2010[4]	3% of the childhood rhabdomyosarcoma survivors were never employed as compared to 1% of the controls (p=0.01)[4] (Childhood Cancer Survivors Study)	*Punyko et al. 2007*
Overall Conclusion		
Across all types of childhood cancer diagnoses including studies focusing on all types of tumors and studies focusing on specific tumor types		
Some evidence suggests that survivors of CAYA cancers are at increased risk of unemployment compared to controls.		43 studies (29 samples) Level B[7,9,11-15,18,21-28,42,43,50-59,61,70-82]
In survivors of CNS tumors		
There is evidence that survivors of CAYA CNS tumors are at increased risk of unemployment compared to controls.		8 studies (5 samples) Level A[27,52,55,58,73-75,82]

2.1 What are the risk factors for poor educational outcomes?	
Conclusion single studies	
2.1.1 What is the risk for poor educational outcomes by sex?	
This study* analyzed risk factors for repeating a grade with multilevel logistic regression (adjusting for sex, age at diagnosis, parental education, financial difficulties, history of repeating a grade, CNS irradiation, relapse, HSCT, time since diagnosis, living in a traditional family unit) and found that male survivors were more likely to repeat a grade: • Male (Ref. Female) OR=1.78 (95%CI:1.21-2.60; p=0.003) (LEA cohort; n=855 ALL & AML survivors; mean 16.2 years at study; Controls: n=1304 siblings mean 18.5 years at study)	*Bonneau et al. 2019*
This study* analyzed risk factors for educational achievement (having basic education only) with univariable logistic regression and found no association between sex and having basic education only (variable was therefore not included in the multivariable model): • Sex: Female (Ref. Male) OR=1.68 (95%CI:0.79-3.54), p=0.175 *(N=160; Lymphoma>CNS tumor>Leukemia>…; Mean age at study 33.5 years; Controls: N=999 from Swiss general population)	*Mader et al. 2017*
This study* used multivariable logistic regression (adjusted for tumor type, sex, age at diagnosis, period of diagnosis, parents' education) and found no significant assocation between sex and completing "compulsory school" or "higher education". Risk factors for completing compulsory school (participants aged ≥14 years): • Male (Ref. Female) OR=0.43 (95%CI:0.13-1.44) Risk factors for completing higher education (participants aged ≥19 years): • Male (Ref. Female) OR=0.43 (95%CI:0.13-1.44) *(n=637 Italian survivors; mixed diagnoses; 0-14 years at diagnosis; Controls: general population)	*Maule et al. 2017*
This study* analyzed risk factors for "no college attendance" (vs. some attendance with or without college degree) using multivariate logistic regression (adjusting for vision problems, age at diagnosis, cranial radiation, medical comorbidity. They found no significant association of sex and education below college: • Sex: Not significant (p>0.20) in univariable logistic regression and was therefore not included in the multivariable model (effect measure not reported) *(Survivors of astroglial tumors from the CCSS; n=587, mean age at study 23.8 years, diagnosis <21 years)	*De Blank et al. 2016*
This study* analyzed risk factors for "less than college graduate" with multiple logistic regression (non-significant factors removed from models, adjusted for neurocognitive outcomes, psychological outcomes, and age at study) and found that sex was not significantly associated with less than college graduate: • Female (Ref. Male): OR=1.04 (95%CI:0.89-1.22) *(CCSS, n=6192 survivors, 58% were <11 years at diagnosis (non-AeYA), 42% were 11-21 years at diagnosis (AeYA); n=390 sibling controls)	*Prasad et al. 2015*
This study* analyzed risk factors for "did not graduate from college". They used multivariable generalized linear models (adjusted for tumor location, age at study, race, tumor type, and age at diagnosis) and found no association between sex and graduating from college: • Female (Ref. male): RR=1.01 (95%CI:0.92-1.11) *(CCSS, n=1094 survivors of bone and soft tissue sarcoma in upper or lower extremity; median age at study 33 years; median age at diagnosis 13 years)	*Marina et al. 2013*
This study* used multivariable logistic regression (including survivors and controls, adjusted for population, age at study, migration background, nationality, language region; standardized on age, sex, migration background, place of living, language region) and found that females were at higher risk of not obtaining upper secondary education or a university degree: Risk factors for completing compulsory school only: • Female (Ref. Male) OR=1.00 (95%CI:0.73-1.38, p=0.999) Risk factors for obtaining upper secondary education or higher (Participants aged ≥27 years) • Female (Ref. Male) OR=0.75 (95%CI:0.60-0.93, p=0.010)	*Kuehni et al. 2012*

Risk factors for obtaining university degree (Participants aged ≥27 years) • Female (Ref. Male) OR=0.62 (95%CI:0.0.45-0.85, p=0.003) *Swiss Childhood Cancer Survivor Cohort (n=961 survivors; mean age at study 27.0 years; mean age at diagnosis 8.1 years; randomly selected control sample from the general population)	
This study* found no significant association between sex and high school degree in multivariable logistic regression (adjusted for age at study, age at diagnosis, diagnosis, duration of treatment, stay on intensive care/bone marrow/stem cell transplantation unit, cancer recurrence, treatment, late effects): • Female (Ref. Male): Effect measures not given, p>0.10 In multivariable logistic regression (adjusted for duration of treatment, age at study, diagnosis, and late effects), they found that female survivors had a lower likelihood of obtaining a college/university degree: • Female (Ref. Male) OR=0.67 (95%CI:0.48-0.95, p=0.025) *German Childhood Cancer Registry (n=820; mean age at study 29.9 years; mean age at diagnosis 15.8 years)	*Dieluweit et al. 2011*
This study* used multivariable logistic regression (adjusted for age at survey, cancer type, treatment, age at diagnosis, second tumor, epilepsy, hearing problems, and vision problems). They analyzed risk factors for level of educational attainment: University degree or higher and found that females (vs. males) were significantly less likely to obtain a university degree: • Sex: Female (Ref. Male) OR=0.77 (95%CI:0.63-0.93) They analyzed risk factors for level of educational attainment: Teaching degree or equivalent and found that no associations between sex and attainment of a teaching degree: • Sex: Female (Ref. Male) OR=0.90 (95%CI:0.76-1.05) They analyzed risk factors for level of educational attainment: A levels and found that females were significantly less likely to obtain an A level: • Sex: Female (Ref. Male) OR=0.79 (95%CI:0.68-0.91) They analyzed risk factors for level of educational attainment: O levels and found no associations between sex and attainment of an O level: • Sex: Female (Ref. Male) OR=0.88 (95%CI:0.75-1.03) *British Childhood Cancer Survivor Study (N=10,183 survivors; Leukemia>CNS neoplasm>Lymphoma>…; Age range at study: 16-50 years).	*Lancashire et al. 2010*
Overall Conclusion	
Some evidence suggests that female survivors of CAYA cancers are at increased risk for lower educational achievement.	8 studies (6 samples) Level C[7,9,12,16,19,52,83,84]
Some evidence suggests that male survivors of CAYA cancers are at increased risk for repeating a grade.	1 study Level C[63]

2.1.2 What is the risk for poor educational outcomes by age at study?	
This study* analyzed risk factors for educational achievement (having basic education only) with univariable logistic regression and found no significant association between age at study and having basic education only (variable was therefore not included in the multivariable model): • Age at study: 30-39 years (Ref. ≥40 years) OR=1.41 (95%CI:0.51-3.94) • Age at study: 20-29 years (Ref. ≥40 years) OR=1.21 (95%CI:0.39-3.78) *(N=160; Lymphoma>CNS tumor>Leukemia>…; Mean age at study 33.5 years; Controls: N=999 from Swiss general population)	*Mader et al. 2017*
This study* analyzed risk factors for "no college attendance" (vs. some attendance with or without college degree) using multivariate logistic regression (adjusting for vision problems, age at diagnosis, cranial radiation, medical comorbidity. They found no significant association of age at interview and education below college: • Age at interview: Not significant (p>0.20) in univariable logistic regression and was therefore not included in the multivariable model (effect measure not reported) *Survivors of astroglial tumors in the CCSS (n=587, mean age at study 23.8 years, diagnosis <21 years)	*De Blank et al. 2016*
This study* analyzed risk factors for "less than college graduate" with multiple logistic regression (non-significant factors removed from models, adjusted for neurocognitive outcomes, psychological outcomes, and sex) and found that older age at study was associated with an decreased risk for less than college graduate: • Current age (per year): OR=0.98 (95%CI:0.97-0.99) *(CCSS, n=6192 survivors, 58% were <11 years at diagnosis (non-AeYA), 42% were 11-21 years at diagnosis (AeYA); n=390 sibling controls)	*Prasad et al. 2015*
This study* analyzed risk factors for "did not graduate from college". They used multivariable generalized linear models (adjusted for tumor type, tumor location, sex, race, and age at diagnosis) and found that survivors aged 30-39 at study (compared to younger) had a lower likelihood of not being a college graduate: • Age at questionnaire: 30–39 years (Ref. <30 years) RR=0.85 (95%CI:0.74-0.97) • Age at questionnaire: 40+ years (Ref. <30 years) RR=0.92 (95%CI:0.80-1.07) *(CCSS, n=1094 survivors of bone and soft tissue sarcoma in upper or lower extremity; median age at study 33 years; median age at diagnosis 13 years)	*Marina et al. 2013*
This study* used multivariable logistic regression (including survivors and controls, adjusted for population, sex, migration background, nationality, language region; standardized on age, sex, migration background, place of living, language region) and found that younger age at study was associated with completing only compulsory school : • Current age: 25-29 years (Ref. 20-24 years) OR=0.60 (95%CI:0.41-0.88, p=0.009) • Current age: 30-34 years (Ref. 20-24 years) OR=0.35 (95%CI:0.23-0.51, p<0.001) • Current age: 35-40 years (Ref. 20-24 years) OR=0.60 (95%CI:0.37-0.98, p=0.040) They found no significant association of age at study and attainment of upper secondary education or higher (in participants aged ≥27 years): • Current age: 30-34 years (Ref. 25-29 years) OR=0.93 (95%CI:0.72-1.20, p=0.559) • Current age: 35-40 years (Ref. 25-29 years) OR=0.81 (95%CI:0.60-1.08, p=0.144) They found no significant association of age at study and attainment of university degree (in participants aged ≥27 years): • Current age: 30-34 years (Ref. 25-29 years) OR=1.03 (95%CI:0.73-1.46, p=0.867) • Current age: 35-40 years (Ref. 25-29 years) OR=0.87 (95%CI:0.57-1.33, p=0.530) *Swiss Childhood Cancer Survivor Cohort (n=961 survivors; mean age at study 27.0 years; mean age at diagnosis 8.1 years; randomly selected control sample from the general population)	*Kuehni et al. 2012*
This study* used multivariable logistic regression (adjusted for sex, diagnosis, age at diagnosis, duration of treatment, stay on intensive care/bone marrow/stem cell transplantation unit, cancer recurrence, treatment, late effects) and found no significant association between age at study and high school degree: • Age at study: Effect measures not given, p>0.10 In multivariable logistic regression (adjusted for duration of treatment, diagnosis, sex, and late effects), they found that older age at study was associated with increased likelihood of obtaining a college/university degree:	*Dieluweit et al. 2011*

- Age at study: OR=1.08 (95%CI:1.05-1.11, p<0.001)

*(German Childhood Cancer Registry; n=820; mean age at study 29.9 years; mean age at diagnosis 15.8 years)

This study* used multivariable logistic regression (adjusted for sex, cancer type, treatment, age at diagnosis, second tumor, epilepsy, hearing problems, and vision problems). They analyzed risk factors for level of educational attainment: University degree or higher and found that older age at study was associated with not obtaining a university degree:

- Age at study: 25-29 years (Ref. 21-24 years) OR=1.19 (95%CI:0.87-1.62)
- Age at study: 30-34 years (Ref. 21-24 years) OR=0.75 (95%CI:0.54-1.05)
- Age at study: 35-39 years (Ref. 21-24 years) OR=0.65 (95%CI:0.44-0.94)
- Age at study: 40-44 years (Ref. 21-24 years) OR=0.64 (95%CI:0.41-0.99)
- Age at study: 45-49 years (Ref. 21-24 years) OR=0.57 (95%CI:0.34-0.96)
- Age at study: ≥50 years (Ref. 21-24 years) OR=0.44 (95%CI:0.25-0.76)

They analyzed risk factors for level of educational attainment: Teaching degree or equivalent and found that older age at study was associated with not obtaining a teaching degree:

- Age at study: 25-29 years (Ref. 21-24 years) OR=1.20 (95%CI:0.92-1.58)
- Age at study: 30-34 years (Ref. 21-24 years) OR=0.83 (95%CI:0.63-1.10)
- Age at study: 35-39 years (Ref. 21-24 years) OR=0.83 (95%CI:0.61-1.13)
- Age at study: 40-44 years (Ref. 21-24 years) OR=0.78 (95%CI:0.54-1.13)
- Age at study: 45-49 years (Ref. 21-24 years) OR=0.77 (95%CI:0.51-1.18)
- Age at study: ≥50 years (Ref. 21-24 years) OR=0.53 (95%CI:0.34-0.83)

They analyzed risk factors for level of educational attainment: A levels and found that older age at study was associated with not obtaining at least one A level:

- Age at study: 20-24 years (Ref. 18-19 years) OR=1.27 (95%CI:0.88-1.83)
- Age at study: 25-29 years (Ref. 18-19 years) OR=1.02 (95%CI:0.71-1.46)
- Age at study: 30-34 years (Ref. 18-19 years) OR=0.63 (95%CI:0.44-0.92)
- Age at study: 35-39 years (Ref. 18-19 years) OR=0.59 (95%CI:0.40-0.88)
- Age at study: 40-44 years (Ref. 18-19 years) OR=0.64 (95%CI:0.42-0.98)
- Age at study: 45-49 years (Ref. 18-19 years) OR=0.58 (95%CI:0.36-0.93)
- Age at study: ≥50 years (Ref. 18-19 years) OR=0.33 (95%CI:0.20-0.53)

They analyzed risk factors for level of educational attainment: O levels and found that older age at study was associated with not obtaining at least one O level:

- Age at study: 20-24 years (Ref. 16-19 years) OR=1.36 (95%CI:0.95-1.93)
- Age at study: 25-29 years (Ref. 16-19 years) OR=1.15 (95%CI:0.82-1.63)
- Age at study: 30-34 years (Ref. 16-19 years) OR=0.73 (95%CI:0.52-1.04)
- Age at study: 35-39 years (Ref. 16-19 years) OR=0.64 (95%CI:0.44-0.93)
- Age at study: 40-44 years (Ref. 16-19 years) OR=0.74 (95%CI:0.48-1.13)
- Age at study: 45-49 years (Ref. 16-19 years) OR=0.44 (95%CI:0.28-0.69)
- Age at study: ≥50 years (Ref. 16-19 years) OR=0.29 (95%CI:0.18-0.45)

*British Childhood Cancer Survivor Study (N=10,183 survivors; Leukemia>CNS neoplasm>Lymphoma>…; Age range at study: 16-50 years)

Lancashire et al. 2010

Overall Conclusion

Some evidence suggest that older age at follow-up is associated with a decreased risk for lower educational achievement in CAYA cancer survivors.	7 studies (5 samples) Level C[7,9,12,16,19,83,84]

2.1.3 What is the risk for poor educational outcomes by race/migration background?	
This study* analyzed risk factors for educational achievement (having basic education only) with multivariable logistic regression (adjusted for population (survivors/controls)), and found that survivors with a migration background were at higher risk for having basic education only: • Migration background: Yes (Ref. No) OR=10.23 (95%CI:4.64-22.55) *(N=160; Lymphoma>CNS tumor>Leukemia>…; Mean age at study 33.5 years; Controls: N=999 from Swiss general population)	*Mader et al. 2017*
This study* analyzed risk factors for "did not graduate from college". They used multivariable generalized linear models (adjusted for tumor location, age at study, sex, tumor type, and age at diagnosis) and found that non-white survivors had a higher risk for not graduating from college: • Race: Non-white (vs. white): RR=1.23 (95% CI:1.07-1.41) *(CCSS, n=1094 survivors of bone and soft tissue sarcoma in upper or lower extremity; median age at study 33 years; median age at diagnosis 13 years)	*Marina et al. 2013*
In this study*, multivariable logistic regression (including survivors and controls, adjusted for population, age at study, sex; standardized on age, sex, place of living, language region of Switzerland) showed that people with a migration background had a higher risk for completing only compulsory school : • Migration background (Ref. No migration background) OR=1.89 (95%CI:1.23-2.88, p=0.003) They found no significant association between migration background and upper secondary education or higher (Participants aged ≥27 years) • Migration background (Ref. No migration background) OR=1.16 (95%CI:0.87-1.56, p=0.318) They found that people with a migration background had a higher likelihood of attaining a university degree (in Participants aged ≥27 years): • Migration background (Ref. No migration background) OR=1.51 (95%CI:1.03-2.21, p=0.034) *Swiss Childhood Cancer Survivor Cohort (n=961 survivors; mean age at study 27.0 years; mean age at diagnosis 8.1 years; randomly selected control sample from the general population)	*Kuehni et al. 2012*
Overall Conclusion	
There is evidence that survivors with a non-white racial background or a migration background in specific geographic regions are at increased risk for lower educational achievement.	3 studies Level A[7,19,84]

2.1.4 What is the risk for poor educational outcomes by parents' education level?	
This study* analyzed risk factors for repeating a grade with multilevel logistic regression (adjusting for sex, age at diagnosis, parental education, financial difficulties, history of repeating a grade, CNS irradiation, relapse, HSCT, time since diagnosis, living in a traditional family unit) and found that lower education level of parents was associated with increased likelihood of the survivor repeating a grade: • Parental educational level: No diploma (Ref. More than high school) OR=4.60 (95%CI:2.27-9.31) • Parental educational level: Less than high school (Ref. More than high school) OR=2.50 (95%CI:1.66-3.75; p<0.001) (LEA cohort; n=855 ALL & AML survivors; mean 16.2 years at study; Controls: n=1304 siblings mean 18.5 years at study)	*Bonneau et al. 2019*
This study* used multivariable logistic regression (adjusted for tumor type, sex, age at diagnosis, period of diagnosis, parents' education) and found no significant assocation between parents' education and completing "compulsory school". They found that higher parents' education was associated with increased likelihood of survivors' completion of "higher education". Risk factors for completing compulsory school (participants aged ≥14 years): • Lower/upper secondary level (Ref. None/primary school) OR=1.47 (95%CI:0.35-6.07) • Parents' education: University degree (Ref. None/primary school) OR=1.18	*Maule et al. 2017*

