Conclusions of evidence tables mental health surveillance

1a. What is the risk of mental health disorders/symptoms in survivors of childhood, adolescent, and young adult (CAYA) cancer?	
Conclusion single studies	
Mental healthcare utilization	
Survivors were more likely to have a mental health visit to family physician (survivors: 68.7/1000 person-years vs. controls: 52.0/1000 person-years; RR=1.32 (95%CI:1.25-1.39), psychiatrist (survivors: 16.2/1000 person-years vs. controls: 10.4/1000 person-years; RR=1.56 (95%CI:1.41-1.72), or all mental healthcare visits (survivors: 79.5/1000 person-years vs. controls: 57.8/1000 person-years; RR=1.38 (95%CI:1.31-1.45). Cumulative Incidence of an Emergency Department Visit or Hospitalization by age 30 years % (95%CI): Psychotic disorder: Survivors: 0.92% (0.57-1.42%) Controls: 0.50% (0.38-0.65%), RR=1.78 (95%CI:1.09-2.89) Mood/affective disorder: Survivors: 3.05% (2.36-3.86%) Controls: 2.27% (2.00-2.55%), RR=1.24 (95%CI:0.96-1.59) Anxiety disorder: Survivors: 6.20% (5.23-7.28%) Controls: 5.44% (5.02-5.89%), RR=1.14 (95%CI:0.96-1.35) Other personality disorder: Survivors: 0.09% (0.04-0.14%) Controls: 0.08% (0.04-0.14%), RR=1.39 (95%CI:0.39-4.99) *Survivors (n=4117; mixed diagnoses; 0-18 yrs at diagnosis; ≥5 yrs since diagnosis). Controls: n=20,269 matched general population controls. Measurement: psychiatric admission retrieved from administrative health databases; ICD-10 and Statistical Manual of Mental Disorders	*Nathan et al. 2018*
10% of survivors* used mental health care in the past year vs. 8% of siblings (p=0.085). *Survivors from the Swiss CCSS cohort (n=1602; mixed diagnoses; mean 7.7 yrs at diagnosis; mean 25.1 yrs at study). Controls: n=703 siblings (≥16 yrs at study). Measurement: survivor self-report	*Gianinazzi et al. 2014*
6.9% of survivors had at least one hospital contact for mental health disorders vs. 8.1% of siblings. Survivors had increased risk of hospital contact for mental disorders (HR= 1.38; 95%CI: 1.26-1.51) as compared to population-based reference (male survivors: HR=1.50, 95%CI: 1.32-1.69; female survivors: HR=1.26 (95%CI: 1.10-1.44). Risk estimates decreased when compared to their siblings (male survivors: 1.31, 95%CI: 1.13-1.51; female survivors: 1.13, 95%CI: 0.97-1.33). *Survivors (n=7085 [82331 person-yrs]; mixed diagnoses; range 0-19 yrs at diagnosis); Controls: n=13105 survivor siblings (225793 person-yrs) and n=140534 individuals from general population (2508513 person yrs) of whom had 251578 sibling comparisons (4307009 person yrs). Measurement: Danish Psychiatric Central Registry	*Lund et al 2013*
3.5% of survivors* self-reported receiving current psychosocial care. *Survivors of adolescent onset cancer with data in German Childhood Cancer Registry (n=820; mixed diagnoses; mean 15.8 yrs at diagnosis [range 15-18 yrs]; mean 13.7 yrs since diagnosis; mean 30.4 yrs at study). Controls: none. Measurement: medical record review and survivor self-report	*Dieluweit et al. 2011*
2.4% of survivors* had a psychiatric hospitalization. Risk of psychiatric hospitalization for all psychiatric diagnoses, schizophrenia, and psychotic disorders was higher among survivors than the general population (standardized hospitalization ratios (SHR) during follow-up). Risk of psychiatric hospitalization for all affective disorders (including unipolar and bipolar psychoses), other reactive psychoses, other neuroses and personality disorders, psychiatric disorders in children, and transient maladaptation did not differ from that of the general population. Risk of psychiatric hospitalization overall: SHR=1.3 (95%CI:1.1-1.4) Schizophrenia and related disorders: SHR=1.6 (95%CI:1.1-2.3) Psychoses of somatic, cerebral cause: SHR=3.0 (95%CI:1.8-4.7) All affective disorders: SHR=0.8 (95%CI:0.5-1.3) Reactive unipolar affective disorders: SHR=1.0 (95%CI:0.4-2.1) Bipolar psychoses: SHR=0.7 (95%CI:0.1-2.9) Nonreactive unipolar psychoses: SHR=1.0 (95%CI:0.5-2.0) Reactive unipolar psychoses: SHR=1.2 (95%CI:0.5-2.4)	*Ross et al. 2003*

Other reactive psychoses: SHR=1.6 (95%CI:0.6-3.5) Other neuroses and personality disorders: SHP=1.0 (95%CI:0.7-1.4) Psychiatric disorders in children: SHR=2.2 (95%CI:0.9-4.6) Transient maladaptation: SHR=1.3 (95%CI:0.8-1.9) *Survivors (n=3710; mixed diagnoses; <20 yrs at diagnosis; age at study not provided). Controls: General population data from Denmark. Measurement: Danish Cancer Registry and Psychiatric Central Registry – admission numbers and primary ICD-8 diagnosis	
Overall Conclusion	
Prevalence of Psychiatric Healthcare Utilization There is evidence that survivors of childhood, adolescent, and young adult (CAYA) cancer utilize psychiatric care. The prevalence of psychiatric healthcare utilization ranged from 2 to 10%.	4 studies (3 samples)[7-10]
Prevalence of Psychiatric Healthcare Utilization in survivors versus controls Some evidence suggests that survivors of CAYA cancer have increased prevalence of psychiatric healthcare utilization as compared to the general population and similar prevalence as siblings.	4 studies (3 samples) Level B[7,8,10,11]

Depression and Mood Disorders	
10.6% of survivors* reported depressive symptoms (vs. 6.2% of siblings, p<0.001). *Survivors from the CCSS cohort (n=4484; mixed diagnoses; mean 10.5 yrs at diagnosis; mean 27.2 yrs at Baseline. Controls: n=1651 siblings. Meaurement: BSI-18 Depression subscale (cutoff ≥63)	*Brinkman et al. 2019*
11.5% of survivors* reported clinical levels of depression. *Survivors from the CCSS cohort (n=6844; mixed diagnoses; mean 7.6 yrs at diagnosis; mean 34.9 yrs at study). Controls: none. Measurement: BSI-18 Depression subscale (n=6059; cut-off: top 10th %tile)	*Crochet et al. 2019*
Survivors* of childhood cancer reported more symptoms of depression as compared with siblings (T-score means for NHW: 48.33 (survivors) vs. 47.25 (siblings), p<0.001; for Hispanics: 49.61 vs. 46.02, p<0.001; for NHB: 48.70 vs. 47.21, p=0.23), adjusting for sex, age at follow-up, year at diagnosis, methotrexate exposure (intravenous and intrathecal), corticosteroid exposure, and any grade 3 and 4 chronic medical condition. *Survivors from the CCSS cohort categorized as non-Hispanic whites (NHW), non-Hispanic blacks (NHB) and Hispanics (n=13708; mixed diagnoses; median 7.2 yrs at diagnosis [range 0-21 yrs]; median 30.9 yrs at study [range 16-54.1 yrs]). Controls: n=3055 siblings. Measurement: BSI-18 Depression subscale	*Dixon et al. 2019*
11.4% of adult survivors* of childhood cancer reported clinically significant depression. *Survivors from the CCSS cohort (n=6199; mixed diagnoses; median 10.0 yrs at diagnosis; mean 34.0 yrs at study). Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Tonorezos et al. 2019*
21% of adolescent, and 20% of adult survivors* of acute lymphoblastic leukemia reported significant depression. Mean T-scores and standard deviations for depression were similar to controls (adolescent survivors: 46.6±8.1 vs. controls 48.1±7.2; adult survivors 6.7±7.5 vs. controls 6.5±5.2, no p-values provided). *Survivors of ALL from the PETALE cohort (n=287 [n=105 adolescents, n=182 adults]; mean 6.2 yrs at diagnosis; mean 21.9 yrs at study; mean 15.7 yrs since diagnosis. Controls: Comparison to scores from n=4 other studies. Measurement: Beck Youth Inventory Depression, Beck Depression Inventory II	*Anestin et al. 2018*
9% of adult survivors* of childhood cancer reported clinically significant depression vs. 4% of controls. Survivors were more likely to report clinically significant depression than controls (OR_{adj}=4.69, 95%CI:2.70-8.16, p<0.001; adjusting for sex, age, marital status, education, income and employment). *Survivors (n=951; mixed diagnoses; median 5.0 yrs at diagnosis [range 0-15 yrs]; median 28.1 yrs since diagnosis [range 23-36 yrs]; median 34.2 yrs at study [range 24-49 yrs]). Controls: n=1130, German Household Panel. Measurement: Patient Health Questionnaire (PHQ-8)	*Burghardt et al. 2019*
More neuroblastoma survivors* than siblings reported depression/anxiety (p=0.003). *Survivors of neuroblastoma from the CCSS cohort (n=859; 97.9% <5 yrs at diagnosis yrs; 8-17 yrs at study. Controls: n=872 siblings. Meaurement: BPI depression/anxiety subscale (cutoff >10th percentile of age-matched siblings).	*Zheng et al. 2018*

11.9% of survivors* vs. 8.0% of siblings reported clinically significant depression (p=0.020). *Survivors from the CCSS cohort (n=7103; mixed diagnoses; <21 yrs at diagnosis; mean 31.8 yrs at study. Controls: n=390 siblings. Meaurement: BSI-18 Depression subscale (cutoff ≥63).	*Huang et al. 2017*
8% of pediatric and adolescent survivors* of acute lymphoblastic leukemia reported high levels of depression (moderate or severe), and 10% of adult survivors of acute lymphoblastic leukemia reported moderate to severe symptoms of depression. *Survivors of ALL from the PETALE-PSY cohort (n=204 [n=84 pediatric and adolescent survivors, n=120 adult survivors]; age at diagnosis 6 ±5 yrs; age at study: ped/ado: 8–18 yrs, adults 19–40 yrs). Measurements: Distress Thermometer; The Beck Youth Inventories (ped/ado), The Positive and Negative Affect Scale for Children (ped/ado), Beck Depression Inventory-II (adults), Beck Anxiety Inventory (adults), Positive and Negative Affect Scale (adults)	*Pépin et al. 2017*
Survivors* of Ewing sarcoma were more likely than comparisons to report symptoms of depression (survivors mean 0.39 vs. controls mean 0.22; p<0.01). *Survivors of Ewing sarcoma (n=618; 70.1% <18 yrs at diagnosis; median 29 yrs at study. Controls: n=316, median 30 yrs at study. Measurement: BSI-18 (0 ”no symptoms” to 4 ”highest symptoms”)	*Ranft et al. 2017*
10.7% of survivors* reported significant depression. *Survivors from the CCSS cohort (n=5021; mixed diagnoses; mean 8.3 yrs at diagnosis; mean 32.0 yrs at study; mean 23.2 yrs since diagnosis). Measurement: BSI-18 Depression subscale (cut-off ≥63)	*Vuotto et al. 2017*
21.9% of survivors* reported major depressive disorder (vs. 11.0% expected, p<0.0001) and 6.0% of survivors reported dysthymia (vs. 2.4% expected, p<0.0001). BSI-18 depression mean score was 3.3 (SD 4.3). *Survivors (n=348; mixed diagnoses; 0-18 yrs at diagnosis; mean 38.5 yrs at study; mean 31.5 yrs since diagnosis). Controls: French norm population n=36,105. Measurement: BSI-18 Depression subscale; Mini-International Neuropsychiatric Interview	*De Laage et al. 2016*
2.3% of survivors* of childhood and adolescent cancers and 2.5% young adult cancers were diagnosed with a mood disorder (ICD10 F3 codes including manic episodes, bipolar disorders, depressive disorders, and mood disorders) according to registry data. Mood disorder diagnoses were more common among survivors of childhood and adolescent cancers (HR=1.3; 95%CI:1.1-1.7) and young adult cancers (HR=1.3; 95%CI:1.1-1.5) than siblings. *Survivors of CAYA cancers (n=13860; mixed diagnoses; age at diagnosis 0-19 yrs: 31% and 20-34 yrs: 69%; age at study not provided). Controls: n=43,392 siblings. Measurement: ICD-10 codes and data from the Finnish Cancer Registry and Central Population Registry	*Ahomaki et al. 2015*
Survivors of retinoblastoma* reported fewer symptoms of depression as compared with siblings from the CCSS cohort (T-score means: 46.1 (survivors) vs. 47.1 (siblings), p=0.02), adjusting for age at study, race/ethnicity, highest educational level, and household income. *Retinoblastoma survivors (n=470; median age at diagnosis 1 yrs; mean 43.3 yrs at study); Controls: n=2820 siblings from the CCSS cohort. Measurement: BSI-18 Depression subscale	*Ford et al. 2015*
11.7% of survivors of AYA cancers* reported clinically significant depression vs. 8.0% of siblings. Survivors were more likely to report clinically significant depression than siblings (OR_{adj}=1.55, 95%CI:1.04-2.30), adjusting for age and sex. *Survivors of adolescent and early young adult cancer from the CCSS cohort (n=2589; mixed diagnoses; 11-21 yrs at diagnosis; ≥75% were ≥35 yrs at study). Controls: n=390 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Prasad et al. 2015*
8.2% of survivors* reported clinically significant depression vs. 7.35% of siblings. Survivors reported equivalent symptoms of depression compared to siblings (T-Score means: 46.4 (survivors) vs. 46.1 (siblings), p=0.266). *Survivors (n=614; mixed diagnoses; <19 yrs at diagnosis; mean 21.9 yrs at study [range 16-39 yrs]). Controls: n=208 siblings. Measurement: BSI-18 Chinese Version Depression subscale (cutoff ≥50)	*Chan et al. 2014*
15.0% of survivors* reported clinically significant depression. *Survivors from the St. Jude Lifetime Cohort Study (n=1863; mixed diagnoses; median 7 yrs at diagnosis; ≥10 yrs since diagnosis; median 32 yrs at study). Controls: none. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Oancea et al. 2014*
40.8% of pediatric brain tumor survivors* reported clinically significant depression.	*Brinkman, Liptak et al 2013*

*Survivors of pediatric brain tumors (n=319; mixed neurooncology diagnoses; mean 10 yrs since diagnosis [SD=5 yrs]; mean 18 yrs at study [SD=5 yrs, range 10-35 yrs]). Controls: none. Measurement: Semi-structured clinical interview based on Diagnostic and Statistical Manual of Mental Disorders IV-TR	
12% of male and 18% of female adolescent aged survivors* reported clinically significant depression. Survivors reported more symptoms of depression compared to healthy adolescents and equivalent symptoms of depression compared to siblings (raw scores: 1.83 (survivors), 1.33 (healthy adolescents), 1.27 (siblings); survivors vs. healthy adolescents p=0.025; survivors vs. siblings p=0.113) *Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥57)	*Gianinazzi et al. 2013*
15.8% of survivors* reported clinically significant depression. *Survivors from the St. Jude Lifetime Cohort Study (n=1667; mixed diagnoses; mean 33.7 yrs at study; mean 25.5 yrs of follow-up [range 11-48]). Controls: none. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Huang et al. 2013*
5.4% of survivors* of adolescent cancers reported clinically significant depression. *Survivors of adolescent onset cancer with data in German Childhood Cancer Registry (n=820; mixed diagnoses; mean 15.8 yrs at diagnosis [range 15-18 yrs]; mean 13.7 yrs since diagnosis; mean 30.4 yrs at study). Controls: none. Measurement: Hospital Anxiety and Depression Scale-Depression subscale (HADS-D) (cutoff > 11)	*Dieluweit et al. 2011*
11.5% of survivors* reported clinically significant depression. *Survivors from the CCSS cohort (n=6440; mixed diagnoses; <21 yrs at diagnosis; >5 yrs since diagnosis; mean 32.0 yrs at study). Controls: Population norms for BSI-18. Measurement: BSI-18 Depression subscale (cutoff: scores reported in ≤10% of the national standardization sample)	*Krull et al. 2011*
11.2% survivors* reported clinically significant depression. *Non-CNS tumor survivors from the CCSS cohort (n=5937; mixed diagnoses; mean 8.5 yrs at diagnosis; mean 32.2 yrs at study). Controls: none. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Kadan-Lottick et al. 2010*
17.1% of survivors' parents* reported clinically significant depression/anxiety for their adolescent vs. 9.1% for siblings (p<0.01). *Parent proxy report from the Adolescent CCSS cohort (n=1652; mixed diagnoses; 12-17 yrs at baseline study; >5 yrs since diagnosis). Controls: n=406 parent proxy report for adolescent siblings aged 12-17 yrs at baseline study. Measurement: Behavior Problem Index (BPI) parent-proxy report of depression/anxiety symptoms (cutoff: depression/anxiety subscale score falling in the bottom 10% of the national standardization sample)	*Krull, Huang et al. 2010*
13.4% of survivors* reported clinically significant depression. A greater proportion of survivors were at risk for clinically significant depression than expected based on norm population (p<0.001); however, survivors reported equivalent symptoms of depression compared to norms (T-Score means: 49.4 (survivors) vs. 50.0 (norms), p=0.053). *Survivors from the Swiss CCSS cohort (n=987; mixed diagnoses; mean 8.4 yrs at diagnosis; mean 19.5 yrs since diagnosis; mean 27.9 yrs at study). Controls: Population norms for BSI. Measurement: BSI Depression subscale (cutoff ≥63)	*Michel et al. 2010*
5.0% / 5.8% of survivors (male/female) reported clinically relevant symptoms of depression. Survivors were more likely to report clinically relevant symptoms of depression than controls (OR 1.69, 95% CI 1.01–2.81,p= 0.045) after controlling for sex, age and education. *Survivors from the German Childhood Cancer Registry (n=820; mixed diagnoses; mean 15.8 yrs at diagnosis; mean 13.7 yrs since diagnosis; mean 30.4 yrs at study). Controls: n=855 normative age-matched sample for HADS. Measurement: Hospital Anxiety and Depression Scale (HADS; cut-off ≥11)	*Seitz et al. 2010*
12.1% survivors* reported clinically significant depression. Survivors reported more symptoms of depression compared to siblings (T-Score means: 49.33 (survivors) vs. 47.46 (siblings), p_{adj}<0.003 adjusted for age, sex, intrafamily correlation), and equivalent symptoms of depression compared to community norms (T-Score mean: 50.00, p_{adj}>0.003 adjusted for age and sex) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Zeltzer et al. 2008*

17.7%* of survivors' parents* reported clinically significant depression/anxiety for their adolescent. Parents were more likely to report clinically significant depression/anxiety for survivors as compared to siblings (RR=1.5; 99%CI:1.1-2.1), adjusted for sex, current age, race/ethnicity and annual household income *Parent proxy report from the Adolescent CCSS cohort (n=2979; mixed diagnoses; mean 3.2 yrs at diagnosis; mean 14.8 yrs at study). Controls: n=649 siblings. Measurement: Behavior Problem Index (BPI) Depression/Anxiety subscale (cutoff ≥ 1.3 SD sibling mean)	*Schultz et al. 2007*
Survivors* of solid tumors reported more symptoms of depression compared to siblings (T-score means: 47.7 (survivors) vs. 46.4 (siblings), p<0.001), but fewer symptoms of depression compared to community norms (Community T-Score mean: 50, p-value not provided). *Survivors of solid tumors diagnosed in childhood from the CCSS cohort (n=2778; renal tumors, STS, and bone tumors; mean 27.1 yrs at study). Controls: n=2925 siblings (mean 29.5 yrs at study) and population norms for BSI. Measurement: BSI-18 Depression subscale	*Zebrack et al. 2007*
Survivors* reported fewer symptoms of depression compared to gender-specific community norms (T-score means: male survivors 48.3, female survivors 48.1, community: 50, p<0.001). *Survivors of childhood cancer from the CCSS cohort (n=8945; mixed diagnoses; median 26 yrs at study [range 18-48 yrs]). Controls: Population norms for BSI-18. Measurement: BSI-18 Depression subscale	*Recklitis, Parsons et al. 2006*
Survivors* of pediatric brain tumors reported more symptoms of depression compared to siblings (T-score means: 49.1 (survivors) vs. 46.5 (siblings), p<0.001), but fewer symptoms of depression compared to community norms (Norm T-Score mean: 50, p-value not provided). *Survivors of childhood brain cancer from the CCSS cohort (n=1101; mixed neurooncology diagnoses; <21 yrs at diagnosis; mean 26.5 yrs at study). Controls: n=2817 siblings (mean 29.4 yrs at study). Measurement: BSI-18 Depression subscale	*Zebrack et al. 2004*
Survivors* were more likely to report clinically significant depression than siblings (OR=1.7, 95%CI:1.4-2.0). *Survivors from the CCSS cohort (n=9535; mixed diagnoses; mean 10.00 yrs at diagnosis [range: 0.1-20.9 yrs]; mean 26.8 yrs age at study [range: 18-48 yrs]). Controls: n=2916 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Hudson et al. 2003*
5.4% of survivors* met criteria for a depressive episode vs. 3.4% of siblings. *Survivors from the CCSS cohort (n=5736; leukemia, Hodgkins lymphoma, and non-Hodgkins lymphoma diagnoses; mean 10.1 yrs at diagnosis [range: 0-20 yrs]; mean 26.9 yrs at study [range: 18-48 yrs]). Controls: n=2565 siblings. Measurement: Brief Symptom Inventory-18 (BSI-18) positive depressive symptoms transposed onto Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria for major depressive episode	*Zebrack et al. 2002*
Survivors* of acute lymphoblastic leukemia (ALL) reported more symptoms of depression compared to siblings (raw means: 8.95 (survivors) vs. 6.97 (siblings), p<0.001). *Survivors of ALL treated on Children's Cancer Group (CCG) protocols (n=580 survivors; <20 yrs at diagnosis; mean 22.6 yrs at study). Controls: n=396 siblings (mean 25.2 yrs at study). Measurement: Profile of Mood Scale-Depression subscale	*Zeltzer et al. 1997*
Overall Conclusion	
Prevalence of Depression and Mood Disorders	
Survivors of CAYA cancer are at risk for depression and mood disorders. The prevalence of clinically significant depression ranged from 5 to 40%, while prevalence of mood disorders ranged from 2.3 to 2.5%.	25 studies (11 samples)[9,12-35]
Prevalence of Depression and Mood Disorders in survivors versus controls	
There is evidence that survivors of CAYA cancer are more likely to experience clinically significant depression than siblings.	7 studies (2 samples) Level A[20-22,29,32,36,37]
There is evidence that survivors of CAYA cancer are more likely to experience clinically significant depression as compared to community norms.	4 studies Level A[18,26-28]
Some evidence suggests that survivors of CAYA cancer are more likely to experience mood disorders than siblings.	1 study Level C[25]
Symptoms of Depression in survivors versus controls	
Some evidence suggests that survivors of CAYA cancer have increased symptoms of depression as compared to siblings.	8 studies (5 samples)

	Level C[17,19,24,38-42]
Some evidence suggests that survivors of CAYA cancer have increased symptoms of depression as compared to the general population.	6 studies (4 samples) Level C[18,19,24,28,43,44]

Anxiety	
6.6% of survivors* reported symptoms of anxiety (vs. 4.9% of siblings, p=0.01). *Survivors from the CCSS cohort (n=4484; mixed diagnoses; mean 10.5 yrs at diagnosis; mean 27.2 yrs at Baseline. Controls: n=1651 siblings. Meaurement: BSI-18 Anxiety subscale (cutoff ≥63)	*Brinkman et al. 2019*
7.5% of survivors* reported clinical levels of anxiety. *Survivors from the CCSS cohort (n=6844; mixed diagnoses; mean 7.6 yrs at diagnosis; mean 34.9 yrs at study). Controls: none. Measurement: BSI-18 Anxiety subscale (n=6059; cut-off: top 10th %tile)	*Crochet et al. 2019*
Survivors* of reported similar levels of anxiety when compared with siblings (T-score means for NHW: 46.86 (survivors) vs. 46.77 (siblings), p=0.68; Hispanics: 45.41 vs. 44.54, p=0.47; NHB: 47.80 vs. 46.16, p=0.10), adjusting for sex, age at follow-up, year at diagnosis, methotrexate exposure (intravenous and intrathecal), corticosteroid exposure, and grade 3 and 4 chronic medical condition. *Survivors from the CCSS cohort categorized as non-Hispanic whites (NHW), non-Hispanic blacks (NHB) and Hispanics (n=13708; mixed diagnoses; median 7.2 yrs at diagnosis [range 0-21 yrs]; median 30.9 yrs at study [range 16-54.1 yrs]). Controls: n=3055 siblings. Measurement: BSI-18 Anxiety subscale	*Dixon et al. 2019*
7.4% of adult survivors* of childhood cancer reported clinically significant anxiety. *Survivors from the CCSS cohort (n=6199; mixed diagnoses; median 10.0 yrs at diagnosis; mean 34.0 yrs at study). Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	*Tonorezos et al. 2019*
14% of adolescent, and 27% of adult survivors* of acute lymphoblastic leukemia reported significant anxiety. In adolescents, mean T-scores and standard deviations for anxiety were similar to controls (adolescent survivors: 47.9±9.2 vs. controls 48.2±7.0, no p-value provided). In adults, means and standard deviations for anxiety were slightly higher (adult survivors 6.0±6.8 vs. controls 4.1±5.1, no p-value provided). *Survivors of ALL from the PETALE cohort (n=287 [n=105 adolescents, n=182 adults]; mean 6.2 yrs at diagnosis; mean 21.9 yrs at study; mean 15.7 yrs since diagnosis. Controls: Comparison to scores from n=4 other studies. Measurement: Beck Youth Inventory for Anxiety, Beck Anxiety Inventory	*Anestin et al. 2018*
8% of adult survivors of childhood cancer reported clinically significant generalized anxiety vs. 3% of controls, and 9% reported social anxiety vs. 5% of controls. Survivors were more likely to report clinically significant generalized anxiety and social anxiety than controls (generalized anxiety OR_{adj}=7.66, 95%CI:3.41-17.22; social anxiety OR_{adj}=2.75, 95%CI:1.40-5.42; adjusting for sex, age, marital status, education, income and employment.) *Survivors (n=951; mixed diagnoses; median 5.0 yrs at diagnosis [range 0-15 yrs]; median 28.1 yrs since diagnosis [range 23-36 yrs]; median 34.2 yrs at study [range 24-49 yrs]). Controls: n=569, German Household Panel. Measurement: Generalized Anxiety Disorder Scale (GAD-2), Mini-Spin	*Burghardt et al. 2019*
7.8% of survivors* vs. 4.4% of siblings reported clinically significant anxiety (p=0.015). *Survivors from the CCSS cohort (n=7103; mixed diagnoses; <21 yrs at diagnosis; mean 31.8 yrs at study. Controls: n=390 siblings. Meaurement: BSI-18 Anxiety subscale (cutoff ≥63).	*Huang et al. 2017*
11% of pediatric and adolescent survivors* of acute lymphoblastic leukemia reported high levels of anxiety (moderate or severe), and 8% of adult survivors reported moderate to severe symptoms of anxiety. *Survivors of ALL from the PETALE-PSY cohort (n=204 [n=84 pediatric and adolescent survivors, n=120 adult survivors]; age at diagnosis 6 ±5 yrs; age at study: ped/ado: 8–18 yrs, adults 19–40 yrs). Measurements: Distress Thermometer; The Beck Youth Inventories (ped/ado), The Positive and Negative Affect Scale for Children (ped/ado), Beck Depression Inventory-II (adults), Beck Anxiety Inventory (adults), Positive and Negative Affect Scale (adults)	*Pépin et al. 2017*
Survivors* of Ewing sarcoma were more likely than comparisons to report symptoms of anxiety (survivors mean 0.41 vs. controls mean 0.32; p<0.01).	*Ranft et al. 2017*

*Survivors of Ewing sarcoma (n=618; 70.1% <18 yrs at diagnosis; median 29 yrs at study. Controls: n=316, median 30 yrs at study. Measurement: BSI-18 Anxiety subscale (0 "no symptoms" to 4 "highest symptoms")	
6.8% of survivors* reported significant anxiety. *Survivors from the CCSS cohort (n=5021; mixed diagnoses; mean 8.3 yrs at diagnosis; mean 32.0 yrs at study; mean 23.2 yrs since diagnosis). Measurement: BSI-18 Anxiety subscale (cut-off ≥63)	*Vuotto et al. 2017*
19.5% of survivors* reported generalized anxiety disorders (vs. 13.5% expected, p<0.01). BSI-18 anxiety mean score was 3.8 (SD 4.2). *Survivors (n=348; mixed diagnoses; 0-18 yrs at diagnosis; mean 38.5 yrs at study; mean 31.5 yrs since diagnosis). Controls: French norm population n=36,105. Measurement: BSI-18 Anxiety subscale; Mini-International Neuropsychiatric Interview	*De Laage et al. 2016*
2.0% of survivors* of childhood and adolescent cancers and 1.2% young adult cancers were diagnosed with neurotic/anxiety disorders (ICD10 F4 codes including phobic anxiety disorders, other anxiety disorders, obsessive-compulsive disorder, reaction to severe stress and adjustment disorders, dissociative disorders, other neurotic disorders) according to registry data. Anxiety disorder diagnoses were more common among survivors of childhood and adolescent cancers (HR=1.3; 95%CI:1.0-1.7) and young adult cancers (HR=1.2; 95%CI:1.0-1.5) than siblings. *Survivors of CAYA cancers (n=13860; mixed diagnoses; age at diagnosis 0-19 yrs: 31% and 20-34 yrs: 69%; age at study not provided). Controls: n=43,392 siblings. Measurement: ICD-10 codes and data from the Finnish Cancer Registry and Central Population Registry	*Ahomaki et al. 2015*
Survivors of retinoblastoma* reported fewer symptoms of anxiety as compared with siblings from the CCSS cohort (T-score means: 44.6 (survivors) vs. 46.8 (siblings), p<0.01), adjusting for age at study, race/ethnicity, highest educational level, household income. *Retinoblastoma survivors (n=470; median age at diagnosis 1 yrs; mean 43.3 yrs at study); Controls: n=2820 siblings from the CCSS cohort. Measurement: BSI-18 Anxiety subscale	*Ford et al. 2015*
Prevalence of cancer-related anxiety ranged from 12.5% to 13.5% among survivors* across age groups (18-24, 25-29, 30-34, 35-39, 40-44, ≥45 yrs). *Survivors from the CCSS cohort (n=22,568; mixed diagnoses; mean 9.5 yrs at diagnosis; mean 22.4 yrs of follow-up; 18-48 yrs at study). Controls: n=7504 siblings. Measurement: Cancer-related anxiety measured with 1 item (medium/a lot/very many/extreme fears versus no/small amount of fears)	*Hudson et al. 2015*
13% of survivors* reported medium to extreme anxiety/fears as a result of cancer or its treatment. *Survivors from the CCSS cohort and Surveillance Epidemiology end results (SEER) data from 9 registries (n=181330; mixed diagnoses; ≤ 19 yrs at diagnosis; 5 –36 yrs since diagnosis; 20-49 yrs at study). Controls: none. Measurement: Cancer-related anxiety measured with 1 item (medium/a lot/very many/extreme fears versus no/small amount of fears)	*Phillips et al. 2015*
7.4% of survivors of AYA cancers* reported clinically significant anxiety vs. 4.4% of siblings. Survivors were more likely to report clinically significant anxiety than siblings (OR_{adj}=2.00, 95%CI:1.17-3.43), adjusting for age and sex. *Survivors of adolescent and early young adult cancer from the CCSS cohort (n=2589; mixed diagnoses; 11-21 yrs at diagnosis; ≥75% were ≥35 yrs at study). Controls: n=390 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	*Prasad et al. 2015*
8.2% of survivors* reported clinically significant anxiety vs. 9.0% of siblings. Survivors reported equivalent symptoms of anxiety compared to siblings (T-Score means: 43.2 (survivors) vs. 44.7 (siblings), p=0.347). *Survivors (n=614; mixed diagnoses; <19 yrs at diagnosis; mean 21.9 yrs at study [range 16-39 yrs]). Controls: n=208 siblings. Controls: n=208 siblings. Measurement: BSI-18 Chinese Version Anxiety subscale (cutoff ≥50)	*Chan et al. 2014*
11.7% of survivors* reported clinically significant anxiety. *Survivors from the St. Jude Lifetime Cohort Study (n=1863; mixed diagnoses; median 7 yrs at diagnosis; ≥10 yrs since diagnosis; median 32 yrs at study). Controls: none. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	*Oancea et al. 2014*
27.6% of pediatric brain tumor survivors* reported clinically significant anxiety. *Survivors of pediatric brain tumors (n=319; mixed neurooncology diagnoses; mean 10 yrs since diagnosis [SD=5 yrs]; mean 18 yrs at study [SD=5 yrs, range 10-35 yrs]). Controls: none. Measurement: Semi-structured clinical interview based on Diagnostic and Statistical Manual of Mental Disorders IV-TR	*Brinkman, Liptak et al 2013*

10% of male and 17% of female adolescent aged survivors* reported clinically significant anxiety. Survivors reported more symptoms of anxiety compared to healthy adolescents and equivalent symptoms of anxiety compared to siblings (raw scores: 1.85 (survivors), 1.19 (healthy adolescents), 1.55 (siblings); survivors vs. healthy adolescents p<0.001; survivors vs. siblings p=0.334) *Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥57)	*Gianinazzi et al 2013*
13.1% of survivors* reported clinically significant anxiety. *Survivors from the St. Jude Lifetime Cohort Study (n=1667; mixed diagnoses; mean 33.7 yrs at study; mean 25.5 yrs of follow-up [range 11-48]). Controls: none. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	*Huang et al. 2013*
14.7% of survivors* of adolescent cancers reported clinically significant anxiety. *Survivors of adolescent onset cancer with data in German Childhood Cancer Registry (n=820; mixed diagnoses; mean 15.8 yrs at diagnosis [range 15-18 yrs]; mean 13.7 yrs since diagnosis; mean 30.4 yrs at study). Controls: none. Measurement: Hospital Anxiety and Depression Scale- Anxiety subscale (HADS-A) (cutoff > 11)	*Dieluweit et al. 2011*
7.7% of survivors* reported clinically significant anxiety. *Survivors from the CCSS cohort (n=6440; mixed diagnoses; <21 yrs at diagnosis; >5 yrs since diagnosis; mean 32.0 yrs at study). Controls: Population norms for BSI-18. Measurement: BSI-18 Anxiety subscale (cutoff: scores reported in ≤10% of the national standardization sample)	*Krull et al. 2011*
7.5% survivors* reported clinically significant anxiety. *Non-CNS tumor survivors from the CCSS cohort (n=5937; mixed diagnoses; mean 8.5 yrs at diagnosis; mean 32.2 yrs at study). Controls: none. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	*Kadan-Lottick et al. 2010*
12.8% of survivors* reported clinically significant anxiety. A greater proportion of survivors were at risk for clinically significant anxiety than expected based on norm population (p=0.004); however, survivors reported fewer symptoms of anxiety compared to norms (T-Score means: 48.4 (survivors) vs. 50.0 (norms), p<0.001). *Survivors from the Swiss CCSS cohort (n=987; mixed diagnoses; mean 8.4 yrs at diagnosis; mean 19.5 yrs since diagnosis; mean 27.9 yrs at study). Controls: Population norms for BSI. Controls: Population norms for BSI. Measurement: BSI Anxiety subscale (cutoff ≥63)	*Michel et al. 2010*
10.0% / 19.2% of survivors (male/female) reported clinically relevant symptoms of anxiety. Survivors were more likely to report clinically relevant symptoms of anxiety than controls (OR=1.66, 95%CI:1.16–2.12, p=0.004) after controlling for sex, age and education. *Survivors from the German Childhood Cancer Registry (n=820; mixed diagnoses; mean 15.8 yrs at diagnosis; mean 13.7 yrs since diagnosis; mean 30.4 yrs at study). Controls: n=855 normative age-matched sample for HADS. Measurement: Hospital Anxiety and Depression Scale (HADS; cut-off ≥11).	*Seitz et al. 2010*
8.2% survivors* reported clinically significant anxiety. Survivors reported more symptoms of anxiety compared to siblings (T-Score means: 47.87 (survivors) vs. 46.36 (siblings), p_{adj}<0.003 adjusted for age, sex, intrafamily correlation), and fewer symptoms of anxiety compared to community norms (T-Score mean: 50.00, p_{adj}<0.003 adjusted for age and sex) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	*Zeltzer et al. 2008*
Survivors* of solid tumors reported more symptoms of anxiety compared to siblings (T-score means: 46.2 (survivors) vs. 45.4 (siblings), p<0.001), but fewer symptoms of anxiety compared to community norms (Norm T-Score mean: 50, p-value not provided). *Survivors of solid tumors diagnosed in childhood from the CCSS cohort (n=2778; renal tumors, STS, and bone tumors; mean 27.1 yrs at study). Controls: n=2925 siblings (mean 29.5 yrs at study) and population norms for BSI. Measurement: BSI-18 Anxiety subscale	*Zebrack et al. 2007*
Survivors* reported fewer symptoms of anxiety compared to gender-specific community norms (T-score means: male survivors 46.1, female survivors 47.1, community: 50, p<0.001). *Survivors of childhood cancer from the CCSS cohort (n=8945; mixed diagnoses; median 26 yrs at study [range 18-48 yrs]). Controls: Population norms for BSI-18. Measurement: BSI-18 Anxiety subscale	*Recklitis, Parsons et al. 2006*

Survivors* of pediatric brain tumors reported equivalent symptoms of anxiety compared to siblings (T-score means: 45.9 (survivors) vs. 45.4 (siblings), p=0.09), but fewer symptoms of anxiety compared to community norms (Community T-Score mean: 50, p-value not provided). *Survivors of childhood brain cancer from the CCSS cohort (n=1101; mixed neurooncology diagnoses; <21 yrs at diagnosis; mean 26.5 yrs at study). Controls: n=2817 siblings (mean 29.4 yrs at study). Measurement: BSI-18 Anxiety subscale	*Zebrack et al. 2004*
Survivors* were more likely to report clinically significant anxiety than siblings (OR=1.9, 95%CI:1.5-2.4). *Survivors from the CCSS cohort (n=9535; mixed diagnoses; mean 10.00 yrs at diagnosis [range: 0.1-20.9 yrs]; mean 26.8 yrs age at study [range: 18-48 yrs]). Controls: n=2916 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	*Hudson et al. 2003*
Child and adolescent aged survivors* reported more symptoms of total anxiety and worry compared to healthy controls (Total anxiety raw means: 49.50 (survivors) vs. 47.58 (controls), p<0.001; Worry raw means: 9.71 (survivors) vs. 9.35 (controls); p<0.001). *Child and adolescent aged survivors (n=309 survivors; mixed diagnoses; mean 5.83 yrs at diagnosis [range 1-17 yrs]; mean 13.53 yrs at study [range 8-20 yrs]). Controls: n=219 healthy children (mean 12.27 yrs at study [range 8-20 yrs]). Measurement: Revised Children's Manifest Anxiety Scale (RCMAS) Total anxiety and Physical Anxiety, Worry, and Social/Concentration subscales	*Barakat et al. 1997*
Survivors* of acute lymphoblastic leukemia (ALL) reported more symptoms of anxiety compared to siblings (raw means: 7.17 (survivors) vs. 6.087 (siblings), p=0.005). *Survivors of ALL treated on Children's Cancer Group (CCG) protocols (n=580 survivors; <20 yrs at diagnosis; mean 22.6 yrs at study). Controls: n=396 siblings (mean 25.2 yrs at study). Measurement: Profile of Mood Scale-Anxiety subscale	*Zeltzer et al. 1997*
Overall Conclusion	
Prevalence of Anxiety	
Survivors of CAYA cancer are at risk for anxiety. The prevalence of clinically significant anxiety ranged from 1 to 27%.	24 studies (11 samples)[9,12-19,21,24-35,45,46]
Prevalence of Anxiety in survivors versus controls	
There is evidence suggests that survivors of survivors of CAYA cancer cancers are more likely to experience clinically significant anxiety than siblings.	5 studies (2 samples) Level A[21,25,29,32,36]
Evidence suggests that survivors of CAYA cancer are more likely to experience clinically significant anxiety as compared to community norms.	4 studies Level A[18,26-28]
Symptoms of Anxiety in survivors versus controls	
Some evidence suggests that survivors of CAYA cancer have increased symptoms of anxiety as compared to siblings.	8 studies (5 samples) Level C[17,19,24,38-42]
Some evidence suggests that survivors of CAYA cancer have increased symptoms of anxiety as compared to community norms.	7 studies (5 samples) Level C[18,19,24,28,43,44,47]

Psychological distress	
9.9% of survivors* reported clinical levels of psychological distress. *Survivors from the CCSS cohort (n=6844; mixed diagnoses; mean 7.6 yrs at diagnosis; mean 34.9 yrs at study). Controls: none. Measurement: BSI-18 GSI (n=6059; cut-off: cut-off: top 10th %tile)	*Crochet et al. 2019*
Survivors* of childhood cancer were more likely to report symptoms of psychological distress as compared with siblings (T-score means for NHW: 47.52 (survivors) vs. 46.74 (siblings), p<0.001; for Hispanics: 48.95 vs. 46.11, p=0.005; for NHB: 47.60 vs. 45.08, p=0.08), adjusting for sex, age at follow-up, year at diagnosis, methotrexate exposure (intravenous and intrathecal), corticosteroid exposure, and any grade 3 and 4 chronic medical condition.	*Dixon et al. 2019*

*Survivors from the CCSS cohort categorized as non-Hispanic whites (NHW), non-Hispanic blacks (NHB) and Hispanics (n=13708; mixed diagnoses; median 7.2 yrs at diagnosis [range 0-21 yrs]; median 30.9 yrs at study [range 16-54.1 yrs]). Controls: n=3055 siblings. Measurement: BSI-18 GSI	
Survivors* of astrocytoma were more likely to experience poor mental health when compared to siblings (RR=1.6; 95%CI:1.4-1.8; adjusting for age, sex, race, and presence of chronic conditions). *Survivors from the CCSS cohort (n=1841; astrocytoma; <21 yrs at diagnosis; 44.5% <30 yrs at study). Controls: n=4023 siblings. Measurement: BSI-18 GSI (cut-off ≥63)	*Effinger et al. 2019*
15.6% of survivors* experienced psychological distress in the clinical range. BSI-18 GSI mean was 50.0 (SD 11.3; median 48.0). *Survivors from the St. Jude cohort (n=2969; mixed diagnoses; mean 8.4 yrs at diagnosis; mean 32.5 yrs at study; mean 24.1 yrs since diagnosis). Measurement: BSI-18 GSI (cut-off ≥63)	*Allen et al. 2018*
30% of adolescent, and 19% of adult survivors* of acute lymphoblastic leukemia reported significant psychological distress. *Survivors of ALL from the PETALE cohort (n=287 [n=105 adolescents, n=182 adults]; mean 6.2 yrs at diagnosis; mean 21.9 yrs at study; mean 15.7 yrs since diagnosis) Controls: none. Measurement: Distress Thermometer (cut-off ≥4)	*Anestin et al. 2018*
32% of adult survivors of childhood cancer reported clinically relevant distress ("any distress"). *Survivors (n=951; mixed diagnoses; median 5.0 yrs at diagnosis [range 0-15 yrs]; median 28.1 yrs since diagnosis [range 23-36 yrs]; median 34.2 yrs at study [range 24-49 yrs]). Controls: none for this outcome. Measurement: "Any distress" defined as the occurrence of ≥1 of the following: depression, somatic distress, suicidal ideation, generalized anxiety, panic, social anxiety or sleep disturbance.	*Burghardt et al. 2019*
33% of pediatric and adolescent survivors* of acute lymphoblastic leukemia had DT scores ≥3, and 25% had scores ≥4. 33% of adult survivors had DT scores ≥3, and 23% had scores ≥4. *Survivors of ALL from the PETALE-PSY cohort (n=204 (n=84 pediatric and adolescent survivors, n=120 adult survivors); 6 ±5 yrs at diagnosis; age at study (ped/ado: 8–18 yrs, adults 19–40 yrs). Measurement: Distress Thermometer (DT)	*Pépin et al. 2017*
35.3% of survivors* reported clinically significant distress. BSI-18 mean score was 10.7 (SD 10.6). *Survivors (n=348; mixed diagnoses; 0-18 yrs at diagnosis; mean 38.5 yrs at study; mean 31.5 yrs since diagnosis). Controls: French norm population n=36,105. Measurement: BSI-18 GSI (cutoffs: males ≥10, females ≥13)	*De Laage et al. 2016*
Survivors* of retinoblastoma (2.8%) were less likely to report clinically significant psychological distress than siblings (6.0%, p<0.01). Survivors of retinoblastoma reported fewer symptoms of distress as compared with sibling controls from CCSS cohort (T-score means: 43.7 (survivors) vs. 46.7 (siblings), p<0.01), adjusting for age at study, race/ethnicity, highest educational level, and household income. *Retinoblastoma survivors (n=470; median age at diagnosis 1 yrs; mean 43.3 yrs at study); Controls: n=2820 siblings from the CCSS cohort. Measurement: BSI-18 (cutoff ≥63 on GSI or any 2 of the 3 BSI-18 subscales)	*Ford et al. 2015*
Prevalence of clinically significant psychological distress ranged from 16.8% to 18.4% among survivors across age groups (18-24, 25-29, 30-34, 35-39, 40-44, ≥45 yrs), as compared to 10.0% to 12.6% in siblings. Survivors were more likely to report distress than siblings (Prevalence Ratio=1.66; 95%CI:1.52-1.80). *Survivors from the CCSS cohort (n=22,568; mixed diagnoses; mean 9.5 yrs at diagnosis; mean 22.4 yrs of follow-up; 18-48 yrs at study). Controls: n=7504 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Hudson et al. 2015*
17% of survivors* reported clinically significant psychological distress. *Survivors from the CCSS cohort and Surveillance Epidemiology end results (SEER) data from 9 registries (n=181330; mixed diagnoses; ≤ 19 yrs at diagnosis; 5 –36 yrs since diagnosis; 20-49 yrs at study). Controls: none. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Phillips et al. 2015*
10.0% of survivors* reported clinically significant psychological distress vs. 9.2% of siblings. Survivors reported equivalent symptoms of distress compared to siblings (T-Score means: 41.6 (survivors) vs. 43.3 (siblings), p=0.378). *Survivors (n=614; mixed diagnoses; <19 yrs at diagnosis; mean 21.9 yrs at study [range 16-39 yrs]). Controls: n=208 siblings. Controls: n=208 siblings. Measurement: BSI-18 Chinese Version GSI (cutoff ≥50)	*Chan et al. 2014*

