Evidence tables mental health surveillance

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?

Ford et al. Psychosocial Outcomes in Adult Survivors of Retinoblastoma. 2015

Study Design Treatment era Years of follow-up	Participants	Treatment	Main outcomes	Quality assessment Remarks
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1932-1994** **Years of follow-up:** **Not specified** **Country:** **United States** **Study center:** **New York area; Memorial Sloan Kettering Cancer Center and others identified by the National Cancer Insitute** **Measurement tool:** **<u>Psychological distress:</u> Brief symptom inventory – 18 (BSI-18): Age and sex adjusted T-scores <u>≥</u>63 on the Global Severity Index or on subscales of anxiety, depression, and somatization** **<u>Posttraumatic stress symptoms:</u> Impact of events scale (IES): At least one reexperiencing symptom, three avoidance symptoms, two arousal symptoms, and significant distress on the BSI-18**	**Sample size:** N=470 **Diagnoses:** Retinoblastoma (RB) Unilateral n=218 Bilateral n=252 **Age at diagnosis:** Median = 1 year Range 0-17 years **Age at study:** M = 43.3 years (SD=11 years) **Controls:** 2,820 Childhood Cancer Survivor Study (CCSS) siblings	Radiation therapy (y/n): Unilateral (15.6% yes) Bilateral (91.7% yes) Chemotherapy (y/n): Unilateral (11.5% yes) Bilateral (37.3% yes) Surgery: enucleation (one eye, both eyes, no) Unilateral (87.2% one eye; 0% both eyes) Bilateral (63.5% one eye; 21.4% both eyes)	<u>Psychological distress</u>: 2.8% of RB survivors reported significant distress as compared to 6.0% of CCSS Siblings (p<0.01). RB survivors were significantly less likely to report global symptoms (P<0.01), depression (P=0.02), anxiety (P<0.01) and somatic distress (P<0.01) as compared with CCSS siblings, after adjusting for age at study, race/ethnicity, highest educational level, and household income: RB Survivors Standardized T-Score / CCSS Siblings Standardized T-Score / p-value Global Severity Index: 43.7 / 46.7 / <0.01 Depression: 46.1 / 47.1 / 0.02 Somatic distress: 45.2 / 48.2 / <0.01 Anxiety: 44.6 / 46.8 / <0.01 Significant distress: 2.8% / 6.0% / <0.01 <u>Posttraumatic stress symptoms</u>: RB survivors were significantly more likely to report symptoms of avoidance (P<0.01) and hyperarousal (P<0.01) as compared to siblings, after adjusting for age at study, race/ethnicity, highest educational level, and household income. No differences in symptoms of re-experiencing and intrusive thinking (unadjusted P=0.38, adjusted P=0.55): RB Survivors / CCSS Siblings / $p\text{-value}_{adj}$ Reexperiencing: 0.68 (1.1) / 0.62 (1.2) / 0.55 Avoidance: 1.19 (1.7) / 0.73 (1.4) / <0.01 Hyperarousal: 1.03 (1.5) / 0.63 (1.2) / <0.01 Only 5 out of N=463 RB survivors (1.1%) met criteria for post-traumatic stress disorder (PTSD).	**Quality assessment:** 1. Is the study group representative? ☐Yes/☒no/ ☐unclear <75% of original cohort assessed 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear Main outcome assessed for >75% of participants 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Prasad et al. **Psychosocial and Neurocognitive Outcomes in Adult Survivors of Adolescent and Early Young Adult Cancer: A Report From the Childhood Cancer Survivor Study. 2015**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☐ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1970-1986** **Years of follow-up:** **At least 5 years from diagnosis at the time of recruitment** **Country:** **US** **Study center:** **Multi-institutional (CCSS)** **Measurement tool:** **BSI-18: T score ≥ 63 classified as having emotional distress**	**Sample size:** N=6192 survivors (n=2589 AeYA (11-21y), n=3603 Non-AeYA (<11)) **Diagnoses:** Leukemia n=2458 (39.7%) CNS malignancies n=902 (14.6%) Hodgkin lymphoma n=980 (15.8%) Non-Hodgkin lymphoma n=553 (8.9%) Soft tissue sarcoma n=656 (10.6%) Osteosarcoma/Ewing n=643 (10.4%) **Age at diagnosis:** AeYA: 11-21 years (48.5% 11-14 years; 51.5% 15-21 years) Non-AeYA: 0-10 years (62.1% <6 years, 37.9% 6-10 years) **Age at study:** 15-39 years AeYAs: 15-19 years: n=0 20-24 years: n=0 25-29 years: n=62 30-34 years: n=568 ≥35 years: n=1959 **Controls:** 390 siblings	**AeYA** *Overall treatment* Surgery only n=204 (7.9%) Chemotherapy n=540 (20.9%) Radiotherapy n=494 (19.1%) Chemotherapy and radiotherapy n= 540 (20.9%) *Chemotherapy:* Antimetabolites n=959 (37.0%) Corticosteroids n=1055 (40.8%) *CNS irradiation:* None n=825 (31.9%) Indirect n=966 (37.3%) Direct < 20 Gy n=274 (10.6%) Direct ≥ 20 Gy n=405 (15.6%) **Non-AeYA:** *Overall treatment:* Surgery only n=211 (5.9%) Chemo n=903 (25.1%) Radio n=332 (9.2%) Chemo and Radio: n=1920 (53.3%) *Chemo:* Antimetabolites n=2249 (62.4%) Corticosteroids n=2232 (62.0%) *CNS irradiation:* None n=1226 (34.0%) Indirect n=424 (11.8%) Direct < 20 Gy n=648 (18.0%) Direct ≥ 20Gy n=1108 (30.8%)	**Risk:** Risk in survivors diagnosed between 11 and 21 years of age (and siblings): Somatization: n=405 (15.6%); Siblings n=26 (6.7%) Depression: n=302 (11.7%); Siblings n=31 (8.0%) Anxiety: n=192 (7.4%); Siblings n=17 (4.4%) After adjusting for current age and sex, survivors between 11 and 21 years of age reported greater emotional distress, including anxiety (OR=2.00; 95%CI:1.17-3.43), somatization (OR=2.36; 95%CI:1.55-3.60), and depression (OR=1.55; 95%CI:1.04-2.30), compared with siblings.	**Quality assessment:** 1. Is the study group representative? ☐Yes/☒no/ ☐unclear <75% of original FU2 survey participated 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear >75% of participants completed main outcomes 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?

Phillips et al. Survivors of childhood cancer in the United States: prevalence and burden of morbidity. 2015

Study Design Treatment era Years of follow-up	Participants	Treatment	Main outcomes	Quality assessment Remarks
Study Design: ☐ **Cross-sectional study** ☐ **Case-control study** ☐ **Cohort study** ☐ **Qualitative study (→ exclude!)** ☐ **Systematic/narrative review (→ exclude!)** ☐ **RCT** ☒ **Other: (specify!)** **Surveillance Epidemiology end results (SEER)** **Treatment era:** **1975-2011** **Years of follow-up:** **83.5% survived ≥5 years** **44.9% survived ≥20 years** **Country:** **USA** **Study center:** **9 SEER registries: Connecticut, Hawaii, Iowa, New Mexico, Utah, metropolitain areas of atlanta, Detroit, San Francisco-Oakland, Seattle/Puget Sound; data from the CCSS** **Measurement tool:** **Mental health: BSI-18, T-scores> 63** **Anxiety: Do you currently have anxiety/fear as a result of your cancer?**	**Sample size:** Mental health: N=181,330 **Diagnoses:** To match CCSS and SEER data, cancer sites were restricted to those in the CCSS study: leukemia, brain and central nervous system tumors, Hodgkin lymphoma, non-Hodgkin lymphoma, renal tumors, neuroblastoma, soft tissue, and bone tumors. CCSS brain tumors that were either germ cells or benign/borderline were excluded from CCSS data to better align with the SEER histology data. **Age at diagnosis:** ≤19 years at diagnosis **Age at study:** 0-60+ years. CCS ≥60 years represented 5% of all CCS. **Controls:** n.a	n.a.	**Risk:** Impaired mental health: n=31,305 (17%) Impaired mental health by current age and years since diagnosis: Current age: Total: 20-29 years 18%; 30-39 years 17%; 40-49 years 16%; Total 17% 5-14 years since dx: 18% 15-24 years since dx: 18% 25-36 years since dx: 16% Anxiety/fear: n=23,660 (13%) Anxiety by current age and years since diagnosis: Current age: Total: 20-29 years 13%; 30-39 years 13%; 40-49 years 14%; Total 13% 5-14 years since dx: 14% 15-24 years since dx: 13% 25-36 years since dx: 13% Prevalence rates were similar for survivors aged 20-49 years. Impaired mental health remained stable by age and time since diagnosis.	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Hudson et al. **Age-dependent changes in health status in the Childhood Cancer Survivor cohort. 2015**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: ☐ **Cross-sectional study** ☐ **Case-control study** ☒ **Cohort study** ☐ **Qualitative study (→ exclude!)** ☐ **Systematic/narrative review (→ exclude!)** ☐ **RCT** ☐ **Other: (specify!)** **Treatment era:** **1970-1986** **Years of follow-up:** **Mean 22.4 years since diagnosis (Range 6-39 years)** **Country:** **USA** **Study center:** **26 centers in US & Canada (CCSS)** **Measurement tool:** **<u>"Poor" or "Adverse" Mental Health:</u> BSI-18: T score > 63 on Global Severity Index or any of the Depression, Anxiety, or Somatization subscales classified as having "poor" or "adverse" mental health** **<u>Cancer-related Anxiety:</u> 1 item; Dichotomized as "Yes" (medium, a lot, very many, or extreme fears or anxiety related to cancer/treatment) versus "No" (no or small amount of fears or anxiety related to cancer/treatment**	**Sample size:** 22,568 survivors **Diagnoses:** **L**eukemia 30.4% CNS malignancies 12.4% Hodgkin lymphoma 17.1% Non-Hodgkin lymphoma 9.1% Wilms tumor 6.7% Neuroblastoma 4.1% Soft tissue sarcoma 9.6% Bone malignancy 10.6% **Age at diagnosis:** M=9.5 years (SD= 5.6 yrs) Range: 0-20 yrs **Age at study:** 18-48 yrs at baseline survey **Controls:** 7,504 siblings	Anthracyclines: 26.9% Alkylators: 52.0% Brain radiation: None 66.9% 3-23.9 Gy 9.2% 24.0-29.9 Gy 11.4% 30+ Gy 11.1% Chest radiation: None 71.6% 6.2-23.9 Gy 7.4% 24.0-37.9 Gy 11.4% 38+ Gy 9.6% Abdominal radiation: None 74.2% 1.4-23.9 Gy 7.0% 24.0-34.9 Gy 8.6% 35+ Gy 10.2% Crainotomy 10.1% Thoracotomy 4.4% Nephrectomy 5.8% Cystectomy 0.7% Lower extremity amputation 4.8% Upper extremity amputation 0.5%	**Risk:** **<u>"Poor" or "Adverse" Mental Health:</u>** Reported by 16.8% to 18.4% of survivors by age group versus 10.0% to 12.6% of siblings by age group; In adjusted models, survivors were more likely than siblings to report adverse mental health; Prevalence Ratio (PR)=1.66 (95%CI:1.52-1.80) **<u>Cancer-related Anxiety:</u>** Reported by 12.5% to 13.5% of survivors by age group	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear >75% participated in they surveys 2. Is the follow-up adequate? ☐Yes/☒no/ ☐unclear <75% of participants responded to T3 survey (5982/9711) 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Ahomaki et al. **Late psychiatric morbidity in survivors of cancer at a young age: a nationwide registry-based study. 2015**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: ☐ **Cross-sectional study** ☐ **Case-control study** ☒ **Cohort study** ☐ **Qualitative study (→ exclude!)** ☐ **Systematic/narrative review (→ exclude!)** ☐ **RCT** ☐ **Other: (specify!)** **Treatment era:** **1975-1982; 1983-1992; 1993-2004** **Years of follow-up: n.a.** **Country: Finland** **Study center:** **South-West Finland Hospital District** **Measurement tool:** **Diagnoses coded according to ICD-10**	**Sample size:** N=13860 **Diagnoses:** Leukemia / other hematological n=1318 Lymphomas n=2138 CNS n=1903 Sympathetic nervous system n=196 Retinoblastoma n=98 Renal- (n=315), hepatic- (n=33), malignant bone-tumors (n=296) Soft tissue sarcomas n=973 Germ cell / other gonadal n=1402 Carcinomas / other malignant n=4188 **Age at diagnosis:** 0-19 years: 31% 20-34 years: 69% **Age at study:** unclear **Controls:** N=43,392 siblings	Mixed	**Risk:** <u>Organic memory and brain disorders (F0), total new diagnoses:</u> 0-19 years at dx: n=19; 20-34 years at dx: n=35 - Risk for organic memory/brain disorders was significantly increased for both childhood (HR 4.9; 95% CI 2.7-8.9) and young adults (YA) (HR 2.1; 95% CI 1.4-3.1) compared with siblings. <u>Alcohol/drug abuse (F1), total new diagnoses</u> 0-19 years at dx: n=59; 20-34 years at dx: n=202 - The risk of alcohol/drug abuse was not significantly elevated overall, but female survivors of YA cancers had a trend for an elevated risk (HR 1.2; 1.0-1.6) <u>Schizophrenia/psychotic disorders (F2), total new diagnoses:</u> 0-19 years at dx: n=56; 20-34 years at dx: n=95 - The risk for psychotic disorders was slightly elevated in survivors of childhood malignancies (HR 1.4; 1.0–1.9) compared with siblings, this finding being most pronounced in female childhood cancer survivors (HR 1.9; 1.3-2.7). <u>Mood disorders (F3), total new diagnoses:</u> 0-19 years at dx: n=101; 20-34 years at dx: n=240 - Mood disorders more common in childhood (HR 1.3; 95% CI 1.1-1.7) and YA (1.3; 95% CI 1.1-1.5) than in siblings. <u>Neurotic/anxiety disorders (F4), total new diagnoses:</u> 0-19 years at dx: n=84; 20-34 years at dx: n=116 - Regarding neurotic/anxiety disorders, the HRs were slightly elevated in both survivors of childhood (HR 1.3; 1.0–1.7), and YA (HR 1.2; 1.0–1.5) malignancies compared with siblings. In both childhood ($p < 0.001$), and YA ($p < 0.03$) cancer survivors, the difference in HRs between female survivors and siblings was significantly higher than the difference between male survivors and siblings for this outcome ($HR_{femaleCCS}$ 2.0; 1.4-2.7; $HR_{femaleYA}$ 1.6; 1.2-2.1) <u>Somatization/eating disorders (F5), total new diagnoses:</u> 0-19 years at dx: n=16; 20-34 years at dx: n=24 - Overall, HRs for somatization/eating disorders were not elevated in either survivor group, but female childhood cancer survivors had a significantly increased HR for this outcome (HR 2.0; 1.1-3.8). <u>Personality disorders (F0), total new diagnoses:</u> 0-19 years at dx: n=48; 20-34 years at dx: n=67 - Nonorganic personality disorders were slightly more common in childhood cancer survivors than in siblings (HR 1.4; 1.0–2.0). The finding was explained by female survivors having significantly higher risk for this outcome than female siblings (HR 2.4;1.6-3.5).	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Yi et al. **Postcancer experiences of childhood cancer survivors: how is posttraumatic stress related to posttraumatic growth? 2014**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **N.a.** **Years of follow-up:** **Not reported** **Country:** **Korea** **Study center:** **N.a.** **Measurement tool:** **Posttraumatic Stress Diagnostic Scale (PDS) – total score (values from 0-51). No cutoffs for caseness were used.**	**Sample size:** 225 cancer survivors **Diagnoses:** Hematological cancer (n = 159, 71.9%), Solid or soft tissue tumor (n = 32, 14.5%), CNS or brain tumor (n = 30, 13.6%) **Age at diagnosis:** M = 9.89 yrs, SD = 4.38 **Age at study:** M = 21.95 yrs, SD = 4.76 Range: 15 to 38 yrs **Controls:** No control group.	No information provided	**Risk:** Post-traumatic stress symptoms on the PDS: 4.5% (n=10) reported “moderate to severe” (21-35) stress symptoms 26.3% (n=59) reported moderate (11-20) stress symptoms 64.3% (n=144) reported mild (1-10) stress symptoms The average PDS score was 8.20 (SD=6.13), ranging from 0-26. No cutoffs for caseness were used, no tests of significance or confidence intervals given	**Quality assessment:** 1. Is the study group representative? ☐Yes/☒no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☐Yes/☐no/ ☐unclear/ ☒n.a. **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Klosky et al. **Relations between posttraumatic stress and posttraumatic growth in long-term survivors of childhood cancer: a report from the Childhood Cancer Survivor Study. 2014**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☐ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1970-1986** **Years of follow-up:** **23.1 years (SD=4.5) since diagnosis** **Country:** **USA and Canada** **Study center:** **Multi-institutional CCSS – 26 centers** **Measurement tool:** **Posttraumatic Stress Diagnostic Scale (PSDS; Foa, Cashman, Jaycox, & Perry, 1997)**	**Sample size:** N=6162 survivors **Diagnoses:** Available in supplemental tables **Age at diagnosis:** Average 8.2 years (SD = 5.9) at diagnosis (range = 0 – 20 years) **Age at study:** Average 31.6 years (SD = 7.6) at survey completion (range = 18 –53 years), **Controls:** n/a	Reported in detail elsewhere (Robison, Armstrong, Boice, et al., 2009)	**Risk:** Over 71% of the sample reported some PTSS. Mean Total Severity Score for **PTSS** was 5.43 (SD=7.14), and the mean subtest scores were 1.06 (SD=1.89), 2.33 (SD=3.44), and 2.04 (SD=2.87) for Re-experiencing, Avoidance, and Arousal, respectively	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☐Yes/☐no/ ☒ n/a/☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Oancea et al. **Emotional distress among adult survivors of childhood cancer. 2014**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **Not specified** **Years of follow-up:** **≥ 10 years after diagnosis** **18+ years at study enrollment** **Country:** **USA** **Study center:** **St Jude Children's Research Hospital, St. Jude Lifetime Cohort Study** **Measurement tool:** **BSI-18: T-score≥63 clinically relevant distress**	**Sample size:** N=1863 **Diagnoses:** Leukemia 41% Other diagnoses not specified, survivors of childhood cancer **Age at diagnosis:** Median age 7 years **Age at study:** Median age 32 years (Interquartile range 26-38 years) **Controls:** NA	Not specified	**Risk:** Elevated global emotional distress (Global severity index: n=281; 15.1%) Anxiety problems (n=218; 11.7%) Depression problems (n=279; 15.0%) Somatization problems (n=331; 17.8%) Same sample as Huang et al. (2013)!! (St. Jude Lifetime Cohort Study)	**Quality assessment:** 1. Is the study group representative? ☐Yes/☒no/ ☐unclear <75% of eligible participated (n=1863/4129) 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Huang et al. **Association between the prevalence of symptoms and health-related quality of life in adult survivors of childhood cancer: a report from the St Jude Lifetime Cohort study. 2013**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1962-2002** **Years of follow-up:** **M=25.5 years (SD=7.8)** **Range: 11-48 years** **Country:** **USA** **Study center:** **St. Jude Children's Research Hospital** **Measurement tool:** **BSI-18: cutoff T-score≥63**	**Sample size:** N=1667 **Diagnoses:** CNS tumors (7.9%) Leukemia (47.1%) ALL (44.5%) AML (2.2%) Other leukemia (0.5%) Lymphoma (18.5%), Hodgkin lymphoma (14.9%) Non-Hodgkin lymphoma (3.5%) Solid tumors (26.5%) Ewing sarcoma (3.3%) Nasopharyngeal carcinoma (0.7%) Neuroblastoma (3.5%) Osteosarcoma (4.1%) Retinoblastoma (4.0%) Rhabdomyosarcoma (2.8%) Wilms tumor (4.9%) Other solid tumor (3.3%) **Age at diagnosis:** Not reported **Age at study:** M= 33.7 years (SD= 8.2) Range: 18.9 - 63.3 years **Controls:** No controls	Chemotherapy (88.1%) Radiotherapy (66.3%) Amputation (4%)	**Risk:** Proportion of survivors with elevated scores (t-scores ≥ 63, top 10%-ile of symptoms elevations in the community sample) on the BSI-18 symptom scales: Anxiety scale- 13.1% Depression scale- 15.8% Somatization scale- 19.3% Same sample as Oancea et al. (2014)!! (St. Jude Lifetime Cohort Study)	**Quality assessment:** 1. Is the study group representative? ☐Yes/☒no/ ☐unclear <75% of eligible participated 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Brinkman, Zhang et al. **Suicide ideation and associated mortality in adult survivors of childhood cancer. 2014**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☐ Cross-sectional study** **☐ Case-control study** **☒ Cohort study including longitudinal assessment (3 time-points)** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1970-1986** **Years of follow-up:** **1992-2010** **Country:** **USA** **Study center:** **Multi-site (CCSS)** **Measurement tool:** **BSI-18: single item assessing suicidal ideation (SI)**	**Sample size:** N=7708 survivors **Diagnoses:** Leukemia, CNS tumor, Hodgkin disease, Non-Hodgkin lymphoma, wilms tumor, neuroblastoma, soft tissue sarcoma, osteosarcoma **Age at diagnosis:** ≤21 years **Age at study:** ≥ 18 years at baseline survey, mean age (SD) was 25.1 (7.4) years- 26.3 (7.3) years, depending on suicidal ideation status (3 groups) **Controls:** N=2776 randomly selected sibling controls	All treatment data were reported according to suicidal ideation status (3 groups, therefor 3 values are reported in each category Chemotherapy Yes 72.2- 76.9% No 17.4- 19.3% (not explained why this did not add up to 100%) Radiation None: 27.4-30.1% Noncranial: 24.3-29.5% CRT ≤20 Gy: 10.3-13.2% CRT ≥20 Gy: 18.9-27.4%	**Risk:** Suicidal ideation (SI) was ascertained at 3 separate time points over the follow-up period (Baseline (beginning in 1992), follow-up 2003, follow-up 2007) Risk of Suicidal ideation was analyzed as 1) Late Report (none at baseline but reported at one of two later time points) and as 2) Recurrent (SI at least 2 of the 3 timepoints) No SI: n=6655 (86.3%) Late Report SI: n=575 (7.5%) Recurrent SI: n=234 (3.0%) Compared to sibling controls: Late Report SI in Survivors: OR = 1.9, 95% CI= 1.5-2.5 Recurrent SI in Survivors: OR=2.6, 95% CI= 1.8-38 Mortality: Of the 10,072 survivors who completed the suicide item at any survey, 644 were found to have died, with 10 of these deaths (1.6%) listed as suicides.	**Quality assessment:** 1. Is the study group representative? ☐Yes/☐no/ ☒unclear Unclear how many were eligible. 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear >75% of baseline participants responded to T3 assessment 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Gianinazzi et al. **Mental health-care utilization in survivors of childhood cancer and siblings: the Swiss childhood cancer survivor study. 2014**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1976-2003** **Years of follow-up:** **Time since diagnosis:** **≥5 years post-diagnosis** **M=20.5 years (SD=7.4)** **Country:** **Switzerland** **Study center:** **Swiss Childhood Cancer Study** **Measurement tool:** **Psychological distress: Brief Symptom Inventory – 18: T-score ≥57 on the Global Severity Index (GSI) or two subscales of anxiety, depression, or somatization** **Mental health care: Self-reported utilization within the past year, including a visit to a psychologist or psychiatrist**	**Sample size:** N=1,602 survivors **Diagnoses:** Leukemia 574 (36%) Lymphoma 291 (18%) CNS tumors 212 (13%) Neuroblastomas 69 (4%) Retinoblastomas 38 (2%) Renal tumors 108 (7%) Hepatic tumors 10 (1%) Bone tumors 77 (5%) Soft tissue sarcoma 90 (6%) Germ cell tumors 45 (3%) Langerhans cell hystiocytosis 69 (5%) Other 19 (1%) **Age at diagnosis:** M=7.7 years (SD=4.7) **Age at study:** M=25.1 years (SD=8.1) **Controls:** 703 siblings	Chemotherapy (y/n; n=1346 84% yes) **Radiotherapy** Body and limbs (n=318, 20% yes) Craniospinal (n=298, 18% yes) BMT (y/n; n=68, 4% yes) Surgery (y/n; n=505, 42% yes)	**Risk:** Psychological distress: 14% of survivors and 12% of siblings reported psychological distress (T score ≥57 on two scales or GSI, p-value not provided). Mental health care utilization: Similar proportions of survivors (10%) used mental health care in the past year as compared to siblings (8%; P=0.085).	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☐Yes/☐no/ ☒unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Van der Geest et al. **Emotional distress in 652 Dutch very long-term survivors of childhood cancer, using the hospital anxiety and depression scale (HADS). 2013**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **2001-2009** **Years of follow-up:** **Median follow-up time: 15 years, Range: 5-42yrs** **Country:** **Netherlands** **Study center:** **Erasmus MC-Sophia Children's Hospital** **Measurement tool:** **<u>Emotional Distress:</u> Hospital Anxiety and Depression Scale (HADS) Dutch validated version, total score, clinical cutoff <u>≥</u> 15**	**Sample size:** 652 survivors of childhood cancer **Diagnoses:** ALL (n= 203, 31%) Renal tumor (n= 84, 13%) Non-Hodgkin Lymphoma (n= 73, 11%) Sarcoma (n= 71, 11%, included Rhabdomyosarcoma, Ewing sarcoma, osteosarcoma) Hodgkin lymphoma (n= 51, 8%) Neuroblastoma (n= 48, 7%) Brain tumor (n= 34, 5%) AML (n= 22, 4%) various tumor (n= 66, 10%; included Langerhans cell histiocytosis, germ cell tumors, other rare tumors) **Age at diagnosis:** Median: 6 years, Range: 0-18 yrs **Age at study:** Median: 23 yrs, Range: 15-46 yrs **Controls:** 440 Dutch participants Mean age: 51 years, Range: 17-89 yrs	**Radiotherapy type (Y/N):** Global CNS radiotherapy (n= 77, 12%) focal brain radiotherapy (n= 21, 3%) limbs (n= 6, 1%) abdomen (n= 41, 6%) total body irradiation (n= 9, 1%) SCT – allogenous (Y/N): n= 20, 3% Limb amputation or rotation plastic (Y/N): n= 11, 2%	**Risk:** Mean HADS score was similar between cancer survivors (M = 6.6, SD = 5.3, p=0.38) and the control group. Total of 43 survivors (7% of total sample) had clinically significant elevations on the HADS.	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Chan et al. **Health-related quality-of-life and psychological distress of young adult survivors of childhood cancer in Hong Kong. 2014**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **Completed therapy 1990-2010** **Years of follow-up:** **Off treatment ≥2 years** **≥5 years post diagnosis** **Elapsed time since diagnosis mean 14.1 years (SD 6.8)** **Country:** **Hong Kong** **Study center:** **Multisite (3 hospitals)** **Measurement tool:** **Chinese version of the Brief Symptom Inventory (BSI-18) ≥ 50 on the global severity index (GSI) used to identify survivors with emotional distress**	**Sample size:** 614 survivors **Diagnoses:** Leukemia: 279 (45.4%) Lymphoma: 62 (10.1%) Bone and soft tissue: 75 (12.2%) Brain and CNS malignancies 52 (8.5%) Others: 146 (23.8%) **Age at diagnosis:** <19 years **Age at study:** 16-39 years Mean 21.9 years (SD 5.6) **Controls:** 208 siblings	Chemotherapy/Radiation therapy/Surgery only: n=241, 46.4% Chemotherapy + Surgery: n=145, 27.9% Chemotherapy + Radiation therapy: n=62, 11.9% Chemotherapy + Radiation therapy + Surgery: n=71, 13.7%	**Risk:** Compared to sibling controls, childhood cancer survivors had no significant differences in adjusted model (adjusted for age, gender, marital status, educational level, employment status, personal monthly income, housing ownership): -Somatization: survivors 43.1 (6.9%) vs sibling 44.6 (6.2%), p=0.174 -Depression: survivors 46.4 (8.2%) vs siblings 46.1 (7.35%), p=0.266 -Anxiety: survivors 43.2 (8.2%) vs siblings 44.7 (9.0%), p=0.347 -Global severity index: survivors 41.6 (10.0%) vs siblings 43.3 (9.2%), p=0.378	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☐n.a./☒unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:** Survey was administered by telephone interviewers but unclear if they were blinded to survivor vs. control status