(95%CI:0.21-6.79) Risk factors for completing higher education (participants aged ≥19 years): • Parents' education: Lower/upper secondary level (Ref. None/primary school) OR=2.08 (95%CI:1.03-4.23) • Parents' education: University degree (Ref. None/primary school) OR=9.54 (95%CI:2.60-35.02) *(n=637 Italian survivors; mixed diagnoses; 0-14 years at diagnosis; Controls: general population)	
In this study*, multivariable logistic regression (adjusted for sex, age, migration background, nationality, language region, place of living, siblings, diagnosis, age at diagnosis, therapy, and relapse) showed that parents' highest degree being compulsory school only was associated with an increased likelihood of the survivor completing compulsory school only: • Parental education (highest degree): Compulsory schooling (Ref. Vocational training) OR=3.31 (95%CI:1.54-7.09, p=0.002) • Parental education (highest degree): Upper secondary education (Ref. Vocational training) OR=0.76 (95%CI:0.40-1.44, p=0.398) • Parental education (highest degree): University education (Ref. Vocational training) OR=0.80 (95%CI:0.33-1.98, p=0.633) They found that parents' highest degree being upper secondary education or university education was associated with an increased likelihood of the survivor attaining upper secondary education (in participants aged ≥27 years): • Parental education (highest degree): Compulsory schooling (Ref. Vocational training) OR=0.63 (95%CI:0.29-1.40, p=0.259) • Parental education (highest degree): Upper secondary education (Ref. Vocational training) OR=1.92 (95%CI:1.14-3.23, p=0.014) • Parental education (highest degree): University education (Ref. Vocational training) OR=14.76 (95%CI:4.22-51.61, p<0.001) They found that parents' highest degree being university education was associated with an increased likelihood of the survivor attaining university education (in participants aged ≥27 years): • Parental education (highest degree): Compulsory schooling (Ref. Vocational training) OR=0.23 (95%CI:0.03-1.49, p=0.123) • Parental education (highest degree): Upper secondary education (Ref. Vocational training) OR=1.17 (95%CI:0.48-2.83, p=0.727) • Parental education (highest degree): University education (Ref. Vocational training) OR=9.13 (95%CI:3.61-23.09, p<0.001) *Swiss Childhood Cancer Survivor Cohort (n=961 survivors; mean age at study 27.0 years; mean age at diagnosis 8.1 years; randomly selected control sample from the general population)	*Kuehni et al. 2012*
This study* analyzed risk factors for repeating a grade. They used multivariable logistic regression (adjusting for diagnosis, BMT, child's education level, educational support, physical sequelae) and found that lower education level of fathers was associated with increased likelihood of the survivor repeating a grade: • Education level of father: Low (Ref. High) OR=7.0 (95%CI:2.4-20.6) In univariable analyzes (student t-test, Chi2, Fisher tests) they found that lower education level of mothers was associated with increased likelihood of the survivor repeating a grade: • Education level of mother: Low (vs. high): higher percentage of grade repetition among survivors with lower education level of mother (p=0.001) *(N=148 survivors; ALL/Lymphoblastic lymphoma>Solid tumor>Hodgkin lymphoma>…; mean age at study 15 years; N=194 siblings and >50,000 healthy schoolchildren)	*Bonneau et al. 2011*
Overall Conclusion	
Evidence suggests that lower parental education is associated with an increased risk for lower educational achievement in CAYA cancer survivors.	2 studies Level B[19,52]
Evidence suggests that lower education level of parents is associated with an increased risk for repeating a grade in CAYA cancer survivors.	2 studies Level B[63,64]

2.1.5 What is the risk for poor educational outcomes by <u>having siblings</u>?	
In this study*, multivariable logistic regression (adjusted for sex, age, migration background, nationality, language region, place of living, parents' education level, diagnosis, age at diagnosis, therapy, and relapse) showed no significant association between having siblings and completing compulsory school only: • Siblings: Yes (Ref. No) OR=0.53 (95%CI:0.26-1.06, p=0.071) They found no significant association between having siblings and attaining upper secondary education (in participants aged ≥27 years): • Siblings: Yes (Ref. No) OR=1.32 (95%CI:0.63-2.76, p=0.458) They found no significant association between having siblings and attaining university education (in participants aged ≥27 years): • Siblings: Yes (Ref. No) OR=0.88 (95%CI:0.27-2.85, p=0.830) *Swiss Childhood Cancer Survivor Cohort (n=961 survivors; mean age at study 27.0 years; mean age at diagnosis 8.1 years; randomly selected control sample from the general population)	*Kuehni et al. 2012*
Overall Conclusion	
Some evidence suggests that having siblings is not significantly associated with educational achievement in CAYA cancer survivors.	1 study Level C[19]

2.1.6 What is the risk for poor educational outcomes by educational support?	
This study* analyzed risk factors for repeating a grade with multilevel logistic regression (adjusting for sex, age at diagnosis, parental education, financial difficulties, history of repeating a grade, CNS irradiation, relapse, HSCT, time since diagnosis, living in a traditional family unit) and found that educational support was associated with increased likelihood of the survivor repeating a grade: • Educational support at home/hospital during treatment: Yes (Ref. No) OR=3.79 (95%CI:2.45-5.88; p<0.001) (LEA cohort; n=855 ALL & AML survivors; mean 16.2 years at study; Controls: n=1304 siblings mean 18.5 years at study)	*Bonneau et al. 2019*
This study* analyzed risk factors for repeating a grade. They used multivariable logistic regression (adjusting for fathers' education level, child's education level at time of diagnosis, diagnosis, physical sequelae, and BMT) and found that no educational help at school was associated with repeating a grade: • Educational help at home: Parental help at home (Ref. Unclear) OR=0.4 (95%CI:0.1-1.7) • Educational help at school: No (Ref. Yes) OR=4.9 (95%CI:1.5-16.0) In univariable analyzes (student t-test, Chi2, Fisher tests) they found no significant associations between educational support at hospital or individual education plan and repeating a grade: • Educational support at hospital: Yes (vs. No): no statistically significant differences (p=0.83) • Individual education plan: Yes (vs. No): no statistically significant differences (p=0.53) (N=148 survivors; ALL/Lymphoblastic lymphoma>Solid tumor>Hodgkin lymphoma>…; mean age at study 15 years; N=194 siblings and >50,000 health schoolchildren)	*Bonneau et al. 2011*
Overall Conclusion	
There is conflicting evidence regarding the association of educational support with repeating a grade in CAYA cancer survivors.	2 studies Conflicting evidence[63,64]

2.1.7 What is the risk for poor educational outcomes by primary cancer diagnosis?	
This study* analyzed risk factors for educational achievement (having basic education only) with univariable logistic regression and found no significant association between diagnosis and having basic education only (variable was therefore not included in the multivariable model): • Diagnosis: CNS tumors (Ref. Leukemia/lymphoma) OR=0.68 (95%CI:0.01-6.00) • Diagnosis: Other cancer (Ref. Leukemia/lymphoma) OR=0.72 (95%CI:0.17-2.77) *(N=160; Lymphoma>CNS tumor>Leukemia>…; Mean age at study 33.5 years; Controls: N=999 from Swiss general population)	*Mader et al. 2017*
This study* used multivariable logistic regression (adjusted for tumor type, sex, age at diagnosis, period of diagnosis, parents' education) and found no significant assocation between tumor type and completing "compulsory school". They found that "other tumor type" was associated with increased likelihood of survivors' completion of "higher education". Risk factors for completing compulsory school (participants aged ≥14 years): • CNS (Ref. Lymph.-hem. system) OR=0.88 (95%CI:0.27-2.84) • Other (Ref. Lymph.-hem. system) OR=1.31 (95%CI:0.31-5.45) Risk factors for completing higher education (participants aged ≥19 years): • CNS (Ref. Lymph.-hem. system) OR=0.74 (95%CI:0.35-1.54) • Other (Ref. Lymph.-hem. system) OR=2.10 (95%CI:1.07-4.15) *(n=637 Italian survivors; mixed diagnoses; 0-14 years at diagnosis; Controls: general population)	*Maule et al. 2017*
This study* analyzed risk factors for "did not graduate from college". They used multivariable generalized linear models (adjusted for tumor location, age at study, sex,	*Marina et al. 2013*

race, and age at diagnosis) and found that survivors of Ewings sarcoma (compared to soft tissue sarcoma) had an increased likelihood of graduating from college: • Tumor Type: Ewings sarcoma (Ref. soft tissue sarcoma (STS)) RR=0.84 (95%CI:0.71-0.99) • Tumor Type: Osteosarcoma (Ref. STS) RR=1.07 (95%CI:0.95-1.20) • Tumor Type: Other bone (Ref. STS) RR=0.73 (95%CI:0.50-1.06) *(CCSS, n=1094 survivors of bone and soft tissue sarcoma in upper or lower extremity; median age at study 33 years; median age at diagnosis 13 years)	
In this study*, multivariable logistic regression (adjusted for sex, age, migration background, nationality, language region, place of living, siblings, age at diagnosis, therapy, and relapse) found that survivors of CNS neoplasms were at an increased risk of completing compulsory school only: • Diagnosis (ICCC3): Lymphoma (Ref. Leukemia) OR=0.54 (95%CI:0.22-1.33, p=0.179) • Diagnosis (ICCC3): CNS neoplasms (Ref. Leukemia) OR=2.64 (95%CI:1.15-6.06, p=0.022) • Diagnosis (ICCC3): Other tumors (Ref. Leukemia) OR=1.37 (95%CI:0.74-2.54, p=0.314) They found no association between diagnosis and obtaining upper secondary education or more (in participants aged ≥27 years): • Diagnosis (ICCC3): Lymphoma (Ref. Leukemia) OR=1.60 (95%CI:0.86-2.97, p=0.135) • Diagnosis (ICCC3): CNS neoplasms (Ref. Leukemia) OR=0.39 (95%CI:0.15-1.02, p=0.056) • Diagnosis (ICCC3): Other tumors (Ref. Leukemia) OR=0.97 (95%CI:0.53-1.78, p=0.919) They found no association between diagnosis and obtaining a university degree (in participants aged ≥27 years): • Diagnosis (ICCC3): Lymphoma (Ref. Leukemia) OR=1.86 (95%CI:0.70-4.98, p=0.215) • Diagnosis (ICCC3): CNS neoplasms (Ref. Leukemia) OR=0.74 (95%CI:0.15-3.71, p=0.716) • Diagnosis (ICCC3): Other tumors (Ref. Leukemia) OR=0.79 (95%CI:0.28-2.22, p=0.651) *Swiss Childhood Cancer Survivor Cohort (n=961 survivors; mean age at study 27.0 years; mean age at diagnosis 8.1 years; randomly selected control sample from the general population)	*Kuehni et al. 2012*
This study* analyzed risk factors for repeating a grade. They used multivariable logistic regression (adjusting for fathers' education level, BMT, child's education level, educational support, physical sequelae) and found no significant associations of diagnosis with survivors repeating a grade: • Diagnosis: Cerebral tumor (Ref. Hematological malignancy) OR=2.8 (95%CI:0.5-15.3) • Diagnosis: Solid tumor (Ref. Hematological malignancy) OR=0.5 (95%CI:0.1-1.5) *(N=148 survivors; ALL/Lymphoblastic lymphoma>Solid tumor>Hodgkin lymphoma>…; mean age at study 15 years; N=194 siblings and >50,000 health schoolchildren)	*Bonneau et al. 2011*
This study* used multivariable logistic regression (adjusted for sex, age at study, age at diagnosis, duration of treatment, stay on intensive care/bone marrow/stem cell transplantation unit, cancer recurrence, treatment, late effects) and found no significant association between diagnosis and high school degree: • Diagnosis: Effect measures not given, p>0.10 In multivariable logistic regression (adjusted for duration of treatment, age at study, sex, and late effects), they found that CNS tumor survivors (compared to leukemia and lymphoma survivors) had a lower likelihood of obtaining a college/university degree: • Diagnosis: CNS tumors (Ref. Leukemia and lymphoma) OR=0.39 (95%CI:0.17-0.92, p=0.031) • Diagnosis: Solid tumors (Ref. Leukemia and lymphoma) OR=0.76 (95%CI:0.53-1.10, p=0.143) *(German Childhood Cancer Registry; n=820; mean age at study 29.9 years; mean age at diagnosis 15.8 years)	*Dieluweit et al. 2011*

This study* used logistic regression on the log scale of education, adjusted for year of birth, residency, socioeconomic status and maternal country of birth. They analyzed risk factors for basic education only (≤9 years) and found that CNS tumor survivors were more likely to have basic education only (compared to the cancer-free population). No association for the other diagnoses: • Diagnosis: Leukemia/Lymphoma (Ref. Cancer-free population) OR=1.07 (95%CI:0.79-1.45) • Diagnosis: CNS tumors (Ref. Cancer-free population) OR=1.80 (95%CI:1.45-2.23) • Diagnosis: Other cancer (Ref. Cancer-free population) OR=1.05 (95%CI:0.82-1.36) They analyzed risk factors for postsecondary education (≥14 years) and found that CNS tumor survivors had a lower likelihood of having a postsecondary education than the cancer-free population. No association for the other diagnoses: • Diagnosis: Leukemia/Lymphoma (Ref. Cancer-free population) OR=0.92 (95%CI:0.79-1.07) • Diagnosis: CNS tumors (Ref. Cancer-free population) OR=0.69 (95%CI:0.58-0.81) • Diagnosis: Other cancer (Ref. Cancer-free population) OR=1.09 (95%CI:0.97-1.22) *(N=1716, CNS tumor>Leukemia>Lymphoma>…; mean age at study 31.6 years; N=1,456,089 controls (Swedish national registers))	*Boman et al. 2010*
This study* used generalized estimating equation logistic regression (taking into account the general household survey (GHS) weighting factor and controlling for age and sex). They analyzed risk factors for level of educational attainment: University degree or higher and found that survivors of leukemia and CNS neoplasms (compared to the general population) had a significantly decreased likelihood of obtaining a university degree: • Leukemia with radiotherapy (Ref. population data from the GHS) OR=0.60 (99%CI:0.49-0.75, p<0.001) • Hodgkin's disease (Ref. population data) OR=1.00 (99%CI:0.77-1.29, p=0.97) • Non-Hodgkin lymphoma (Ref. population data) OR=1.01 (99%CI:0.74-1.38, p=0.93) • CNS neoplasm with radiotherapy (Ref. population data) OR=0.31 (99%CI:0.23-0.43, p<0.001) • CNS neoplasm without radiotherapy (Ref. population data) OR=0.58 (99%CI:0.42-0.80, p<0.001) • Neuroblastoma (Ref. population data) OR=0.72 (99%CI:0.46-1.14, p=0.07) • Retinoblastoma (Ref. population data) OR=1.17 (99%CI:0.89-1.55, p=0.14) • Wilms tumor (Ref. population data) OR=0.87 (99%CI:0.68-1.14, p=0.18) • Bone sarcomas (Ref. population data) OR=1.22 (99%CI:0.88-1.69, p=0.11) • Soft tissue sarcomas (Ref. population data) OR=1.02 (99%CI:0.77-1.35, p=0.86) • Other neoplasm (Ref. population data) OR=1.12 (99%CI:0.87-1.44, p=0.24) *British Childhood Cancer Survivor Study (N=10,183 survivors; Leukemia>CNS neoplasm>Lymphoma>…; Age range at study: 16-50 years)	*Lancashire et al. 2010*
This study* used multivariable logistic regression (adjusted for sex, urban/rural status, and socioeconomic status quintile) to analyze risk factors for special education. They found that survivors of all diagnoses were more likely to receive special education than controls: • Diagnosis: Leukemias (Ref. Controls) OR=3.06 (95%CI:2.34-3.99) • Diagnosis: CNS tumors (Ref. Controls) OR=6.11 (95%CI:4.40-8.49) • Diagnosis: Neuroblastomas (Ref. Controls) OR=2.29 (95%CI:1.21-4.32) • Diagnosis: Others (Ref. Controls) OR=2.06 (95%CI:1.56-2.72) *(N=782; Leukemia>CNS>Lymphoma>…; Mean age at diagnosis was 4.6 years; Controls N=8386 randomly selected school children)	*Lorenzi et al. 2009*
Overall Conclusion	
Evidence suggests that CNS tumor survivors are at an increased risk for lower educational achievement.	6 studies Level B[7,12,14,16,19,52]
Some evidence suggests that leukemia survivors (treated with cranial radiotherapy) are at an increased risk for lower educational achievement.	2 studies Level C[14,16]

Some evidence suggests that survivors of Ewing's sarcoma (compared to survivors of soft tissue sarcoma) are at a decreased risk for lower education achievement.	1 study Level C[84]
Some evidence suggests that CAYA cancer survivors of all diagnoses are at risk for special education.	1 study Level C[65]
Some evidence suggests that diagnosis is not significantly associated with repeating a grade in survivors of CAYA cancers.	1 study Level C[64]

2.1.8 What is the risk for poor educational outcomes by tumor location?	
This study* analyzed risk factors for "did not graduate from college". They used multivariable generalized linear models (adjusted for tumor type, age at study, sex, race, and age at diagnosis) and found that survivors of lower extremity tumors (compared to upper extremity) had an increased likelihood of graduating from college: • Tumor location: Lower Extremity (Ref. Upper Extremity) RR=0.87 (95%CI:0.77-0.97) *(CCSS, n=1094 survivors of bone and soft tissue sarcoma in upper or lower extremity; median age at study 33 years; median age at diagnosis 13 years)	*Marina et al. 2013*
Overall Conclusion	
Some evidence suggests that survivors of upper extremity bone tumors are at an increased risk for lower educational achievement (compared to survivors of lower extremity bone tumors).	1 study Level C[84]

2.1.9 What is the risk for poor educational outcomes by stay at an intensive care unit?	
This study* used multivariable logistic regression (adjusted for late effects), they found that stay at an intensive care unit/bone marrow/stem cell transplantation unit was associated with a lower likelihood of obtaining a high school degree: • Intensive care/Bone marrow/stem cell plantation unit: Yes (Ref. No) OR=0.73 (95%CI:0.54-0.99, p=0.042) In multivariable logistic regression (adjusted for sex, age at study, age at diagnosis, diagnosis, duration of treatment, stay on intensive care/bone marrow/stem cell transplantation unit, cancer recurrence, late effects), they found no significant association between stay at an intensive care unit/bone marrow/stem cell transplantation unit and obtaining a college/university degree: • Intensive care/Bone marrow/stem cell transplantation unit: Effect measures not given, p>0.10 *(German Childhood Cancer Registry; n=820; mean age at study 29.9 years; mean age at diagnosis 15.8 years)	*Dieluweit et al. 2011*
Overall Conclusion	
Some evidence suggests that stay at an intensive care unit is associated with lower likelihood of obtaining a high school degree in CAYA cancer survivors.	1 study Level C[12]
Some evidence suggests that stay at an intensive care unit is not significantly associated with obtaining a college/university degree.	1 study Level C[12]