Survivors* (14%) were equally likely to report clinically significant psychological distress as compared to siblings (14%, p=0.923). *Survivors from the Swiss CCSS cohort (n=1602; mixed diagnoses; mean 7.7 yrs at diagnosis; mean 25.1 yrs at study). Controls: n=703 siblings (≥16 yrs at study). Measurement: BSI-18 (cutoff ≥57 on GSI or any 2 of the 3 BSI-18 subscales)	*Gianinazzi et al. 2014*
15.1% of survivors* reported clinically significant psychological distress. *Survivors from the St. Jude Lifetime Cohort Study (n=1863; mixed diagnoses; median 7 yrs at diagnosis; ≥10 yrs since diagnosis; median 32 yrs at study). Controls: none. Measurement: BSI-18 GSI (cutoff ≥63)	*Oancea et al. 2014*
13% of adolescent aged survivors* reported clinically significant psychological distress (9% of males and 16% of females) vs. 11% of siblings. Survivors reported more symptoms of distress to healthy adolescents and equivalent symptoms of distress compared to siblings (raw scores: 4.85 (survivors), 3.30 (healthy adolescents), 3.76 (siblings); survivors vs. healthy adolescents p<0.001; survivors vs. siblings p=0.177). *Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 (cutoff ≥57 on GSI or any 2 of the 3 BSI-18 subscales)	*Gianinazzi et al 2013*
20.6% of survivors* reported clinically significant psychological distress. Survivors reported more symptoms of distress compared to norms (T-score means: 54.9 (survivors) vs 50 (norms), p<0.001). *Survivors' (n=223; mixed diagnoses; mean 9.91 yrs at diagnosis; mean 21.92 yrs at study). Controls: Population norms. Measurement: BSI-18 GSI (cutoff ≥63)	*Kim et al. 2013*
7% of survivors* reported clinically significant psychological distress. Survivors reported equivalent symptoms of distress compared to controls (mean scores: 6.6 (survivors), not provided (controls), survivors vs. controls p=0.38). *Survivors (n=652; mixed diagnoses; median 6 yrs at diagnosis; median 23 yrs at study [range 15-46 yrs]). Controls: n=440 Dutch HADS controls (mean age 51 yrs [range 17-89 yrs]). Measurement: Hospital Anxiety and Depression scale (HADS) (cutoff ≥15)	*Van der Geest et al. 2013*
22.2% of survivors* reported clinically significant psychological distress. *Survivors (n=621; mixed diagnoses; mean 11.1 yrs at diagnosis; mean 15.8 yrs since diagnosis; mean 26.9 yrs at study). Controls: none. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Zebrack et al. 2011*
9.7% survivors* reported clinically significant psychological distress. *Non-CNS tumor survivors from the CCSS cohort (n=5937; mixed diagnoses; mean 8.5 yrs at diagnosis; mean 32.2 yrs at study). Controls: none. Measurement: BSI-18 (cutoff ≥63 on GSI)	*Kadan-Lottick et al. 2010*
24.6% of survivors* reported clinically significant psychological distress (≥63 on two or more domain scales or GSI ≥63), while 14.4% of survivors reported clinically significant global distress (GSI ≥63). A significantly greater proportion of survivors were at risk for clinically significant global distress than expected based on norm population (p<0.001); however, survivors reported fewer symptoms of global distress compared to norms (GSI T-Score means: 46.2 [survivors] vs. 50.0 [norms], p<0.001). *Survivors from the Swiss CCSS cohort (n=987; mixed diagnoses; mean 8.4 yrs at diagnosis; mean 19.5 yrs since diagnosis; mean 27.9 yrs at study). Controls: Population norms for BSI-18. Measurement: BSI-18	*Michel et al. 2010*
Survivors* (15.0%) were more likely to report clinically significant psychological distress as comparted to siblings (9.8%) (OR=1.7, 95%CI:1.4-2.0, p<0.001). *Survivors from the CCSS cohort (n=4151 ALL survivors; median 4 yrs at diagnosis; mean 21.2 yrs since diagnosis; median 26 yrs at study. Controls: n=3083 siblings. Measurement: BSI-18 (cutoff ≥63 on any subscale)	*Mody et al. 2008*
10.5% survivors* reported clinically significant psychological distress. Survivors reported more symptoms of distress compared to siblings (T-Score means: 49.17 (survivors) vs. 46.64 (siblings), p_{adj}<0.003 adjusted for age, sex, intrafamily correlation), and equivalent symptoms of distress compared to community norms (T-Score mean: 50.00, p_{adj}>0.003 adjusted for age and sex). *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI)	*Zeltzer et al. 2008*
8% of survivors* of solid tumors reported clinically significant psychological distress vs. 5% of siblings. Survivors reported more symptoms of psychological distress compared to siblings (T-score means: 46.3 (survivors) vs. 44.8 (siblings); p<0.001 (univariable) and p_{adj}<0.05 adjusted for sociodemographic, SES, health status), but fewer symptoms of	*Zebrack et al. 2007*

distress compared to community norms (Norms T-Score mean: 50, p-value not provided). *Survivors of solid tumors diagnosed in childhood from the CCSS cohort (n=2778; renal tumors, STS, and bone tumors; mean 27.1 yrs at study). Controls: n=2925 siblings (mean 29.5 yrs at study) and population norms for BSI. Measurement: BSI-18 (cutoff ≥63 on GSI)	
Survivors* (7.4% of men and 9% of women) were less likely to report clinically significant psychological distress as compared to gender-specific community norms (10% expected from norms; men vs. norms: p<0.001, women vs. norms: p<0.05). Survivors reported fewer symptoms of distress compared to norms (T-score means: 46.6 (male survivors), 46.9 (female survivors), 50 (norms), p<0.001). *Survivors of childhood cancer from the CCSS cohort (n=8945; mixed diagnoses; median 26 yrs at study [range 18-48 yrs]). Controls: Population norms for BSI-18. Measurement: BSI-18 (cutoff ≥63 on GSI)	*Recklitis, Parsons et al. 2006*
11% of survivors* of pediatric brain tumors reported clinically significant psychological distress vs. 5% of siblings. Survivors reported more symptoms of distress compared to siblings (T-score means: 46.9 (survivors) vs. 44.8 (siblings), p<0.001), but fewer symptoms of distress compared to community norms (Norms T-Score mean: 50, p-value not provided). *Survivors of childhood brain cancer from the CCSS cohort (n=1101; mixed neurooncology diagnoses; <21 yrs at diagnosis; mean 26.5 yrs at study). Controls: n=2817 siblings (mean 29.4 yrs at study). Measurement: BSI-18 (cutoff ≥63 on GSI)	*Zebrack et al. 2004*
24% of survivors of acute lymphoblastic leukemia* reported clinically significant negative affect. *Survivors treated on Children's Cancer Group (CCG) acute lymphoblastic leukemia protocols (n=555; <20 yrs at diagnosis; 18-33 yrs at study). Controls: none. Measurement: Profile of Mood Scale-Total score (cutoff >33)	*Glover et al. 2003*
Survivors* were more likely to report clinically significant distress than siblings (OR=2.2, 95%CI:1.8-2.8). *Survivors from the CCSS cohort (n=9535; mixed diagnoses; mean 10.00 yrs at diagnosis [range: 0.1-20.9 yrs]; mean 26.8 yrs age at study [range: 18-48 yrs]). Controls: n=2916 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Hudson et al. 2003*
Survivors* of acute lymphoblastic leukemia (ALL) reported more symptoms of negative affect compared to siblings (raw means: 17.90 (survivors) vs. 12.52 (siblings), p<0.001). *Survivors of ALL treated on Children's Cancer Group (CCG) protocols (n=580 survivors; <20 yrs at diagnosis; mean 22.6 yrs at study). Controls: n=396 siblings (mean 25.2 yrs at study). Measurement: Profile of Mood Scale-Total score	Zeltzer et al. 1997
Overall Conclusion	
Prevalence of Psychological Distress	
Survivors of CAYA cancer are at risk for psychological distress. The prevalence of clinically significant psychological distress ranged from 2 to 35%.	25 studies (12 samples)[7,14,15,17-19,24,26,27,30,33-35,38,39,41,43,45,46,48-53]
Prevalence of Psychological Distress in survivors versus controls	
Some evidence suggests that survivors of CAYA cancer are more likely to experience clinically significant psychological distress as compared to siblings.	6 studies (3 samples) Level C[7,36,38,46,51,54]
There is conflicting evidence regarding clinically significant psychological distress in survivors of CAYA cancer as compared to community norms. One study found survivors were more likely to report clinically significant distress compared to community norms, while another found survivors were less likely to report clinically significant distress as compared to norms.	2 studies Conflicting Evidence[18,43]
Symptoms of Psychological Distress in survivors versus controls	
Some evidence suggests that survivors of CAYA cancer have increased symptoms of psychological distress as compared to siblings.	8 studies (5 samples) Level C[17,19,24,38-42]
There is conflicting evidence regarding symptoms of psychological distress in survivors of CAYA cancer as compared to the general population. In 2 studies, survivors reported more symptoms of distress as compared to norms. No difference was found between	6 studies (4 samples)

survivors and norms symptoms of distress in 2 studies. In 2 studies, survivors reported fewer symptoms of distress compared norms.	Conflicting Evidence[18,19,24,43,48,49]

Post-traumatic stress disorder (PTSD), Stress-related mental disorders (SRMD), and post-traumatic stress symptoms (PTSS)	
16.8% of survivors* reported PTSS (vs. 4.0% of siblings, p<0.001). *Survivors from the CCSS cohort (n=4484; mixed diagnoses; mean 10.5 yrs at diagnosis; mean 27.2 yrs at Baseline. Controls: n=1651 siblings. Measurement: Posttraumatic Stress Diagnostic Scale (cutoff: ≥1 re-experiencing symptom, ≥3 avoidance symptoms, and ≥2 arousal symptoms)	*Brinkman et al. 2019*
14.5% of survivors* reported symptoms of PTSS. *Survivors from the CCSS cohort (n=6844; mixed diagnoses; mean 7.6 yrs at diagnosis; mean 34.9 yrs at study). Controls: none. Measurement: Post-traumatic Stress Scale (cutoff: ≥13)	*Crochet et al. 2019*
11.8% of survivors* experienced PTSD in the clinical range. PTSD mean score was 27.7 (SD 12.4; median 23.0). *Survivors from the St. Jude cohort (n=2969; mixed diagnoses; mean 8.4 yrs at diagnosis; mean 32.5 yrs at study; mean 24.1 yrs since diagnosis). Measurement: PTSD Checklist-Civilian (cut-off ≥44)	*Allen et al. 2018*
16.1% of survivors* reported symptoms of PTSS. *Survivors from the CCSS cohort (n=5021; mixed diagnoses; mean 8.3 yrs at diagnosis; mean 32.0 yrs at study; mean 23.2 yrs since diagnosis). Measurement: Post-traumatic Stress Diagnostic Scale	*Vuotto et al. 2017*
15.2% of survivors* reported reported severe IES scores (≥26); 27.8% reported moderate IES scores (8-25). 43% had significant IES scores (≥8). IES mean score was 11.0 (SD 13.5), while subscale means included intrusion at 5.6 (SD 7.5) and avoidance at 5.8 (SD 8.3). *Survivors (n=348; mixed diagnoses; 0-18 yrs at diagnosis; mean 38.5 yrs at study; mean 31.5 yrs since diagnosis). Controls: French norm population n=36,105. Measurement: Impact of Event Scale (IES)	*De Laage et al. 2016*
1.1% of survivors of retinoblastoma* met criteria for PTSD. Survivors were more likely to report symptoms of avoidance and hyperarousal as compared with siblings from the CCSS cohort (Score means: avoidance- 1.19 (survivors) vs. 0.73 (CCSS siblings), p_{adj}<0.01; hyperarousal- 1.03 (survivors) vs. 0.63 (CCSS siblings), p_{adj}<0.01; p-values adjusted for age at study, race/ethnicity, educational level, household income). No differences were found between survivors and CCSS siblings on symptoms of re-experiencing and intrusive thinking (p_{adj}=0.55). *Retinoblastoma survivors (n=470; median age at diagnosis 1 yrs; mean 43.3 yrs at study); Controls: n=2820 siblings from the CCSS cohort. Measurement: Impact of Event Scale	*Ford et al. 2015*
71% of survivors* reported symptoms of PTSS (mean PSDS Total Severity=5.43 [SD=7.14]; mean subtest scores: Re-experiencing=1.06 [SD=1.89]; Avoidance=2.33[SD=3.44]; Arousal=2.04 [SD=2.87]). *Survivors from the CCSS cohort (n=6162; mixed diagnoses; mean 8.2 yrs at diagnosis; mean 23.1 yrs since diagnosis; mean 31.6 yrs at study). Controls: none. Measurement: Post-traumatic Stress Diagnostic Scale (PSDS)	*Klosky et al. 2014*
4.5% of survivors* reported moderate to severe PTSS, 26.3% reported moderate PTSS, and 64.3% reported mild PTSS (mean PSDS Total Severity Score=8.20 [SD=6.13]). *Survivors (n=225; mixed diagnoses; mean 9.89 yrs at diagnosis; mean 21.95 yrs at study). Controls: none. Measurement: Post-traumatic Stress Diagnostic Scale (PSDS)	*Yi et al. 2014*
14.4% of survivors* of adolescent cancers met diagnostic criteria for PTSD. *Survivors of adolescent onset cancer with data in German Childhood Cancer Registry (n=820; mixed diagnoses; mean 15.8 yrs at diagnosis [range 15-18 yrs]; mean 13.7 yrs since diagnosis; mean 30.4 yrs at study). Controls: none. Measurement: Post-traumatic Stress Diagnostic Scale (PDS)- German version	*Dieluweit et al. 2011*
10.5%/18.0% of survivors (male/female) met diagnostic criteria for PTSD. Survivors were more likely to meet diagnostic criteria for PTSD than controls (OR 3.26, 95%CI 2.25–4.74,p<0.001) after controlling for sex, age and education. *Survivors from the German Childhood Cancer Registry (n=820; mixed diagnoses; mean 15.8 yrs at diagnosis; mean 13.7 yrs since diagnosis; mean 30.4 yrs at study). Controls: n=1027 friends and snowball-sample for PDS. Measurement: Posttraumatic Stress Diagnostic Scale (case cutoff: All six DSM-IV diagnosis criteria A–F met)	*Seitz et al. 2010*

Prevalence of PTSD in survivors* compared to siblings differs according to how PTS is operationalized: • Survivors (9.0%) were more likely to meet full symptom criteria for PTSD with impairment/distress as compared to siblings (2.1%); OR=4.21, (95%CI: 2.11-8.38), p <0.0001 • Survivors (7.5%) were more likely to meet full symptom criteria for PTSD without impairment/distress as compared to siblings (2.7%); OR=2.85, (95% CI:1.51–5.39), p=0.0013 • Survivors (11.4%) were more likely to meet partial symptom criteria for PTSD without impairment or distress as compared to siblings (8.0%); OR=1.71, (95%CI: 1.13–2.60), p=0.012 • Survivors (4.8%) were equally likely to meet partial symptom criteria for PTSD with impairment/distress as compared to siblings (3.2%); OR=1.42, (95%CI: 0.79-2.56), p=0.24 *Survivors from the CCSS cohort (n=6542; mixed diagnoses; mean 8.2 yrs at diagnosis; mean 31.85 yrs at study). Controls: n=368 siblings (mean 33.44 yrs at study). Measurement: Post-traumatic Stress Diagnostic Scale (PSDS)- (PTSD symptoms), BSI-18 (distress criterion), and RAND Health Status Survey, Short Form-36 (impairment criterion).	*Stuber, Meeske, Leisenring et al. 2011*
Survivors* (9.0%) were more likely to meet diagnostic criteria for PTSD as compared to siblings (2%); OR=4.14, 95%CI:2.08-8.25, adjusted for age at interview, race, gender, & within-family correlation between survivor & sibling *Survivors from the CCSS cohort (n=6542; mixed diagnoses; mean 8.2 yrs at diagnosis; mean 31.85 yrs at study). Controls: n=368 siblings (mean 33.44 yrs at study). Measurement: Post-traumatic Stress Diagnostic Scale (PSDS)- (PTSD symptoms), BSI-18 (distress criterion), and RAND Health Status Survey, Short Form-36 (impairment criterion).	*Stuber, Meeske, Krull et al. 2010*
Survivors* (18.6%) were more likely to have been diagnosed with any stress related mental disorder (SRMD) as compared to children without cancer (7.3%) (p<0.0001 cumulative incidence comparison; SRMD HR=3.22, 95% CI= 2.17-4.76, adjusted for race) • 0.77% of survivors were diagnosed with PTSD vs 0.60% of children without cancer • 0.26% of survivors were diagnosed with acute stress disorder vs 0.0% of children without cancer • 11.5% of survivors were diagnosed with adjustment disorder vs 3.5% of children without cancer *Medicaid eligible survivors identified from the South Carolina Central Cancer Registry (n=390; mixed diagnoses; age at study entry: 0-5 yrs (n=175), 6-11 yrs (n=118), 12-15 yrs (n=97)). Controls: n=1329 Medicaid eligible children without cancer. Measurement: SRMD diagnoses from Medicaid claims database	*Schrag et al. 2008*
12% of survivors* reported severe PTSS and 28% reported moderate PTSS (raw score means: IES intrusion=5.6 [SD 7.3], IES avoidance=4.7 [SD 7.1], IES total= 10.3 [SD 13.3]). *Survivors (n=500; mixed diagnoses; median 8 yrs at diagnosis; mean 24 yrs at study). Controls: none. Measurement: Impact of Event Scale (IES)	*Langeveld et al. 2004*
Survivors* were equally likely to report clinically significant PTSS as compared to healthy peers (Severe PTSS: 2.6% of survivors vs. 3.4% of controls; Moderate PTSS: 12.5% of survivors vs. 12.3% of controls). Survivors reported equivalent symptoms of post-traumatic stress compared to healthy peers (mean scores: IES-Intrusion 5.34 (survivors) vs. 4.92 (controls), IES-Avoidance (survivors) 6.81 vs. 6.87 (controls), IES-total score 12.15 (survivors) vs. 11.80 (controls), TSC-Post-traumatic-stress 6.65 (survivors) vs. 6.85 (controls), TSC-anger 7.16 (survivors) vs. 7.11 (controls). Survivors reported more dissociation symptoms compared to healthy peers (mean scores: TSC-dissociation 5.96 (survivors) vs. 5.82 (controls), p<0.001, with child age serving as a significant covariate). *Child and adolescent aged survivors (n=309 survivors; mixed diagnoses; mean 5.83 yrs at diagnosis [range 1-17 yrs]; mean 13.53 yrs at study [range 8-20 yrs]). Controls: n=219 healthy children (mean 12.27 yrs at study [range 8-20 yrs]). Measurement: Impact of Event Scale (IES); Post-traumatic Stress Disorder Reaction Index (PTSDRI); Trauma Symptom Checklist for Children (TSC)	*Barakat et al. 1997*
Overall Conclusion	
Prevalence of Post-traumatic stress disorder (PTSD), Stress-related mental disorders (SRMD), and post-traumatic stress symptoms (PTSS)	
Survivors of CAYA cancer are at risk for PTSD, PTSS, and SRMD. Across 9 studies, the prevalence of PTSD ranged from 1 to 18%. One study found a cumulative incidence of 18% for all SRMD diagnoses. Across 5 studies, the prevalence of significant PTSS ranged from 12 to 71%.	14 studies (10 samples)[9,27-30,38,47,53,55-60]

Prevalence of PTSD, SRMD, and significant PTSS in survivors versus controls	
Evidence suggests that survivors of CAYA cancer are more likely to experience PTSD or any SRMD as compared to controls: Survivors were more likely to meet full or partial diagnosic criteria for PTSD as compared to siblings (3 studies, 1 sample) and the general population (1 study). One study found survivors were more likely to have been diagnosed with any SRMD as compared to children without cancer. Survivors were equally likely to experience significant PTSS compared to healthy peers (1 study). As compared to siblings, survivors of retinoblastoma reported more symptoms of avoidance and hyperarousal and equivalent symptoms of re-experiencing and intrusive thinking (1 study).	6 studies (4 samples) Level B[28,29,38,47,57,58]

Externalizing problems	
More neuroblastoma survivors* than siblings reported behavior problems, including attention deficit (p<0.001), peer conflict/social withdrawal (p<0.001), headstrong behavior (p<0.001), and antisocial behavior (p=0.01). *Survivors of neuroblastoma from the CCSS cohort (n=859; 97.9% <5 yrs at diagnosis yrs; 8-17 yrs at study. Controls: n=872 siblings. Meaurement: BPI (cutoff >10th percentile of age-matched siblings).	*Zheng et al. 2018*
21.9% of pediatric brain tumor survivors* reported behavior problems. *Survivors of pediatric brain tumors (n=319; mixed neurooncology diagnoses; mean 10 yrs since diagnosis [SD=5 yrs]; mean 18 yrs at study [SD=5 yrs, range 10-35 yrs]). Controls: none. Measurement: Semi-structured clinical interview based on Diagnostic and Statistical Manual of Mental Disorders IV-TR	*Brinkman, Liptak et al 2013*
Survivors' parents* were more likely to report clinically significant headstrong (13.2%) and antisocial (12.3%) for their adolescent as compared to siblings (p<0.01). *Parent proxy report from the Adolescent CCSS cohort (n=1652; mixed diagnoses; 12-17 yrs at baseline study; >5 yrs since diagnosis). Controls: n=406 parent proxy report for adolescent siblings aged 12-17 yrs at baseline study. Measurement: Behavior Problem Index (BPI) parent-proxy report (cutoff: Headstrong behavior and Antisocial behavior subscale scores falling in the bottom 10% of the national standardization sample)	*Krull, Huang et al. 2010*
Survivors' parents* were more likely to report clinically significant headstrong (22.8%) and antisocial (14.6%) behavior for their adolescent as compared to siblings (Antisocial behavior: RR=1.7; 99%CI:1.3-2.2; Headstrong behavior: RR=1.3; 99%CI:1.0-1.8; adjusted for sex, current age, race/ethnicity and annual household income) *Parent proxy report from the Adolescent CCSS cohort (n=2979; mixed diagnoses; mean 3.2 yrs at diagnosis; mean 14.8 yrs at study). Controls: n=649 siblings. Measurement: Behavior Problem Index (BPI) Headstrong behavior and Antisocial behavior subscales (cutoff ≥ 1.3 SD sibling mean)	*Schultz et al. 2007*
Survivors* of acute lymphoblastic leukemia (ALL) reported more symptoms of anger compared to siblings (raw means: 9.62 (survivors) vs. 8.09 (siblings), p=0.002). *Survivors of ALL treated on Children's Cancer Group (CCG) protocols (n=580 survivors; <20 yrs at diagnosis; mean 22.6 yrs at study). Controls: n=396 siblings (mean 25.2 yrs at study). Measurement: Profile of Mood Scale-Anger subscale	*Zeltzer et al. 1997*
Overall Conclusion	
Prevalence of Externalizing Problems	
Survivors of CAYA cancer are at risk for externalizing behavior problems. The prevalence of behavior problems ranged from 12 to 22%.	3 studies (2 samples)[12,20,22]
Prevalence of Externalizing Problems in survivors versus controls	
Some evidence suggests that survivors of CAYA cancer are more likely to experience clinically significant behavioral problems as compared to siblings.	3 studies (1 sample) Level C[20,22,37]
Symptoms of Externalizing Problems in survivors versus controls	
Some evidence suggests that survivors of CAYA cancer have increased symptoms of anger compared to controls.	1 study Level C[40]

Suicidal ideation & death by suicide	
0.56% of survivors* died due to suicide vs. 17.1% of comparisons. The risk of death by suicide was found to be increased when compared to comparisons: RR=1.37; 95%CI:1.02-1.83).	*Korhonen et al. 2019*

*Survivors from the SALiCCS cohort (n=29,285; mixed diagnoses; <20 yrs at diagnosis; median 19.0 yrs at study; median 9.4 yrs since diagnosis). Controls: population-based comparisonsn n=146,282. Measurement: Causes of death classified according to the International Classification of Diseases (ICD)	
8% of adult survivors of childhood cancer reported suicidal ideation vs. 6% of controls. Survivors were more likely to report suicidal ideation than controls (OR_{adj}=2.22, 95%CI:1.38-3.57, p<0.001), adjusting for sex, age, marital status, education, income and employment.) *Survivors (n=951; mixed diagnoses; median 5.0 yrs at diagnosis [range 0-15 yrs]; median 28.1 yrs since diagnosis [range 23-36 yrs]; median 34.2 yrs at study [range 24-49 yrs]). Controls: n=11.30, German Household Panel. Measurement: Single question for suicidal ideation.	*Burghardt et al. 2019*
Cumulative incidence of suicide by age 30 yrs did not differ significantly between survivors and controls: Survivors: 0.13% (0.03-0.39%) Controls: 0.03% (0.01-0.08%), RR=2.92 (95%CI:0.70-12.23) *Survivors (n=4117; mixed diagnoses; age at diagnosis 0-18 yrs; ≥5 yrs since diagnosis). Controls: n=20,269 matched general population controls. Measurement: psychiatric admission retrieved from administrative health databases; ICD-10 and Statistical Manual of Mental Disorders	*Nathan et al. 2018*
5.9% of survivors* reported suicidal ideation (expected: 13.6%, p<0.0001). *Survivors (n=348; mixed diagnoses; 0-18 yrs at diagnosis; mean 38.5 yrs at study; mean 31.5 yrs since diagnosis). Controls: French norm population n=36,105. Measurement: Mini-International Neuropsychiatric Interview	*De Laage et al. 2016*
86.3% of survivors* reported no suicidal ideation (SI), 7.5% of survivors reported SI at follow-up, and 3.0% reported recurrent SI. 1.6% of deaths in the survivor sample were attributed to suicide. Survivors were more likely to report SI at follow-up (OR=1.9, 95%CI:1.5-2.5) and more likely to report recurrent SI as compared to siblings (OR=2.5, 95%CI:1.8-3.8). *Survivors from the CCSS cohort (n=7798; mixed diagnoses; ≤21 yrs at diagnosis; ≥18 yrs at study, mean 25.1-26.3 yrs at study time points). Controls: n=2776 siblings. Measurement: SI was assessed at three time points (1992, 2003, 2007) using single item from BSI-18	*Brinkman, Zhang et al. 2014*
11.7% of pediatric brain tumor survivors* reported suicidal ideation (SI), 0.9% reported recurrent SI, and 1.6% had documented suicide attempts. *Survivors of pediatric brain tumors (n=319; mixed neurooncology diagnoses; mean 10 yrs since diagnosis [SD=5 yrs]; mean 18 yrs at study [SD=5 yrs, range 10-35 yrs]). Controls: none. Measurement: Semi-structured clinical interview based on Diagnostic and Statistical Manual of Mental Disorders IV-TR and record review	*Brinkman, Liptak et al 2013*
0.18% of survivor* deaths in the survivor sample were attributed to suicide. Risk of death by suicide was equivalent in childhood cancer survivors as compared to the general population (observed probability=0.18%, 95%CI:0.04%-0.53% vs. expected probability=0.19%; p=1.00). *Survivors (n= 1647; mixed diagnoses; mean 8.2 yrs at diagnosis; mean 22.3 yrs at study 22.3 yrs). Controls: General population of Slovenia. Measurement: Data from the Cancer Registry of Slovenia (1978-2008) and the Statistical Office of the Republic of Slovenia	*Cizek Sajko et al. 2012*
Survivors* (7.8%) were more likely to report suicidal ideation as compared to siblings (4.6%) (OR=2.5, 95%CI:1.8-3.8). *Survivors from the CCSS cohort (n=9126; mixed diagnoses; <18 yrs at diagnosis, 6-29 yrs since diagnosis; 18-48 yrs at study). Controls: n=2968 siblings. Measurement: single item on BSI-18	*Recklitis, Diller et al. 2010*
12.8% of survivors* reported suicidality, with 8.4% reporting suicidal ideation alone, 0.4% reporting past attempts without current ideation, and 4.0% reporting past attempts and current ideation. *Survivors (n=226; mixed diagnoses; mean 10.08 yrs at diagnosis; mean 18.3 yrs since diagnosis; mean 28.38 yrs at study). Controls: none. Measurement: single item from Symptom Checklist-90 revised (SCL-90 R) and Beck Scale for Suicidal Ideation (BDSI)	*Recklitis, Lockwood et al. 2006*
Overall Conclusion	
Prevalence of Suicidal ideation and Death by suicide	
Survivors of CAYA cancer are at risk for suicidal ideation, attempted suicide, and death by suicide. Across 6 studies (5 samples), the prevalence of suicidal ideation ranged from 5 to 12%. Across 2 studies, the prevalence of attempted suicide ranged from 1 to 4%. Across 4 studies, the prevalence of death by suicide ranged from 0.1 to 1.6%.	9 studies (8 samples)[11,12,26,27,61-65]
Prevalence of Suicidal ideation versus controls	

Some evidence suggests that survivors of CAYA cancer are more likely to experience suicidal ideation as compared to controls.	4 studies (3 samples) Level C[26,27,61,62]
Prevalence of Death by suicide versus controls	
Some evidence suggests that survivors of CAYA cancer are more likely to experience death by suicide as compared to controls.	3 studies Level C[11,64,65]

Other mental health disorders and symptoms	
13.1% of survivors* had documentation of ADHD, 14.5% of them inattentive type, 13% hyperactive/impulsive type, 10.1% combined type. Taking together those without ADHD diagnosis, but with symptom related to ADHD, 32.6% survivors experienced ADHD-related symptoms. Prevalence of ADHD was higher than in the general population (9.4%; p=0.002) *Survivors of pediatric brain tumor (n=528; mean 8.2 yrs at diagnosis; mean 15.5 yrs at study). Controls: general population, no statistical testing. Measurement: Clinical Attention deficit/Hyperactivity disorder (ADHD) diagnosis as documented in the medical record	*Shabason et al. 2019*
7% of adult survivors* reported panic vs. 3% of controls. Survivors were more likely to report panic than controls (OR_{adj}=4.36, 95%CI:1.88-10.09, p<0.001), adjusting for sex, age, marital status, education, income and employment.) *Survivors (n=951; mixed diagnoses; median 5.0 yrs at diagnosis [range 0-15 yrs]; median 28.1 yrs since diagnosis [range 23-36 yrs]; median 34.2 yrs at study [range 24-49 yrs]). Controls: n=11.30, German Household Panel. Measurement: Brief PHQ panic module.	*Burghardt et al. 2019*
6.5% of survivors* reported panic disorders (expected: 4.65%, p<0.05) and 4.3% of survivors reported agoraphobia (expected: 2.1%, p<0.0001). *Survivors (n=348; mixed diagnoses; 0-18 yrs at diagnosis; mean 38.5 yrs at study; mean 31.5 yrs since diagnosis). Controls: French norm population n=36,105. Measurement: Mini-International Neuropsychiatric Interview	*De Laage et al. 2016*
Schizophrenia and psychotic disorder diagnoses were more common among survivors* of childhood and adolescent cancers as compared to siblings (HR=1.4, 95%CI:1.0–1.9). Non-organic personality disorder diagnoses were more common among survivors* of childhood and adolescent cancers as compared to siblings (HR=1.4, 95%CI:1.0–2.0). *Survivors of CAYA cancers (n=13860; mixed diagnoses; age at diagnosis 0-19 yrs: 31% and 20-34 yrs: 69%; age at study not provided). Controls: n=43,392 siblings. Measurement: ICD-10 codes and data from the Finnish Cancer Registry and Central Population Registry	*Ahomaki et al. 2015*
10.5% of survivors* reported clinically significant obsessive-compulsive symptoms. No difference was observed between proportion of survivors reporting obsessive-compulsive symptoms than expected from the norm population (p=0.574). Survivors reported fewer symptoms of obsessive compulsive disorder as compared to norms (T-Score means: 46.9 (survivors) vs. 50.0 (norms), p<0.001). *Survivors from the Swiss CCSS cohort (n=987; mixed diagnoses; mean 8.4 yrs at diagnosis; mean 19.5 yrs since diagnosis; mean 27.9 yrs at study). Controls: Population norms for BSI. Controls: Population norms for BSI. Measurement: BSI Obsessive Compulsive subscale (cutoff ≥63)	*Michel et al. 2010*
Overall Conclusion	
Prevalence of other mental health disorders and symptoms	
Survivors of CAYA cancer are at risk for obsessive compulsive symptoms: the prevalence of clinically significant obsessive compulsive symptoms was 10.5%	1 study[18]
Survivors of CAYA cancer are at risk for attention deficit/hyperactivity disorders: the prevalence of attention deficit/hyperactivity disorders was 13%.	1 study[66]
Survivors of CAYA cancer are at risk for panic: the prevalence of panic was 7%.	1 study[26]
Prevalence of other mental health disorders and symptoms vs. comparisons	
Evidence suggests that survivors of CAYA cancer are more likely to experience schizophrenia and psychotic disorder as compared to controls.	1 study Level C[25]
Some evidence suggests that survivors of CAYA cancer are more likely to experience personality disorders as compared to controls.	1 study Level C[25]

Some evidence suggests that survivors of CAYA cancer are equally likely to experience obsessive-compulsive symptoms as compared to controls, but more likely to report fewer symptoms.	1 study Level C[18]
Some evidence suggests that survivors of CAYA cancer are more likely to experience attention deficit/hyperactivity disorders as compared to the general population.	1 study Level C[66]
Some evidence suggests that survivors of CAYA cancer are more likely to experience panic as compared to the general population.	1 study Level C[26]

1b-1. What are the key clinical, demographic and treatment-related risk factors for developing depression among survivors of childhood, adolescent, and young adult (CAYA) cancer?	
Conclusion single studies	
Clinical risk factors: Age at diagnosis	
Survivor* age at diagnosis was not associated with depression/anxiety using log-binomial models (adjusted for age at diagnosis, age at study, sex, annual household income). • Age at diagnosis: <1 year (Ref. ≥1 year) not significant *Survivors of neuroblastoma from the CCSS cohort (n=859; 97.9% <5 yrs at diagnosis yrs; 8-17 yrs at study. Controls: n=872 siblings. Meaurement: BPI depression/anxiety subscale (cutoff >10th percentile of age-matched siblings).	*Zheng et al. 2018*
Survivor* age at diagnosis was not associated with depression using multivariable logistic regression (stratified by diagnostic groups): • CNS tumors and leukemia survivors: Age at diagnosis, years: 11-21 (Ref. ≤10 years) OR=1.11 (95%CI:0.87-1.42) (adjusted for chemotherapy) • Lymphoma and sarcoma survivors: Age at diagnosis, years: 11-21 (Ref. ≤10 years) OR=0.75 (95%CI:0.59-0.97) *Survivors of adolescent and early young adult cancer from the CCSS cohort (n=2589; mixed diagnoses; 11-21 yrs at diagnosis; ≥75% were ≥35 yrs at study). Controls: n=3603 survivors diagnosed ≤10 yrs old. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Prasad et al. 2015*
Survivor* age at diagnosis was not associated with depression using generalized estimating equations (adjusting for scarring/disfigurement, hair loss, recurrence, SMN, age at study, sex, race, educational achievement, marital status, cranial radiation, surgery): • Age at diagnosis: 5-9 years (Ref. 0-4 years) OR=1.02 (95%CI:0.84-1.23, p=0.87) • Age at diagnosis: 10-21 years (Ref. 0-4 years) OR=1.02 (95%CI:0.81-1.29, p=0.86) *Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥ 90th %tile on standardized norms)	*Kinahan et al. 2012*
Survivor* age at diagnosis was not associated with depression using multivariable logistic regression (adjusted for sex, survival time, surgery, chemotherapy, radiation): • Age at diagnosis: 0-3 years (Ref. 15-20 years) OR=1.0 (95%CI:0.8-1.2) • Age at diagnosis: 4-9 years (Ref. 15-20 years) OR=1.0 (95%CI:0.8-1.2) • Age at diagnosis: 10-14 years (Ref. 15-20 years) OR=0.9 (95%CI:0.7-1.1) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Zeltzer et al. 2008*
Survivor* age at diagnosis was not associated with depression/anxiety using multiple variable models (adjusted for sex, current age group, age at diagnosis, race/ethnicity, annual household income, disfigurement, treatment): • Age at diagnosis: <2 years (Ref. 5-9) RR=1.1 (99%CI:0.7-1.4) • Age at diagnosis: 2-4 years (Ref. 5-9) RR=0.8 (99%CI:0.6-1.1) *Parent proxy report from the Adolescent CCSS cohort (n=2979; mixed diagnoses; mean 3.2 yrs at diagnosis; mean 14.8 yrs at study). Controls: n=649 siblings. Measurement: Behavior Problem Index (BPI) Depression/Anxiety subscale (cutoff ≥ 1.3 SD sibling mean)	*Schultz et al. 2007*
Overall Conclusion	
Evidence suggests that age at diagnosis is not related to the risk of developing depression among survivors of childhood, adolescent, and young adult (CAYA) cancer.	5 studies (2 samples) Level B[21,22,24,37,67]

Clinical risk factors: Time since diagnosis	
Time since diagnosis was not associated with depression using multivariable logistic regression (adjusted for sex, age at diagnosis, surgery, chemotherapy, radiation): • Survival time: <20 years (Ref. 30+ years) OR=1.0 (95%CI:0.8-1.3) • Survival time: 20-24 years (Ref. 30+ years) OR=0.9 (95%CI:0.7-1.2) • Survival time: 25-29 years (Ref. 30+ years) OR=1.0 (95%CI:0.7-1.2) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Zeltzer et al. 2008*
Overall Conclusion	
Some evidence suggests that time since diagnosis is not related to the risk of developing depression among survivors of CAYA cancer.	1 study Level C[24]

Clinical risk factors: Diagnosis	
Diagnosis type was not associated with depression using multivariable logistic regression (adjusted for age at study, sex, parents' education, perceived parents' support, diagnosis, treatment modality, late effects, time since diagnosis): • Diagnosis: CNS tumors (Ref. Leukemia, lymphoma) OR=1.41 (95%CI:0.54-3.70, p=0.215) • Diagnosis: Other (Ref. Leukemia, lymphoma) OR=0.67 (95%CI:0.31-1.41, p=0.215) *Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥57)	*Gianinazzi et al 2013*
Overall Conclusion	
Some evidence suggests that diagnosis type is not related to the risk of developing depression among survivors of CAYA cancer.	1 study Level C[19]

Clinical risk factors: Second malignant neoplasm (SMN) or recurrence	
No association was found between SMN or recurrence and depression using multivariable logistic regression (stratified by diagnostic groups): • CNS tumors and leukemia survivors: SMN or recurrence not included in final model • Lymphoma and sarcoma survivors: SMN or recurrence not included in final model *Survivors of adolescent and early young adult cancer from the CCSS cohort (n=2589; mixed diagnoses; 11-21 yrs at diagnosis; ≥75% were ≥35 yrs at study). Controls: n=3603 survivors diagnosed ≤10 yrs old. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Prasad et al. 2015*
No association was found between recurrence or SMN and depression using generalized estimating equations (adjusting for scarring/disfigurement, hair loss, age at diagnosis, age at study, sex, race, educational achievement, marital status, cranial radiation, surgery): • Recurrence: Yes (Ref. No) OR=1.19 (95%CI:0.99-1.44, p=0.07) • Second malignant neoplasm: Yes (Ref. No) OR=1.09 (95%CI:0.79-1.50, p=0.61) *Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥ 90th %tile on standardized norms)	*Kinahan et al. 2012*
Overall Conclusion	
Some evidence suggests that second malignant neoplasm or recurrence is not related to the risk of developing depression among survivors of CAYA cancer.	2 studies (1 sample) Level C[21,67]

Clinical risk factors: Tumor location	
No association was found between tumor location and depression using multivariable binary logistic regression. • Axial (Ref. Pelvis) OR=0.65 (95%CI:0.39 to 1.08) • Lower extremity (Ref. Pelvis) OR=0.89 (95%CI:0.53 to 1.48) • Upper extremity (Ref. Pelvis) OR=0.69 (95%CI:0.35 to 1.38)	*Ranft et al. 2017*

*Survivors of Ewing sarcoma (n=618; 70.1% <18 yrs at diagnosis; median 29 yrs at study. Controls: n=316, median 30 yrs at study. Measurement: BSI-18 Depression subscale (0 "no symptoms" to 4 "highest symptoms")	
Overall Conclusion	
Some evidence suggests that tumor location is not related to the risk of developing depression among survivors of CAYA cancer.	1 study Level C[44]

Clinical risk factors: Metastases/Localized disease	
No association was found between risk group and depression using multivariable binary logistic regression. • Pulmonary metastases (Ref. localized disease) OR=1.27 (95%CI:0.69 to 2.33) • Extrapulmonary metastases (Ref. localized disease) OR=1.75 (95%CI:0.81 to 3.79) *Survivors of Ewing sarcoma (n=618; 70.1% <18 yrs at diagnosis; median 29 yrs at study. Controls: n=316, median 30 yrs at study. Measurement: BSI-18 Depression subscale (0 "no symptoms" to 4 "highest symptoms")	*Ranft et al. 2017*
Overall Conclusion	
Some evidence suggests that risk group is not related to the risk of developing depression among survivors of CAYA cancer.	1 study Level C[44]

Clinical risk factors: Scarring/disfigurement	
Head/neck scarring/disfigurement, arm/leg scarring/disfigurement, chest/abdomen scarring/disfigurement (in never married survivors), and persistent hair loss (in female survivors) were associated with increased risks for depression using generalized estimating equations (adjusting for age at diagnosis, age at study, sex, race, educational achievement, marital status, recurrence, SMN, cranial radiation, surgery): • Head/neck scarring or disfigurement: Yes (Ref. No) OR=1.19 (95%CI:1.01-1.41, p=0.03) • Arm/leg scarring or disfigurement: Yes (Ref. No) OR=1.22 (95%CI:1.02-1.45, p=0.03) • Chest/abdomen scarring or disfigurement: Yes (married) (Ref. No) OR=1.24 (95%CI:0.96-1.62, p=0.10) Yes (div/sep) (Ref. No) OR=1.27 (95%CI:0.87-1.84, p=0.22) Yes (never married) (Ref. No) OR=0.80 (95%CI:0.65-0.98, p=0.03) • Persistent hair loss: Yes (male) (Ref. No) OR=1.15 (95%CI:0.86-1.54, p=0.34) Yes (female) (Ref. No) OR=1.60 (95%CI:1.22-2.11, p=0.001) *Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: Scarring and disfigurement items (yes/no) for head/neck, arm/leg, and chest/abdomen areas; persistent hair loss (yes/no); BSI-18 Depression subscale (cutoff ≥ 90th %tile on standardized norms)	*Kinahan et al. 2012*
Disfigurement was not associated with depression/anxiety using multiple variable models (adjusted for sex, current age group, age at diagnosis, race/ethnicity, annual household income, disfigurement, treatment): • Head/neck/scalp/eye: Yes (Ref. No) RR=1.2 (99%CI:0.9-1.6) • Limb: Yes (Ref. No) RR=1.2 (99%CI:0.9-1.6) • Chest or abdomen: Yes (Ref. No) RR=1.3 (99%CI:1.0-1.6) *Parent proxy report from the Adolescent CCSS cohort (n=2979; mixed diagnoses; mean 3.2 yrs at diagnosis; mean 14.8 yrs at study). Controls: n=649 siblings. Measurement: Behavior Problem Index (BPI) Depression/Anxiety subscale (cutoff ≥ 1.3 SD sibling mean) and scarring and disfigurement items (yes/no) for head/neck, arm/leg, and chest/abdomen areas	*Schultz et al. 2007*
Overall Conclusion	
Some evidence suggests scarring/disfigurement is related to higher risk of developing depression among survivors of CAYA cancer. Specifically, having head/neck or arm leg scarring/disfigurement, having persistent hair loss for females, or having chest/abdomen scarring/disfigurement for individuals who are not married increases the risk of depression among survivors.	2 studies Level C[22,67]

Clinical risk factors: Survivor health and late effects	
Poor or fair physical health was associated with an increased risk for depression using Poisson regression (adjusted for heavy/risky drinking, sex, physical health, radiation, race, age at diagnosis, age at follow-up, educational attainment, and employment status). • Physical health: Poor, fair (Ref. good, very good, excellent) RR=2.6 (95%CI:2.1-3.2; P≤0.01) *Survivors from the CCSS cohort (n=4484; mixed diagnoses; mean 10.5 yrs at diagnosis; mean 27.2 yrs at Baseline. Controls: n=1651 siblings. Meaurement: BSI-18 Depression subscale (cutoff ≥63) and single item assessing self-reported health (fair/poor vs. good/very good/excellent)	*Brinkman et al. 2019*
In adolescent survivors of acute lymphoblastic leukemia, poor functional health status was associated with an increased risk for depression using multivariable binary logistic regression (adjusted for sex, age, age at diagnosis and treatment risk status): • Functional health status: OR=1.32 (95%CI:1.13-1.60; p<0.0001) In adult survivors, poor functional health status was associated with an increased risk for depression using multivariable binary logistic regression (adjusted for sex, age, age at diagnosis and treatment risk status): • Functional health status: OR=1.19 (95%CI:1.11-1.28; p<0.0001) *Survivors of ALL from the PETALE cohort (n=287 [n=105 adolescents, n=182 adults]; mean 6.2 yrs at diagnosis; mean 21.9 yrs at study; mean 15.7 yrs since diagnosis. Controls: Comparison to scores from n=4 other studies. Measurement: Beck Youth Inventory Depression, Beck Depression Inventory II; functional health status measured with self-rated 16D (adolescents) and 15D (adults)	*Anestin et al. 2018*
Peripheral neuropathy and Grade ≥2 pulmonary disease were associated with an increased risk for depression/anxiety using log-binomial models (adjusted for age at diagnosis, age at evaluation, sex, and annual household income). No association was found between Grade ≥2 endocrine disease and depression/anxiety. • Peripheral neuropathy: Yes (Ref. No) PR=1.86 (95%CI:1.28-2.56; p=0.002) • Grade ≥2 pulmonary disease: Yes (Ref. No) PR=1.92 (95%CI:1.31-2.65; p<0.001) • Grade ≥2 endocrine disease: Yes (Ref. No) not significant *Survivors of neuroblastoma from the CCSS cohort (n=859; 97.9% <5 yrs at diagnosis yrs; 8-17 yrs at study. Controls: n=872 siblings. Meaurement: BPI depression/anxiety subscale (cutoff >10th percentile of age-matched siblings); health conditions graded according to the Common Terminology Criteria for Adverse Events, version 4.03	*Zheng et al. 2018*
Endocrine conditions and pulmonary conditions were associated with an increased risk for depression using log-binomial multivariable regression (adjusting for endocrine conditions, pulmonary conditions, and sex). • Endocrine conditions: Yes (Ref. No) RR=1.34 (95%CI:1.13-1.59) • Pulmonary conditions: Yes (Ref. No) RR=1.38 (1.14-1.66) *Survivors from the CCSS cohort (n=5021; mixed diagnoses; mean 8.3 yrs at diagnosis; mean 32.0 yrs at study; mean 23.2 yrs since diagnosis). Measurement: BSI-18 Depression subscale (cut-off ≥63); health conditions self-reported by survivors	*Vuotto et al. 2017*
Survivor self-reported somatic/physical late effects were associated with an increased risk for depression using multivariable logistic regression (adjusted for age at study, sex, parents' education, perceived parents' support, diagnosis, treatment modality, time since diagnosis). • Late effects: Somatic/physical problems (Ref. No late effects) OR=4.23 (95%CI:2.01-8.95, p<0.001) *Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥57); Late effects self-reported by survivors and classified as psychological or somatic/physical problems	*Gianinazzi et al 2013*
No association between survivor reported major medical conditions and depression were found using multivariable logistic regression (adjusted for sex, age at study, race, educational achievement, marital status, employment, income, health insurance). • Major medical condition (Ref. no major medical condition) OR=1.2 (95%CI:1.0-1.4) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥63); Survivors reporting complete deafness, kidney dialysis, congestive heart failure, myocardial infarction, angioplasty, bypass surgery, stroke, liver cirrhosis, a heart, lung, or kidney transplant,	*Zeltzer et al. 2008*

amputation, joint replacement or second cancer, and/or current use of seizure medications, medications for heart problems or high blood pressure, chemotherapy, immune suppressants, or oxygen were classified as having a major medical condition	
Perceived good or fair health was associated with increased depressive symptoms using generalized linear mixed modeling (adjusted for sex, income, major medical condition, brain radiation dosage, age, income & health; higher least square (LS) mean indicates more problems). • Self-rated health: Poor or fair: LS mean 5.21 (SE 0.37), compared to good/very good/excellent: LS mean 2.46 (SE 0.37), p<0.001 *Survivors of childhood brain cancer from the CCSS cohort (n=1101; mixed neurooncology diagnoses; <21 yrs at diagnosis; mean 26.5 yrs at study). Controls: n=2817 siblings (mean 29.4 yrs at study). Measurement: BSI-18 Depression subscale and single item assessing self-reported health (fair/poor vs. good/very good/excellent)	*Zebrack et al. 2004*
Overall Conclusion	
Some evidence suggests that survivor-reported physical late effects and perceived poor health status are related to an increased risk of developing depression among survivors of CAYA cancer.	7 studies (3 samples) Level B[19,24,29,33,34,37,39]

Clinical risk factors: Pain	
Medium amount, a lot, and very bad cancer-related pain was associated with an increased risk for depression using Poisson regression (adjusted for heavy/risky drinking, sex, physical health, radiation, race, age at diagnosis, age at follow-up, educational attainment, and employment status). • Cancer-related pain: Medium amount, a lot, very bad (Ref. none, small amount) RR=1.5 (95%CI:1.2-1.8; P≤0.01) *Survivors from the CCSS cohort (n=4484; mixed diagnoses; mean 10.5 yrs at diagnosis; mean 27.2 yrs at Baseline. Controls: n=1651 siblings. Meaurement: BSI-18 Depression subscale (cutoff ≥63)	*Brinkman et al. 2019*
Cancer-related pain was associated with an increased risk for depression using multivariable logistic regression (adjusted for education, employment, health insurance, learning or memory problems, age at clinical evaluation): • Cancer-related pain: Very bad, excruciating pain (Ref. No pain) OR=6.63 (95%CI:2.76-15.90) • Cancer-related pain: A lot of pain (Ref. No pain) OR=4.50 (95%CI:2.75-7.36) • Cancer-related pain: Medium amount of pain (Ref. No pain) OR=1.41 (95%CI:0.89-2.23) • Cancer-related pain: Small amount of pain (Ref. No pain) OR=1.71 (95%CI:1.18-2.47) *Survivors from the St. Jude Lifetime Cohort Study (n=1863; mixed diagnoses; median 7 yrs at diagnosis; ≥10 yrs since diagnosis; median 32 yrs at study). Controls: none. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Oancea et al. 2014*
Overall Conclusion	
Evidence suggests that cancer-related pain is related to an increased risk of developing depression among survivors of CAYA cancer.	2 studies Level B[14,29]

Demographic risk factors: Physical exercise	
Meeting national guidelines for vigorous exercise (≥9 MET-hrs wk^{-1} as compared to <9) was associated with lower prevalence of depression using multivariable log-binomial regression (adjusted for age at follow-up, age at diagnosis, sex, race, smoking, education, cancer diagnosis, cancer treatment variables (alkylating agents, anthracyclines, chest radiation, brain or head radiation), baseline anxiety, depression, somatization or cancer pain, and baseline or interim severe, disabling, or life threatening chronic health conditions). • Meeting national guidelines for vigorous exercise: Yes (≥9 MET-hrs wk-1) (Ref. No (<9 MET-hrs wk-1)) PR=0.80 (95%CI:0.68-0.94; p=0.007) *Survivors from the CCSS cohort (n=6199; mixed diagnoses; median 10.0 yrs at diagnosis; mean 34.0 yrs at study). Controls: none. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Tonorezos et al. 2019*
Overall Conclusion	

Some evidence suggests that sufficient physical activity was associated with a decreased risk of developing depression among survivors of CAYA cancer.	1 study Level C[31]

Clinical risk factors: Drinking behavior	
Lower age at drinking initiation was associated with an increased risk for depression using Poisson regression (adjusted for sex, physical health, radiation, race, age at diagnosis, age at follow-up, educational attainment, and employment status). No association between heavy/risky drinking and depression was found using Poisson regression (adjusted for, sex, physical health, radiation, race, age at diagnosis, age at follow-up, educational attainment, and employment status). • Age at drinking initiation: <18 years (Ref. ≥18 years) RR=1.3 (95%CI:1.1-1.5; P≤0.01) • Heavy drinking: Yes (Ref. No) RR=1.2 (95%CI:1.0-1.5) *Survivors from the CCSS cohort (n=4484; mixed diagnoses; mean 10.5 yrs at diagnosis; mean 27.2 yrs at Baseline. Controls: n=1651 siblings. Meaurement: BSI-18 Depression subscale (cutoff ≥63).	*Brinkman et al. 2019*
Overall Conclusion	
Some evidence suggests that lower age at drinking initiation was associated with an increased risk of developing depression among survivors of CAYA cancer.	1 study Level C[29]
Some evidence suggests that heavy/risky drinking is not related to the risk of developing depression among survivors of CAYA cancer.	1 study Level C[29]

Demographic risk factors: Sex	
No association between sex and depression was found using Poisson regression (adjusted for heavy/risky drinking, sex, physical health, radiation, race, age at diagnosis, age at follow-up, educational attainment, and employment status). • Female (Ref. Male) RR=0.8 (95%CI:0.6-0.9) *Survivors from the CCSS cohort (n=4484; mixed diagnoses; mean 10.5 yrs at diagnosis; mean 27.2 yrs at Baseline. Controls: n=1651 siblings. Meaurement: BSI-18 Depression subscale (cutoff ≥63).	*Brinkman et al. 2019*
No association between sex and depression was found using multivariable logistic regression (adjusted for sex, age, marital status, education, income and employment). • Female (Ref. Male) OR=1.23 (95%CI: 0.69-2.18) *Survivors (n=951; mixed diagnoses; median 5.0 yrs at diagnosis [range 0-15 yrs]; median 28.1 yrs since diagnosis [range 23-36 yrs]; median 34.2 yrs at study [range 24-49 yrs]). Controls: n=1130, German Household Panel. Measurement: Patient Health Questionnaire (PHQ-8)	*Burghardt et al. 2019*
No association between sex and depression/anxiety was found using log-binomial models (adjusted for age at diagnosis, age at study, sex, annual household income). • Male (Ref. Female) not significant *Survivors of neuroblastoma from the CCSS cohort (n=859; 97.9% <5 yrs at diagnosis yrs; 8-17 yrs at study. Controls: n=872 siblings. Meaurement: BPI depression/anxiety subscale (cutoff >10th percentile of age-matched siblings).	*Zheng et al. 2018*
Female survivors of Ewing sarcoma are at increased risk for depression using multivariable binary logistic regression. • Female (Ref. Male) OR=1.71 (95%CI:1.20 to 2.45) *Survivors of Ewing sarcoma (n=618; 70.1% <18 yrs at diagnosis; median 29 yrs at study. Controls: n=316, median 30 yrs at study. Measurement: BSI-18 Depression subscale (0 ”no symptoms” to 4 ”highest symptoms”)	*Ranft et al. 2017*
No association between sex and depression was found using multivariable logistic regression (stratified by diagnostic groups). • CNS tumors and leukemia survivors: Sex not included in final model • Lymphoma and sarcoma survivors: Sex not included in final model *Survivors of adolescent and early young adult cancer from the CCSS cohort (n=2589; mixed diagnoses; 11-21 yrs at diagnosis; ≥75% were ≥35 yrs at study). Controls: n=3603 survivors diagnosed ≤10 yrs old. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Prasad et al. 2015*
Male survivors are at an increased risk for depression using multivariable logistic regression (adjusted for education, employment, health insurance, cancer-related pain, learning or memory problems, age at clinical evaluation). • Male (Ref. female) OR=1.56 (95%CI:1.17-2.09)	*Oancea et al. 2014*