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?			
Lund et al. **Hospital contact for mental disorders in survivors of childhood cancer and their siblings in Denmark: a population-based cohort study. 2013**			
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: ☐ **Cross-sectional study** ☐ **Case-control study** ☒ **Cohort study** ☐ **Qualitative study (→ exclude!)** ☐ **Systematic/narrative review (→ exclude!)** ☐ **RCT** ☐ **Other: (specify!)** **Treatment era:** **01.01.1975-15.12.2009** **Years of follow-up:** **The follow-up extended to 37 years, with a median of 8·82 (IQR 2·41–19·25) years for childhood cancer survivors and 17·32 (2·99–26·25) years for comparisons.** **Country:** **Denmark, nationwide registry study** **Measurement tool:** **Hospital contacts for mental disorders registered in the Danish Psychiatric Central Registry (This contains dates and complete discharge diagnoses for all inpatient contacts to Danish psychiatric departments since April, 1969, and all outpatient contacts since 1995. All diagnoses of mental disorders from 1975 to 2011 were categorised into two main groups: psychotic disorders, consisting of the subcategories of organic psychosis, schizophrenia and other psychoses, and bipolar depression; and nonpsychotic disorders, including other affective disorders (mainly unipolar depression), anxiety, personality disorder, and two groups we defined for this study: "neurodevelopmental and other non-psychotic organic disorders" and "emotional and behavioural disorders". The latter group consisted of mental and behavioural disorders related to psychoactive substance misuse, diagnoses of emotional and behavioural disorder specific to childhood and adolescence (except for attention deficit hyperactivity disorder, which was categorised in the group of neurobehavioural disorders), and emotional and behavioural reactions and syndromes (appendix). Multiple diagnoses in the same person were recorded, but only the fi rst contact within each main diagnostic group (or subgroups within main groups) was counted. If a person had had a contact for a psychotic disorder, any subsequent non-psychotic disorder was disregarded.)**	**Sample size:** N=7085 (82331 person-years) **Diagnoses:** Leukaemia: 1707 (24) Lymphoma: 904 (13%) Central nervous system (CNS) tumours: 1774 (25%) Neuroblastoma and other tumours of the sympathetic nervous system: 317 (5%) Retinoblastoma: 136 (2%) Renal tumours: 257 (4%) Hepatic tumours: 66 (1%) Malignant bone tumours: 347 (5%) Soft-tissue sarcomas: 404 (6%) Germ-cell, trophoblastic and other gonadal tumours: 503 (7%) Carcinomas and other malignant epithelial neoplasms: 580 (8%) Other and unspecified malignant neoplasm: 90 (%) **Age at diagnosis:** 0-4: 2198 (31%), 5-9: 1294 (18%), 10-14:1338 (19%), 15-19: 2255 (32%) **Age at study:** Not reported **Controls:** 13105 siblings (225793 person-year) respectively 140534 (2508513 person-year) population based survivor comparisons (of whom have had 251578 (4307009 person year) sibling comparisons)	**Risk:** The excess absolute risk for hospital contact for mental disorders was: 0.92 contacts per 1000 person-years for male survivors of childhood cancer (95% CI: 0.30–1.54) and 0.84 for females (95% CI: 0.24–1.46) in the period with only inpatient contacts (1975–1994). The excess absolute risk during 1995–2009 was 2.25 contacts per 1000 person-years for males (95% CI: 1.45–3.04) and 1.26 for females (95%CI: 0.26–2.26) including both inpatient and outpatient contacts. With the population-based comparisons as reference, we noted a Hazard Ratio for a first hospital contact in male survivors of 1.50 (95% CI: 1.32–1.69) and of 1.26 (1.10–1.44) in females. In the analyses of both sexes combined, the Hazard Ratio for any hospital contact in survivors was 1.38 (95% CI: 1.26–1.51). When survivors were compared directly with their siblings, the risk estimates slightly decreased (1.31, 1.13–1.51 for males and 1.13, 0.97–1.33 for females). Overall, no increased risk for hospital contact was noted for brothers (HR 0.99, 95% CI: 0.91–1.08) or sisters (1.01, 0.93–1.10) of survivors, or for any specific psychiatric subtype	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Brinkman, Liptak et al. **Suicide ideation in pediatric and adult survivors of childhood brain tumors. 2013**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☒ Other: (specify!) Retrospective medical record view and semi-structured clinical interviews** **Treatment era:** **n.a.** **Years of follow-up:** **n.a** **Country:** **United States of America** **Study center:** **Neuro-oncology outcomes program at Dana Farber Cancer Institute and Children's Hospital Boston.** **Measurement tool: Medical record view and semi-structured clinical interviews based on criteria set forth by DSM IV-TR and included assessment of depression, anxiety, behavior and social functioning**	**Sample size:** 319 Survivors of pediatric brain tumors. **Diagnoses:** Pediatric brain tumor: most common = low-grade glioma n=162 (50.8%), embryonal tumor n=64 (20.1%) Craniopharyngioma n=23, (7.2%) Germ cell tumor n=28, (8.8%) Ependymoma n=14, (4.4%) Other n=28 (8.8%) **Age at diagnosis:** Mean = 10 years before study (SD = 5.0) Approx. 40% were ≥10 years from diagnosis. **Age at study:** Mean = 18 years (SD = 5.0), range 10-35 years **Controls:** n.a.	Surgery only (observation) n=99 (31%) Surgery + radiation n=95 (29.8%) surgery, radiation + chemotherapy n=84 (26.3%) other n=41 (12.9%)	**Risk:** 37 patients (11.7%) reported suicidal ideation (SI) during at least one clinic visit and three reported SI at more than one screening. Five patients (1.6%) had documented suicide attempts, two of whom reported ideation at multiple screenings. All those 5 patients had a history of depression, though data to establish a temporal relationship between the onset of depression and suicidality were unavailable. Mean age of SI: 16.9 years (range 7-26) Depression: 130 (40.8%) Anxiety: 88 (27.6%) Social probems 147 (46.1%) Behavior problems 70 (21.9%) Psychoactive medication: 72 (23.7%)	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Kim et al. **Psychological distress in adolescent and young adult survivors of childhood cancer in Korea. 2013**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **Not reported; recruited for the study June – November 2010** **Years of follow-up:** **Time from diagnosis M=11.99 years (SD=5.91 years), range 2 to 29 years** **Country:** **Korea** **Study center:** **Multiple hospital sites in Korea (exact N unknown)** **Measurement tool:** **Brief Symptom Inventory (BSI-18)** **T-score ≥63 used to identify survivors with emotional distress: anxiety, depression, somatization, global severity index (GSI)**	**Sample size:** 223 survivors of childhood cancer **Diagnoses:** Hematological cancers 157 (71.7%) Solid or soft tissue tumors 32 (14.6%) Central nervous system or brain tumors 30 (13.7%) **Age at diagnosis:** 0-18 years of age, M=9.91, SD=4.39 **Age at study:** 15-38 years, M=21.92, SD=4.69 **Controls:** n/a	Not reported	**Risk:** Survivors mean GSI T scores (M=54.9, SD=9.15) were significantly higher than the normative mean of 50 (t=8.00; P<0.001). Overall prevalence of distress was 20.6%, (n=46) 80.4% had not significant values (n=177)	**Quality assessment:** 1. Is the study group representative? ☐Yes/☐no/ ☒unclear 2. Is the follow-up adequate? ☐Yes/☐no/ ☒unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:** Employed a convenience sample so unlikely a representative sample of survivors in Korea. Limited generalizability. Analyses were not adjusted for relevant treatment exposures. No comparison group with other non-cancer Koreans of the same age. US normative data and cut-off scores used for the BSI.