2.1.10 What is the risk for poor educational outcomes by surgery?	
This study* analyzed risk factors for "did not graduate from college". They used multivariable generalized linear models (adjusted for chemotherapy, tumor location, age at study, and race) and found that amputation was associated with a lower likelihood of graduating from college: • Limb Surgery: Above Knee Amputation (Ref. None) RR=1.36 (95%CI:1.18-1.56) • Limb Surgery: Below Knee Amputation (Ref. None) RR=1.46 (95%CI:1.15-1.86 • Limb Surgery: Upper Extremity Amputation (Ref. None) RR=1.80 (95%CI:1.48-2.18) • Limb Surgery: Limb sparing (Ref. None) RR=1.11 (95%CI:0.95-1.30) *(CCSS, n=1094 survivors of bone and soft tissue sarcoma in upper or lower extremity; median age at study 33 years; median age at diagnosis 13 years)	*Marina et al. 2013*
In this study*, multivariable logistic regression (adjusted for sex, age, migration background, nationality, language region, place of living, siblings, diagnosis, age at diagnosis, and relapse) showed no significant association of surgery only (compared to chemotherapy) and completing compulsory school only: • Therapy: Surgery only (Ref. Chemotherapy) OR=0.62 (95%CI:0.22-1.72, p=0.314) They found no significant association of surgery only (compared to chemotherapy) and obtaining upper secondary education or more (in participants aged ≥27 years): • Therapy: Surgery only (Ref. Chemotherapy) OR=1.74 (95%CI:0.55-5.52, p=0.919) They found no significant association of surgery only (compared to chemotherapy) and obtaining a university degree (in participants aged ≥27 years): • Therapy: Surgery only (Ref. Chemotherapy) OR=0.24 (95%CI:0.02-3.39, p=0.053) *Swiss Childhood Cancer Survivor Cohort (n=961 survivors; mean age at study 27.0 years; mean age at diagnosis 8.1 years; randomly selected control sample from the general population)	*Kuehni et al. 2012*
This study* used multivariable logistic regression (adjusted for sex, age at study, age at diagnosis, diagnosis, second tumor, epilepsy, hearing problems, and vision problems). They analyzed risk factors for level of educational attainment: University degree or higher and found no significant association between surgery and attainment of a university degree: • Surgery: Yes (Ref. No) OR=1.08 (95%CI:0.78-1.48) They analyzed risk factors for level of educational attainment: Teaching degree or equivalent and found no significant assocations between surgery and attainment of a teaching degree: • Surgery: Yes (Ref. No) OR=1.05 (95%CI:0.81-1.39) They analyzed risk factors for level of educational attainment: A levels and found no significant assocations between surgery and attainment of at least one A level: • Surgery: Yes (Ref. No) OR=1.17 (95%CI:0.91-1.49) They analyzed risk factors for level of educational attainment: O levels and found no significant assocations between surgery and attainment of at least one O level: • Surgery: Yes (Ref. No) OR=1.10 (95%CI:0.84-1.45) British Childhood Cancer Survivor Study (N=10,183 survivors; Leukemia>CNS neoplasm>Lymphoma>…; Age range at study: 16-50 years)	*Lancashire et al. 2010*
Overall Conclusion	
Some evidence suggests that an amputation is associated with an increased risk for lower educational achievement in CAYA cancer survivors.	1 study Level C[84]
Evidence suggests that surgery (not further specified) is not significantly associated with educational achievement in CAYA cancer survivors.	2 studies Level B[16,19]

2.1.11 What is the risk for poor educational outcomes by chemotherapy?	
This study* analyzed risk factors for educational achievement (having basic education only) with univariable logistic regression and found no significant association between chemotherapy (vs. surgery only) and having basic education only (variable was therefore not included in the multivariable model): • Treatment: Chemotherapy (Ref. surgery only) OR=1.39 (95%CI:0.19-8.84), p=0.827 *(N=160; Lymphoma>CNS tumor>Leukemia>…; Mean age at study 33.5 years; Controls: N=999 from Swiss general population)	*Mader et al. 2017*
This study* analyzed risk factors for "did not graduate from college". They used multivariable generalized linear models (adjusted for limb surgery, tumor location, age at study, and race) and found that alkylating agents was associated with a lower, whereas anthracyclines was associated with an increased likelihood of graduating from college: • Alkylating agent: Any (Ref. None) RR=1.21 (95%CI:1.07-1.37) • Anthracyclines: Any (Ref. None) RR=0.81 (95%CI:0.71-0.91) *(CCSS, n=1094 survivors of bone and soft tissue sarcoma in upper or lower extremity; median age at study 33 years; median age at diagnosis 13 years)	*Marina et al. 2013*
This study* used multivariate logistic regression analyzes (adjusting for radiotherapy, and age at diagnosis) to analyze the risk of "achievement of high school certificate" vs. less than high school certificate. They found that chemotherapy was not significantly associated with achieving a high school diploma: • Chemotherapy (Ref. No chemotherapy): OR=2.00 (95%CI:0.98-4.04, p=0.058) *Survivors of brain tumors in Germany (n=203, median age at diagnosis 11 years, median age at study 22 years)	*Pfitzer et al. 2013*
In this study*, multivariable logistic regression (adjusted for sex, age, migration background, nationality, language region, place of living, siblings, diagnosis, age at diagnosis, and relapse) showed no significant association of treatment and completing compulsory school only: • Therapy: Surgery only (Ref. Chemotherapy) OR=0.62 (95%CI:0.22-1.72, p=0.314) • Therapy: Radiotherapy (Ref. Chemotherapy) OR=1.14 (95%CI:0.63-2.08, p=0.381) • Therapy: Bone marrow transplantation (Ref. Chemotherapy) OR=0.75 (95%CI:0.26-2.14, p=0.584) They found no significant association of treatment and obtaining upper secondary education or more (in participants aged ≥27 years): • Therapy: Surgery only (Ref. Chemotherapy) OR=1.74 (95%CI:0.55-5.52, p=0.919) • Therapy: Radiotherapy (Ref. Chemotherapy) OR=0.75 (95%CI:0.45-1.24, p=0.875) • Therapy: Bone marrow transplantation (Ref. Chemotherapy) OR=0.72 (95%CI:0.30-1.73, p=0.465) They found no significant association of treatment and obtaining a university degree (in participants aged ≥27 years): • Therapy: Surgery only (Ref. Chemotherapy) OR=0.24 (95%CI:0.02-3.39, p=0.053) • Therapy: Radiotherapy (Ref. Chemotherapy) OR=0.95 (95%CI:0.42-2.14, p=0.123) • Therapy: Bone marrow transplantation (Ref. Chemotherapy) OR=0.55 (95%CI:0.11-2.83, p=0.472) *Swiss Childhood Cancer Survivor Cohort (n=961 survivors; mean age at study 27.0 years; mean age at diagnosis 8.1 years; randomly selected control sample from the general population)	*Kuehni et al. 2012*
This study* used multivariable logistic regression (adjusted for sex, age at study, age at diagnosis, diagnosis, second tumor, epilepsy, hearing problems, and vision problems). They analyzed risk factors for level of educational attainment: University degree or higher and found no significant associations between treatment with chemotherapy and obtaining a university degree: • Chemotherapy: Yes (Ref. No) OR=1.14 (95%CI:0.86-1.52) They analyzed risk factors for level of educational attainment: Teaching degree or equivalent and found no significant associations between treatment with chemotherapy and obtaining a teaching degree: • Chemotherapy: Yes (Ref. No) OR=1.13 (95%CI:0.88-1.45)	*Lancashire et al. 2010*

They analyzed risk factors for level of educational attainment: A levels and found no significant associations between treatment with chemotherapy and obtaining at least one A level: • Chemotherapy: Yes (Ref. No) OR=1.08 (95%CI:0.86-1.35) They analyzed risk factors for level of educational attainment: O levels and found no significant associations between treatment with chemotherapy and obtaining at least one O level: • Chemotherapy: Yes (Ref. No) OR=1.05 (95%CI:0.81-1.37) *British Childhood Cancer Survivor Study (N=10,183 survivors; Leukemia>CNS neoplasm>Lymphoma>…; Age range at study: 16-50 years)	
This study* used multivariable logistic regression (adjusted for sex, urban/rural status, and socioeconomic status quintile) to analyze risk factors for special education. They found no significant association between treatment with intrathecal methotrexate and receiving special education: • Treatment: Intrathecal methotrexate (Ref. No IT MTX) OR=0.66 (95%CI:0.34-1.31) *(N=782; Leukemia>CNS>Lymphoma>…; Mean age at diagnosis was 4.6 years; Controls N=8386 randomly selected school children)	*Lorenzi et al. 2009*
Overall Conclusion	
Evidence suggests that there is no significant association between chemotherapy treatment (not further specified) and educational achievement in CAYA cancer survivors.	4 studies Level B[7,16,19,85]
Some evidence suggests that treatment with alkylating agents is associated with an increased risk for lower educational achievement in childhood bone and soft tissue cancer survivors.	1 study Level C[84]
Some evidence suggests that treatment with anthracyclines is associated with a decreased risk for lower educational achievement in childhood bone and soft tissue cancer survivors.	1 study Level C[84]
Some evidence suggests no significant association of intrathecal methotrexate with special education in CAYA cancer survivors.	1 study Level C[65]

2.1.12 What is the risk for poor educational outcomes by radiation?	
This study* analyzed risk factors for repeating a grade with multilevel logistic regression (adjusting for sex, age at diagnosis, parental education, financial difficulties, history of repeating a grade, CNS irradiation, relapse, HSCT, time since diagnosis, living in a traditional family unit) and found no significant association between CNS irradiation and repeating a grade: • CNS irradiation: n.s. (LEA cohort; n=855 ALL & AML survivors; mean 16.2 years at study; Controls: n=1304 siblings mean 18.5 years at study)	*Bonneau et al. 2019*
This study* analyzed risk factors for educational achievement (having basic education only) with univariable logistic regression and found no significant association between radiotherapy (vs. surgery only) and having basic education only (variable was therefore not included in the multivariable model): • Treatment: Radiotherapy (Ref. surgery only) OR=0.69 (95%CI:0.06-5.08), p=0.827 *(N=160; Lymphoma>CNS tumor>Leukemia>…; Mean age at study 33.5 years; Controls: N=999 from Swiss general population)	*Mader et al. 2017*
This study* analyzed risk factors for "no college attendance" (vs. some attendance with or without college degree) using multivariate logistic regression (adjusting for vision problems, age at diagnosis, age at interview, medical comorbidity). They found that cranial radiation with 30 Gy or more was associated with increased risk of not attending college: • Cranial radiation: ≤30 Gy (Ref. None) OR=0.53 (95%CI:0.14-1.98) • Cranial radiation: >30 Gy (Ref. None) OR=2.05 (95%CI:1.37-3.06) *Survivors of astroglial tumors in the CCSS (n=587, mean age at study 23.8 years, diagnosis <21 years)	*De Blank et al. 2016*

This study* used multivariate logistic regression analyzes (adjusting for chemotherapy, and age at diagnosis) to analyze the risk of "achievement of high school certificate" vs. less than high school certificate. They found no significant association of irradiation and achievement of high school certificate: • Irradiation: either craniospinal irradiation or irradiation of the tumor (Ref. no irradiation): OR=0.54 (95%CI:0.08-3.76, p=0.536) • Irradation: craniospinal irradiation and irradiation of the tumor (Ref. no irradiation): OR=0.51 (95%CI:0.07-3.59, p=0.502) • Irradiation: not defined (Ref. no irradiation): OR=0.34 (95%CI:0.05-2.24, p=0.262) *Survivors of brain tumors in Germany (n=203, median age at diagnosis 11 years, median age at study 22 years)	*Pfitzer et al. 2013*
In this study*, multivariable logistic regression (adjusted for sex, age, migration background, nationality, language region, place of living, siblings, diagnosis, age at diagnosis, and relapse) showed no significant association of radiotherapy (compared to chemotherapy) and completing compulsory school only: • Therapy: Radiotherapy (Ref. Chemotherapy) OR=1.14 (95%CI:0.63-2.08, p=0.381) They found no significant association of radiotherapy (compared to chemotherapy) and obtaining upper secondary education or more (in participants aged ≥27 years): • Therapy: Radiotherapy (Ref. Chemotherapy) OR=0.75 (95%CI:0.45-1.24, p=0.875) They found no significant association of radiotherapy (compared to chemotherapy) and obtaining a university degree (in participants aged ≥27 years): • Therapy: Radiotherapy (Ref. Chemotherapy) OR=0.95 (95%CI:0.42-2.14, p=0.123) *Swiss Childhood Cancer Survivor Cohort (n=961 survivors; mean age at study 27.0 years; mean age at diagnosis 8.1 years; randomly selected control sample from the general population)	*Kuehni et al. 2012*
This study* used multivariable logistic regression (adjusted for sex, age at study, age at diagnosis, diagnosis, second tumor, epilepsy, hearing problems, and vision problems). They analyzed risk factors for level of educational attainment: University degree or higher and found no significant association between radiotherapy (cranial or other vs. no radiotherapy) and attainment of a university degree: • Radiotherapy: Other radiotherapy (noncranial) (Ref. No radiotherapy) OR=1.10 (95%CI:0.85-1.44) • Radiotherapy: Cranial radiotherapy (Ref. No radiotherapy) OR=0.80 (95%CI:0.54-1.17) They analyzed risk factors for level of educational attainment: Teaching degree or equivalent and found no significant association between radiotherapy (cranial or other vs. no radiotherapy) and attainment of a teaching degree: • Radiotherapy: Other radiotherapy (noncranial) (Ref. No radiotherapy) OR=1.06 (95%CI:0.84-1.34) • Radiotherapy: Cranial radiotherapy (Ref. No radiotherapy) OR=0.91 (95%CI:0.66-1.23) They analyzed risk factors for level of educational attainment: A levels and found that cranial radiotherapy was associated with a decreased likelihood of obtaining at least one A level: • Radiotherapy: Other radiotherapy (noncranial) (Ref. No radiotherapy) OR=1.16 (95%CI:0.94-1.44) • Radiotherapy: Cranial radiotherapy (Ref. No radiotherapy) OR=0.73 (95%CI:0.56-0.96) They analyzed risk factors for level of educational attainment: O levels and found that cranial radiotherapy was associated with a decreased likelihood of obtaining at least one O level: • Radiotherapy: Other radiotherapy (noncranial) (Ref. No radiotherapy) OR=1.06 (95%CI:0.82-1.37) • Radiotherapy: Cranial radiotherapy (Ref. No radiotherapy) OR=0.58 (95%CI:0.44-0.77)	*Lancashire et al. 2010*

*British Childhood Cancer Survivor Study (N=10,183 survivors; Leukemia>CNS neoplasm>Lymphoma>…; Age range at study: 16-50 years)	
This study* used log-binomial generalized linear models, adjusted for sex, age at diagnosis, and the maximum radiation dose to any of the other three segments. They analyzed risk factors for education below college graduate and found no significant associations between radiation (dose and brain region) and education below college graduate: • Posterior fossa: <30Gy (Ref. None) RR=1.0 (95%CI:0.8-1.3) • Posterior fossa: 30-49Gy (Ref. None) RR=1.0 (95%CI:0.8-1.3) • Posterior fossa: ≥50Gy (Ref. None) RR=1.0 (95%CI:0.8-1.3) • Temporal lobe: <30Gy (Ref. None) RR=0.9 (95%CI:0.7-1.2) • Temporal lobe: 30-49Gy (Ref. None) RR=1.2 (95%CI:0.9-1.5) • Temporal lobe: ≥50Gy (Ref. None) RR=1.2 (95%CI:1.0-1.5) • Frontal lobe: <30Gy (Ref. None) RR=1.0 (95%CI:0.8-1.2) • Frontal lobe: 30-49Gy (Ref. None) RR=1.1 (95%CI:0.8-1.4) • Frontal lobe: ≥50Gy (Ref. None) RR=1.2 (95%CI:0.9-1.6) • Occipital lobe: <30Gy (Ref. None) RR=0.9 (95%CI:0.8-1.2) • Occipital lobe: 30-49Gy (Ref. None) RR=0.9 (95%CI:0.8-1.2) • Occipital lobe: ≥50Gy (Ref. None) RR=1.0 (95%CI:0.8-1.3) *(CCSS, N=1877; CNS tumor survivors; 56.8% <25 years at study; Controls: N=3899 siblings)	*Armstrong et al. 2009*
This study* used multivariable logistic regression (adjusted for sex, urban/rural status, and socioeconomic status quintile) to analyze risk factors for special education. They found no significant association between radiotherapy or cranial radiotherapy and receiving special education: • Treatment: Radiotherapy (Ref. No radiotherapy) OR=1.03 (95%CI:0.72-1.48) • Treatment: Cranial radiotherapy (Ref. No cranial radiotherapy) OR=1.09 (95%CI:0.71-1.69) *(N=782; Leukemia>CNS>Lymphoma>…; Mean age at diagnosis was 4.6 years; Controls N=8386 randomly selected BC school children)	*Lorenzi et al. 2009*
Overall Conclusion	
Some evidence suggests that cranial radiotherapy is associated with an increased risk for lower educational achievement in CAYA cancer survivors.	6 studies (5 samples) Level C[7,16,19,27,83,85]
Some evidence suggests that radiotherapy is not significantly associated with receiving special education in CAYA cancer survivors.	1 study Level C[65]
Some evidence suggests that CNS irradiation among ALL and AML survivors is not significantly associated with repeating a grade in CAYA cancer survivors.	1 study Level C[63]

2.1.13 What is the risk for poor educational outcomes by <u>bone marrow/stem cell transplantation</u>?	
This study* analyzed risk factors for repeating a grade with multilevel logistic regression (adjusting for sex, age at diagnosis, parental education, financial difficulties, history of repeating a grade, CNS irradiation, relapse, HSCT, time since diagnosis, living in a traditional family unit) and found no significant association between HSCT and repeating a grade: • HSCT: n.s. (LEA cohort; n=855 ALL & AML survivors; mean 16.2 years at study; Controls: n=1304 siblings mean 18.5 years at study)	*Bonneau et al. 2019*
In this study*, multivariable logistic regression (adjusted for sex, age, migration background, nationality, language region, place of living, siblings, diagnosis, age at diagnosis, and relapse) showed no significant association of bone marrow transplantation (compared to chemotherapy) and completing compulsory school only: • Therapy: Bone marrow transplantation (Ref. Chemotherapy) OR=0.75 (95%CI:0.26-2.14, p=0.584) They found no significant association of bone marrow transplantation (compared to chemotherapy) and obtaining upper secondary education or more (in participants	*Kuehni et al. 2012*

aged ≥27 years): • Therapy: Bone marrow transplantation (Ref. Chemotherapy) OR=0.72 (95%CI:0.30-1.73, p=0.465) They found no significant association of bone marrow transplantation (compared to chemotherapy) and obtaining a university degree (in participants aged ≥27 years): • Therapy: Bone marrow transplantation (Ref. Chemotherapy) OR=0.55 (95%CI:0.11-2.83, p=0.472) *Swiss Childhood Cancer Survivor Cohort (n=961 survivors; mean age at study 27.0 years; mean age at diagnosis 8.1 years; randomly selected control sample from the general population)	
This study* analyzed risk factors for repeating a grade. They used multivariable logistic regression (adjusting for fathers' education level, child's education level at time of diagnosis, diagnosis, educational support, physical sequelae) and found no significant associations of BMT with repeating a grade: • Bone marrow transplant: Yes (Ref. No) OR=3.2 (95%CI:0.8-12.8) *(N=148 survivors; ALL/Lymphoblastic lymphoma>Solid tumor>Hodgkin lymphoma>…; mean age at study 15 years; N=194 siblings and >50,000 health schoolchildren)	*Bonneau et al. 2011*
Overall Conclusion	
Some evidence suggests that there is no significant association between stem cell transplantation and educational achievement.	1 study Level C[19]
Evidence suggests that there is no significant association between stem cell transplantation and repeating a grade.	2 studies Level B[63,64]

2.1.14 What is the risk for poor educational outcomes by duration of primary cancer treatment?	
This study* used multivariable logistic regression (adjusted for sex, age at study, age at diagnosis, diagnosis, stay on intensive care/bone marrow/stem cell transplantation unit, cancer recurrence, treatment, late effects) and found no significant association between duration of treatment and high school degree: • Duration of treatment (months): Effect measures not given, p>0.10 In multivariable logistic regression (adjusted for age at study, sex, diagnosis, and late effects), they found no significant association between duration of treatment and obtaining a college/university degree: • Duration of treatment (months): OR=0.99 (95%CI:0.99-1.00, p=0.133) *(German Childhood Cancer Registry; n=820; mean age at study 29.9 years; mean age at diagnosis 15.8 years)	*Dieluweit et al. 2011*
Overall Conclusion	
Some evidence suggests that there is no significant association between duration of primary cancer treatment and educational achievement.	1 study Level C[12]