*Survivors from the St. Jude Lifetime Cohort Study (n=1863; mixed diagnoses; median 7 yrs at diagnosis; ≥10 yrs since diagnosis; median 32 yrs at study). Controls: none. Measurement: BSI-18 Depression subscale (cutoff ≥63)	
No association between sex and depression was found using multivariable logistic regression (adjusted for age at study, parents' education, perceived parents' support, diagnosis, treatment modality, late effects, time since diagnosis). • Female (Ref. Male) OR=1.59 (95%CI:0.86-2.98, p=0.143) *Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥57)	*Gianinazzi et al 2013*
No association between sex and depression was found using generalized estimating equations (adjusting for scarring/disfigurement, hair loss, age at diagnosis, recurrence, SMN, age at study, race, educational achievement, marital status, cranial radiation, surgery). • Sex: An overall RR estimate is not shown for this demographic factor as a result of the presence of significant interactions with other variables in the model *Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥ 90th %tile on standardized norms)	*Kinahan et al. 2012*
Female survivors were at an increased risk for depression using multivariable logistic regression (adjusted for age at study, race, educational attainment, marital status, employment, annual income, health insurance, major medical condition). • Female (Ref. Male) OR=1.3 (95%CI:1.1-1.5) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Zeltzer et al. 2008*
No association between sex and depression/anxiety was found using multiple variable models (adjusted for current age group, age at diagnosis, race/ethnicity, annual household income, disfigurement, treatment). • Female (Ref. Male) RR=1.2 (99%CI:1.0-1.5) *Parent proxy report from the Adolescent CCSS cohort (n=2979; mixed diagnoses; mean 3.2 yrs at diagnosis; mean 14.8 yrs at study). Controls: n=649 siblings. Measurement: Behavior Problem Index (BPI) Depression/Anxiety subscale (cutoff ≥ 1.3 SD sibling mean)	*Schultz et al. 2007*
No association between sex and depressive symptoms was found using generalized linear mixed modeling (adjusted for income, self-rated health, major medical condition, brain radiation dosage, age, income & health; higher least square (LS) mean indicates more problems): • Female: LS mean 3.98 (SE 0.26), compared to male: LS mean 3.66 (SE 0.26), p=0.215 *Survivors of childhood brain cancer from the CCSS cohort (n=1101; mixed neurooncology diagnoses; <21 yrs at diagnosis; mean 26.5 yrs at study). Controls: n=2817 siblings (mean 29.4 yrs at study). Measurement: BSI-18 Depression subscale	*Zebrack et al. 2004*
Female survivors were at an increased risk for depression using logistic regression with general estimating equations (adjusted for intensive chemotherapy, income, education). • Female (Ref. Male) RR=2.06 (95%CI:1.53-2.76, p<0.0001) *Survivors from the CCSS cohort (n=5736; leukemia, Hodgkins lymphoma, and non-Hodgkins lymphoma diagnoses; mean 10.1 yrs at diagnosis [range: 0-20 yrs]; mean 26.9 yrs at study [range: 18-48 yrs]). Controls: n=2565 siblings. Measurement: Brief Symptom Inventory-18 (BSI-18) positive depressive symptoms transposed onto Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria for major depressive episode	*Zebrack et al. 2002*
Overall Conclusion	
Some evidence suggests that female sex is related to an increased risk of depression. One study suggests that male sex is related to increased risk of depression, while 3 studies (2 samples) suggests that female sex is related to an increased risk of depression, and 8 studies (3 samples) find no association	12 studies (5 samples) Level C[14,19,21-24,26,29,37,39,44,67]

Demographic risk factors: Age at study	
Higher age was associated with a decreased risk for depression, using multivariable logistic regression (adjusted for sex, age, marital status, education, income and employment). • Age at clinical evaluation (continuous): OR=0.92 (95%CI: 0.87, 0.97, p=0.004) *Survivors (n=951; mixed diagnoses; median 5.0 yrs at diagnosis [range 0-15 yrs]; median 28.1 yrs since diagnosis [range 23-36 yrs]; median 34.2 yrs at study [range 24-49 yrs]). Controls: n=1130, German Household Panel. Measurement: Patient Health Questionnaire (PHQ-8)	*Burghardt et al. 2019*
No association between age at study and depression was found using multivariable binary logistic regression. • Age at study, years: 20-29 (Ref. <20) OR= 1.65 (95%CI:0.93 to 2.94) • Age at study, years: 30-39 (Ref. <20) OR= 1.45 95%CI: (0.75 to 2.83) • Age at study, years: 40-64 (Ref. <20) OR= 1.60 (95%CI:0.79 to 3.23) *Survivors of Ewing sarcoma (n=618; 70.1% <18 yrs at diagnosis; median 29 yrs at study. Controls: n=316, median 30 yrs at study. Measurement: BSI-18 Depression subscale (0 "no symptoms" to 4 "highest symptoms")	*Ranft et al. 2017*
No association between age at study and depression was found using multivariable logistic regression (stratified by diagnostic groups). • CNS tumors and leukemia survivors: Age at study not included in final model • Lymphoma and sarcoma survivors: Age at study not included in final model *Survivors of adolescent and early young adult cancer from the CCSS cohort (n=2589; mixed diagnoses; 11-21 yrs at diagnosis; ≥75% were ≥35 yrs at study). Controls: n=3603 survivors diagnosed ≤10 yrs old. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Prasad et al. 2015*
Older age at study was associated with an increased risk for depression using multivariable logistic regression (adjusted for education, employment, health insurance, cancer-related pain, learning or memory problems). • Age at clinical evaluation (continuous): OR=1.027 (95%CI:1.008-1.045) *Survivors from the St. Jude Lifetime Cohort Study (n=1863; mixed diagnoses; median 7 yrs at diagnosis; ≥10 yrs since diagnosis; median 32 yrs at study). Controls: none. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Oancea et al. 2014*
No association between age at study and depression was found using multivariable logistic regression (adjusted for sex, parents' education, perceived parents' support, diagnosis, treatment modality, late effects, time since diagnosis). • Age at study, years: 18-19 (Ref. 16-17) OR=1.01 (95%CI:0.53-1.89, p=0.992) *Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥57)	*Gianinazzi et al 2013*
No association between age at study and depression was found using generalized estimating equations (adjusting for scarring/disfigurement, hair loss, recurrence, SMN, age at diagnosis, sex, race, educational achievement, marital status, cranial radiation, surgery). • Age at study: 30-39 years (Ref. <30 years) OR=1.00 (95%CI:0.81-1.22, p=0.98) • Age at study: ≥40 years (Ref. <30 years) OR=1.23 (95%CI:0.92-1.66, p=0.16) *Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥ 90th %tile on standardized norms)	*Kinahan et al. 2012*
No association between age at study and depression was found using multivariable logistic regression (adjusted for sex, race, educational attainment, marital status, employment, annual income, health insurance, major medical condition). • Age at second follow-up: 25-34 years (Ref. 18-24 years) OR=1.0 (95%CI:0.8-1.2) • Age at second follow-up: 35+ years (Ref. 18-24 years) OR=1.3 (95%CI:1.0-1.6) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Zeltzer et al. 2008*
No association between age at study was found with depression/anxiety using multiple variable models (adjusted for sex, age at diagnosis, race/ethnicity, annual household income, disfigurement, treatment). • Current age group: 12-14 years (Ref. 15-17) RR=1.1 (99%CI:0.9-1.4)	*Schultz et al. 2007*

*Parent proxy report from the Adolescent CCSS cohort (n=2979; mixed diagnoses; mean 3.2 yrs at diagnosis; mean 14.8 yrs at study). Controls: n=649 siblings. Measurement: Behavior Problem Index (BPI) Depression/Anxiety subscale (cutoff ≥ 1.3 SD sibling mean)	
Overall Conclusion	
There is conflicting evidence regarding the association between age at study and risk of depression among survivors of CAYA cancer.	8 studies (6 samples) Conflicting evidence[14,19,21,22,24,26,44,67]

Demographic risk factors: Race/ethnicity	
No association between race and depression was found using generalized estimating equations (adjusting for scarring/disfigurement, hair loss, recurrence, SMN, age at diagnosis, age at study, sex, educational achievement, marital status, cranial radiation, surgery). • Black (Ref. White) OR=0.86 (95%CI:0.55-1.34, p=0.50) • Other/mixed (Ref. White) OR=1.10 (95%CI:0.80-1.51, p=0.57) *Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥ 90th %tile on standardized norms)	*Kinahan et al. 2012*
No association between race and depression was found using multivariable logistic regression (adjusted for sex, age at study, educational attainment, marital status, employment, annual income, health insurance, major medical condition). • Black (Ref. White) OR=0.7 (95%CI:0.4-1.1) • Hispanic (Ref. White) OR=1.2 (95%CI:0.8-1.7) • Other (Ref. White) OR=1.1 (95%CI:0.7-1.7) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Zeltzer et al. 2008*
No association between race/ethnicity and depression/anxiety was found using multiple variable models (adjusted for sex, current age group, age at diagnosis, annual household income, disfigurement, treatment). • Black (Ref. White) RR=1.3 (99%CI:0.8-1.9) • Hispanic (Ref. White) RR=1.2 (99%CI:0.8-1.9) • Other (Ref. White) RR=1.0 (99%CI:0.6-1.7) *Parent proxy report from the Adolescent CCSS cohort (n=2979; mixed diagnoses; mean 3.2 yrs at diagnosis; mean 14.8 yrs at study). Controls: n=649 siblings. Measurement: Behavior Problem Index (BPI) Depression/Anxiety subscale (cutoff ≥ 1.3 SD sibling mean)	*Schultz et al. 2007*
Overall Conclusion	
Evidence suggests that race/ethnicity is not associated with the risk of depression among survivors of CAYA cancer.	3 studies (2 samples) Level B[22,24,67]

Demographic risk factors: Marital status	
No association between marital status and depression was found using multivariable logistic regression (adjusted for sex, age, marital status, education, income and employment). • Married (Ref. Not married) OR=1.21 (95%CI:0.62-2.36) *Survivors (n=951; mixed diagnoses; median 5.0 yrs at diagnosis [range 0-15 yrs]; median 28.1 yrs since diagnosis [range 23-36 yrs]; median 34.2 yrs at study [range 24-49 yrs]). Controls: n=1130, German Household Panel. Measurement: Patient Health Questionnaire (PHQ-8)	*Burghardt et al. 2019*
No association between marital status and depression was found using generalized estimating equations (adjusting for scarring/disfigurement, hair loss, recurrence, SMN, age at diagnosis, age at study, sex, educational achievement, race, cranial radiation, surgery). • Marital status: An overall RR estimate is not shown for this demographic factor as a result of the presence of significant interactions with other variables in the model	*Kinahan et al. 2012*

*Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥ 90th %tile on standardized norms)	
Not being married was associated with increased risk for depression using multivariable logistic regression (adjusted for sex, age at study, race, educational achievement, employment, annual income, health insurance, major medical condition). • Single (Ref. married/living as married) OR=1.9 (95%CI:1.6-2.3) • Divorced/separated (Ref. married/living as married) OR=2.2 (95%CI:1.7-2.9) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Zeltzer et al. 2008*
Not being married/not living as married was associated with increased depressive symptoms using generalized linear mixed modeling (adjusted for sex, income, self-rated health, major medical condition, brain radiation dosage, age, income & health; higher least square (LS) mean indicates more problems): • Marital status: Not currently married: LS mean 4.46 (SE 0.22), compared to married/living as married: LS mean 3.18 (SE 0.31), p<0.001 *Survivors of childhood brain cancer from the CCSS cohort (n=1101; mixed neurooncology diagnoses; <21 yrs at diagnosis; mean 26.5 yrs at study). Controls: n=2817 siblings (mean 29.4 yrs at study). Measurement: BSI-18 Depression subscale	*Zebrack et al. 2004*
Overall Conclusion	
Evidence suggests that not being married/not living as married is associated with increased risk of depression among survivors of CAYA cancer.	4 studies (2 samples) Level B[24,26,39,67]

Demographic risk factors: Educational achievement	
Low education was associated with increased risk for depression, using multivariable logistic regression (adjusted for sex, age, marital status, education, income and employment). • Education: Low (Ref. High) OR=2.33 (95%CI: 1.08, 5.02) • Education: Middle (Ref. High) OR=1.84 (95%CI:0.97-3.48) *Survivors (n=951; mixed diagnoses; median 5.0 yrs at diagnosis [range 0-15 yrs]; median 28.1 yrs since diagnosis [range 23-36 yrs]; median 34.2 yrs at study [range 24-49 yrs]). Controls: n=1130, German Household Panel. Measurement: Patient Health Questionnaire (PHQ-8)	*Burghardt et al. 2019*
Completing high school, but not graduating from college, was associated with an increased risk for depression using multivariable logistic regression (adjusted for employment, health insurance, cancer-related pain, learning or memory problems, age at clinical evaluation). • Education: Did not graduate high school (Ref. College graduate or post-graduate level) OR=1.16 (95%CI:0.68-1.97) • Education: Completed high school/GED or received training after high school (Ref. College graduate or post-graduate level) OR=1.52 (95%CI:1.03-2.24) • Education: Some college (Ref. College graduate or post-graduate level) OR=1.37 (95%CI:0.94-2.01) *Survivors from the St. Jude Lifetime Cohort Study (n=1863; mixed diagnoses; median 7 yrs at diagnosis; ≥10 yrs since diagnosis; median 32 yrs at study). Controls: none. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Oancea et al. 2014*
Being a college graduate was associated with a lower risk for depression using generalized estimating equations (adjusting for scarring/disfigurement, hair loss, recurrence, SMN, age at diagnosis, age at study, sex, marital status, race, cranial radiation, surgery). • College graduate: Yes (Ref. No) OR=0.79 (95%CI:0.68-0.92, p<0.01) *Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥ 90th %tile on standardized norms)	*Kinahan et al. 2012*

No association between educational achievement and depression was found using multivariable logistic regression (adjusted for sex, age at study, race, marital status, employment, annual income, health insurance, major medical condition). • Below high school (Ref. college graduate) OR=1.2 (95%CI:0.9-1.8) • High school graduate (Ref. college graduate) OR=1.2 (95%CI:1.0-1.4) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Zeltzer et al. 2008*
Higher educational achievement was associated with decreased depressive symptoms using generalized linear mixed modeling (adjusted for sex, income, self-rated health, major medical condition, brain radiation dosage, age, income & health; higher least square (LS) mean indicates more problems): • Education: <High school graduate: LS mean 4.55 (SE 0.41), compared to HS graduate or some college: LS mean 3.42 (SE 0.23), compared to college graduate: LS mean 3.49 (SE 0.41), p=0.030 *Survivors of childhood brain cancer from the CCSS cohort (n=1101; mixed neurooncology diagnoses; <21 yrs at diagnosis; mean 26.5 yrs at study). Controls: n=2817 siblings (mean 29.4 yrs at study). Measurement: BSI-18 Depression subscale	*Zebrack et al. 2004*
Lower educational achievement was associated with increased risk for depression using logistic regression with general estimating equations (adjusted for sex, intensive chemotherapy, & income). • Below high school graduate (Ref. College-postgraduate) RR=2.27 (95%CI:1.39-3.70, p=0.001) • High school graduate-some college (Ref. College-postgraduate) RR=1.41 (95%CI:1.01-1.97, p=0.04) *Survivors from the CCSS cohort (n=5736; leukemia, Hodgkins lymphoma, and non-Hodgkins lymphoma diagnoses; mean 10.1 yrs at diagnosis [range: 0-20 yrs]; mean 26.9 yrs at study [range: 18-48 yrs]). Controls: n=2565 siblings. Measurement: Brief Symptom Inventory-18 (BSI-18) positive depressive symptoms transposed onto Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria for major depressive episode	*Zebrack et al. 2002*
Overall Conclusion	
Evidence suggests that lower levels of educational achievement are associated with greater risk for depression among survivors of CAYA cancer.	6 studies (3 samples) Level B[14,23,24,26,39,67]

Demographic risk factors: Employment	
No association between employment and depression was found using multivariable logistic regression (adjusted for sex, age, marital status, education, income and employment). • Unemployed (Ref. Employed) OR=2.63 (95%CI:0.88-7.88) *Survivors (n=951; mixed diagnoses; median 5.0 yrs at diagnosis [range 0-15 yrs]; median 28.1 yrs since diagnosis [range 23-36 yrs]; median 34.2 yrs at study [range 24-49 yrs]). Controls: n=1130, German Household Panel. Measurement: Patient Health Questionnaire (PHQ-8)	*Burghardt et al. 2019*
No significant association was found between employment and depression using multivariable logistic regression (adjusted for education, health insurance, cancer-related pain, learning or memory problems, age at clinical evaluation). • Employment: Unable to work due to illness or disability (Ref. Caring for home or family (not seeking paid work)/Student/Retired/Working part- or full-time) OR=1.37 (95%CI:0.74-2.52) • Employment: Never had a job, or not currently working or unemployed and looking for work (Ref. Caring for home or family (not seeking paid work)/Student/Retired/Working part- or full-time) OR=1.39 (95%CI:0.96-2.02) *Survivors from the St. Jude Lifetime Cohort Study (n=1863; mixed diagnoses; median 7 yrs at diagnosis; ≥10 yrs since diagnosis; median 32 yrs at study). Controls: none. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Oancea et al. 2014*
Unemployment was associated with increased risk for depression using multivariable logistic regression (adjusted for sex, age at study, race, educational achievement, marital status, annual income, health insurance, major medical condition). • Student (Ref. employed/caring for home) OR=1.0 (95%CI:0.7-1.4)	*Zeltzer et al. 2008*

• Looking for work/unable to work (Ref. employed/caring for home) OR=2.5 (95%CI:2.0-3.0) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥63)	
Overall Conclusion	
Some evidence suggests that looking for work or being unable to work is associated with greater risk for depression among survivors of CAYA cancer.	3 studies Level C[14,24,26]

Demographic risk factors: Income	
No association between income and depression was found using multivariable logistic regression (adjusted for sex, age, marital status, education, income and employment). • Income in 100 Euros per month (continuous): OR=0.98 (95%CI:0.96-1.00) *Survivors (n=951; mixed diagnoses; median 5.0 yrs at diagnosis [range 0-15 yrs]; median 28.1 yrs since diagnosis [range 23-36 yrs]; median 34.2 yrs at study [range 24-49 yrs]). Controls: n=1130, German Household Panel. Measurement: Patient Health Questionnaire (PHQ-8)	*Burghardt et al. 2019*
No association between annual household income and depression/anxiety was found using log-binomial models (adjusted for age at diagnosis, age at study, sex, annual household income). • Unknown (Ref. ≥$60,000) PR=0.89 (95%CI:0.4-1.73) • <$20,000 (Ref. ≥$60,000) PR=1.45 (95%CI:0.9-2.33) • $20,000-$39,999 (Ref. ≥$60,000) PR=1.32 (95%CI:0.87-2.04) • $40,000-$59,999 (Ref. ≥$60,000) PR=0.85 (95%CI:0.57-1.29) *Survivors of neuroblastoma from the CCSS cohort (n=859; 97.9% <5 yrs at diagnosis yrs; 8-17 yrs at study. Controls: n=872 siblings. Meaurement: BPI depression/anxiety subscale (cutoff >10th percentile of age-matched siblings).	*Zheng et al. 2018*
Low annual income was associated with increased risk for depression using multivariable logistic regression (adjusted for sex, age at study, race, educational achievement, marital status, employment, health insurance, major medical condition). • Annual income below $20,000 (Ref. $20,000+) OR=1.8 (95%CI:1.5-2.2) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Zeltzer et al. 2008*
Household income was not associated with depression/anxiety using multiple variable models (adjusted for sex, current age group, age at diagnosis, race/ethnicity, disfigurement, treatment). • <20,000 (Ref. 60,000+) RR=1.3 (99%CI:1.0-1.9) • 20,000-60,000 (Ref. 60,000+) RR=1.3 (99%CI:0.7-1.3) *Parent proxy report from the Adolescent CCSS cohort (n=2979; mixed diagnoses; mean 3.2 yrs at diagnosis; mean 14.8 yrs at study). Controls: n=649 siblings. Measurement: Behavior Problem Index (BPI) Depression/Anxiety subscale (cutoff ≥ 1.3 SD sibling mean)	*Schultz et al. 2007*
Low income was associated with an increased risk for depression using logistic regression with general estimating equations (adjusted for sex, intensive chemotherapy, education). • Income <$20,000 (Ref. $20,000-$60,000+) RR=2.21 (95%CI:1.64-2.99, p<0.0001) *Survivors from the CCSS cohort (n=5736; leukemia, Hodgkins lymphoma, and non-Hodgkins lymphoma diagnoses; mean 10.1 yrs at diagnosis [range: 0-20 yrs]; mean 26.9 yrs at study [range: 18-48 yrs]). Controls: n=2565 siblings. Measurement: Brief Symptom Inventory-18 (BSI-18) positive depressive symptoms transposed onto Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria for major depressive episode	*Zebrack et al. 2002*
Overall Conclusion	
Some evidence suggests that a lower annual income is associated with greater risk for depression among survivors of CAYA cancer.	5 studies (3 samples) Level C[22-24,26,37]

Demographic risk factors: Health insurance	
No association between health insurance and depression was found using multivariable logistic regression (adjusted for education, employment, cancer-related pain, learning or memory problems, age at clinical evaluation). • Health insurance: none (Ref. Canadian resident/Through spouse's or parent's policy/Through place of employment/Through self-purchased policy) OR=1.32 (95%CI:0.92-1.89) • Health insurance: Through Medicare or Medicaid or other public assistance programs, or military dependent/veteran's benefits (Ref. Canadian resident/Through spouse's or parent's policy/Through place of employment/Through self-purchased policy) OR=1.01 (95%CI:0.64-1.60) *Survivors from the St. Jude Lifetime Cohort Study (n=1863; mixed diagnoses; median 7 yrs at diagnosis; ≥10 yrs since diagnosis; median 32 yrs at study). Controls: none. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Oancea et al. 2014*
No association was found between health insurance and depression using multivariable logistic regression (adjusted for sex, age at study, race, educational achievement, marital status, employment, income, major medical condition). • No health insurance (Ref. health insurance) OR=1.3 (95%CI:1.0-1.7) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Zeltzer et al. 2008*
Overall Conclusion	
Evidence suggests that health insurance status is not associated with the risk of depression among survivors of CAYA cancer.	2 studies Level B[14,24]

Demographic risk factors: Parents' educational achievement	
No association between parents' education and depression was found using multivariable logistic regression (adjusted for age at study, sex, perceived parents' support, diagnosis, treatment modality, late effects, time since diagnosis). • Parents' education: Secondary, tertiary (Ref. Compulsory, primary) OR=1.47 (95%CI:0.66-3.28, p=0.346) *Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥57)	*Gianinazzi et al 2013*
Overall Conclusion	
Some evidence suggests that parents' educational achievement is not associated with the risk of depression among survivors of CAYA cancer.	1 study Level C[19]

Treatment-related risk factors: Bone marrow transplantation	
No association between bone marrow transplantation and depression was found using multivariable logistic regression (adjusted for age at study, sex, parents' education, perceived parents' support, diagnosis, late effects, time since diagnosis). • Treatment: Bone marrow transplantation (Ref. Chemotherapy) OR=1.04 (95%CI:0.33-3.29, p=0.537) *Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥57)	*Gianinazzi et al 2013*
Overall Conclusion	
Some evidence suggests that bone marrow transplantation is not associated with the risk of depression among survivors of CAYA cancer.	1 study Level C[19]

Treatment-related risk factors: Chemotherapy	
No association between treatment with anthracyclines and depression/anxiety was found using log-binomial models (adjusted for cranial radiation, abdominal radiation, total body irradiation, anthracycline, interaction between age at diagnosis and platinum agent, interaction between age at diagnosis and anthracycline, age at diagnosis, age at evaluation, sex, and annual household income). • Anthracycline: Yes (Ref. No) not significant	*Zheng et al. 2018*

*Survivors of neuroblastoma from the CCSS cohort (n=859; 97.9% <5 yrs at diagnosis yrs; 8-17 yrs at study. Controls: n=872 siblings. Meaurement: BPI depression/anxiety subscale (cutoff >10th percentile of age-matched siblings).	
No association between high-dose chemotherapy and depression was found using multivariable binary logistic regression. • High-dose chemotherapy: Yes (Ref. No) OR= 1.12 (95%CI:0.58 to 2.15) *Survivors of Ewing sarcoma (n=618; 70.1% <18 yrs at diagnosis; median 29 yrs at study. Controls: n=316, median 30 yrs at study. Measurement: BSI-18 Depression subscale (0 ”no symptoms” to 4 ”highest symptoms”)	*Ranft et al. 2017*
Treatment with antimetabolites was associated with a lower risk for depression in CNS tumor/leukemia survivors using multivariable logistic regression (stratified by diagnostic groups). • CNS tumors and leukemia survivors: Chemotherapy: Antimetabolites (Ref. yes) OR=0.72 (95%CI:0.58-0.90) (adjusted for age at diagnosis) • CNS tumors and leukemia survivors: Chemotherapy: Corticosteroids not included in final model • Lymphoma and sarcoma survivors: Chemotherapy not included in final model *Survivors of adolescent and early young adult cancer from the CCSS cohort (n=2589; mixed diagnoses; 11-21 yrs at diagnosis; ≥75% were ≥35 yrs at study). Controls: n=3603 survivors diagnosed ≤10 yrs old. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Prasad et al. 2015*
No associations between different treatment type modalities and depression was were found using multivariable logistic regression (adjusted for age at study, sex, parents’ education, perceived parents’ support, diagnosis, late effects, time since diagnosis). • Treatment: Surgery (Ref. Chemotherapy) OR=0.89 (95%CI:0.31-2.66, p=0.537) • Treatment: Radiotherapy (Ref. Chemotherapy) OR=0.57 (95%CI:0.26-1.31, p=0.537) • Treatment: Bone marrow transplantation (Ref. Chemotherapy) OR=1.04 (95%CI:0.33-3.29, p=0.537) *Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥57)	*Gianinazzi et al 2013*
No association of chemotherapy and depression was found using multivariable logistic regression (adjusted for sex, age at diagnosis, survival time, surgery, radiation). • Chemotherapy (Ref. no surgery) OR=1.0 (95%CI:0.8-1.2) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Zeltzer et al. 2008*
Intensive chemotherapy was associated with an increased risk for depression using logistic regression with general estimating equations (adjusted for sex, income, education). • Intensive chemotherapy: Yes (Ref. No) RR=1.46 (95%CI:1.09-1.96, p=0.01) *Survivors from the CCSS cohort (n=5736; leukemia, Hodgkins lymphoma, and non-Hodgkins lymphoma diagnoses; mean 10.1 yrs at diagnosis [range: 0-20 yrs]; mean 26.9 yrs at study [range: 18-48 yrs]). Controls: n=2565 siblings. Measurement: Brief Symptom Inventory-18 (BSI-18) positive depressive symptoms transposed onto Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria for major depressive episode	*Zebrack et al. 2002*
Overall Conclusion	
Some evidence suggests that more intense chemotherapy is associated with an increased risk of depression among survivors of CAYA cancer.	6 studies (3 samples) Level C[19,21,23,24,37,44]

Treatment-related risk factors: Radiation	
No association between radiation and depression was found using Poisson regression (adjusted for heavy/risky drinking, sex, physical health, radiation, race, age at diagnosis, age at follow-up, educational attainment, and employment status). • Radiation: Non-cranial (Ref. None) RR=0.8 (0.6-1.0) • Radiation: CRT≤20Gy (Ref. None) RR=0.9 (0.7-1.2) • Radiation: CRT>20Gy (Ref. None) RR=1.0 (0.8-1.3)	*Brinkman et al. 2019*

*Survivors from the CCSS cohort (n=4484; mixed diagnoses; mean 10.5 yrs at diagnosis; mean 27.2 yrs at Baseline. Controls: n=1651 siblings. Meaurement: BSI-18 Depression subscale (cutoff ≥63).	
No association between radiation and depression/anxiety was found using log-binomial models (adjusted for cranial radiation, abdominal radiation, total body irradiation, anthracycline, interaction between age at diagnosis and platinum agent, interaction between age at diagnosis and anthracycline, age at diagnosis, age at evaluation, sex, and annual household income). • Cranial radiation: Yes (Ref. No) not significant • Abdominal radiation: Yes (Ref. No) not significant • Total body irradiation: Yes (Ref. No) not significant *Survivors of neuroblastoma from the CCSS cohort (n=859; 97.9% <5 yrs at diagnosis yrs; 8-17 yrs at study. Controls: n=872 siblings. Meaurement: BPI depression/anxiety subscale (cutoff >10th percentile of age-matched siblings).	*Zheng et al. 2018*
No association between radiotherapy, or radiotherapy + surgery and depression was found using multivariable binary logistic regression. • Local treatment: Surgery + Radiotherapy (Ref. Surgery) OR= 0.94 (95%CI:0.61 to 1.44) • Local treatment: Radiotherapy (Ref. Surgery) OR= 0.70 (95%CI:0.37 to 1.31) *Survivors of Ewing sarcoma (n=618; 70.1% <18 yrs at diagnosis; median 29 yrs at study. Controls: n=316, median 30 yrs at study. Measurement: BSI-18 Depression subscale (0 ”no symptoms” to 4 ”highest symptoms”)	*Ranft et al. 2017*
No association between cranial irradiation and depression was found using multivariable logistic regression. • CNS tumors and leukemia survivors: Cranial irradiation not included in final model *Survivors of adolescent and early young adult cancer from the CCSS cohort (n=2589; mixed diagnoses; 11-21 yrs at diagnosis; ≥75% were ≥35 yrs at study). Controls: n=3603 survivors diagnosed ≤10 yrs old. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Prasad et al. 2015*
No association between radiotherapy and depression was found using multivariable logistic regression (adjusted for age at study, sex, parents’ education, perceived parents’ support, diagnosis, late effects, time since diagnosis). • Treatment: Radiotherapy (Ref. Chemotherapy) OR=0.57 (95%CI:0.26-1.31, p=0.537) *Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥57)	*Gianinazzi et al 2013*
Cranial radiation ≤20 Gy (considered scatter exposure only) was associated with a lower risk for depression using generalized estimating equations (adjusting for scarring/disfigurement, hair loss, recurrence, SMN, age at diagnosis, age at study, sex, race, educational achievement, marital status, surgery). • Cranial radiation: Scatter exposure only (Ref. none) OR=0.82 (95%CI:0.68-0.99, p=0.04) • Cranial radiation: Direct, ≤20 Gy (Ref. none) OR=1.00 (95%CI:0.79-1.26, p=0.99) • Cranial radiation: Direct, 20-36 Gy (Ref. none) OR=1.01 (95%CI:0.80-1.27, p=0.93) • Cranial radiation: Direct, ≥36 Gy (Ref. none) OR=0.88 (95%CI:0.68-1.15, p=0.35) *Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥ 90th %tile on standardized norms)	*Kinahan et al. 2012*
No association between radiation and depression was found using multivariable logistic regression (adjusted for sex, age at diagnosis, survival time, surgery, chemotherapy). • Cranial radiation (Ref. none) OR=1.2 (95%CI:1.0-1.5) • Other than cranial radiation (Ref. none) OR=0.9 (95%CI:0.7-1.1) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Zeltzer et al. 2008*
Treatment with cranial radiation, or both intrathecal methotrexate and cranial radiation was associated with an increased risk for depression/anxiety using multiple variable models (adjusted for sex, current age group, age at diagnosis, race/ethnicity, annual household income, & disfigurement).	*Schultz et al. 2007*

• Intrathecal methotrexate (Ref. No IT Mtx or CR) RR=1.3 (99%CI:1.0-1.7) • Cranial radiation (Ref. No IT Mtx or CR) RR=1.7 (99%CI:1.2-2.6) • Both IT Mtx and CR (Ref. No IT Mtx or CR) RR=1.8 (99%CI:1.3-2.4) *Parent proxy report from the Adolescent CCSS cohort (n=2979; mixed diagnoses; mean 3.2 yrs at diagnosis; mean 14.8 yrs at study). Controls: n=649 siblings. Measurement: Behavior Problem Index (BPI) Depression/Anxiety subscale (cutoff ≥ 1.3 SD sibling mean).	
Overall Conclusion	
There is conflicting evidence as to whether radiation is associated with a risk of depression among survivors of CAYA cancer. One study found that cranial scatter exposure was associated with decreased risk of depression, while another study found cranial radiation was associated with increased risk of depression/anxiety.	8 studies (4 samples) Conflicting evidence[19,21,22,24,29,37,44,67]

Treatment-related risk factors: Surgery	
No association between surgery and depression was found using multivariable logistic regression (adjusted for age at study, sex, parents' education, perceived parents' support, diagnosis, late effects, time since diagnosis). • Treatment: Surgery (Ref. Chemotherapy) OR=0.89 (95%CI:0.31-2.66, p=0.537) *Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥57)	*Gianinazzi et al 2013*
Having had surgery was associated with an increased risk for depression using generalized estimating equations (adjusting for scarring/disfigurement, hair loss, recurrence, SMN, age at diagnosis, age at study, sex, race, educational achievement, marital status, cranial radiation). • Surgery: Yes (Ref. No) OR=1.24 (95%CI:1.06-1.45, p=0.01) *Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥ 90th %tile on standardized norms)	*Kinahan et al. 2012*
No association between surgery and depression was found using multivariable logistic regression (adjusted for sex, age at diagnosis, survival time, chemotherapy, radiation). • Surgery (Ref. no surgery) OR=1.1 (95%CI:0.9-1.4) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Zeltzer et al. 2008*
Overall Conclusion	
Some evidence suggests that having had surgery (not further specified) is associated with an increased risk of depression among survivors of CAYA cancer.	3 studies (2 samples) Level C[19,24,67]

1b-2. What are the key clinical, demographic and treatment-related risk factors for developing anxiety among survivors of childhood, adolescent, and young adult (CAYA) cancer?	
Conclusion single studies	
Clinical risk factors: Age at diagnosis	
Survivors who were older at diagnosis were at lower risk for anxiety using multivariable logistic regression (stratified by diagnostic groups). • CNS tumors and leukemia survivors: Age at diagnosis, years: 11-21 (Ref. ≤10 years) OR=1.44 (95%CI:0.97-2.13) (adjusted for current age) • Lymphoma and sarcoma survivors: Age at diagnosis, years: 11-21 (Ref. ≤10 years) OR=0.73 (95%CI:0.54-0.98) (adjusted for chemotherapy) *Survivors of adolescent and early young adult cancer from the CCSS cohort (n=2589; mixed diagnoses; 11-21 yrs at diagnosis; ≥75% were ≥35 yrs at study). Controls: n=3603 survivors diagnosed ≤10 yrs old. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	*Prasad et al. 2015*
No association between age at diagnosis and anxiety was found using generalized estimating equations (adjusting for scarring/disfigurement, hair loss, recurrence, SMN, sex, race, educational achievement, marital status, cranial radiation, surgery). • Age at diagnosis: 5-9 years (Ref. 0-4 years) OR=0.96 (95%CI:0.74-1.23, p=0.73)	*Kinahan et al. 2012*

• Age at diagnosis: 10-21 years (Ref. 0-4 years) OR=1.08 (95%CI:0.81-1.45, p=0.60) *Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥ 90th %tile on standardized norms)	
No association between age at diagnosis and anxiety was found using multivariable logistic regression (adjusted for sex, survival time, surgery, chemotherapy, radiation). • Age at diagnosis: 0-3 years (Ref. 15-20 years) OR=1.1 (95%CI:0.8-1.4) • Age at diagnosis: 4-9 years (Ref. 15-20 years) OR=1.1 (95%CI:0.8-1.5) • Age at diagnosis: 10-14 years (Ref. 15-20 years) OR=0.9 (95%CI:0.7-1.2) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	*Zeltzer et al. 2008*
Overall Conclusion	
Some evidence suggests that older age at diagnosis is related to a decreased risk for for developing anxiety; however, this was only among survivors of CAYA cancer with lymphoma and sarcoma diagnoses.	3 studies (1 sample) Level C[21,24,67]

Clinical risk factors: Time since diagnosis	
No association between survival time and anxiety was found using multivariable logistic regression (adjusted for sex, age at diagnosis, surgery, chemotherapy, radiation). • Survival time: <20 years (Ref. 30+ years) OR=1.1 (95%CI:0.8-1.6) • Survival time: 20-24 years (Ref. 30+ years) OR=1.0 (95%CI:0.8-1.4) • Survival time: 25-29 years (Ref. 30+ years) OR=1.0 (95%CI:0.7-1.3) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	*Zeltzer et al. 2008*
Overall Conclusion	
Some evidence suggests that time since diagnosis is not related to the risk of developing anxiety among survivors of CAYA cancer.	1 study Level C[24]

Clinical risk factors: Diagnosis	
No association between diagnosis and anxiety was found using multivariable logistic regression (adjusted for age at study, sex, parents' education, perceived parents' support, treatment modality, late effects, time since diagnosis). • Diagnosis: CNS tumors (Ref. Leukemia, lymphoma) OR=0.44 (95%CI:0.44-3.38, p=0.141) • Diagnosis: Other (Ref. Leukemia, lymphoma) OR=0.69 (95%CI:0.14-1.21, p=0.141) *Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥57)	*Gianinazzi et al 2013*
Ewing sarcoma survivors were at increased risk for cancer-related anxiety using generalized linear models (adjusted for tumor location, age at questionnaire, sex, race, age at diagnosis). • Tumor Type: Ewing sarcoma (Ref. Soft tissue sarcoma) RR=2.08 (95%CI:1.09-3.98) • Tumor Type: Osteosarcoma (Ref. Soft tissue sarcoma) RR=1.32 (95%CI:0.74-2.35) • Tumor Type: Other bone (Ref. Soft tissue sarcoma) RR=1.37 (95%CI:0.32-5.93) *Survivors from the CCSS cohort (n=1094; upper and lower extremity sarcoma diadnoses; median 13 yrs at diagnosis, median 33 yrs at study). Controls: none. Measurement: Cancer-related anxiety measured with 1 item (medium/a lot/very many fears versus no/small amount of fears)	*Marina et al. 2013*
Survivors of Hodgkin disease, sarcoma, and bone cancers were at increased risk for cancer-related anxiety using multivariable logistic regression analysis (adjusted for age at interview, sex, race/ethnicity, education, household income, health insurance). • Diagnosis: CNS (Ref. Leukemia) OR=1.0 (95%CI:0.8-1.3) • Diagnosis: Hodgkin disease (Ref. Leukemia) OR=1.4 (95%CI:1.2-1.8) • Diagnosis: NHL (Ref. Leukemia) OR=1.1 (95%CI:0.8-1.4) • Diagnosis: Wilms (Ref. Leukemia) OR=0.9 (95%CI:0.7-1.2) • Diagnosis: Neuroblastoma (Ref. Leukemia) OR=0.9 (95%CI:0.6-1.2)	*Hudson et al. 2003*

• Diagnosis: Sarcoma (Ref. Leukemia) OR=1.4 (95%CI:1.2-1.8) • Diagnosis: Bone (Ref. Leukemia) OR=1.4 (95%CI:1.1-1.7) *Survivors from the CCSS cohort (n=9535; mixed diagnoses; mean 10.00 yrs at diagnosis [range: 0.1-20.9 yrs]; mean 26.8 yrs age at study [range: 18-48 yrs]). Controls: n=2916 siblings. Measurement: Cancer-related anxiety measured with 1 item (medium/a lot/very many/extreme fears versus no/small amount of fears)	
Overall Conclusion	
Some evidence suggests that diagnosis type is related to an increased risk of developing anxiety among survivors of CAYA cancer. Specifically, being diagnosed with Hodgins disease, sarcoma, or bone cancer was related to increased risk of anxiety (1 study), as was specifically Ewing sarcoma (1 study).	3 studies (2 samples) Level C[19,36,68]

Clinical risk factors: Second malignant neoplasm (SMN) or recurrence	
No association between SMN or recurrence and anxiety was found using multivariable logistic regression (stratified by diagnostic groups). • CNS tumors and leukemia survivors: SMN or recurrence not included in final model • Lymphoma and sarcoma survivors: SMN or recurrence not included in final model *Survivors of adolescent and early young adult cancer from the CCSS cohort (n=2589; mixed diagnoses; 11-21 yrs at diagnosis; ≥75% were ≥35 yrs at study). Controls: n=3603 survivors diagnosed ≤10 yrs old. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	*Prasad et al. 2015*
No association between recurrence or SMN and anxiety was found using generalized estimating equations (adjusting for scarring/disfigurement, hair loss, age at diagnosis, age at study, sex, race, educational achievement, marital status, cranial radiation, surgery). • Recurrence: Yes (Ref. No) OR=0.98 (95%CI:0.75-1.29, p=0.91) • Second malignant neoplasm: Yes (Ref. No) OR=0.85 (95%CI:0.54-1.36, p=0.50) *Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥ 90th %tile on standardized norms)	*Kinahan et al. 2012*
Overall Conclusion	
Some evidence suggests that having a second malignant neoplasm or recurrence is not related to the risk of developing anxiety among survivors of CAYA cancer.	2 studies (1 sample) Level C[21,67]

Clinical risk factors: Tumor location	
No association was found between tumor location and anxiety using multivariable binary logistic regression. • Axial (Ref. Pelvis) OR= 1.01 (95%CI:0.63 to 1.63) • Lower extremity (Ref. Pelvis) OR= 0.80 (95%CI:0.49 to 1.31) • Upper extremity (Ref. Pelvis) OR= 0.45 (95%CI:0.22 to 0.91) *Survivors of Ewing sarcoma (n=618; 70.1% <18 yrs at diagnosis; median 29 yrs at study. Controls: n=316, median 30 yrs at study. Measurement: BSI-18 Anxiety subscale (0 ”no symptoms” to 4 ”highest symptoms”)	*Ranft et al. 2017*
No association between tumor location and cancer-related anxiety was found using generalized linear models (adjusted for age at questionnaire, sex, race, tumor type, age at diagnosis). • Tumor location: Lower Extremity (Ref. Upper) RR=0.93 (95%CI:0.57-1.50) *Survivors from the CCSS cohort (n=1094; upper and lower extremity sarcoma diadnoses; median 13 yrs at diagnosis, median 33 yrs at study). Controls: none. Measurement: Cancer-related anxiety measured with 1 item (medium/a lot/very many fears versus no/small amount of fears)	*Marina et al. 2013*
Overall Conclusion	
Evidence suggests that tumor location is not related to the risk of developing anxiety among survivors of CAYA cancer.	2 studies Level B[44,68]

Clinical risk factors: Metastases/localized disease	
No association was found between risk group and anxiety using multivariable binary logistic regression. • Pulmonary metastases (Ref. localized disease) OR= 1.13 (95%CI:0.63 to 2.01) • Extrapulmonary metastases (Ref. localized disease) OR= 1.17 (95%CI:0.54 to 2.53) *Survivors of Ewing sarcoma (n=618; 70.1% <18 yrs at diagnosis; median 29 yrs at study. Controls: n=316, median 30 yrs at study. Measurement: BSI-18 Anxiety subscale (0 "no symptoms" to 4 "highest symptoms")	*Ranft et al. 2017*
Overall Conclusion	
Some evidence suggests that risk group is not related to the risk of developing anxiety among survivors of CAYA cancer.	1 study Level C[44]

Clinical risk factors: Scarring/disfigurement	
Chest/abdomen scarring/disfigurement (in divorced/separated survivors) and persistent hair loss were associated with increased risk for anxiety using generalized estimating equations (adjusting for age at diagnosis, age at study, sex, race, educational achievement, marital status, recurrence, SMN, cranial radiation, surgery). • Head/neck scarring or disfigurement: Yes (Ref. No) OR=1.19 (95%CI:0.95-1.48, p=0.12) • Arm/leg scarring or disfigurement: Yes (Ref. No) OR=1.11 (95%CI:0.88-1.40, p=0.38) • Chest/abdomen scarring or disfigurement: Yes (married) (Ref. No) OR=1.08 (95%CI:0.79-1.47, p=0.64) Yes (div/sep) (Ref. No) OR=1.94 (95%CI:1.21-3.10, p=0.01) Yes (never married) (Ref. No) OR=1.03 (95%CI:0.78-1.35, p=0.85) • Persistent hair loss: Yes (Ref. No) OR=1.60 (95%CI:1.23-2.07, p<0.001) *Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: Scarring and disfigurement items (yes/no) for head/neck, arm/leg, and chest/abdomen areas; persistent hair loss (yes/no); BSI-18 Anxiety subscale (cutoff ≥ 90th %tile on standardized norms)	*Kinahan et al. 2012*
Overall Conclusion	
Some evidence suggests that scarring/disfigurement is related to increased risk of developing anxiety among survivors of CAYA cancer. Specifically, experiencing persistent hair loss was related to increased risk.	1 study Level C[67]

Clinical risk factors: Survivor health and late effects	
Poor or fair physical health was associated with an increased risk for anxiety using Poisson regression (adjusted for heavy/risky drinking, sex, physical health, radiation, race, age at diagnosis, age at follow-up, educational attainment, and employment status). • Physical health: Poor, fair (Ref. good, very good, excellent) RR=3.2 (95%CI:3.4-4.3; P≤0.01) *Survivors from the CCSS cohort (n=4484; mixed diagnoses; mean 10.5 yrs at diagnosis; mean 27.2 yrs at Baseline. Controls: n=1651 siblings. Meaurement: BSI-18 Anxiety subscale (cutoff ≥63) and single item assessing self-reported health (fair/poor vs. good/very good/excellent)	*Brinkman et al. 2019*
In adolescent survivors of acute lymphoblastic leukemia, poor functional health status was associated with an increased risk for anxiety using multivariable binary logistic regression (adjusted for sex, age, age at diagnosis and treatment risk status): • Functional health status: OR=1.36 (95%CI:1.16-1.60; p<0.0001) In adult survivors, poor functional health status was associated with an increased risk for anxiety using multivariable binary logistic regression (adjusted for sex, age, age at diagnosis and treatment risk status): • Functional health status: OR=1.18 (95%CI:1.10-1.25; p<0.0001) *Survivors of ALL from the PETALE cohort (n=287 [n=105 adolescents, n=182 adults]; mean 6.2 yrs at diagnosis; mean 21.9 yrs at study; mean 15.7 yrs since diagnosis. Controls: Comparison to scores from n=4 other studies. Measurement: Beck Youth Inventory for Anxiety, Beck Anxiety Inventory; functional health status measured with self-rated 16D (adolescents) and 15D (adults)	*Anestin et al. 2018*

Cardiac and pulmonary conditions were associated with an increased risk for anxiety using log-binomial multivariable regression (adjusting for cardiac conditions, pulmonary conditions, and time since diagnosis). • Cardiac conditions: Yes (Ref. No) RR=1.48 (95%CI:1.19-1.84) • Pulmonary conditions: Yes (Ref. No) RR=1.58 (95%CI:1.25-1.99) *Survivors from the CCSS cohort (n=5021; mixed diagnoses; mean 8.3 yrs at diagnosis; mean 32.0 yrs at study; mean 23.2 yrs since diagnosis). Measurement: BSI-18 Anxiety subscale (cut-off ≥63); health conditions self-reported by survivors	*Vuotto et al. 2017*
Having a chronic condition was associated with an increased risk for cancer-related anxiety using generalized estimating equations (adjusted for sex, race/ethnicity, age at questionnaire administration, age at diagnosis, body mass index, smoking status, physical activity level, within-person correlation). • Any chronic condition, grade 3-4 (Ref. no chronic condition): PR=1.56 (95%CI:1.42-1.72) • One chronic condition, grade 3-4 (Ref. no chronic condition): PR=1.41 (95%CI:1.26-1.57) • Two chronic conditions, grade 3-4 (Ref. no chronic condition): PR=2.03 (95%CI:1.76-2.34) • Second malignancy (Ref. No organ-specific chronic condition): PR=1.70 (95%CI:1.41-2.05) • Vision/hearing/speech chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): PR=1.15 (0.97-1.37) • Endocrine chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): PR=1.24 (95%CI:1.06-1.46) • Respiratory chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): PR=2.14 (95%CI:1.44-3.17) • Cardiac chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): PR=1.23 (95%CI:1.01-1.50) • Gastrointestinal chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): PR=1.48 (95%CI:1.17-1.87) • Renal chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): PR=0.98 (0.55-1.75) • Musculoskeletal chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): PR=1.10 (0.91-1.32) • Neurologic chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): PR=1.59 (95%CI:1.33-1.92) • Other hematologic chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): PR=1.21 (0.95-1.55) *Survivors from the CCSS cohort (n=22,568; mixed diagnoses; mean 9.5 yrs at diagnosis; mean 22.4 yrs of follow-up; 18-48 yrs at study). Controls: n=7504 siblings. Measurement: Cancer-related anxiety measured with 1 item (medium/a lot/very many/extreme fears versus no/small amount of fears); Chronic conditions graded according to the Common Terminology Criteria for Adverse Events, version 4.0	*Hudson et al. 2015*
Survivor self-reported somatic/physical late effects were associated with with an increased risk for anxiety using multivariable logistic regression (adjusted for age at study, sex, parents' education, perceived parents' support, diagnosis, treatment modality, time since diagnosis) • Late effects: Somatic/physical problems (Ref. No late effects) OR=4.06 (95%CI:1.84-8.97, p<0.001) *Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥57); Late effects self-reported by survivors and classified as psychological or somatic/physical problems	*Gianinazzi et al 2013*
No association between survivor reported major medical condition and anxiety was found using multivariable logistic regression (adjusted for sex, age at study, race, educational achievement, marital status, employment, income, health insurance). • Major medical condition (Ref. no major medical condition) OR=1.2 (95%CI:1.0-1.6) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥63); Survivors reporting complete deafness, kidney dialysis, congestive heart failure, myocardial	*Zeltzer et al. 2008*

infarction, angioplasty, bypass surgery, stroke, liver cirrhosis, a heart, lung, or kidney transplant, amputation, joint replacement or second cancer, and/or current use of seizure medications, medications for heart problems or high blood pressure, chemotherapy, immune suppressants, or oxygen were classified as having a major medical condition	
Survivor perceived poor or fair health was associated with increased anxiety symptoms using generalized linear mixed modeling (adjusted for sex, income, major medical condition, brain radiation dosage, age, income & health; higher least square (LS) mean indicates more problems): • Self-rated health: Poor or fair: LS mean 4.38 (SE 0.38), compared to good/very good/excellent: LS mean 2.52 (SE 0.25), p<0.001 *Survivors of childhood brain cancer from the CCSS cohort (n=1101; mixed neurooncology diagnoses; <21 yrs at diagnosis; mean 26.5 yrs at study). Controls: n=2817 siblings (mean 29.4 yrs at study). Measurement: BSI-18 Anxiety subscale	*Zebrack et al. 2004*
Overall Conclusion	
Evidence suggests that survivor reported chronic conditions, physical late effects, and perceived poor health status are related to increased risk of developing anxiety among survivors of CAYA cancer.	7 studies (3 samples) Level B[19,24,29,33,34,39,46]