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Gianinazzi et al. **Adolescent survivors of childhood cancer: are they vulnerable for psychological distress? 2013**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1976-2003** **Years of follow-up:** **Time since diagnosis:** **M= 12.2 years (SD=4.0)** **Country:** **Switzerland** **Study center:** **Swiss Childhood Cancer Registry** **Measurement tool:** **BSI-18, T-score of ≥57 was defined as distressed**	**Sample size:** N=407 **Diagnoses:** Leukemias- 33% Lymphomas- 13% CNS tumors- 17% Neuroblastomas- 6% Retinoblastomas- 3% Renal tumors- 10% Hepatic tumors- 1% Bone tumors- 3% Soft tissue sarcomas- 5% Germ cell tumors- 3% Langerhans cell hystiocytosis- 5% Other- 1% **Age at diagnosis:** M= 5.7 years (SD= 3.9) **Age at study:** M = 17.9 years (SD = 1.5) Range: 16.0-19.9 years **Controls:** Three comparison groups: • N=93 healthy German adolescents • N=56 German adolescent psychotherapy patients • N=102 siblings of survivors	Chemotherapy with or without surgery- 53% Radiation with or without chemotherapy/ surgery- 26% BMT- 7% Surgery only- 14%	**Risk:** Outcomes ○ Raw scores on BSI-18 scales ○ Proportion with either GSI or two other BSI-18 subscale t-scores ≥ 57 ○ Raw scores on BSI-18 scales among those with a BSI-18 scale t-score ≥ 57 ▪ 13% of survivors reported elevations (t-scores ≥ 57) in either GSI or two other BSI-18 subscale. ▪ Proportion of male survivors reporting elevated (t-scores ≥ 57) distress: Somatization- 5%; Depression- 12%; Anxiety- 10%; GSI- 9%). ▪ Proportion of female survivors reporting elevated (t-scores ≥ 57) distress: Somatization- 19%; Depression- 18%; Anxiety- 17%; GSI- 16%). ▪ Survivors have significantly higher BSI-18 raw scores compared to healthy German adolescents on all BSI-18 scales: ○ BSI-18 GSI: 4.85, 95%CI:4.01-5.64 vs. 3.30, 95%CI:1.98-4.61, p<0.001 ○ BSI-18 Somatization subscale: 1.28, 95%CI:1.05-1.50 vs. 0.76, 95%CI:0.38-1.15, p<0.001 ○ BSI-18 Depression subscale: 1.83, 95%CI:1.51-2.16 vs. 1.33, 95%CI:0.71-1.96, p=0.025 ○ BSI-18 Anxiety subscale: 1.85, 95%CI:1.56-2.14 vs. 1.19, 95%CI:0.72-1.67, p<0.001 ▪ Survivors as a whole did not differ from siblings on any BSI-18 scale. Female survivors did not differ from siblings on any BSI-18 scale. Male survivors did have higher BSI-18 raw scales than male siblings on the Somatization (P=0.025), Depression (P<0.001), and GSI (P=0.008). Male survivors did not differ from male siblings on the Anxiety subscale. • The proportion of survivors and siblings with either GSI or two other BSI-18 subscale t-scores ≥ 57 did not differ significantly—52 of 407 survivors (13%) and 11 of 102 siblings (11%). ▪ Distressed survivors had higher Somatization (P<0.001) and Anxiety (P=0.002) scores than distressed German psychotherapy patients. There were no differences between distressed survivors & distressed psychotherapy patients on the GSI or the depression subscale.	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Cizek Sajko et al. **Suicide among childhood cancer survivors in Slovenia. 2012**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: ☐ **Cross-sectional study** ☐ **Case-control study** ☒ **Cohort study** ☐ **Qualitative study (→ exclude!)** ☐ **Systematic/narrative review (→ exclude!)** ☐ **RCT** ☐ **Other: (specify!)** **Treatment era:** **1978-2008** **Years of follow-up:** **Mean time of observation (years) 13.9 (SD 10.7), range 1-33 years** **Country:** **Slovenia** **Study center:** **University Children's Hospital in Ljubljana** **Measurement tool:** **Medical chart review – data was collected from medical records on cause of death by suicide**	**Sample size:** 1647 **Diagnoses:** Leukemia (n = 430, 36%) Central nervous system tumor (n = 317, 19%) Hodgkins disease (n = 150, 9%) Non-Hodgkin lymphoma (n = 140, 9%) Renal tumors (n = 94, 6%), Neuroblastoma (n = 59, 4%) Rhabdomyosarcoma (n = 62, 4%) Malignancy bone tumors (n = 111, 7%) Soft tissue sarcoma (n = 54, 3%) Gonadal cancer (n = 55, 3%) Carcinomas (n = 109, 7%) Other neoplasms (n = 51, 3%) Unspecified malignant neoplasm (n = 15, 1%) **Age at diagnosis:** Mean 8.2 years (SD = 4.9) Range 0-18 years **Age at study:** Beginning of follow-up: mean 9.4 years (SD = 4.4), range 5-34 years **End of follow-up:** mean 22.3 years (SD = 11.9), range 5-66 **Controls:** General population: vital status determined from database maintained by Statistical Office of the Republic of Slovenia	Surgery (S) only Radiation therapy (RT) Chemotherapy (C): S only (n = 232, 14%) RT only (n = 41, 2%) C only (n = 235, 14%) S + RT (n = 169, 10%) RT + C (n = 478, 29%) S + C (n = 230, 14%) S + R + C (n = 243, 15%)	**Risk:** Compared to the general population (vital status maintained by the government database), there is no increased risk of suicide in childhood cancer survivors. 3/1647 survivors committed suicide (0.18%), all were male. Risk of suicide in childhood cancer survivors - Observed probability = 0.18% (95% CI 0.04%-0.53%) Risk of suicide in general population – Expected probability = 0.19% No statistically significant difference between the two (p = 1.00)	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:** Patients in the cohort did not necessarily have been long-term survivors (so included patients on therapy)

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Stuber et al. **Defining medical posttraumatic stress among young adult survivors in the Childhood Cancer Survivor Study. 2011**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RC** **☐ Other: (specify!)** **Treatment era:** **1970-1986** **Years of follow-up:** **Taken from Stuber et al., 2010 article:** **Years since dx:** **15-19 (27.1%)** **20-24 (35.8%)** **25-29 (25.5%)** **30-34 (11.6%)** **Country:** **USA** **Study center:** **Various in USA and Canada (CCSS)** **Measurement tool:** **Posttraumatic stress response Diagnostic Scale (PDS), 17 questions based on DSM IV related diagnostic criteria; scale measures severity (occurrence) of symptoms on scale 0-3. PDS in study used in 3 ways: 1. Criteria for DSM symptoms cluster, 2. Number of 17 symptoms , 3. Severity/frequency of symptoms; Brief Symptom Inventory-18 (BSI-18) T-score ≥ 63 considered as clinically significant distress on the global stress index (GSI) or subscales of depression, anxiety, or somatization; RAND Health Status Survey, Short Form-36 (RAND SF-36) T-score ≤ 40 considered clinically impaired; Diagnostic Criterion F for PTSD attributed if BSI-18 GSI) ≥ 63, or two subscale scores ≥ 63; SF-36 ≤ 40 functional limitations caused by emotional stress; 5 different groups of survivors and siblings (combined) using different operational definitions of posttraumatic stress: 1. Posttraumatic stress defined as meeting full symptoms**	**Sample size:** 6542 survivors of childhood cancer **Diagnoses:** Bone cancer (9.2%), Central Nervous System Malignancies (10.5%), Hodgkin Lymphoma (14.2%), Kidney-Wilms (9.6%), Leukemia (33.4%), Non-Hodgkin Lymphoma (7.7%), Neuroblastoma (6.2%), Soft tissue sarcoma (9.2%) **Age at diagnosis:** Mean age = 8.2 yrs, SD = 5.87 yrs Range: 0-20 yrs **Age at study:** Mean age = 31.85 yrs, SD = 7.55 yrs Range: 18-53 yrs **Controls:** 368 siblings Mean age = 33.44 yrs, SD = 8.2 yrs Range: 18-54	Taken from Stuber et al., 2010 article: Chemotherapy Y/N • None (20.3%) • Anthracycline/ Alkylating (59.8%) • Other drugs (19.9%) Radiation Therapy (RT) Y/N • RT to brain (29.6%) • RT, but not brain (33.5%) • RT site unknown (2.9%) • No RT (34.0%)	Prevalence of posttraumatic stress in survivors of childhood cancer compared to siblings differs according to how posttraumatic stress is operationalized. 9.0% of survivors (n = 589) met full symptom criteria for PTSD with impairment or distress, as compared to 2.1% of siblings (n=8) 7.5% of survivors (n = 490) met full symptom criteria for PTSD but had no impairment or distress, as compared to 2.7% of siblings (n=10) 4.8% of survivors (n = 314) met partial symptom criteria for PTSD with impairment or distress, as compared to 3.2% of siblings (n=12) 11.4% of survivors (n = 744) met partial symptom criteria for PTSD but had no impairment or distress, as compared to 8.0% of siblings (n=30) Survivors had higher prevalence than siblings when: • Posttraumatic stress defined as meeting full symptoms in the presence of functional impairment: OR= 4.21; (95%CI 2.11 - 8.38), p <.0001 • Posttraumatic stress defined as meeting full symptoms without functional impairment OR =2.85; (95%CI 1.51 – 5.39), p = .0013 • Posttraumatic stress defined as meeting partial symptoms without functional impairment OR = 1.71, (95%CI 1.13 – 2.60), p = 0.012	**Quality assessment:** 1. Is the study group representative? ☒ Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒ Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒ n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:** Same sample population as Stuber, Meeske, Leinsenring, Stratton, Zeltzer, Dawson…Krull, 2010

and the presence of distress or functional impairment, 2. Posttraumatic stress defined as meeting full symptoms without functional impairment or significant distress, 3. Presence of partial symptoms (2 of 3) and the presence of functional impairment or distress, 4. Presence of partial symptoms (2 of 3) and the absence of functional impairment or distress, 5. Less than two clusters of symptoms			No difference between survivors and siblings using: • Presence of partial symptoms in the presence of functional impairment OR = 1.42, (95%CI 0.79 - 2.56), p = 0.24	

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Dieluweit et al. **Utilization of psychosocial care and oncological follow-up assessments among German long-term survivors of cancer with onset during adolescence. 2011**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **< 2015 but otherwise not specified.** **Years of follow-up:** **Time since diagnosis: M=13.7 years; SD=6.0 years** **Country:** **Germany** **Study center:** **German Childhood Cancer Registry** **Measurement tool:** **<u>Posttraumatic stress symptoms:</u>** **Posttraumatic Stress Diagnostic Scale (PDS). Clinically relevant score achieved when all 6 DSM-IV diagnostic criteria were met.** **<u>Depression and anxiety:</u> Hospital anxiety and depression scale (HADS). A score of 11 or higher on the Depression or Anxiety subscales indicated probable presence of an anxiety or mood disorder.**	**Sample size:** N=820 survivors of adolescent onset cancer **Diagnoses:** Leukemia (19.3%) Lymphoma (30.5%) CNS tumors (9.5%) Bone tumors (21.2%) Soft tissue sarcomas (9.2%) Germ cell tumors (6.6%) Other (2.4%) **Age at diagnosis:** M=15.8 years (SD=0.9 years) Range: 15-18 years **Age at study:** M=30.4 years (SD=6.0 years) **Controls:** n/a	Surgery (y/n; yes=71.8%) Chemotherapy (y/n; yes=90.5%) Radiation (y/n; yes=57.8%)	**Risk:** At the time of follow-up: • 14.7% reported clinically significant anxiety (HADS-A ≥ 11) • 5.4% clinically significant depression (HADS-D ≥ 11) • 14.4% met posttraumatic stress criteria at follow-up (PDS) • 3.5% of participants reported receiving psychosocial care • 4.9% reported utilization of psychotropic medication	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☐Yes/☐no/ ☒unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Krull et al. **Neurocognitive functioning and health-related behaviours in adult survivors of childhood cancer: a report from the Childhood Cancer Survivor Study. 2011**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1970 - 1986** **Years of follow-up:** **All survivors were ≥5 years from diagnosis. Included all completed data from CCSS 2003 Follow-Up Survey until data freeze in 2008.** **Country:** **US** **Study center:** **Childhood Cancer Survivor Study (CCSS)** **Measurement tool:** **Brief Symptom Inventory-18 (BSI-18)** **Clinical impairment for anxiety, depression, and somatization was defined as scores falling in the bottom 10% of the national standardization sample.**	**Sample size:** 6,440 adult survivors **Diagnoses:** Leukaemia: 2145 (33.3%) CNS tumours: 660 (10.3%) Hodgkin lymphoma: 872 (13.5%) Non-hodgkin lymphoma: 505 (7.8%) Wilms tumour: 646 (10.0%) Neuroblastoma: 418 (6.5%) Soft tissue sarcoma: 606 (9.4%) Bone cancer: 588 (9.1%) **Age at diagnosis:** <21 years of age **Age at study:** M=32.0 yrs (SD=7.6) **Controls:** N/A	<u>Radiation</u> Brain: 1765 (27.4%) Chest: 1215 (18.9%) Neck: 1026 (15.9%) Abdomen: 1166 (18.1%) Spine: 413 (6.4%) Pelvis: 906 (14.1%) Limb: 263 (4.1%) Total body: 79 (1.2%) <u>Chemotherapy</u> Alkylator: 3,125 (48.5%) Anthracycline: 2,466 (38.3%) Epipodophyllotoxin: 460 (7.1%) Antimetabolite (IV): 2,773 (43.1%) Antimetabolite (IT): 4,430 (68.8%) Corticosteroids: 2,890 (44.9%)	**Risk:** For anxiety, 7.7% of survivors (N=493) scored in in the impaired range. For depression, 11.5% of survivors (N=740) scored in in the impaired range. For somatization, 13.4% of survivors (N=860) scored in in the impaired range.	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☐Yes/☐no/ ☒n.a./☐unclear 3. Are the outcome assessors blinded? ☒Yes/☐no/ ☐n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:** Data on health behaviors and neurocognitive outcomes from this paper were not abstracted as they were not relevant to the question.

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Zebrack et al. **The perceived impact of cancer on quality of life for post-treatment survivors of childhood cancer. 2011**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1968-2005** **Years of follow-up:** **Years since diagnosis-** ***M* 15.8 yrs (SD =7.0 yrs)** **Range 2–37 yrs** **Country:** **US** **Study center:** **3 childhood cancer centers** **Measurement tool:** **Brief Symptom Inventory (BSI-18)**	**Sample size:** 621 survivors of childhood cancer **Diagnoses:** Hematological (n= 379, 61.0%), brain tumor (n= 79, 12.7%), solid tumors/soft tissue tumors/other (n= 163, 26.2%; included germ cell tumors, retinoblastoma, neuroblastoma, and other tumors not specified) **Age at diagnosis:** M = 11.1 yrs, SD = 5.5 yrs Range: 0-21 yrs **Age at study:** M = 26.9 yrs, SD = 5.5 Range: 18-39 yrs **Controls:** n.a.	No information provided	**Risk:** <u>Psychological Distress</u> On the BSI-18, 22.2% (N=134) endorsed clinically significant levels of distress as defined by a T-score > 63 on any 2 of the 3 Anxiety, Depression, or Somatization subscales and/or a T-score > 63 on the Global Severity Index (GSI).	**Quality assessment:** 1. Is the study group representative? ☐Yes/☒no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:** Only 29.3% of those eligible participated in the study