2.1.15 What is the risk for poor educational outcomes by age at primary cancer diagnosis?	
This study* analyzed risk factors for repeating a grade with multilevel logistic regression (adjusting for sex, age at diagnosis, parental education, financial difficulties, history of repeating a grade, CNS irradiation, relapse, HSCT, time since diagnosis, living in a traditional family unit) and found that being adolescent (11-17 years) at diagnosis was associated with repeating a grade: • Age at diagnosis: 11-17 years (Ref. <11 years) OR=2.70 (95%CI:1.63-4.48; p<0.001) (LEA cohort; n=855 ALL & AML survivors; mean 16.2 years at study; Controls: n=1304 siblings mean 18.5 years at study)	*Bonneau et al. 2019*
This study* analyzed risk factors for educational achievement (having basic education only) with univariable logistic regression and found no significant association between age at diagnosis (16-20 vs. 21-25 years) and having basic education only (variable was therefore not included in the multivariable model): • Age at diagnosis: 16-20 years (Ref. 21-25 years) OR=0.56 (95%CI:0.12-2.10) *(N=160; Lymphoma>CNS tumor>Leukemia>…; Mean age at study 33.5 years; Controls: N=999 from Swiss general population)	*Mader et al. 2017*

This study* used multivariable logistic regression (adjusted for tumor type, sex, age at diagnosis, period of diagnosis, parents' education) and found no significant assocation between age at diagnosis and completing "compulsory school". They found that being younger at diagnosis (0-4 years vs. 10-14 years) was associated with decreased likelihood of survivors' completion of "higher education". Risk factors for completing compulsory school (participants aged ≥14 years): • Age at diagnosis: 0-4 years (Ref. 10-14 years) OR=3.32 (95%CI:0.46-33.35) • Age at diagnosis: 5-9 years (Ref. 10-14 years) OR=1.08 (95%CI:0.35-3.32) Risk factors for completing higher education (participants aged ≥19 years): • Age at diagnosis: 0-4 years (Ref. 10-14 years) OR=0.34 (95%CI:0.16-0.72) • Age at diagnosis: 5-9 years (Ref. 10-14 years) OR=0.62 (95%CI:0.31-1.25) *(n=637 Italian survivors; mixed diagnoses; 0-14 years at diagnosis; Controls: general population)	*Maule et al. 2017*
This study* analyzed risk factors for "no college attendance" (vs. some attendance with or without college degree) using multivariate logistic regression (adjusting for vision problems, age at diagnosis, cranial radiation, medical comorbidity. They found that younger age at diagnosis was associated with increased likelihood of not attending college: • Age at diagnosis: ≤4 years (Ref. ≥10 years) OR 2.01 (95%CI:1.29-3.12) • Age at diagnosis: 5-9 years (Ref. ≥10 years) OR 1.41 (95%CI:0.86-2.30) *Survivors of astroglial tumors in the CCSS (n=587, mean age at study 23.8 years, diagnosis <21 years)	*De Blank et al. 2016*
This study* analyzed risk factors for intermediate education, undergraduate education, and graduate education using Cox regression models (adjusted for sex, year of birth, treatment era, and parental education). We report results for intermediate education (equivalent to high school education) and graduate education (equivalent to university/college master level). They found that survivors had significantly lower hazard of completing intermediate education if diagnosed at age 0-4 years (compared to the cancer-free population): • Age at diagnosis: 0-4 (Ref. CFP) HR 0.8 (95%CI:0.7-0.9) • Age at diagnosis: 5-9 (Ref. CFP) HR 0.9 (95%CI:0.8-1.0) • Age at diagnosis: 10-14 (Ref. CFP) HR 0.9 (95%CI:0.8-1.1) They found that survivors had significantly lower hazard of completing graduate education if diagnosed at age 5-9 years (compared to the cancer-free population): • Age at diagnosis: 0-4 (Ref. CFP) HR 0.8 (95%CI:0.6-1.0) • Age at diagnosis: 5-9 (Ref. CFP) HR 0.4 (95%CI:0.3-0.7) • Age at diagnosis: 10-14 (Ref. CFP) HR 1.0 (95%CI:0.7-1.4) • Age at diagnosis: 15-18 (Ref. CFP) HR 1.1 (95%CI:0.8-1.4) *Norwegian population-based cohort study (n=2213 survivors and 1,212,623 cancer-free population controls)	*Ghaderi et al. 2016*
In this study* used multivariable logistic regression (adjusted for sex, age, migration background, nationality, language region, place of living, siblings, diagnosis, therapy, and relapse) found no significant association of age at diagnosis and compulsory school only: • Age at diagnosis: 5-9 years (Ref. 0-4 years) OR=1.12 (95%CI:0.60-2.07, p=0.721) • Age at diagnosis: ≥10 years (Ref. 0-4 years) OR=0.98 (95%CI:0.51-1.85, p=0.940) They found no significant associations of age at diagnosis and upper secondary education or more (in participants aged >27 years): • Age at diagnosis: 5-9 years (Ref. 0-4 years) OR=1.66 (95%CI:0.90-3.07, p=0.108) • Age at diagnosis: ≥10 years (Ref. 0-4 years) OR=1.28 (95%CI:0.70-2.34, p=0.431) They found no significant associations of age at diagnosis and obtaining university degree (in participants aged >27 years): • Age at diagnosis: 5-9 years (Ref. 0-4 years) OR=1.64 (95%CI:0.59-4.56, p=0.346) • Age at diagnosis: ≥10 years (Ref. 0-4 years) OR=1.04 (95%CI:0.36-2.99, p=0.944) *Swiss Childhood Cancer Survivor Cohort (n=961 survivors; mean age at study 27.0 years; mean age at diagnosis 8.1 years; randomly selected control sample from the general population)	*Kuehni et al. 2013*
This study*used multivariate logistic regression analyzes (adjusting for radiotherapy, and chemotherapy) to analyze the risk of "achievement of high school certificate" vs.	*Pfitzer et al. 2013*

less than high school certificate. They found no significant association of age at diagnosis and achievement of high school certificate: • Age at diagnosis: 6-10 years (Ref. 1-5 years): OR=2.24 (95%CI:0.45-11.25, p=0.326) • Age at diagnosis: older than 10 years (Ref. 1-5 years): OR=2.65 (95%CI:0.54-13.01, p=0.231) *Survivors of brain tumors in Germany (n=203, median age at diagnosis 11 years, median age at study 22 years)	
This study* analyzed risk factors for repeating a grade. They used multivariable logistic regression (adjusting for fathers' education level, BMT, diagnosis, educational support, physical sequelae) and found that being in primary school at time of diagnosis (vs. secondary school) was associated with repeating a grade: • Children's education level at time of diagnosis: primary school (Ref. secondary school) OR=4.4 (95%CI:1.7-11.6) *(N=148 survivors; ALL/Lymphoblastic lymphoma>Solid tumor>Hodgkin lymphoma>…; mean age at study 15 years; N=194 siblings and >50,000 health schoolchildren)	*Bonneau et al. 2011*
This study* used multivariable logistic regression (adjusted for sex, age at study, diagnosis, duration of treatment, stay on intensive care/bone marrow/stem cell transplantation unit, cancer recurrence, treatment, late effects) and found no significant association between age at diagnosis and high school degree: • Age at diagnosis: Effect measures not given, p>0.10 In multivariable logistic regression (adjusted for sex, age at study, diagnosis, duration of treatment, stay on intensive care/bone marrow/stem cell transplantation unit, cancer recurrence, treatment, late effects), they found no significant association between age at diagnosis and obtaining a college/university degree: • Age at diagnosis: Effect measures not given, p>0.10 *German Childhood Cancer Registry (n=820; mean age at study 29.9 years; mean age at diagnosis 15.8 years)	*Dieluweit et al. 2011*
This study* analyzed risk factors for level of education: Completion of high school. They used ANOVA and found that being older at diagnosis was associated with lower likelihood of high school completion: • Age at diagnosis: 10-17 years (Ref. 5-9 years): OR=0.16 (95%CI:0.05-0.92) They analyzed risk factors for level of education: College or university degree at age 25. They used ANOVA and found that younger age at diagnosis was associated with lower likelihood of having a college or university degree at 25 years: • Age at diagnosis: <5 years (Ref. ≥5 years) OR=0.36 (95%CI:0.17-0.77) They analyzed risk factors for level of education: College or university degree at age 30. They used ANOVA and found that younger age at diagnosis was associated with lower likelihood of having a college or university degree at 30 years: • Age at diagnosis: <5 years (Ref. ≥5 years) OR=0.07 (95%CI:0.02-0.31) *(N=167 survivors; ALL; 61.6%<30 years at study) and the Swedish Total Population Register (N=8350 matched controls)	*Holmqvist et al. 2010*
This study* used multivariable logistic regression (adjusted for sex, age at study, treatment, diagnosis, second tumor, epilepsy, hearing problems, and vision problems). They analyzed risk factors for level of educational attainment: University degree or higher and found no significant associations of age at diagnosis and obtaining a university degree: • Age at diagnosis: 1-4 years (Ref. 0 years) OR=0.68 (95%CI:0.44-1.03) • Age at diagnosis: 5-9 years (Ref. 0 years) OR=0.92 (95%CI:0.58-1.45) • Age at diagnosis: 10-14 years (Ref. 0 years) OR=1.02 (95%CI:0.64-1.63) They analyzed risk factors for level of educational attainment: Teaching degree or equivalent and found no significant associations of age at diagnosis and obtaining a teaching degree: • Age at diagnosis: 1-4 years (Ref. 0 years) OR=0.84 (95%CI:0.58-1.22) • Age at diagnosis: 5-9 years (Ref. 0 years) OR=1.14 (95%CI:0.77-1.70) • Age at diagnosis: 10-14 years (Ref. 0 years) OR=1.18 (95%CI:0.78-1.77)	*Lancashire et al. 2010*

They analyzed risk factors for level of educational attainment: A levels and found no significant associations of age at diagnosis and obtaining at least one A level: • Age at diagnosis: 1-4 years (Ref. 0 years) OR=0.84 (95%CI:0.61-1.16) • Age at diagnosis: 5-9 years (Ref. 0 years) OR=1.16 (95%CI:0.82-1.65) • Age at diagnosis: 10-14 years (Ref. 0 years) OR=1.27 (95%CI:0.88-1.83) They analyzed risk factors for level of educational attainment: O levels and found that older age at diagnosis was associated with increased likelihood of obtaining at least one O level: • Age at diagnosis: 1-4 years (Ref. 0 years) OR=1.04 (95%CI:0.73-1.48) • Age at diagnosis: 5-9 years (Ref. 0 years) OR=1.49 (95%CI:1.00-2.21) • Age at diagnosis: 10-14 years (Ref. 0 years) OR=1.78 (95%CI:1.18-2.68) *British Childhood Cancer Survivor Study (N=10,183 survivors; Leukemia>CNS neoplasm>Lymphoma>…; Age range at study: 16-50 years)	
Overall Conclusion	
Some evidence suggests that younger age at primary cancer diagnosis is associated with an increased risk for lower educational achievement.	8 studies Level C[7,8,12,16,19,22,83,85]
There is conflicting evidence regarding the association between age at primary cancer diagnosis and risk for repeating a grade.	2 studies Conflicting evidence[63,64]

2.1.16 What is the risk for poor educational outcomes by time since primary cancer diagnosis?	
This study* analyzed risk factors for educational achievement (having basic education only) with univariable logistic regression and found no significant association between time since diagnosis and having basic education only (variable was therefore not included in the multivariable model): • Time since diagnosis: 11-15 years (Ref. ≥16 years) OR=0.71 (95%CI:0.10-4.42) • Time since diagnosis: 5-10 years (Ref. ≥16 years) OR=1.27 (95%CI:0.28-6.52) *(N=160; Lymphoma>CNS tumor>Leukemia>…; Mean age at study 33.5 years; Controls: N=999 from Swiss general population)	*Mader et al. 2017*
Overall Conclusion	
Some evidence suggests that time since primary cancer diagnosis is not significantly associated with educational achievement.	1 study Level C[7]

2.1.17 What is the risk for poor educational outcomes after diagnosis of a relapse/second cancer?	
This study* analyzed risk factors for repeating a grade with multilevel logistic regression (adjusting for sex, age at diagnosis, parental education, financial difficulties, history of repeating a grade, CNS irradiation, relapse, HSCT, time since diagnosis, living in a traditional family unit) and found no significant association between relapse and repeating a grade: • Relapse: n.s. (LEA cohort; n=855 ALL & AML survivors; mean 16.2 years at study; Controls: n=1304 siblings mean 18.5 years at study)	*Bonneau et al. 2019*
This study* analyzed risk factors for educational achievement (having basic education only) with univariable logistic regression and found no significant association between relapse and having basic education only (variable was therefore not included in the multivariable model): • Self-reported relapse: Yes (Ref. No) OR=0.45 (95%CI:0.01-3.31) *(N=160; Lymphoma>CNS tumor>Leukemia>…; Mean age at study 33.5 years; Controls: N=999 from Swiss general population)	*Mader et al. 2017*
This study* used multivariable logistic regression (adjusted for sex, age, migration background, nationality, language region, place of living, siblings, diagnosis, treatment, and age at diagnosis) found that relapse was associated with an increased likelihood of completing compulsory school only:	*Kuehni et al. 2012*

• Relapse: Yes (Ref. No) OR=2.11 (95%CI:1.08-4.12, p=0.028) They found no significant association of relapse and obtaining upper secondary education or more (in participants aged ≥27 years): • Relapse: Yes (Ref. No) OR=0.52 (95%CI:0.25-1.05, p=0.069) They found no significant association of relapse and obtaining a university degree (in participants aged ≥27 years): • Relapse: Yes (Ref. No) OR=0.99 (95%CI:0.28-3.45, p=0.983) *Swiss Childhood Cancer Survivor Cohort (n=961 survivors; mean age at study 27.0 years; mean age at diagnosis 8.1 years; randomly selected control sample from the general population)	
This study* used multivariable logistic regression (adjusted for sex, age at study, age at diagnosis, diagnosis, duration of treatment, stay on intensive care/bone marrow/stem cell transplantation unit, treatment, late effects) and found no significant association between recurrence and high school degree: • Recurrence: Effect measures not given, p>0.10 In multivariable logistic regression (adjusted for sex, age at study, age at diagnosis, diagnosis, duration of treatment, stay on intensive care/bone marrow/stem cell transplantation unit, cancer recurrence, treatment, late effects), they found no significant association between recurrence and obtaining a college/university degree: • Recurrence: Effect measures not given, p>0.10 *German Childhood Cancer Registry (n=820; mean age at study 29.9 years; mean age at diagnosis 15.8 years)	*Dieluweit et al. 2011*
This study* used multivariable logistic regression (adjusted for sex, age at study, age at diagnosis, diagnosis, treatment, epilepsy, hearing problems, and vision problems). They analyzed risk factors for level of educational attainment: University degree or higher and found no significant assocations between second primary tumor and attainment of a university degree: • Second primary tumor: Yes at age ≤21 years (Ref. None) OR=0.68 (95%CI:0.21-2.18) • Second primary tumor: Yes at age ≥22 years (Ref. None) OR=0.97 (95%CI:0.64-1.48) They analyzed risk factors for level of educational attainment: Teaching degree or equivalent and found no significant assocations between second primary tumor and attainment of a teaching degree: • Second primary tumor: Yes at age ≤21 years (Ref. None) OR=0.45 (95%CI:0.15-1.32) • Second primary tumor: Yes at age ≥22 years (Ref. None) OR=1.10 (95%CI:0.79-1.55) They analyzed risk factors for level of educational attainment: A levels and found no significant assocations between second primary tumor and attainment of at least one A level: • Second primary tumor: Yes at age ≤21 years (Ref. None) OR=0.56 (95%CI:0.21-1.53) • Second primary tumor: Yes at age ≥22 years (Ref. None) OR=1.10 (95%CI:0.82-1.49) They analyzed risk factors for level of educational attainment: O levels and found no significant assocations between second primary tumor and attainment of at least one O level: • Second primary tumor: Yes at age ≤21 years (Ref. None) OR=0.72 (95%CI:0.24-2.14) • Second primary tumor: Yes at age ≥22 years (Ref. None) OR=0.97 (95%CI:0.70-1.33) *British Childhood Cancer Survivor Study (N=10,183 survivors; Leukemia>CNS neoplasm>Lymphoma>…; Age range at study: 16-50 years)	*Lancashire et al. 2010*
Overall Conclusion	
Some evidence suggests that a relapse is associated with an increased risk for lower educational achievement.	4 studies Level C[7,12,16,19]
Some evidence suggests that a relapse is not significantly associated with the risk for repeating a grade.	1 study Level C[63]

2.1.18 What is the risk for poor educational outcomes by late effects (not further specified)?	
This study* analyzed risk factors for educational achievement (having basic education only) with univariable logistic regression and found no significant association between late effects and having basic education only (variable was therefore not included in the multivariable model): • Self-reported late effects: Yes (Ref. No) OR=0.83 (95%CI:0.14-3.55) *(N=160; Lymphoma>CNS tumor>Leukemia>…; Mean age at study 33.5 years; Controls: N=999 from Swiss general population)	*Mader et al. 2017*
This study* tumoranalyzed risk factors for "no college attendance" (vs. some attendance with or without college degree) using multivariate logistic regression (adjusting for vision problems, age at diagnosis, age at interview, radiotherapy). They found that a medical comorbidity was associated with increased risk for not attending college: • Medical comorbidity: Yes (Ref. No) OR 1.84 (95%CI:1.25-2.72) *Survivors of astroglial tumors in the CCSS (n=587, mean age at study 23.8 years, diagnosis <21 years)	*De Blank et al. 2016*
This study* analyzed risk factors for repeating a grade. They used multivariable logistic regression (adjusting for fathers' education level, child's education level at time of diagnosis, diagnosis, educational support, BMT) and found no significant association between late effects and repeating a grade: • Late effects: Yes (Ref. No) OR=2.1 (95%CI:0.8-5.8) *(N=148 survivors; ALL/Lymphoblastic lymphoma>Solid tumor>Hodgkin lymphoma>…; mean age at study 15 years; N=194 siblings and >50,000 health schoolchildren)	*Bonneau et al. 2011*
Overall Conclusion	
Some evidence suggests that late effects are associated with an increased risk for lower educational achievement.	2 studies Level C[7,83]
Some evidence suggest that late effects are not significantly associated with repeating a grade.	1 study Level C[64]