Clinical risk factors: Pain	
Medium amount, a lot, and very bad cancer-related pain was associated with an increased risk for anxiety using Poisson regression (adjusted for heavy/risky drinking, sex, physical health, radiation, race, age at diagnosis, age at follow-up, educational attainment, and employment status). • Cancer-related pain: Medium amount, a lot, very bad (Ref. none, small amount) RR=1.8 (95%CI:1.3-2.4; P≤0.01) *Survivors from the CCSS cohort (n=4484; mixed diagnoses; mean 10.5 yrs at diagnosis; mean 27.2 yrs at Baseline. Controls: n=1651 siblings. Meaurement: BSI-18 Anxiety subscale (cutoff ≥63).	*Brinkman et al. 2019*
Cancer-related pain was associated with an increased risk for anxiety using multivariable logistic regression (adjusted for education, employment, health insurance, learning or memory problems, age at clinical evaluation). • Cancer-related pain: very bad, excruciating pain (Ref. No pain) OR=11.11 (95%CI:4.60-26.82) • Cancer-related pain: A lot of pain (Ref. No pain) OR=5.84 (95%CI:3.49-9.76) • Cancer-related pain: Medium amount of pain (Ref. No pain) OR=2.69 (95%CI:1.68-4.33) • Cancer-related pain: Small amount of pain (Ref. No pain) OR=2.30 (95%CI:1.51-3.49) *Survivors from the St. Jude Lifetime Cohort Study (n=1863; mixed diagnoses; median 7 yrs at diagnosis; ≥10 yrs since diagnosis; median 32 yrs at study). Controls: none. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	*Oancea et al. 2014*
Overall Conclusion	
Evidence suggests that cancer-related pain is related to increased risk of developing anxiety among survivors of CAYA cancer.	2 studies Level B[14,29]

Clinical risk factors: Smoking	
Former or current smoking was associated with an increased risk for cancer-related anxiety using generalized linear models with a log-link function to allow direct estimation of prevalence ratios (PR, adjusted for sex, income, education, physical activity, anthracyclines, alkylating agents, abdominal radiation, thoracotomy, nephrectomy, within-person correlation). • Smoking: Former (Ref. Never): PR=1.24 (95%CI:1.06-1.45) • Smoking: Current (Ref. Never): PR=1.25 (95%CI:1.09-1.44) *Survivors from the CCSS cohort (n=22,568; mixed diagnoses; mean 9.5 yrs at diagnosis; mean 22.4 yrs of follow-up; 18-48 yrs at study). Controls: n=7504 siblings. Measurement: Cancer-related anxiety measured with 1 item (medium/a lot/very many/extreme fears versus no/small amount of fears)	*Hudson et al. 2015*
Overall Conclusion	

Some evidence suggests that former or current smoking is related to increased risk of developing anxiety among survivors of CAYA cancer.	1 study Level C[46]

Clinical risk factors: Physical activity	
No association between meeting national guidelines for vigorous exercise (≥9 MET-hrs wk^{-1} as compared to <9) was found using multivariable log-binomial regression (adjusted for age at follow-up, age at diagnosis, sex, race, smoking, education, cancer diagnosis, cancer treatment variables (alkylating agents, anthracyclines, chest radiation, brain or head radiation), baseline anxiety, depression, somatization or cancer pain, and baseline or interim severe, disabling, or life threatening chronic health conditions). • Meeting national guidelines for vigorous exercise: Yes (≥9 MET-hrs wk-1) (Ref. No (<9 MET-hrs wk-1)) PR=1.01 (95%CI:0.83-1.23; p=0.941) *Survivors from the CCSS cohort (n=6199; mixed diagnoses; median 10.0 yrs at diagnosis; mean 34.0 yrs at study). Controls: none. Measurement: BSI-18 Depression subscale (cutoff ≥63)	*Tonorezos et al. 2019*
No association between meeting U.S. Center for Disease Control and Prevention (CDC) physical activity guidelines and cancer-related anxiety was found using generalized linear models with a log-link function to allow direct estimation of prevalence ratios (PR, adjusted for sex, income, education, smoking, anthracyclines, alkylating agents, abdominal radiation, thoracotomy, nephrectomy, within-person correlation). • Meets CDC guidelines for physical activity: No (Ref. Yes) PR=1.10 (95%CI:0.99-1.22) *Survivors from the CCSS cohort (n=22,568; mixed diagnoses; mean 9.5 yrs at diagnosis; mean 22.4 yrs of follow-up; 18-48 yrs at study). Controls: n=7504 siblings. Measurement: Cancer-related anxiety measured with 1 item (medium/a lot/very many/extreme fears versus no/small amount of fears); CDC guidelines recommend ≥150 minutes moderate physical activity per week	*Hudson et al. 2015*
Overall Conclusion	
Some evidence suggests that physical activity is not related to the risk of developing anxiety among survivors of CAYA cancer.	2 studies (1 sample) Level C[31,46]

Clinical risk factors: Drinking behavior	
Lower age at drinking initiation was associated with an increased risk for anxiety using Poisson regression (adjusted for sex, physical health, radiation, race, age at diagnosis, age at follow-up, educational attainment, and employment status). No association between heavy/risky drinking and anxiety was found using Poisson regression (adjusted for, sex, physical health, radiation, race, age at diagnosis, age at follow-up, educational attainment, and employment status). • Age at drinking initiation: <18 years (Ref. ≥18 years) RR=1.6 (95%CI:1.3-2.1; P≤0.01) • Heavy drinking: Yes (Ref. No) RR=1.3 (95%CI:1.0-1.7) *Survivors from the CCSS cohort (n=4484; mixed diagnoses; mean 10.5 yrs at diagnosis; mean 27.2 yrs at Baseline. Controls: n=1651 siblings. Meaurement: BSI-18 Anxiety subscale (cutoff ≥63).	*Brinkman et al. 2019*
Overall Conclusion	
Some evidence suggests that lower age at drinking initiation was associated with an increased risk of anxiety among survivors of CAYA cancer.	1 study Level C[29]
Some evidence suggests that heavy/risky drinking is not related to the risk of anxiety among survivors of CAYA cancer.	1 study Level C[29]

Demographic risk factors: Sex	
No association between sex and anxiety was found using Poisson regression (adjusted for heavy/risky drinking, sex, physical health, radiation, race, age at diagnosis, age at follow-up, educational attainment, and employment status). • Female (Ref. Male) RR=0.8 (95%CI:0.6-1.0) *Survivors from the CCSS cohort (n=4484; mixed diagnoses; mean 10.5 yrs at diagnosis; mean 27.2 yrs at Baseline. Controls: n=1651 siblings. Meaurement: BSI-18 Anxiety subscale (cutoff ≥63).	*Brinkman et al. 2019*

No association between sex and generalized anxiety or social anxiety was found using multivariable logistic regression (adjusted for sex, age, marital status, education, income and employment). • Generalized anxiety: Female (Ref. Male) OR=1.11 (95%CI: 0.63-1.96) • Social anxiety: Female (Ref. Male) OR=1.17 (95%CI: 0.70-1.95) *Survivors (n=951; mixed diagnoses; median 5.0 yrs at diagnosis [range 0-15 yrs]; median 28.1 yrs since diagnosis [range 23-36 yrs]; median 34.2 yrs at study [range 24-49 yrs]). Controls: n=1130, German Household Panel. Measurement: Generalized Anxiety Disorder Scale (GAD-2); Mini-Spin (social anxiety)	*Burghardt et al. 2019*
Female survivors of Ewing sarcoma are at increased risk for anxiety using multivariable binary logistic regression. • Female (Ref. Male) OR= 1.49 (95%CI:1.06 to 2.09) *Survivors of Ewing sarcoma (n=618; 70.1% <18 yrs at diagnosis; median 29 yrs at study. Controls: n=316, median 30 yrs at study. Measurement: BSI-18 Anxiety subscale (0 ”no symptoms” to 4 ”highest symptoms”)	*Ranft et al. 2017*
Female survivors were at an increased risk for cancer-related anxiety using generalized linear models with a log-link function to allow direct estimation of prevalence ratios (PR, adjusted for income, education, smoking, physical activity, anthracyclines, alkylating agents, abdominal radiation, thoracotomy, nephrectomy, within-person correlation). • Female sex (Ref. Male): PR=1.73 (95%CI:1.55-1.94) *Survivors from the CCSS cohort (n=22,568; mixed diagnoses; mean 9.5 yrs at diagnosis; mean 22.4 yrs of follow-up; 18-48 yrs at study). Controls: n=7504 siblings. Measurement: Cancer-related anxiety measured with 1 item (medium/a lot/very many/extreme fears versus no/small amount of fears)	*Hudson et al. 2015*
No association between sex and anxiety was found using multivariable logistic regression (stratified by diagnostic groups). • CNS tumors and leukemia survivors: Sex not included in final model • Lymphoma and sarcoma survivors: Sex not included in final model *Survivors of adolescent and early young adult cancer from the CCSS cohort (n=2589; mixed diagnoses; 11-21 yrs at diagnosis; ≥75% were ≥35 yrs at study). Controls: n=3603 survivors diagnosed ≤10 yrs old. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	*Prasad et al. 2015*
Female survivors were at an increased risk for anxiety using multivariable logistic regression (adjusted for age at study, parents’ education, perceived parents’ support, diagnosis, treatment modality, late effects, time since diagnosis). • Female (Ref. Male) OR=3.01 (95%CI:1.45-6.24, p=0.003) *Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥57)	*Gianinazzi et al 2013*
Female survivors were at increased risk for cancer-related anxiety using generalized linear models (adjusted for tumor location, age at questionnaire, race, tumor type, age at diagnosis). • Female (Ref. Male) RR=1.73 (95%CI:1.08-2.77) *Survivors from the CCSS cohort (n=1094; upper and lower extremity sarcoma diadnoses; median 13 yrs at diagnosis, median 33 yrs at study). Controls: none. Measurement: Cancer-related anxiety measured with 1 item (medium/a lot/very many fears versus no/small amount of fears)	*Marina et al. 2013*
No association between sex and anxiety was found using generalized estimating equations (adjusting for scarring/disfigurement, hair loss, age at diagnosis, recurrence, SMN, age at study, race, educational achievement, marital status, cranial radiation, surgery). • Female (Ref. Male) OR=0.98 (95%CI:0.82-1.17, p=0.84) *Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥ 90th %tile on standardized norms)	*Kinahan et al. 2012*
Female survivors were at an increased risk for anxiety using multivariable logistic regression (adjusted for age at study, race, educational attainment, marital status, employment, annual income, health insurance, major medical condition). • Female (Ref. Male) OR=1.7 (95%CI:1.4-2.0)	*Zeltzer et al. 2008*

*Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	
Female survivors were at an increased risk for cancer-related anxiety using multivariable logistic regression analysis (adjusted for age at interview, race/ethnicity, education, household income, health insurance, diagnosis). • Female (Ref. Male) OR=1.6 (95%CI:1.4-1.9) *Survivors from the CCSS cohort (n=9535; mixed diagnoses; mean 10.00 yrs at diagnosis [range: 0.1-20.9 yrs]; mean 26.8 yrs age at study [range: 18-48 yrs]). Controls: n=2916 siblings. Cancer-related anxiety measured with 1 item (medium/a lot/very many/extreme fears versus no/small amount of fears)	*Hudson et al. 2003*
Overall Conclusion	
Evidence suggests that female sex is related to increased risk of developing anxiety among survivors of CAYA cancer.	10 studies (4 samples) Level B[19,21,24,26,29,36,44,46,67,68]

Demographic risk factors: Age at study	
No association between age at study and generalized anxiety or social anxiety was found using multivariable logistic regression (adjusted for sex, age, marital status, education, income and employment). • Generalized anxiety: Age (continuous): OR=0.96 (95%CI: 0.91-1.01) • Social anxiety: Age (continuous): OR=0.98 (95%CI: 0.93-1.03) *Survivors (n=951; mixed diagnoses; median 5.0 yrs at diagnosis [range 0-15 yrs]; median 28.1 yrs since diagnosis [range 23-36 yrs]; median 34.2 yrs at study [range 24-49 yrs]). Controls: n=1130, German Household Panel. Measurement: Generalized Anxiety Disorder Scale (GAD-2); Mini-Spin (social anxiety)	*Burghardt et al. 2019*
No association between age at study and anxiety was found using multivariable binary logistic regression. • Age at study, years: 20-29 (Ref. <20) OR= 1.05 (95%CI:0.62 to 1.78) • Age at study, years: 30-39 (Ref. <20) OR= 1.24 (95%CI:0.67 to 2.28) • Age at study, years: 40-64 (Ref. <20) OR= 0.97 (95%CI:0.50 to 1.88) *Survivors of Ewing sarcoma (n=618; 70.1% <18 yrs at diagnosis; median 29 yrs at study. Controls: n=316, median 30 yrs at study. Measurement: BSI-18 Anxiety subscale (0 ”no symptoms” to 4 ”highest symptoms”)	*Ranft et al. 2017*
No association between age at study and anxiety was found using multivariable logistic regression (stratified by diagnostic groups). • CNS tumors and leukemia survivors: Current age (per year): OR=0.98 (95%CI:0.95-1.00) (adjusted for age at diagnosis) • Lymphoma and sarcoma survivors: Age at study not included in final model *Survivors of adolescent and early young adult cancer from the CCSS cohort (n=2589; mixed diagnoses; 11-21 yrs at diagnosis; ≥75% were ≥35 yrs at study). Controls: n=3603 survivors diagnosed ≤10 yrs old. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	*Prasad et al. 2015*
Older age at clinical evaluation was associated with an increased risk for anxiety using multivariable logistic regression (adjusted for education, employment, health insurance, cancer-related pain, learning or memory problems). • Age at clinical evaluation (continuous): OR=1.021 (95%CI:1.001-1.041) *Survivors from the St. Jude Lifetime Cohort Study (n=1863; mixed diagnoses; median 7 yrs at diagnosis; ≥10 yrs since diagnosis; median 32 yrs at study). Controls: none. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	*Oancea et al. 2014*
No association between age at study and anxiety was found using multivariable logistic regression (adjusted for sex, parents’ education, perceived parents’ support, diagnosis, treatment modality, late effects, time since diagnosis). • Age at study, years: 18-19 (Ref. 16-17) OR=1.17 (95%CI:0.58-2.39, p=0.659) *Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥57)	*Gianinazzi et al 2013*

No association between age at questionnaire and cancer-related anxiety was found using generalized linear models (adjusted for tumor location, sex, race, tumor type, age at diagnosis). • Age at questionnaire: 30-39 years (Ref. <30) RR=0.81 (95%CI:0.48-1.38) • Age at questionnaire: 40+ years (Ref. <30) RR=0.70 (95%CI:0.36-1.36) *Survivors from the CCSS cohort (n=1094; upper and lower extremity sarcoma diadnoses; median 13 yrs at diagnosis, median 33 yrs at study). Controls: none. Measurement: Cancer-related anxiety measured with 1 item (medium/a lot/very many fears versus no/small amount of fears)	*Marina et al. 2013*
No association between age at study and anxiety was found using generalized estimating equations (adjusting for scarring/disfigurement, hair loss, recurrence, SMN, age at diagnosis, sex, race, educational achievement, marital status, cranial radiation, surgery). • Age at study: 30-39 years (Ref. <30 years) OR=1.01 (95%CI:0.78-1.30, p=0.96) • Age at study: ≥40 years (Ref. <30 years) OR=0.88 (95%CI:0.60-1.27, p=0.49) *Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥ 90th %tile on standardized norms)	*Kinahan et al. 2012*
No association between age at study and anxiety was found using multivariable logistic regression (adjusted for sex, race, educational attainment, marital status, employment, annual income, health insurance, major medical condition). • Age at second follow-up: 25-34 years (Ref. 18-24 years) OR=0.8 (95%CI:0.6-1.0) • Age at second follow-up: 35+ years (Ref. 18-24 years) OR=0.9 (95%CI:0.6-1.1) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	*Zeltzer et al. 2008*
No association between age at study and cancer-related anxiety was found using multivariable logistic regression analysis (adjusted for sex, race/ethnicity, education, household income, health insurance, diagnosis). • Age at interview: 25-29 years (Ref. 18-24) OR=1.1 (95%CI:0.9-1.2) • Age at interview: 30-34 years (Ref. 18-24) OR=1.0 (95%CI:0.8-1.2) • Age at interview: ≥35 years (Ref. 18-24) OR=1.1 (95%CI:0.9-1.3) *Survivors from the CCSS cohort (n=9535; mixed diagnoses; mean 10.00 yrs at diagnosis [range: 0.1-20.9 yrs]; mean 26.8 yrs age at study [range: 18-48 yrs]). Controls: n=2916 siblings. Cancer-related anxiety measured with 1 item (medium/a lot/very many/extreme fears versus no/small amount of fears)	*Hudson et al. 2003*
Overall Conclusion	
Some evidence suggests that older age at participation in the study is related to increased risk of developing anxiety in among survivors of CAYA cancer.	9 studies (5 samples) Level C[14,19,21,24,26,36,44,67,68]

Demographic risk factors: Race/ethnicity	
No association between race and cancer-related anxiety was found using generalized linear models (adjusted for tumor location, age at questionnaire, sex, tumor type, age at diagnosis). • Non-white (Ref. White) RR=0.96 (95%CI:0.47-1.97) *Survivors from the CCSS cohort (n=1094; upper and lower extremity sarcoma diadnoses; median 13 yrs at diagnosis, median 33 yrs at study). Controls: none. Measurement: Cancer-related anxiety measured with 1 item (medium/a lot/very many fears versus no/small amount of fears)	*Marina et al. 2013*
No association between race and anxiety was found using generalized estimating equations (adjusting for scarring/disfigurement, hair loss, recurrence, SMN, age at diagnosis, age at study, sex, educational achievement, marital status, cranial radiation, surgery). • Black (Ref. White) OR=1.04 (95%CI:0.61-1.77, p=0.88) • Other/mixed (Ref. White) OR=1.02 (95%CI:0.67-1.57, p=0.91) *Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-	*Kinahan et al. 2012*

49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥ 90th %tile on standardized norms)	
No association between race and anxiety was found using multivariable logistic regression (adjusted for sex, age at study, educational attainment, marital status, employment, annual income, health insurance, major medical condition). • Black (Ref. White) OR=1.0 (95%CI:0.6-1.6) • Hispanic (Ref. White) OR=1.3 (95%CI:0.9-2.0) • Other (Ref. White) OR=0.8 (95%CI:0.4-1.4) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	*Zeltzer et al. 2008*
Being a survivor with non-white ethnicity was associated with increased anxiety symptoms using generalized linear mixed modeling (adjusted for sex, income, self-rated health, major medical condition, brain radiation dosage, age, income & health; higher least square (LS) mean indicates more problems): • Ethnicity: Non-white: LS mean 4.04 (SE 0.44), compared to white: LS mean 2.85 (SE 0.20), p=0.007 *Survivors of childhood brain cancer from the CCSS cohort (n=1101; mixed neurooncology diagnoses; <21 yrs at diagnosis; mean 26.5 yrs at study). Controls: n=2817 siblings (mean 29.4 yrs at study). Measurement: BSI-18 Anxiety subscale	*Zebrack et al. 2004*
No association between race/ethnicity and cancer-related anxiety was found using multivariable logistic regression analysis (adjusted for age at interview, sex, education, household income, health insurance, diagnosis). • Minority (Ref. White, non-hispanic) OR=0.9 (95%CI:0.7-1.1) *Survivors from the CCSS cohort (n=9535; mixed diagnoses; mean 10.00 yrs at diagnosis [range: 0.1-20.9 yrs]; mean 26.8 yrs age at study [range: 18-48 yrs]). Controls: n=2916 siblings. Cancer-related anxiety measured with 1 item (medium/a lot/very many/extreme fears versus no/small amount of fears)	*Hudson et al. 2003*
Overall Conclusion	
Some evidence suggests that race/ethnicity is related to increased risk of developing anxiety among survivors of CAYA cancer. One study found that non-white survivors reported increased anxiety as compared to white survivors.	5 studies (1 sample) Level C[24,36,39,67,68]

Demographic risk factors: Marital status	
No association between marital status and generalized anxiety or social anxiety was found using multivariable logistic regression (adjusted for sex, age, marital status, education, income and employment). • Generalized anxiety: Married (Ref. Not married) OR=0.73 (95%CI: 0.37-1.43) • Social anxiety: Married (Ref. Not married) OR=0.58 (95%CI: 0.31-1.07) *Survivors (n=951; mixed diagnoses; median 5.0 yrs at diagnosis [range 0-15 yrs]; median 28.1 yrs since diagnosis [range 23-36 yrs]; median 34.2 yrs at study [range 24-49 yrs]). Controls: n=1130, German Household Panel. Measurement: Generalized Anxiety Disorder Scale (GAD-2); Mini-Spin (social anxiety)	*Burghardt et al. 2019*
No association between marital status and anxiety was found using generalized estimating equations (adjusting for scarring/disfigurement, hair loss, recurrence, SMN, age at diagnosis, age at study, sex, educational achievement, race, cranial radiation, surgery). • Marital status: An overall RR estimate is not shown for this demographic factor as a result of the presence of significant interactions with other variables in the model *Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥ 90th %tile on standardized norms)	*Kinahan et al. 2012*
Being divorced/separated was associated with increased risk for anxiety using multivariable logistic regression (adjusted for sex, age at study, race, educational achievement, employment, annual income, health insurance, major medical condition). • Single (Ref. married/living as married) OR=1.1 (95%CI:0.9-1.4) • Divorced/separated (Ref. married/living as married) OR=1.6 (95%CI:1.1-2.1)	*Zeltzer et al. 2008*

*Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	
Overall Conclusion	
Some evidence suggests being divorced/separated is related to increased risk of developing anxiety among survivors of CAYA cancer.	3 studies (2 samples) Level C[24,26,67]

Demographic risk factors: Educational achievement	
Low education and medium education (as compared to high education) were associated with increased risk for generalized anxiety, using multivariable logistic regression (adjusted for sex, age, marital status, education, income and employment). • Low education: Yes (Ref. High education) OR=2.68 (95%CI: 1.25, 5.73) • Medium education: Yes (Ref. High education) OR=2.36 (95%CI: 1.25, 4.45) No association between educational achievement and social anxiety was found using multivariable logistic regression (adjusted for sex, age, marital status, education, income and employment). • Education: Low (Ref. High) OR=1.34 (95%CI:0.63-2.85) • Education: Middle (Ref. High) OR=1.32 (95%CI:0.74-2.37) *Survivors (n=951; mixed diagnoses; median 5.0 yrs at diagnosis [range 0-15 yrs]; median 28.1 yrs since diagnosis [range 23-36 yrs]; median 34.2 yrs at study [range 24-49 yrs]). Controls: n=569, German Household Panel. Measurement: Generalized Anxiety Disorder Scale (GAD-2); Mini-Spin (social anxiety)	*Burghardt et al. 2019*
No association between education level and cancer-related anxiety was found using generalized linear models with a log-link function to allow direct estimation of prevalence ratios (PR, adjusted for sex, income, smoking, physical activity, anthracyclines, alkylating agents, abdominal radiation, thoracotomy, nephrectomy, within-person correlation). • No high school graduate (Ref. High school graduate): PR=1.23 (95%CI:0.99-1.51) *Survivors from the CCSS cohort (n=22,568; mixed diagnoses; mean 9.5 yrs at diagnosis; mean 22.4 yrs of follow-up; 18-48 yrs at study). Controls: n=7504 siblings. Measurement: Cancer-related anxiety measured with 1 item (medium/a lot/very many/extreme fears versus no/small amount of fears)	*Hudson et al. 2015*
No association between level of education and anxiety was found using multivariable logistic regression (adjusted for employment, health insurance, cancer-related pain, learning or memory problems, age at clinical evaluation). • Education: Did not graduate high school (Ref. College graduate or post-graduate level) OR=1.44 (95%CI:0.82-2.55) • Education: Completed high school/GED or received training after high school (Ref. College graduate or post-graduate level) OR=1.43 (95%CI:0.92-2.21) • Education: Some college (Ref. College graduate or post-graduate level) OR=1.29 (95%CI:0.85-1.98) *Survivors from the St. Jude Lifetime Cohort Study (n=1863; mixed diagnoses; median 7 yrs at diagnosis; ≥10 yrs since diagnosis; median 32 yrs at study). Controls: none. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	*Oancea et al. 2014*
Being a college graduate was associated with a lower risk for anxiety using generalized estimating equations (adjusting for scarring/disfigurement, hair loss, recurrence, SMN, age at diagnosis, age at study, sex, marital status, race, cranial radiation, surgery). • College graduate: Yes (Ref. No) OR=0.71 (95%CI:0.59-0.86, p<0.001) *Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥ 90th %tile on standardized norms)	*Kinahan et al. 2012*
Having an education level below high school was associated with increased risk for anxiety using multivariable logistic regression (adjusted for sex, age at study, race, marital status, employment, annual income, health insurance, major medical condition). • Below high school (Ref. college graduate) OR=1.6 (95%CI:1.1-2.3) • High school graduate (Ref. college graduate) OR=1.2 (95%CI:1.0-1.4)	*Zeltzer et al. 2008*

*Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	
No association between level of education and cancer-related anxiety was found using multivariable logistic regression analysis (adjusted for age at interview, sex, race/ethnicity, household income, health insurance, diagnosis). • High school or less (Ref. High school + some college) OR=1.1 (95%CI:1.0-1.3) *Survivors from the CCSS cohort (n=9535; mixed diagnoses; mean 10.00 yrs at diagnosis [range: 0.1-20.9 yrs]; mean 26.8 yrs age at study [range: 18-48 yrs]). Controls: n=2916 siblings. Cancer-related anxiety measured with 1 item (medium/a lot/very many/extreme fears versus no/small amount of fears)	*Hudson et al. 2003*
Overall Conclusion	
Evidence suggests that lower education level is related to increased risk of developing anxiety among survivors of CAYA cancer.	6 studies (3 samples) Level B[14,24,26,36,46,67]

Demographic risk factors: Employment	
Being unemployed was associated with increased risk for generalized anxiety, using multivariable logistic regression (adjusted for sex, age, marital status, education, income and employment). • Unemployed (Ref. Employed) OR=4.57 (95%CI: 1.68, 12.37) No association between employment and social anxiety was found using multivariable logistic regression (adjusted for sex, age, marital status, education, income and employment). • Unemployed (Ref. Employed) OR=1.35 (95%CI: 0.38-4.79) *Survivors (n=951; mixed diagnoses; median 5.0 yrs at diagnosis [range 0-15 yrs]; median 28.1 yrs since diagnosis [range 23-36 yrs]; median 34.2 yrs at study [range 24-49 yrs]). Controls: n=569, German Household Panel. Measurement: Generalized Anxiety Disorder Scale (GAD-2); Mini-Spin (social anxiety)	*Burghardt et al. 2019*
Being unable to work due to illness or disability was associated with an increased risk for anxiety using multivariable logistic regression (adjusted for education, health insurance, cancer-related pain, learning or memory problems, age at clinical evaluation). • Employment: Unable to work due to illness or disability (Ref. Caring for home or family [not seeking paid work]/Student/Retired/Working part- or full-time) OR=2.17 (95%CI:1.18-4.01) • Employment: Never had a job, or not currently working or unemployed and looking for work (Ref. Caring for home or family [not seeking paid work]/Student/Retired/Working part- or full-time) OR=1.41 (95%CI:0.94-2.11) *Survivors from the St. Jude Lifetime Cohort Study (n=1863; mixed diagnoses; median 7 yrs at diagnosis; ≥10 yrs since diagnosis; median 32 yrs at study). Controls: none. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	*Oancea et al. 2014*
Unemployment was associated with increased risk for anxiety using multivariable logistic regression (adjusted for sex, age at study, race, educational achievement, marital status, annual income, health insurance, major medical condition). • Student (Ref. Employed/Caring for home) OR=1.0 (95%CI:0.6-1.5) • Looking for work/unable to work (Ref. Employed/Caring for home) OR=2.5 (95%CI:2.0-3.1) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	*Zeltzer et al. 2008*
No significant association between employment status and anxiety symptoms was found using generalized linear mixed modeling (adjusted for sex, income, self-rated health, major medical condition, brain radiation dosage, age, income & health; higher least square (LS) mean indicates more problems): • Employment status: Not employed in last year: LS mean 3.69 (SE 0.31), compared to currently employed: LS mean 3.20 (SE 0.28), p=0.085 *Survivors of childhood brain cancer from the CCSS cohort (n=1101; mixed neurooncology diagnoses; <21 yrs at diagnosis; mean 26.5 yrs at study). Controls: n=2817 siblings (mean 29.4 yrs at study). Measurement: BSI-18 Anxiety subscale	*Zebrack et al. 2004*
Overall Conclusion	

Evidence suggests that unemployed working status is related to increased risk of developing anxiety among survivors of CAYA cancer.	4 studies (3 samples) Level B[14,24,26,39]

Demographic risk factors: Income	
No association between income and generalized anxiety or social anxiety was found using multivariable logistic regression (adjusted for sex, age, marital status, education, income and employment). • Generalized anxiety: Income in 100 Euros per month (continuous): OR=0.99 (95%CI: 0.98-1.01) • Social anxiety: Income in 100 Euros per month (continuous): OR=1.00 (95%CI: 0.99-1.01) *Survivors (n=951; mixed diagnoses; median 5.0 yrs at diagnosis [range 0-15 yrs]; median 28.1 yrs since diagnosis [range 23-36 yrs]; median 34.2 yrs at study [range 24-49 yrs]). Controls: n=1130, German Household Panel. Measurement: Generalized Anxiety Disorder Scale (GAD-2); Mini-Spin (social anxiety)	*Burghardt et al. 2019*
Low household income (<$20,000 USD) was associated with increased risk for cancer-related anxiety using generalized linear models with a log-link function to allow direct estimation of prevalence ratios (PR, adjusted for sex, education, smoking, physical activity, anthracyclines, alkylating agents, abdominal radiation, thoracotomy, nephrectomy, within-person correlation). • Income <$20,000/yr (Ref. ≥$20,000/yr): PR=1.51 (95%CI:1.33-1.72) *Survivors from the CCSS cohort (n=22,568; mixed diagnoses; mean 9.5 yrs at diagnosis; mean 22.4 yrs of follow-up; 18-48 yrs at study). Controls: n=7504 siblings. Measurement: Cancer-related anxiety measured with 1 item (medium/a lot/very many/extreme fears versus no/small amount of fears)	*Hudson et al. 2015*
Low household income (<$20,000 USD) was associated with increased risk for anxiety using multivariable logistic regression (adjusted for sex, age at study, race, educational achievement, marital status, employment, health insurance, major medical condition). • Annual income below $20,000 (Ref. $20,000+) OR=1.6 (95%CI:1.3-2.0) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	*Zeltzer et al. 2008*
Low household income (<$20,000 USD) was associated with increased anxiety symptoms using generalized linear mixed modeling (adjusted for sex, self-rated health, major medical condition, brain radiation dosage, age, income & health; higher least square (LS) mean indicates more problems): • Income $USD: <20,000: LS mean 4.50 (SE 0.39), ≥20,000+: LS mean 2.10 (SE 0.33), p<0.001 • Income $USD and ethnicity: <20K, non-white: LS mean 5.93 (SE 0.67), compared to <20K, white: LS mean 3.67 (SE 0.30), compared to ≥20K, non-white: LS mean 2.16 (SE 0.56), compared to ≥20K, white: LS mean 2.04 (SE 0.24), p=0.014 • Income $USD and health: <$20K, poor or fair: LS mean 6.39 (SE 0.57), compared to <$20K, good or better: LS mean 3.20 (SE 0.37), compared to $20K, poor or fair: LS mean 2.36 (SE 0.49), compared to $20K, good or better: LS mean: 1.83 (SE 0.30), p<0.001 *Survivors of childhood brain cancer from the CCSS cohort (n=1101; mixed neurooncology diagnoses; <21 yrs at diagnosis; mean 26.5 yrs at study). Controls: n=2817 siblings (mean 29.4 yrs at study). Measurement: BSI-18 Anxiety subscale	*Zebrack et al. 2004*
Low household income (<$20,000 USD) was associated with an increased risk for cancer-related anxiety using multivariable logistic regression analysis (adjusted for age at interview, sex, race/ethnicity, education, household income, health insurance, diagnosis). • Household income <$20,000 (Ref. ≥$20,000) OR=1.4 (95%CI:1.2-1.7) *Survivors from the CCSS cohort (n=9535; mixed diagnoses; mean 10.00 yrs at diagnosis [range: 0.1-20.9 yrs]; mean 26.8 yrs age at study [range: 18-48 yrs]). Controls: n=2916 siblings. Cancer-related anxiety measured with 1 item (medium/a lot/very many/extreme fears versus no/small amount of fears)	*Hudson et al. 2003*
Overall Conclusion	

Evidence suggests that lower annual income is related to increased risk of developing anxiety among survivors of CAYA cancer.	5 studies (2 samples) Level B[24,26,36,39,46]

Demographic risk factors: Health insurance	
No association between health insurance and anxiety was found using multivariable logistic regression (adjusted for education, employment, cancer-related pain, learning or memory problems, age at clinical evaluation). • Health insurance: None (Ref. Canadian resident/Through spouse's or parent's policy/Through place of employment/Through self-purchased policy) OR=1.47 (95%CI:0.99-2.19) • Health insurance: Through Medicare or Medicaid or other public assistance programs, or military dependent/veteran's benefits (Ref. Canadian resident/Through spouse's or parent's policy/Through place of employment/Through self-purchased policy) OR=0.85 (95%CI:0.52-1.42) *Survivors from the St. Jude Lifetime Cohort Study (n=1863; mixed diagnoses; median 7 yrs at diagnosis; ≥10 yrs since diagnosis; median 32 yrs at study). Controls: none. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	*Oancea et al. 2014*
No association between health insurance and anxiety was found using multivariable logistic regression (adjusted for sex, age at study, race, educational achievement, marital status, employment, income, major medical condition). • No health insurance (Ref. Health insurance) OR=1.3 (95%CI:1.0-1.7) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	*Zeltzer et al. 2008*
No association between health insurance and cancer-related anxiety was found using multivariable logistic regression analysis (adjusted for age at interview, sex, race/ethnicity, education, household income, diagnosis). • Health insurance: No (Ref. Yes or Canadian) OR=1.1 (95%CI:0.9-1.3) *Survivors from the CCSS cohort (n=9535; mixed diagnoses; mean 10.00 yrs at diagnosis [range: 0.1-20.9 yrs]; mean 26.8 yrs age at study [range: 18-48 yrs]). Controls: n=2916 siblings. Cancer-related anxiety measured with 1 item (medium/a lot/very many/extreme fears versus no/small amount of fears)	*Hudson et al. 2003*
Overall Conclusion	
Evidence suggests that health insurance is not related to increased risk of developing anxiety among survivors of CAYA cancer.	3 studies (2 samples) Level B[14,24,36]

Demographic risk factors: Parents' educational achievement	
No association between parents' education and anxiety was found using multivariable logistic regression (adjusted for age at study, sex, perceived parents' support, diagnosis, treatment modality, late effects, time since diagnosis). • Parents' education: Secondary, tertiary (Ref. Compulsory, primary) OR=0.88 (95%CI:0.33-2.36, p=0.807) *Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥57)	*Gianinazzi et al 2013*
Overall Conclusion	
Some evidence suggests that parents' educational achievement is not related to increased risk of developing anxiety among survivors of CAYA cancer.	1 study Level C[19]

Treatment-related risk factors: Bone marrow transplantation	
No association between bone marrow transplantation and anxiety was found using multivariable logistic regression (adjusted for age at study, sex, parents' education, perceived parents' support, diagnosis, late effects, time since diagnosis). • Treatment: Bone marrow transplantation (Ref. Chemotherapy) OR=0.36 (95%CI:0.73-1.73, p=0.404)	*Gianinazzi et al 2013*

*Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥57)	
Overall Conclusion	
Some evidence suggests that bone marrow transplantation is not related to risk of anxiety among survivors of CAYA cancer.	1 study Level C[19]

Treatment-related risk factors: Chemotherapy	
No association between high-dose chemotherapy and anxiety was found using multivariable binary logistic regression. • High-dose chemotherapy: Yes (Ref. No) OR= 1.43 (95%CI:0.76 to 2.67) *Survivors of Ewing sarcoma (n=618; 70.1% <18 yrs at diagnosis; median 29 yrs at study. Controls: n=316, median 30 yrs at study. Measurement: BSI-18 Anxiety subscale (0 "no symptoms" to 4 "highest symptoms")	*Ranft et al. 2017*
Survivors treated with alkylating agents were at an increased risk for cancer-related anxiety using generalized linear models with a log-link function to allow direct estimation of prevalence ratios (PR, adjusted for sex, income, education, smoking, physical activity, abdominal radiation, thoracotomy, nephrectomy, within-person correlation). • Anthracyclines (Ref. No anthracyclines): PR=1.14 (95%CI:1.00-1.29) • Alkylating agents (Ref. No alkylating agents): PR=1.20 (95%CI:1.06-1.36) *Survivors from the CCSS cohort (n=22,568; mixed diagnoses; mean 9.5 yrs at diagnosis; mean 22.4 yrs of follow-up; 18-48 yrs at study). Controls: n=7504 siblings. Measurement: Cancer-related anxiety measured with 1 item (medium/a lot/very many/extreme fears versus no/small amount of fears)	*Hudson et al. 2015*
Treatment with corticosteroids was associated with an increased risk for anxiety in lymphoma/sarcoma survivors using multivariable logistic regression (stratified by diagnostic groups). • CNS tumors and leukemia survivors: Chemotherapy not included in final model • Lymphoma and sarcoma survivors: Chemotherapy: Antimetabolites (Ref. no) not included in final model • Lymphoma and sarcoma survivors: Chemotherapy: Corticosteroids (Ref. no) OR=1.48 (95%CI:1.11-1.99) (adjusted for age at diagnosis) *Survivors of adolescent and early young adult cancer from the CCSS cohort (n=2589; mixed diagnoses; 11-21 yrs at diagnosis; ≥75% were ≥35 yrs at study). Controls: n=3603 survivors diagnosed ≤10 yrs old. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	*Prasad et al. 2015*
No association between treatment modality (i.e., surgery, chemotherapy, or bone marrow transplant) and anxiety was found using multivariable logistic regression (adjusted for age at study, sex, parents' education, perceived parents' support, diagnosis, late effects, time since diagnosis). • Treatment: Surgery (Ref. Chemotherapy) OR=1.12 (95%CI:0.31-4.02, p=0.404) • Treatment: Radiotherapy (Ref. Chemotherapy) OR=0.65 (95%CI:0.27-1.50, p=0.404) • Treatment: Bone marrow transplantation (Ref. Chemotherapy) OR=0.36 (95%CI:0.73-1.73, p=0.404) *Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥57)	*Gianinazzi et al 2013*
No association between chemotherapy and anxiety was found using multivariable logistic regression (adjusted for sex, age at diagnosis, survival time, surgery, radiation). • Chemotherapy (Ref. no chemotherapy) OR=1.2 (95%CI:0.9-1.5) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	*Zeltzer et al. 2008*
Survivors treated with alkylating and anthracycline drugs are at an increased risk for cancer-related anxiety using multivariable logistic regression analysis (adjusted for age at interview, sex, race/ethnicity, diagnosis, surgery, radiation therapy). • Chemotherapy: Alkylating agent (Ref. none) OR=1.2 (95%CI:1.0-1.5) • Chemotherapy: Anthracycline (Ref. none) OR=1.1 (95%CI:0.8-1.5) • Chemotherapy: Alkylating + Anthracycline (Ref. none) OR=1.5 (95%CI:1.2-1.9)	*Hudson et al. 2003*

• Chemotherapy: Other (Ref. none) OR=1.1 (95%CI:0.9-1.5) *Survivors from the CCSS cohort (n=9535; mixed diagnoses; mean 10.00 yrs at diagnosis [range: 0.1-20.9 yrs]; mean 26.8 yrs age at study [range: 18-48 yrs]). Controls: n=2916 siblings. Cancer-related anxiety measured with 1 item (medium/a lot/very many/extreme fears versus no/small amount of fears)	
Overall Conclusion	
Some evidence suggests that having received specific types of chemotherapy is related to increased risk of developing anxiety among survivors of CAYA cancer. One study found that alkylating agents increased risk of anxiety, while another study found that alkylating agents with anthracycline increased the risk of anxiety. One study also found that lymphoma and sarcoma survivors who received corticosteroids were at increased risk of anxiety.	6 studies (3 samples) Level C[19,21,24,36,44,46]

Treatment-related risk factors: Radiation	
No association between radiation and anxiety was found using Poisson regression (adjusted for heavy/risky drinking, sex, physical health, radiation, race, age at diagnosis, age at follow-up, educational attainment, and employment status). • Radiation: Non-cranial (Ref. None) RR=0.8 (0.6-1.1) • Radiation: CRT≤20Gy (Ref. None) RR=0.7 (0.5-1.1) • Radiation: CRT>20Gy (Ref. None) RR=0.7 (0.5-1.0) *Survivors from the CCSS cohort (n=4484; mixed diagnoses; mean 10.5 yrs at diagnosis; mean 27.2 yrs at Baseline. Controls: n=1651 siblings. Meaurement: BSI-18 Anxiety subscale (cutoff ≥63).	*Brinkman et al. 2019*
No association between radiotherapy, or radiotherapy + surgery and anxiety was found using multivariable binary logistic regression. • Local treatment: Surgery + Radiotherapy (Ref. Surgery) OR= 0.84 (95%CI:0.56 to 1.27) • Local treatment: Radiotherapy (Ref. Surgery) OR= 1.26 (95%CI:0.71 to 2.24) *Survivors of Ewing sarcoma (n=618; 70.1% <18 yrs at diagnosis; median 29 yrs at study. Controls: n=316, median 30 yrs at study. Measurement: BSI-18 Anxiety subscale (0 ”no symptoms” to 4 ”highest symptoms”)	*Ranft et al. 2017*
Abdominal radiation with ≥35.0 Gy was associated with an increased risk for cancer-related anxiety using generalized linear models with a log-link function to allow direct estimation of prevalence ratios (PR, adjusted for sex, income, education, smoking, physical activity, anthracyclines, alkylating agents, thoracotomy, nephrectomy, within-person correlation). • Abdominal radiation: 1.4-23.9 Gy (Ref. none): PR=0.96 (95%CI:0.75-1.22) • Abdominal radiation: 24.0-34.9 Gy (Ref. none): PR=1.11 (95%CI:0.90-1.37) • Abdominal radiation: 35.0+ Gy (Ref. none): PR=1.34 (95%CI:1.12-1.60) *Survivors from the CCSS cohort (n=22,568; mixed diagnoses; mean 9.5 yrs at diagnosis; mean 22.4 yrs of follow-up; 18-48 yrs at study). Controls: n=7504 siblings. Measurement: Cancer-related anxiety measured with 1 item (medium/a lot/very many/extreme fears versus no/small amount of fears)	*Hudson et al. 2015*
No association between cranial irradiation and anxiety was found using multivariable logistic regression. • CNS tumors and leukemia survivors: Cranial irradiation not included in final model *Survivors of adolescent and early young adult cancer from the CCSS cohort (n=2589; mixed diagnoses; 11-21 yrs at diagnosis; ≥75% were ≥35 yrs at study). Controls: n=3603 survivors diagnosed ≤10 yrs old. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	*Prasad et al. 2015*
No association between radiotherapy and anxiety was found using multivariable logistic regression (adjusted for age at study, sex, parents' education, perceived parents' support, diagnosis, late effects, time since diagnosis). • Treatment: Radiotherapy (Ref. Chemotherapy) OR=0.65 (95%CI:0.27-1.50, p=0.404) *Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥57)	*Gianinazzi et al 2013*

Survivors treated with abdominal or limb radiation were at an increased risk for cancer-related anxiety using generalized linear models (adjusted for tumor location, sex). • Abdominal Radiation: Any (Ref. none) RR=4.17 (95%CI:1.42-12.26) • Limb Radiation: Any (Ref. none) RR=1.68 (95%CI:1.04-2.7) *Survivors from the CCSS cohort (n=1094; upper and lower extremity sarcoma diadnoses; median 13 yrs at diagnosis, median 33 yrs at study). Controls: none. Measurement: Cancer-related anxiety measured with 1 item (medium/a lot/very many fears versus no/small amount of fears)	*Marina et al. 2013*
Cranial radiation with 20 Gy or more was associated with a lower risk for anxiety using generalized estimating equations (adjusting for scarring/disfigurement, hair loss, recurrence, SMN, age at diagnosis, age at study, sex, race, educational achievement, marital status, surgery). • Cranial radiation: Scatter exposure only (Ref. none) OR=0.73 (95%CI:0.58-0.92, p=0.01) • Cranial radiation: Direct, ≤20 Gy (Ref. none) OR=0.69 (95%CI:0.50-0.95, p=0.02) • Cranial radiation: Direct, 20-36 Gy (Ref. none) OR=0.76 (95%CI:0.56-1.05, p=0.09) • Cranial radiation: Direct, ≥36 Gy (Ref. none) OR=0.79 (95%CI:0.56-1.11, p=0.17) *Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥ 90th %tile on standardized norms)	*Kinahan et al. 2012*
No association between radiation and anxiety was found using multivariable logistic regression (adjusted for sex, age at diagnosis, survival time, surgery, chemotherapy). • Cranial radiation (Ref. none) OR=0.9 (95%CI:0.7-1.1) • Other than cranial radiation (Ref. none) OR=0.9 (95%CI:0.7-1.1) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	*Zeltzer et al. 2008*
No association between brain radiation dosage and anxiety symptoms was found using generalized linear mixed modeling (adjusted for sex, income, self-rated health, major medical condition, age, income & health; higher least square (LS) mean indicates more problems): • Brain radiation dosage: 0-29 Gy LS mean 3.74 (SE 0.0.31), compared to 30-49 Gy LS mean 3.37 (SE 0.39), compared to 50 Gy+ LS mean 3.23 (SE 0.27), p=0.112 *Survivors of childhood brain cancer from the CCSS cohort (n=1101; mixed neurooncology diagnoses; <21 yrs at diagnosis; mean 26.5 yrs at study). Controls: n=2817 siblings (mean 29.4 yrs at study). Measurement: BSI-18 Anxiety subscale	*Zebrack et al. 2004*
No association between radiation and cancer-related anxiety was found using multivariable logistic regression analysis (adjusted for age at interview, sex, race/ethnicity, diagnosis, surgery, chemotherapy). • Radiation: Head/brain (Ref. none) OR=1.1 (95%CI:0.9-1.3) • Radiation: Chest/mantle (Ref. none) OR=1.2 (95%CI:0.9-1.5) • Radiation: Brain/chest (Ref. none) OR=1.2 (95%CI:0.7-2.0) • Radiation: Other (Ref. none) OR=1.2 (95%CI:1.0-1.5) *Survivors from the CCSS cohort (n=9535; mixed diagnoses; mean 10.00 yrs at diagnosis [range: 0.1-20.9 yrs]; mean 26.8 yrs age at study [range: 18-48 yrs]). Controls: n=2916 siblings. Cancer-related anxiety measured with 1 item (medium/a lot/very many/extreme fears versus no/small amount of fears)	*Hudson et al. 2003*
Overall Conclusion	
Some evidence suggests that abdominal radiation is associated with an increased risk of anxiety among survivors of CAYA cancer.	2 studies (1 sample) Level C[46,68]
Some evidence suggests that low doses of cranial irradiation are associated with a decreased risk for anxiety among survivors of CAYA cancer.	6 studies (1 sample) Level C[21,24,29,36,39,67]
Some evidence suggests that limb radiation is associated with an increased risk of anxiety among survivors of CAYA cancer.	1 study Level C[68]
Evidence suggests that there is no association between radiotherapy (not further specified) and anxiety among survivors of CAYA cancer.	5 studies (3 samples)

	Level B[19,24,29,36,44]

Treatment-related risk factors: Surgery	
Thoracotomy was associated with an increased risk for cancer-related anxiety using generalized linear models with a log-link function to allow direct estimation of prevalence ratios (PR, adjusted for sex, income, education, smoking, physical activity, anthracyclines, alkylating agents, abdominal radiation, nephrectomy, within-person correlation). • Thoracotomy (Ref. No thoracotomy): PR=1.32 (95%CI:1.05-1.67) • Nephrectomy (Ref. No nephrectomy): PR=0.79 (95%CI:0.61-1.03) *Survivors from the CCSS cohort (n=22,568; mixed diagnoses; mean 9.5 yrs at diagnosis; mean 22.4 yrs of follow-up; 18-48 yrs at study). Controls: n=7504 siblings. Measurement: Cancer-related anxiety measured with 1 item (medium/a lot/very many/extreme fears versus no/small amount of fears)	*Hudson et al. 2015*
No association between surgery and anxiety was found using multivariable logistic regression (adjusted for age at study, sex, parents' education, perceived parents' support, diagnosis, late effects, time since diagnosis). • Treatment: Surgery (Ref. Chemotherapy) OR=1.12 (95%CI:0.31-4.02, p=0.404) *Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥57)	*Gianinazzi et al 2013*
No association was found between having had surgery and anxiety using generalized estimating equations (adjusting for scarring/disfigurement, hair loss, recurrence, SMN, age at diagnosis, age at study, sex, race, educational achievement, marital status, cranial radiation). • Surgery: Yes (Ref. No) OR=1.18 (95%CI:0.97-1.44, p=0.10) *Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥ 90th %tile on standardized norms)	*Kinahan et al. 2012*
No association between surgery and anxiety was found using multivariable logistic regression (adjusted for sex, age at diagnosis, survival time, chemotherapy, radiation). • Surgery (Ref. no surgery) OR=1.1 (95%CI:0.8-1.4) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 Anxiety subscale (cutoff ≥63)	*Zeltzer et al. 2008*
No association between surgery and cancer-related anxiety was found using multivariable logistic regression analysis (adjusted for age at interview, sex, race/ethnicity, diagnosis, radiation therapy, chemotherapy). • Surgery: Yes (Ref. No) OR=1.2 (95%CI:1.0-1.6) *Survivors from the CCSS cohort (n=9535; mixed diagnoses; mean 10.00 yrs at diagnosis [range: 0.1-20.9 yrs]; mean 26.8 yrs age at study [range: 18-48 yrs]). Controls: n=2916 siblings. Cancer-related anxiety measured with 1 item (medium/a lot/very many/extreme fears versus no/small amount of fears)	*Hudson et al. 2003*
Overall Conclusion	
Some evidence suggests that having undergone thoracotomy is related to increased risk of developing anxiety among survivors of CAYA cancer.	1 study Level C[46]
Some evidence suggests that there is no association between surgery (not further specified) and anxiety among survivors of CAYA cancer.	4 studies (2 samples) Level B[19,24,36,67]