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Kadan-Lottick et al. **Neurocognitive functioning in adult survivors of childhood non-central nervous system cancers. 2010**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☒ Cohort study - retrospective** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **Jan 1970- Dec 1986** **Years of follow-up:** **n/a** **Country:** **US** **Study center:** **26 institutions in US & Canada (CCSS)** **Measurement tool:** **<u>BSI-18</u>: Subscale scores ≥63** • **Depression subscale** • **Anxiety subscale** • **Global Severity Index ≥63 =”Emotional Distress”**	**Sample size:** N: 5937 non-CNS survivors **Diagnoses:** • ALL: 1939 (32.7%) • Myeloid leukemia (AML or CML): 292 (4.9%) • Hodgkin disease: 908 (15.3) • Non-Hodgkin lymphoma: 509 (8.6%) • Neuroblastoma: 433 (7.3%) • Soft tissue sarcoma: 613 (10.3%) • Osteosarcoma: 382 (6.4%) • Ewings and other bone tumors: 212 (3.6%) • Wilms tumor: 649 (10.9%) **Age at diagnosis:** Mean (SD): 8.5 (6.0) Range: 0–20 **Age at study:** Mean (SD): 32.2 (7.6) Range: 17.0–54.1 **Controls:** n/a – did not compare siblings on BSI data	Chemotherapy: 1663 (29.8%) Radiotherapy (RT): 452 (8.1%) Chemotherapy and RT: 3178 (57%) No chemotherapy or RT: 284 (5.1%)	**Risk**: (univariate analysis for association with self-reported impaired neurocognitive functioning outcomes) • Global Severity Index (“Emotional Distress”) Yes: 576 No: 5345 • Depression subscale Yes: 665 No: 5259 • Anxiety subscale Yes: 444 No: 5479 Somatization subscale not reported.	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☐Yes/☐no/ ☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Stuber et al. **Prevalence and predictors of posttraumatic stress disorder in adult survivors of childhood cancer. 2010**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1970-1986** **Years of follow-up:** **Years since dx:** **15-19 years (27.1%); 20-24 years (35.8%)** **25-29 years (25.5%); 30-34 years (11.6%)** **Country:** **USA** **Study center:** **Various in USA and Canada (CCSS)** **Measurement tool:** **Posttraumatic stress response Diagnostic Scale (PDS): PTSD coded as dichotomous categorical variable: yes/no** **Brief Symptom Inventory-18 (BSI-18) T-score ≥ 63 considered as clinically significant distress on the global stress index (GSI) or subscales of depression, anxiety, or somatization** **RAND Health Status Survey, Short Form-36 (RAND SF-36) T-score ≤ 40 considered clinically impaired** **Diagnostic Criterion F for PTSD Met if BSI-18 GSI ≥ 63, two subscale scores ≥ 63 or SF-36 score ≤ 40 indicating functional limitations caused by emotional stress**	**Sample size:** 6542 survivors of childhood cancer **Diagnoses:** Bone cancer (9.2%), Central Nervous System Malignancies (10.5%), Hodgkin Lymphoma (14.2%), Kidney-Wilms (9.6%), Leukemia (33.4%), Non-Hodgkin Lymphoma (7.7%), Neuroblastoma (6.2%), Soft tissue sarcoma (9.2%) **Age at diagnosis:** Mean age = 8.2 yrs, SD = 5.87 yrs Range: 0-20 yrs **Age at study:** Mean age = 31.85 yrs, SD = 7.55 yrs Range: 18-53 yrs **Controls:** 368 siblings Mean age = 33.44 yrs, SD = 8.2 yrs Range: 18-54	Chemotherapy Y/N • None (20.3%) • Anthracycline/ Alkylating (59.8%) • Other drugs (19.9%) Radiation Therapy (RT) Y/N • RT to brain (29.6%) • RT, but not brain (33.5%) • RT site unknown (2.9%) • No RT (34.0%)	**Risk:** 9% of survivors (n = 589) met criteria for PTSD , as compared to 2% of siblings (n=8) Survivors risk of PTSD was more than 4 times higher than siblings (OR= 4.41; 95%CI= 2.08 to 8.25)	**Quality assessment:** 1. Is the study group representative? ☒ Yes/☐ no/ ☐ unclear 2. Is the follow-up adequate? ☒ Yes/☐ no/ ☐ unclear 3. Are the outcome assessors blinded? ☐ Yes/ ☐ no/ ☒ n.a./ ☐ unclear 4. Are the analyses adjusted for important confounding factors? ☒ Yes/☐ no/ ☐ unclear **Remarks:** Adjusted for age at interview, race, gender, within family correlation

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Krull et al. **Adolescent behavior and adult health status in childhood cancer survivors. 2010**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☐ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1970-1986** **Years of follow-up:** **All survivors were ≥5 years from diagnosis at baseline.** **Country:** **US** **Study center:** **Childhood Cancer Survivor Study (CCSS)** **Measurement tool:** **Behavior Problem Index (BPI) was used to obtain parent-proxy report of depression/anxiety symptoms, headstrong behavior, attention deficit, social withdrawal, and antisocial behavior at baseline. Participants' impairment was categorized dichotomously and defined as a reported level of problematic symptoms occurring in ≤10% of the original normative standardization sample.**	**Sample size:** 1,652 survivors **Diagnoses:** Leukemia= 790 (47.8%) CNS tumor= 150 (9.1%) Other= 712 (43.1%) **Age at diagnosis:** n.a. **Age at study:** 12-17 years of age at baseline **Controls:** 406 siblings	<u>Cranial Radiation:</u> Yes= 452 (27.4%) No= 1084 (65.6%) Unknown= 116 (7.0%)	**Risk:** Parents reported significant impairment for survivors on measures of depression/anxiety (17.1% impaired), headstrong behavior (13.2% impaired), attention deficit (19.0% impaired), social withdrawal (21.1% impaired), and antisocial behavior (12.3% impaired). As compared to siblings, significantly more survivors were classified as having depression/anxiety ($p<0.01$), headstrong behavior ($p<0.01$), attention deficit ($p<0.01$), social withdrawal ($p<0.01$), and antisocial behavior ($p<0.01$).	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:** Mental health outcomes only assessed at baseline via parent report. Follow-up outcomes included health behaviors as reported by survivors.

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Michel et al. **Psychological distress in adult survivors of childhood cancer: the Swiss Childhood Cancer Survivor study. 2010**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**

Study Design:
☒ Cross-sectional study
☐ Case-control study
☒ Cohort study
☐ Qualitative study (→ exclude!)
☐ Systematic/narrative review (→ exclude!)
☐ RCT
☐ Other: (specify!)
 	
Treatment era:
1976-2003
 	
Years of follow-up:
Time since diagnosis
***M*= 19.5 yrs (SD=6.5 yrs)**
Range: 5.8 - 37.9 yrs
 	
5-14 yrs = 26.3%
15-19 yrs =26.6%
20-24 yrs =26.1%
≥25 yrs = 20.9%
 	
Country:
Switzerland
 	
Study center:
 	
Swiss Childhood Cancer Registry (SCCR)
 	
Measurement tool:
Brief symptom Inventory (53 items, T-scores ≥63)
	Sample size:
	1076 responders to invitation to participate
	987 with valid BSI
	623 non-responders to invitation
	
	Diagnoses:
	Leukemia (36.9%), lymphoma (21.5%), CNS tumor (11.7%), neuroblastoma (3.2%), retinoblastoma (1.9%), renal tumor (5.3%), hepatic tumor (0.5%), malignant bone tumor (5.3%), soft tissue sarcoma (5.3%), germ cell tumor (2.7%), carcinamo (1%), other malignancy (0.3%) or Langerhans cell histiocytosis (4.3%)
	
	Age at diagnosis:
	M=8.4 yrs (SD=4.7 yrs)
	Range: 0.0 - 16.0 yrs
	
	Age at study:
	M=27.9 yrs (SD=6.0 yrs)
	Range: 20.0 - 49.1 yrs
	
	20-24.9 yrs = 38.0%
	25-29.9 yrs = 29.7%
	≥30 yrs = 32.3%
	
	Controls:
	Population Norms for BSI
		Surgerly only (8.8%)
		
		Chemotherapy (49.6%)
		
		Radiotherapy (40.7%)
		
		Bone marrow transplantation (4%)
			Risk:
			• Two hundred forty-three survivors (24.6%; 95% CI, 21.9% to 27.3%) were 'cases' (T-score **≥**63) on two or more domain scales or on the GSI.
			  ○ 14.4% had Global Severity Index (GSI) scores **≥**63
			  ○ 8.1% had somatization scores **≥**63
			  ○ 10.5% had obsessive-compulsive tendencies scores **≥**63
			  ○ 13.4% had depression scores **≥**63
			  ○ 12.8% had anxiety scores **≥**63
			
			• Survivors had significantly lower T-scores than norm population for general severity index (p<0.001), somatization (p<0.001), obsessive-compulsive tendencies (p<0.001), and anxiety (p<0.001). No significant difference was observed between survivor T-scores and norm population for depression (p=0.053).
			
			• A significantly greater proportion of childhood cancer survivors were at risk for significant psychological distress on GSI (p<0.001), depression (p<0.001), somatization (p=0.047), and anxiety (p=0.004) than expected from the norm population. No significant difference was observed between proportion of survivors reporting obsessive-compulsive tendencies (p=0.574) than expected from the norm population.
				Quality assessment:
				1. Is the study group representative?
				☒Yes/☐no/
				☐unclear
				2. Is the follow-up adequate?
				☒Yes/☐no/
				☐unclear
				3. Are the outcome assessors blinded?
				☐Yes/☐no/
				☒n.a./☐unclear
				4. Are the analyses adjusted for important confounding factors?
				☒Yes/☐no/
				☐unclear
				
				Remarks:

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Recklitis, Diller et al. **Suicide ideation in adult survivors of childhood cancer: a report from the Childhood Cancer Survivor Study. 2010**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1.1.1970-31.12.1986** **Years of follow-up:** **≥5 years from diagnosis** **Country:** **US** **Study center:** **Multicenter, 26 institutions US & Canada (CCSS)** **Measurement tool:** **BSI-18, specifically item 9: Suicidal ideation**	**Sample size:** N: 9126 (4312 female, 4814 male) **Diagnoses:** Leukemia: 2681 (29.4%) Hodgkins Lymphoma: 1645 (18.0%) CNS: 1136 (12.5%) Bone: 991 (10.9%) Sarcoma: 88 (9.7) NHL 842 (9.2%) Wilms tumor 584 (6.4%) Neuroblastoma 360 (3.9%) **Age at diagnosis:** <3 years: 820 (9.0%) 3-6 years: 2043 (22.4%) 7-10 years: 1764 (19.3%) 11-17: 3509 (10.9%) **Age at study:** 18-24 years: 3566 (39.1%) 25-29 years: 2501 (27.5%) 30-34 years: 1859 (20.4%) ≥ 35 years: 1200 (13.2%) **Controls:** Siblings: 2968 (1585 female, 4814 male)	Surgery only: 578 (7.3%) RT only: 23 (0.3%) Chemo only: 307 (3.9%) Chemo and RT: 910 (11.5%) Chemo and surgery: 1310 (16.6%) RT and surgery: 1143 (14.5%) Chemo and RT and surgery 3632 (46.0%)	**Risk:** Survivors 7.8% (n=713) compared with 4.6% controls (n=135) (OR=1.79, 95%CI 1.4-2.4) at risk of SI Not associated with sex, age at diagnosis, time since diagnosis, type of cancer therapy, recurrence, or second malignancy (chronic conditions, pain and poor global health rating).	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Mody et al. **Twenty-five-year follow-up among survivors of childhood acute lymphoblastic leukemia: a report from the Childhood Cancer Survivor Study. 2008**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1.1.1970-31.12.1986** **Years of follow-up:** **Mean 21.2 years (range 5-35 years)** **Country:** **USA** **Study center:** **26 institutions in USA & Canada (CCSS)** **Measurement tool:** **Cfr Hudson et al, 2003** **BSI-18-item : Cutoff T-score≥63 was used. Participants who had a significant elevation on any of the 3 symptom specific subscales were classified as having adverse mental health.**	**Sample size:** 4151 survivors, 1939 (46.7%) female, 2212 (53%) male (5778 eligible) For mental health analysis n=2599 (>18 years) including n=735 (17.7% relapsed) **Diagnoses:** ALL **Age at diagnosis:** Median=4 years (range 0-21 years) **Age at study:** Median=26 years **Controls:** Siblings (n=3899) For mental health analysis n=3083	Chemotherapy: Anthracyclines, n=1782 (48.7%); Alkylating, n=2006 (54.9%) Both anthracyclines plus alkylating, n= 1444 (39.5%) Radiation: Cranial/craniospinal: n=2266 (92.2%) Total body irradiation, n=134 (5.5%) Other sites: n=62 (2.3%) Bone marrow transplant: n=205, (4.9%) (numbers may not add up to the total number of subjects due to missing values)	**Risk:** Increased risk for adverse mental health in survivors (vs. siblings): Survivors: n=389 (15.0%) Siblings: n=302 (9.8%) OR for adverse mental health: Survivors (Ref. siblings) OR=1.7* (95%CI:1.4-2.0, p<0.001) OR for adverse mental health: Nonrelapsed, nonirradiated survivors (vs. siblings) OR=1.6* (95%CI:1.1-2.1, p=0.1*) *adjusted for age at interview, age at diagnosis, sex, ethnicity, cumulative anthracycline dose, alkylator score	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Zeltzer et al. **Psychosocial outcomes and health-related quality of life in adult childhood cancer survivors: a report from the childhood cancer survivor study. 2008**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1970-1986** **Years of follow-up:** **Mean survival time 23 (range 15-34) years** **Country:** **USA and Canada** **Study center:** **Multi-centre 26 sites (CCSS)** **Measurement tool:** **BSI-18: T-scores ≥ 63 classified as poor outcome** **SF-36: 1 SD below mean (T-score ≤ 40) on MH or MCS classified as poor**	**Sample size:** 7147 survivors **Diagnoses:** Acute lymphoblastic leukemia: n = 2090, 29.2% Acute myeloid leukemia: n = 170, 2.4% Other leukemia: n = 146, 2.0% Astrocytomas: n = 548, 7.7% Medulloblastoma, PNET: n = 195, 2.7% Other CNS tumors: n = 143, 2.0% Hodgkins disease: n = 955, 13.4 % Non-Hodgkins lymphoma: n = 533, 7.5% Wilm's tumor: n = 671, 9.4% Neuroblastoma: n = 448, 6.3% Soft tissue sarcoma: n = 631, 8.8% Ewing's sarcoma: n = 194, 2.7% Osteosarcoma: n = 395, 5.5% Other bone: n = 28, 0.4% **Age at diagnosis:** Median age at diagnosis: 7 yrs 0-3 yrs: n = 2211, 30.9% 4-9 yrs: n = 2137, 29.9% 10-14 yrs: n = 1497, 20.9% 15-20 yrs: n = 1302, 18.2% **Age at study:** Median age: 32 yrs 18-24 yrs: n = 1482, 20.7% 25-34 yrs: n = 3169, 44.3% 35+ yrs: n = 2496, 34.9% **Controls:** 388 siblings of survivors from random sample of sibling pool Siblings median age: 33 yrs	**Chemotherapy:** Yes: n = 5326, 74.5% No: n = 1411, 19.7% Medical record unavailable: n = 410, 5.7% **Radiation** Cranial: n = 2057, 28.8% Other than cranial: n = 2415, 33.8% None: n = 2265, 31.7% Medical record unavailable: n = 410, 5.7%	**Risk:** Frequencies and percents of survivors with poor outcomes: Depression subscale: n=868 (12.1%) Anxiety subscale: n=589 (8.2%) Somatization: n=980 (13.7%) Global status index: n=752 (10.5%) <u>BSI-18</u> **Survivors referenced against general population (adjusted for age and sex) and siblings (adjusted for age, sex, and intrafamilial correlation):** mean T-scores (95% CI) • Depression subscale: Survivors 49.33 (49.11-49.55) ; US Population 50.00 (49.44-50.56); Siblings 47.46 (46.50-48.42, p_{adj}<0.003) • Anxiety subscale: Survivors 47.87 (47.65-48.09); US Population 50.00 (49.44-50.56, p_{adj}<0.003); Siblings 46.36 (45.46-47.26, p_{adj}<0.003) • Somatization subscale: Survivors 49.03 (50.19-50.59); US Population 50.00 (49.44-50.56); Siblings 47.80 (46.92-48.68, p_{adj}<0.003) • Global status index: Survivors 49.17 (48.93-49.41); US Population 50.00 (49.44-50.56), Siblings 46.64 (45.64-47.64, p_{adj}<0.003) "Compared with siblings, survivors reported more symptoms of global distress, depression, anxiety, and somatization, although scores are lower (better) than population norms for both groups."	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☒Yes/☐no/ ☐n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:** BSI scores not transposed to DSM-IV; e.g. Matcham et al. (2016) suggests SF-36 MH and MCS can predict DSM-IV diagnoses at a similar cut-off