2.1.19 What is the risk for poor educational outcomes by neurocognitive functioning?	
This study* analyzed risk factors for "less than college graduate" with multiple logistic regression (non-significant factors removed from models, adjusted for current age, psychological outcomes, and sex) and found that impaired task efficiency and impaired memory were associated with an increased risk for less than college degree, whereas impaired organization was associated with a decreased risk for less than college degree: • Task efficiency: Impaired (Ref. Not impaired) OR=1.31 (95%CI:1.02-1.69) • Memory: Impaired (Ref. Not impaired) OR=10.45 (95%CI:1.17-1.79) • Organization: Impaired (Ref. Not impaired) OR=0.73 (95%CI:0.56-0.95) • Emotional regulation: removed from the model, no effect measure reported *(CCSS, n=6192 survivors, 58% were <11 years at diagnosis (non-AeYA), 42% were 11-21 years at diagnosis (AeYA); n=390 sibling controls)	*Prasad et al. 2015*
This study* examined neurocognitive risk factors for reduced educational attainment and unemployment. Poisson models were used examining 8 neurocognitive impairment domains, current age, and sex as predictors of no college graduation (vs. college graduation). They found that impaired intellect, academics, executive function and self-reported behavior problems were associated with an increased risk for not graduating from college: • Impaired intellect RR=1.33 (95%CI:1.18-1.49) • Impaired academics RR=1.28 (95%:CI 1.14-1.44) • Impaired executive function RR=1.21 (95%CI:1.04-1.41) • Self-reported behavior problems RR=1.18 (95%CI:1.07-1.31) • Attention, memory, processing speed, and cognitive rating, current age, and sex were also tested but no results reported *Survivors of Acute Lymphoblastic Leukemia (n=567, mean age at diagnosis 6.5 years, mean age at study 33 years)	*Krull et al. 2013*

This study* used multivariable logistic regression (adjusted for duration of treatment, age at study, sex, and late effects), they found neuropsychological late effects was associated with a lower likelihood of obtaining a college/university degree: • Late effects: Neuropsychological: Yes (Ref. No) OR=0.50 (95%CI:0.27-0.91, p=0.024) *German Childhood Cancer Registry (n=820; mean age at study 29.9 years; mean age at diagnosis 15.8 years)	*Dieluweit et al. 2011*
Overall Conclusion	
There is evidence that impaired neurocognitive/neuropsychological functioning is associated with an increased risk for lower educational achievement.	3 studies Level A[9,12,86]

2.1.20 What is the risk for poor educational outcomes by psychological outcomes?	
This study* analyzed risk factors for "less than college graduate" with multiple logistic regression (non-significant factors removed from models, adjusted for current age, neurocognitive functioning, and sex) and found that impaired somatization was associated with an increased risk for less than a college degree: • Somatization: Impaired (Ref. Not impaired) OR=1.48 (95%CI:1.18-1.85) • Depression: removed from the model, no effect measure reported • Anxiety: removed from the model, no effect measure reported *(CCSS, n=6192 survivors, 58% were <11 years at diagnosis (non-AeYA), 42% were 11-21 years at diagnosis (AeYA); n=390 sibling controls)	*Prasad et al. 2015*
Overall Conclusion	
Some evidence suggests that higher somatization is associated with an increased risk for lower educational achievement.	1 study Level C[9]

2.1.21 What is the risk for poor educational outcomes by epilepsy/seizure?	
This study* used multivariable logistic regression (adjusted for sex, age at study, age at diagnosis, diagnosis, treatment, second cancer, hearing problems, and vision problems). They analyzed risk factors for level of educational attainment: University degree or higher and found that epilepsy at age ≤21 years was associated with decreased likelihood of obtaining a university degree: • Epilepsy or repeated seizures at age ≤21 years (Ref. None) OR=0.59 (95%CI:0.35-0.98) • Epilepsy or repeated seizures at age ≥22 years (Ref. None) OR=0.75 (95%CI:0.33-1.68) They analyzed risk factors for level of educational attainment: Teaching degree or equivalent and found that epilepsy was associated with decreased likelihood of obtaining a teaching degree: • Epilepsy or repeated seizures at age ≤21 years (Ref. None) OR=0.56 (95%CI:0.37-0.84) • Epilepsy or repeated seizures at age ≥22 years (Ref. None) OR=0.44 (95%CI:0.21-0.93) They analyzed risk factors for level of educational attainment: A levels and found that epilepsy was associated with decreased likelihood of obtaining at least one A level: • Epilepsy or repeated seizures at age ≤21 years (Ref. None) OR=0.52 (95%CI:0.37-0.73) • Epilepsy or repeated seizures at age ≥22 years (Ref. None) OR=0.43 (95%CI:0.25-0.73) They analyzed risk factors for level of educational attainment: O levels and found that epilepsy was associated with decreased likelihood of obtaining at least one O level: • Epilepsy or repeated seizures at age ≤21 years (Ref. None) OR=0.37 (95%CI:0.27-0.52)	*Lancashire et al. 2010*

• Epilepsy or repeated seizures at age ≥22 years (Ref. None) OR=0.60 (95%CI:0.39-0.93) *British Childhood Cancer Survivor Study (N=10,183 survivors; Leukemia>CNS neoplasm>Lymphoma>…; Age range at study: 16-50 years)	
Overall Conclusion	
Some evidence suggests that epilepsy/seizures at younger age (≤21 years) is associated with an increased risk for lower educational achievement.	1 study Level C[16]

2.1.22 What is the risk for poor educational outcomes by visual or hearing problems?	
This study* analyzed risk factors for "no college attendance" (vs. some attendance with or without college degree) using multivariate logistic regression (adjusting for medical comorbidity, age at diagnosis, age at interview, radiotherapy). They found that vision problems were not significantly associated with risk for not attending college: • Vision with impairment (Ref. vision without impairment) OR=0.93 (95%CI:0.56-1.55) • Bilateral vision loss (Ref. vision without impairment) OR=2.05 (95%CI:0.99-4.23) *Survivors of astroglial tumors in the CCSS (n=587, mean age at study 23.8 years, diagnosis <21 years)	*De Blank et al. 2016*
This study* used multivariable logistic regression (adjusted for stay at intensive care/Bone marrow/stem cell plantation unit), they found that having visual or hearing late effect was associated with a lower likelihood of obtaining a high school degree: • Late effects: Visual or hearing: Yes (Ref. No) OR=0.69 (95%CI:0.48-0.99, p=0.048) *German Childhood Cancer Registry (n=820; mean age at study 29.9 years; mean age at diagnosis 15.8 years)	*Dieluweit et al. 2011*
This study* used multivariable logistic regression (adjusted for sex, age at study, age at diagnosis, diagnosis, treatment, epilepsy, second cancer, and vision problems). They analyzed risk factors for level of educational attainment: University degree or higher and found no significant association between hearing problems and attainment of a university degree: • One or more hearing problems at ≤21 years (Ref. None) OR=0.78 (95%CI:0.45-1.34) • One or more hearing problems at ≥22 years (Ref. None) OR=0.70 (95%CI:0.35-1.40) They analyzed risk factors for level of educational attainment: Teaching degree or equivalent and found no significant association between hearing problems and attainment of a teaching degree: • One or more hearing problems at ≤21 years (Ref. None) OR=0.89 (95%CI:0.58-1.38) • One or more hearing problems at ≥22 years (Ref. None) OR=0.82 (95%CI:0.49-1.39) They analyzed risk factors for level of educational attainment: A levels and found no significant association between hearing problems and attainment of at least one A level: • One or more hearing problems at ≤21 years (Ref. None) OR=0.98 (95%CI:0.66-1.47) • One or more hearing problems at ≥22 years (Ref. None) OR=0.78 (95%CI:0.51-1.19) They analyzed risk factors for level of educational attainment: O levels and found no significant association between hearing problems and attainment of at least one O'leve: • One or more hearing problems at ≤21 years (Ref. None) OR=0.76 (95%CI:0.49-1.18) • One or more hearing problems at ≥22 years (Ref. None) OR=0.88 (95%CI:0.58-1.33) *British Childhood Cancer Survivor Study (N=10,183 survivors; Leukemia>CNS neoplasm>Lymphoma>…; Age range at study: 16-50 years)	*Lancashire et al. 2010*
Overall Conclusion	
Some evidence suggests that hearing and visual problems are associated with an increased risk for lower educational achievement.	3 studies Level C[12,16,83]

2.1.23 What is the risk for poor educational outcomes by financial difficulties?	
This study* analyzed risk factors for repeating a grade with multilevel logistic regression (adjusting for sex, age at diagnosis, parental education, financial difficulties, history of repeating a grade, CNS irradiation, relapse, HSCT, time since diagnosis, living in a traditional family unit) and found that financial difficulties at diagnosis were associated with repeating a grade: • Financial difficulties at diagnosis: Yes (Ref. No) OR=2.62 (95%CI:1.61-4.28; p<0.001) (LEA cohort; n=855 ALL & AML survivors; mean 16.2 years at study; Controls: n=1304 siblings mean 18.5 years at study)	*Bonneau et al. 2019*
Overall Conclusion	
Some evidence suggests that financial difficulties at diagnosis are associated with an increased risk for repeating a grade.	1 study Level C[63]

2.1.24 What is the risk for poor educational outcomes by history of repeating a grade?	
This study* analyzed risk factors for repeating a grade with multilevel logistic regression (adjusting for sex, age at diagnosis, parental education, financial difficulties, history of repeating a grade, CNS irradiation, relapse, HSCT, time since diagnosis, living in a traditional family unit) and found no significant association between history of repeating a grade and repeating a grade: • History of repeating a grade: n.s. (LEA cohort; n=855 ALL & AML survivors; mean 16.2 years at study; Controls: n=1304 siblings mean 18.5 years at study)	*Bonneau et al. 2019*
Overall Conclusion	
Some evidence suggests that history of repeating a grade is not significantly associated with an risk for repeating a grade.	1 study Level C[63]

2.2 What are the risk factors for poor employment outcomes?	
Conclusion single studies	
2.2.1 What is the risk for poor employment outcomes by sex?	
This study* analyzed risk factors for employment with multivariable logistic regression (adjusted for sex, age, cancer type, age at diagnosis, second primary tumour, epilepsy/seizures, hearing problem, vision problem, recurrence) and found that females are less likely to be employed than males: • Female (Ref. Male) OR=0.58 (99%CI:0.51-0.66) *(n=10,257; British Childhood Cancer Survivor Study; Controls from general population study)	*Frobisher et al. 2017*
This study* analyzed risk factors for unemployment with multivariable logistic regression (adjusted for sex, educational level, marital status, age at diagnosis, and late effects) and found that females were more likely to be unemployed than males: • Female (Ref. Male) OR=2.52 (95%CI:1.36-4.68) *(N=160; Lymphoma>CNS tumor>Leukemia>…; Mean age at study 33.5 years; Controls: N=999 from Swiss general population)	*Mader et al. 2017*
This study* analyzed risk factors for employment using multivariable logistic regression (adjusted for tumor type, sex, age at diagnosis, period of diagnosis, parents' education) and found no significant assocation between sex and employment: • Male (Ref. Female) OR=2.18 (95%CI:0.90-5.28) *(n=637 Italian survivors; mixed diagnoses; 0-14 years at diagnosis; Controls: general population)	*Maule et al. 2017*
This study* analyzed risk factors for "not employed" (vs. part- or full-time employment) using multivariate logistic regression (adjusting for medical comorbidity, radiotherapy, and vision problems). They found that female sex was associated with higher risk for unemployment: • Female (Ref. male) OR 1.68 (95%CI:1.16-2.44) *Survivors of astroglial tumors in the CCSS (n=587, mean age at study 23.8 years, diagnosis <21 years)	*De Blank et al. 2016*
This cohort study* analyzed risk factors for "unemployed" with multiple logistic regression (non-significant factors removed from models, adjusted for current age, psychological outcomes, and neurocognitive outcomes) and found that female sex was associated with a decreased risk for unemployment: • Female (Ref. male): OR=0.41 (95%CI:0.33-0.52) *(CCSS, n=6192 survivors, 58% were <11 years at diagnosis (non-AeYA), 42% were 11-21 years at diagnosis (AeYA); n=390 sibling controls)	*Prasad et al. 2015*
This cross-sectional survey* analyzed risk factors for unemployment using multivariable logistic regression analysis (n=156, excluding homemakers and students, adjusting for education, diagnosis, and late effects). They found no significant association of sex and risk for unemployment: • Male (Ref. Female) OR=2.05 (95%CI:0.71-5.90; p=0.183) *Childhood cancer survivors in Japan (n=240, mean age at study 24.3 years, mean age at diagnosis 7.5 years)	*Ishida et al. 2014*
This study* used Poisson models to examine eight neurocognitive impairment domains, and current age as predictors of "not maintaining full-time employment". They found that female sex was associated with an increased risk for not maintaining full-time employment: • Female (Ref. male): RR=1.33 (95%CI:1.06-1.66) *St. Jude cohort study; survivors of ALL (n=567, mean age at diagnosis 6.5 years, mean age at study 33 years)	*Krull et al. 2013*
This study* analyzed risk factors for unemployment. They used multivariable generalized linear models (adjusted for tumor location, age at study, race, tumor type, and age at diagnosis) and found that female survivors were at higher risk for unemployment than males: • Female (Ref. Male) RR=1.44 (95%CI:1.16-1.80) *(CCSS, n=1094 survivors of bone and soft tissue sarcoma in upper or lower extremity; median age at study 33 years; median age at diagnosis 13 years)	*Marina et al. 2013*

This study* used multivariable logistic regression (adjusted for age at study, age at diagnosis, having children, and neuropsychological late effects) to analyze risk factors for employment. They found that female survivors were less likely to be employed than males: • Female (Ref. Male) OR=0.59 (95%CI:0.34-0.89, p=0.016) *German Childhood Cancer Registry (n=820; mean age at study 29.9 years; mean age at diagnosis 15.8 years)	*Dieluweit et al. 2011*
This study* used multivariable relative risk regression (adjusted for current age, race, age at diagnosis, cranial radiation, CNS tumor resection, amputation, limb-sparing, and treatment era) to analyze risk factors for unemployment, physical occupations, nonphysical occupations, and professional occupations. Only risk factors for unemployment are presented here. The authors found that female survivors were at higher risk for unemployment than males : • Female (Ref. Male) RR=1.93 (95%CI:1.76-2.11, p<0.001) *(CCSS, n=7144 survivors; 57% were below 35 years of age at study; 52% were below 10 years at diagnosis)	*Kirchhoff et al. 2011b*
This study* analyzed risk factors for health-related unemployment. They used multivariable logistic regression (adjusted for age at study, race, years since diagnosis, cranial radiation, recurrence, secondary cancer, CNS tumor resection, amputation, and limb-saving), and found that females were more likely to be unemployed (health-related) than males: • Female (Ref. Male) OR=1.73 (95%CI:1.43-2.08, p<0.001) They also analyzed risk factors for unemployed but seeking work with multivariable logistic regression (adjusted for age at study, race, years since diagnosis, cranial radiation, recurrence, secondary cancer, CNS tumor resection, amputation, and limb-saving), and found no significant associations between sex and being unemployed but seeking work: • Female (Ref. Male) OR=1.19 (95%CI:0.94-1.51, p=0.15) (CCSS; N=6339 survivors; Leukemia>Lymphoma>CNS malignancies>…; mean age 34.2 years at study; N=1967 sibling controls (mean age 36.1 years at study))	*Kirchhoff et al. 2010*
DCOG 2010[4] Female survivors of childhood cancer are at higher risk of being unemployed than male survivors of childhood cancer[4] (Childhood Cancer Survivor Study)	*Pang et al. 2008*
DCOG 2010[4] Female survivors of childhood cancer are at higher risk of being unemployed than male survivors of childhood cancer[4]	*De Boer et al. 2006*
Overall Conclusion	
Evidence suggests that female survivors are at increased risk of unemployment compared with male survivors.	13 studies (9 samples) Level B[7,9,12,52,70,71,73,75,78,83,84,86,87]

2.2.2 What is the risk for poor employment outcomes by <u>age at study</u>?	
This study* analyzed risk factors for employment with multivariable logistic regression (adjusted for sex, age, cancer type, age at diagnosis, second primary tumour, epilepsy/seizures, hearing problem, vision problem, recurrence) and found that likelihood of employment increases with age, but declines after 45-49 years: • Age at study: 20-24 years (Ref. 16-19 years) OR=5.64 (99%CI:4.60-6.92) • Age at study: 25-29 years (Ref. 16-19 years) OR=11.76 (99%CI:9.42-14.68) • Age at study: 30-34 years (Ref. 16-19 years) OR=10.87 (99%CI:8.64-13.67) • Age at study: 35-39 years (Ref. 16-19 years) OR=11.44 (99%CI:8.88-14.73) • Age at study: 40-44 years (Ref. 16-19 years) OR=9.10 (99%CI:6.82-12.14)	*Frobisher et al. 2017*

• Age at study: 45-49 years (Ref. 16-19 years) OR=10.50 (99%CI:7.41-14.87) • Age at study: 50-54 years (Ref. 16-19 years) OR=7.96 (99%CI:5.43-11.67) • Age at study: ≥55 years (Ref. 16-19 years) OR=3.07 (99%CI:1.94-4.88) *(n=10,257; British Childhood Cancer Survivor Study; Controls from general population study)	
This study* analyzed risk factors for unemployment with univariable logistic regression and found no association of age at study with unemployment (and was therefore not included in the multivariable model): • Age at study: 30-39 years (Ref. ≥40 years) OR=1.40 (95%CI:0.62-3.17) • Age at study: 20-29 years (Ref. ≥40 years) OR=2.04 (95%CI:0.88-4.74) *(N=160; Lymphoma>CNS tumor>Leukemia>…; Mean age at study 33.5 years; Controls: N=999 from Swiss general population)	*Mader et al. 2017*
This study analyzed risk factors for "not employed" (vs. part- or full-time employment) using multivariate logistic regression (adjusting for sex, medical comorbidity, radiotherapy, and vision problems). They found no association of age at interview with risk for unemployment: • Age at interview: Not significant (p>0.20) in univariable logistic regression and was therefore not included in the multivariable model (effect measure not reported) *Survivors of astroglial tumors in the CCSS (n=587, mean age at study 23.8 years, diagnosis <21 years)	*De Blank et al. 2016*
This cohort study* analyzed risk factors for "unemployed" with multiple logistic regression (non-significant factors removed from models, adjusted for sex, psychological outcomes, and neurocognitive outcomes) and found no association with risk for unemployment: • Current age (per year): OR=0.98 (95%CI:0.97-1.00) *(CCSS, n=6192 survivors, 58% were <11 years at diagnosis (non-AeYA), 42% were 11-21 years at diagnosis (AeYA); n=390 sibling controls)	*Prasad et al. 2015*
This cross-sectional survey* analyzed risk factors for unemployment using univariable analysis (Chi^2 tests; n=156, excluding homemakers and students). They found no significant association of age at survey and risk for unemployment (variable was therefore not included in the multivariable model): • Age at survey (20 years or younger, 21-24 years, 25-29 years, 30 years or older): p=0.608 *Childhood cancer survivors in Japan (n=240, mean age at study 24.3 years, mean age at diagnosis 7.5 years)	*Ishida et al. 2014*
This study* used Poisson models to examine eight neurocognitive impairment domains, and sex as predictors of "not maintaining full-time employment". They found that older age at study was associated with a lower risk for not maintaining full-time employment: • Older current age (years) RR=0.98 (95%:CI 0.96-0.99) *St. Jude cohort study; survivors of ALL (n=567, mean age at diagnosis 6.5 years, mean age at study 33 years)	*Krull et al. 2013*
This study* analyzed risk factors for unemployment. They used multivariable generalized linear models (adjusted for tumor location, sex, race, tumor type, and age at diagnosis) and found no significant association between age at study and unemployment: • Age at questionnaire: 30–39 years (Ref. <30 years) RR=0.96 (95%CI:0.69-1.33) • Age at questionnaire: 40+ years (Ref. <30 years) RR=1.25 (95%CI:0.88-1.78) *(CCSS, n=1094 survivors of bone and soft tissue sarcoma in upper or lower extremity; median age at study 33 years; median age at diagnosis 13 years)	*Marina et al. 2013*
This study* used multivariable logistic regression (adjusted for sex, age at diagnosis, having children, and neuropsychological late effects) to analyze risk factors for employment. They found that survivors older at study were more likely to be employed: • Age at study: OR=1.04 (95%CI:1.01-1.08, p=0.017) *German Childhood Cancer Registry (n=820; mean age at study 29.9 years; mean age at diagnosis 15.8 years)	*Dieluweit et al. 2011*
This study* used multivariable relative risk regression (adjusted for sex, race, age at diagnosis, cranial radiation, CNS tumor resection, amputation, limb-sparing, and	*Kirchhoff et al. 2011b*