1b-3. What are the key clinical, demographic and treatment-related risk factors for developing psychological distress among survivors of childhood, adolescent, and young adult (CAYA) cancer?	
Conclusion single studies	
Clinical risk factors: Age at diagnosis	
No association between age at diagnosis and emotional distress was found using multivariable linear regression analysis (adjusted for sex, age at study, duration of treatment, global CNS irradiation, educational achievement). • Age at diagnosis (years) β=0.07, p=0.14 *Survivors (n=652; mixed diagnoses; median 6 yrs at diagnosis; median 23 yrs at study [range 15-46 yrs]). Controls: n=440 Dutch HADS controls (mean age 51 yrs [range 17-89 yrs]). Measurement: Hospital Anxiety and Depression scale (HADS) (cutoff ≥15)	*Van der Geest et al. 2013*
No association between age at diagnosis and psychological distress was found using generalized estimating equations (adjusting for scarring/disfigurement, hair loss, recurrence, SMN, age at study, sex, race, educational achievement, marital status, cranial radiation, surgery). • Age at diagnosis: 5-9 years (Ref. 0-4 years) OR=0.98 (95%CI:0.79-1.22, p=0.86) • Age at diagnosis: 10-21 years (Ref. 0-4 years) OR=1.05 (95%CI:0.81-1.36, p=0.73) *Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: BSI-18 GSI subscale (cutoff ≥ 90th %tile on standardized norms)	*Kinahan et al. 2012*
No association between age at diagnosis and psychological distress was found using multivariable hierarchical regression (adjusted for sex, employment status, education, marital/relationship status, income, health problems, years since diagnosis, cancer type, negative/positive impact of cancer). • Standardized beta coefficient- Age at diagnosis: 0.022, p≥0.05 *Survivors (n=621; mixed diagnoses; mean 11.1 yrs at diagnosis; mean 15.8 yrs since diagnosis; mean 26.9 yrs at study). Controls: none. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Zebrack et al. 2011*
No association between age at diagnosis and psychological distress was found using multivariable logistic regression (adjusted for sex, current age, siblings, immigration status, late effects). • Age at diagnosis: 5-9 years (Ref. 0-4 years): OR=1.53 (95%CI:0.88-2.65), p=0.129 • Age at diagnosis: 10-15 years (Ref. 0-4 years): OR=1.31 (95%CI:0.79-2.16), p=0.295 *Survivors from the Swiss CCSS cohort (n=987; mixed diagnoses; mean 8.4 yrs at diagnosis; mean 19.5 yrs since diagnosis; mean 27.9 yrs at study). Controls: Population norms for BSI. Controls: Population norms for BSI. Measurement: BSI (cutoff ≥63 on GSI and/or ≥ 2 BSI domains)	*Michel et al. 2010*
No association between age at diagnosis and psychological distress was found using multivariable logistic regression (adjusted for sex, survival time, surgery, chemotherapy, radiation). • Age at diagnosis: 0-3 years (Ref. 15-20 years) OR=1.1 (95%CI:0.8-1.4) • Age at diagnosis: 4-9 years (Ref. 15-20 years) OR=1.1 (95%CI:0.9-1.4) • Age at diagnosis: 10-14 years (Ref. 15-20 years) OR=1.0 (95%CI:0.8-1.3) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI)	*Zeltzer et al. 2008*
Survivors' younger age at diagnosis was associated with an increased risk for psychological distress using multivariable logistic regression (adjusted for treatment, level of education, ethnicity, sex, special education, influence of cancer on employment, self-reported health, age at interview, relapse, mother's highest level of education). • Age at diagnosis: <12.5 years (Ref. >12.5 years) OR=3.7 (95%CI:2.0-6.6, p<0.001) *Survivors treated on Children's Cancer Group (CCG) protocols (n=555; acute lymphoblastic leukemia; <20 yrs at diagnosis; 18-33 yrs at study). Controls: none. Measurement: Profile of Mood Scale-Total score (cutoff >33)	*Glover et al. 2003*
Overall Conclusion	
Some evidence suggests that younger age at diagnosis is related to increased risk of developing psychological distress among survivors of CAYA cancer.	6 studies (5 samples) Level C[18,24,48,50,52,67]

Clinical risk factors: Time Since Diagnosis	
No association between time since diagnosis and psychological distress was found using modified multivariable Poisson models (adjusting for age, sex, race/ethnicity, employment status, household income, marital status, years since diagnosis, second malignant neoplasm, disease recurrence, and treatment type). • Years since diagnosis: Per year (continuous): RR=0.99 (95%CI:0.97–1.01; p= 0.54) *Survivors from the CCSS cohort (n=4798; mixed diagnoses; mean 7.6 yrs at diagnosis; mean 34.9 yrs at study). Controls: none. Measurement: BSI-18 GSI (cut-off: top 10th %tile)	*Crochet et al. 2019*
Longer time since diagnosis was related to an increased risk of psychological distress using multivariable logistic regression (adjusted for age, economic status). • Time since diagnosis: 10-14 years (Ref. <10 years) OR=0.36 (95%CI:0.12-1.09; p=0.071) • Time since diagnosis: 15-19 years (Ref. <10 years) OR=1.36 (95%CI:0.50-3.67; p=0.544) • Time since diagnosis: >20 years (Ref. <10 years) OR=3.67 (95%CI:1.05-12.88; p=0.042) *Survivors' (n=223, Hematological cancers, solid or soft tissue tumors, central nervous system tumors or brain tumors, mean age at diagnosis=9.91 years (SD=4.69) and mean age at study 21.92 (SD=4.69); measurement: BSI-18 (cutoff ≥63)	*Kim et al 2013*
No association between time since diagnosis and psychological distress was found using multivariable hierarchical regression (adjusted for sex, employment status, education, marital/relationship status, income, health problems, age at diagnosis, cancer type, negative/positive impact of cancer). • Standardized beta coefficient- Years since diagnosis: -0.019, p≥0.05 *Survivors (n=621; mixed diagnoses; mean 11.1 yrs at diagnosis; mean 15.8 yrs since diagnosis; mean 26.9 yrs at study). Controls: none. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Zebrack et al. 2011*
No association between survival time and psychological distress was found using multivariable logistic regression (adjusted for sex, age at diagnosis, surgery, chemotherapy, radiation). • Survival time: <20 years (Ref. 30+ years) OR=0.9 (95%CI:0.7-1.2) • Survival time: 20-24 years (Ref. 30+ years) OR=0.7 (95%CI:0.6-1.0) • Survival time: 25-29 years (Ref. 30+ years) OR=0.9 (95%CI:0.7-1.1) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI)	*Zeltzer et al. 2008*
Overall Conclusion	
Some evidence suggests that longer time since diagnosis is related to the increased risk of developing psychological distress among survivors of CAYA cancer.	4 studies (3 samples) Level C[24,30,49,50]

Clinical risk factors: Diagnosis	
No association between diagnosis and psychological distress was found using multivariable logistic regression (adjusted for age at study, sex, parents' education, perceived parents' support, treatment modality, late effects, time since diagnosis). • Diagnosis: CNS tumors (Ref. Leukemia, lymphoma) OR=1.11 (95%CI:0.37-3.38, p=1.000) • Diagnosis: Other (Ref. Leukemia, lymphoma) OR=1.33 (95%CI:0.59-2.97, p=1.000) *Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 (cutoff ≥57 on GSI or any 2 of the 3 BSI-18 subscales)	*Gianinazzi et al 2013*
No association between diagnosis and poor mental health was found using generalized linear models (adjusted for tumor location, age at questionnaire, sex, race, tumor type). • Tumor Type: Ewing sarcoma (Ref. Soft tissue sarcoma) RR=1.21 (95%CI:0.92-1.59) • Tumor Type: Osteosarcoma (Ref. Soft tissue sarcoma) RR=1.14 (95%CI:0.91-1.43) • Tumor Type: Other bone (Ref. Soft tissue sarcoma) RR=0.76 (95%CI:0.38-1.49)	*Marina et al. 2013*

*Survivors from the CCSS cohort (n=1094; upper and lower extremity sarcoma diadnoses; median 13 yrs at diagnosis, median 33 yrs at study). Controls: none. Measurement: BSI-18 (cutoff ≥63 on GSI or any of the BSI-18 subscales)	
No association between diagnosis and psychological distress was found using multivariable hierarchical regression (adjusted for sex, employment status, education, marital/relationship status, income, health problems, age at diagnosis, years since diagnosis, cancer type, negative/positive impact of cancer). • Standardized beta coefficient- Cancer type (1 = brain tumor): 0.024; Cancer type (1 = solid tumor): -0.018, p≥0.05 *Survivors (n=621; mixed diagnoses; mean 11.1 yrs at diagnosis; mean 15.8 yrs since diagnosis; mean 26.9 yrs at study). Controls: none. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Zebrack et al. 2011*
No association between diagnosis and psychological distress was found using multivariable logistic regression analysis (adjusted for age at interview, sex, race/ethnicity, education, household income, health insurance). • Diagnosis: CNS (Ref. Leukemia) OR=1.1 (95%CI:0.9-1.3) • Diagnosis: Hodgkin disease (Ref. Leukemia) OR=1.1 (95%CI:1.0-1.4) • Diagnosis: NHL (Ref. Leukemia) OR=1.0 (95%CI:0.8-1.3) • Diagnosis: Wilms (Ref. Leukemia) OR=0.8 (95%CI:0.6-1.0) • Diagnosis: Neuroblastoma (Ref. Leukemia) OR=0.9 (95%CI:0.6-1.2) • Diagnosis: Sarcoma (Ref. Leukemia) OR=1.0 (95%CI:0.8-1.2) • Diagnosis: Bone (Ref. Leukemia) OR=1.0 (95%CI:0.9-1.3) *Survivors from the CCSS cohort (n=9535; mixed diagnoses; mean 10.00 yrs at diagnosis [range: 0.1-20.9 yrs]; mean 26.8 yrs age at study [range: 18-48 yrs]). Controls: n=2916 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Hudson et al. 2003*
Overall Conclusion	
Evidence suggests that cancer diagnosis type is not related to the risk of developing psychological distress among survivors of CAYA cancer.	4 studies (3 samples) Level B[19,36,50,68]

Clinical risk factors: Second malignant neoplasm (SMN) or recurrence	
No association between SMN or recurrence and psychological distress was found using modified multivariable Poisson models (adjusting for age, sex, race/ethnicity, employment status, household income, marital status, years since diagnosis, second malignant neoplasm, disease recurrence, and treatment type). • Second malignant neoplasm: Yes RR=1.16 (95%CI:0.87–1.55; p= 0.32 • Recurrence: Yes RR=1.00 (95%CI:0.77–1.31; p= 0.97) *Survivors from the CCSS cohort (n=4798; mixed diagnoses; mean 7.6 yrs at diagnosis; mean 34.9 yrs at study). Controls: none. Measurement: BSI-18 GSI (cut-off: top 10th %tile)	*Crochet et al. 2019*
Having a second malignancy was associated with an increased risk for overall psychological distress using generalized estimating equation (adjusted for sex, race/ethnicity, age at questionnaire administration, age at diagnosis, body mass index, smoking status, physical activity level, within-person correlation). • Second malignancy (Ref. No organ-specific chronic condition): PR=1.22 (95%CI:1.01-1.46) *Survivors from the CCSS cohort (n=22,568; mixed diagnoses; mean 9.5 yrs at diagnosis; mean 22.4 yrs of follow-up; 18-48 yrs at study). Controls: n=7504 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales); Chronic conditions graded according to the Common Terminology Criteria for Adverse Events, version 4.0	*Hudson et al. 2015*
No association between recurrence or SMN and psychological distress was found using generalized estimating equations (adjusting for scarring/disfigurement, hair loss, age at diagnosis, age at study, sex, race, educational achievement, marital status, cranial radiation, surgery). • Recurrence: Yes (Ref. No) OR=1.10 (95%CI:0.88-1.37, p=0.41) • Second malignant neoplasm: Yes (Ref. No) OR=0.95 (95%CI:0.67-1.35, p=0.78) *Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: BSI-18 GSI subscale (cutoff ≥ 90th %tile on standardized norms)	*Kinahan et al. 2012*

Overall Conclusion	
Some evidence suggests that experiencing a second malignancy is related to increased risk of developing psychological distress among survivors of CAYA cancer.	3 studies (1 sample) Level C[30,46,67]

Clinical risk factors: Tumor location	
No association between tumor location and overall psychological distress was found using generalized linear models (adjusted for age at questionnaire, sex, race, tumor type, age at diagnosis). • Tumor location: Lower Extremity (Ref. Upper) RR=0.87 (95%CI:0.71-1.08) *Survivors from the CCSS cohort (n=1094; upper and lower extremity sarcoma diadnoses; median 13 yrs at diagnosis, median 33 yrs at study). Controls: none. Measurement: BSI-18 (cutoff ≥63 on GSI or any of the BSI-18 subscales)	*Marina et al. 2013*
Overall Conclusion	
Some evidence suggests that tumor location is not related to the risk of developing psychological distress among survivors of CAYA cancer.	1 study Level C[68]

Clinical risk factors: Scarring/disfigurement	
Arm/leg scarring/disfigurement and persistent hair loss were associated with an increased risk for psychological distress using generalized estimating equations (adjusting for age at diagnosis, age at study, sex, race, educational achievement, marital status, recurrence, SMN, cranial radiation, surgery). • Head/neck scarring or disfigurement: Yes (Ref. No) OR=1.19 (95%CI:1.00-1.43, p=0.05) • Arm/leg scarring or disfigurement: Yes (Ref. No) OR=1.25 (95%CI:1.04-1.51, p=0.02) • Chest/abdomen scarring or disfigurement: Yes (Ref. No) OR=1.07 (95%CI:0.90-1.27, p=0.44) • Persistent hair loss: Yes (Ref. No) OR=1.44 (95%CI:1.15-1.80, p<0.01) *Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: Scarring and disfigurement items (yes/no) for head/neck, arm/leg, and chest/abdomen areas; persistent hair loss (yes/no); BSI-18 GSI subscale (cutoff ≥ 90th %tile on standardized norms)	*Kinahan et al. 2012*
Overall Conclusion	
Some evidence suggests that arm/leg scarring/disfigurement and persistent hair loss are associated with an increased risk of developing psychological distress among survivors of CAYA cancer.	1 study Level C[67]

Clinical risk factors: Survivor health and late effects	
In adolescent survivors of acute lymphoblastic leukemia, poor functional health status was associated with an increased risk for psychological distress using multivariable binary logistic regression (adjusted for sex, age, age at diagnosis and treatment risk status): • Functional health status: OR=1.17 (95%CI:1.07–1.30; p=0.003) In adult survivors, poor functional health status was associated with an increased risk for psychological distress using multivariable binary logistic regression (adjusted for sex, age, age at diagnosis and treatment risk status): • Functional health status: OR=1.10 (95%CI:1.04–1.17; p=0.001) *Survivors of ALL from the PETALE cohort (n=287 [n=105 adolescents, n=182 adults]; mean 6.2 yrs at diagnosis; mean 21.9 yrs at study; mean 15.7 yrs since diagnosis. Controls: Comparison to scores from n=4 other studies. Measurement: Distress Thermometer (cut-off ≥4), functional health status measured with self-rated 16D (adolescents) and 15D (adults)	*Anestin et al. 2018*
Self-reported late effects were associated with an increased risk for psychological distress using multivariable logistic regression (adjusted for sex and marital status). • Self-reported late effects: Yes (Ref. No) OR=2.23 (95%CI:1.30-3.8; p=0.003)	*De Laage et al. 2016*

*Survivors (n=348; mixed diagnoses; 0-18 yrs at diagnosis; mean 38.5 yrs at study; mean 31.5 yrs since diagnosis). Controls: French norm population n=36,105. Measurement: BSI-18 GSI	
Having a chronic condition was associated with an increased risk for overall psychological distress using generalized estimating equation (adjusted for sex, race/ethnicity, age at questionnaire administration, age at diagnosis, body mass index, smoking status, physical activity level, within-person correlation). • Any chronic condition, grade 3-4 (Ref. no chronic condition): PR=1.78 (95%CI:1.63-1.95) • One chronic condition, grade 3-4 (Ref. no chronic condition): PR=1.53 (95%CI:1.38-1.69) • Two chronic conditions, grade 3-4 (Ref. no chronic condition): PR=2.63 (95%CI:2.32-2.98) • Vision/hearing/speech chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): PR=1.47 (95%CI:1.26-1.70) • Endocrine chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): PR=1.41 (95%CI:1.23-1.62) • Respiratory chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): PR=2.63 (95%CI:1.83-3.78) • Cardiac chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): PR=1.72 (95%CI:1.47-2.03) • Gastrointestinal chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): PR=1.29 (95%CI:1.04-1.61) • Renal chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): PR=1.55 (95%CI:1.02-2.35) • Musculoskeletal chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): PR=1.05 (95%CI:0.89-1.25) • Neurologic chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): PR=2.13 (95%CI:1.81-2.52) • Other hematologic chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): PR=1.30 (95%CI:1.04-1.63) *Survivors from the CCSS cohort (n=22,568; mixed diagnoses; mean 9.5 yrs at diagnosis; mean 22.4 yrs of follow-up; 18-48 yrs at study). Controls: n=7504 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales); Chronic conditions graded according to the Common Terminology Criteria for Adverse Events, version 4.0	*Hudson et al. 2015*
Survivor self-reported somatic/physical late effects were associated with an increased risk for psychological distress using multivariable logistic regression (adjusted for age at study, sex, parents' education, perceived parents' support, diagnosis, treatment modality, time since diagnosis). • Late effects: Somatic/physical problems (Ref. No late effects) OR=6.98 (95%CI:3.07-15.91, p<0.001) *Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 (cutoff ≥57 on GSI or any 2 of the 3 BSI-18 subscales); Late effects self-reported by survivors and classified as psychological or somatic/physical problems	*Gianinazzi et al 2013*
Survivor self-reported recent health problems were related to increased symptoms of psychological distress using multivariable hierarchical regression (adjusted for sex, employment status, education, marital/relationship status, income, age at diagnosis, years since diagnosis, cancer type, negative/positive impact of cancer). • Standardized beta coefficient- Health problems (1 = yes, present): 0.077, p<0.05 *Survivors (n=621; mixed diagnoses; mean 11.1 yrs at diagnosis; mean 15.8 yrs since diagnosis; mean 26.9 yrs at study). Controls: none. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales); Health problems self-reported by survivors as "experiencing any recent health problems for which they have seen a doctor" (yes/no)	*Zebrack et al. 2011*
Somatic/physical late effects were associated with an increased risk for psychological distress using multivariable logistic regression (adjusted for sex, current age, siblings, immigration status, age at diagnosis). • Late effects: Somatic problems only (Ref. No late effects): OR=2.00 (95%CI:1.29-3.11), p=0.002 *Survivors from the Swiss CCSS cohort (n=987; mixed diagnoses; mean 8.4 yrs at diagnosis; mean 19.5 yrs since diagnosis; mean 27.9 yrs at study). Controls: Population norms for BSI.	*Michel et al. 2010*

Controls: Population norms for BSI. Measurement: BSI (cutoff ≥63 on GSI and/or ≥ 2 BSI domains); Late effects self-reported by survivors and classified as psychological or somatic/physical problems	
No association between survivor self-reported major medical condition and psychological distress was found using multivariable logistic regression (adjusted for sex, age at study, race, educational achievement, marital status, employment, income, health insurance). • Major medical condition (Ref. no major medical condition) OR=1.2 (95%CI:1.0-1.4) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI); Survivors reporting complete deafness, kidney dialysis, congestive heart failure, myocardial infarction, angioplasty, bypass surgery, stroke, liver cirrhosis, a heart, lung, or kidney transplant, amputation, joint replacement or second cancer, and/or current use of seizure medications, medications for heart problems or high blood pressure, chemotherapy, immune suppressants, or oxygen were classified as having a major medical condition	*Zeltzer et al. 2008*
Survivors with a major medical condition and perceived poor or fair health were at an increased risk for symptoms of psychological distress using generalized linear mixed modeling (adjusted for sex, income, brain radiation dosage, age, income & health; higher least square (LS) mean indicates more problems): • Major medical condition: Yes: LS mean 11.24 (SE 0.64), compared to No: LS mean 9.30 (SE 0.63), p=0.007 • Self-rated health: Poor or fair: LS mean 14.15 (SE 0.92), compared to good/very good/excellent: LS mean 6.38 (SE 0.46), p<0.001 *Survivors of childhood brain cancer from the CCSS cohort (n=1101; mixed neurooncology diagnoses; <21 yrs at diagnosis; mean 26.5 yrs at study). Controls: n=2817 siblings (mean 29.4 yrs at study). Measurement: BSI-18 (cutoff ≥63 on GSI); Major medical condition defined as survivor self-reported chronic conditions (i.e., complete deafness, dialysis, congestive heart failure, myocardial infarction, stroke or cerebrovascular incident, current use of oxygen, cirrhosis, coronary artery bypass surgery, angioplasty, heart transplant, lung transplant, kidney transplant, repeated seizures, convulsions, or blackouts, diagnosis of a second cancer, amputation, joint replacement) during the last 2 years AND/OR use of anticonvulsants, cardiovascular medications, or chemotherapy/immune suppressants within a 2-year period post treatment.	*Zebrack et al. 2004*
Perception of poorer health was associated with an increased risk for psychological distress using multivariable logistic regression (adjusted for age at diagnosis, treatment, level of education, ethnicity, sex, special education, influence of cancer on employment, age at interview, relapse, mother's highest level of education). • Self-rated health: Good (Ref. Excellent) OR=1.71 (95%CI:0.0-2.7, p=0.04) • Self-rated health: Poor (Ref. Excellent) OR=4.7 (95%CI:2.2-10.5, p<0.001) *Survivors treated on Children's Cancer Group (CCG) protocols (n=555; acute lymphoblastic leukemia; <20 yrs at diagnosis; 18-33 yrs at study). Controls: none. Measurement: Profile of Mood Scale-Total score (cutoff >33)	*Glover et al. 2003*
Overall Conclusion	
Evidence suggests that survivor reported chronic conditions, physical late effects, and perceived poor health status are related to increased risk of developing psychological distress among survivors of CAYA cancer.	9 studies (6 samples) Level B[18,19,24,27,34,39,46,50,52]

Clinical risk factors: Pain	
Cancer-related pain was associated with an increased risk for psychological distress using multivariable logistic regression (adjusted for education, employment, health insurance, cancer-related pain, learning or memory problems, age at clinical evaluation). • Cancer-related pain: very bad, excruciating pain (Ref. No pain) OR=10.83 (95%CI:4.42-26.50) • Cancer-related pain: A lot of pain (Ref. No pain) OR=8.72 (95%CI:5.32-14.31) • Cancer-related pain: Medium amount of pain (Ref. No pain) OR=2.38 (95%CI:1.53-3.71) • Cancer-related pain: Small amount of pain (Ref. No pain) OR=1.97 (95%CI:1.34-2.90)	*Oancea et al. 2014*

*Survivors from the St. Jude Lifetime Cohort Study (n=1863; mixed diagnoses; median 7 yrs at diagnosis; ≥10 yrs since diagnosis; median 32 yrs at study). Controls: none. Measurement: BSI-18 GSI (cutoff ≥63)	
Overall Conclusion	
Some evidence suggests that cancer-related pain is related to increased risk of developing psychological distress among survivors of CAYA cancer.	1 study Level C[14]

Clinical risk factors: Posttraumatic stress	
Survivors with posttraumatic stress had an increased risk for global emotional distress using modified multivariable Poisson models (adjusting for age, sex, race/ethnicity, employment status, household income, marital status, years since diagnosis, second malignant neoplasm, disease recurrence, and treatment type). • PTSS: Yes (Ref. No) RR=8.58 (95%CI:7.13-10.32, p<0.001) *Survivors from the CCSS cohort (n=6844; mixed diagnoses; mean 7.6 yrs at diagnosis; mean 34.9 yrs at study). Controls: none. Measurement: Post-traumatic Stress Scale (cutoff: ≥13); BSI-18 GSI (cutoff: not reported)	*Crochet et al. 2019*
Overall Conclusion	
Some evidence suggests that posttraumatic stress is related to increased risk of psychological distress among survivors of CAYA cancer.	1 study Level C[30]

Clinical risk factors: Obesity	
Survivors with obesity were at an increased risk for overall psychological distress using generalized linear models with a log-link function to allow direct estimation of prevalence ratios (PR, adjusted for sex, race/ethnicity, income, education, smoking, physical activity, alkylating agents, craniotomy, within-person correlation). • BMI <18.5kg/m^2 (Ref. BMI 18.5-24.9kg/m^2): PR=1.12 (95%CI:0.92-1.38) • BMI 25.0-29.9kg/m^2 (Ref. BMI 18.5-24.9kg/m^2): PR=1.08 (95%CI:0.97-1.20) • BMI ≥30kg/m^2 (Ref. BMI 18.5-24.9kg/m^2): PR=1.24 (95%CI:1.10-1.41) *Survivors from the CCSS cohort (n=22,568; mixed diagnoses; mean 9.5 yrs at diagnosis; mean 22.4 yrs of follow-up; 18-48 yrs at study). Controls: n=7504 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Hudson et al. 2015*
Overall Conclusion	
Some evidence suggests that obesity (BMI≥30) is related to an increased risk of developing psychological distress among survivors of CAYA cancer.	1 study Level C[46]

Clinical risk factors: Smoking	
Survivors who were either former or current smokers were at an increased risk for overall psychological distress using generalized linear models with a log-link function to allow direct estimation of prevalence ratios (PR, adjusted for sex, race/ethnicity, income, education, BMI, physical activity, alkylating agents, craniotomy, within-person correlation). • Smoking: Former (Ref. Never): PR=1.53 (95%CI:1.33-1.75) • Smoking: Current (Ref. Never): PR=1.92 (95%CI:1.71-2.16) *Survivors from the CCSS cohort (n=22,568; mixed diagnoses; mean 9.5 yrs at diagnosis; mean 22.4 yrs of follow-up; 18-48 yrs at study). Controls: n=7504 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Hudson et al. 2015*
Overall Conclusion	
Some evidence suggests that being a former or current smoker is related to an increased risk of developing psychological distress among survivors of CAYA cancer.	1 study Level C[46]

Clinical risk factors: Physical activity	
Survivors who did not meet U.S. Center for Disease Control and Prevention (CDC) guidelines for physical activity were at increased risk for overall psychological distress using generalized linear models with a log-link function to allow direct estimation of prevalence ratios (PR, adjusted for sex, race/ethnicity, income, education, BMI, smoking, alkylating agents, craniotomy, within-person correlation).	*Hudson et al. 2015*

• Meets CDC guidelines for physical activity: No (Ref. Yes) PR=1.26 (95%CI:1.15-1.38) *Survivors from the CCSS cohort (n=22,568; mixed diagnoses; mean 9.5 yrs at diagnosis; mean 22.4 yrs of follow-up; 18-48 yrs at study). Controls: n=7504 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales); CDC guidelines recommend ≥150 minutes moderate physical activity per week	
Overall Conclusion	
Some evidence suggests that not meeting the CDC guidelines for physical activity is related to an increased risk of developing psychological distress among survivors of CAYA cancer.	1 study Level C[46]

Demographic risk factors: Sex	
No association between sex and psychological distress was found using modified multivariable Poisson models (adjusting for age, sex, race/ethnicity, employment status, household income, marital status, years since diagnosis, second malignant neoplasm, disease recurrence, and treatment type). • Female RR=1.03 (95%CI:0.88–1.20; p= 0.75) *Survivors from the CCSS cohort (n=4798; mixed diagnoses; mean 7.6 yrs at diagnosis; mean 34.9 yrs at study). Controls: none. Measurement: BSI-18 GSI (cut-off: top 10th %tile)	*Crochet et al. 2019*
No association was found between psychological distress and sex using multivariable logistic regression (adjusted for self-reported late effects and marital status). • Male (Ref. Female) OR=0.82 (95%CI:0.51-1.32; p=0.28) *Survivors (n=348; mixed diagnoses; 0-18 yrs at diagnosis; mean 38.5 yrs at study; mean 31.5 yrs since diagnosis). Controls: French norm population n=36,105. Measurement: BSI-18 GSI	*De Laage et al. 2016*
Female survivors were at an increased risk for psychological distress using generalized linear models with a log-link function to allow direct estimation of prevalence ratios (PR, adjusted for race/ethnicity, income, education, BMI, smoking, physical activity, alkylating agents, craniotomy, within-person correlation). • Female (Ref. Male) PR=1.16 (95%CI:1.05-1.29) *Survivors from the CCSS cohort (n=22,568; mixed diagnoses; mean 9.5 yrs at diagnosis; mean 22.4 yrs of follow-up; 18-48 yrs at study). Controls: n=7504 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Hudson et al. 2015*
Female survivors were at an increased risk for psychological distress using multivariable logistic regression (adjusted for age at study, parents' education, perceived parents' support, diagnosis, treatment modality, late effects, time since diagnosis). • Female (Ref. Male) OR=3.59 (95%CI:1.71-7.52, p=0.001) *Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 (cutoff ≥57 on GSI or any 2 of the 3 BSI-18 subscales)	*Gianinazzi et al 2013*
No association was found between psychological distress and sex using generalized linear models (adjusted for tumor location, age at questionnaire, race, tumor type, age at diagnosis). • Female (Ref. Male) RR=0.96 (95%CI:0.81-1.15) *Survivors from the CCSS cohort (n=1094; upper and lower extremity sarcoma diadnoses; median 13 yrs at diagnosis, median 33 yrs at study). Controls: none. Measurement: BSI-18 (cutoff ≥63 on GSI or any of the BSI-18 subscales)	*Marina et al. 2013*
No association was found between emotional distress and sex using multivariable linear regression analysis (adjusted for age at study, age at diagnosis, duration of treatment, global CNS irradiation, educational achievement). • Sex (m vs. f) β=0.58, p=0.18 *Survivors (n=652; mixed diagnoses; median 6 yrs at diagnosis; median 23 yrs at study [range 15-46 yrs]). Controls: n=440 Dutch HADS controls (mean age 51 yrs [range 17-89 yrs]). Measurement: Hospital Anxiety and Depression scale (HADS) (cutoff ≥15)	*Van der Geest et al. 2013*
No association was found between psychological distress and sex using generalized estimating equations (adjusting for scarring/disfigurement, hair loss, age at diagnosis, recurrence, SMN, age at study, race, educational achievement, marital status, cranial radiation, surgery). • Female (Ref. Male) OR=1.16 (95%CI:1.00-1.34, p=0.06)	*Kinahan et al. 2012*

*Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: BSI-18 GSI subscale (cutoff ≥ 90th %tile on standardized norms)	
No association was found between psychological distress and sex using multivariable hierarchical regression (adjusted for employment status, education, marital/relationship status, income, health problems, age at diagnosis, years since diagnosis, cancer type, negative/positive impact of cancer). • Standardized beta coefficient- Gender (1 = male): 0.065, p≥0.05 *Survivors (n=621; mixed diagnoses; mean 11.1 yrs at diagnosis; mean 15.8 yrs since diagnosis; mean 26.9 yrs at study). Controls: none. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Zebrack et al. 2011*
Female survivors were at an increased risk for psychological distress using multivariable logistic regression (adjusted for current age, siblings, immigration status, age at diagnosis, late effects). • Female (Ref. male): OR=1.79 (95%CI:1.22-2.64), p=0.003 *Survivors from the Swiss CCSS cohort (n=987; mixed diagnoses; mean 8.4 yrs at diagnosis; mean 19.5 yrs since diagnosis; mean 27.9 yrs at study). Controls: Population norms for BSI. Controls: Population norms for BSI. Measurement: BSI (cutoff ≥63 on GSI and/or ≥ 2 BSI domains)	*Michel et al. 2010*
Female survivors were at an increased risk for psychological distress using multivariable logistic regression (adjusted for age at study, race, educational attainment, marital status, employment, annual income, health insurance, major medical condition). • Female (Ref. Male) OR=1.5 (95%CI:1.3-1.8) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI)	*Zeltzer et al. 2008*
Female survivors were at an increased risk for symptoms of psychological distress using generalized linear mixed modeling (adjusted for income, self-rated health, major medical condition, brain radiation dosage, age, income & health; higher least square (LS) mean indicates more problems): • Female: LS mean 11.00 (SE 0.62), compared to male: LS mean 9.53 (SE 0.62), p=0.023 *Survivors of childhood brain cancer from the CCSS cohort (n=1101; mixed neurooncology diagnoses; <21 yrs at diagnosis; mean 26.5 yrs at study). Controls: n=2817 siblings (mean 29.4 yrs at study). Measurement: BSI-18 (cutoff ≥63 on GSI)	*Zebrack et al. 2004*
White females and non-white males had an increased risk for psychological distress (compared to white males) using multivariable logistic regression (adjusted for age at diagnosis, treatment, level of education, special education, influence of cancer on employment, self-reported health, age at interview, relapse, mother's highest level of education). • Female X White (Ref. Male X White) OR=3.1 (95%CI:1.4-6.8, p=0.006) • Male X Non-white (Ref. Male X White) OR=3.8 (95%CI:1.6-9.2, p=0.004) • Female X Non-white (Ref. Male X White) OR=2.3 (95%CI:0.7-7.2, p=0.15) *Survivors treated on Children's Cancer Group (CCG) protocols (n=555; acute lymphoblastic leukemia; <20 yrs at diagnosis; 18-33 yrs at study). Controls: none. Measurement: Profile of Mood Scale-Total score (cutoff >33)	*Glover et al. 2003*
Female survivors were at an increased risk for psychological distress using multivariable logistic regression analysis (adjusted for age at interview, race/ethnicity, education, household income, health insurance, diagnosis). • Female (Ref. Male) OR=1.2 (95%CI:1.1-1.3) *Survivors from the CCSS cohort (n=9535; mixed diagnoses; mean 10.00 yrs at diagnosis [range: 0.1-20.9 yrs]; mean 26.8 yrs age at study [range: 18-48 yrs]). Controls: n=2916 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Hudson et al. 2003*
Overall Conclusion	
Evidence suggests that female sex is related to an increased risk of developing psychological distress among survivors of CAYA cancer.	13 studies (6 samples) Level B[18,19,24,27,30,36,39,46,48,50,52,67,68]

Demographic risk factors: Age at study	
No association between age at evaluation and psychological distress was found using modified multivariable Poisson models (adjusting for age, sex, race/ethnicity, employment status, household income, marital status, years since diagnosis, second malignant neoplasm, disease recurrence, and treatment type). • Age at evaluation: Per year (continuous): RR=1.01 (95%CI:0.99–1.02; p= 0.23) *Survivors from the CCSS cohort (n=4798; mixed diagnoses; mean 7.6 yrs at diagnosis; mean 34.9 yrs at study). Controls: none. Measurement: BSI-18 GSI (cut-off: top 10th %tile)	*Crochet et al. 2019*
Older age at study was associated with an increased risk for psychological distress using multivariable logistic regression (adjusted for education, employment, health insurance, cancer-related pain, learning or memory problems). • Age at clinical evaluation (continuous): OR=1.036 (95%CI:1.017-1.055) *Survivors from the St. Jude Lifetime Cohort Study (n=1863; mixed diagnoses; median 7 yrs at diagnosis; ≥10 yrs since diagnosis; median 32 yrs at study). Controls: none. Measurement: BSI-18 GSI (cutoff ≥63)	*Oancea et al. 2014*
No association between age at study and psychological distress was found using multivariable logistic regression (adjusted for sex, parents' education, perceived parents' support, diagnosis, treatment modality, late effects, time since diagnosis). • Age at study, years: 18-19 (Ref. 16-17) OR=1.41 (95%CI:0.69-2.89, p=0.343) *Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 (cutoff ≥57 on GSI or any 2 of the 3 BSI-18 subscales)	*Gianinazzi et al 2013*
No association between age at study and psychological distress was found using multivariable logistic regression (adjusted for economic status, time since diagnosis). • Age: 19-25 years (Ref. 15-18) OR=2.64 (95%CI:0.83-8.39; p=0.100) • Age: 26-39 years (Ref. 15-18) OR=2.82 (95%CI:0.63-12.60; p=0.176) * Survivors (n=223, Hematological cancers, solid or soft tissue tumors, central nervous system tumors or brain tumors, mean age at diagnosis=9.91 years (SD=4.69) and mean age at study 21.92 (SD=4.69); measurement: BSI-18 (cutoff ≥63)	*Kim et al 2013*
No association between age at study and psychological distress was found using generalized linear models (adjusted for tumor location, sex, race, tumor type, age at diagnosis). • Age at questionnaire: 30-39 years (Ref. <30) RR=0.88 (95%CI:0.70-1.11) • Age at questionnaire: 40+ years (Ref. <30) RR=1.02 (95%CI:0.78-1.32) *Survivors from the CCSS cohort (n=1094; upper and lower extremity sarcoma diadnoses; median 13 yrs at diagnosis, median 33 yrs at study). Controls: none. Measurement: BSI-18 (cutoff ≥63 on GSI or any of the BSI-18 subscales)	*Marina et al. 2013*
Older age at study was associated with an increased risk for psychological distress using multivariable linear regression analysis (adjusted for sex, age at diagnosis, duration of treatment, global CNS irradiation, educational achievement). • Age at study (years) β=0.08, p=0.03 *Survivors (n=652; mixed diagnoses; median 6 yrs at diagnosis; median 23 yrs at study [range 15-46 yrs]). Controls: n=440 Dutch HADS controls (mean age 51 yrs [range 17-89 yrs]). Measurement: Hospital Anxiety and Depression scale (HADS) (cutoff ≥15)	*Van der Geest et al. 2013*
No association between age at study and psychological distress was found using generalized estimating equations (adjusting for scarring/disfigurement, hair loss, recurrence, SMN, age at diagnosis, sex, race, educational achievement, marital status, cranial radiation, surgery). • Age at study: 30-39 years (Ref. <30 years) OR=1.00 (95%CI:0.80-1.26, p=0.99) • Age at study: ≥40 years (Ref. <30 years) OR=1.15 (95%CI:0.84-1.58, p=0.39) *Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: BSI-18 GSI subscale (cutoff ≥ 90th %tile on standardized norms)	*Kinahan et al. 2012*
Older age at study was associated with an increased risk for psychological distress using multivariable logistic regression (adjusted for sex, siblings, immigration status, age at diagnosis, late effects). • Current age: 25-29 years (Ref. 20-24 years): OR=1.65 (95%CI:1.01-2.67), p=0.044) • Current age: ≥30 years (Ref. 20-24 years): OR=1.90 (95%CI:1.18-3.04), p=0.008)	*Michel et al. 2010*

*Survivors from the Swiss CCSS cohort (n=987; mixed diagnoses; mean 8.4 yrs at diagnosis; mean 19.5 yrs since diagnosis; mean 27.9 yrs at study). Controls: Population norms for BSI. Controls: Population norms for BSI. Measurement: BSI (cutoff ≥63 on GSI and/or ≥ 2 BSI domains)	
No association between age at study and psychological distress was found using multivariable logistic regression (adjusted for sex, race, educational attainment, marital status, employment, annual income, health insurance, major medical condition). • Age at second follow-up: 25-34 years (Ref. 18-24 years) OR=0.9 (95%CI:0.7-1.1) • Age at second follow-up: 35+ years (Ref. 18-24 years) OR=1.1 (95%CI:0.9-1.5) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI)	*Zeltzer et al. 2008*
No association between age at study and symptoms of psychological distress was found using using generalized linear mixed modeling (adjusted for sex, income, self-rated health, major medical condition, brain radiation dosage, income & health; higher least square (LS) mean indicates more problems): • Age: LS mean -0.114 (SE 0.06), p=0.057 *Survivors of childhood brain cancer from the CCSS cohort (n=1101; mixed neurooncology diagnoses; <21 yrs at diagnosis; mean 26.5 yrs at study). Controls: n=2817 siblings (mean 29.4 yrs at study). Measurement: BSI-18 (cutoff ≥63 on GSI)	*Zebrack et al. 2004*
No association between age at study and psychological distress was found using multivariable logistic regression analysis (adjusted for sex, race/ethnicity, education, household income, health insurance, diagnosis) • Age at interview: 25-29 years (Ref. 18-24) OR=1.0 (95%CI:0.8-1.1) • Age at interview: 30-34 years (Ref. 18-24) OR=1.0 (95%CI:0.8-1.1) • Age at interview: ≥35 years (Ref. 18-24) OR=0.9 (95%CI:0.8-1.1) *Survivors from the CCSS cohort (n=9535; mixed diagnoses; mean 10.00 yrs at diagnosis [range: 0.1-20.9 yrs]; mean 26.8 yrs age at study [range: 18-48 yrs]). Controls: n=2916 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Hudson et al. 2003*
Overall Conclusion	
Some evidence suggests that older age at study participation is related to an increased risk of developing psychological distress among survivors of CAYA cancer.	11 studies (5 samples) Level C[18,19,24,30,36,39,48,49,67-69]

Demographic risk factors: Race/ethnicity	
No association between race/ethnicity and psychological distress was found using modified multivariable Poisson models (adjusting for age, sex, race/ethnicity, employment status, household income, marital status, years since diagnosis, second malignant neoplasm, disease recurrence, and treatment type). • Race/ethnicity: Black/Hispanic/Other RR=1.02 (95%CI:0.82–1.27; p= 0.85) *Survivors from the CCSS cohort (n=4798; mixed diagnoses; mean 7.6 yrs at diagnosis; mean 34.9 yrs at study). Controls: none. Measurement: BSI-18 GSI (cut-off: top 10th %tile)	*Crochet et al. 2019*
No association between race/ethnicity and psychological distress was found using generalized linear models with a log-link function to allow direct estimation of prevalence ratios (PR, adjusted for sex, income, education, BMI, smoking, physical activity, alkylating agents, craniotomy, within-person correlation). • Nonwhite race/ethnicity (Ref. White): PR=1.10 (95%CI:0.93-1.29) *Survivors from the CCSS cohort (n=22,568; mixed diagnoses; mean 9.5 yrs at diagnosis; mean 22.4 yrs of follow-up; 18-48 yrs at study). Controls: n=7504 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Hudson et al. 2015*
No association between race/ethnicity and psychological distress was found using generalized linear models (adjusted for tumor location, age at questionnaire, sex, tumor type, age at diagnosis). • Non-white (Ref. White) RR=1.07 (95%CI:0.80-1.41) *Survivors from the CCSS cohort (n=1094; upper and lower extremity sarcoma diadnoses; median 13 yrs at diagnosis, median 33 yrs at study). Controls: none. Measurement: BSI-18 (cutoff ≥63 on GSI or any of the BSI-18 subscales)	*Marina et al. 2013*

No association between race/ethnicity and psychological distress was found using generalized estimating equations (adjusting for scarring/disfigurement, hair loss, recurrence, SMN, age at diagnosis, age at study, sex, educational achievement, marital status, cranial radiation, surgery). • Black (Ref. White) OR=1.03 (95%CI:0.67-1.60, p=0.88) • Other/mixed (Ref. White) OR=1.01 (95%CI:0.69-1.46, p=0.98) *Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: BSI-18 GSI subscale (cutoff ≥ 90th %tile on standardized norms)	*Kinahan et al. 2012*
No association between race/ethnicity and psychological distress was found using multivariable logistic regression (adjusted for sex, age at study, educational attainment, marital status, employment, annual income, health insurance, major medical condition). • Black (Ref. White) OR=1.0 (95%CI:0.7-1.6) • Hispanic (Ref. White) OR=1.4 (95%CI:1.0-2.0) • Other (Ref. White) OR=0.8 (95%CI:0.5-1.4) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI)	*Zeltzer et al. 2008*
Non-white ethnicity was associated with an increased risk for psychological distress using multivariable logistic regression (adjusted for age at diagnosis, treatment, level of education, sex, special education, influence of cancer on employment, self-reported health, age at interview, relapse, mother's highest level of education). • Minority (Ref. White) OR=1.7 (95%CI:0.1-3.2, p=0.01) *Survivors treated on Children's Cancer Group (CCG) protocols (n=555; acute lymphoblastic leukemia; <20 yrs at diagnosis; 18-33 yrs at study). Controls: none. Measurement: Profile of Mood Scale-Total score (cutoff >33)	*Glover et al. 2003*
No association between race/ethnicity and psychological distress was found using multivariable logistic regression analysis (adjusted for age at interview, sex, education, household income, health insurance, diagnosis). • Minority (Ref. White, non-Hispanic) OR=0.9 (95%CI:0.8-1.1) *Survivors from the CCSS cohort (n=9535; mixed diagnoses; mean 10.00 yrs at diagnosis [range: 0.1-20.9 yrs]; mean 26.8 yrs age at study [range: 18-48 yrs]). Controls: n=2916 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Hudson et al. 2003*
Overall Conclusion	
Some evidence suggests that non-white race/ethnicity is related to an increased risk of developing psychological distress among survivors of CAYA cancer.	7 studies (2 samples) Level C[24,30,36,46,52,67,68]

Demographic risk factors: Immigration status	
Survivors with the citizenship status of immigrant were at an increased risk of psychological distress using multivariable logistic regression (adjusted for sex, current age, siblings, immigration status, age at diagnosis, late effects). • Immigration status: Immigrant (Ref. Native Swiss): OR=2.11 (95%CI:1.05-4.26), p=0.037 *Data from the Swiss Childhood Cancer Registry; n=987; mixed diagnoses; mean age at study 27.9 yrs; mean age at diagnosis 8.4 yrs; mean time since diagnosis 19.5 yrs. Control sample: Population norms for BSI. Measurement: Brief Symptom Inventory (BSI, 53 items) T-scores ≥63 on the Global Severity Index (GSI).	*Michel et al. 2010*
Overall Conclusion	
Some evidence suggests that having immigrant citizenship status is related to an increased risk of psychological distress among survivors of CAYA cancer.	1 study Level C[18]

Demographic risk factors: Sibling status	
Survivors without siblings were at an increased risk for psychological distress using multivariable logistic regression (adjusted for sex, current age, siblings, immigration status, age at diagnosis, late effects).	*Michel et al. 2010*

• Siblings: No (Ref. Yes): OR=2.53 (95%CI:1.48-4.32), p=0.001 *Survivors from the Swiss CCSS cohort (n=987; mixed diagnoses; mean 8.4 yrs at diagnosis; mean 19.5 yrs since diagnosis; mean 27.9 yrs at study). Controls: Population norms for BSI. Controls: Population norms for BSI. Measurement: BSI (cutoff ≥63 on GSI and/or ≥ 2 BSI domains)	
Overall Conclusion	
Some evidence suggests that not having a sibling is related to an increased risk of developing psychological distress among survivors of CAYA cancer.	1 study Level C[18]

Demographic risk factors: Marital status	
Being single or separated was associated with an increased risk for psychological distress using modified multivariable Poisson models (adjusting for age, sex, race/ethnicity, employment status, household income, marital status, years since diagnosis, second malignant neoplasm, disease recurrence, and treatment type). • Marital status: Single or separated RR=1.29 (95%CI:1.08–1.53; p= 0.005) *Survivors from the CCSS cohort (n=4798; mixed diagnoses; mean 7.6 yrs at diagnosis; mean 34.9 yrs at study). Controls: none. Measurement: BSI-18 GSI (cut-off: top 10th %tile)	*Crochet et al. 2019*
No association was found between psychological distress and marital status using multivariable logistic regression (adjusted for sex and self-reported late effects). • Couple (Ref. Single) OR=0.59 (95%CI:0.33-1.03) *Survivors (n=348; mixed diagnoses; 0-18 yrs at diagnosis; mean 38.5 yrs at study; mean 31.5 yrs since diagnosis). Controls: French norm population n=36,105. Measurement: BSI-18 GSI	*De Laage et al. 2016*
Not being married/living as married was associated with increased risk for psychological distress using used generalized estimating equations (adjusting for scarring/disfigurement, hair loss, recurrence, SMN, age at diagnosis, age at study, sex, educational achievement, race, cranial radiation, surgery). • Marital status: Divorced, separated, widowed, or no longer living as married (Ref. Married/living as married) OR=1.95 (95%CI:1.54-2.47, p<0.001) • Marital status: Never married or lived as married (Ref. Married/living as married) OR=1.88 (95%CI:1.55-2.29, p<0.001) *Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: BSI-18 GSI subscale (cutoff ≥ 90th %tile on standardized norms)	*Kinahan et al. 2012*
Not being married was associated with increased risk for psychological distress using multivariable hierarchical regression (adjusted for sex, employment status, education, income, health problems, age at diagnosis, years since diagnosis, cancer type, negative/positive impact of cancer). • Standardized beta coefficients- Marital/relationship status (1 = yes): -0.115, p <0.01 *Survivors (n=621; mixed diagnoses; mean 11.1 yrs at diagnosis; mean 15.8 yrs since diagnosis; mean 26.9 yrs at study). Controls: none. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Zebrack et al. 2011*
Not being married was associated with increased risk for psychological distress using multivariable logistic regression (adjusted for sex, age at study, race, educational achievement, employment, annual income, health insurance, major medical condition). • Single (Ref. married/living as married) OR=1.3 (95%CI:1.1-1.6) • Divorced/separated (Ref. married/living as married) OR=1.7 (95%CI:1.2-2.2) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI)	*Zeltzer et al. 2008*
Overall Conclusion	
Evidence suggests that not being married/living as married is related to an increased risk of developing psychological distress among survivors of CAYA cancer.	5 studies (3 samples) Level B[24,27,30,50,67]

Demographic risk factors: Educational achievement	
Survivors that did not graduate from high school were at an increased risk for psychological distress using generalized linear models with a log-link function to allow direct estimation of prevalence ratios (PR, adjusted for sex, race/ethnicity, income, BMI, smoking, physical activity, alkylating agents, craniotomy, within-person correlation). • No high school graduate (Ref. High school graduate): PR=1.43 (95%CI:1.19-1.73) *Survivors from the CCSS cohort (n=22,568; mixed diagnoses; mean 9.5 yrs at diagnosis; mean 22.4 yrs of follow-up; 18-48 yrs at study). Controls: n=7504 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Hudson et al. 2015*
Having graduated from high school but not having completed any college education was associated with an increased risk of psychological distress using multivariable logistic regression (adjusted for education, employment, health insurance, cancer-related pain, learning or memory problems, age at clinical evaluation). • Education: Did not graduate high school (Ref. College graduate or post-graduate level) OR=1.58 (95%CI:0.93-2.69) • Education: Completed high school/GED or received training after high school (Ref. College graduate or post-graduate level) OR=1.65 (95%CI:1.10-2.48) • Education: Some college (Ref. College graduate or post-graduate level) OR=1.45 (95%CI:0.97-2.16) *Survivors from the St. Jude Lifetime Cohort Study (n=1863; mixed diagnoses; median 7 yrs at diagnosis; ≥10 yrs since diagnosis; median 32 yrs at study). Controls: none. Measurement: BSI-18 GSI (cutoff ≥63)	*Oancea et al. 2014*
Higher educational achievement was associated with a lower risk for emotional distress using linear regression analysis (adjusted for sex, age at study, age at diagnosis, duration of treatment, global CNS irradiation). • High educational achievement (Ref. Medium educational achievement) β=-1.28, p<0.01 • Low educational achievement (Ref. Medium educational achievement) β=0.44, p=0.53 *Survivors (n=652; mixed diagnoses; median 6 yrs at diagnosis; median 23 yrs at study [range 15-46 yrs]). Controls: n=440 Dutch HADS controls (mean age 51 yrs [range 17-89 yrs]). Measurement: Hospital Anxiety and Depression scale (HADS) (cutoff ≥15)	*Van der Geest et al. 2013*
Being a college graduate was associated with a lower risk for psychological distress using generalized estimating equations (adjusting for scarring/disfigurement, hair loss, recurrence, SMN, age at diagnosis, age at study, sex, marital status, race, cranial radiation, surgery). • College graduate: Yes (Ref. No) OR=0.64 (95%CI:0.54-0.75, p<0.001) *Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: BSI-18 GSI subscale (cutoff ≥ 90th %tile on standardized norms)	*Kinahan et al. 2012*
Educational achievement below a college degree was associated with an increased risk for psychological distress using multivariable hierarchical regression (adjusted for sex, employment status, marital/relationship status, income, health problems, age at diagnosis, years since diagnosis, cancer type, negative/positive impact of cancer). • Standardized beta coefficients- Education (1 = some college): 0.097, *p*<0.05; Education (1 = having college degree): 0.062, p≥0.05 *Survivors (n=621; mixed diagnoses; mean 11.1 yrs at diagnosis; mean 15.8 yrs since diagnosis; mean 26.9 yrs at study). Controls: none. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Zebrack et al. 2011*
Educational achievement below a college education was associated with an increased risk for psychological distress using multivariable logistic regression (adjusted for sex, age at study, race, marital status, employment, annual income, health insurance, major medical condition). • Below high school (Ref. college graduate) OR=1.6 (95%CI:1.1-2.2) • High school graduate (Ref. college graduate) OR=1.3 (95%CI:1.1-1.5) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI)	*Zeltzer et al. 2008*