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Schultz et al. **Behavioral and social outcomes in adolescent survivors of childhood cancer: a report from the childhood cancer survivor study. 2007**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1.1.1970-31.12.1986** **Years of follow-up:** **≥ 5 years post diagnosis, mean 11.5 years from diagnosis** **Country:** **USA** **Study center:** **26 institutions in USA & Canada (CCSS)** **Measurement tool:** **Behavior Problem Index (BPI):** **clinically significant was ≥1.3 SD above comparison sibling group's mean score in each domain: depression/anxiety, headstrong, peer conflict/social withdrawal, attention deficit, antisocial and social competence.**	**Sample size:** 2979 survivors **Diagnoses:** leukemia (n= 1345, 45.2%), CNS cancer (n= 376, 12.6%), Hodgkin's disease (n= 39, 1.3%), non-Hodgkin's lymphoma (n= 132, 4.4%), Wilms' tumor (n= 474, 15.9%), neuroblastoma (n= 382, 12.8%), soft tissue sarcoma (n= 200, 6.7%), bone cancer (n= 31, 1.0%) **Age at diagnosis: yrs(SD)** Mean (M): 3.2 (2.9) Range: 0-9.9 **Age at study:** M = 14.8 (1.6) Range: 12-17 **Controls:** 649 siblings M = 14.9 (1.6) Range: 12-17	Overall treatment Surgery only: n= 215 (7.2%) Chemotherapy: n= 1015 (34.1%) Radiation: n= 206 (6.9%) Chemotherapy & radiation: n= 1236 (41.5%) No surgery, chemotherapy, or radiation: n= 5 (0.2%) Unknown: n= 9 (0.3%) CNS treatment Neither IT Mtx or cranial radiation: n= 1369 (46.0%) IT Mtx: n= 739 (24.8%) Cranial radiation: n= 232 (7.8%) Both IT Mtx and cranial radiation: n= 639 (21.4%) Disfigurement: Head/neck/scalp/eye: n = 663 (22.3%) Limb: n = 392 (13.2%) Chest or abdomen: n = 1122 (37.7%)	**Risk:** % in clinically significant range, risk ratio (RR), and 99% CI presented in comparison to sibling sample – adjusted for sex, current age, race/ethnicity and annual household income (Table 4) In overall survivor sample Depression/anxiety: 17.7%; RR = 1.5; 99% CI, 1.1-2.1 Headstrong: 14.6%; RR = 1.3; 99%CI, 1.0-1.8 Attention deficit: 20.6%; RR = 1.4; 99% CI, 1.1-1.9 Peer conflict/social withdrawal: 14.4%; RR = 1.2; 99% CI, 0.9-1.6 Antisocial: 22.8%; RR = 1.7; 99% CI, 1.3-2.2 Social Competence: 19.8%; RR = 1.3; 99% CI, 1.0-1.6	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Schrag et al. **Stress-related mental disorders in childhood cancer survivors. 2008**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: ☐ **Cross-sectional study** ☐ **Case-control study** ☒ **Cohort study** ☐ **Qualitative study (→ exclude!)** ☐ **Systematic/narrative review (→ exclude!)** ☐ **RCT** ☐ **Other: (specify!)** **Treatment era:** **n.a.** **Years of follow-up:** **"at least one year of survival", more detailed information not available** **Country:** **USA** **Study center:** **South Carolina division of the Department of Health and Human Services; South Carolina Central Cancer Registry** **Measurement tool:** **SRMD diagnosis**	**Sample size:** N=390, 170 (43.59%) female, 219 (56.15%) male **Diagnoses:** Hematologic n=180 Bone or joint n=21 Brain, CNS, eye, or orbital n=72 Other tissues n=117 **Age at diagnosis:** 0-5 years: n=175 6-11 years: n=116 12-15 years: n=99 **Age at study:** 0-5 years: n=175 (44.87%) 6-11 years: n=118 (30.26%) 12-15 years: n=97 (24.87) **Controls:** Children with no history of malignancy (n=1329)	Chemotherapy only n=140 Any radiation, no BMT n=87 BMT n=13 None in Medicaid records n=150	**Risk:** Survivors vs. controls: Any stress-related mental disorder(SRMD): n=47/390 (12.05%) vs. n=53/1329 (3.99%) Posttraumatic stress disorder: n=3 (0.77%) vs. n=8 (0.60%) Acute stress disorder: n=1 (0.26%) vs. 0 (0%) Adjustment disorders: n=45 (11.54%) vs. n=47 (3.54%) None of these: n=343 (87.95%) vs. n=1276 (96.01%) The cumulative incidence of SRMD diagnoses was 18.60% (95% CI=12.37-24.83) among cancer survivors and 7.31% (95% CI=5.02-9.60) in children without cancer (p<0.0001). Adjusting for previous mental disorder diagnosis, race, and sex, a diagnosis of pediatric cancer significantly increased the risk for SRMD (HR=3.00, 95%CI:2.02-4.45). No stat.sign. interaction between surviving pediatric cancer and previous mental disorders (p=0.95, data not shown)	**Quality assessment:** 1. Is the study group representative? ☐Yes/☐no/ ☒unclear 2. Is the follow-up adequate? ☐Yes/☐no/ ☒unclear 3. Are the outcome assessors blinded? ☐Yes/☒no/ ☐n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Recklitis, Lockwood et al. **Suicidal ideation and attempts in adult survivors of childhood cancer. 2006**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **n.a.** **Years of follow-up:** **Mean time since diagnosis 18.3 years (SD 7.9)** **Country:** **USA** **Study center: Multidisciplinary Survivor clinic** **Measurement tool:** • **Short Form-36 (higher scores indicate better functioning)** • **Beck Depression Inventory (BDI)(total score of ≥16 = depressed)** • **Suicide item from the Symptom Checklist-90 Revised (question 15)** • **Beck Scale for Suicidal Ideation**	**Sample size:** N=226 (126 female, 100 male) **Diagnoses:** Lymphomas 32.7% Leukemias 32.3% Sarcomas 14.2% Wilm's tumor 7.5% Other solid tumors such as (neuroblastoma, germ cell tumors) 13.3% **Age at diagnosis:** Mean: 10.08 years (SD 5.47) **Age at study:** Mean: 28.38 years (SD 7.91, range 18 to 64) **Controls:** n.a.	Cranial radiation 34.07%	**Risk:** N=29 participants (12.83%; 95%CI: 8.90%-18.07%) reported suicidality. N=19 participants (8.41%, 95%CI: 5.27%-13.02%) reported suicidal ideation alone One participant (0.44%; 95%CI: 0.02%-2.82%) reported past attempts without current ideation N=9 participants (3.98%; 95%CI: 1.95%-7.67%) reported both current ideation and past attempts. N=15 participants reported suicidal ideation on both the SCL-90-R and the BDI. N= 9 participants reported suicidality on the BDI only N=5 reported suicidality on the SCL-90-R only Complete data from 200 participants.	**Quality assessment:** 1. Is the study group representative? ☐Yes/☒no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Zebrack et al. **Psychological distress in long-term survivors of solid tumors diagnosed in childhood: a report from the childhood cancer survivor study. 2007**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1.1.1970-31.12.1986** **Years of follow-up:** **Years since diagnosis** **Mean: 16.3, SD 4.8 (range 5-29)** **Country:** **USA & Canada** **Study center:** **25 institutions in USA & Canada** **Measurement tool:** **BSI-18: 'positive risk' for psychological distress = T-scores ≥ 63 for any 2 of 3 sub-scales**	**Sample size:** 2778 survivors of 'solid' tumours **Diagnoses:** 'Solid tumours' including renal tumours, soft tissue sarcomas, bone tumours n=985 (36%) **Age at diagnosis:** ≤20 years **Age at study:** Mean: 27.1 years, SD 6.0 (range 18-56) **Controls:** 2925 sibling controls Mean: 29.5 years, SD 7.2 (range 18-56)	• Chemotherapy: n=2016 (83%) • combined alkylating agent + anthracyclines: n=889 (37%) • Radiation therapy: n=1329 (55%) • Limb amputation: n=486 (20%)	**Risk:** 8% of survivors, compared to 5% of siblings, fit the criteria for "positive risk" for psychological distress The overall sample mean GSI was lower (score of 2 or less) for both survivors (46%) and siblings (51%), as compared to community norms. And for each of the three subscales depression, anxiety and somatization 71-78% of survivors and 76-85% of siblings scored 2 or less. Global status index: Survivors 46.3; community norm 50.0; Siblings 44.8 (survivors vs. siblings p<0.001) Depression subscale: Survivors 47.7; community norm 50.00; Siblings 46.4 (survivors vs. siblings p<0.001); Anxiety subscale: Survivors 46.2; community norm 50.00; Siblings 45.4 (survivors vs. siblings p<0.001); Somatization subscale: Survivors 47.6; community norm 50.00; Siblings 46.2 (survivors vs. siblings p<0.001) On multivariate analyses, once accounting for statistically significant sociodemographic, SES, health status variables, survivors scored significantly higher (P<0.05) than siblings on GSI, which was accounted for by a statistically higher somatic distress score (P<0.05), but no statistically significant differences on depression and anxiety subscales.	**Quality assessment:** 1. Is the study group representative? ☐Yes/☒no/☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/☐unclear **Remarks:** BSI scores not transposed to DSM-IV

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?

Recklitis, Parsons et al. **Factor structure of the brief symptom inventory--18 in adult survivors of childhood cancer: results from the childhood cancer survivor study. 2006**

Study Design Treatment era Years of follow-up	Participants	Treatment	Main outcomes	Quality assessment Remarks
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1.1.1970-31.12.1986** **Years of follow-up:** **Time since diagnosis:** **Median: 17 years (range 6-29)** **Country:** **USA and Canada** **Study center:** **Childhood cancer survivor study. 25 institutions USA and Canada** **Measurement tool:** **BSI-18** **Case definition: GSI T-score≥63**	**Sample size:** N=8945, 4233 (47.3%)female, 4712 (52.7%) male **Diagnoses:** Leukemias 29.4% Non-hodgkin lymphomas 18.2% Hodgin's disease 12.3% Bone tumors 11.0% Soft tissue sarcoma 9.7% Central nervous system tumors 9.2% Kidney tumors 6.3% Neuroblastomas 4.0% **Age at diagnosis:** Less than 21 years at diagnosis; n.a. in detail **Age at study:** Median of 26 years (range 18-48 years) 18-22y: 26.4% 23-26y: 24.4% 27-34y: 26% 35+y: 13.2% **Controls:** - Community norms - Adult oncology groups	n.a.	**Risk:** "Compared with their gender-specific community norms, survivors' mean T scores were all significantly smaller than the normative mean of 50, indicating that survivors reported less symptom distress. Though significant, the magnitude of the differences between survivor and community means were small, […]" **T-scores** Men Women Depression 48.3 (SD 9.20) 48.1 (SD 9.50) Anxiety 46.1 (SD 8.80) 47.1 (SD 9.50) Somatization 46.8 (SD 7.30) 48.7 (SD 8.80) GSI 46.6 (SD 9.70) 46.9 (SD 10.60) "Compared with the 10% [cases with psychological distress] that would be expected on the basis of the community norms, a significantly smaller proportion of survivors, 7.4% (348 of 4712) of men and 9% (380 of 4233) of women, were classified as having significant psychological distress (men: z= -5.98, p<0.001; women: z= -2.22, p<0.05)." "The childhood cancer survivors' average GSI raw score of 6.18 was significantly lower than the score of 8.42 reported in adult cancer patients in another study (p<0.001)." Caseness (BSI-18 GSI T-score≥57 survivors vs. adult cancer patients: Survivors: 18.9% (1687 of 8945) Adult cancer patients: 22.3% (344 of 1543; p<0.01) → Survivors reported less distress than cancer patient group.	**Quality assessment:** 1. Is the study group representative? ☐Yes/☒no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?

Langeveld et al. **Posttraumatic stress symptoms in adult survivors of childhood cancer. 2004**

Study Design Treatment era Years of follow-up

Study Design:
☒ Cross-sectional study
☐ Case-control study
☐ Cohort study
☐ Qualitative study (→ exclude!)
☐ Systematic/narrative review (→ exclude!)
☐ RCT
☐ Other: (specify!)

Treatment era:
5-33 years ago

Years of follow-up:
33 years ago

Country:
The Netherlands

Study center:
Academic medical centre

Measurement tool:
Impact of Events Scale (IES)
- **Subscales of intrusion and avoidance**
- **15 items**
- **Score of 8-25=”moderate’, 26+=”severe”**

Participants

Sample size:
500

Diagnoses:

Leukemia or Non-Hodgkins lymphoma without CRT: n = 136, 27%

Leukemia or Non-Hodgkins lymphoma with CRT: n = 105, 21%

Solid tumor: n = 214, 45%

Brain/CNS tumor: n = 45, 9%

Age at diagnosis:
Median = 8 years
Range: 0-19

Age at study:
Mean = 24 years, SD = 5.1
Range: 16-49

Controls:
none

Treatment

Chemotherapy (with or without surgery): n = 226, 45%

Radiation therapy (with or without surgery): n = 40, 8%

Combination therapy (chemotherapy and radiation with or without surgery): n = 234, 47%

Main outcomes

Risk:
Post-traumatic stress symptoms:
28% (n = 137) had scores in the moderate range
12% (n = 62) had scores in the severe range

Women had higher scores than men in both the moderate range (28% females, 25% o males) and severe range (20%females, 6% males)
T-test results presented below with M (SD) presented

Scale of IES	All	Males (n=266)	Female (n=234)	p value
Intrusion	5.6 (7.3)	3.4 (5.0)	8.0 (8.7)	<0.001
Avoidance	4.7 (7.1)	3.9 (6.0)	5.7 (8.1)	0.004
Total	10.3 (13.3)	7.3 (9.90)	13.8 (15.7)	<0.001

Chi-square results with n (%)

Total of IES	All	Males (n=266)	Female (n=234)	p value
8-28	137 (28)	65 (25)	66 (28)	0.34
≥ 26	62 (12)	16 (6)	46 (20)	<0.001

Quality assessment Remarks

Quality assessment:
1. Is the study group representative?
☒Yes/☐no/☐unclear
2. Is the follow-up adequate?
☒Yes/☐no/☐unclear
3. Are the outcome assessors blinded?
☐Yes/☐no/☒n.a./☐unclear
4. Are the analyses adjusted for important confounding factors?
☒Yes/☐no/☐unclear

Remarks:

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Zebrack et al. **Psychological outcomes in long-term survivors of childhood brain cancer: a report from the childhood cancer survivor study. 2004**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **Year of diagnosis** **1970-1973: n=177 (16.1%)** **1974-1978: n=335 (30.4%)** **1979-1986: n=589 (53.5%)** **Years of follow-up:** **Not stated; survival at least 5y from diagnosis** **Country:** **USA + Canada** **Study center:** **Multicenter 25 institutions (CCSS)** **Measurement tool:** **BSI-18: main outcome was T-score ≥ 63 for GSI or any 2 of 3 sub-scales, classified as positive risk for psychological distress** **Subscales: depression, somatization and anxiety**	**Sample size:** 1101 survivors of childhood brain cancer, 507 (46%) female, 594 (54%) male **Diagnoses:** Astrocytoma/glial cell: n=714 (64.9%) PNET / Medulloblastoma: n=202 (18.3%) Other CNS: 185 (16.8%) **Age at diagnosis:** 0-4: n=186 (16.9%) 5-11: n=508 (46.1%) 12-20: n=407 (37.0%) **Age at study:** Mean 26.5y SD 5.5y Range 18-44y **Controls:** 2817 siblings of childhood cancer survivors Controls age at study Mean 29.4y SD 7.2y Range 18-56y	Chemotherapy: yes: n= 205 (21.1%) Chemotherapy: no: n=766 (78.9%) Missings: n=127 Radiotherapy • Max brain radiation dose: - 0-29 Gy: n=313 (35.1%) - 30-49 Gy: n=112 (12.6%) - ≥ 50 Gy: n=467 (52.3%) • Localisation: - Localised: n=289 5(1.6%) - Whole brain: n=280 (48.4%) - missings: n=314	**Risk:** Overall, 11% of survivors compared to 5% of sibling controls met criteria for positive risk for psychological distress. Survivors scored significantly higher on GSI (T-score 46.9 vs. 44.8 in siblings, p<0.001), depression subscale (T-score 49.1 vs. 46.5 in siblings, p<0.001), and somatic distress subscale (T-score 47.8 vs. 46.2 in siblings, p<0.001). No difference in anxiety subscale (T-score 45.9 vs. 45.4 in siblings, p=0.09). Standardized T-Scores for survivors were significantly lower than for community norms (mean 50, SD 10 for GSI and three subscales): GSI 46.9; Depression: 49.1; Somatic distress: 47.8, Anxiety 45.9	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☒Yes/☐no/ ☐n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:** Positive risk on BSI-18 was not transposed to DSM-IV criteria 180/1281 (14%) eliminated from analyses because of incomplete data, may have been more impaired

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Glover et al. **Impact of CNS treatment on mood in adult survivors of childhood leukemia: a report from the Children's Cancer Group. 2003**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1970-1986** **Years of follow-up:** **Not reported** **Country:** **USA** **Study center:** **23 institutions participating in the Children's Cancer Group (CCG)** **Measurement tool:** **Profile of mood scale (POMS) Measure of mood states (tension/anxiety, depression, anger, confusion, vigor, fatigue) where higher scores indicated greater mood disturbance. Total Mood Disturbance (TMD) scores greater than 33 labeled as mood-disturbed and lower than 33, as healthy**	**Sample size:** 555 **Diagnoses:** ALL leukemia **Age at diagnosis:** Not reported **Age at study:** 18-33 years **Controls:** n.a.	ALL therapy in CCG trials Including cranial radiation, methotrexate for many participants 1. No/ Low MTX (< 83 mg) & CRT (< 21 Gy)- 23.6% 2. High MTX (> 83 mg) & No/Low CRT- 33.7% 3. High CRT (> 21 Gy) & No/Low MTX- 32.3% 4. High CRT & MTX- 10.5%	**Risk: Elevated POM Total Mood Disturbance (TMD) Score (≥33)** Overall, 24% of the sample had elevated TMD score. By treatment group, 20.3 - 28.5% of the of the sample had elevated TMD scores: 1. No/Low MTX (< 83 mg) & CRT (< 21 Gy)- 24.1% elevated TMD score 2. High MTX (> 83 mg) & No/Low CRT- 20.3% elevated TMD score 3. High CRT (> 21 Gy) & No/Low MTX- 28.5% elevated TMD score 4. High CRT & MTX- 20.7% elevated TMD score	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☐Yes/☐no/ ☒unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Hudson et al. **Health status of adult long-term survivors of childhood cancer: a report from the Childhood Cancer Survivor Study. 2003**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1970-1986** **Years of follow-up:** **n/a** **Country:** **United States** **Study center:** **26 centres in US & Canada (CCSS)** **Measurement tool:** **BSI-18:** • **Global Severity Index** • **Depression, Anxiety, & Somatization subscales** • **T score > 63 on any of the Depression, Anxiety, or Somatization subscales classified as having "poor" or "adverse" mental health** **Cancer-related Anxiety: 1 item; Dichotomized as "Yes" (medium, a lot, very many, or extreme fears or anxiety related to cancer/treatment) versus "No" (no or small amount of fears or anxiety related to cancer/treatment**	**Sample size:** N=9535 **Diagnoses:** Leukemia: n = 2865, 30.1% CNS malignancies: n = 1186, 12.4% Hodgkin disease: n = 1666, 17.5% Non-Hodgkin lymphoma: n = 867, 9.1% Wilms tumor: n = 636, 6.7% Neuroblastoma: n = 403, 4.2% Sarcoma: n = 902, 9.5% Bone malignancy: n = 1010, 10.6% **Age at diagnosis:** M= 10.0 yrs (SD= 5.6 yrs) Range: 0.1-20.9 yrs **Age at study:** M= 26.8 yrs (SD= 6.2 yrs) Range: 18-48 yrs **Controls:** 2916 siblings	Radiotherapy • Any 5925/9535= 62.1% Chemotherapy • Any 6434/9535= 67.5% Combination • Surgery only: n = 624, 7.3% • Radiation only: n = 23, 0.3% • Chemo only: n = 340, 4.1% • Chemo+radiation: n = 959, 11.6% • Chemo+surgery: n = 1362, 16.5% • Radiation+surgery: n = 1172, 14.2% • Chemo+radiation+surgery: n = 3754, 45.5%	**"Poor" or "Adverse" Mental Health:** Reported by 17.2% survivors versus 10.2% of siblings In adjusted models, survivors were more likely than siblings to report: • Adverse mental health; Odds Ratio (OR)= 1.8 (CI: 1.6-2.1) • Global Distress OR= 2.2 (CI:1.8-2.8) • Depression OR= 1.7 (CI:1.4-2.0) • Somatization OR= 2.2 (CI:1.8-2.7) • Anxiety OR= 1.9 (CI:1.5-2.4) **Cancer-related Anxiety:** Reported by 13.2% of survivors	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?