treatment era) to analyze risk factors for unemployment, physical occupations, nonphysical occupations, and professional occupations. Only risk factors for unemployment are presented here. The authors found no significant association between current age and unemployment: • Current age: 35-44 years (Ref. 25-34 years) RR=1.04 (95%CI:0.90-1.20, p=0.60) • Current age: 45+ years (Ref. 25-34 years) RR=0.96 (95%CI:0.74-1.26, p=0.79) *(CCSS, n=7144 survivors; 57% were below 35 years of age at study; 52% were below 10 years at diagnosis)	
This study* analyzed risk factors for health-related unemployment. They used multivariable logistic regression (adjusted for sex, race, years since diagnosis, cranial radiation, recurrence, secondary cancer, CNS tumor resection, amputation, and limb-saving), and found that being 35-44 years at study (compared to 25-34 years) was associated with increased risk for health-related unemployment: • Current age: 35-44 years (Ref. 25-34 years) OR=1.31 (95%CI:1.07-1.61, p=0.01) • Current age: 45+ years (Ref. 25-34 years) OR=1.03 (95%CI:0.71-1.49, p=0.87) They also analyzed risk factors for unemployed but seeking work with multivariable logistic regression (adjusted for sex, race, years since diagnosis, cranial radiation, recurrence, secondary cancer, CNS tumor resection, amputation, and limb-saving), and found that being 35-44 years at study (compared to 25-34 years) was associated with decreased risk for being unemployed but seeking work: • Current age: 35-44 years (Ref. 25-34 years) OR=0.62 (95%CI:0.46-0.81, p<0.001) • Current age: 45+ years (Ref. 25-34 years) OR=0.68 (95%CI:0.39-1.15) (CCSS; N=6339 survivors; Leukemia>Lymphoma>CNS malignancies>…; mean age 34.2 years at study; N=1967 sibling controls (mean age 36.1 years at study))	*Kirchhoff et al. 2010*
DCOG 2010[4] Younger survivors of childhood cancer (at time of investigation) are at higher risk of being unemployed than older survivors of childhood cancer[4]	*De Boer et al. 2006*
Overall Conclusion	
Some evidence suggests that survivors younger at follow-up are at increased risk of unemployment.	11 studies (7 samples) Level C[7,9,12,70,71,73,78,83,84,86,87]

2.2.3 What is the risk for poor employment outcomes by <u>race/migration background</u>?	
This study* analyzed risk factors for unemployment with univariable logistic regression and found no significant association of migration background and unemployment (and was therefore not included in the multivariable model): • Migration background (Ref. no migration background) OR=1.47 (95%CI:0.73-2.96) *(N=160; Lymphoma>CNS tumor>Leukemia>…; Mean age at study 33.5 years; Controls: N=999 from Swiss general population)	*Mader et al. 2017*
This study* analyzed risk factors for unemployment. They used multivariable generalized linear models (adjusted for tumor location, age at study, sex, tumor type, and age at diagnosis) and found that non-white survivors were at higher risk for unemployment: • Race: Non-white (Ref. White) RR=1.42 (95%CI:1.04-1.93) *(CCSS, n=1094 survivors of bone and soft tissue sarcoma in upper or lower extremity; median age at study 33 years; median age at diagnosis 13 years)	*Marina et al. 2013*
This study* used multivariable relative risk regression (adjusted for sex, race, age at diagnosis, cranial radiation, CNS tumor resection, amputation, limb-sparing, and treatment era) to analyze risk factors for unemployment, physical occupations, nonphysical occupations, and professional occupations. Only risk factors for unemployment are presented here. The authors found that non-white survivors were at higher risk for unemployment:	*Kirchhoff et al. 2011b*

• Race: Black, non-Hispanic (Ref. White, non-Hispanic) RR=1.36 (95%CI:1.09-1.70, p=0.007) • Race: Hispanic (Ref. White, non-Hispanic) RR=1.33 (95%CI:1.09-1.61, p=0.004) • Race: Other/mixed (Ref. White, non-Hispanic) RR=1.34 (95%CI:1.17-1.55, p<0.001) *(CCSS, n=7144 survivors; 57% were below 35 years of age at study; 52% were below 10 years at diagnosis)	
This study* analyzed risk factors for health-related unemployment. They used multivariable logistic regression (adjusted for sex, age at study, years since diagnosis, cranial radiation, recurrence, secondary cancer, CNS tumor resection, amputation, and limb-saving), and found that Black, Hispanic and other/mixed (compared to White, non-Hispanic) were at increased risk for health-related unemployment: • Race: Black, non-Hispanic (Ref. White, non-Hispanic) OR=1.89 (95%CI:1.16-3.10, p=0.01) • Race: Hispanic (Ref. White, non-Hispanic) OR=1.66 (95%CI:1.05-2.63, p=0.03) • Race: Other/mixed (Ref. White, non-Hispanic) OR=1.43 (95%CI:1.03-1.99, p=0.03) They also analyzed risk factors for unemployed but seeking work with multivariable logistic regression (adjusted for sex, age at study, years since diagnosis, cranial radiation, recurrence, secondary cancer, CNS tumor resection, amputation, and limb-saving), and found that Black, and other/mixed (compared to White, non-Hispanic) were at increased risk for being unemployed but seeking work: • Race: Black, non-Hispanic (Ref. White, non-Hispanic) OR=2.16 (95%CI:1.21-3.84, p=0.001) • Race: Hispanic (Ref. White, non-Hispanic) OR=1.51 (95%CI:0.85-2.67, p=0.15) • Race: Other/mixed (Ref. White, non-Hispanic) OR=1.57 (95%CI:1.06-2.35, p=0.03) (CCSS; N=6339 survivors; Leukemia>Lymphoma>CNS malignancies>…; mean age 34.2 years at study; N=1967 sibling controls (mean age 36.1 years at study))	*Kirchhoff et al. 2010*
Overall Conclusion	
Some evidence suggests that survivors with non-white racial backgrounds are at increased risk of unemployment.	4 studies (2 samples) Level C[7,70,71,84]

2.2.4 What is the risk for poor employment outcomes by <u>marital status</u>?	
This study* analyzed risk factors for unemployment with multivariable logistic regression (adjusted for sex, educational achievement, marital status, age at diagnosis, and late effects) and found that not being married was associated with decreased likelihood of unemployment: • Not married (Ref. Married) OR=0.53 (95%CI:0.29-0.98) *(N=160; Lymphoma>CNS tumor>Leukemia>…; Mean age at study 33.5 years; Controls: N=999 from Swiss general population)	*Mader et al. 2017*
Overall Conclusion	
Some evidence suggests that being unmarried is associated with a lower likelihood of unemployment.	1 study Level C[7]

2.2.5 What is the risk for poor employment outcomes by <u>educational achievement</u>?	
This study* analyzed risk factors for unemployment with multivariable logistic regression (adjusted for sex, educational achievement, marital status, age at diagnosis, and late effects) and found that basic education was associated with increased likelihood of unemployment: • Basic education (Ref. higher education) OR=2.78 (95%CI:1.01-7.65) *(N=160; Lymphoma>CNS tumor>Leukemia>…; Mean age at study 33.5 years; Controls: N=999 from Swiss general population)	*Mader et al. 2017*
This cross-sectional survey* analyzed risk factors for unemployment using multivariable logistic regression analysis (n=156, excluding homemakers and students, adjusting for sex, diagnosis, and late effects). They found that dropping out of school (compared to university degree) was associated with an increased risk for unemployment:	*Ishida et al. 2014*

• Education: Dropout (Ref. University) OR=8.46 (95%CI:1.66-43.1; p=0.010) • Education: Junior high school (Ref. University) OR=1.66 (95%CI:0.11-24.8; p=0.713) • Education: High school (Ref. University) OR=1.78 (95%CI:0.52-6.12; p=0.359) • Education: College or vocational school (Ref. University) OR=1.26 (95%CI:0.29-5.54; p=0.757) *Childhood cancer survivors in Japan (n=240, mean age at study 24.3 years, mean age at diagnosis 7.5 years)	
DCOG 2010[4] "Lower educational status is associated with poor employment outcomes in survivors of childhood bone tumors"[4]	*De Boer et al. 2006*
Overall Conclusion	
There is evidence that lower educational achievement is associated with an increased risk of unemployment.	3 studies Level A[7,73,87]

2.2.6 What is the risk for poor employment outcomes by <u>having children</u>?	
This study* used multivariable logistic regression (adjusted for sex, age at study, age at diagnosis, and late effects) to analyze risk factors for employment. They found that survivors with children were less likely to be employed: • Having children: Yes (Ref. No) OR=0.36 (95%CI:0.23-0.56, p<0.001) *German Childhood Cancer Registry (n=820; mean age at study 29.9 years; mean age at diagnosis 15.8 years)	*Dieluweit et al. 2011*
Overall Conclusion	
Some evidence suggests that having children is associated with an increased risk of unemployment.	1 study Level C[12]

2.2.7 What is the risk for poor employment outcomes by <u>primary cancer diagnosis</u>?	
This study* analyzed risk factors for employment with multivariable logistic regression (adjusted for sex, age, cancer type, age at diagnosis, second primary tumour, epilepsy/seizures, hearing problem, vision problem, recurrence) and found that survivors of CNS tumors and bone sarcoma were less likely to be employed: • Leukaemia (Ref. CNS neoplasm) OR=1.57 (99%CI:1.28-1.92) • Hodgkin's lymphoma (Ref. CNS neoplasm) OR=2.03 (99%CI:1.49-2.78) • Non-hodgkin's lymphoma (Ref. CNS neoplasm) OR=1.79 (99%CI:1.29-2.48) • Neuroblastoma (Ref. CNS neoplasm) OR=1.46 (99%CI:1.01-2.10) • Retinoblastoma (Ref. CNS neoplasm) OR=2.38 (99%CI:1.72-3.28) • Wilms' tumour (Ref. CNS neoplasm) OR=1.53 (99%CI:1.17-2.00) • Bone sarcoma (Ref. CNS neoplasm) OR=1.29 (99%CI:0.91-1.85) • Soft tissue sarcoma (Ref. CNS neoplasm) OR=1.60 (99%CI:1.20-2.13) • Other neoplasm (Ref. CNS neoplasm) OR=1.92 (99%CI:1.46-2.51) *(n=10,257; British Childhood Cancer Survivor Study; Controls from general population study)	*Frobisher et al. 2017*
This study* analyzed risk factors for unemployment with univariable logistic regression and found no significant associations between diagnosis and unemployment (and was therefore not included in the multivariable model): • Diagnosis: CNS tumors (Ref. Leukemia/lymphoma) OR=2.24 (95%CI:0.19-15.79) • Diagnosis: Other cancer (Ref. Leukemia/lymphoma) OR=1.46 (95%CI:0.38-6.15) *(N=160; Lymphoma>CNS tumor>Leukemia>…; Mean age at study 33.5 years; Controls: N=999 from Swiss general population)	*Mader et al. 2017*
This study* analyzed risk factors for employment using multivariable logistic regression (adjusted for tumor type, sex, age at diagnosis, period of diagnosis, parents' education) and found that diagnosis of a CNS tumor was associated with a decreased likelihood for employment: • Tumor type: CNS (Ref. Lymph.-hem. system) OR=0.19 (95%CI:0.06-0.57) • Tumor type: Other (Ref. Lymph.-hem. system) OR=0.57 (95%CI:0.19-1.68)	*Maule et al. 2017*

*(n=637 Italian survivors; mixed diagnoses; 0-14 years at diagnosis; Controls: general population)	
This cross-sectional survey* analyzed risk factors for unemployment using multivariable logistic regression analysis (n=156, excluding homemakers and students, adjusting for sex, education, and late effects). They found no significant association of diagnosis with risk for unemployment: • Lymphoma (Ref. Leukemia) OR=1.55 (95%CI:0.34-7.19, p=0.575) • Other solid cancers (Ref. Leukemia) OR=0.22 (95%CI:0.02-2.32, p=0.210) • Bone/soft tissue sarcoma (Ref. Leukemia) OR=1.05 (95%CI:0.14-7.92, p=0.964) • Brain tumor (Ref. Leukemia) OR=2.73 (95%CI:0.83-8.96, p=0.098) *Childhood cancer survivors in Japan (n=240, mean age at study 24.3 years, mean age at diagnosis 7.5 years)	*Ishida et al. 2014*
This study* analyzed risk factors for unemployment. They used multivariable generalized linear models (adjusted for tumor location, age at study, sex, race, and age at diagnosis) and found that osteosarcoma survivors (compared to soft tissue sarcoma survivors) were at higher risk for unemployment: • Ewings sarcoma (Ref. soft tissue sarcoma (STS)) RR=1.38 (95%CI:0.96-2.00) • Osteosarcoma (Ref. STS) RR=1.64 (95%CI:1.23-2.20) • Other bone (Ref. STS) RR=1.44 (95%CI:0.74-2.80) *(CCSS, n=1094 survivors of bone and soft tissue sarcoma in upper or lower extremity; median age at study 33 years; median age at diagnosis 13 years)	*Marina et al. 2013*
This study* used multivariable logistic regression (adjusted for sex, age at study, age at diagnosis, stay on intensive care/bone marrow/stem cell transplantation unit, cancer recurrence, treatment, family status, having children, duration of treatment, late effects) to analyze risk factors for employment. They found no significant association of diagnosis and employment: • Diagnosis: Effect measure not given, p>0.10 (and was therefore not included in the final model) *German Childhood Cancer Registry (n=820; mean age at study 29.9 years; mean age at diagnosis 15.8 years)	*Dieluweit et al. 2011*
This study* used logistic regression on the log scale of employment, adjusted for year of birth, residency, socioeconomic status and maternal country of birth. They analyzed risk factors for employment (excluding students) and found that CNS tumor survivors (compared to cancer-free population) were at increased risk for unemployment: • Diagnosis: Leukemia/Lymphoma (Ref. Cancer-free population) OR=0.98 (95%CI:0.89-1.08) • Diagnosis: CNS tumors (Ref. Cancer-free population) OR=0.85 (95%CI:0.77-0.94) • Diagnosis: Other cancer (Ref. Cancer-free population) OR=0.95 (95%CI:0.87-1.03) *(N=1716, CNS tumor>Leukemia>Lymphoma>…; mean age at study 31.6 years; N=1,456,089 controls (Swedish national registers))	*Boman et al. 2010*
Overall Conclusion	
Some evidence suggests that osteosarcoma survivors have an increased risk of unemployment (as compared to soft tissue sarcoma survivors).	1 study Level C[84]
Some evidence suggests that CNS tumor survivors have an increased risk of unemployment.	4 studies Level B[7,14,52,78]
Other evidence did not show that primary cancer diagnosis is associated with the risk of unemployment in survivors.	3 studies Level B[7,12,87]

2.2.8 What is the risk for poor employment outcomes by tumor location?	
This study* analyzed risk factors for unemployment. They used multivariable generalized linear models (adjusted for diagnosis, age at study, sex, race, and age at diagnosis) and found no significant association between tumor location and unemployment: • Tumor location: Lower Extremity (Ref. Upper Extremity) RR=0.81 (95%CI:0.62-1.06) *(CCSS, n=1094 survivors of bone and soft tissue sarcoma in upper or lower extremity; median age at study 33 years; median age at diagnosis 13 years)	*Marina et al. 2013*
Overall Conclusion	
Some evidence suggests that tumor location (lower vs. upper extremity) is not significantly associated with risk of unemployment in bone and soft tissue sarcoma survivors.	1 study Level C[84]

2.2.9 What is the risk for poor employment outcomes by stem cell transplantation?	
This cross-sectional survey* analyzed risk factors for unemployment using univariable analysis (Chi^2 tests; n=156, excluding homemakers and students). They found no significant association of four treatment modalities with risk for unemployment: • Treatment (chemotherapy/radiation/surgery/stem cell transplantation) all p>0.30 and therefore excluded from multivariate analyzes *Childhood cancer survivors in Japan (n=240, mean age at study 24.3 years, mean age at diagnosis 7.5 years)	*Ishida et al. 2014*
This study* used multivariable logistic regression (adjusted for sex, age at study, age at diagnosis, cancer recurrence, family status, having children, duration of treatment, late effects) to analyze risk factors for employment. They found no significant association of intensive care/bone marrow/stem cell transplantation unit and employment: • Intensive care/Bone marrow/Stem cell plantation unit: Effect measure not given, p>0.10 (and was therefore not included in the final model) *German Childhood Cancer Registry (n=820; mean age at study 29.9 years; mean age at diagnosis 15.8 years)	*Dieluweit et al. 2011*
Overall Conclusion	
Evidence suggests stem cell transplantation is not associated with risk of unemployment.	2 studies Level B[12,87]

2.2.10 What is the risk for poor employment outcomes by surgery?	
This study* analyzed risk factors for employment with multivariable logistic regression (adjusted for sex, age, treatment, age at diagnosis, second primary tumour, epilepsy/seizures, hearing problem, vision problem, recurrence) and found surgery was associated with lower likelihood of being employed: • Surgery: Yes (Ref. No) OR=0.79 (99%CI:0.64-0.96) *(n=10,257; British Childhood Cancer Survivor Study; Controls from general population study)	*Frobisher et al. 2017*
This cross-sectional survey* analyzed risk factors for unemployment using univariable analysis (Chi^2 tests; n=156, excluding homemakers and students). They found no significant association of four treatment modalities with risk for unemployment: • Treatment (chemotherapy/radiation/surgery/stem cell transplantation) all p>0.30 and therefore excluded from multivariate analyzes *Childhood cancer survivors in Japan (n=240, mean age at study 24.3 years, mean age at diagnosis 7.5 years)	*Ishida et al. 2014*
This study* used multivariable logistic regression (adjusted for sex, age at study, age at diagnosis, cancer recurrence, family status, having children, duration of treatment, late effects) to analyze risk factors for employment. They found no significant association of treatment (surgery, radiotherapy, or chemotherapy) and employment: • Treatment (surgery, radiotherapy, or chemotherapy): Effect measure not given, p>0.10 (and was therefore not included in the final model) *German Childhood Cancer Registry (n=820; mean age at study 29.9 years; mean age at diagnosis 15.8 years)	*Dieluweit et al. 2011*
Overall Conclusion	
Some evidence suggests that surgery (not further specified) is associated with increased risk of unemployment.	3 studies Level C[12,78,87]