No significant association between educational achievement and psychological distress was founf using multivariable logistic regression (adjusted for age at diagnosis, treatment, ethnicity, sex, special education, influence of cancer on employment, self-reported health, age at interview, relapse, mother's highest level of education). • Highest education: High school graduate (Ref. Some college) OR=1.63 (95%CI:0.6-4.8, p=0.37) • Highest education: Dropout (Ref. Some college) OR=2.87 (95%CI:0.6-13.1, p=0.17) *Survivors treated on Children's Cancer Group (CCG) protocols (n=555; acute lymphoblastic leukemia; <20 yrs at diagnosis; 18-33 yrs at study). Controls: none. Measurement: Profile of Mood Scale-Total score (cutoff >33)	*Glover et al. 2003*
Lower educational achievement was associated with an increased risk for psychological distress using multivariable logistic regression analysis (adjusted for age at interview, sex, race/ethnicity, household income, health insurance, diagnosis). • High school or less (Ref. High school + some college) OR=1.3 (95%CI:1.1-1.5) *Survivors from the CCSS cohort (n=9535; mixed diagnoses; mean 10.00 yrs at diagnosis [range: 0.1-20.9 yrs]; mean 26.8 yrs age at study [range: 18-48 yrs]). Controls: n=2916 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Hudson et al. 2003*
Overall Conclusion	
Evidence suggests that lower levels of educational achievement are related to increased risk of developing psychological distress among survivors of CAYA cancer.	8 studies (5 samples) Level B[14,24,36,46,48,50,52,67]

Demographic risk factors: Employment	
Being unemployed was associated with an increased risk for psychological distress using modified multivariable Poisson models (adjusting for age, sex, race/ethnicity, employment status, household income, marital status, years since diagnosis, second malignant neoplasm, disease recurrence, and treatment type). • Employment status: Unemployed RR=1.85 (95%CI:1.54–2.22; p < 0.001) *Survivors from the CCSS cohort (n=4798; mixed diagnoses; mean 7.6 yrs at diagnosis; mean 34.9 yrs at study). Controls: none. Measurement: BSI-18 GSI (cut-off: top 10th %tile)	*Crochet et al. 2019*
Being unable to work due to illness or disability was associated with an increased risk for psychological distress using multivariable logistic regression (adjusted for education, health insurance, cancer-related pain, learning or memory problems, age at clinical evaluation). • Employment: Unable to work due to illness or disability (Ref. Caring for home or family, student, retired, working part- or full-time) OR=1.83 (95%CI:1.01-3.34) • Employment: Never had a job, or not currently working, or unemployed and looking for work (Ref. Caring for home or family, student, retired, working part- or full-time) OR=1.20 (95%CI:0.82-1.77) *Survivors from the St. Jude Lifetime Cohort Study (n=1863; mixed diagnoses; median 7 yrs at diagnosis; ≥10 yrs since diagnosis; median 32 yrs at study). Controls: none. Measurement: BSI-18 GSI (cutoff ≥63)	*Oancea et al. 2014*
Unemployment was associated with increased risk for psychological distress using multivariable hierarchical regression (adjusted for sex, education, marital/relationship status, income, health problems, age at diagnosis, years since diagnosis, cancer type, negative/positive impact of cancer). • Standardized beta coefficients- Employment status (1 = employed): -0.075, p <0.05 *Survivors (n=621; mixed diagnoses; mean 11.1 yrs at diagnosis; mean 15.8 yrs since diagnosis; mean 26.9 yrs at study). Controls: none. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Zebrack et al. 2011*
Unemployment was associated with increased risk for psychological distress using multivariable logistic regression (adjusted for sex, age at study, race, educational achievement, marital status, annual income, health insurance, major medical condition). • Student (Ref. employed/caring for home) OR=1.0 (95%CI:0.7-1.5) • Looking for work/unable to work (Ref. employed/caring for home) OR=3.1 (95%CI:2.5-3.7)	*Zeltzer et al. 2008*

*Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI)	
Survivors' perception of the cancer limiting the their ability to work was associated with an increased risk for psychological distress using multivariable logistic regression (adjusted for age at diagnosis, treatment, level of education, ethnicity, sex, special education, self-reported health, age at interview, relapse, mother's highest level of education). • Cancer limiting ability to work: Yes (Ref. No) OR=3.3 (95%CI:1.8-5.8, p<0.001) *Survivors treated on Children's Cancer Group (CCG) protocols (n=555; acute lymphoblastic leukemia; <20 yrs at diagnosis; 18-33 yrs at study). Controls: none. Measurement: Profile of Mood Scale-Total score (cutoff >33)	*Glover et al. 2003*
Overall Conclusion	
There is evidence that being unemployed is related to an increased risk of developing psychological distress among survivors of CAYA cancer.	5 studies (4 samples) Level A[14,24,30,50,52]

Demographic risk factors: Income/Economic status	
Lower household income was associated with an increased risk for psychological distress using modified multivariable Poisson models (adjusting for age, sex, race/ethnicity, employment status, household income, marital status, years since diagnosis, second malignant neoplasm, disease recurrence, and treatment type). • Household income: < 20,000 (Ref. 60,000+) RR=1.70 (95%CI:1.34–2.15; p< 0.001*) • Household income: 20,000–39,999 (Ref. 60,000+) RR=1.33 (95%CI:1.07–1.66; p= 0.009) • Household income: 40,000–59,999 (Ref. 60,000+) RR=1.36 (95%CI:1.08–1.72; p= 0.010) *Survivors from the CCSS cohort (n=4798; mixed diagnoses; mean 7.6 yrs at diagnosis; mean 34.9 yrs at study). Controls: none. Measurement: BSI-18 GSI (cut-off: top 10th %tile)	*Crochet et al. 2019*
Survivors with a low income were at an increased risk for psychological distress using generalized linear models with a log-link function to allow direct estimation of prevalence ratios (PR, adjusted for sex, race/ethnicity, education, BMI, smoking, physical activity, alkylating agents, craniotomy, within-person correlation). • Income <$20,000 USD/yr (Ref. ≥$20,000/yr): PR=1.84 (95%CI:1.65-2.05) *Survivors from the CCSS cohort (n=22,568; mixed diagnoses; mean 9.5 yrs at diagnosis; mean 22.4 yrs of follow-up; 18-48 yrs at study). Controls: n=7504 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Hudson et al. 2015*
Having an unstable economic status was related to an increased risk for psychological distress using multivariable logistic regression (adjusted for age, time since diagnosis). • Economic status: Unstable (Ref. Stable) OR=2.58 (95%CI:1.20-5.54; p=0.016) * Survivors (n=223, Hematological cancers, solid or soft tissue tumors, central nervous system tumors or brain tumors, mean age at diagnosis=9.91 yrs (SD=4.69) and mean age at study 21.92 (SD=4.69); measurement: BSI-18 (cutoff ≥63)	*Kim et al 2013*
No association was found between annual income and psychological distress using multivariable hierarchical regression (adjusted for sex, employment status, education, marital/relationship status, income, health problems, age at diagnosis, years since diagnosis, cancer type, negative/positive impact of cancer). • Standardized beta coefficient- Income (1 ≥ $25,000 USD): -0.053, p≥0.05 *Survivors (n=621; mixed diagnoses; mean 11.1 yrs at diagnosis; mean 15.8 yrs since diagnosis; mean 26.9 yrs at study). Controls: none. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Zebrack et al. 2011*
Low annual income was associated with increased risk for psychological distress using multivariable logistic regression (adjusted for sex, age at study, race, educational achievement, marital status, employment, health insurance, major medical condition). • Annual income below $20,000 USD (Ref. $20,000+) OR=1.8 (95%CI:1.5-2.3) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI)	*Zeltzer et al. 2008*
Survivors with an income of <$20,000 USD were at an increased risk for symptoms of psychological distress using generalized linear mixed modeling (adjusted for sex,	*Zebrack et al. 2004*

income, self-rated health, major medical condition, brain radiation dosage, age, health; higher least square (LS) mean indicates more problems): • Income $USD: <20,000: LS mean 12.31 (SE 0.79), ≥20,000+: LS mean 8.23 (SE 0.65), p<0.001 • Income $USD and health: <$20K, poor or fair: LS mean 17.51 (SE 1.38), compared to <$20K, good or better: LS mean 7.10 (SE 0.73), compared to $20K, poor or fair: LS mean 10.79 (SE 1.20), compared to $20K, good or better: LS mean: 5.67 (SE 0.48), p=0.008 *Survivors of childhood brain cancer from the CCSS cohort (n=1101; mixed neurooncology diagnoses; <21 yrs at diagnosis; mean 26.5 yrs at study). Controls: n=2817 siblings (mean 29.4 yrs at study). Measurement: BSI-18 (cutoff ≥63 on GSI)	
Survivors with a low household income were at increased risk for psychological distress using multivariable logistic regression analysis (adjusted for age at interview, sex, race/ethnicity, education, health insurance, diagnosis). • Household income <$20,000 USD (Ref.≥$20,000) OR=1.8 (95%CI:1.5-2.0) *Survivors from the CCSS cohort (n=9535; mixed diagnoses; mean 10.00 yrs at diagnosis [range: 0.1-20.9 yrs]; mean 26.8 yrs age at study [range: 18-48 yrs]). Controls: n=2916 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Hudson et al. 2003*
Overall Conclusion	
Evidence suggests that lower or unstable household income is related to an increased risk of developing psychological distress among survivors of CAYA cancer.	7 studies (3 samples) Level B[24,30,36,39,46,49,50]

Demographic risk factors: Health insurance	
Survivors without health insurance were at an increased risk for psychological distress using multivariable logistic regression (adjusted for education, employment, cancer-related pain, learning or memory problems, age at clinical evaluation). • Health insurance: None (Ref. Canadian resident/Through spouse's or parent's policy/Through place of employment/Through self-purchased policy) OR=1.60 (95%CI:1.11-2.32) • Health insurance: Through Medicare or Medicaid or other public assistance programs/Military dependent or veteran's benefits (Ref. Canadian resident/Through spouse's or parent's policy/Through place of employment/Through self-purchased policy) OR=1.07 (95%CI:0.67-1.71) *Survivors from the St. Jude Lifetime Cohort Study (n=1863; mixed diagnoses; median 7 yrs at diagnosis; ≥10 yrs since diagnosis; median 32 yrs at study). Controls: none. Measurement: BSI-18 GSI (cutoff ≥63)	*Oancea et al. 2014*
Survivors without health insurance were at an increased risk for psychological distress using multivariable logistic regression (adjusted for sex, age at study, race, educational achievement, marital status, employment, income, major medical condition). • No health insurance (Ref. health insurance) OR=1.3 (95%CI:1.1-1.7) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI)	*Zeltzer et al. 2008*
Survivors without health insurance were at increased risk for psychological distress using multivariable logistic regression analysis (adjusted for age at interview, sex, race/ethnicity, education, household income, diagnosis). • Health insurance: No (Ref. Yes or Canadian) OR=1.4 (95%CI:1.2-1.6) *Survivors from the CCSS cohort (n=9535; mixed diagnoses; mean 10.00 yrs at diagnosis [range: 0.1-20.9 yrs]; mean 26.8 yrs age at study [range: 18-48 yrs]). Controls: n=2916 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Hudson et al. 2003*
Overall Conclusion	
There is evidence that not having health insurance is related to an increased risk of developing psychological distress among survivors of CAYA cancer.	3 studies (2 samples) Level A[14,24,36]

Demographic risk factors: Parents' educational achievement	
No association between parents' education and psychological distress was found using multivariable logistic regression (adjusted for age at study, sex, perceived parents' support, diagnosis, treatment modality, late effects, time since diagnosis). • Parents' education: Secondary, tertiary (Ref. Compulsory, primary) OR=1.30 (95%CI:0.52-3.27, p=0.574) *Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 (cutoff ≥57 on GSI or any 2 of the 3 BSI-18 subscales)	*Gianinazzi et al 2013*
Overall Conclusion	
Some evidence suggests that parents' education is not related to the risk of developing psychological distress among survivors of CAYA cancer.	1 study Level C[19]

Treatment-related risk factors: Bone marrow transplantation	
No association between bone marrow transplantation and psychological distress was found using multivariable logistic regression (adjusted for age at study, sex, parents' education, perceived parents' support, diagnosis, late effects, time since diagnosis). • Treatment: Bone marrow transplantation (Ref. Chemotherapy) OR=0.79 (95%CI:0.19-3.22, p=0.848) *Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 (cutoff ≥57 on GSI or any 2 of the 3 BSI-18 subscales)	*Gianinazzi et al 2013*
Overall Conclusion	
Evidence suggests that bone marrow transplantation is not associated with the risk for psychological distress among survivors of CAYA cancer.	1 study Level C[19]

Treatment-related risk factors: Chemotherapy	
No association of chemotherapeutic treatments with psychological distress was found using modified multivariable Poisson models (adjusting for age, sex, race/ethnicity, employment status, household income, marital status, years since diagnosis, second malignant neoplasm, disease recurrence, and treatment type). • Anthracycline dose 1st 5 years: Per 100 g/m2 (continuous): RR=0.96 (95%CI:0.91–1.01; p= 0.12) • Alkylating agents dose 1st 5 years: Per 100 g/m2 (continuous) RR=1.15 (95%CI:0.46–2.87; p= 0.76) • Methotrexate IV dose 1st 5 years: Per 100 g/m2 (continuous): RR=0.98 (95%CI:0.76–1.26; p= 0.87) • Methotrexate IT dose 1st 5 years: Per 100 g/m2 (continuous): RR=1.03 (95%CI:0.99–1.07; p= 0.18) *Survivors from the CCSS cohort (n=4798; mixed diagnoses; mean 7.6 yrs at diagnosis; mean 34.9 yrs at study). Controls: none. Measurement: BSI-18 GSI (cut-off: top 10th %tile)	*Crochet et al. 2019*
Treatment with alkylating agents was associated with increased risk for psychological distress using generalized linear models with a log-link function to allow direct estimation of prevalence ratios (PR, adjusted for sex, race/ethnicity, income, education, BMI, smoking, physical activity, craniotomy, within-person correlation). • Alkylating agents: Yes (Ref. No) PR=1.19 (95%CI:1.08-1.32) *Survivors from the CCSS cohort (n=22,568; mixed diagnoses; mean 9.5 yrs at diagnosis; mean 22.4 yrs of follow-up; 18-48 yrs at study). Controls: n=7504 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Hudson et al. 2015*
No association between treatment modality and psychological distress was found using multivariable logistic regression (adjusted for age at study, sex, parents' education, perceived parents' support, diagnosis, late effects, time since diagnosis). • Treatment: Surgery (Ref. Chemotherapy) OR=0.70 (95%CI:0.19-2.48, p=0.848) • Treatment: Radiotherapy (Ref. Chemotherapy) OR=0.68 (95%CI:0.28-1.64, p=0.848) • Treatment: Bone marrow transplantation (Ref. Chemotherapy) OR=0.79 (95%CI:0.19-3.22, p=0.848)	*Gianinazzi et al 2013*

*Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 (cutoff ≥57 on GSI or any 2 of the 3 BSI-18 subscales)	
No association between chemotherapy and psychological distress was found using multivariable logistic regression (adjusted for sex, age at diagnosis, survival time, surgery, radiation). • Chemotherapy (Ref. no chemotherapy) OR=1.1 (95%CI:0.9-1.4) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI)	*Zeltzer et al. 2008*
No association between treatment modality and psychological distress was found using multivariable logistic regression (adjusted for age at diagnosis, level of education, ethnicity, sex, special education, influence of cancer on employment, self-reported health, age at interview, relapse, mother's highest level of education). • Treatment: High methotrexate (Ref. No-low treatment) OR=0.4 (95%CI:0.2-1.2, p=0.11) • Treatment: High CNS irradiation (Ref. No-low treatment) OR=0.4 (95%CI:0.2-1.2, p=0.10) • Treatment: High both (Ref. No-low treatment) OR=1.7 (95%CI:0.4-6.8, p=0.45) *Survivors treated on Children's Cancer Group (CCG) protocols (n=555; acute lymphoblastic leukemia; <20 yrs at diagnosis; 18-33 yrs at study). Controls: none. Measurement: Profile of Mood Scale-Total score (cutoff >33)	*Glover et al. 2003*
No association was found between chemotherapy and psychological distress using multivariable logistic regression analysis (adjusted for age at interview, sex, race/ethnicity, diagnosis, surgery, radiation therapy). • Chemotherapy: Alkylating agent (Ref. none) OR=1.2 (95%CI:1.0-1.4) • Chemotherapy: Anthracycline (Ref. none) OR=1.1 (95%CI:0.8-1.5) • Chemotherapy: Alkylating+ Anthracycline (Ref. none) OR=1.2 (95%CI:1.0-1.5) • Chemotherapy: Other (Ref. none) OR=1.0 (95%CI:0.8-1.3) *Survivors from the CCSS cohort (n=9535; mixed diagnoses; mean 10.00 yrs at diagnosis [range: 0.1-20.9 yrs]; mean 26.8 yrs age at study [range: 18-48 yrs]). Controls: n=2916 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Hudson et al. 2003*
Overall Conclusion	
Some evidence suggests that treatment with alkylating agents is related to an increased risk of developing psychological distress among survivors of CAYA cancer.	6 studies (3 samples) Level C[19,24,30,36,46,52]

Treatment-related risk factors: Radiation	
Cranial radiation was associated with a decreased risk for psychological distress using modified multivariable Poisson models (adjusting for age, sex, race/ethnicity, employment status, household income, marital status, years since diagnosis, second malignant neoplasm, disease recurrence, and treatment type). • Cranial radiation: Per 10 Gy (continuous): RR=0.94 (95%CI:0.90–0.9; p= 0.022) *Survivors from the CCSS cohort (n=4798; mixed diagnoses; mean 7.6 yrs at diagnosis; mean 34.9 yrs at study). Controls: none. Measurement: BSI-18 GSI (cut-off: top 10th %tile)	*Crochet et al. 2019*
Abdominal radiation was associated with an increased risk for poor mental health using generalized linear models (adjusted for tumor location, age at diagnosis). • Abdominal Radiation: Any (Ref. none) RR=2.24 (95%CI:1.25-4.02) *Survivors from the CCSS cohort (n=1094; upper and lower extremity sarcoma diadnoses; median 13 yrs at diagnosis, median 33 yrs at study). Controls: none. Measurement: BSI-18 (cutoff ≥63 on GSI or any of the BSI-18 subscales)	*Marina et al. 2013*
No association between radiotherapy and psychological distress was found using multivariable logistic regression (adjusted for age at study, sex, parents' education, perceived parents' support, diagnosis, late effects, time since diagnosis). • Treatment: Radiotherapy (Ref. Chemotherapy) OR=0.68 (95%CI:0.28-1.64, p=0.848) *Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 (cutoff ≥57 on GSI or any 2 of the 3 BSI-18 subscales)	*Gianinazzi et al 2013*

No association between global CNS irradiation and emotional distress was found using multivariable linear regression analysis (adjusted for sex, age at study, age at diagnosis, duration of treatment, educational achievement). • Global CNS irradiation (yes vs. no) β=0.63, p=0.40 *Survivors (n=652; mixed diagnoses; median 6 yrs at diagnosis; median 23 yrs at study [range 15-46 yrs]). Controls: n=440 Dutch HADS controls (mean age 51 yrs [range 17-89 yrs]). Measurement: Hospital Anxiety and Depression scale (HADS) (cutoff ≥15)	*Van der Geest et al. 2013*
No association between cranial radiation and psychological distress was found using generalized estimating equations (adjusting for scarring/disfigurement, hair loss, recurrence, SMN, age at diagnosis, age at study, sex, race, educational achievement, marital status, surgery). • Cranial radiation: Scatter exposure only (Ref. none) OR=0.88 (95%CI:0.73-1.07, p=0.21) • Cranial radiation: Direct, ≤20 Gy (Ref. none) OR=0.77 (95%CI:0.58-1.02, p=0.07) • Cranial radiation: Direct, 20-36 Gy (Ref. none) OR=1.01 (95%CI:0.78-1.30, p=0.93) • Cranial radiation: Direct, ≥36 Gy (Ref. none) OR=0.77 (95%CI:0.57-1.05, p=0.09) *Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: BSI-18 GSI subscale (cutoff ≥ 90th %tile on standardized norms)	*Kinahan et al. 2012*
No association between radiation and psychological distress was found using multivariable logistic regression (adjusted for sex, age at diagnosis, survival time, surgery, chemotherapy). • Cranial radiation (Ref. none) OR=1.0 (95%CI:0.8-1.2) • Other than cranial radiation (Ref. none) OR=1.0 (95%CI:0.8-1.2) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI)	*Zeltzer et al. 2008*
No association between brain radiation dosage and symptoms of psychological distress was found using generalized linear mixed modeling (adjusted for sex, income, self-rated health, major medical condition, age, income & health; higher least square (LS) mean indicates more problems): • Brain radiation dosage: 0-29 Gy LS mean 11.03 (SE 0.68), 30-49 Gy LS mean 9.57 (SE 0.96), 50 Gy+ LS mean 10.20 (SE 0.58), p=0.302 *Survivors of childhood brain cancer from the CCSS cohort (n=1101; mixed neurooncology diagnoses; <21 yrs at diagnosis; mean 26.5 yrs at study). Controls: n=2817 siblings (mean 29.4 yrs at study). Measurement: BSI-18 (cutoff ≥63 on GSI)	*Zebrack et al. 2004*
No association between treatment modality and psychological distress was found using multivariable logistic regression (adjusted for age at diagnosis, level of education, ethnicity, sex, special education, influence of cancer on employment, self-reported health, age at interview, relapse, mother's highest level of education). • Treatment: High methotrexate (Ref. No-low treatment) OR=0.4 (95%CI:0.2-1.2, p=0.11) • Treatment: High CNS irradiation (Ref. No-low treatment) OR=0.4 (95%CI:0.2-1.2, p=0.10) • Treatment: High both (Ref. No-low treatment) OR=1.7 (95%CI:0.4-6.8, p=0.45) *Survivors treated on Children's Cancer Group (CCG) protocols (n=555; acute lymphoblastic leukemia; <20 yrs at diagnosis; 18-33 yrs at study). Controls: none. Measurement: Profile of Mood Scale-Total score (cutoff >33)	*Glover et al. 2003*
No association between radiation and psychological distress was found using multivariable logistic regression analysis (adjusted for age at interview, sex, race/ethnicity, diagnosis, surgery, chemotherapy). • Radiation: Head/brain (Ref. none) OR=1.0 (95%CI:0.8-1.2) • Radiation: Chest/mantle (Ref. none) OR=1.1 (95%CI:0.9-1.3) • Radiation: Brain/chest (Ref. none) OR=1.1 (95%CI:0.7-1.7) • Radiation: Other (Ref. none) OR=1.1 (95%CI:0.9-1.3) *Survivors from the CCSS cohort (n=9535; mixed diagnoses; mean 10.00 yrs at diagnosis [range: 0.1-20.9 yrs]; mean 26.8 yrs age at study [range: 18-48 yrs]). Controls: n=2916 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Hudson et al. 2003*
Overall Conclusion	

Some evidence suggests that abdominal radiation is related to an increased risk of developing psychological distress among survivors of CAYA cancer.	1 study Level C[68]
Some evidence suggests that higher doses of cranial irradiation are associated with a decreased risk of psychological distress among survivors of CAYA cancer.	7 studies (3 samples) Level C[24,30,36,39,48,52,67]
Evidence suggests that there is no association between radiotherapy (not further specified) and risk of psychological distress among survivors of CAYA cancer.	3 studies Level B[19,24,36]

Treatment-related risk factors: Surgery	
Craniotomy was associated with an increased risk for poor or adverse mental health using generalized linear models with a log-link function to allow direct estimation of prevalence ratios (PR, adjusted for sex, race/ethnicity, income, education, BMI, smoking, physical activity, alkylating agents, within-person correlation). • Craniotomy: Yes (Ref. No) PR=1.23 (95%CI:1.05-1.44) *Survivors from the CCSS cohort (n=22,568; mixed diagnoses; mean 9.5 yrs at diagnosis; mean 22.4 yrs of follow-up; 18-48 yrs at study). Controls: n=7504 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Hudson et al. 2015*
No association between treatment modality and psychological distress was found using multivariable logistic regression (adjusted for age at study, sex, parents' education, perceived parents' support, diagnosis, late effects, time since diagnosis). • Treatment: Surgery (Ref. Chemotherapy) OR=0.70 (95%CI:0.19-2.48, p=0.848) *Survivors from the Swiss CCSS cohort (n=407; mixed diagnoses; mean 5.7 yrs at diagnosis; mean 17.9 yrs at study). Controls: n=93 healthy adolescents and n=102 siblings. Measurement: BSI-18 (cutoff ≥57 on GSI or any 2 of the 3 BSI-18 subscales)	*Gianinazzi et al 2013*
Having had surgery was associated with an increased risk of psychological distress using generalized estimating equations (adjusting for scarring/disfigurement, hair loss, recurrence, SMN, age at diagnosis, age at study, sex, race, educational achievement, marital status, cranial radiation). • Surgery: Yes (Ref. No) OR=1.35 (95%CI:1.14-1.60, p<0.001) *Survivors from the CCSS cohort (n=14358; mixed diagnoses; ≤21 yrs at diagnosis; mean 16.1 yrs from diagnosis to baseline [SD=4.9 yrs], mean 7.7 yrs from baseline to follow-up [SD=1.2 yrs]; 5-49 yrs at basline study, ≥18 yrs follow-up). Controls: n= 4023 siblings. Measurement: BSI-18 GSI subscale (cutoff ≥ 90th %tile on standardized norms)	*Kinahan et al. 2012*
No association between surgery and psychological distress was found using multivariable logistic regression (adjusted for sex, age at diagnosis, survival time, chemotherapy, radiation). • Surgery (Ref. no surgery) OR=1.2 (95%CI:0.9-1.5) *Survivors from the CCSS cohort (n=7147; mixed diagnoses; median 7 yrs at diagnosis; median 32 yrs at study). Controls: n=388 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI)	*Zeltzer et al. 2008*
No association between surgery and psychological distress was found using multivariable logistic regression analysis (adjusted for age at interview, sex, race/ethnicity, diagnosis, radiation therapy, chemotherapy). • Surgery: Yes (Ref. No) OR=1.1 (95%CI:0.9-1.3) *Survivors from the CCSS cohort (n=9535; mixed diagnoses; mean 10.00 yrs at diagnosis [range: 0.1-20.9 yrs]; mean 26.8 yrs age at study [range: 18-48 yrs]). Controls: n=2916 siblings. Measurement: BSI-18 (cutoff ≥63 on GSI or any BSI-18 subscales)	*Hudson et al. 2003*
Overall Conclusion	
Some evidence suggests that having undergone surgery (not further specified) is related to an increased risk of developing psychological distress among survivors of CAYA cancer.	4 studies (2 samples) Level C[19,24,36,67]
Some evidence suggests that having undergone craniotomy is associated with an increased risk of psychological distress among survivors of CAYA cancer.	1 study Level C[46]

Treatment-related risk factors: Duration of treatment	
No association between duration of treatment and emotional distress was found using multivariable linear regression analysis (adjusted for sex, age at study, age at diagnosis, global CNS irradiation, educational achievement).	*Van der Geest et al. 2013*

• Duration of treatment (years) β=0.03, p=0.78 *Survivors (n=652; mixed diagnoses; median 6 yrs at diagnosis; median 23 yrs at study [range 15-46 yrs]). Controls: n=440 Dutch HADS controls (mean age 51 yrs [range 17-89 yrs]). Measurement: Hospital Anxiety and Depression scale (HADS) (cutoff ≥15)	
Overall Conclusion	
Some evidence suggests that the duration of treatment is not related to the risk of developing psychological distress among survivors of CAYA cancer.	1 study Level C[48]

1b-4. What are the key clinical, demographic and treatment-related risk factors for post-traumatic stress or stress-related mental disorders among survivors of childhood, adolescent, and young adult (CAYA) cancer?	
Conclusion single studies	
Clinical risk factors: Age at diagnosis	
No association between age at diagnosis and post-traumatic stress was found using multiple linear regression (adjusting for GSI Total Score, Worry total score, perceived stress scale, diagnosis, age at diagnosis, sex, and education): • Age at diagnosis (1 year): β=0.02, p=0.47 *Survivors from the St. Jude cohort (n=2969; mixed diagnoses; mean 8.4 yrs at diagnosis; mean 32.5 yrs at study; mean 24.1 yrs since diagnosis). Measurement: PTSD Checklist-Civilian: cut-off ≥44; BSI-18: cut-off ≥63	*Allen et al. 2018*
Survivors diagnosed at 6-11 years of age were found to have an increased risk for any stress-related mental disorder using multivariable cox proportional hazards models (adjusted for diagnosis, treatment, previous mental disorder diagnosis). • Age at diagnosis: 6-11 years (Ref. 0-5) HR=2.36 (95%CI:1.19-4.65) • Age at diagnosis: 12-15 years (Ref. 0-5) HR=0.49 (95%CI:0.16-1.55) *Medicaid eligible survivors identified from the South Carolina Central Cancer Registry (n=390; mixed diagnoses; age at study entry: 0-5 yrs (n=175), 6-11 yrs (n=118), 12-15 yrs (n=97)). Controls: n=1329 Medicaid eligible children without cancer. Measurement: SRMD diagnoses from Medicaid claims database	*Schrag et al. 2008*
No association between age at diagnosis and post-traumatic stress symptoms was found using simultaneous linear regression (adjusted for sex, age at follow-up, marital status, educational level, employment, diagnosis, treatment duration, years since completion of therapy, late effects, treatment). • Age at diagnosis (years): β= 0.35 (p≥0.05) *Survivors (n=500; mixed diagnoses; median 8 yrs at diagnosis; mean 24 yrs at study). Controls: none. Measurement: Impact of Event Scale (IES)	*Langeveld et al. 2004*
No association between age at diagnosis and post-traumatic stress symptoms was found using multivariable regression (adjusted for age, sex, race, treatment intensity, years off treatment, past perceived life threat, mother support network, mother family cohesion, mother family satisfaction, mother family adaptability). • Age at diagnosis: β= 0.28 (not significant) *Child and adolescent aged survivors (n=309 survivors; mixed diagnoses; mean 5.83 yrs at diagnosis [range 1-17 yrs]; mean 13.53 yrs at study [range 8-20 yrs]). Controls: n=219 healthy children (mean 12.27 yrs at study [range 8-20 yrs]). Measurement: Impact of Event Scale (IES); Post-traumatic Stress Disorder Reaction Index (PTSDRI)	*Barakat et al. 1997*
Overall Conclusion	
Some evidence suggests that being diagnosed between 6-11 years of age (compared to younger than 6 years or 12 years and older) is related to an increased risk of developing a stress-related mental disorder among survivors of CAYA cancer.	1 study Level C[59]
Evidence suggests that age at diagnosis is not related to the risk of developing post-traumatic stress symptoms among survivors of CAYA cancer.	3 studies Level A[47,53,60]
Clinical risk factors: Time since diagnosis	
No significant association between years since completion of therapy and post-traumatic stress symptoms was found using simultaneous linear regression (adjusted for sex, age at follow-up, marital status, educational level, employment, age at	*Langeveld et al. 2004*

diagnosis, diagnosis, treatment duration, years since completion of therapy, late effects, treatment). • Years since completion of therapy: β= 0.35 (p≥0.05) *Survivors (n=500; mixed diagnoses; median 8 yrs at diagnosis; mean 24 yrs at study). Controls: none. Measurement: Impact of Event Scale (IES)	
No association between years off treatment and post-traumatic stress symptoms was found using multivariable regression (adjusted for age, sex, race, treatment intensity, years off treatment, age at diagnosis, past perceived life threat, mother support network, mother family cohesion, mother family satisfaction, mother family adaptability). • Years off treatment: β= -0.03 (not significant) *Child and adolescent aged survivors (n=309 survivors; mixed diagnoses; mean 5.83 yrs at diagnosis [range 1-17 yrs]; mean 13.53 yrs at study [range 8-20 yrs]). Controls: n=219 healthy children (mean 12.27 yrs at study [range 8-20 yrs]). Measurement: Impact of Event Scale (IES); Post-traumatic Stress Disorder Reaction Index (PTSDRI)	*Barakat et al. 1997*
Overall Conclusion	
Evidence suggests that time since diagnosis is not related to the risk of developing post-traumatic stress symptoms among survivors of CAYA cancer.	2 studies Level B[47,60]

Clinical risk factors: Diagnosis	
Diagnosis of a CNS tumor was associated with less post-traumatic stress, whereas no association between diagnosis of leukemia/lymphoma with post-traumatic stress was found using multiple linear regression (adjusting for GSI Total Score, Worry total score, perceived stress scale, diagnosis, age at diagnosis, sex, and education): • CNS tumor vs. other β=-1.15, p=0.022 • Leukemia/lymphoma vs. other β=0.12, p=0.69 *Survivors from the St. Jude cohort (n=2969; mixed diagnoses; mean 8.4 yrs at diagnosis; mean 32.5 yrs at study; mean 24.1 yrs since diagnosis). Measurement: PTSD Checklist-Civilian (cut-off ≥44)	*Allen et al. 2018*
Survivors of hematological cancers, or brain/CNS/eye/orbital cancers had an increased risk for any stress-related mental disorder using multivariable cox proportional hazards models (adjusted for age at diagnosis, treatment, previous mental disorder diagnosis). • Diagnosis: Hematologic cancers (Ref. Other) HR=5.10 (95%CI:1.51-17.16) • Diagnosis: Brain/CNS/eye/orbital (Ref. Other) HR=5.25 (95%CI:1.45-19.08) • Diagnosis: Bone/joint cancers (Ref. Other) n/a (none in this category had SRMD diagnosis) *Medicaid eligible survivors identified from the South Carolina Central Cancer Registry (n=390; mixed diagnoses; age at study entry: 0-5 yrs (n=175), 6-11 yrs (n=118), 12-15 yrs (n=97)). Controls: n=1329 Medicaid eligible children without cancer. Measurement: SRMD diagnoses from Medicaid claims database	*Schrag et al. 2008*
Survivors of leukemia/non-Hodgkin Lymphoma with CRT were at a decreased risk for post-traumatic stress symptoms (compared to survivors of leukemia/non-Hodgkin Lymphoma without CRT) using simultaneous linear regression (adjusted for sex, age at follow-up, marital status, educational level, employment, age at diagnosis, treatment duration, years since completion of therapy, late effects, treatment). • Leukemia/non-Hodgkin Lymphoma with CRT (Ref. Leukemia/non-Hodgkin Lymphoma without CRT): β= -0.12 (p<0.05) • Solid tumor (Ref. Leukemia/non-Hodgkin Lymphoma without CRT): β= -0.07 (p≥0.05) • Brain/CNS tumor (Ref. Leukemia/non-Hodgkin Lymphoma without CRT): β= -0.07 (p≥0.05) *Survivors (n=500; mixed diagnoses; median 8 yrs at diagnosis; mean 24 yrs at study). Controls: none. Measurement: Impact of Event Scale (IES)	*Langeveld et al. 2004*
Overall Conclusion	
Some evidence suggests that diagnosis type is related to the increased risk of developing a stress-related mental disorder among survivors of CAYA cancer. Specifically, survivors of hematologic cancers or cancers of the brain/CNS/eye/orbital area were at increased risk for a stress-related mental disorder.	1 study Level C[59]

Some evidence suggests that diagnosis type is related to the risk of developing post-traumatic stress symptoms among survivors of CAYA cancer. Specifically, survivors of leukemia/non-Hodgkin lymphoma who received cranial radiation (1 study) and survivors of CNS tumors (1 study) were at decreased risk for symptoms.	2 studies Level C[53,60]

Clinical risk factors: Second malignant neoplasm (SMN) or recurrence	
No association between SMN or recurrence and post-traumatic stress disorder was found using multivariable logistic regression models (adjusted for sex and race, age at interview, education, employment, personal income, marital status, radiation and age at diagnosis, chemotherapy). • Secondary Malignant Neoplasm: Yes (Ref. No): OR=1.01 (95%CI:0.72 – 1.41), p=0.097 • Recurrence: Yes (Ref. No): OR=1.22 (95%CI:0.91 – 1.62), p=0.18 *Survivors from the CCSS cohort (n=6542; mixed diagnoses; mean 8.2 yrs at diagnosis; mean 31.85 yrs at study). Controls: n=368 siblings (mean 33.44 yrs at study). Measurement: Post-traumatic Stress Diagnostic Scale (PSDS)- (PTSD symptoms), BSI-18 (distress criterion), and RAND Health Status Survey, Short Form-36 (impairment criterion).	*Stuber, Meeske, Krull et al. 2010*
Overall Conclusion	
Some evidence suggests that experiencing a second malignant neoplasm or recurrence is not related to the risk of developing a post-traumatic stress disorder among survivors of CAYA cancer.	1 study Level C[58]

Clinical risk factors: Survivor health and late effects	
Poor or fair physical health was associated with an increased risk for post-traumatic stress using Poisson regression (adjusted for heavy/risky drinking, sex, physical health, radiation, race, age at diagnosis, age at follow-up, educational attainment, and employment status). • Physical health: Poor, fair (Ref. good, very good, excellent) RR=1.9 (95%CI:1.6-2.2; P≤0.01) *Survivors from the CCSS cohort (n=4484; mixed diagnoses; mean 10.5 yrs at diagnosis; mean 27.2 yrs at Baseline. Controls: n=1651 siblings. Meaurement: Posttraumatic Stress Diagnostic Scale and single item assessing self-reported health (fair/poor vs. good/very good/excellent)	*Brinkman et al. 2019*
Cardiac, endocrine, and pulmonary conditions were associated with an increased risk for posttraumatic stress using log-binomial multivariable regression. • Cardiac conditions: Yes (Ref. No) RR=1.32 (95%CI:1.15-1.51) • Endocrine conditions: Yes (Ref. No) RR=1.33 (95%CI:1.16-1.52) • Pulmonary conditions: Yes (Ref. No) RR=1.40 (95%CI:1.21-1.62) *Survivors from the CCSS cohort (n=5021; mixed diagnoses; mean 8.3 yrs at diagnosis; mean 32.0 yrs at study; mean 23.2 yrs since diagnosis). Measurement: Post-traumatic Stress Diagnostic Scale; health conditions self-reported by survivors	*Vuotto et al. 2017*
No association between self-reported late effects and post-traumatic stress disorder using multivariable logistic regression (adjusted for sex and marital status). • Self-reported late effects: Yes (Ref. No) OR=2.05 (95%CI:0.95-4.43; p=0.07) *Survivors (n=348; mixed diagnoses; 0-18 yrs at diagnosis 0-18 yrs; mean 38.5 yrs at study; mean 31.5 yrs since diagnosis). Controls: French norm population n=36,105. Measurement: Impact of Event Scale; Mini-International Neuropsychiatric Interview	*De Laage et al. 2016*
Survivors with late effects/health problems were at an increased risk for post-traumatic stress symptoms using simultaneous linear regression (adjusted for sex, age at follow-up, marital status, educational level, employment, age at diagnosis, diagnosis, treatment duration, years since completion of therapy, late effects, treatment). • Late effects/health problems: β= 0.15 (p<0.05) *Survivors (n=500; mixed diagnoses; median 8 yrs at diagnosis; mean 24 yrs at study). Controls: none. Measurement: Impact of Event Scale (IES); Late effects and health problems were scored by oncology clinicans on an adapted version of the Greenberg, Meadows, and Kazak's Scale for Medical Limitations	*Langeveld et al. 2004*
Overall Conclusion	

Evidence suggests that the experience of late effects or poor physical health is related to the increased risk of developing post-traumatic stress symptoms among survivors of CAYA cancer.	4 studies (3 samples) Level B[27,29,33,60]

Clinical risk factors: Pain	
Medium amount, a lot, and very bad cancer-related pain was associated with an increased risk for post-traumatic stress using Poisson regression (adjusted for heavy/risky drinking, sex, physical health, radiation, race, age at diagnosis, age at follow-up, educational attainment, and employment status). • Cancer-related pain: Medium amount, a lot, very bad (Ref. none, small amount) RR=2.0 (95%CI:1.6-2.3; P≤0.01) *Survivors from the CCSS cohort (n=4484; mixed diagnoses; mean 10.5 yrs at diagnosis; mean 27.2 yrs at Baseline. Controls: n=1651 siblings. Meaurement: Posttraumatic Stress Diagnostic Scale.	*Brinkman et al. 2019*
Overall Conclusion	
Some evidence suggests that experiencing pain was associated with an increased risk of developing post-traumatic stress among survivors of CAYA cancer.	1 study Level C[29]

Clinical risk factors: Drinking behavior	
No association between age at drinking initiation and post-traumatic stress using Poisson regression (adjusted for sex, physical health, radiation, race, age at diagnosis, age at follow-up, educational attainment, and employment status). No association between heavy/risky drinking and post-traumatic stress was found using Poisson regression (adjusted for, sex, physical health, radiation, race, age at diagnosis, age at follow-up, educational attainment, and employment status). • Age at drinking initiation: <18 years (Ref. ≥18 years) RR=1.1 (95%CI:1.0-1.3) • Heavy drinking: Yes (Ref. No) RR=1.2 (95%CI:1.0-1.4) *Survivors from the CCSS cohort (n=4484; mixed diagnoses; mean 10.5 yrs at diagnosis; mean 27.2 yrs at Baseline. Controls: n=1651 siblings. Meaurement: Posttraumatic Stress Diagnostic Scale.	*Brinkman et al. 2019*
Overall Conclusion	
Some evidence suggests that lower age at drinking initiation is not related to the risk of developing post-traumatic stress among survivors of CAYA cancer.	1 study Level C[29]
Some evidence suggests that heavy/risky drinking is not related to the risk of developing post-traumatic stress among survivors of CAYA cancer.	1 study Level C[29]

Clinical risk factors: Past perceived life threat	
Past perceived life threat was associated with an increased risk for post-traumatic stress symptoms using multivariable regression (adjusted for age, sex, race, treatment intensity, years off treatment, age at diagnosis, mother support network, mother family cohesion, mother family satisfaction, mother family adaptability). • Past perceived life threat: β= 0.41 (p=0.001) *Child and adolescent aged survivors (n=309 survivors; mixed diagnoses; mean 5.83 yrs at diagnosis [range 1-17 yrs]; mean 13.53 yrs at study [range 8-20 yrs]). Controls: n=219 healthy children (mean 12.27 yrs at study [range 8-20 yrs]). Measurement: Impact of Event Scale (IES); Post-traumatic Stress Disorder Reaction Index (PTSDRI)	*Barakat et al. 1997*
Overall Conclusion	
Some evidence suggests that past perceived life threat is related to the increased risk of developing post-traumatic stress symptoms among survivors of CAYA cancer.	1 study Level C[47]

Clinical risk factors: Mental health problems	
More psychological distress, more worries, and higher perceived stress was associated with more post-traumatic stress using multiple linear regression (adjusting for GSI Total Score, Worry total score, perceived stress scale, diagnosis, age at diagnosis, sex, and education): • BSI GSI T-Score (1 unit): β=0.67, p<0.001 • Worry total score (1 unit): β=0.10, p=0.001	*Allen et al. 2018*

• Perceived Stress Scale (1 unit): β=0.76, p<0.0001 *Survivors from the St. Jude cohort (n=2969; mixed diagnoses; mean 8.4 yrs at diagnosis; mean 32.5 yrs at study; mean 24.1 yrs since diagnosis). Measurement: PTSD Checklist-Civilian (cut-off ≥44), BSI-18 (cut-off ≥63)	
Survivors with a previous mental disorder diagnosis had an increased risk for any stress-related mental disorder using multivariable cox proportional hazards models (adjusted for diagnosis, age at diagnosis, treatment). • Previous mental disorder diagnosis (Ref. none) HR=2.83 (95%CI:1.02-7.84) *Medicaid eligible survivors identified from the South Carolina Central Cancer Registry (n=390; mixed diagnoses; age at study entry: 0-5 yrs (n=175), 6-11 yrs (n=118), 12-15 yrs (n=97)). Controls: n=1329 Medicaid eligible children without cancer. Measurement: SRMD diagnoses from Medicaid claims database	*Schrag et al. 2008*
Overall Conclusion	
Evidence suggests that having a previous diagnosis of a mental health disorder or experiencing mental health problems is related to the increased risk of developing a stress-related mental disorder among survivors of CAYA cancer.	2 studies Level B[53,59]

Demographic risk factors: Sex	
No association between sex and post-traumatic stress was found using Poisson regression (adjusted for heavy/risky drinking, sex, physical health, radiation, race, age at diagnosis, age at follow-up, educational attainment, and employment status). • Female (Ref. Male) RR=1.2 (95%CI:1.1-1.4) *Survivors from the CCSS cohort (n=4484; mixed diagnoses; mean 10.5 yrs at diagnosis; mean 27.2 yrs at Baseline. Controls: n=1651 siblings. Meaurement: Posttraumatic Stress Diagnostic Scale.	*Brinkman et al. 2019*
Female sex was associated with more post-traumatic stress using multiple linear regression (adjusting for GSI Total Score, Worry total score, perceived stress scale, diagnosis, age at diagnosis, sex, and education): • Female vs. male β=1.64, p<0.0001 *Survivors from the St. Jude cohort (n=2969; mixed diagnoses; mean 8.4 yrs at diagnosis; mean 32.5 yrs at study; mean 24.1 yrs since diagnosis). Measurement: PTSD Checklist-Civilian (cut-off ≥44)	*Allen et al. 2018*
Male sex was associated with a decreased risk for post-traumatic stress disorder using multivariable logistic regression (adjusted for self-reported late effects and marital status). • Male (Ref. Female) OR=0.48 (95%CI:0.25-0.90; p=0.01) *Survivors (n=348; mixed diagnoses; 0-18 yrs at diagnosis; mean 38.5 yrs at study; mean 31.5 yrs since diagnosis). Controls: French norm population n=36,105. Measurement: Impact of Event Scale; Mini-International Neuropsychiatric Interview	*De Laage et al. 2016*
No association between sex, race and post-traumatic stress disorder was found using multivariable logistic regression models (adjusted for race, age at interview, education, employment, personal income, marital status, radiation and age at diagnosis, chemotherapy, SMN, recurrence). • Sex and Race: Female, non-white (Ref. Male, non-white): OR=1.56 (95%CI:0.93-2.62), p=0.09 • Sex and Race: Male, White non-Hispanic (Ref. Male, non-white): OR=1.23 (95%CI:0.79-1.90), p=0.36 • Sex and Race: Female, White non-Hispanic (Ref. Male, non-white): OR=1.1 (95%CI:0.72-1.72), p=0.62 *Survivors from the CCSS cohort (n=6542; mixed diagnoses; mean 8.2 yrs at diagnosis; mean 31.85 yrs at study). Controls: n=368 siblings (mean 33.44 yrs at study). Measurement: Post-traumatic Stress Diagnostic Scale (PSDS)- (PTSD symptoms), BSI-18 (distress criterion), and RAND Health Status Survey, Short Form-36 (impairment criterion).	*Stuber, Meeske, Krull et al. 2010*
Female sex was associated with an increased risk for post-traumatic stress symptoms using simultaneous linear regression (adjusted for age at follow-up, marital status, educational level, employment, age at diagnosis, diagnosis, treatment duration, years since completion of therapy, late effects, treatment). • Female (Ref. Male): β= 0.23 (p<0.001) *Survivors (n=500; mixed diagnoses; median 8 yrs at diagnosis; mean 24 yrs at study). Controls: none. Measurement: Impact of Event Scale (IES)	*Langeveld et al. 2004*

No association between sex and post-traumatic stress symptoms was found using multivariable regression (adjusted for age, race, treatment intensity, years off treatment, age at diagnosis, past perceived life threat, mother support network, mother family cohesion, mother family satisfaction, mother family adaptability). • Female (Ref. Male): β= 0.12 (not significant) *Child and adolescent aged survivors (n=309 survivors; mixed diagnoses; mean 5.83 yrs at diagnosis [range 1-17 yrs]; mean 13.53 yrs at study [range 8-20 yrs]). Controls: n=219 healthy children (mean 12.27 yrs at study [range 8-20 yrs]). Measurement: Impact of Event Scale (IES); Post-traumatic Stress Disorder Reaction Index (PTSDRI)	*Barakat et al. 1997*
Overall Conclusion	
Evidence suggests that female sex is related to the increased risk of developing post-traumatic stress symptoms among survivors of CAYA cancer.	6 studies (5 samples) Level B[27,29,47,53,58,60]

Demographic risk factors: Age at study	
Older age at interview was associated with an increased risk for post-traumatic stress disorder using multivariable logistic regression models (adjusted for sex and race, education, employment, personal income, marital status, radiation and age at diagnosis, chemotherapy, SMN, recurrence). • Age at interview: 30-39 years (Ref. 18-29 years): OR=1.52 (95%CI:1.16-2.00), p<0.01 • Age at interview: 40+ (Ref. 18-29 years): OR=1.57 (95%CI:1.05-2.43), p=0.03 *Survivors from the CCSS cohort (n=6542; mixed diagnoses; mean 8.2 yrs at diagnosis; mean 31.85 yrs at study). Controls: n=368 siblings (mean 33.44 yrs at study). Measurement: Post-traumatic Stress Diagnostic Scale (PSDS)- (PTSD symptoms), BSI-18 (distress criterion), and RAND Health Status Survey, Short Form-36 (impairment criterion).	*Stuber, Meeske, Krull et al. 2010*
No association between age at follow-up and post-traumatic stress symptoms was found using simultaneous linear regression (adjusted for sex, marital status, educational level, employment, age at diagnosis, diagnosis, treatment duration, years since completion of therapy, late effects, treatment). • Age at follow-up (years): β= -0.35 (p≥0.05) *Survivors (n=500; mixed diagnoses; median 8 yrs at diagnosis; mean 24 yrs at study). Controls: none. Measurement: Impact of Event Scale (IES)	*Langeveld et al. 2004*
No association between age at study and post-traumatic stress symptoms was found using multivariable regression (adjusted for sex, race, treatment intensity, years off treatment, age at diagnosis, past perceived life threat, mother support network, mother family cohesion, mother family satisfaction, mother family adaptability). • Age: β= -0.05 (not significant) *Child and adolescent aged survivors (n=309 survivors; mixed diagnoses; mean 5.83 yrs at diagnosis [range 1-17 yrs]; mean 13.53 yrs at study [range 8-20 yrs]). Controls: n=219 healthy children (mean 12.27 yrs at study [range 8-20 yrs]). Measurement: Impact of Event Scale (IES); Post-traumatic Stress Disorder Reaction Index (PTSDRI)	*Barakat et al. 1997*
Overall Conclusion	
Some evidence suggests that older age at study participation is related to an increased risk of developing post-traumatic stress disorder among survivors of CAYA cancer.	3 studies Level C[47,58,60]