Ross et al. Psychiatric hospitalizations among survivors of cancer in childhood or adolescence. 2003

Study Design Treatment era Years of follow-up	Participants	Treatment	Main outcomes	Quality assessment Remarks
Study Design: ☐ **Cross-sectional study** ☐ **Case-control study** ☒ **Cohort study** ☐ **Qualitative study (→ exclude!)** ☐ **Systematic/narrative review (→ exclude!)** ☐ **RCT** ☐ **Other: (specify!)** **Treatment era:** **1943 to 1990** **Years of follow-up: Follow-up started 3 years after diagnosis or January 1, 1970. They excluded the first 3 years of follow-up after cancer diagnosis. Follow-up for psychiatric admissions continued until the date of death, or December 31 1993 – Mean=14.9 years** **Country:** **Denmark** **Study center: n.a.** **Measurement tool:** **Retrospective Cancer Registry & Psychiatric Central Register. Admissions to psychiatric hospitals & primary psychiatric diagnosis (ICD-8).**	**Sample size:** 3710 **Diagnoses:** CNS tumors: 973 (26%) Leukemia: 586 (16%) Malignant lymphoma: 497 (13%) Carcinomas and other malignant epithelial neoplasms: 425 (11%) Tumor of sympathetic nervous system: 111(3%) Renal tumor: 177 (5%) Hepatic tumor: 8 (<1) Germ cell: 286 (8%) Soft-tissue sarcoma: 274 (7%) Bone tumor: 161 (4%) Retinoblastoma: 166 (4%) Other neoplasm: 46 (1%) **Age at diagnosis:** <20 years of age 0-4 years (1087), 5-9 years (656), 10-14 years (734), 15-19 years (1233) **Age at study:** Not reported **Controls:** General population data from Denmark	Not reported, aside from radiotherapy.	**Risk:** Standardized Hospitalization Ratio (SHR), 95% CI Risk of hospitalization for any psychiatric disease was higher among survivors than in the general population (SHR 1.3, 1.1-1.4), though this was largely driven by brain tumor survivors (see next table). There was increased risk of psychoses of somatic, cerebral cause (SHR 3.0, 1.8-4.7), psychiatric disorders in somatic diseases (SHR 2.5, 1.5-3.9), and psychiatric disorders in children (SHR 2.2, 0.9-4.6) among survivors. Significant increase in risk for schizophrenia and related disorders (SHR 1.6, 1.1-2.3) among survivors. No evidence to support increased risk of major depressive disorder in survivors. **Standardized hospitalization ratios during follow-up for all cancers** **Psychiatric diagnosis** — **SHR (95% CI)** All diagnoses — 1.3 (1.1–1.4) Psychoses of somatic, cerebral causes — 3.0 (1.8–4.7) Psychiatric disorders in somatic diseases — 2.5 (1.5–3.9) All other diagnoses — 1.1 (1.0–1.3) Schizophrenia and related disorders — 1.6 (1.1–2.3) All affective disorders — 0.8 (0.5–1.3) Bipolar psychoses — 0.7 (0.1–2.0) Nonreactive unipolar psychoses — 1.0 (0.5–2.0) Reactive unipolar psychoses — 1.2 (0.5–2.4) Neuroses and personality disorders — 0.6 (0.2–1.5) Other reactive psychoses — 1.6 (0.6–3.5) Other neuroses and personality disorders — 1.0 (0.7–1.4) Dementia — 1.1 (0.0–5.9) Substance abuse or alcohol — 1.0 (0.7–1.4) Psychiatric disorders in children — 2.2 (0.9–4.6) Transient maladaptation — 1.3 (0.8–1.9) Others — 1.2 (0.6–2.0)	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Zebrack et al. **Psychological outcomes in long-term survivors of childhood leukemia, Hodgkin's disease, and non-Hodgkin's lymphoma: a report from the Childhood Cancer Survivor Study. 2002**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **Diagnosed 1970-1986** **Years of follow-up:** **Years since diagnosis** **Mean 16.3 yrs (5-29), SD 4.8 yrs** **Country:** **USA & Canada** **Study center:** **25 centers** **Measurement tool:** **BSI-18: positive depressive symptoms transposed onto DSM-IV criteria for Major Depressive Episode; somatic distress ≥ 90thcentile**	**Sample size:** 5736 subset of CCSS survivors with leukemia or lymphoma **Diagnoses:** Leukemia (n=2991), Hodgkin's (n=1843) and Non-Hodgkin's Lymphoma (n=902) **Age at diagnosis:** Mean=10.1 yrs, SD=5.5 Range 0-20 **Age at study:** Survivors Mean= 26.9 yrs, SD=6.2 Range: 18-48 **Controls:** 2565 siblings of survivors	Received intensive chemotherapy (includes various protocols and cumulative doses of chemotherapeutic agents, defined by disease-specific criteria): (n=1685) 36.4% Received cranial radiotherapy: (n=1725) 40.1%	**Risk:** <u>DSM-IV Depressive symptoms</u> 5.4% of leukemia/lymphoma survivors reached the cutoff score indicative of a depressive episode, compared with 3.4% of sibling controls. This gives an overall RR = 1.6 <u>BSI-18 Somatic distress</u> 12.7% of leukemia / lymphoma survivors reached the symptomatic score for somatic distress, compared with 8.0% of sibling controls. This gives an overall RR = 1.6	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:** DSM-IV depressive symptoms, but non-standardised cutoffs

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?

Barakat et al. Families surviving childhood cancer: a comparison of posttraumatic stress symptoms with families of healthy children. 1997

Study Design Treatment era Years of follow-up	Participants	Treatment	Main outcomes	Quality assessment Remarks
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era: n.a** **Years of follow-up: n.a** **Country: USA** **Study center: Two different sites** **Measurement tool:** **Child factors** • **Impact of Event Scale (IES)- assessment of response to traumatic stress** • **Posttraumatic Stress Disorder Reaction Index – assessment of post-traumatic stress total scores are moderate (25-39) and severe (>40)** • **Assessment of Life Threat and Treatment Intensity Questionnaire (ALTTIQ) – assessed past life threat from cancer** • **Revised Children's Manifest Anxiety Scale (RCMAS)- assessed child trait anxiety** • **Trauma Symptom Checklist for Children (TSC) – assessed posttraumatic stress, dissociation, and anger**	**Sample size:** 309 survivors, 309 mothers, 213 fathers **Diagnoses:** ALL 38% Wilms tumor 10% Sarcoma 9% Acute nonlymphoblastic leukemia 8% Lymphoma 8% Hodgkins disease 6% Other cancers 21% including neuroblastoma and retinoblastoma **Age at diagnosis:** Mean = 5.83 years, range 1-17 years. **Age at study:** Range 8-20 years Mean = 13.53 years (SD=3.37) **Controls:** 219 healthy children, 211 mothers, and 114 fathers.	Treatment intensity was rated on a 3-point scale from mild (e.g., surgery only) to severe (e.g., bone marrow transplant) by a pediatric oncologist.	**<u>Comparison between survivor's scores and comparison children</u>** MANCOVA for omnibus differences was nonsiginficant, including covariates of child age, household income, mother-father education, and race. **Children's score** / **Survivors Mean** / **Comparison Mean** / **F** / **Effect size** **IES-Intrusion** 5.34 4.92 2.60 .06 **IES-Avoidance** 6.81 6.87 2.18 .00 **IES-Total score** 12.15 11.80 2.65 .03 **RCMAS-Physical anxiety** 9.59 8.97 7.21 .19 **RCMAS-Worry** 9.71 9.35 5.78* .11 **RCMAS-Social/ concentration** 14.89 15.02 0.85 .01 **RCMAS-Total anxiety** 49.50 47.58 7.99* .16 **Reaction Index** 13.28 13.88 1.16 .05 **TSC-Post-traumatic stress** 6.65 6.85 1.49 .04 **TSC-dissociation** 5.96 5.82 3.46* .03 **TSC-Anger** 7.16 7.11 1.48 .01 • p<.001 Follow-up univariate tests indicated that childhood cancer survivors themselves did not differ in post-traumatic stress symptoms (PTSS) compared to their healthy counterparts. Child anxiety (RCMAS worry and total) and scores of TSC-dissociation did differ significantly, with child age $F(11, 436) = 6.43$, $p < .001$, serving as a significant covariate (older age with greater symptoms). For cancer survivors, 2.6% had scores of post-traumatic stress in the severe range, compared with 3.4% in the comparison group. For cancer survivors, 12.1% had post-traumatic stress scores in the moderate range, compared to 12.3% of the comparison group. There were no significant differences in the percentages of children falling in each range.	**Quality assessment:** 1. Is the study group representative? ☐Yes/☐no/ ☒unclear 2. Is the follow-up adequate? ☐Yes/☐no/ ☒unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:** 56% response rate for participants who were cancer survivors and 39% for healthy controls

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?

Zeltzer et al. **Comparison of psychologic outcome in adult survivors of childhood acute lymphoblastic leukemia versus sibling controls: a cooperative Children's Cancer Group and National Institutes of Health study. 1997**

Study Design Treatment era Years of follow-up

Study Design:
☒ Cross-sectional study
☐ Case-control study
☒ Cohort study
☐ Qualitative study (→ exclude!)
☐ Systematic/narrative review (→ exclude!)
☐ RCT
☐ Other: (specify!)

Treatment era:
1970-1990

Years of follow-up:
Survivors were at least 2 yrs after diagnosis; 95% at least 5 yrs after diagnosis

Country:
USA

Study center:
Multi-center 23 sites of the Children's Cancer Group

Measurement tool:
Profile of Mood States-(POMS)-higher scores indicate more affective disturbance including anxiety/tension, depression, anger, confusion, vigor, and fatigue.

Participants

Sample size:
580 survivors of childhood ALL who completed the interview and POMS

Diagnoses:
ALL (100%)

Age at diagnosis:
< 20y

Age at study:
≥ 18y
Mean=22.6 yrs
SD=3.2 yrs

Controls:
396 siblings who completed the interview and POMS

Survivors were younger than controls (mean=25.2y; SD=4.8).

Treatment

Not reported

Main outcomes

Risk:
Per t-tests, survivors of childhood ALL had higher total scores, tension/anxiety, depression, anger, and confusion.
Per regression analyses controlling for age, sex, and survivor-sex interactions, survivors of childhood ALL again had higher total scores, tension/anxiety, depression, anger, and confusion.

However, survivors' total POMS were noted to not be as high as in McNair et al.'s (1971) sample of psychiatric outpatients

Comparisons to sibling controls

POMS Scale	*Survivor Mean*	*Sibling Mean*	*t*-test	*p*	*F*	*p*
Total	17.90	12.52	3.61	<0.001	4.35	<0.02
Tension/ Anxiety	7.17	6.08	2.84	0.005	3.92	<0.02
Depression	8.95	6.97	3.62	<0.001	4.41	<0.02
Anger	9.62	8.09	3.10	0.002	3.51	<0.03
Vigor	19.19	19.67	-1.32	0.19	2.86	0.06
Fatigue	7.87	8.36	-1.31	0.19	1.61	0.20
Confusion	3.67	2.59	3.91	<0.001	3.98	<0.02

Two-tail t-test with equal variances assumed
F reflects regression analyses predicting POMS total and subscale scores from survivor status, controlling for age, sex, and survivor-sex interactions

Quality assessment Remarks

Quality assessment:
1. Is the study group representative?
☒Yes/☐no/☐unclear
2. Is the follow-up adequate?
☒Yes/☐no/☐unclear
3. Are the outcome assessors blinded?
☒Yes/☐no/☐n.a./☐unclear
4. Are the analyses adjusted for important confounding factors?
☒Yes/☐no/☐unclear

Remarks:
Cutoffs for poor outcomes were not defined or reported. There was a significant difference between siblings and survivors on age.

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Seitz et al. **Posttraumatic stress, depression and anxiety among adult long-term survivors of cancer in adolescence. 2010**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **n.a.** **Years of follow-up:** **Responders: mean 13.68 years ± SD 6.02 years** **Country:** **Germany** **Study center:** **n.a.** **Measurement tool:** • **Posttraumatic Stress Diagnostic Scale (PDS): A clinically relevant questionnaire score was achieved when all six DSM-IV diagnosis criteria (A–F) were met.** • **Hospital Anxiety and Depression Scale (HADS): a score of 11 or higher indicates a probable presence of an anxiety or mood disorder and is thus clinically relevant** • **Expert System for Diagnosing Mental Disorders DIA-X/M-CIDI: section D 'Anxiety Disorders', section E 'Mood Disorders' and section N 'PTSD'**	**Sample size:** N=820 (N=202 for clinical interviews) **Diagnoses:** Lymphoma: n=250 (30.5%) Leukaemia: n=158 (19.3%) Malignant bone tumors: n=174 (21.2%) CNS: n=78 (9.5%) Other: n=160 (19.5%) **Age at diagnosis:** Mean 15.78 years ± 0.89 years (SD) **Age at study:** Mean 30.44 years ± 6.05 years (SD) **Controls:** N=1027 (N=140 for clinical interviews) (recruited through survivors (friends) and snowball-system) Age at study: Mean 31.52 years ± 7.00 years (SD) N=855: normative age-matched	Surgery: n=589 (71.8%) Chemotherapy n=742 (90.5%) Radiation n=474 57.8%) Other n=70 (8.5%)	More survivors than controls had clinically relevant scores (HADS or PDS) for symptoms of posttraumatic stress, depression or anxiety: At least one clinically relevant symptom in 22.4% (n= 184) of the survivors compared to 14.0% (n= 144) in the healthy controls (p<0.001). Survivors: 13.9% in one, 5.9% in two, 2.7% in all three conditions at the same time. Controls: 10.6% in one, 3.1% in two, 0.3% in three conditions at the same time In a logistic regression the effect of group (survivors versus control) remained significant for symptoms of PTSD (OR 3.26,95% CI 2.25–4.74,p< .001), depression (OR 1.69, 95% CI 1.01–2.81,p= 0.045) and anxiety (OR 1.657, 95% CI 1.16–2.12,p= 0.004) after statistical control for sex, age and education. Posttraumatic stress: Males: 10.5% of survivors vs. 2.9% of controls reported clinically relevant symptoms of PTSD (p<0.001) Females: 18.0% of survivors vs. 5.4% of controls reported clinically relevant symptoms of PTSD (p<0.001) Clinical interview: PTSD was diagnosed more often in survivors (5.7% (n= 25) versus controls (2.1% (n= 11), p= 0.004; OR 2.79; 95%CI 1.36-5.73). Depression: Males: 5.0% of survivors vs. 3.6% of controls reported clinically relevant symptoms of depression (n.s.) Females: 5.8% of survivors vs. 2.8% of controls reported clinically relevant symptoms of depression (p<0.05) Clinical interview: 14.9% (n= 65) of survivors fulfilled the diagnostic criteria for a depressive mood disorder (vs. 9.3% (n= 48) of controls; p= 0.008; OR 1.70; 95% CI 1.15-2.53). Anxiety: Males: 10.0% of survivors vs. 6.5% of controls reported clinically relevant symptoms of anxiety (n.s.) Females: 19.2% of survivors vs. 11.4% of controls reported clinically relevant symptoms of anxiety (p<0.001) Clinical interview: anxiety disorders were found in 16.5% (n= 72) of survivors and were significantly more common than in controls 11.0% (n= 57, p= 0.015; OR 1.59; 95%CI 1.09–2.31).	**Quality assessment:** 1. Is the study group representative? ☐Yes/☒no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

	reference group for HADS			

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
De Laage et al. **Screening for psychological distress in very long-term adult survivors of childhood cancer. 2016**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **n.a.** **Years of follow-up:** **Mean time since the diagnosis 31.5 years (SD = 9.1 years; range: 8.8–56.1 years)** **Country:** **France** **Study center:** **Long-Term Follow-up Clinic (LTFUC) for childhood cancer survivors at Institut Gustave-Roussy and Institut Curie** **Measurement tool:** • **Brief Symptom Inventory-18 (BSI-18): gender-specific cutoff score to identify patients who experience clinically significant distress: male score ≥10, female score ≥13** • **Impact of Event Scale (IES): score between 8 and 25 to consider that a person is at risk for developing PTSD and a score of 26 or more to indicate that a person is unable to cope with the impact of the event and needs professional help** • **Mini-International Neuropsychiatric Interview (MINI): MINI data of the survivors were compared with the**	**Sample size:** N=348 **Diagnoses:** Hodgkin: n=45 Sarcoma: n=93 Nephroblastoma: n=59 Neuroblastoma: n=50 LNH: 36 CNS tumor: n=33 Others: n=32 **Age at diagnosis:** Mean age at cancer diagnosis 7 years (SD = 5.1 years; range: 0.0–18.0 years) **Age at study:** Mean 38.5 years (SD = 8.5 years; range: 18.1–65.8 years) **Controls:** French norm population using the Mental Health in General Population (MHGP) database derived from a representative national survey of the French adult population (N = 36,105)	Surgery: n=284 Chemotherapy n=313 Radiation n=235	Brief symptom Inventory-18: BSI-18 GSI: Mean 10.7 (SD 10.6) BSI-18 depression: Mean 3.3 (SD 4.3) BSI-18 anxiety: Mean 3.8 (SD 4.2) BSI-18 somatization: Mean 3.6 (SD 4.2) Prevalence: 35.3% of survivors reported clinically significant distress (male score ≥10, female score ≥13) Impact of event scale: IES: Mean 11.0 (SD 13.5) IES intrusion: Mean 5.6 (SD 7.5) IES avoidance: Mean 5.8 (SD 8.3) Prevalence: 15.2% of survivors reported severe IES score (≥26); 27.8% reported moderate IES scores (8-25) → 43% had a significant IES score (≥8) MINI: Major depressive disorder: 21.92% (expected: 11.03%, p<0.0001 vs. French general population) Dysthimia: 5.98% (expected: 2.39%, p<0.0001 vs. French general population) Panic disorders: 6.54% (expected: 4.65%, p<0.05 vs. French general population) Generalized anxiety disorders: 19.51% (expected: 13.49%, p<0.01 vs. French general population) Agoraphobia: 4.27% (expected: 2.13%, p<0.0001 vs. French general population) Suicide ideation: 5.85% (expected: 13.6%, p<0.0001 vs. French general population)	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

French norm population using the Mental Health in General Population (MHGP) database derived from a representative national survey of the French adult population (N = 36,105)				

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?