2.2.11 What is the risk for poor employment outcomes by limb surgery (i.e. amputation or limb-saving)?	
This study* analyzed risk factors for unemployment. They used multivariable generalized linear models (adjusted for chemotherapy, tumor location, sex, and race) and found that limb sparing surgery was not significantly associated with unemployment. Lower extremity amputation was associated with an increased risk for unemployment: • Limb Surgery: Above Knee Amputation (Ref. None) RR=1.88 (95%CI:1.38-2.55) • Limb Surgery: Below Knee Amputation (Ref. None) RR=1.78 (95%CI:1.00-3.17 • Limb Surgery: Upper Extremity Amputation (Ref. None) RR=1.65 (95%CI:0.97-2.80) • Limb Surgery: Limb sparing (Ref. None) RR=0.84 (95%CI:0.58-1.24) *(CCSS, n=1094 survivors of bone and soft tissue sarcoma in upper or lower extremity; median age at study 33 years; median age at diagnosis 13 years)	*Marina et al. 2013*
This study* used multivariable relative risk regression (adjusted for sex, race, current age, age at diagnosis, cranial radiation, amputation, limb-sparing, and treatment era) to analyze risk factors for unemployment, physical occupations, nonphysical occupations, and professional occupations. Only risk factors for unemployment are presented here. The authors found that limb sparing surgery was not significantly associated with unemployment. Amputation was associated with an increased risk for unemployment: • Amputation: Yes (Ref. No) RR=1.30 (95%CI:1.09-1.55, p=0.003) • Limb-sparing: Yes (Ref. No) RR=1.40 (95%CI:1.00-1.97, p=0.05) *(CCSS, n=7144 survivors; 57% were below 35 years of age at study; 52% were below 10 years at diagnosis)	*Kirchhoff et al. 2011b*
This study* analyzed risk factors for health-related unemployment. They used multivariable logistic regression (adjusted for sex, age at study, race, time since diagnosis, recurrence, secondary cancer, cranial radiation, CNS tumor resection, and amputation), and found that limb-saving and amputation were associated with an increased risk for health-related unemployment: • Limb-saving: Yes (Ref. No) OR=4.23 (95%CI:2.33-7.69, p<0.001) • Amputation: Yes (Ref. No) OR=2.18 (95%CI:1.54-3.10, p<0.001)	*Kirchhoff et al. 2010*

They also analyzed risk factors for unemployed but seeking work with multivariable logistic regression and found no significant association of limb-saving and amputation with unemployed but seeking work: • Limb-saving: Yes (Ref. No) OR=0.28 (95%CI:0.04-2.00, p=0.21) • Amputation: Yes (Ref. No) OR=0.90 (95%CI:0.52-1.58, p=0.72) (CCSS; N=6339 survivors; Leukemia>Lymphoma>CNS malignancies>…; mean age 34.2 years at study; N=1967 sibling controls (mean age 36.1 years at study))	
Overall Conclusion	
Some evidence suggests that amputation is associated with an increased risk of unemployment.	3 studies (1 sample) Level C[70,71,84]
Some evidence suggests that limb-saving surgery is associated with an increased risk of unemployment.	3 studies (1 sample) Level C[70,71,84]

2.2.12 What is the risk for poor employment outcomes by cerebral surgery?	
This study* used multivariable relative risk regression (adjusted for sex, race, current age, age at diagnosis, cranial radiation, amputation, limb-sparing, and treatment era) to analyze risk factors for unemployment, physical occupations, nonphysical occupations, and professional occupations. Only risk factors for unemployment are presented here. The authors found that CNS tumor resection was associated with an increased risk for unemployment: • CNS tumor resection: Yes (Ref. No) RR=1.29 (95%CI:1.12-1.48, p<0.001) *(CCSS, n=7144 survivors; 57% were below 35 years of age at study; 52% were below 10 years at diagnosis)	*Kirchhoff et al. 2011b*
This study* analyzed risk factors for health-related unemployment. They used multivariable logistic regression (adjusted for sex, age at study, race, time since diagnosis, recurrence, secondary cancer, cranial radiation, amputation, and limb-saving), and found that CNS tumor resection was associated with an increased risk for health-related unemployment: • CNS tumor resection: Yes (Ref. No) OR=2.02 (95%CI:1.53-2.66,p<0.001) They also analyzed risk factors for unemployed but seeking work with multivariable logistic regression and found no significant associations of CNS tumor resection with unemployed but seeking work: • CNS tumor resection: Yes (Ref. No) OR=1.06 (95%CI:0.72-1.56, p=0.75) (CCSS; N=6339 survivors; Leukemia>Lymphoma>CNS malignancies>…; mean age 34.2 years at study; N=1967 sibling controls (mean age 36.1 years at study))	*Kirchhoff et al. 2010*
Overall Conclusion	
Some evidence suggests that cerebral surgery is associated with an increased risk of unemployment.	2 studies (1 sample) Level C[70,71]

2.2.13 What is the risk for poor employment outcomes by chemotherapy?	
This study* analyzed risk factors for employment with multivariable logistic regression (adjusted for sex, age, treatment, age at diagnosis, second primary tumour, epilepsy/seizures, hearing problem, vision problem, recurrence) and found no significant association between chemotherapy and employment: • Chemotherapy: Yes (Ref. No) OR=1.09 (99%CI:0.88-1.34) *(n=10,257; British Childhood Cancer Survivor Study; Controls from general population study)	*Frobisher et al. 2017*
This study* analyzed risk factors for unemployment with univariable logistic regression and found no significant association between chemotherapy (vs. surgery only) and unemployment (and was therefore not included in the multivariable model): • Chemotherapy (Ref. surgery only) OR=1.04 (95%CI:0.20-4.52) *(N=160; Lymphoma>CNS tumor>Leukemia>…; Mean age at study 33.5 years; Controls: N=999 from Swiss general population)	*Mader et al. 2017*

This cross-sectional survey* analyzed risk factors for unemployment using univariable analysis (Chi^2 tests; n=156, excluding homemakers and students). They found no significant association of four treatment modalities with risk for unemployment: • Treatment (chemotherapy/radiation/surgery/stem cell transplantation) all p>0.30 and therefore excluded from multivariate analyzes *Childhood cancer survivors in Japan (n=240, mean age at study 24.3 years, mean age at diagnosis 7.5 years)	*Ishida et al. 2014*
This study* analyzed risk factors for unemployment. They used multivariable generalized linear models (adjusted for limb surgery, tumor location, sex, and race) and found that alkylating agents, as well as vincristine were associated with an increased risk for unemployment: • Alkylating agent: Any (Ref. None) RR=1.44 (95%CI:1.11-1.86) + • Vincristine: Any (Ref. None) RR=1.33 (95%CI:1.03-1.71) *(CCSS, n=1094 survivors of bone and soft tissue sarcoma in upper or lower extremity; median age at study 33 years; median age at diagnosis 13 years)	*Marina et al. 2013*
This study* used multivariable logistic regression (adjusted for sex, age at study, age at diagnosis, cancer recurrence, family status, having children, duration of treatment, late effects) to analyze risk factors for employment. They found no significant association of treatment (surgery, radiotherapy, or chemotherapy) and employment: • Treatment (surgery, radiotherapy, or chemotherapy): Effect measure not given, p>0.10 (and was therefore not included in the final model) *German Childhood Cancer Registry (n=820; mean age at study 29.9 years; mean age at diagnosis 15.8 years)	*Dieluweit et al. 2011*
Overall Conclusion	
Evidence suggests that chemotherapy (not further specified) is not associated with an increased risk of unemployment.	4 studies Level B[7,12,78,87]
Some evidence suggests that vincristine and alkylating agents are associated with an increased risk of unemployment.	1 study Level C[84]

2.2.14 What is the risk for poor employment outcomes by radiotherapy?	
This study* analyzed risk factors for employment with multivariable logistic regression (adjusted for sex, age, treatment, age at diagnosis, second primary tumour, epilepsy/seizures, hearing problem, vision problem, recurrence) and found no statistically significant association between non-cranial radiotherapy and employment: • Radiotherapy: Yes, non-cranial (Ref. No) OR=0.96 (99%CI:0.77-1.19) *(n=10,257; British Childhood Cancer Survivor Study; Controls from general population study)	*Frobisher et al. 2017*
This study* analyzed risk factors for unemployment with univariable logistic regression and found no significant association between radiotherapy (vs. surgery only) and unemployment (and was therefore not included in the multivariable model): • Radiotherapy (Ref. surgery only) OR=0.37 (95%CI:0.04-2.10) *(N=160; Lymphoma>CNS tumor>Leukemia>…; Mean age at study 33.5 years; Controls: N=999 from Swiss general population)	*Mader et al. 2017*
This cross-sectional survey* analyzed risk factors for unemployment using univariable analysis (Chi^2 tests; n=156, excluding homemakers and students). They found no significant association of four treatment modalities with risk for unemployment: • Treatment (chemotherapy/radiation/surgery/stem cell transplantation) all p>0.30 and therefore excluded from multivariate analyzes *Childhood cancer survivors in Japan (n=240, mean age at study 24.3 years, mean age at diagnosis 7.5 years)	*Ishida et al. 2014*
This study* used multivariable logistic regression (adjusted for sex, age at study, age at diagnosis, cancer recurrence, family status, having children, duration of treatment, late effects) to analyze risk factors for employment. They found no significant association of treatment (surgery, radiotherapy, or chemotherapy) and employment: • Treatment (surgery, radiotherapy, or chemotherapy): Effect measure not given, p>0.10 (and was therefore not included in the final model) *German Childhood Cancer Registry (n=820; mean age at study 29.9 years; mean age at diagnosis 15.8 years)	*Dieluweit et al. 2011*
Overall Conclusion	

Some evidence suggests that radiotherapy (not further specified) is not associated with an increased risk of unemployment.	4 studies Level B[7,12,78,87]

2.2.15 What is the risk for poor employment outcomes by cranial radiation?	
This study* analyzed risk factors for employment with multivariable logistic regression (adjusted for sex, age, treatment, age at diagnosis, second primary tumour, epilepsy/seizures, hearing problem, vision problem, recurrence) and found that cranial radiotherapy was associated with a lower likelihood of being employed: • Radiotherapy: Yes, cranial (Ref. No) OR=0.62 (99%CI:0.50-0.77) *(n=10,257; British Childhood Cancer Survivor Study; Controls from general population study)	*Frobisher et al. 2017*
This study* analyzed risk factors for "not employed" (vs. part- or full-time employment) using multivariate logistic regression (adjusting for medical comorbidity, sex, and vision problems). They found that cranial radiation with 30 Gy or more was associated with an increased risk for unemployment: • Cranial radiation: ≤30 Gy (Ref. None) OR=2.41 (95%CI:0.78-7.46) • Cranial radiation: >30 Gy (Ref. None) OR=1.74 (95%CI:1.17-2.59) *Survivors of astroglial tumors in the CCSS (n=587, mean age at study 23.8 years, diagnosis <21 years)	*De Blank et al. 2016*
This study* used multivariable relative risk regression (adjusted for sex, race, current age, age at diagnosis, CNS tumor resection, amputation, limb-sparing, and treatment era) to analyze risk factors for unemployment, physical occupations, nonphysical occupations, and professional occupations. Only risk factors for unemployment are presented here. The authors found that cranial radiation with 35 Gy or more was associated with an increased risk for unemployment: • Cranial radiation: Scatter low (Ref. None) RR=0.98 (95%CI:0.87-1.11, p=0.79) • Cranial radiation: Scatter high (Ref. None) RR=0.97 (95%CI:0.72-1.31, p=0.85) • Cranial radiation: <18 Gy (Ref. None) RR=0.91 (95%CI:0.76-1.10, p=0.35) • Cranial radiation: 18-24 Gy (Ref. None) RR=1.00 (95%CI:0.85-1.16, p=0.96) • Cranial radiation: 25-34 Gy (Ref. None) RR=1.04 (95%CI:0.76-1.42, p=0.81) • Cranial radiation: ≥35 Gy (Ref. None) RR=1.61 (95%CI:1.39-1.87, p<0.001) *(CCSS, n=7144 survivors; 57% were below 35 years of age at study; 52% were below 10 years at diagnosis)	*Kirchhoff et al. 2011b*
This study* analyzed risk factors for health-related unemployment. They used multivariable logistic regression (adjusted for sex, age at study, race, time since diagnosis, recurrence, secondary cancer, CNS tumor resection, amputation, and limb-saving), and found that cranial radiation with 18 Gy or higher was associated with increased risk for health-related unemployment: • Cranial radiation: Scatter low (Ref. None) OR=0.91 (95%CI:0.69-1.20, p=0.51) • Cranial radiation: Scatter high (Ref. None) OR=1.18 (95%CI: 0.65-2.13, p=0.59) • Cranial radiation: <18 Gy (Ref. None) OR=0.97 (95%CI:0.63-1.48, p=0.87) • Cranial radiation: 18-24 Gy (Ref. None) OR=1.45 (95%CI:1.06-1.98, p=0.02) • Cranial radiation: ≥25 Gy (Ref. None) OR=3.47 (95%CI:2.54-4.74, p<0.001) They also analyzed risk factors for unemployed but seeking work with multivariable logistic regression (adjusted for sex, age at study, race, time since diagnosis, recurrence, secondary cancer, CNS tumor resection, amputation, and limb-saving), and found that cranial radiation with 25 Gy or higher was associated with increased risk for unemployed but seeking work: • Cranial radiation: Scatter low (Ref. None) OR=0.78 (95%CI:0.55-1.11, p=0.17) • Cranial radiation: Scatter high (Ref. None) OR=0.9 (95%CI: 0.42-1.92, p=0.78) • Cranial radiation: <18 Gy (Ref. None) OR=1.06 (95%CI:0.69-1.64, p=0.78) • Cranial radiation: 18-24 Gy (Ref. None) OR=1.1 (95%CI:0.75-1.63, p=0.62) • Cranial radiation: ≥25 Gy (Ref. None) OR=1.77 (95%CI:1.15-2.71, p=0.009) *(CCSS; N=6339 survivors; Leukemia>Lymphoma>CNS malignancies>…; mean age 34.2 years at study; N=1967 sibling controls (mean age 36.1 years at study))	*Kirchhoff et al. 2010*
This study* used log-binomial generalized linear models, adjusted for sex, age at diagnosis, and the maximum radiation dose to any of the other three segments. They analyzed risk factors for unemployment and found that exposure of the temporal or	*Armstrong et al. 2009*

frontal lobe to 50 Gy or more was significantly associated with higher risk of unemployment: • Posterior fossa: <30Gy (Ref. None) RR=1.1 (95%CI:0.6-1.8) • Posterior fossa: 30-49Gy (Ref. None) RR=1.3 (95%CI:0.8-2.4) • Posterior fossa: ≥50Gy (Ref. None) RR=1.2 (95%CI:0.7-1.9) • Temporal lobe: <30Gy (Ref. None) RR=1.1 (95%CI:0.7-1.9) • Temporal lobe: 30-49Gy (Ref. None) RR=1.5 (95%CI:1.0-2.4) • Temporal lobe: ≥50Gy (Ref. None) RR=1.7 (95%CI:1.1-2.6) • Frontal lobe: <30Gy (Ref. None) RR=1.2 (95%CI:0.7-2.3) • Frontal lobe: 30-49Gy (Ref. None) RR=1.6 (95%CI:0.9-3.0) • Frontal lobe: ≥50Gy (Ref. None) RR=2.1 (95%CI:1.1-4.1) • Occipital lobe: <30Gy (Ref. None) RR=1.1 (95%CI:0.6-1.9) • Occipital lobe: 30-49Gy (Ref. None) RR=1.2 (95%CI:0.7-2.2) • Occipital lobe: ≥50Gy (Ref. None) RR=1.5 (95%CI:0.8-2.7) *(CCSS, N=1877; CNS tumor survivors; 56.8% <25 years at study; Controls: N=3899 siblings)		
DCOG 2010[4]	Survivors of childhood cancer treated with (cranial) radiotherapy are at higher risk of being unemployed[4]	*Pang et al. 2008*
DCOG 2010[4]	Survivors of childhood cancer treated with (cranial) radiotherapy are at higher risk of being unemployed[4]	*De Boer et al. 2006*
Overall Conclusion		
There is evidence that higher doses of cranial radiation are associated with an increased risk of unemployment as compared to no cranial radiation.		7 studies (3 samples) Level A[27,70,71,73,75,78,83]

2.2.16 What is the risk for poor employment outcomes by <u>treatment duration</u>?	
This study* used multivariable logistic regression (adjusted for sex, age at study, age at diagnosis, stay on intensive care/bone marrow/stem cell transplantation unit, treatment, family status, having children, cancer recurrence, and late effects) to analyze risk factors for employment. They found no significant association of treatment duration and employment: • Treatment duration: Effect measure not given, p>0.10 (and was therefore not included in the final model) *German Childhood Cancer Registry (n=820; mean age at study 29.9 years; mean age at diagnosis 15.8 years)	*Dieluweit et al. 2011*
Overall Conclusion	
Some evidence suggests that treatment duration is not significantly associated with the risk of unemployment.	1 study Level C[12]

2.2.17 What is the risk for poor employment outcomes by <u>age at primary cancer diagnosis</u>?	
This study* analyzed risk factors for employment with multivariable logistic regression (adjusted for sex, age, cancer type, age at diagnosis, second primary tumour, epilepsy/seizures, hearing problem, vision problem, recurrence) and found that older age at diagnosis was associated with increased likelihood of employment: • Age at diagnosis: 1-4 years (Ref. 0 years) OR=1.07 (99%CI:0.83-1.40) • Age at diagnosis: 5-9 years (Ref. 0 years) OR=1.41 (99%CI:1.05-1.88) • Age at diagnosis: 10-14 years (Ref. 0 years) OR=1.43 (99%CI:1.05-1.94) *(n=10,257; British Childhood Cancer Survivor Study; Controls from general population study)	*Frobisher et al. 2017*