Demographic risk factors: Race/ethnicity	
No association between sex, race and post-traumatic stress disorder was found using multivariable logistic regression models (adjusted for sex, age at interview, education, employment, personal income, marital status, radiation and age at diagnosis, chemotherapy, SMN, recurrence). • Sex and Race: Female, non-white (Ref. Male, non-white): OR=1.56 (95%CI:0.93-2.62), p=0.09 • Sex and Race: Male, White non-Hispanic (Ref. Male, non-white): OR=1.23 (95%CI:0.79-1.90), p=0.36 • Sex and Race: Female, White non-Hispanic (Ref. Male, non-white): OR=1.1 (95%CI:0.72-1.72), p=0.62 *Survivors from the CCSS cohort (n=6542; mixed diagnoses; mean 8.2 yrs at diagnosis; mean 31.85 yrs at study). Controls: n=368 siblings (mean 33.44 yrs at study). Measurement: Post-	*Stuber, Meeske, Krull et al. 2010*

traumatic Stress Diagnostic Scale (PSDS)- (PTSD symptoms), BSI-18 (distress criterion), and RAND Health Status Survey, Short Form-36 (impairment criterion).	
No association between race and post-traumatic stress symptoms was found using multivariable regression (adjusted for age, sex, treatment intensity, years off treatment, age at diagnosis, past perceived life threat, mother support network, mother family cohesion, mother family satisfaction, mother family adaptability). • Black (Ref. White): β= 0.12 (not significant) • Hispanic (Ref. White): β= -0.01 (not significant) • Asian (Ref. White): β= 0.09 (not significant) *Child and adolescent aged survivors (n=309 survivors; mixed diagnoses; mean 5.83 yrs at diagnosis [range 1-17 yrs]; mean 13.53 yrs at study [range 8-20 yrs]). Controls: n=219 healthy children (mean 12.27 yrs at study [range 8-20 yrs]). Measurement: Impact of Event Scale (IES); Post-traumatic Stress Disorder Reaction Index (PTSDRI)	*Barakat et al. 1997*
Overall Conclusion	
Evidence suggests that race/ethnicity is not related to the risk of developing post-traumatic stress symptoms among survivors of CAYA cancer.	2 studies Level B[47,58]

Demographic risk factors: Marital status	
Being in a relationship was associated with a decreased risk for post-traumatic stress disorder using multivariable logistic regression (adjusted for self-reported late effects and sex). • Couple (Ref. Single) OR=0.51 (95%CI:0.26-0.97; p=0.02) *Survivors (n=348; mixed diagnoses; 0-18 yrs at diagnosis; mean 38.5 yrs at study; mean 31.5 yrs since diagnosis). Controls: French norm population n=36,105. Measurement: Impact of Event Scale; Mini-International Neuropsychiatric Interview	*De Laage et al. 2016*
Survivors who were single or widowed/divorced/separated are at an increased risk for post-traumatic stress disorder using multivariable logistic regression models (adjusted for sex and race, age at interview, education, employment, personal incomeradiation and age at diagnosis, chemotherapy, SMN, recurrence). • Marital Status: Single (Ref. married/living as married): OR=1.99 (95%CI:1.58-2.50), p<0.0001 • Marital Status: Widowed/divorced/separated (Ref. married/living as married): OR=2.27 (95%CI:1.66-3.11), p<0.0001 *Survivors from the CCSS cohort (n=6542; mixed diagnoses; mean 8.2 yrs at diagnosis; mean 31.85 yrs at study). Controls: n=368 siblings (mean 33.44 yrs at study). Measurement: Post-traumatic Stress Diagnostic Scale (PSDS)- (PTSD symptoms), BSI-18 (distress criterion), and RAND Health Status Survey, Short Form-36 (impairment criterion).	*Stuber, Meeske, Krull et al. 2010*
No association between marital status and post-traumatic stress was found using simultaneous linear regression (adjusted for sex, age at follow-up, educational level, employment, age at diagnosis, diagnosis, treatment duration, years since completion of therapy, late effects, treatment). • Married: β= 0.05 (p≥0.05) *Survivors (n=500; mixed diagnoses; median 8 yrs at diagnosis; mean 24 yrs at study). Controls: none. Measurement: Impact of Event Scale (IES)	*Langeveld et al. 2004*
Overall Conclusion	
Evidence suggests that being single or widowed/divorced/separated is related to the increased risk of developing post-traumatic stress disorder among survivors of CAYA cancer.	3 studies Level B[27,58,60]

Demographic risk factors: Educational achievement	
Less than college education was associated with more post-traumatic stress using multiple linear regression (adjusting for GSI Total Score, Worry total score, perceived stress scale, diagnosis, age at diagnosis, sex, and education): • < college graduate vs. ≥college graduate β=0.90, p=0.002 *Survivors from the St. Jude cohort (n=2969; mixed diagnoses; mean 8.4 yrs at diagnosis; mean 32.5 yrs at study; mean 24.1 yrs since diagnosis). Measurement: PTSD Checklist-Civilian (cut-off ≥44)	*Allen et al. 2018*
Lower education was associated with an increased risk for post-traumatic stress disorder using multivariable logistic regression models (adjusted for sex and race, age	*Stuber, Meeske, Krull et al. 2010*

at interview, employment, personal income, marital status, radiation and age at diagnosis, chemotherapy, SMN, recurrence). • Education: ≤High school graduate (Ref. ≥College graduate): OR=1.51 (95%CI:1.16-1.98), p<0.01 • Education: Some college (Ref. ≥College graduate): OR=1.12 (95%CI:0.90-1.39), p=0.32 *Survivors from the CCSS cohort (n=6542; mixed diagnoses; mean 8.2 yrs at diagnosis; mean 31.85 yrs at study). Controls: n=368 siblings (mean 33.44 yrs at study). Measurement: Post-traumatic Stress Diagnostic Scale (PSDS)- (PTSD symptoms), BSI-18 (distress criterion), and RAND Health Status Survey, Short Form-36 (impairment criterion).	
Higher educational level was associated with a decreased risk for post-traumatic stress using simultaneous linear regression (adjusted for sex, age at follow-up, marital status, employment, age at diagnosis, diagnosis, treatment duration, years since completion of therapy, late effects, treatment). • Higher educational level: β= -0.15 (p<0.05) *Survivors (n=500; mixed diagnoses; median 8 yrs at diagnosis; mean 24 yrs at study). Controls: none. Measurement: Impact of Event Scale (IES)	*Langeveld et al. 2004*
Overall Conclusion	
There is evidence that lower educational achievement is related to the increased risk of developing post-traumatic stress disorder among survivors of CAYA cancer.	3 studies Level A[53,58,60]

Demographic risk factors: Employment	
Unemployed survivors were at an increased risk for post-traumatic stress disorder using multivariable logistic regression models (adjusted for sex and race, age at interview, education, personal income, marital status, radiation and age at diagnosis, chemotherapy, SMN, recurrence). • Employment: Unemployed (Ref. employed): OR=2.01 (95%CI:1.62-2.51), p<0.0001 *Survivors from the CCSS cohort (n=6542; mixed diagnoses; mean 8.2 yrs at diagnosis; mean 31.85 yrs at study). Controls: n=368 siblings (mean 33.44 yrs at study). Measurement: Post-traumatic Stress Diagnostic Scale (PSDS)- (PTSD symptoms), BSI-18 (distress criterion), and RAND Health Status Survey, Short Form-36 (impairment criterion).	*Stuber, Meeske, Krull et al. 2010*
Having employment or being a student/homemaker was associated with a decreased risk of post-traumatic stress (compared to unemployment) using simultaneous linear regression (adjusted for sex, age at follow-up, marital status, educational level, age at diagnosis, diagnosis, treatment duration, years since completion of therapy, late effects, treatment). • Student/homemaker (Ref. unemployed): β= -0.20 (p<0.05) • Employed (Ref. unemployed): β= -0.17 (p<0.05) *Survivors (n=500; mixed diagnoses; median 8 yrs at diagnosis; mean 24 yrs at study). Controls: none. Measurement: Impact of Event Scale (IES)	*Langeveld et al. 2004*
Overall Conclusion	
There is evidence that being unemployed is related to the increased risk of developing post-traumatic stress disorder among survivors of CAYA cancer.	2 studies Level B[58,60]

Demographic risk factors: Income	
Income below $20,000 USD was associated with an increased risk for post-traumatic stress disorder using multivariable logistic regression models (adjusted for sex and race, age at interview, education, employment, marital status, radiation and age at diagnosis, chemotherapy, SMN, recurrence). • Personal income: $20,000-39,999 (Ref. $40,000+): OR=1.02 (95%CI:0.76-1.37), p=0.89 • Personal income: <$20,000 (Ref. $40,000+): OR=1.63 (95%CI:1.21-2.20), p<0.01 *Survivors from the CCSS cohort (n=6542; mixed diagnoses; mean 8.2 yrs at diagnosis; mean 31.85 yrs at study). Controls: n=368 siblings (mean 33.44 yrs at study). Measurement: Post-traumatic Stress Diagnostic Scale (PSDS)- (PTSD symptoms), BSI-18 (distress criterion), and RAND Health Status Survey, Short Form-36 (impairment criterion).	*Stuber, Meeske, Krull et al. 2010*
Overall Conclusion	

Some evidence suggests that income below $20,000 USD is related to the increased risk of developing post-traumatic stress disorder among survivors of CAYA cancer.	1 study Level C[58]

Treatment-related risk factors: Chemotherapy	
No association between chemotherapy and post-traumatic stress disorder was found using multivariable logistic regression models (adjusted for sex and race, age at interview, education, employment, personal income, marital status, radiation and age at diagnosis, SMN, recurrence). • Chemotherapy: Anthracycline/Alkylating (Ref. none): OR=1.07 (95%CI:0.83-1.38), p=0.59 • Chemotherapy: Other drugs (Ref. none): OR=1.32 (95%CI:0.96-1.81), p=0.08 *Survivors from the CCSS cohort (n=6542; mixed diagnoses; mean 8.2 yrs at diagnosis; mean 31.85 yrs at study). Controls: n=368 siblings (mean 33.44 yrs at study). Measurement: Post-traumatic Stress Diagnostic Scale (PSDS)- (PTSD symptoms), BSI-18 (distress criterion), and RAND Health Status Survey, Short Form-36 (impairment criterion).	*Stuber, Meeske, Krull et al. 2010*
Overall Conclusion	
Some evidence suggests that chemotherapy status is not related to the risk of developing post-traumatic stress disorder among survivors of CAYA cancer.	1 study Level C[58]

Treatment-related risk factors: Radiation	
No association between radiation and post-traumatic stress was found using Poisson regression (adjusted for heavy/risky drinking, sex, physical health, radiation, race, age at diagnosis, age at follow-up, educational attainment, and employment status). • Radiation: Non-cranial (Ref. None) RR=1.1 (0.9-1.3) • Radiation: CRT≤20Gy (Ref. None) RR=1.2 (1.0-1.6) • Radiation: CRT>20Gy (Ref. None) RR=1.1 (0.9-1.3) *Survivors from the CCSS cohort (n=4484; mixed diagnoses; mean 10.5 yrs at diagnosis; mean 27.2 yrs at Baseline. Controls: n=1651 siblings. Meaurement: Posttraumatic Stress Diagnostic Scale.	*Brinkman et al. 2019*

Cranial radiation or radiotherapy to other sites between ages 0-4 years, and radiotherapy to other sites between ages 5-9 years was associated with an increased risk for post-traumatic stress disorder using multivariable logistic regression models (adjusted for sex, race, age at interview, education, employment, personal income, marital status, age at diagnosis, chemotherapy, SMN, recurrence).
• Age at dx 0-4:
  ○ Cranial RT (Ref. No RT): OR=2.05 (95%CI:1.41-2.97), p<0.001
  ○ RT other site (Ref. No RT): OR=1.57 (95%CI:1.02-2.43), p=0.04
• Age at dx 5-9:
  ○ Cranial RT (Ref. No RT): OR=1.25 (95%CI:0.76-2.04), p=0.39
  ○ RT other site (Ref. No RT): OR=1.83 (95%CI:1.09-3.06), p=0.02
• Age at dx 10-14:
  ○ Cranial RT (Ref. No RT): OR=0.58 (95%CI:0.34-1.00), p=0.05
  ○ RT other site (Ref. No RT): OR=1.10 (95%CI:0.69-1.75), p=0.69
• Age at dx 15-20:
  ○ Cranial RT (Ref. No RT): OR=0.82 (95%CI:0.42-1.59), p=0.56
  ○ RT other site (Ref. No RT): OR=1.09 (95%CI:0.67-1.77), p=0.74
*Survivors from the CCSS cohort (n=6542; mixed diagnoses; mean 8.2 yrs at diagnosis; mean 31.85 yrs at study). Controls: n=368 siblings (mean 33.44 yrs at study). Measurement: Post-traumatic Stress Diagnostic Scale (PSDS)- (PTSD symptoms), BSI-18 (distress criterion), and RAND Health Status Survey, Short Form-36 (impairment criterion).
	Stuber, Meeske, Krull et al. 2010

No significant relationship between treatment modality and post-traumatic stress symptoms was found using simultaneous linear regression (adjusted for sex, age at follow-up, marital status, educational level, employment, age at diagnosis, diagnosis, treatment duration, years since completion of therapy, late effects). • Radiation therapy (with or without surgery; Ref. chemotherapy (with or without surgery): β= -0.04 (p≥0.05) • Combination therapy (with or without surgery; Ref. chemotherapy (with or without surgery): β= -0.00 (p≥0.05)	*Langeveld et al. 2004*

*Survivors (n=500; mixed diagnoses; median 8 yrs at diagnosis; mean 24 yrs at study). Controls: none. Measurement: Impact of Event Scale (IES)	
Overall Conclusion	
Some evidence suggests that undergoing radiation is related to the increased risk of developing post-traumatic stress disorder among survivors of CAYA cancer. Specifically, for patients diagnosed at ages 0-4 years, receiving cranial radiation or radiation to another site increased risk. For patients diagnosed ages 5-9, radiation at another site increased risk of post-traumatic stress disorder.	3 studies (2 samples) Level C[29,58,60]

Treatment-related risk factors: Bone marrow transplant	
Survivors treated with bone marrow transplantation had an increased risk for any stress-related mental disorder using multivariable cox proportional hazards models (adjusted for diagnosis, age at diagnosis, previous mental disorder diagnosis). • Treatment: Any radiation without BMT (Ref. Chemotherapy only) HR=1.55 (95%CI:0.74-3.27) • Treatment: BMT (Ref. Chemotherapy only) HR=2.82 (95%CI:1.02-7.80) *Medicaid eligible survivors identified from the South Carolina Central Cancer Registry (n=390; mixed diagnoses; age at study entry: 0-5 yrs (n=175), 6-11 yrs (n=118), 12-15 yrs (n=97)). Controls: n=1329 Medicaid eligible children without cancer. Measurement: SRMD diagnoses from Medicaid claims database	*Schrag et al. 2008*
Overall Conclusion	
Some evidence suggests that undergoing bone marrow transplant is related to the increased risk of developing a stress-related mental disorder among survivors of CAYA cancer.	1 study Level C[59]

Treatment-related risk factors: Treatment intensity	
No association of treatment intensity and post-traumatic stress symptoms was found using multivariable regression (adjusted for age, sex, race, years off treatment, age at diagnosis, past perceived life threat, mother support network, mother family cohesion, mother family satisfaction, mother family adaptability). • Treatment intensity: β= 0.06 (not significant) *Child and adolescent aged survivors (n=309 survivors; mixed diagnoses; mean 5.83 yrs at diagnosis [range 1-17 yrs]; mean 13.53 yrs at study [range 8-20 yrs]). Controls: n=219 healthy children (mean 12.27 yrs at study [range 8-20 yrs]). Measurement: Impact of Event Scale (IES); Post-traumatic Stress Disorder Reaction Index (PTSDRI)	*Barakat et al. 1997*
Overall Conclusion	
Some evidence suggests that treatment intensity is not related to the risk of post-traumatic stress symptoms among survivors of CAYA cancer.	1 study Level C[47]

1b-5. What are the key clinical, demographic and treatment-related risk factors for suicidal ideation or suicide among survivors of childhood, adolescent, and young adult (CAYA) cancer?	
Conclusion single studies	
Clinical risk factors: Age at diagnosis	
Risk of suicide was increased in survivors as compared to controls when survivors were diagnosed between ages 15 and 19 years using Poisson regression (adjusting for country, sex, age, and diagnostic period). However, risk of suicide did not differ statistically significantly by age at diagnosis (p=0.50, from likelihood ratio test). • Birth to 4 years, Survivors (Ref. Comparisons) RR=1.43 (95%CI:0.68-3.02) • 5-9 years, Survivors (Ref. Comparisons) RR=1.10 (95%CI:0.44-2.79) • 10-14 years, Survivors (Ref. Comparisons) RR=0.97 (95%CI:0.50-1.86) • 15-19 years, Survivors (Ref. Comparisons) RR=1.61 (95%CI:1.09-2.39) • No statistical difference by age at diagnosis was found (p=0.50, from likelihood ratio test) *Survivors from the SALiCCS cohort (n=29,285; mixed diagnoses; <20 yrs at diagnosis; median 19.0 yrs at study; median 9.4 yrs since diagnosis). Controls: population-based comparisonsn	*Korhonen et al. 2019*

n=146,282. Measurement: Causes of death classified according to the International Classification of Diseases (ICD)	
No association between age at diagnosis and report of suicidal ideation was found using multivariable logistic regression (adjusted for physical health status, seizure, pain, chronic health conditions, depression). • Age at diagnosis (continuous): OR=0.98 (95%CI:0.96-1.00) *Survivors from the CCSS cohort (n=7798; mixed diagnoses; ≤21 yrs at diagnosis; ≥18 yrs at study, mean 25.1-26.3 yrs at study time points). Controls: n=2776 siblings. Measurement: SI was assessed at three time points (1992, 2003, 2007) using single item from BSI-18	*Brinkman, Zhang et al. 2014*
No association between age at diagnosis and suicidal ideation was found using multivariable logistic regression analysis (adjusted for sex, age, depression history, psychoactive medication, surgery only treatment, seizures). • Age at diagnosis: OR=1.1 (95%CI:0.97-1.2) *Survivors of pediatric brain tumors (n=319; mixed neurooncology diagnoses; mean 10 yrs since diagnosis [SD=5 yrs]; mean 18 yrs at study [SD=5, range 10-35 yrs]). Controls: none. Measurement: Semi-structured clinical interview based on Diagnostic and Statistical Manual of Mental Disorders IV-TR and record review	*Brinkman, Liptak et al 2013*
Younger age at diagnosis was associated with an increased risk for suicidal ideation using hierarchical logistic regression (adjusting for sex, age at study, diagnosis, depression score, physical health, no. of chronic conditions, cancer pain, no. of hospital admissions). • Age at diagnosis, <3 years (Ref. ≥18): OR=1.9 (95%CI:1.2-3.0, p<0.05) • Age at diagnosis, 3-6 years (Ref. ≥18): OR=1.4 (95%CI:1.0-2.2, p≥0.05) • Age at diagnosis, 7-10 years (Ref. ≥18): OR=1.7 (95%CI:1.1-2.5, p<0.05) • Age at diagnosis, 11-17 years (Ref. ≥18): OR=1.5 (95%CI:1.1-2.2, p<0.05) *Survivors from the CCSS cohort (n=9126; mixed diagnoses; <18 yrs at diagnosis, 6-29 yrs since diagnosis; 18-48 yrs at study). Controls: n=2968 siblings. Measurement: single item on BSI-18	*Recklitis, Diller et al. 2010*
Overall Conclusion	
Some evidence suggests that younger age at diagnosis is related to an increased risk of suicidal ideation among survivors of CAYA cancer.	3 studies (2 samples) Level C[12,61,62]
Some evidence suggests that survivors diagnosed between 15 and 19 years are at an increased risk of suicide among survivors of CAYA cancer when compared to controls.	1 study Level C[65]

Clinical risk factors: Time period of diagnosis	
Risk of suicide was increased in survivors diagnosed and treated during the time periods of 1971 through 1979 and 1990 through 1999 as compared to controls using Poisson regression (adjusting for country, sex, age, and diagnostic period). However, risk of suicide did not differ statistically significantly by time period of diagnosis (p=0.40, from likelihood ratio test). • 1971-1979, Survivors (Ref. Comparisons) RR=1.56 (95%CI:1.00-2.43) • 1980-1989, Survivors (Ref. Comparisons) RR=1.04 (95%CI:0.60-1.82) • 1990-1999, Survivors (Ref. Comparisons) RR=1.79 (95%CI:1.01-3.18) • 2000-2009, Survivors (Ref. Comparisons) RR=0.72 (95%CI:0.17-3.14) • No statistical difference by time period of diagnosis was found (p=0.40, from likelihood ratio test) *Survivors from the SALiCCS cohort (n=29,285; mixed diagnoses; <20 yrs at diagnosis; median 19.0 yrs at study; median 9.4 yrs since diagnosis). Controls: population-based comparisonsn n=146,282. Measurement: Causes of death classified according to the International Classification of Diseases (ICD)	*Korhonen et al. 2019*
Overall Conclusion	
Some evidence suggests that survivors diagnosed between 1971-1979, and 1990-1999 are at an increased risk of suicide among survivors of CAYA cancer when compared to controls.	1 study Level C[65]

Clinical risk factors: Time since diagnosis	
No association was found between time since diagnosis and risk of suicide using Poisson regression (adjusting for country, sex, age, and diagnostic period).	*Korhonen et al. 2019*

• Follow-up time since diagnosis: <1 year, Survivors (Ref. Comparisons) RR=5.34 (95%CI:0.75-37.95) • Follow-up time since diagnosis: 1-4 years, Survivors (Ref. Comparisons) RR=1.33 (95%CI:0.59-3.01) • Follow-up time since diagnosis: ≥5 years, Survivors (Ref. Comparisons) RR=1.33 (95%CI:0.97-1.83) • Follow-up time since diagnosis: No statistical difference by time since diagnosis was found (p=0.57, from likelihood ratio test) *Survivors from the SALiCCS cohort (n=29,285; mixed diagnoses; <20 yrs at diagnosis; median 19.0 yrs at study; median 9.4 yrs since diagnosis). Controls: population-based comparisonsn n=146,282. Measurement: Causes of death classified according to the International Classification of Diseases (ICD)	
Overall Conclusion	
Some evidence suggests that time since diagnosis is not related to risk of suicide among survivors of CAYA cancer when compared to controls.	1 study Level C[65]

Clinical risk factors: Diagnosis	
No association was found between cancer site and risk of suicide using Poisson regression (adjusting for country, sex, age, and diagnostic period). • Leukemia, Survivors (Ref. Comparisons) RR=0.84 (95%CI:0.34-2.08) • Lymphoma, Survivors (Ref. Comparisons) RR=1.43 (95%CI:0.75-2.74) • CNS, Survivors (Ref. Comparisons) RR=1.22 (95%CI:0.60-2.45) • Other, Survivors (Ref. Comparisons) RR=1.56 (95%CI:1.04-2.34) • No statistical difference by cancer site was found (p=0.62, from likelihood ratio test) *Survivors from the SALiCCS cohort (n=29,285; mixed diagnoses; <20 yrs at diagnosis; median 19.0 yrs at study; median 9.4 yrs since diagnosis). Controls: population-based comparisonsn n=146,282. Measurement: Causes of death classified according to the International Classification of Diseases (ICD)	*Korhonen et al. 2019*
Being diagnosed with a CNS disease was associated with an increased risk for suicidal ideation using hierarchical logistic regression (adjusting for sex, age at study, age at diagnosis, depression score, physical health, no. of chronic conditions, cancer pain, no. of hospital admissions). • Diagnosis (Ref. Other solid tumors): Hematologic malignancies OR=1.0 (95%CI:0.8-1.3, p≥0.05) • Diagnosis (Ref. Other solid tumors): CNS disease OR=1.5 (95%CI:1.1-1.9, p<0.01) *Survivors from the CCSS cohort (n=9126; mixed diagnoses; <18 yrs at diagnosis, 6-29 yrs since diagnosis; 18-48 yrs at study). Controls: n=2968 siblings. Measurement: single item on BSI-18	*Recklitis, Diller et al. 2010*
Overall Conclusion	
Some evidence suggests that being diagnosed with a CNS cancer is related to an increased risk of suicidal ideation among survivors of CAYA cancer.	1 study Level C[62]
Some evidence suggests that cancer diagnosis type is not related to risk of suicide among survivors of CAYA cancer when compared to controls.	1 study Level C[65]

Clinical risk factors: Survivor health and late effects	
Having a chronic health condition was associated with an increased risk for late-report suicidal ideation using multivariable logistic regression (adjusted for age at diagnosis, physical health status, seizure, pain, depression). • Chronic health conditions: Grade 1 or 2 (Ref. none) OR=1.51 (95%CI:1.10-2.09) • Chronic health conditions: Grade 3 or 4 (Ref. none) OR=1.63 (95%CI:1.16-2.28) Survivor perceived fair/poor physical health status was associated with an increased risk for late-report suicidal ideation using multivariable logistic regression (adjusted for age at diagnosis, seizure, pain, chronic health conditions, depression). • Physical health status: Fair/Poor (Ref. ≥good): OR=1.88 (95%CI:1.29-5.74)	*Brinkman, Zhang et al. 2014*

Fair/poor physical health status was associated with an increased risk for recurrent suicidal ideation using multivariable logistic regression (adjusted for age at study, marital status, health insurance, physical health status, seizure, pain, depression). Physical health status: Fair/Poor (Ref. ≥good): OR 1.87 (95%CI:1.20-2.91) *Survivors from the CCSS cohort (n=7798; mixed diagnoses; ≤21 yrs at diagnosis; ≥18 yrs at study, mean 25.1-26.3 yrs at study time points). Controls: n=2776 siblings. Measurement: SI was assessed at three time points (1992, 2003, 2007) using single item from BSI-18; Chronic conditions graded according to the Common Terminology Criteria for Adverse Events, version 3.0	
No association between number of chronic conditions and suicidal ideation was found using hierarchical logistic regression (adjusting for sex, age at study, diagnosis, age at diagnosis, depression score, physical health, cancer pain, no. of hospital admissions). • Number of chronic conditions: 1 (Ref. 0): OR=1.1 (95%CI:0.8-1.3, p≥0.05) • Number of chronic conditions: 2 (Ref. 0): OR=0.8 (95%CI:0.6-1.1, p≥0.05) • Number of chronic conditions: ≥3 (Ref. 0): OR=0.9 (95%CI:0.7-1.2, p≥0.05) Poorer self-ratings of health were associated with an increased risk for suicidal ideation using hierarchical logistic regression (adjusting for sex, age at study, diagnosis, age at diagnosis, depression score, physical health, no. of chronic conditions, cancer pain, no. of hospital admissions). • Physical health: poor (Ref. excellent): OR=2.6 (95%CI:1.5-4.5, p<0.001) • Physical health: fair (Ref. excellent): OR=2.1 (95%CI:1.5-3.0, p<0.001) • Physical health: good (Ref. excellent): OR=1.8 (95%CI:1.3-2.5, p<0.001) • Physical health: very good (Ref. excellent): OR=1.2 (95%CI:0.9-1.7, p≥0.05) *Survivors from the CCSS cohort (n=9126; mixed diagnoses; <18 yrs at diagnosis, 6-29 yrs since diagnosis; 18-48 yrs at study). Controls: n=2968 siblings. Measurement: single item on BSI-18; Chronic conditions graded according to the Common Terminology Criteria for Adverse Events, version 3.0	*Recklitis, Diller et al. 2010*
Overall Conclusion	
Some evidence suggests that having a chronic health condition or poor self-perceived ratings of health is related to an increased risk of suicidal ideation among survivors of CAYA cancer.	2 studies (1 sample) Level C[61,62]

Clinical risk factors: Seizures	
Seizures were associated with an increased risk for late-report suicidal ideation using multivariable logistic regression (adjusted for age at diagnosis, physical health status, pain, chronic health conditions, depression). • Seizure: Yes (Ref. No) OR=2.04 (95%CI:1.32-3.16) Seizures were associated with an increased risk for recurrent suicidal ideation using multivariable logistic regression (adjusted for age at study, marital status, health insurance, physical health status, seizure, pain, depression). • Seizure: Yes (Ref. No) OR=2.25 (95%CI:1.29-3.93) *Survivors from the CCSS cohort (n=7798; mixed diagnoses; ≤21 yrs at diagnosis; ≥18 yrs at study, mean 25.1-26.3 yrs at study time points). Controls: n=2776 siblings. Measurement: SI was assessed at three time points (1992, 2003, 2007) using single item from BSI-18	*Brinkman, Zhang et al. 2014*
History of seizures was associated with an increased risk for suicidal ideation using multivariable logistic regression analysis (adjusted for sex, age, depression history, psychoactive medication, age at diagnosis, surgery only treatment). • History of seizures: Yes (Ref. No) OR=3.6 (95%CI:1.1-11.1) *Survivors of pediatric brain tumors (n=319; mixed neurooncology diagnoses; mean 10 yrs since diagnosis [SD=5 yrs]; mean 18 yrs at study [SD=5 yrs, range 10-35 yrs]). Controls: none. Measurement: Semi-structured clinical interview based on Diagnostic and Statistical Manual of Mental Disorders IV-TR and record review	*Brinkman, Liptak et al 2013*
Overall Conclusion	
Some evidence suggests that having a history of seizures is related to an increased risk of suicidal ideation among survivors of CAYA cancer.	2 studies Level B[12,61]

Clinical risk factors: Depression	
Depression was associated with an increased risk for late-report suicidal ideation using multivariable logistic regression (adjusted for age at diagnosis, physical health status, seizure, pain, chronic health conditions). • Depression: Yes (Ref. No) OR=2.95 (95%CI:2.10-4.14) Depression was associated with an increased risk for recurrent suicidal ideation using multivariable logistic regression (adjusted for age at study, marital status, health insurance, physical health status, seizure, pain). • Depression: Yes (Ref. No) OR=9.12 (95%CI:6.32-13.2) *Survivors from the CCSS cohort (n=7798; mixed diagnoses; ≤21 yrs at diagnosis; ≥18 yrs at study, mean 25.1-26.3 yrs at study time points). Controls: n=2776 siblings. Measurement: SI was assessed at three time points (1992, 2003, 2007) using single item from BSI-18 and BSI-18 Depression subscale (cutoff score ≥63)	*Brinkman, Zhang et al. 2014*
History of depression was associated with an increased risk for suicidal ideation using multivariable logistic regression analysis (adjusted for sex, age, psychoactive medication, age at diagnosis, surgery only treatment, seizures). • History of depression: Yes (Ref. No) OR=20.5 (95%CI:4.2-101.1) *Survivors of pediatric brain tumors (n=319; mixed neurooncology diagnoses; mean 10 yrs since diagnosis [SD=5 yrs]; mean 18 yrs at study [SD=5 yrs, range 10-35 yrs]). Controls: none. Measurement: Semi-structured clinical interview based on Diagnostic and Statistical Manual of Mental Disorders IV-TR and record review	*Brinkman, Liptak et al 2013*
Higher depression score was associated with an increased risk for suicidal ideation using hierarchical logistic regression (adjusting for sex, age at study, diagnosis, age at diagnosis, physical health, no. of chronic conditions, cancer pain, no. of hospital admissions). • BSI-Depression score ≥63 (Ref. <63): OR=16.4 (95%CI:13.7-19.7, p<0.001) *Survivors from the CCSS cohort (n=9126; mixed diagnoses; <18 yrs at diagnosis, 6-29 yrs since diagnosis; 18-48 yrs at study). Controls: n=2968 siblings. Measurement: single item on BSI-18 and BSI-18 Depression subscale	*Recklitis, Diller et al. 2010*
Overall Conclusion	
There is evidence that a history of depression is related to an increased risk of suicidal ideation among survivors of CAYA cancer.	3 studies (2 samples) Level A[12,61,62]

Clinical risk factors: Pain	
Headache was associated with an increased risk for late-report suicidal ideation using multivariable logistic regression (adjusted for age at diagnosis, physical health status, seizure, chronic health conditions, depression). • Pain: Headache (Ref. none) OR=1.38 (95%CI:1.05-1.82) • Pain: Other (Ref. none) OR=1.00 (95%CI:0.57-1.73) Headache was associated with an increased risk for recurrent suicidal ideation using multivariable logistic regression (adjusted for age at study, marital status, health insurance, physical health status, seizure, depression). • Pain: Headache (Ref. none) OR=1.62 (95%CI:1.11-2.36) • Pain: Other (Ref. none) OR=1.30 (95%CI:0.66-2.53) *Survivors from the CCSS cohort (n=7798; mixed diagnoses; ≤21 yrs at diagnosis; ≥18 yrs at study, mean 25.1-26.3 yrs at study time points). Controls: n=2776 siblings. Measurement: SI was assessed at three time points (1992, 2003, 2007) using single item from BSI-18	*Brinkman, Zhang et al. 2014*
Cancer pain was associated with an increased risk for suicidal ideation using hierarchical logistic regression (adjusting for sex, age at study, diagnosis, age at diagnosis, depression score, physical health, no. of chronic conditions, no. of hospital admissions). • Cancer pain: small amount (Ref. none): OR=1.9 (95%CI:1.4-2.4, p<0.001) • Cancer pain: medium amount (Ref. none): OR=1.7 (95%CI:1.3-2.3, p<0.001) • Cancer pain: very bad (Ref. none): OR=2.0 (95%CI:1.4-2.9, p<0.001)	*Recklitis, Diller et al. 2010*

*Survivors from the CCSS cohort (n=9126; mixed diagnoses; <18 yrs at diagnosis, 6-29 yrs since diagnosis; 18-48 yrs at study). Controls: n=2968 siblings. Measurement: single item on BSI-18	
Overall Conclusion	
There is evidence that experiencing pain is related to an increased risk of suicidal ideation among survivors of CAYA cancer.	2 studies (1 sample) Level C[61,62]

Clinical risk factors: Hospital admission	
No association between number of hospital admissions and suicidal ideation was found using hierarchical logistic regression (adjusting for sex, age at study, diagnosis, age at diagnosis, depression score, physical health, no. of chronic conditions, cancer pain). • Number of hospital admissions: 1-5 (Ref. 0): OR=1.0 (95%CI:0.8-1.3, p≥0.05) • Number of hospital admissions: ≥5 (Ref. 0): OR=1.3 (95%CI:0.7-2.6, p≥0.05) *Survivors from the CCSS cohort (n=9126; mixed diagnoses; <18 yrs at diagnosis, 6-29 yrs since diagnosis; 18-48 yrs at study). Controls: n=2968 siblings. Measurement: single item on BSI-18	*Recklitis, Diller et al. 2010*
Overall Conclusion	
Some evidence suggests that the number of hospital admissions is not related to the risk of suicidal ideation among survivors of CAYA cancer.	1 study Level C[62]

Clinical risk factors: Medication	
Psychoactive medication use was associated with an increased risk for suicidal ideation using multivariable logistic regression analysis (adjusted for sex, age, depression history, age at diagnosis, surgery only treatment, seizures). • Psychoactive medication use: Yes (Ref. No) OR=4.5 (95%CI:1.8-11.2) *Survivors of pediatric brain tumors (n=319; mixed neurooncology diagnoses; mean 10 yrs since diagnosis [SD=5 yrs]; mean 18 yrs at study [SD=5 yrs, range 10-35 yrs]). Controls: none. Measurement: Semi-structured clinical interview based on Diagnostic and Statistical Manual of Mental Disorders IV-TR and record review	*Brinkman, Liptak et al 2013*
Overall Conclusion	
Some evidence suggests that psychoactive medication use is related to an increased risk of suicidal ideation among survivors of CAYA cancer.	1 study Level C[12]

Demographic risk factors: Sex	
No association was found between sex and risk of suicide using Poisson regression (adjusting for country, sex, age, and diagnostic period). • Male, Survivors (Ref. Comparisons) RR=1.30 (95%CI:0.93-1.82) • Female, Survivors (Ref. Comparisons) RR=1.61 (95%CI:0.91-2.88) • No statistical difference by sex was found (p=0.47, from likelihood ratio test) *Survivors from the SALiCCS cohort (n=29,285; mixed diagnoses; <20 yrs at diagnosis; median 19.0 yrs at study; median 9.4 yrs since diagnosis). Controls: population-based comparisonsn n=146,282. Measurement: Causes of death classified according to the International Classification of Diseases (ICD)	*Korhonen et al. 2019*
No association between sex and suicidal ideation was found using multivariable logistic regression (adjusted for sex, age, marital status, education, income and employment). • Female (Ref. Male) OR=1.15 (95%CI: 0.65-2.03) *Survivors (n=951; mixed diagnoses; median 5.0 yrs at diagnosis [range 0-15 yrs]; median 28.1 yrs since diagnosis [range 23-36 yrs]; median 34.2 yrs at study [range 24-49 yrs]). Controls: n=1130, German Household Panel. Measurement: Single question for suicidal ideation.	*Burghardt et al. 2019*
No association between sex and suicidal ideation was found using multivariable logistic regression analysis (adjusted for age, depression history, psychoactive medication, age at diagnosis, surgery only treatment, seizures). • Female (Ref. Male) OR=1.6 (95%CI:0.7-3.8) *Survivors of pediatric brain tumors (n=319; mixed neurooncology diagnoses; mean 10 yrs since diagnosis [SD=5 yrs]; mean 18 yrs at study [SD=5 yrs, range 10-35 yrs]). Controls: none. Measurement: Semi-structured clinical interview based on Diagnostic and Statistical Manual of Mental Disorders IV-TR and record review	*Brinkman, Liptak et al 2013*

No association between sex and suicidal ideation was found using hierarchical logistic regression (adjusting for age at study, diagnosis, age at diagnosis, depression score, physical health, no. of chronic conditions, cancer pain, no. of hospital admissions). • Female (Ref. Male): OR=1.2 (95%CI:1.0-1.4, p≥0.05) *Survivors from the CCSS cohort (n=9126; mixed diagnoses; <18 yrs at diagnosis, 6-29 yrs since diagnosis; 18-48 yrs at study). Controls: n=2968 siblings. Measurement: single item on BSI-18	*Recklitis, Diller et al. 2010*
Overall Conclusion	
Evidence suggests that sex is not related to the risk of suicidal ideation among survivors of CAYA cancer.	3 studies Level B[12,26,62]
Some evidence suggests that sex is not related to risk of suicide among survivors of CAYA cancer when compared to controls.	1 study Level C[65]

Demographic risk factors: Age at study	
No association was found between age and risk of suicide using Poisson regression (adjusting for country, sex, age, and diagnostic period). • Age: <10 years, Survivors (Ref. Comparisons) no cases • Age: 10-19 years, Survivors (Ref. Comparisons) RR=1.18 (95%CI:0.53-2.64) • Age: 20-29 years, Survivors (Ref. Comparisons) RR=1.31 (95%CI:0.86-2.00) • Age: 30-39 years, Survivors (Ref. Comparisons) RR=1.56 (95%CI:0.90-2.69) • Age: ≥40 years, Survivors (Ref. Comparisons) RR=1.45 (95%CI:0.62-3.39) • Age: No statistical difference by age was found (p=0.99, from likelihood ratio test) *Survivors from the SALiCCS cohort (n=29,285; mixed diagnoses; <20 yrs at diagnosis; median 19.0 yrs at study; median 9.4 yrs since diagnosis). Controls: population-based comparisonsn n=146,282. Measurement: Causes of death classified according to the International Classification of Diseases (ICD)	*Korhonen et al. 2019*
No association between age and suicidal ideation was found using multivariable logistic regression (adjusted for sex, age, marital status, education, income and employment). • Age (continuous): OR=0.99 (95%CI: 0.94-1.04) *Survivors (n=951; mixed diagnoses; median 5.0 yrs at diagnosis [range 0-15 yrs]; median 28.1 yrs since diagnosis [range 23-36 yrs]; median 34.2 yrs at study [range 24-49 yrs]). Controls: n=1130, German Household Panel. Single question for suicidal ideation.	*Burghardt et al. 2019*
No association between age at study and suicidal ideation was found using multivariable logistic regression (adjusted for marital status, health insurance, physical health status, seizure, pain, depression). • Age at baseline (continuous): OR=1.04 (95%CI:1.00-1.07) *Survivors from the CCSS cohort (n=7798; mixed diagnoses; ≤21 yrs at diagnosis; ≥18 yrs at study, mean 25.1-26.3 yrs at study time points). Controls: n=2776 siblings. Measurement: SI was assessed at three time points (1992, 2003, 2007) using single item from BSI-18	*Brinkman, Zhang et al. 2014*
No association between age at study and suicidal ideation was found using multivariable logistic regression analysis (adjusted for sex, depression history, psychoactive medication, age at diagnosis, surgery only treatment, seizures). • Current age: OR=1.1 (95%CI:0.99-1.2) *Survivors of pediatric brain tumors (n=319; mixed neurooncology diagnoses; mean 10 yrs since diagnosis [SD=5 yrs]; mean 18 yrs at study [SD=5 yrs, range 10-35 yrs]). Controls: none. Measurement: Semi-structured clinical interview based on Diagnostic and Statistical Manual of Mental Disorders IV-TR and record review	*Brinkman, Liptak et al 2013*
No association between age at study and suicidal ideation was found using hierarchical logistic regression (adjusting for sex, diagnosis, age at diagnosis, depression score, physical health, no. of chronic conditions, cancer pain, no. of hospital admissions). • Age at interview, 25-29 years (Ref. 18-24): OR=1.0 (95%CI:0.8-1.2, p≥0.05) • Age at interview, 30-34 years (Ref. 18-24): OR=1.0 (95%CI:0.7-1.3, p≥0.05) • Age at interview, ≥35 years (Ref. 18-24): OR=1.1 (95%CI:0.8-1.6, p≥0.05) *Survivors from the CCSS cohort (n=9126; mixed diagnoses; <18 yrs at diagnosis, 6-29 yrs since diagnosis; 18-48 yrs at study). Controls: n=2968 siblings. Measurement: single item on BSI-18;	*Recklitis, Diller et al. 2010*
Overall Conclusion	
Evidence suggests that age at study is not related to the risk of suicidal ideation among survivors of CAYA cancer.	4 studies (3 samples)

	Level B[12,26,61,62]
Some evidence suggests that age at study is not related to risk of suicide among survivors of CAYA cancer when compared to controls.	1 study Level C[65]

Demographic risk factors: Country	
In Denmark, risk of suicide was increased in survivors as compared to controls using Poisson regression (adjusting for country, sex, age, and diagnostic period). However, risk of suicide did not differ statistically significantly by country (p=0.42, from likelihood ratio test). • Country: Denmark, Survivors (Ref. Comparisons) RR=2.05 (95%CI:1.12-3.74) • Country: Finland, Survivors (Ref. Comparisons) RR=1.18 (95%CI:0.74-1.86) • Country: Sweden, Survivors (Ref. Comparisons) RR=1.32 (95%CI:0.81-2.14) • Country: No statistical difference by country was found (p=0.42, from likelihood ratio test) *Survivors from the SALiCCS cohort (n=29,285; mixed diagnoses; <20 yrs at diagnosis; median 19.0 yrs at study; median 9.4 yrs since diagnosis). Controls: population-based comparisonsn n=146,282. Measurement: BSI-18; Causes of death classified according to the International Classification of Diseases (ICD)	*Korhonen et al. 2019*
Overall Conclusion	
Some evidence suggests that risk of suicide among survivors of CAYA cancer was increased in Denmark, but not Finland or Sweden, when compared to controls.	1 study Level C[65]

Demographic risk factors: Marital status	
Being married was associated with a decreased risk for suicidal ideation, using multivariable logistic regression (adjusted for sex, age, marital status, education, income and employment). • Married: Yes (Ref. No) OR=0.37 (95%CI: 0.17, 0.82) *Survivors (n=951; mixed diagnoses; median 5.0 yrs at diagnosis [range 0-15 yrs]; median 28.1 yrs since diagnosis [range 23-36 yrs]; median 34.2 yrs at study [range 24-49 yrs]). Controls: n=11.30, German Household Panel. Measurement: Single question for suicidal ideation.	*Burghardt et al. 2019*
Being married or divorced was associated with a decreased risk for recurrent suicidal ideation using multivariable logistic regression (adjusted for age at study, health insurance, physical health status, seizure, pain, depression). • Marital status: divorced (Ref. single) OR=0.42 (95%CI:0.20-0.87) • Marital status: married (Ref. single) OR=0.62 (95%CI:0.41-0.95) *Survivors from the CCSS cohort (n=7798; mixed diagnoses; ≤21 yrs at diagnosis; ≥18 yrs at study, mean 25.1-26.3 yrs at study time points). Controls: n=2776 siblings. Measurement: SI was assessed at three time points (1992, 2003, 2007) using single item from BSI-18	*Brinkman, Zhang et al. 2014*
Overall Conclusion	
Some evidence suggests that being married or divorced is related to a decreased risk of suicidal ideation among survivors of CAYA cancer.	2 studies Level B[26,61]

Demographic risk factors: Educational achievement	
No association between educational achievement and suicidal ideation was found using multivariable logistic regression (adjusted for sex, age, marital status, education, income and employment). • Education: Low (Ref. High) OR=1.41 (95%CI:0.61-3.26) • Education: Middle (Ref. High) OR=1.72 (95%CI:0.92-3.23) *Survivors (n=951; mixed diagnoses; median 5.0 yrs at diagnosis [range 0-15 yrs]; median 28.1 yrs since diagnosis [range 23-36 yrs]; median 34.2 yrs at study [range 24-49 yrs]). Controls: n=1130, German Household Panel. Measurement: Single question for suicidal ideation.	*Burghardt et al. 2019*
Overall Conclusion	
Some evidence suggests that educational achievement is not related to the risk of suicidal ideation among survivors of CAYA cancer.	1 study Level C[26]

Demographic risk factors: Employment	
Unemployment was associated with an increased risk for suicidal ideation using multivariable logistic regression (adjusted for sex, age, marital status, education, income and employment). • Unemployed (Ref. Employed) OR=3.26 (95%CI:1.17-9.14) *Survivors (n=951; mixed diagnoses; median 5.0 yrs at diagnosis [range 0-15 yrs]; median 28.1 yrs since diagnosis [range 23-36 yrs]; median 34.2 yrs at study [range 24-49 yrs]). Controls: n=1130, German Household Panel. Measurement: Single question for suicidal ideation.	*Burghardt et al. 2019*
Overall Conclusion	
Some evidence suggests that unemployment is associated with an increased risk for suicidal ideation among survivors of CAYA cancer.	1 study Level C[26]

Demographic risk factors: Income	
No association between income and suicidal ideation was found using multivariable logistic regression (adjusted for sex, age, marital status, education, income and employment). • Income in 100 Euros per month (continuous): OR=0.99 (95%CI:0.97-1.01) *Survivors (n=951; mixed diagnoses; median 5.0 yrs at diagnosis [range 0-15 yrs]; median 28.1 yrs since diagnosis [range 23-36 yrs]; median 34.2 yrs at study [range 24-49 yrs]). Controls: n=1130, German Household Panel. Measurement: Single question for suicidal ideation.	*Burghardt et al. 2019*
Overall Conclusion	
Some evidence suggests that income is not related to the risk for suicidal ideation among survivors of CAYA cancer.	1 study Level C[26]

Demographic risk factors: Health insurance	
Having health insurance was associated with a decreased risk of recurrent suicidal ideation using multivariable logistic regression (adjusted for age at study, marital status, physical health status, seizure, pain, depression). • Health insurance: Yes (Ref. No) OR=0.51 (95%CI:0.33-0.78) *Survivors from the CCSS cohort (n=7798; mixed diagnoses; ≤21 yrs at diagnosis; ≥18 yrs at study, mean 25.1-26.3 yrs at study time points). Controls: n=2776 siblings. Measurement: SI was assessed at three time points (1992, 2003, 2007) using single item from BSI-18	*Brinkman, Zhang et al. 2014*
Overall Conclusion	
Some evidence suggests that having health insurance is related to a decreased risk of suicidal ideation among survivors of CAYA cancer.	1 study Level C[61]

Treatment-related risk factors: Surgery	
Observation or surgery only was associated with an increased risk for suicidal ideation using multivariable logistic regression analysis (adjusted for sex, age, depression history, psychoactive medication, age at diagnosis, seizures). • Observation or surgery only treatment: Yes (Ref. No) OR=3.7 (95%CI:1.5-9.1) *Survivors of pediatric brain tumors (n=319; mixed neurooncology diagnoses; mean 10 yrs since diagnosis [SD=5 yrs]; mean 18 yrs at study [SD=5 yrs, range 10-35 yrs]). Controls: none. Measurement: Semi-structured clinical interview based on Diagnostic and Statistical Manual of Mental Disorders IV-TR and record review	*Brinkman, Liptak et al 2013*
Overall Conclusion	
Some evidence suggests that observation or surgery only treatment is related to an increased risk of suicidal ideation among survivors of CAYA cancer.	1 study Level C[12]

1b-6. What are the key clinical, demographic and treatment-related risk factors for behavioral problems among survivors of childhood, adolescent, and young adult (CAYA) cancer?	
Conclusion single studies	
Clinical risk factors: Age at diagnosis	
No association between age at diagnosis and headstrong behavior was found using log-binomial models (adjusted for age at diagnosis, age at study, sex, annual household income). • Age at diagnosis: <1 year (Ref. ≥1 year) not significant No association between age at diagnosis and antisocial behavior was found using log-binomial models (adjusted for age at diagnosis, age at study, sex, annual household income). • Age at diagnosis: <1 year (Ref. ≥1 year) not significant *Survivors of neuroblastoma from the CCSS cohort (n=859; 97.9% <5 yrs at diagnosis yrs; 8-17 yrs at study. Controls: n=872 siblings. Meaurement: BPI (cutoff >10th percentile of age-matched siblings).	*Zheng et al. 2018*
No association between age at diagnosis and headstrong behavior was found using multiple variable models (adjusted for sex, current age group, race/ethnicity, annual household income, disfigurement, treatment): • Age at diagnosis: <2 years (Ref. 5-9) RR=0.9 (99%CI:0.6-1.4) • Age at diagnosis: 2-4 years (Ref. 5-9) RR=0.9 (99%CI:0.6-1.2) No association between age at diagnosis and antisocial behavior was found using multiple variable models (adjusted for sex, current age group, race/ethnicity, annual household income, disfigurement, treatment): • Age at diagnosis: <2 years (Ref. 5-9) RR=1.1 (99%CI:0.8-1.6) • Age at diagnosis: 2-4 years (Ref. 5-9) RR=1.0 (99%CI:0.7-1.3) *Parent proxy report from the Adolescent CCSS cohort (n=2979; mixed diagnoses; mean 3.2 yrs at diagnosis; mean 14.8 yrs at study). Controls: n=649 siblings. Measurement: Behavior Problem Index (BPI) Headstrong behavior and Antisocial behavior subscales (cutoff ≥ 1.3 SD sibling mean)	*Schultz et al. 2007*
Overall Conclusion	
Some evidence suggests that age at diagnosis is not related to behavioral problems, including headstrong and antisocial behavior, among survivors of CAYA cancer.	2 studies (1 sample) Level C[22,37]