Brinkman et al. **Alcohol consumption behaviors and neurocognitive dysfunction and emotional distress in adult survivors of childhood cancer: A report from the Childhood Cancer Survivor Study. 2019**

Study Design Treatment era Years of follow-up	Participants	Treatment	Main outcomes	Quality assessment Remarks
Study Design: **☐ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1970-1986** **Years of follow-up:** **≥ 5years** **Three timepoints:** **Baseline, Follow-up 2, Follow-up 4** **Country:** **USA and Canada** **Study center:** **Multi-site (CCSS)** **Measurement tool:** • **BSI-18: T-score of ≥63 defined as distress** • **Posttraumatic Stress Diagnostic Scale (PDS): at least one re-experiencing symptom, at least three avoidance**	**Sample size:** N=4484 survivors **Diagnoses:** Leukemia 1353 (30.2%) CNS tumor 453 (10.1%) Hodgkin lymphoma 874 (19.5%) Non-Hodgkin lymphoma 382 (8.5%) Wilms tumor 290 (6.5%) Neuroblastoma 165 (3.7%) Soft tissue sarcoma 456 (10.2%) Bone tumors 511 (11.4%) **Age at diagnosis:** <21 years Mean 10.5 years (SD 5.6) **Age at study:** >18 years at baseline Baseline: Mean 27.2 years (SD 6.2) Follow-up 2: Mean 34.8 years (SD 6.1) Follow-up 4: Mean 39.5 years (SD 6.0) **Controls:** N=1651 siblings	Radiation: None n=1240 (29.9%) Non-cranial n=1435 (34.6%) ≤20Gy Cranial n=523 (12.6%) >20Gy Cranial n=946 (22.8%) Intravenous Methotrexate: Yes n=791 (19.1%) No n=3359 (80.9%) No. of intrathecal injections: None n=2819 (66.7%) 1 n=1052 (24.9%) ≥2 n=355 (8.4%)	"Compared with siblings survivors reported a higher prevalence of depressive (P < 0.001, somatic (P < 0.001), and posttraumatic stress symptoms (P < 0.001)." Survivors: n, %; Siblings: n, %; p-value Emotional distress Depression[a]: 474, 10.6, 106, 6.2, <0.001 Anxiety[a]: 296, 6.6, 83, 4.9, 0.010 Somatization[a]: 602, 13.5, 109, 6.4, <0.001 Posttraumatic stress[b,c]: 696, 16.8, 10, 4.0, <0.001 [a]Impairment defined as level of symptoms above the 90th percentile of the reference group. [b]Impairment defined as ≥1 re-experiencing symptom, ≥3 avoidance symptoms, and ≥2 arousal symptoms. [c]Data only available for 248 siblings. Unclear whether this data is from Baseline survey, Follow-up 2 or Follow-up 4.	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/☐unclear 2. Is the follow-up adequate? ☐Yes/☒no/☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/☐unclear **Remarks:** Longitudinally persisting distress (T-score ≥63 at baseline, follow-up 2 and follow-up 4), and/or increasing emotional distress (non-significant distress at baseline (T-score <63) that increased at follow-up 2 or follow-up 4

symptoms and at least two arousal symptoms, with or without functional impairment was defined as positive endorsement of PTSS				for any of the three BSI subscales).

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Zheng et al. **Long-Term Psychological and Educational Outcomes for Survivors of Neuroblastoma: A Report from the Childhood Cancer Survivor Study. 2018**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☐ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1970-1999** **Years of follow-up:** **≥5 years from diagnosis** **Country:** **USA and Canada** **Study center:** **Multi-site (CCSS)** **Measurement tool:** • **Behavior Problem Index (BPI), parent reported: higher scores indicate worse behavioral symptoms; impairment defined as beyond the highest 10th percentile of age-matched siblings controls**	**Sample size:** N=859 **Diagnoses:** Neuroblastoma n=859 **Age at diagnosis:** <1 years: n=534 (62.2%) 1-1.99 years: n=184 (21.4%) 2-4.99 years: n=123 (14.3%) ≥5 years: n=18 (2.1%) **Age at study:** <18 years at baseline survey: 8-11 years: n=157 (18.3%) 12-13 years: n=206 (24.0%) 14-15 years: n=250 (29.1%) 16-17 years: n=246 (28.6%) **Controls:** N=872 siblings	Surgery only n=259 (32.8%) Surgery and chemotherapy n=292 (37.0%) Surgery and radiation n=59 (7.5%) Surgery, chemotherapy, and radiation n=163 (20.6%) None/other combinations n=17 (2.1%)	"Compared with siblings, survivors had a greater proportion impaired in every domain of the BPI (Fig. 2), including anxiety/depression (P=.003), attention deficit (P<.001), peer conflict/social withdrawal (P<.001), headstrong behavior (P<.001), and antisocial behavior (P=0.01)." Percent impairment for the different BPI Domains is displayed in Figure 1. The percent impairments for the different BPI Domains are not reported in numbers, and it is not possible to read the correct prevalence off from Figure 1.	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☐n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Dixon et al. **Racial and Ethnic Disparities in Neurocognitive, Emotional, and Quality of Life Outcomes in Survivors of Childhood Cancer: A report From the Childhood Cancer Survivor Study. 2019**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: ☐ **Cross-sectional study** ☐ **Case-control study** ☒ **Cohort study** ☐ **Qualitative study (→ exclude!)** ☐ **Systematic/narrative review (→ exclude!)** ☐ **RCT** ☐ **Other: (specify!)** **Treatment era:** **Diagnosed from 1970-1999** **Years of follow-up:** **Not stated; survival at least 5y from diagnosis** **Country:** **US & Canada** **Study center: Multicenter, 31 institutions (CCSS)** **Measurement tool:** • **Brief Symptom Inventory-18: depression, anxiety, somatization subscales: higher scores indicate more distress; scores were reported as standardized T-scores with a general population mean ± SD score of 50 ± 10**	**Sample size:** 13'708 CCS non-Hispanic white: NHW n=12'287 (89.6%) non-Hispanic black: NHB n=600 (4.4%) Hispanic n=821 (6%) **Diagnoses:** Acute lymphoblastic leukemia n=3216 (33.0%) Acute myeloid leukemia n=421 (3.1%) Other leukemia n=118 (0.9%) Astrocytoma n=1279 (9.4%) Medulloblastoma, PNET n=468 (3.5%) Other CNS tumors n=331 (2.4%) Hodgkin lymphoma n=1569 (11.6%) Non-Hodgkin lymphoma n=992 (7.3%) Kidney tumors n=1097 (8.1%) Neuroblastoma n=864 (6.4%) Soft-tissue sarcoma n=919 (6.8%) Ewing sarcoma n=377 (2.8%) Osteosarcoma n=575 (4.2%) Other bone tumors n=61 (0.5%) **Age at diagnosis:** Median age at dx [range] 7.2 years [0.0-21.0 years] **Age at study:** Median age at follow-up [range] 30.9 years [16.0-54.1 years] **Controls:** Random sample of CCS siblings. N=3055	Cranial radiation, maxTD in Gy None: n=7902 (70.3%) >0 to <20: n=1121 (10.5%) 20 to <30: n=969 (8.2%) 30 to <50: n=335 (2.7%) ≥50: n=1037 (8.2%) Intravenous methotrexate, g/m2 None: n=9060 (75.2%) <4.3: n=1265 (11.7%) ≥4.3: n=1094 (13.2%) Intrathecal methotrexate, mg/m2 None: n=7756 (62.6%) <230: n=2602 (24.7%) ≥230: n=900 (12.7%) Systemic corticosteroid None: n=6697 (53.4%) Prednisone only: n=4510 (43.6%) Any dexamethasone: n=383 (3.0%)	**Risk:** Depression Within racial/ethnic groups, NHW and Hispanic survivors were more likely than siblings to have higher scores for **depression**. No statistically significant difference was found between NHB survivors and siblings.[a] (survivors vs. siblings, p-value) **NHW: 48.33 vs. 47.25, p<0.001** **Hispanics: 49.61 vs. 46.02, p<0.001** NHB: 48.70 vs. 47.21, p=0.23 Anxiety No statistically significant difference was found between survivors and siblings for **anxiety**.[a] (survivors vs. siblings, p-value) NHW: 46.86 vs. 46.77, p=0.68 Hispanics: 45.41 vs. 44.54, p=0.47 NHB: 47.80 vs. 46.16, p=0.10 Global Severity Index Within racial/ethnic groups, NHW and Hispanic survivors were more likely than siblings to have higher GSI scores. No statistically significant difference was found between NHB survivors and siblings.[a] (survivors vs. siblings, p-value) **NHW: 47.52 vs. 46.74, p<0.001** **Hispanics: 48.95 vs. 46.11, p=0.005** NHB: 47.60 vs. 45.08, p=0.08 [a]all analyses adjusted for sex, age at follow-up, year at diagnosis, methotrexate exposure (intravenous and intrathecal), corticosteroid exposure, and any Common Terminology Criteria for Adverse Events grade 3 and 4 chronic medical condition.	**Quality assessment:** 1. Is the study group representative? ☐Yes/☒no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:** Participants aged <18 years were excluded from analyses using the BSI-18

	Median age: 33.4 years (range 9.6-54.1 years) non-Hispanic white: NHW n=2882 (94.3%) non-Hispanic black: NHB n=70 (2.3%) Hispanic n=103 (3.4%)			

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Allen et al. **Posttraumatic stress-related psychological functioning in adult survivors of childhood cancer. 2018**				
Study Design Treatment era Years of follow-up	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment Remarks**
Study Design: **☐ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **n.a.** **Years of follow-up:** **Mean 24.1 years (SD 8.2 years); range 10.2-48.3 years** **Country:** **USA** **Study center:** **St. Jude Lifetime Cohort; St. Jude**	**Sample size:** N=2969 **Diagnoses:** Leukemia n=1108 (37.3%) Lymphoma n=612 (20.6%) CNS tumors n=293 (9.9%) Neuroblastoma n=193 (6.5%) Osteosarcoma/Ewing sarcoma n=203 (6.8%) Wilms tumor n=126 (4.2%) Retinoblastoma n=88 (3.0%) Rhabdomyosarcoma n=97 (3.3%) Other solid tumors (e.g., germ cell tumor, melanoma) n=238 (8.0%) Other n=11 (0.4%) **Age at diagnosis:** Mean 8.4 years (SD 5.6 years); range 0-21.8 years **Age at study:** Mean 32.5 years (SD 8.5); range 18.3-63.8 years **Controls:**	Chemotherapy n=2547 (85.8%) Radiation therapy n=1784 (60.1%) Surgery n=1365 (46.0%) Bone marrow transplant n=127 (4.3%)	Post-traumatic stress disorder: PTSD Checklist-Civilian: Mean 27.7 (SD 12.4); Median 23.0; 11.8% in clinical range Psychological distress: BSI-18: Global Symptoms Index Mean 50.0 (SD 11.3); Median 48.0; 15.6% in clinical range	**Quality assessment:** 1. Is the study group representative? ☐Yes/☒no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

Children's Research Hospital **Measurement tool:** • **PTSD Checklist-Civilian (PCL-C): cut-off ≥44 was used for caseness** • **BSI-18: cut-off ≥63 was used for caseness**				

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Anestin et al. **Psychological risk in long-term survivors of childhood acute lymphoblastic leukemia and its association with functional health status: A PETALE cohort study. 2018**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **87-01, 91-01, 95-01, 2000-01, 2005-01** **Years of follow-up:** **≥5 years postdiagnosis** **Mean 15.7 years (SD 5.1 years)** **Country:** **Canada; PETALE cohort** **Study center:** **Sainte-Justine University Health Center, Laval University Health Center** **Measurement tool:** • **Adolescents: Beck Youth Inventories for Anxiety and Depression (BYI-AD): standardized T scores, significant anxiety T score ≥55 (BYI-A), and significant depression T score ≥55 (BYI-D)** • **Young adults: Beck Anxiety Inventory (BAI), Beck Depression Inventory II (BDI-II): significant anxiety scores ≥8 (BAI), and significant depression scores ≥14 (BDI-II)** • **Distress thermometer: cut-off for psychological distress≥4**	**Sample size:** Total N=287: n=105 adolescent survivors n=182 adult survivors **Diagnoses:** Acute lymphoblastic leukemia **Age at diagnosis:** <19 years Mean 6.2 years (SD 4.5 years) **Age at study:** Mean 21.9 years (SD 6 years) **Controls:** Control values from other studies, see references[a,b,c,d]	Radiotherapy: Yes n=161 (56.1%) No n=126 (43.9%)	Adolescents: 14% of adolescent survivors experienced significant anxiety 21% of adolescent survivors experienced significant depression 30% of adolescent survivors experienced significant psychological distress "Mean T scores and standard deviations for anxiety (47.9 ± 9.2) and depression (46.6 ± 8.1) were similar to matched control groups (48.2 ± 7.0, d = −0.04 for anxiety) and (48.1 ± 7.2, d = −0.2 for depression)."[a] Adults: 27% of adult survivors experienced significant anxiety 20% of adult survivors experienced significant depression 19% of adult survivors experienced significant psychological distress "Means and standard deviations for anxiety (6.0 ± 6.8) and depression (6.7 ± 7.5) were slightly higher than a control group for anxiety (4.1 ± 5.1, d = 0.3) but not for the depression (6.5 ± 5.2, d = 0.04)."[b,c] "However, the control group for adults with anxiety symptoms were older (45.8 years old) and both scores are to be interpreted as minimal anxiety symptoms as scores ranged from 0 to 7."[d] [a] Beck JS, Beck AT, Jolly JB, Steer RA. The Beck Youth Inventories for Children and Adolescents. 2nd ed. San Antonio, TX: Pearson; 2005. [b,c] Pemberger S, Jagsch R, Frey E, et al. Quality of life in long-term childhood cancer survivors and the relation of late effects and subjective well-being. Support Care Cancer. 2005;13:49–56. Muntingh AD, van der Feltz-Cornelis CM, van Marwijk HW, Spinhoven P, Penninx BW, van Balkom AJ. Is the Beck Anxiety Inventory a good tool to assess the severity of anxiety? A primary care study in the Netherlands Study of Depression and Anxiety (NESDA). BMC Fam Pract. 2011;12:66. [d]Beck AT, Steer RA, Ball R, Ranieri W. Comparison of Beck Depression Inventories -IA and -II in psychiatric outpatients. J Pers Assess. 1996;67:588–597.	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Pépin et al. **How to interpret high levels of distress when using the Distress Thermometer in the long-term follow-up clinic? A study with Acute Lymphoblastic Leukemia survivors. 2017**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **n.a.** **Years of follow-up:** **n.a.** **Country:** **Canada, PETALE-PSY survivor cohort** **Study center:** **Sainte-Justine UHC and Québec UHC** **Measurement tool:** **Children and adolescents:** • **The Beck Youth Inventories** • **The Positive and Negative Affect Scale for Children** • **Distress thermometer** **Adults:**	**Sample size:** N=204 n=84 children and adolescent survivors n=120 adult survivors **Diagnoses:** Acute lymphoblastic leukemia **Age at diagnosis:** Age at diagnosis was 6 years (±5 years) **Age at study:** Children and adolescent survivors: Mean age of 15±2 years (8–18 years) Adult survivors: Mean age of 26 ± 5 years (19–40 years) **Controls:** n.a.	Radiotherapy 57%	Children and adolescent survivors: "11% (N = 9) reported high levels of anxiety (moderate or severe) and 8% (N = 7) displayed high levels of depression (moderate or severe). Thirty-three percent (N = 28) of children and adolescents had a DT score ≥3, and 25% (N = 21) obtained scores ≥4." Adult survivors: "8% (N = 10) reported moderate to severe symptoms of anxiety and 10% (N = 12) had moderate to severe symptoms of depression. Thirty-three percent (N = 39) had a score ≥3, and 23% (N = 28) had ≥4."	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

• **Beck Depression Inventory-II** • **Beck Anxiety Inventory** • **Positive and Negative Affect Scale** • **Distress thermometer**				

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?