This study* analyzed risk factors for unemployment with multivariable logistic regression (adjusted for sex, educational achievement, marital status, age at diagnosis, and late effects) and found that being 16-20 years at diagnosis (vs. 21-25 years) was associated with higher risk for unemployment: • Age at diagnosis: 16-20 years (Ref. 21-25 years) OR=5.29 (95%CI:1.32-30.79) *(N=160; Lymphoma>CNS tumor>Leukemia>…; Mean age at study 33.5 years; Controls: N=999 from Swiss general population)	*Mader et al. 2017*
This study* analyzed risk factors for employment using multivariable logistic regression (adjusted for tumor type, sex, age at diagnosis, period of diagnosis, parents' education) and found no significant associations between age at diagnosis and employment: • Age at diagnosis: 0-4 years (Ref. 10-14 years) OR=0.35 (95%CI:0.09-1.32) • Age at diagnosis: 5-9 years (Ref. 10-14 years) OR=0.34 (95%CI:0.11-1.00) *(n=637 Italian survivors; mixed diagnoses; 0-14 years at diagnosis; Controls: general population)	*Maule et al. 2017*
This study* analyzed risk factors for "not employed" (vs. part- or full-time employment) using multivariate logistic regression (adjusting for sex, medical comorbidity, radiotherapy, and vision problems). They found no association of age at diagnosis with risk for unemployment: • Age at diagnosis: Not significant (p>0.20) in univariable logistic regression and was therefore not included in the multivariable model (effect measure not reported) *Survivors of astroglial tumors in the CCSS (n=587, mean age at study 23.8 years, diagnosis <21 years)	*De Blank et al. 2016*
This study* used multivariable relative risk regression (adjusted for sex, race, current age, cranial radiation, CNS tumor resection, amputation, limb-sparing, and treatment era) to analyze risk factors for unemployment, physical occupations, nonphysical occupations, and professional occupations. Only risk factors for unemployment are presented here. The authors found no significant association of age at diagnosis and unemployment: • Age at diagnosis: 5-9 years (Ref. ≤4 years) RR=0.94 (95%CI:0.82-1.07, p=0.34) • Age at diagnosis: 10-14 years (Ref. ≤4 years) RR=0.88 (95%CI:0.75-1.03, p=0.11) • Age at diagnosis: ≥15 years (Ref. ≤4 years) RR=0.85 (95%CI:0.68-1.06, p=0.14) *(CCSS, n=7144 survivors; 57% were below 35 years of age at study; 52% were below 10 years at diagnosis)	*Kirchhoff et al. 2011b*
This study* used multivariable logistic regression (adjusted for sex, age at study, having children, and neuropsychological late effects) to analyze risk factors for employment. They found that survivors older at diagnosis were less likely to be employed: • Age at diagnosis: OR=0.80 (95%CI:0.66-0.98, p=0.032) *German Childhood Cancer Registry (n=820; mean age at study 29.9 years; 15-18 years at diagnosis)	*Dieluweit et al. 2011*
Overall Conclusion	
There is conflicting evidence on the association of age at diagnosis and risk of unemployment. Some evidence suggests that diagnosis at <5 years of age or during adolescence might be associated with an increased risk for unemployment.	6 studies (5 samples) Conflicting evidence[7,12,52,70,78,83]

2.2.18 What is the risk for poor employment outcomes by time since primary cancer diagnosis?	
This study* analyzed risk factors for unemployment with univariable logistic regression and found no significant association between time since diagnosis and unemployment (and was therefore not included in the multivariable model): • Time since diagnosis: 11-15 years (Ref. ≥16 years) OR=1.49 (95%CI:0.33-7.70) • Time since diagnosis: 5-10 years (Ref. ≥16 years) OR=0.82 (95%CI:0.14-4.65) *(N=160; Lymphoma>CNS tumor>Leukemia>…; Mean age at study 33.5 years; Controls: N=999 from Swiss general population)	*Mader et al. 2017*
This study* analyzed risk factors for health-related unemployment. They used multivariable logistic regression (adjusted for sex, age at study, race, cranial radiation, recurrence, secondary cancer, CNS tumor resection, amputation, and limb-saving), and found that longer time since diagnosis was associated with increased risk for health-related unemployment:	*Kirchhoff et al. 2010*

• Years since diagnosis: 21-30 years (Ref. ≤20 years) OR=1.36 (95%CI:1.06-1.75, p=0.02) • Years since diagnosis: >30 years (Ref. ≤20 years) OR=1.89 (95%CI:1.35-2.64, p<0.001) They also analyzed risk factors for unemployed but seeking work with multivariable logistic regression (adjusted for sex, age at study, race, cranial radiation, recurrence, secondary cancer, CNS tumor resection, amputation, and limb-saving), and found no significant association between time since diagnosis and unemployed but seeking work: • Years since diagnosis: 21-30 years (Ref. ≤20 years) OR=0.90 (95%CI:0.68-1.18, p=0.43) • Years since diagnosis: >30 years (Ref. ≤20 years) OR=0.64 (95%CI:0.40-1.04, p=0.07) (CCSS; N=6339 survivors; Leukemia>Lymphoma>CNS malignancies>…; mean age 34.2 years at study; N=1967 sibling controls (mean age 36.1 years at study))	
Overall Conclusion	
Some evidence suggests that a longer time since primary cancer diagnosis is associated with an increased risk of unemployment.	2 studies Level C[7,71]

2.2.19 What is the risk for poor employment outcomes by relapse/second cancer?	
This study* analyzed risk factors for employment with multivariable logistic regression (adjusted for sex, age, cancer type, age at diagnosis, second primary tumour, epilepsy/seizures, hearing problem, vision problem, recurrence) and found that a second primary tumour or a recurrence were associated with decreased likelihood of employment: • Second primary tumour: Yes (Ref. No) OR=0.68 (99%CI:0.52-0.88) • Recurrence: Yes (Ref. No) OR=0.69 (99%CI:0.58-0.84) *(n=10,257; British Childhood Cancer Survivor Study; Controls from general population study)	*Frobisher et al. 2017*
This study* used multivariable logistic regression (adjusted for sex, age at study, age at diagnosis, stay on intensive care/bone marrow/stem cell transplantation unit, treatment, family status, having children, duration of treatment, and late effects) to analyze risk factors for employment. They found no significant association of cancer recurrence and employment: • Cancer recurrence: Effect measure not given, p>0.10 (and was therefore not included in the final model) *German Childhood Cancer Registry (n=820; mean age at study 29.9 years; mean age at diagnosis 15.8 years)	*Dieluweit et al. 2011*
This study* analyzed risk factors for health-related unemployment. They used multivariable logistic regression (adjusted for sex, age at study, race, time since diagnosis, secondary cancer, cranial radiation, CNS tumor resection, amputation, and limb-saving), and found that recurrence, as well as secondary cancer were associated with an increased risk for health-related unemployment: • Recurrence: Yes (Ref. No) OR=1.35 (95%CI:1.02-1.78, p=0.03) • Secondary cancer: Yes (Ref. No) OR=1.5 (95%CI:1.04-2.14, p=0.03) They also analyzed risk factors for unemployed but seeking work with multivariable logistic regression and found no significant associations of recurrence, as well as secondary cancer with unemployed but seeking work: • Recurrence: Yes (Ref. No) OR=1.01 (95%CI:0.69-1.49, p=0.95) • Secondary cancer: Yes (Ref. No) OR=1.28 (95%CI:0.76-2.15, p=0.38) (CCSS; N=6339 survivors; Leukemia>Lymphoma>CNS malignancies>…; mean age 34.2 years at study; N=1967 sibling controls (mean age 36.1 years at study))	*Kirchhoff et al. 2010*
Overall Conclusion	
Evidence suggests that diagnosis of a secondary cancer is associated with an increased risk of unemployment.	2 studies Level B[71,78]
Evidence suggests that cancer recurrence is associated with an increased risk of unemployment.	3 studies Level B[12,71,78]

2.2.20 What is the risk for poor employment outcomes by late effects?	
This study* analyzed risk factors for unemployment with multivariable logistic regression (adjusted for sex, educational achievement, marital status, age at diagnosis, and late effects) and found that late effects were associated with an increased risk for unemployment: • Self-reported late effects: Yes (Ref. No) OR=4.70 (95%CI:1.26-19.49) *(N=160; Lymphoma>CNS tumor>Leukemia>…; Mean age at study 33.5 years; Controls: N=999 from Swiss general population)	*Mader et al. 2017*
This study* analyzed risk factors for "not employed" (vs. part- or full-time employment) using multivariate logistic regression (adjusting for sex, radiation, and vision problems). They found that a medical comorbidity was associated with an increased risk for unemployment: • Medical comorbidity: Yes (Ref. No) OR 2.83 (95%CI:1.92-4.15) *Survivors of astroglial tumors in the CCSS (n=587, mean age at study 23.8 years, diagnosis <21 years)	*De Blank et al. 2016*
This cross-sectional survey* analyzed risk factors for unemployment using multivariable logistic regression analysis (n=156, excluding homemakers and students, adjusting for sex, education, and diagnosis). They found that late effects were associated with an increased risk for unemployment: • Late effects: Yes (Ref. No) OR=6.22 (95%CI:1.80-21.4, p=0.004) *Childhood cancer survivors in Japan (n=240, mean age at study 24.3 years, mean age at diagnosis 7.5 years)	*Ishida et al. 2014*
Overall Conclusion	
There is evidence that late effects are associated with an increased risk of unemployment.	3 studies Level A[7,83,87]

2.2.21 What is the risk for poor employment outcomes by neurocognitive functioning?	
This study* analyzed risk factors for "unemployed" with multiple logistic regression (non-significant factors removed from models, adjusted for sex, psychological outcomes, and age at study) and found that impaired task efficiency was associated with an increased risk for unemployment: • Task efficiency: Impaired (Ref. Not impaired) OR=2.93 (95%CI:2.28-3.77) • Memory, Emotional regulation, and Organization were removed from the model as non-significant predictors of being unemployed. *(CCSS, n=6192 survivors, 58% were <11 years at diagnosis (non-AeYA), 42% were 11-21 years at diagnosis (AeYA); n=390 sibling controls)	*Prasad et al. 2015*
This study* used Poisson models to examine eight neurocognitive impairment domains, current age, and sex as predictors of "not maintaining full-time employment". They found that impaired intellect, academics, attention, processing speed, and self-reported cognitive problems were associated with an increased risk for not maintaining full-time employment: • Impaired intellect RR=1.42 (95%CI:1.10-1.84) • Impaired academics RR=1.31 (95%CI:1.01-1.68) • Impaired attention RR=1.29 (95%CI 1.02-1.64) • Impaired processing speed RR=1.31 (95%CI:1.01-1.70) • Executive function, memory, and behavior problems were also tested but no results reported *St. Jude cohort study; survivors of ALL (n=567, mean age at diagnosis 6.5 years, mean age at study 33 years)	*Krull et al. 2013*
This study* used multivariable logistic regression (adjusted for sex, age at study, age at diagnosis, and having children) to analyze risk factors for employment. They found that survivors with neuropsychological late effects were less likely to be employed: • Late effects: Neuropsychological: Yes (Ref. No) OR=0.55 (95%CI:0.34-0.89, p=0.016) *German Childhood Cancer Registry (n=820; mean age at study 29.9 years; mean age at diagnosis 15.8 years)	*Dieluweit et al. 2011*
This study* used generalized linear models, adjusted for sex, age, race, time since treatment, recurrence and secondary cancers to analyze risk factors for health-related unemployment, unemployed but seeking work and not in the labor force. Only risk factors for health-related unemployment and unemployed but seeking work are presented here. They found that high scores on the NCQ (neurocognitive	*Kirchhoff et al. 2011a*

questionnaire) task efficiency and memory subscales were associated with an increased risk for health-related unemployment: • NCQ Task efficiency: ≥63 (Ref. <63) RR=2.38 (95%CI:1.89-3.01, p<0.001) • NCQ Emotional regulation: ≥63 (Ref. <63) RR=0.92 (95%CI:0.75-1.13) • NCQ Memory: ≥63 (Ref. <63) RR=1.23 (95%CI:1.01-1.50, p<0.05) They found that high scores on the NCQ task efficiency subscale were associated with an increased risk for unemployed but seeking work: • NCQ Task efficiency: ≥63 (Ref. <63) RR=1.39 (95%CI:1.02-1.91, p<0.05) • NCQ Emotional regulation: ≥63 (Ref. <63) RR=1.08 (95%CI:0.79-1.49) • NCQ Memory: ≥63 (Ref. <63) RR=0.91 (95%CI:0.67-1.24) *(CCSS, n=3763 survivors; 56% were below 35 years of age at study; <21 years at diagnosis)	
DCOG 2010[4] Executive functional problems, like cognitive control and behaviour control, are associated with being unemployed[4]	*Ness et al. 2005*
Overall Conclusion	
There is evidence that neuropsychological functioning deficits are associated with an increased risk of unemployment.	5 studies (4 samples) Level A[9,12,29,86,88]

2.2.22 What is the risk for poor employment outcomes by psychological outcomes?	
This cohort study* analyzed risk factors for "unemployed" with multiple logistic regression (non-significant factors removed from models, adjusted for sex, neurocognitive functioning, and age at study) and found that somatization and depression were associated with an increased risk for unemployment: • Somatization: Impaired (Ref. Not impaired) OR=2.29 (95%CI:1.77-2.98) • Depression: Impaired (Ref. Not impaired) OR=1.94 (95%CI:1.43-2.63) • Anxiety was removed from the model as non-significant predictor of being unemployed *(CCSS, n=6192 survivors, 58% were <11 years at diagnosis (non-AeYA), 42% were 11-21 years at diagnosis (AeYA); n=390 sibling controls)	*Prasad et al. 2015*
This study* used generalized linear models, adjusted for sex, age, race, time since treatment, recurrence and secondary cancers to analyze risk factors for health-related unemployment, unemployed but seeking work and not in the labor force. Only risk factors for health-related unemployment and unemployed but seeking work are presented here. They found that high scores of the BSI Somatization subscale were associated with an increased risk for health-related unemployment: • BSI Depression: ≥63 (Ref. <63) RR=1.15 (95%CI:0.92-1.43) • BSI Somatization: ≥63 (Ref. <63) RR=1.32 (95%CI:1.08-1.61, p<0.01) • BSI Anxiety: ≥63 (Ref. <63) RR=0.88 (95%CI:0.69-1.12) They found that high scores of the BSI Depression subscale were associated with an increased risk for unemployed but seeking work: • BSI Depression: ≥63 (Ref. <63) RR=1.57 (95%CI:1.10-2.24, p<0.05) • BSI Somatization: ≥63 (Ref. <63) RR=1.14 (95%CI:0.79-1.66) • BSI Anxiety: ≥63 (Ref. <63) RR=0.77 (95%CI:0.52-1.15) *(CCSS, n=3763 survivors; 56% were below 35 years of age at study; <21 years at diagnosis)	*Kirchhoff et al. 2011a*
DCOG 2010[4] Emotional problems, like depression and anxiety, are associated with being unemployed[4]	*Ness et al. 2005*
Overall Conclusions	

Some evidence suggests that impaired somatization is associated with an increased risk of unemployment.	2 studies (1 sample) Level C[9,88]
Evidence suggests that increased depression is associated with an increased risk of unemployment.	3 studies (2 samples) Level B[9,29,88]
Some evidence suggests that increased anxiety is associated with an increased risk of unemployment.	3 studies (2 samples) Level C[9,29,88]

2.2.23 What is the risk for poor employment outcomes by vision/hearing problems?	
This study* analyzed risk factors for employment with multivariable logistic regression (adjusted for sex, age, cancer type, age at diagnosis, second primary tumour, epilepsy/seizures, hearing problem, vision problem, recurrence) and found that vision and hearing problems were associated with decreased likelihood of employment: • Vision problems: Yes (Ref. No) OR=0.44 (99%CI:0.36-0.54) • Hearing problems: Yes (Ref. No) OR=0.75 (99%CI:0.61-0.93) *(n=10,257; British Childhood Cancer Survivor Study; Controls from general population study)	*Frobisher et al. 2017*
This study* analyzed risk factors for "not employed" (vs. part- or full-time employment) using multivariate logistic regression (adjusting for sex, radiation, and medical comorbidity). They found that bilateral vision loss was associated with an increased risk for unemployment: • Vision with impairment (Ref. vision without impairment) OR 1.29 (95%CI:0.79-2.09) • Bilateral vision loss (Ref. vision without impairment) OR 2.17 (95%CI:1.06-4.46) *Survivors of astroglial tumors in the CCSS (n=587, mean age at study 23.8 years, diagnosis <21 years)	*De Blank et al. 2016*
Overall Conclusions	
Evidence suggests that vision problems are associated with an increased risk of unemployment.	2 studies Level B[78,83]
Some evidence suggests that hearing problems are associated with an increased risk of unemployment.	1 study Level C[78]

2.2.24 What is the risk for poor employment outcomes in survivors with epilepsy?	
This study* analyzed risk factors for employment with multivariable logistic regression (adjusted for sex, age, cancer type, age at diagnosis, second primary tumour, epilepsy/seizures, hearing problem, vision problem, recurrence) and found that epilepsy/repeated seizures/fits were associated with decreased likelihood of employment: • Epilepsy/repeated seizures: Yes (Ref. No) OR=0.33 (99%CI:0.27-0.42) *(n=10,257; British Childhood Cancer Survivor Study; Controls from general population study)	*Frobisher et al. 2017*
DCOG 2010[4] Motor impairments or epilepsy are associated with poor employment outcomes in survivors of childhood CNS tumors[4]	*De Boer et al. 2006*
Overall Conclusion	
Some evidence suggests that epilepsy/seizures is associated with an increased risk of unemployment.	2 studies Level B[73,78]

2.2.25 What is the risk for poor employment outcomes in survivors with physical disabilities?	
DCOG 2010[4] Motor impairments or epilepsy are associated with poor employment outcomes in survivors of childhood CNS tumors[4]	*De Boer et al. 2006*
DCOG 2010[4] Physical disabilities are associated with poor employment outcomes in survivors of childhood cancer[4]	*Ness et al. 2005*
Overall Conclusion	
Evidence suggests that physical disability is associated with an increased risk of unemployment.	2 studies Level B[29,73]

2.2.26 What is the risk for poor employment outcomes by health-related quality of life?	
This study* used generalized linear models, adjusted for sex, age, race, time since treatment, recurrence and secondary cancers to analyze risk factors for health-related unemployment, unemployed but seeking work and not in the labor force. Only risk factors for health-related unemployment and unemployed but seeking work are presented here. They found that low physical health-related quality of life was associated with an increased risk for health-related unemployment: • SF-36 Physical health: <40 (Ref. ≥40) RR=7.83 (95%CI:6.11-10.04, p<0.001) • SF-36 Mental health: <40 (Ref. ≥40) RR=1.20 (95%CI:0.98-1.48) They found that low mental health-related quality of life was associated with an increased risk for unemployed but seeking work: • SF-36 Physical health: <40 (Ref. ≥40) RR=0.94 (95%CI:0.65-1.37) • SF-36 Mental health: <40 (Ref. ≥40) RR=2.08 (95%CI:1.48-2.91, p<0.001) *(CCSS, n=3763 survivors; 56% were below 35 years of age at study; <21 years at diagnosis)	*Kirchhoff et al. 2011a*
Overall Conclusions	
Some evidence suggests that poor physical and mental quality of life is associated with an increased risk of unemployment.	1 study Level C[88]

2.2.27 What is the risk for poor employment outcomes by IQ?	
DCOG 2010[4] Lower IQ is associated with poor employment outcomes in survivors of childhood CNS tumors[4]	*De Boer et al. 2006*
Overall Conclusion	
Some evidence suggests that lower IQ is associated with an increased risk of unemployment.	1 study Level C[73]

2.2.28 What is the risk for poor employment outcomes by parents' education?	
This study* analyzed risk factors for employment using multivariable logistic regression (adjusted for tumor type, sex, age at diagnosis, period of diagnosis, parents' education) and found that parents' lower/upper secondary level education (compared to none/primary school) was associated with an increased likelihood of employment: • Parents' education: Lower/upper secondary level (Ref. None/primary school) OR=3.11 (95%CI:1.18-8.25) • Parents' education: University degree (Ref. None/primary school) OR=1.02 (95%CI:0.21-4.85)	*Maule et al. 2017*

*(n=637 Italian survivors; mixed diagnoses; 0-14 years at diagnosis; Controls: general population)	
Overall Conclusion	
Some evidence suggests that parents' lower/upper secondary level education (Ref. None/primary school) is associated with an increased likelihood of employment.	1 study Level C[52]

3. Which interventions can improve educational/employment outcomes among childhood cancer survivors?	
Conclusion single studies	
No studies evaluating interventions to improve education or employment outcomes in survivors of childhood, adolescent and young adult cancers identified.	No studies