Clinical risk factors: Scarring/disfigurement	
No association between disfigurement and headstrong behavior was found using multiple variable models (adjusted for sex, current age group, age at diagnosis, race/ethnicity, annual household income, treatment): • Head/neck/scalp/eye: Yes (Ref. No) RR=1.1 (99%CI:0.7-1.4) • Limb: Yes (Ref. No) RR=1.1 (99%CI:0.8-1.6) • Chest or abdomen: Yes (Ref. No) RR=1.2 (99%CI:0.9-1.6) No association between disfigurement and antisocial behavior was found using multiple variable models (adjusted for sex, current age group, age at diagnosis, race/ethnicity, annual household income, treatment): • Head/neck/scalp/eye: Yes (Ref. No) RR=1.1 (99%CI:0.9-1.5) • Limb: Yes (Ref. No) RR=1.1 (99%CI:0.8-1.5) • Chest or abdomen: Yes (Ref. No) RR=1.1 (99%CI:0.8-1.3) *Parent proxy report from the Adolescent CCSS cohort (n=2979; mixed diagnoses; mean 3.2 yrs at diagnosis; mean 14.8 yrs at study). Controls: n=649 siblings. Measurement: Behavior Problem Index (BPI) Headstrong behavior and Antisocial behavior subscales (cutoff ≥ 1.3 SD sibling mean) and scarring and disfigurement items (yes/no) for head/neck, arm/leg, and chest/abdomen areas	*Schultz et al. 2007*
Overall Conclusion	
Some evidence suggests that disfigurement from treatment is not related to behavioral problems, including headstrong behavior and antisocial behavior, among survivors of CAYA cancer.	1 study Level C[22]

Clinical risk factors: Survivor health and late effects	
Peripheral neuropathy, grade ≥2 pulmonary disease and grade ≥2 endocrine disease were associated with an increased risk for headstrong behavior using log-binomial models (adjusted for age at diagnosis, age at study, sex, annual household income). • Peripheral neuropathy: Yes (Ref. No) PR=1.78 (95%CI:1.21-2.48; p=0.005) • Grade ≥2 pulmonary disease: Yes (Ref. No) PR=1.75 (95%CI:1.16-1.91; p=0.003) • Grade ≥2 endocrine disease: Yes (Ref. No) PR=1.74 (95%CI:1.16-1.91; p=0.004) Grade ≥2 pulmonary disease and grade ≥2 endocrine disease were associated with an increased risk for antisocial behavior using log-binomial models (adjusted for age at diagnosis, age at study, sex, annual household income). • Peripheral neuropathy: Yes (Ref. No) not significant • Grade ≥2 pulmonary disease: Yes (Ref. No) PR=1.83 (95%CI:1.17-2.27; p=0.004) • Grade ≥2 endocrine disease: Yes (Ref. No) PR=1.80 (95%CI:1.13-2.09; p=0.006) *Survivors of neuroblastoma from the CCSS cohort (n=859; 97.9% <5 yrs at diagnosis yrs; 8-17 yrs at study. Controls: n=872 siblings. Meaurement: BPI (cutoff >10th percentile of age-matched siblings); health conditions graded according to the Common Terminology Criteria for Adverse Events, version 4.03	*Zheng et al. 2018*
Overall Conclusion	
Some evidence suggests that late effects are associated with an increased risk for behavioral problems (headstrong and antisocial behavior) among survivors of CAYA cancer.	1 study Level C[37]

Demographic risk factors: Sex	
No association between sex and headstrong behavior was found using log-binomial models (adjusted for age at diagnosis, age at study, sex, annual household income). • Male (Ref. Female) not significant No association between sex and antisocial behavior was found using log-binomial models (adjusted for age at diagnosis, age at study, sex, annual household income). • Male (Ref. Female) not significant *Survivors of neuroblastoma from the CCSS cohort (n=859; 97.9% <5 yrs at diagnosis yrs; 8-17 yrs at study. Controls: n=872 siblings. Meaurement: BPI (cutoff >10th percentile of age-matched siblings).	*Zheng et al. 2018*
No association between sex and headstrong behavior was found using multiple variable models (adjusted for current age group, age at diagnosis, race/ethnicity, annual household income, disfigurement, treatment): • Female (Ref. Male) RR=0.9 (99%CI:0.7-1.1) No association between sex and antisocial behavior was found using multiple variable models (adjusted for current age group, age at diagnosis, race/ethnicity, annual household income, disfigurement, treatment): • Female (Ref. Male) RR=1.1 (99%CI:0.9-1.3) *Parent proxy report from the Adolescent CCSS cohort (n=2979; mixed diagnoses; mean 3.2 yrs at diagnosis; mean 14.8 yrs at study). Controls: n=649 siblings. Measurement: Behavior Problem Index (BPI) Headstrong behavior and Antisocial behavior subscales (cutoff ≥ 1.3 SD sibling mean)	*Schultz et al. 2007*
Overall Conclusion	
Some evidence suggests that sex is not related to behavioral problems, including headstrong behavior and antisocial behavior, among survivors of CAYA cancer.	2 studies (1 sample) Level C[22,37]

Demographic risk factors: Age at study	
No association between age at study and headstrong behavior was found using multiple variable models (adjusted for sex, age at diagnosis, race/ethnicity, annual household income, disfigurement, treatment): • Current age group: 12-14 years (Ref. 15-17) RR=1.1 (99%CI:0.8-1.3)	*Schultz et al. 2007*

No association between age at study and antisocial behavior was found using multiple variable models (adjusted for sex, age at diagnosis, race/ethnicity, annual household income, disfigurement, treatment):

- Current age group: 12-14 years (Ref. 15-17) RR=1.0 (99%CI:0.8-1.3)

*Parent proxy report from the Adolescent CCSS cohort (n=2979; mixed diagnoses; mean 3.2 yrs at diagnosis; mean 14.8 yrs at study). Controls: n=649 siblings. Measurement: Behavior Problem Index (BPI) Headstrong behavior and Antisocial behavior subscales (cutoff ≥ 1.3 SD sibling mean)

Overall Conclusion	
Some evidence suggests that age at study is not related to behavioral problems, including headstrong behavior and antisocial behavior, among survivors of CAYA cancer.	1 study Level C[22]

Demographic risk factors: Race/ethnicity

No association between race/ethnicity and headstrong behavior was found using multiple variable models (adjusted for sex, current age group, age at diagnosis, annual household income, disfigurement, treatment):

- Black (Ref. White) RR=1.2 (99%CI:0.7-1.9)
- Hispanic (Ref. White) RR=1.1 (99%CI:0.7-1.9)
- Other (Ref. White) RR=1.1 (99%CI:0.6-2.0)

No association between race/ethnicity and antisocial behavior was found using multiple variable models (adjusted for sex, current age group, age at diagnosis, annual household income, disfigurement, treatment): *Schultz et al. 2007*

- Black (Ref. White) RR=1.0 (99%CI:0.7-1.6)
- Hispanic (Ref. White) RR=1.0 (99%CI:0.7-1.6)
- Other (Ref. White) RR=0.9 (99%CI:0.6-1.5)

*Parent proxy report from the Adolescent CCSS cohort (n=2979; mixed diagnoses; mean 3.2 yrs at diagnosis; mean 14.8 yrs at study). Controls: n=649 siblings. Measurement: Behavior Problem Index (BPI) Headstrong behavior and Antisocial behavior subscales (cutoff ≥ 1.3 SD sibling mean)

Overall Conclusion	
Some evidence suggests that race/ethnicity is not related to behavioral problems, including headstrong behavior and antisocial behavior, among survivors of CAYA cancer.	1 study Level C[22]

Demographic risk factors: Income

Lower annual household income was associated with an increased risk for headstrong behavior using log-binomial models (adjusted for age at diagnosis, age at study, sex, annual household income).

- Unknown (Ref. ≥$60,000) PR=1.46 (95%CI:0.74-2.69)
- <$20,000 (Ref. ≥$60,000) PR=1.43 (95%CI:0.84-2.41)
- $20,000-$39,999 (Ref. ≥$60,000) PR=1.72 (95%CI:1.12-2.72)
- $40,000-$59,999 (Ref. ≥$60,000) PR=1.02 (95%CI:0.67-1.61)

No association between annual household income and antisocial behavior was found using log-binomial models (adjusted for age at diagnosis, age at study, sex, annual household income). *Zheng et al. 2018*

- Unknown (Ref. ≥$60,000) not significant
- <$20,000 (Ref. ≥$60,000) not significant
- $20,000-$39,999 (Ref. ≥$60,000) not significant
- $40,000-$59,999 (Ref. ≥$60,000) not significant

*Survivors of neuroblastoma from the CCSS cohort (n=859; 97.9% <5 yrs at diagnosis yrs; 8-17 yrs at study. Controls: n=872 siblings. Meaurement: BPI (cutoff >10th percentile of age-matched siblings).

Lower household income was associated with an increased risk for headstrong behavior using multiple variable models (adjusted for sex, current age group, age at diagnosis, race/ethnicity, disfigurement, treatment): *Schultz et al. 2007*

• <20,000 (Ref. 60,000+) RR=1.8 (99%CI:1.2-2.7) • 20,000-60,000 (Ref. 60,000+) RR=1.4 (99%CI:1.0-1.9) Lower household income was associated with an increased risk for antisocial behavior using multiple variable models (adjusted for sex, current age group, age at diagnosis, race/ethnicity, disfigurement, treatment): • <20,000 (Ref. 60,000+) RR=1.5 (99%CI:1.1-2.2) • 20,000-60,000 (Ref. 60,000+) RR=1.1 (99%CI:0.9-1.4) *Parent proxy report from the Adolescent CCSS cohort (n=2979; mixed diagnoses; mean 3.2 yrs at diagnosis; mean 14.8 yrs at study). Controls: n=649 siblings. Measurement: Behavior Problem Index (BPI) Headstrong behavior and Antisocial behavior subscales (cutoff ≥ 1.3 SD sibling mean)	
Overall Conclusion	
Some evidence suggests that lower annual income is related an increased risk of behavioral problems, including headstrong behavior and antisocial behavior, among survivors of CAYA cancer.	2 studies (1 sample) Level C[22,37]

Treatment-related risk factors: Treatment modality	
No associations between treatment modality and headstrong behavior was found using log-binomial models (adjusted for cranial radiation, abdominal radiation, total body irradiation, anthracycline, interaction between age at diagnosis and platinum agent, interaction between age at diagnosis and anthracycline, age at diagnosis, age at evaluation, sex, and annual household income). • Cranial radiation: Yes (Ref. No) not significant • Abdominal radiation: Yes (Ref. No) not significant • Total body irradiation: Yes (Ref. No) not significant • Anthracycline: Yes (Ref. No) not significant Abdominal radiation and treatment with anthracyclines was associated with an increased risk for antisocial behavior using log-binomial models (adjusted for cranial radiation, abdominal radiation, total body irradiation, anthracycline, interaction between age at diagnosis and platinum agent, interaction between age at diagnosis and anthracycline, age at diagnosis, age at evaluation, sex, and annual household income). • Cranial radiation: Yes (Ref. No) not significant • Abdominal radiation: Yes (Ref. No) PR=1.58 (95%CI:1.01-2.36; p=0.04) • Total body irradiation: Yes (Ref. No) not significant • Anthracycline: Yes (Ref. No) PR=1.58 (95%CI:1.07-2.30; p=0.02) *Survivors of neuroblastoma from the CCSS cohort (n=859; 97.9% <5 yrs at diagnosis yrs; 8-17 yrs at study. Controls: n=872 siblings. Meaurement: BPI (cutoff >10th percentile of age-matched siblings).	*Zheng et al. 2018*
No association between treatment modality and headstrong behavior was found using multiple variable models (adjusted for sex, current age group, age at diagnosis, race/ethnicity, annual household income, disfigurement): • Intrathecal methotrexate (Ref. No IT Mtx or CR) RR=1.2 (99%CI:0.8-1.7) • Cranial radiation (Ref. No IT Mtx or CR) RR=1.1 (99%CI:0.7-1.8) • Both IT Mtx and CR (Ref. No IT Mtx or CR) RR=1.2 (99%CI:0.8-1.7) Cranial radiation and both intrathecal methotrexate and cranial radiation was associated with an increased risk for antisocial behavior using multiple variable models (adjusted for sex, current age group, age at diagnosis, race/ethnicity, annual household income, disfigurement): • Intrathecal methotrexate (Ref. No IT Mtx or CR) RR=1.1 (99%CI:0.8-1.5) • Cranial radiation (Ref. No IT Mtx or CR) RR=2.2 (99%CI:1.6-3.1) • Both IT Mtx and CR (Ref. No IT Mtx or CR) RR=1.6 (99%CI:1.2-2.1) *Parent proxy report from the Adolescent CCSS cohort (n=2979; mixed diagnoses; mean 3.2 yrs at diagnosis; mean 14.8 yrs at study). Controls: n=649 siblings. Measurement: Behavior Problem Index (BPI) Headstrong behavior and Antisocial behavior subscales (cutoff ≥ 1.3 SD sibling mean)	*Schultz et al. 2007*
Overall Conclusion	
Some evidence suggests that treatment type is not related to headstrong behavior among survivors of CAYA cancer. Some evidence suggests that the combination of	2 studies (1 sample)

intrathecal methotrexate and cranial radiation, is related to an increased risk of antisocial behavior. Some evidence suggests that cranial radiation, abdominal radiation, and treatment with anthracyclines is related to an increased risk of antisocial behavior among survivors of CAYA cancer.	Level C[22,37]

1b-7. What are the key clinical, demographic and treatment-related risk factors for mental healthcare visit among survivors of childhood, adolescent, and young adult (CAYA) cancer?	
Conclusion single studies	
Clinical risk factors	
Clinical risk factors for mental healthcare visit from Andersen-Gill recurrent event multivariable regression models (adjusting for sex, income, age at diagnosis, diagnosis, and HSCT): Being 15 years or older at diagnosis was associated with an increased risk for mental healthcare visit. • Age at diagnosis: 5-9 years (Ref. 0-4 years) RR=1.15 (95%CI:0.84-1.56, p=0.381) • Age at diagnosis: 10-14 years (Ref. 0-4 years) RR=1.36 (95%CI:0.98-1.88, p=0.068) • Age at diagnosis: ≥15 years (Ref. 0-4 years) RR=1.81 (95%CI:1.17-2.80, p=0.008) • Diagnosis: Other leukemia (Ref. ALL) RR=0.85 (95%CI:0.40-1.82; p=0.676) • Diagnosis: Hodgkin lymphoma (Ref. ALL) RR=0.96 (95%CI:0.61-1.50; p=0.857) • Diagnosis: Other lymphomas (Ref. ALL) RR=1.29 (95%CI:0.77-2.18; p=0.337) • Diagnosis: CNS tumors (Ref. ALL) RR=1.28 (95%CI:0.90-1.82; p=0.167) • Diagnosis: Neuroblastoma (Ref. ALL) RR=1.08 (95%CI:0.66-1.77; p=0.749) • Diagnosis: Soft tissue sarcomas (Ref. ALL) RR=0.99 (95%CI:0.59-1.66; p=0.968) • Diagnosis: Retinoblastoma (Ref. ALL) RR=0.78 (95%CI:0.42-1.44; p=0.426) • Diagnosis: Renal tumors (Ref. ALL) RR=1.23 (95%CI:0.79-1.91; p=0.360) • Diagnosis: Hepatic tumors (Ref. ALL) RR=1.09 (95%CI:0.50-2.38; p=0.820) • Diagnosis: Bone tumors (Ref. ALL) RR=1.17 (95%CI:0.71-1.92; p=0.541) • Diagnosis: Germ cell tumors (Ref. ALL) RR=1.23 (95%CI:0.65-2.32; p=0.529) • Diagnosis: Other epithelial neoplasms (Ref. ALL) RR=1.58 (95%CI:0.89-2.80; p=0.117) • Diagnosis: Unspecified malignancies (Ref. ALL) RR=2.59 (95%CI:0.66-10.18; p=0.173) • Relapse or SMN: not included in final model • Treatment era: not included in final model *Survivors (n=4117; mixed diagnoses; 0-18 years at diagnosis; ≥5 yrs since diagnosis). Controls: n=20,269 matched general population controls. Measurement: psychiatric admission retrieved from administrative health databases; ICD-10 and Statistical Manual of Mental Disorders	*Nathan et al. 2018*
Overall Conclusion	
Some evidence suggests that older age at diagnosis is associated with an increased risk for mental healthcare visit among survivors of CAYA cancer.	1 study Level C[11]
Some evidence suggests that diagnosis is not associated with the risk for mental healthcare visit among survivors of CAYA cancer.	1 study Level C[11]
Some evidence suggests that relapse or SMN are not associated with the risk for mental healthcare visit among survivors of CAYA cancer.	1 study Level C[11]
Some evidence suggests that treatment era is not associated with the risk for mental healthcare visit among survivors of CAYA cancer.	1 study Level C[11]

Demographic risk factors	
Clinical risk factors for mental healthcare visit from Andersen-Gill recurrent event multivariable regression models (adjusting for sex, income, age at diagnosis, diagnosis, and HSCT): Female sex was associated with an increased risk for mental healthcare visit. • Sex: Female (Ref. Male) RR=1.39 (95%CI:1.10-1.75; p=0.006) • Income quintile: 2 (Ref. 1) RR=1.16 (95%CI:0.79-1.70; p=0.463) • Income quintile: 3 (Ref. 1) RR=1.09 (95%CI:0.76-1.56; p=0.650) • Income quintile: 4 (Ref. 1) RR=1.07 (95%CI:0.73-1.56; p=0.737)	*Nathan et al. 2018*

• Income quintile: 5 (Ref. 1) RR=1.31 (95%CI:0.90-1.92; p=0.165) *Survivors (n=4117; mixed diagnoses; 0-18 years at diagnosis; ≥5 yrs since diagnosis). Controls: n=20,269 matched general population controls. Measurement: psychiatric admission retrieved from administrative health databases; ICD-10 and Statistical Manual of Mental Disorders	
Overall Conclusion	
Some evidence suggests that female sex is associated with an increased risk for mental healthcare visit among survivors of CAYA cancer.	1 study Level C[11]
Some evidence suggests that income is not associated with the risk for mental healthcare visit among survivors of CAYA cancer.	1 study Level C[11]

Treatment-related risk factors	
Clinical risk factors for mental healthcare visit from Andersen-Gill recurrent event multivariable regression models (adjusting for sex, income, age at diagnosis, diagnosis, and HSCT): No treatment-related variables were associated with mental healthcare visit. • HSCT: Autologous (Ref. None) RR=0.71 (95%CI:0.43-1.16; p=0.174) • HSCT: Allogeneic (Ref. None) RR=1.68 (95%CI:0.93-3.04; p=0.087) • CNS radiation: not included in final model • ITR: not included in final model • Surgery: not included in final model • Chemotherapy: not included in final model • High-dose methotrexate: not included in final model • Corticosteroids: not included in final model • Cyclophosphamide equivalent dose: not included in final model *Survivors (n=4117; mixed diagnoses; 0-18 years at diagnosis; ≥5 yrs since diagnosis). Controls: n=20,269 matched general population controls. Measurement: psychiatric admission retrieved from administrative health databases; ICD-10 and Statistical Manual of Mental Disorders	*Nathan et al. 2018*
Overall Conclusion	
Some evidence suggests that haematopoietic stem cell transplantation is not related to the risk for mental healthcare visit among survivors of CAYA cancer.	1 study Level C[11]
Some evidence suggests that CNS irradiation is not associated with the risk for mental healthcare visit among survivors of CAYA cancer.	1 study Level C[11]
Some evidence suggests that intensity of treatment is not associated with the risk for mental healthcare visit among survivors of CAYA cancer.	1 study Level C[11]
Some evidence suggests that chemotherapy, or more specifically high-dose methotrexate, corticosteroids, and cyclophosphamide equivalent dose are not associated with the risk for mental healthcare visit among survivors of CAYA cancer.	1 study Level C[11]
Some evidence suggests that surgery is not associated with the risk for mental healthcare visit among survivors of CAYA cancer.	1 study Level C[11]

1b-7. What are the key clinical, demographic and treatment-related risk factors for a first severe mental health event among survivors of childhood, adolescent, and young adult (CAYA) cancer?	
Conclusion single studies	
Clinical risk factors	
Risk factors for first severe mental health event (ED visit, hospitalization, or suicide) from Cox proportional hazard regression (adjusting for sex, income, age, diagnosis, CNS radiation, and high-dose methotrexate): Survivors who were diagnosed at ages 5 to 9, or 10 to 14 years were less likely than those diagnosed at ages 0 to 4 years to experience a severe event. • Age at diagnosis: 5-9 years (Ref. 0-4 years) HR=0.66 (95%CI:0.49-0.89, p=0.006) • Age at diagnosis: 10-14 years (Ref. 0-4 years) HR=0.64 (95%CI:0.46-0.91, p=0.011) • Age at diagnosis: ≥15 years (Ref. 0-4 years) HR=0.66 (95%CI:0.42-1.04, p=0.072) • Diagnosis: Other leukemia (Ref. ALL) HR=1.11 (95%CI:0.62-1.98; p=0.731) • Diagnosis: Hodgkin lymphoma (Ref. ALL) HR= 1.17 (95%CI:0.73-1.88; p=0.511) • Diagnosis: Other lymphomas (Ref. ALL) HR= 1.26 (95%CI:0.79-2.02; p=0.335) • Diagnosis: CNS tumors (Ref. ALL) HR= 1.16 (95%CI:0.81-1.67; p=0.412)	*Nathan et al. 2018*

• Diagnosis: Neuroblastoma (Ref. ALL) HR= 1.15 (95%CI:0.64-2.06; p=0.641) • Diagnosis: Soft tissue sarcomas (Ref. ALL) HR= 1.35 (95%CI:0.83-2.20; p=0.226) • Diagnosis: Retinoblastoma (Ref. ALL) HR= 0.65 (95%CI:0.27-1.54; p=0.327) • Diagnosis: Renal tumors (Ref. ALL) HR= 1.39 (95%CI:0.88-2.20; p=0.157) • Diagnosis: Hepatic tumors (Ref. ALL) HR= 1.38 (95%CI:0.55-3.46; p=0.488) • Diagnosis: Bone tumors (Ref. ALL) HR= 0.77 (95%CI:0.41-1.44; p=0.416) • Diagnosis: Germ cell tumors (Ref. ALL) HR= 0.72 (95%CI:0.35-1.48; p=0.369) • Diagnosis: Other epithelial neoplasms (Ref. ALL) HR= 0.63 (95%CI:0.28-1.40; p=0.255) • Diagnosis: Unspecified malignancies (Ref. ALL) HR= 0.38 (95%CI:0.06-2.54; p=0.316) • Relapse or SMN: not included in final model • Treatment era: not included in final model *Survivors (n=4117; mixed diagnoses; 0-18 years at diagnosis; ≥5 yrs since diagnosis). Controls: n=20,269 matched general population controls. Measurement: psychiatric admission retrieved from administrative health databases; ICD-10 and Statistical Manual of Mental Disorders	
Overall Conclusion	
Some evidence suggests that being diagnosed between 5 and 14 years was associated with a decreased risk for a first severe mental health event among survivors of CAYA cancer.	1 study Level C[11]
Some evidence suggests that diagnosis is not associated with the risk for a first severe mental health event among survivors of CAYA cancer.	1 study Level C[11]
Some evidence suggests that relapse or SMN are not associated with the risk for a first severe mental health event among survivors of CAYA cancer.	1 study Level C[11]
Some evidence suggests that treatment era is not associated with the risk for a first severe mental health event among survivors of CAYA cancer.	1 study Level C[11]

Demographic risk factors	
Risk factors for first severe mental health event (ED visit, hospitalization, or suicide) from Cox proportional hazard regression (adjusting for sex, income, age, diagnosis, CNS radiation, and high-dose methotrexate): Survivors who were in the highest income quintile at diagnosis were significantly less likely to experience a severe event than those in the lowest quintile. • Sex: Female (Ref. Male) HR=1.19 (95%CI:0.96-1.47; p=0.111) • Income quintile: 2 (Ref. 1) HR=0.89 (95%CI:0.64-1.23; p=0.474) • Income quintile: 3 (Ref. 1) HR=0.76 (95%CI:0.55-1.07; p=0.119) • Income quintile: 4 (Ref. 1) HR=0.84 (95%CI:0.61-1.17; p=0.305) • Income quintile: 5 (Ref. 1) HR=0.64 (95%CI:0.45-0.91; p=0.012) *Survivors (n=4117; mixed diagnoses; 0-18 years at diagnosis; ≥5 yrs since diagnosis). Controls: n=20,269 matched general population controls. Measurement: psychiatric admission retrieved from administrative health databases; ICD-10 and Statistical Manual of Mental Disorders	*Nathan et al. 2018*
Overall Conclusion	
Some evidence suggests that sex is not associated with the risk for a first severe mental health event among survivors of CAYA cancer.	1 study Level C[11]
Some evidence suggests that higher income is associated with a decreased risk for a first severe mental health event among survivors of CAYA cancer.	1 study Level C[11]

Treatment-related risk factors	
Risk factors for first severe mental health event (ED visit, hospitalization, or suicide) from Cox proportional hazard regression (adjusting for sex, income, age, diagnosis, CNS radiation, and high-dose methotrexate): Survivors who had received cranial radiation had a reduced risk of a severe event compared with those who did not. • CNS radiation: Yes (Ref. No) HR=0.73 (95%CI:0.55-0.98; p=0.038) • High-dose methotrexate: Yes (Ref. No) HR=0.81 (95%CI:0.56-1.17; p=0.267) • ITR: not included in final model • Surgery: not included in final model • Chemotherapy: not included in final model	*Nathan et al. 2018*

• Corticosteroids: not included in final model • HSCT: not included in final model • Cyclophosphamide equivalent dose: not included in final model *Survivors (n=4117; mixed diagnoses; 0-18 years at diagnosis; ≥5 yrs since diagnosis). Controls: n=20,269 matched general population controls. Measurement: psychiatric admission retrieved from administrative health databases; ICD-10 and Statistical Manual of Mental Disorders	
Overall Conclusion	
Some evidence suggests that haematopoietic stem cell transplantation is not related to the risk for a first severe mental health event among survivors of CAYA cancer.	1 study Level C[11]
Some evidence suggests that CNS irradiation is associated with a decreased risk for a first severe mental health event among survivors of CAYA cancer.	1 study Level C[11]
Some evidence suggests that intensity of treatment is not associated with the risk for a first severe mental health event among survivors of CAYA cancer.	1 study Level C[11]
Some evidence suggests that chemotherapy, or more specifically high-dose methotrexate, corticosteroids, and cyclophosphamide equivalent dose are not associated with the risk for a first severe mental health event among survivors of CAYA cancer.	1 study Level C[11]
Some evidence suggests that surgery is not associated with the risk for a first severe mental health event among survivors of CAYA cancer.	1 study Level C[11]

1b-8. What are the key clinical, demographic and treatment-related risk factors for panic among survivors of childhood, adolescent, and young adult (CAYA) cancer?	
Conclusion single studies	
Demographic risk factors	
No association was found between panic and age, marital status, education, and income using multivariable logistic regression (adjusted for sex, age, marital status, education, income and employment). • Age (continuous): OR=0.97 (95%CI:0.91-1.02) • Marital status: Married (Ref. Not married) OR=1.33 (95%CI:0.67-2.64) • Education: Low (Ref. High) OR=1.58 (95%CI:0.71-3.53) • Education: Middle (Ref. High) OR=0.85 (95%CI:0.42-1.72) • Income in 100 Euros per month (continuous): OR=0.98 (95%CI:0.96-1.01) Female sex and unemployment were associated with an increased risk for panic using multivariable logistic regression (adjusted for sex, age, marital status, education, income and employment). • Female (Ref. Male) OR=1.97 (95%CI:1.09-3.58) • Unemployed (Ref. Employed) OR=3.39 (95%CI:1.14-10.10) *Survivors of childhood cancer (n=951; mixed diagnoses; median 5.0 yrs at diagnosis [range 0-15 yrs]; median 28.1 yrs since diagnosis [range 23-36 yrs]; median 34.2 yrs at study [range 24-49 yrs]). Controls: n=1130, German Household Panel. Measurement: brief PHQ panic module	*Burghardt et al. 2019*
Overall Conclusion	
Some evidence suggests that age is not related to the risk for panic among survivors of CAYA cancer.	1 study Level C[26]
Some evidence suggests that marital status is not related to the risk for panic among survivors of CAYA cancer.	1 study Level C[26]
Some evidence suggests that educational achievement is not related to the risk for panic among survivors of CAYA cancer.	1 study Level C[26]
Some evidence suggests that income is not related to the risk for panic among survivors of CAYA cancer.	1 study Level C[26]
Some evidence suggests that female sex is associated with an increased risk for panic among survivors of CAYA cancer.	1 study Level C[26]
Some evidence suggests that unemployment is associated with an increased risk for panic among survivors of CAYA cancer.	1 study Level C[26]

2. Does the risk of developing poor mental health change over time among survivors of childhood, adolescent, and young adult (CAYA) cancer?	
Conclusion single studies	
More survivors than siblings experienced persistent or increasing symptoms of depression (6.0% vs. 3.7%, p<0.001) and anxiety (3.7% vs. 2.6%, p=0.03). 12.5% of survivors vs. 6.8% of siblings experienced persistent or increasing symptoms of depression, anxiety, and/or somatization (p<0.001). * Survivors from the CCSS cohort (n=4484; mixed diagnoses; mean 10.5 yrs at diagnosis; mean 27.2 yrs at Baseline. Controls: n=1651 siblings. Meaurement: BSI-18 (cutoff ≥63) over 3 time points between 1994-2008	*Brinkman et al. 2019*
Subsets of survivors reported significant increases (depression: 10.2%; anxiety: 11.8%), or significant decreases (depression: 15.1%; anxiety: 15.2%) in mental health symptoms over time. However, the majority of survivors reported persistently few/no symptoms (depression: 65.8%; anxiety: 68.4%) or persistently elevated symptoms (depression: 8.9%; anxiety: 4.8%) over time. *Survivors from the CCSS cohort (n=4569, mixed diagnoses; mean age at diagnosis 10 yrs, range 0-20 yrs; age at study 27.4 yrs). Controls: none. Measurement: Changes in BSI-18 Depression and Anxiety subscales scores (cutoff ≥63) over 3 time points between 1994-2010	*Brinkman, Zhu et al 2013*
Overall Conclusion	
Change of risk over time Some evidence suggests that the risk of anxiety and depression does not change over time in the majority of survivors of CAYA cancer. However, there is also a suggestion that the risk of anxiety and depression may increase for 10-12% of survivors or decrease for 15-16% of survivors over time. Additionally, persistent or increasing symptoms of depression and anxiety were more prevalent in survivors than siblings.	2 studies (1 sample) Level C[29,69]

3. How sensitive are commonly used diagnostic tools for self-reported, parent-reported, different age groups, format and different clinical issues among survivors of childhood, adolescent, and young adult (CAYA) cancer?	
Conclusion single studies	
Brief Symptom Inventory-18 (BSI-18)	
In adult survivors* of pediatric brain tumors, the BSI-18 demonstrated good internal consistency (Cronbach's alphas = 0.74 to 0.90). The concordance between survivor reported BSI-18 scores and clinician GAF ratings was 72%. There was moderate agreement on case classification between GAF and BSI-18 (kappa=0.34, p=0.003). Clinicians rated a higher proportion of survivors as having significant distress on the GAF (32%) as compared to survivors' report of significant distress on the BSI-18 (27%). There was no association between agreement with diagnosis, age at diagnosis, or time since diagnosis. *Survivors of pediatric brain tumors (n=79; mixed neurooncology diagnoses; mean age at study 22.8 yrs [SD=3.2, range 19-30 yrs]). Controls: none. Measurement: BSI-18 (cutoff: GSI ≥57); Clinician rating on the Global Assessment of Functioning (GAF) scale in the Diagnostic and Statistical Manual of Mental Disorders (DSM IV; cutoff: GAF ≤60 following semi-structured interview)	*Liptak et al. 2012*
Among adult survivors* of childhood cancer, receiver operating characteristics analysis showed excellent diagnostic utility of the BSI-18 (area under curve = 0.922) as compared to the SCL-90. Using the standard BSI-18 case rule, sensitivity was 45.2%, specificity was 99.4%, and the total predictive value was 90.7% as compared to the SCL-90. Using the Zabora case rule, sensitivity was 67.7%, specificity was 93.8%, and the total predictive value was 89.6% as compared to the SCL-90. Using the Recklitis case rule, sensitivity was 87.1%, specificity was 83.3%, and the total predictive value was 83.9% as compared to the SCL-90. *Survivors (n=193; mixed diagnoses; median age at diagnosis 11 yrs, range 0-20 yrs; median age at study 26 yrs, range 18-54 yrs). Controls: none. Measurement: BSI-18 (cutoffs: Standard BSI-18 case rule GSI ≥63 or or at least two of subscales ≥63; Zabora case rule GSI ≥57; Recklitis case rule GSI ≥50); Symptom Checklist-90-Revised (SCL-90; GSI ≥63 or or at least two of subscales ≥63)	*Merport et al. 2012*
Among adult survivors* of childhood cancer, the BSI-18 demonstrated acceptable internal consistency (Cronbach's alphas = 0.82 to 0.94). Receiver operating characteristics analysis showed excellent diagnostic utility of the BSI-18 (area under curve = 0.98) as compared to the SCL-90. Using the standard BSI-18 case rule, sensitivity was 41.78%, specificity was 100%, and the total predictive value was 79.19% as compared to the SCL-90. Using an alternate case rule, sensitivity was 83.54%, specificity was 97.89%, and the total predictive value was 92.76% as compared to the SCL-90. Using the study derived case rule, sensitivity was 97.47%, specificity was 85.21%, and the total predictive value was 89.59% as compared to the SCL-90. *Survivors (n=221; mixed diagnoses; median age at diagnosis 11 yrs, range 0-20 yrs; median age at study 26 yrs, range 18-55 yrs). Controls: none. Measurement: BSI-18 (cutoffs: Standard BSI-18 case rule GSI ≥63 or or at least two of subscales ≥63; Alternative case rule GSI ≥57; Study derived case rule GSI ≥50); Symptom Checklist-90-Revised (SCL-90; GSI ≥63 or or at least two of subscales ≥63)	*Recklitis and Rodriguez 2007*
Among adult survivors* of childhood cancer, the BSI-18 demonstrated acceptable internal consistency (Cronbach's alphas = 0.75 to 0.90). Exploratory factor analysis supported a 3-factor structure closely corresponding to the 3 BSI–18 subscales. Confirmatory factor analysis with structural equation modeling validated the 3-dimensional structure in a separate subsample (root-mean-square error of approximation (RMSEA) ≤ 0.05; comparative fit index (CFI) and nonnormed fit index (NNFI) ≥ 0.96). Analysis of the 3-factor model showed consistent fit in male and female participants. *Survivors of childhood cancer from the CCSS cohort (n=8945; mixed diagnoses; median 26 yrs at study [range 18-48 yrs]). Controls: none. Measurement: BSI-18	*Recklitis, Parsons et al. 2006*
Benefit and Burden Scale for Children (BBSC)	
Among pediatric aged survivors*, the BBSC-Dutch version demonstrated good internal consistency (Cronbach's alphas: Benefit α=0.84 and Burden: α=0.72) and satisfactory test-retest reliability (Pearson's correlation coefficient at 21 day re-test: Benefit r=0.74 and Burden r=0.78). Homogeneity was satisfactory with item-total correlations ranging	*Maurice-Stam et al. 2011*

from 0.34 to 0.71 for Benefit and 0.35 to 0.50 for Burden (after deleting one item). Construct validity was supported for Burden with strong correlations (r≥0.5; p<0.001) with 11 out of 15 psychological outcomes (e.g. anxiety, post-traumatic stress, and behavioral problems). Benefit did not correlate with the psychological outcomes. *Pediatric aged survivors (n=77; mixed diagnoses; mean age at study 13.8 yrs, range 8-18 yrs; mean age at diagnosis 10.2 yrs; mean time since diagnosis 3.2 yrs). Control: none. Measurement: BBSC-Dutch; State-Trait Anxiety Inventory for Children (STAI-C); Children's Revised Impact of Event Scale (CRIES); Strengths and Difficulties Questionnaire (SDQ)	
Beck Youth Inventory-II (BYI-II)	
In adolescent survivors* of acute lymphoblastic leukemia, limited agreement was found between parents' and children's ratings of anxiety and depression on the BYI-II. Medium differences on anxiety and depression were found between mothers and children, as well as fathers and children. Both parents had higher ratings than children on anxiety and depression. Parental ratings were associated with parental psychological symptoms: larger disagreement was found with higher parental psychological symptoms. *Survivors of ALL with both parents from the PETALE cohort (n=62; mean 3.6 yrs at diagnosis; mean 11.6 yrs since diagnosis). Measurement: Beck Youth Inventory (anxiety and depression; child version for parent-report).	*Abate et al. 2018*
In adolescent aged survivors* of pediatric brain tumors, the BYI-II demonstrated strong internal consistency (Cronbach's alphas = 0.86 to 0.96). The concordance of case classifications between adolescent-reported BYI-II scores and clinician GAF ratings was 73%. There was low agreement on case classification between GAF and BYI-II (kappa=0.19, p=0.077). Clinicians rated a higher proportion of adolescents as having significant distress on the GAF (24%) as compared to adolescents' report of significant distress on the BYI-II (17%). There was no association between agreement with diagnosis, age at diagnosis, or time since diagnosis. *Survivors of pediatric brain tumors (n=84; mixed neurooncology diagnoses; mean age at study 15.7 yrs [SD=1.9, range 12-18 yrs]). Controls: none. Measurement: BYI-II (cutoff: ≥60 for depression and/or anxiety or ≤40 for self-concept subscales); Clinician rating on the Global Assessment of Functioning (GAF) scale in the Diagnostic and Statistical Manual of Mental Disorders (DSM IV, cutoff: GAF ≤60 following semi-structured interview)	*Liptak et al. 2012*
Distress Thermometer (DT)	
In adolescent survivors of acute lymphoblastic leukemia*, limited agreement was found between parents' and children's ratings of distress on the DT (DT; 0-10 single visual numeric scale measure of distress). Small differences on distress were found between mothers and children, as well as fathers and children. Only mothers had higher ratings than children on distress. Parental ratings were associated with child's sex, parental income, and parental psychological symptoms: larger disagreement for fathers' ratings of child distress was found with the child being female and lower parental income. Larger disagreement for mothers' ratings of child distress was found with higher psychological symptoms. *Survivors of ALL with both parents from the PETALE cohort (n=62; mean 3.6 yrs at diagnosis; mean 11.6 yrs since diagnosis). Measurement: Distress Thermometer.	*Abate et al. 2018*
In adult survivors* of childhood cancer, a score of ≥3 on the DT yielded optimal sensitivity of 92% and specificity of 79% as compared to the Hospital Anxiety and Depression Scale. *Survivors (n=286; mixed diagnoses; median 24 yrs at study; median 6 yrs at diagnosis; median 17 yrs since diagnosis). Controls: None. Measures: Distress Thermometer; Hospital Anxiety and Depression Scale (cut-off ≥15).	*Van der Geest et al. 2018*
In pediatric and adolescent survivors* of acute lymphoblastic leukemia, DT score was associated with the negative affect domain (β=0.523, p<.001; R2=0.273, p<.001), but no association was found with depression or positive affect. In adult survivors*, DT score was associated with anxiety (β=0.343, p=.001; R2=0.291, p<.001), positive affect (β=−0.209, p=.008; R2=0,045, p=.006) and negative affect (β=0.210, p=.045; R2=0,023, p=.045), but no association was found with depression. *Survivors of ALL from the PETALE-PSY cohort (n=204 (n=84 pediatric and adolescent survivors, n=120 adult survivors); 6 ±5 yrs at diagnosis; age at study (ped/ado: 8–18 yrs, adults 19–40 yrs). Measurements: Distress Thermometer; The Beck Youth Inventories-II (ped/ado), The Positive	*Pépin et al. 2017*

and Negative Affect Scale for Children (ped/ado), Beck Depression Inventory-II (adults), Beck Anxiety Inventory (adults), Positive and Negative Affect Scale (adults)	
Among adult survivors* of childhood cancer, receiver operating characteristics analysis showed fair diagnostic utility for the DT (area under curve = 0.72) as compared to the SCL-90-R. Each DT score (0-10) was evaluated as a potential cut-off score by calculating its sensitivity and specificity with the SCL-90-R criterion, and no DT score met the criteria of sensitivity ≥0.90 and specificity ≥0.75. *Survivors (n=119; mixed diagnosis; median age at study 23.5 yrs, range 18-45; median age at diagnosis: 11.2 yrs). Controls: None. Measurement: Distress Thermometer; Symptom Checklist-90-Revised (SCL-90-R, cutoff: GSI ≥63 and/or any 2 subscales ≥63)	*Recklitis, Licht et al. 2007*
Distress Screening Tool (DST)	
Among adolescent survivors of childhood cancer*, the DST demonstrated moderate internal consistency for self-report (Cronbach's α=0.86) and caregiver-report version (Cronbach's α=0.84). Test-retest reliability was assessed over a two week period for self-report (r = 0.70) and caregiver report (r = 0.85, both p<0.001). Convergent validity showed that each self-report item and total score correlated with the respective items of the CDI, RCMAS, DT and PedsQL self-report version, all p<0.001. Caregiver-report was significantly correlated with subscale and total scores of the parent-proxy report of PedsQL and showed significant correlations with the CBCL (all p<0.001). Discriminant validity: mean DST score of survivors with PedsQL scores below the average range was significantly higher than that of survivors with PedsQL scores within the average range, on both self-report, p<0.05, and caregiver-report, p<0.001. Cut-off scores were established using the 1.5~2SD above the mean method: ≥15 for self-report, and ≥16 for caregiver-report. *Survivors (n=168; mixed diagnosis; mean 14.05 yrs at study, range 10-18. Measurement: Distress Screening Tool (DST); Children's Depression Inventory (CDI); Revised Children's Manifest Anxiety Scale (RCMAS); Distress Thermometer (DT); Pediatric Quality of life Generic Score Scale (PedsQL); Child Behaivor Checklist (6-18, CBCL).	*Yoon et al. 2019*
Post-traumatic Stress Diagnostic Scale (PDS)	
Among adult survivors* of childhood cancer, receiver operating characteristics analysis showed good diagnostic utility of the PDS in identifying emotional distress as compared to the BSI-18 [Severity of Symptoms: AUC: 0.84 (95% CI 0.82 – 0.85); Number of Symptoms: AUC: 0.82 (95% CI 0.80 – 0.84)], as well as fair diagnostic utility of the PDS in identifying functional impairment as compared to the BSI-18 [Severity of Symptoms: AUC: 0.84 (95% CI 0.82 – 0.85); Number of Symptoms: AUC: 0.82 (95% CI 0.80 – 0.84)], as well as compared to the RAND SF-36 [Severity of Symptoms: AUC: 0.74 (95% CI 0.73 – 0.76); Number of Symptoms: AUC: 0.74 (95% CI 0.72 – 0.75)]. No difference exists in the predictive value of severity/frequency and number of symptoms on the PDS in the accurate prediction of emotional distress or impaired function using the BSI-18 and SF-36. *Survivors from the CCSS cohort (n=6542; mixed diagnoses; mean age at study 31.85 yrs; mean age at diagnosis 8.2 yrs). Controls: n=368 siblings (mean age at study 33.44 yrs). Measurement: PDS; BSI-18 (cutoff: GSI ≥63 and/or any 2 subscales ≥63); RAND Health Status Survey, Short Form-36 (cutoff: ≤40 on either role limitations subscales)	*Stuber et al. 2011*
Overall Conclusions	
Adult Measures	
There is evidence that the Brief Symptom Inventory-18 (BSI-18) is a reliable and valid measure of clinically significant emotional distress in adult survivors of childhood, adolescent, and young adult cancers.	4 studies Level A[43,70-72]
Some evidence suggests that the Distress Thermometer (DT) with a cut-off of ≥3 can be used as a screening measure for psychological distress in adult survivors of childhood, adolescent, and young adult cancers. The DT score was associated with anxiety, positive and negative affect, but not with depression.	3 studies Level C[35,73,74]
Some evidence suggests that the Post-traumatic stress Diagnostic Scale (PDS) is a valid measure of clinically significant distress in adult survivors of childhood, adolescent, and young adult cancers, but is not able to reliability identify clinically significant functional impairment.	1 study Level C[57]
Youth Measures	

Some evidence suggests that the Distress Thermometer (DT) is not ideal to identify mental health problems in pediatric and adolescent survivors of cancer. Agreement between parent's and children's ratings of the DT is limited in pediatric and adolescent survivors of cancer. The DT score was associated with negative affect, but not with anxiety, depression, or negative affect in pediatric and adolescent survivors of cancer.	2 studies Level B[35,75]
Some evidence suggests that the Distress Screening Tool (DST; self-report and caregiver report) is a reliable and valid measure to screen for distress in pediatric and adolescent survivors of cancer.	1 study Level C[76]
Some evidence suggests that the Benefit and Burden Scale for Children (BBSC) is a reliable and valid measure of psychological adjustment to potentially traumatic experiences in pediatric and adolescent survivors of cancer.	1 study Level C[77]
Some evidence suggests that the Beck Youth Inventories-ll (BYI-II) is a reliable measure of anxiety and depression in pediatric and adolescent survivors of cancer. However, agreement between parent's and children's ratings of the Beck Youth Inventories was limited in pediatric and adolescent survivors of cancer.	2 studies Level C[70,75]

4. What is the effect of any intervention in the treatment of mental health symptoms among survivors of childhood, adolescent, and young adult (CAYA) cancer?	
Conclusion single studies	
Survivors* of pediatric brain tumors participating in a musical training (weekly one-to-one lesson for 52 weeks) reported significant improvement of depressive symptoms (CES-DC: mean=16.27 vs 21.1, p=0.009) after 6 months and at the end of the intervention period (mean=15.03 vs 21.47, p<0.001), compared to placebo-intervention controls. *Survivors of pediatric brain tumors (n=30 in the intervention group and n=30 in control group (CG); mean age at study: 12.5 yrs (IG) and 14.0 (CG). Measurement: Center for Epidemiological Studies Depression Scale for Children (CES-DC)	*Cheung et al. 2019*
Survivors* participating in the Onco-STEP program (10 session internet-based cognitive-behavioral intervention program completed over 5-6 weeks) reported significant improvements pre- vs. post-treatment for PTSS (PDS: t=4.81, p<0.001), anxiety (HADS-A: t=3.44, p=0.003), fear of progression/relapse (FOP-SF: t=2.14, p=0.046), and symptoms of depression (HADS-D: t=5.69, p<0.001). Maintenance of treatment effects were observed three months after completion of intervention for PTSS (F(1,14)=11.16, p=0.005), anxiety (F(1,14)=15.40, p=0.002), and fear of progression/relapse (F1,14=11.92, p=0.004), but not for symptoms of depression. *Survivors (n=20; mixed diagnoses; mean age at diagnosis 13.45 yrs (SD = 4.71); mean yrs of follow-up 13.8 yrs (SD 4.7), range 4-21 yrs; mean age at study 27.25 yrs (SD = 4.8 yrs), range: 20-36 yrs). Measurement: Post-traumatic Diagnostic Scale (PDS), Hospital Anxiety and Depression Scale- Anxiety and Depression subscales (HADS-A & HADS-D), Fear of Progression or Relapse Questionnaire- Short Form (FOP-SF).	*Seitz et al. 2014*
Survivors* of pediatric brain tumors participating in group social skills training (Eight 2-hour weekly group sessions focused on social skills) did not report significant improvements in depression or internalizing, externalizing, or total behavior problems. Survivors* of pediatric brain tumors (n=32, Children n=17, Adolescents n=15; mixed neurooncology diagnoses; mean age at study 9.58 yrs (CBT group) and 9.28 yrs (Controls); mean age at diagnosis 5.53 yrs (CBT group) and 7.59 yrs (Controls). Measurement: Parent proxy report on Child Behavior Checklist (CBCL), Youth Self Report (YSR), & Child Depression Inventory (CDI).	*Barrera et al. 2009*
Survivors* of pediatric brain tumors participating in cognitive behavioral therapy (CBT; 2-3 weekly individual sessions and weekly parent sessions for a duration of 4-8 months) demonstrated significant decreases from baseline to follow-up in internalizing symptoms (p=0.05) and total problems (p=0.012), as compared to a control group. Survivors participating in CBT treatment did not demonstrate significant improvements in anxiety/depression, thought problems, delinquent behavior, aggressive behavior, or total externalizing problems following CBT treatment. *Survivors of pediatric brain tumors (n=40, CBT clinical group n=17, Controls n=23; mixed neurooncology diagnoses; mean age at study 9.58 yrs (CBT group) and 9.28 yrs (Controls); mean age at diagnosis 5.53 yrs (CBT group) and 7.59 yrs (Controls). Measurement: Parent proxy report on Child Behavior Checklist 4-18 (CBCL/4-18).	*Poggi et al. 2009*
Survivors* participating in the Survivor Cancer Competently Intervention Program (SCCIP; manualized 4-session, 1-day family group intervention to reduce post-traumatic stress symptoms (PTSS) in adolescent survivors and their families) reported significant improvements in arousal PTS symptoms compared to wait-list controls (IES-R-Arousal: t(143)=2.77, p=0.01). No differences were found between the treatment and control groups on intrusion or avoidance PTS symptoms (IES-R Intrusion: t(140)=1.32, p=0.19; IES-R Avoidance: t(145)=0.66, p=0.51), anxiety symptoms (RCMAS Total: t(110)=0.46, p=0.65), or on PTSD severity (PTSD-RI - t(143)=1.21, p=0.23). *Survivors (n=74 survivors of childhood cancer in the intervention group and n=75 control survivors in a wait-list control group; mixed diagnoses; age range 10-19 yrs, median age at study: 14.32 yrs; median age at diagnosis: 7.80 yrs). Measurement: Impact of Events Scale-Revised (IES-R), Post-traumatic Stress Disorder Reaction Index (PTSD-RI), Revised Children's Manifest Anxiety Scale (RCMAS).	*Kazak, Alderfer et al., 2004*
Overall Conclusion	

Effect of Cognitive Behavioral Therapy Evidence suggests that cognitive behavioral therapy can be useful in the treatment of anxiety, depression, and post-traumatic stress symptoms among survivors of CAYA cancer.	2 studies Level B[78,79]
Effect of Group Social Skills Training Some evidence suggests that social skills training does not improve mental health symptoms in pediatric and adolescent survivors of cancer.	1 study Level C[80]
Effect of Family Group Intervention for PTSS Some evidence suggests that family group intervention can be useful in the treatment of post-traumatic arousal symptoms in pediatric and adolescent survivors of cancer.	1 study Level C[81]
Effect of participating in musical training Some evidence suggests that participating in weekly musical training can be useful in the treatment of depression in pediatric and adolescent survivors of cancer.	1 study Level C[82]