Vuotto et al. Impact of Chronic Disease on Emotional Distress in Adult Survivors of Childhood Cancer: A Report From the Childhood Cancer Survivor Study. 2017

Study Design Treatment era Years of follow-up	Participants	Treatment	Main outcomes	Quality assessment Remarks
Study Design: **☐ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1970-1986** **Years of follow-up:** **Time since diagnosis, years: mean 23.2 (SD 4.5), median 23 (IQR 19-27)** **Country:** **USA and Canada** **Study center:** **Multi-site (CCSS)** **Measurement tool:** • **Brief Symptom Inventory 18: elevated distress defined as a T-score ≥63** • **Post-traumatic Stress Diagnostic Scale (PDS): positive endorsement of PTSS was defined as at least 1**	**Sample size:** N=5021 **Diagnoses:** Leukemia n=1697 (33.8%) CNS tumor n=499 (9.9%) Hodgkin lymphoma n=720 (14.3%) Non-Hodgkin lymphoma n=377 (7.5%) Wilms tumor n=473 (9.4%) Neuroblastoma n=316 (6.3%) Soft tissue sarcoma n=470 (9.4%) Bone cancer n=469 (9.3%) **Age at diagnosis:** Age at diagnosis, years: mean 8.3 (SD 5.9), median 7.0 (IQR 3-13) **Age at study:** Age at Follow-up 2, years: mean 32.0 (SD 7.6), median 32 (IQR 26-37) **Controls:** n.a.	**Surgery (n= (%))** CNS 550 (11.0) Respiratory system 417 (8.3) Cardiovascular system 50 (1.0) Other surgery 2750 (54.8) None 1208 (24.1) **Radiotherapy (n= (%))** Cranial 1451 (29.0) Thoracic 1035 (20.7) Abdominal 963 (19.2) Pelvic 713 (14.2) Other radiotherapy 421 (8.4) None 1750 (34.9) **Chemotherapy (n= (%))** IT methotrexate or cytarabine (any) 1851 (36.9) 1 injection 1274 (25.4) 2 injections 525 (10.5) ≥3 injections 52 (1.0) Corticosteroids (yes/no) 2425 (48.3) IV methotrexate 940 (18.7) Bleomycin (yes/no) 260 (5.4) Anthracyclines 1777 (36.7)	Supporting Table 4: **Depression** **Anxiety** **PTSS** Grade n (%) n (%) n (%) Leukemia 203 (12.0) 116 (6.8) 290 (17.1) CNS Tumor 74 (14.8) 40 (8.0) 89 (17.8) Hodgkin Lymphoma 60 (8.3) 45 (6.3) 124 (17.2) Non-Hodgkin Lymphoma 40 (10.6) 26 (6.9) 54 (14.3) Wilms Tumor 45 (9.5) 36 (7.6) 62 (13.1) Neuroblastoma 25 (7.9) 23 (7.3) 38 (12.0) Soft Tissue Sarcoma 42 (8.9) 27 (5.7) 71 (15.1) Bone Cancer 49 (10.4) 30 (6.4) 82 (17.5) Prevalence of Depression: 10.7% 203+74+60+40+45+25+42+49=538 -> 538/5021= 10.7% Prevalence of Anxiety: 6.8% 116+40+45+26+36+23+27+30=343 -> 343/5021= 6.8% Prevalence of PTSS: 16.1% 290+89+124+54+62+38+71+82=810 -> 810/5021= 16.1%	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☐Yes/☒no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

reexperiencing symptom, at least 3 avoidance symptoms, and at least 2 arousal symptoms				

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
***Korhonen et al.* Suicides and Deaths Linked to Risky Health Behavior in Childhood Cancer Patients: A Nordic Population-Based Register Study. 2019**				
Study Design Treatment era Years of follow-up	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment Remarks**
Study Design: **☐ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1971-2009** **Years of follow-up:** **Time since diagnosis:** **Median follow-up was 9.4 years (range: 0-42.0 years)** **Country:** **Denmark, Finland and Sweden: SALiCCS cohort**	**Sample size:** N=29'285 **Diagnoses (n= (%)):** Leukemia 7409 (25) Lymphoma 3958 (14 CNS tumors 6616 (23) Neuroblastoma and other peripheral cell tumors 1415 (5) Retinoblastoma 482 (2) Renal tumors 1202 (4) Hepatic tumors 277 (1) Malignant bone tumors 1426 (5) Soft-tissue sarcomas 1741 (6) Germ cell, trophoblastic, and other gonadal neoplasms 1774 (6) Other malignant epithelial neoplasms 2596 (9) Other and unspecified malignant neoplasms 389 (1) **Age at diagnosis (n= (%)):** <20 years Birth to 4 years: 9341 (32) 5-9 years 5327 (18) 10-14 years 5694 (19)	n.a.	Deaths due to suicide: Survivors: 0.56% Comparisons:17.1% "The risk of committing suicide was found to be statistically significantly increased among patients with cancer when compared with population comparison subjects (RR, 1.37; 95% CI, 1.02-1.83)." "The overall risk of dying of risky health behavior was significantly increased among patients with cancer when compared with population comparison subjects (RR, 1.25; 95% CI, 1.06-1.47)." "Increased risk of dying of alcohol poisoning and suicide among patients with cancer compared with population comparison subjects (RR, 2.83 [95% CI, 1.28-6.27] and RR, 1.37 [95% CI, 1.02-1.83], respectively)"	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

Study center: **n.a.** **Measurement tool:** • **Causes of death classified according to the International Classification of Diseases (ICD, different versions used)**	15-19 years 8923 (31) **Age at study:** Median age at the end of follow-up was 19.0 years (range: birth to 59.1 years) **Controls:** N=146'282 population-based comparison subjects (1:5 ratio) identified from national population registries, matched by birth month and year, sex, and country. The median age at the end of follow-up was 27.4 years (range: birth to 58.8 years) for population comparisons			Follow-up began at the date of cancer diagnosis for cases and from the equivalent age for matched population comparisons and ended at death, emigration, or the end of follow-up (December 31, 2008, for Denmark and Sweden and December 31, 2012, for Finland), whichever occurred first.

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Effinger et al. **Long-term health and social function in adult survivors of pediatric astrocytoma: A report from the Childhood Cancer Survivor Study. 2019**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☐ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **Time Period of Diagnosis** **1970–1975: n=273 (25.5%)** **1976–1980: n=307 (28.7%)** **1981–1986: n=490 (45.8%)** **Years of follow-up:** **Data from baseline survey, Follow-up 2 in 2003, and Follow-up 4 in 2007** **Country:** **USA and Canada** **Study center:** **Multi-site (CCSS)** **Measurement tool:** • **Brief Symptom Inventory-18: GSI T-score ≥63 defined as poor mental health**	**Sample size:** N=1182 **Diagnoses:** Astrocytoma **Age at diagnosis:** <21 years at diagnosis 0–4 years: n=430 (36.4%) 5–9 years: n=330 (27.9%) 10–20 years: n=422 (35.7%) **Age at study:** <18 years: n=76 (6.4%) 18–24 years: n=200 (16.9%) 25–29 years: n=250 (21.2%) 30–34 years: n=241 (20.4%) 35–39 years: n=205 (17.3%) ≥40 years: n=210 (17.8%) **Controls:** N=4023 siblings	No chemotherapy or radiation: n=375 (35.9%) Chemotherapy without radiation: n=17 (1.6%) Radiation without chemotherapy: n=454 (43.5%) Chemotherapy plus radiation: n=200 (19.1%) Radiation Therapy: Yes: n=654 (62.5%) No: n=393 (37.5%)	Survivors were more likely to experience poor mental health than siblings RR=1.6 (95%CI:1.4-1.8; adjusting for age, sex, race, and presence of chronic conditions).	**Quality assessment:** 1. Is the study group representative? ☐Yes/☒no/ ☐unclear 2. Is the follow-up adequate? ☐Yes/☐no/ ☒unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Nathan et al. **Adverse Mental Health Outcomes in a Population-Based Cohort of Survivors of Childhood Cancer. 2018**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: ☐ Cross-sectional study ☐ Case-control study ☒ Cohort study ☐ Qualitative study (→ exclude!) ☐ Systematic/narrative review (→ exclude!) ☐ RCT ☐ Other: (specify!) Treatment era (n= (%)): 1987-1993: 1520 (36.9) 1994-2001: 2003 (48.7) 2002-2008: 594 (14.4) Years of follow-up: ≥5 years since the latest of diagnosis, relapse, or subsequent malignant neoplasm Country: Canada Study center: Pediatric Oncology Group of Ontario's Networked Information System (Ontario's 5 pediatric cancer centers) Measurement tool: • A mental health visit was defined as a visit to a family physician, psychiatrist, or emergency department (ED) or a hospitalization. • A severe mental health event was defined as an ED visit, hospitalization, or suicide. • International Statistical Classification of Diseases-10th Revision and Diagnostic and Statistical Manual of	**Sample size:** N=4117 **Diagnoses (n= (%)):** Acute lymphoblastic leukemia 1087 (26.4) Other leukemias 189 (4.6) Hodgkin lymphoma 386 (9.4) Other lymphomas 307 (7.5) Central nervous system tumors 808 (19.6) Neuroblastoma 144 (3.5) Retinoblastoma 92 (2.2) Renal tumors 240 (5.8) Hepatic tumors 39 (0.9) Bone tumors 202 (4.9) Soft tissue sarcomas 256 (6.2) Germ cell tumors 164 (4.0) Other epithelial tumors 170 (4.1) Unspecified malignancies 33 (0.9) **Age at diagnosis (n= (%)):** 0-4 years: 1347 (32.7) 5-9 years: 1052 (25.6) 10-14 years: 1181 (28.7) 15-18 years: 537 (13.0) **Age at study:** n.a. **Controls:** N=20269 controls from the general population, matched by birth year and month, sex, and residential location	Hematopoietic stem cell transplantation No n=3854 (93.6%) Autologous n=114 (2.8%) Allogenic n=149 (3.6%) Surgery No n=1868 (45.4%) Yes n=2249 (54.6%) Chemotherapy No n=1031 (25.0%) Yes n=3021 (73.4%) Unknown n=65 (1.6%) Cranial radiation No n=3230 (78.5%) Yes n=887 (21.5%) High-dose methotrexate No n=3229 (78.4%) Yes n=823 (20.0%) Unknown n=65 (1.6%) Corticosteroid No n=2367 (57.5%) Yes n=1685 (40.9%) Unknown n=65 (1.6%)	Mental healthcare utilization: Mental healthcare visits to family physician (crude rate per 1000 person-years): Survivors: 68.7 (65.4-72.1) Controls: 52.0 (50.8-53.2) Unadjusted RR=1.32 (95%CI:1.25-1.39) Mental healthcare visits to psychiatrist (crude rate per 1000 person-years): Survivors: 16.2 (14.8-17.6) Controls: 10.4 (9.9-10.9) Unadjusted RR=1.56 (95%CI:1.41-1.72) All mental healthcare visits (crude rate per 1000 person-years): Survivors: 79.5 (75.9-83.3) Controls: 57.8 (56.5-59.2) Unadjusted RR=1.38 (95%CI:1.31-1.45) Suicide: Cumulative Incidence by age 30 years % (95%CI): Survivors: 0.13% (0.03-0.39%) Controls: 0.03% (0.01-0.08%), RR=2.92 (95%CI:0.70-12.23) Psychotic disorder: Cumulative Incidence of an Emergency Department Visit or Hospitalization by age 30 years % (95%CI): 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: Cumulative Incidence of an Emergency Department Visit or Hospitalization by age 30 years % (95%CI): 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: Cumulative Incidence of an Emergency Department Visit or Hospitalization by age 30 years % (95%CI): 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: Cumulative Incidence of an Emergency Department Visit or Hospitalization by age 30 years % (95%CI): Survivors: 0.09% (0.04-0.14%) Controls: 0.08% (0.04-0.14%), RR=1.39 (95%CI:0.39-4.99)	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:** During the study period, survivors and controls were followed for a median [range], 7.5 years [1.0-21.9]; vs. controls 7.5 years [1.0-21.9] Total person-years of follow-up survivors: 35,027, controls: 172,409

Mental Disorders, Fourth Edition codes was used to classify ED visits and hospitalizations into the diagnostic subcategories: substance abuse, psychotic disorders, mood/affective disorders, anxiety disorders, and selected disorders of adult personality and behavior				

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?

Huang et al. **Emotional distress impacts quality of life evaluation: a report from the Childhood Cancer Survivor Study. 2017**

Study Design Treatment era Years of follow-up	Participants	Treatment	Main outcomes	Quality assessment Remarks
Study Design: ☐ **Cross-sectional study** ☐ **Case-control study** ☒ **Cohort study** ☐ **Qualitative study (→ exclude!)** ☐ **Systematic/narrative review (→ exclude!)** ☐ **RCT** ☐ **Other: (specify!)** **Treatment era:** **1970-1986** **Years of follow-up:** **10-19 years: n=1916 (27.0%)** **20-29 years: n=4361 (61.4%)** **30+ years: n=826 (11.6%)** **Country:** **USA, Canada** **Study center:** **Multi-center study; CCSS** **Measurement tool:** • **SF-36** • **Brief Symptom Inventory-18, cut-off ≥63**	**Sample size:** N=7103 **Diagnoses** Leukemia n=2,369 (33.4%) Central nervous system tumors n=767 (10.8%) Hodgkin lymphoma n=999 (14.1%) Non-Hodgkin lymphoma n=541 (7.6%) Wilms tumor n=677 (9.5%) Neuroblastoma n=452 (6.4%) Soft tissue sarcoma n=646 (9.1%) Bone cancer n=652 (9.2%) **Age at diagnosis:** <21 years **Age at study:** Mean 31.8 years (SD 7.5) **Controls:** N=390 siblings; mean 33.5 years at study (SD 8.2)	Chemotherapy Yes n=5,301 (80.0%) No n=1,353 (20.0%) Radiotherapy Yes n=4,339 (65.8%) No n=2,288 (34.2%) Amputation Yes n=434 (7.1%) No n=5,716 (92.9%)	**Risk** |	**Cancer survivor *T* score ≥63, %**	**Sibling *T* score ≥63, %**	***p* value**
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Anxiety	7.8%	4.4%	0.015
Depression	11.9%	8.0%	0.020
Somatization	14.1%	6.7%	<0.001		**Quality assessment:** 1. Is the study group representative? ☐Yes/☒no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Ranft et al. **Quality of Survivorship in a Rare Disease: Clinicofunctional Outcome and Physical Activity in an Observational Cohort Study of 618 Long-Term Survivors of Ewing Sarcoma. 2017**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: ☐ **Cross-sectional study** ☐ **Case-control study** ☒ **Cohort study** ☐ **Qualitative study (→ exclude!)** ☐ **Systematic/narrative review (→ exclude!)** ☐ **RCT** ☐ **Other: (specify!)** **Treatment era** **1980-1985** **1986-1991** **1992-1998** **1999-2009** **Years of follow-up** **3-4.9 years: n=35 (5.7%)** **5-9.9 years: n=191 (30.9%)** **10-19.9 years: n=248 (40.1%)** **≥20 years: n=144 (23.3%)** **Country** **Germany** **Study center** **N.a.** **Measurement tool** • **Brief Symptom Inventory**	**Sample size** N=618 **Diagnosis** Ewing sarcoma **Age at diagnosis** 0-9.9 years: n=142 (23.0%) 10-17.9 years: n=291 (47.1%) 18-29.9 years: n=131 (21.2%) ≥30 years: n=54 (8.7%) **Age at study** Median age at study 29 years 0-9.9 years: n=5 (0.8%) 10-17.9 years: n=63 (10.2%) 18-29.9 years: n=272 (44.0%) ≥30 years: n=278 (45.0%) **Controls** N=316 controls, recruited through survivors; median age at study 30 years	Local treatment None n=2 (0.3%) Surgery n=174 (28.2%) Radiotherapy n=96 (15.5%) Surgery + Radiotherapy n=346 (56.0%) High-dose chemotherapy No n=555 (89.8%) Yes n=63 (10.2%)	**Risk:** "Overall, no pronounced symptoms were revealed in the BSI scales, with raw values <0.50, whereas control subjects had significantly lower symptom values (d=0.19 to 0.50; P<0.01)." BSI-Depression (0 "no symptoms" – 4 "highest symptoms"): Survivors: mean 0.39; controls: mean 0.22, p<0.01 BSI-Anxiety (0 "no symptoms" – 4 "highest symptoms"): Survivors: mean 0.41; controls: mean 0.32, p<0.01	**Quality assessment:** 1. Is the study group representative? ☐Yes/☒no/ ☐unclear 2. Is the follow-up adequate? ☐Yes/☐no/ ☒n.a./☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Shabason et al. **Clinical diagnosis of attention-deficit/hyperactivity disorder in survivors of pediatric brain tumors. 2019**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☒ Other: (specify!)** **Retrospective chart review** **Treatment era:** **Diagnosed from 2000-2015** **Years of follow-up:** **≥ 2 years after end of treatment** **Country:** **USA** **Study center:** **Children's Hospital Philadelphia, USA** **Measurement tool:** **None.** **Considered to have a diagnosis of ADHD if listed in the problem list, medical history or documentation of any clinical encounter within the EMR**	**Sample size:** 528 (55.7% male) **Diagnoses:** Brain tumor: Low-grade glioma (54.5%) Medulloblastoma (11.9%) Craniopharyngioma (8.7%) **Age at diagnosis:** Mean=8.15 yrs, SD: 4.4 yrs, Range: 0-16 yrs **Age at study:** Mean=15.5 yrs, SD: 5.1 yrs, Range: 2.4-29.7 yrs **Controls:** N.a. [1]Danielson ML, Bitsko RH, Ghandour RM, Holbrook JR, Kogan MD, Blumberg SJ (2018) Prevalence of parent-reported ADHD diagnosis and associated treatment among U.S. children and adolescents, 2016. J Clin Child Adolesc Psychol 47(2):199–212	Surgery only: 201 (38.1%) Surgery and RT: 69 (13.1%) Surgery and Chemo: 48 (9.1%) Surgery, RT and Chemo: 111 (21.1%) Of those who received RT: • Focal radiation only:59.2% • Whole brain or craniospinal RT: 42.7% • Both: 1.9%	**Risk:** 69 (13.1%) Survivors had documentation of ADHD. • Diagnosed before cancer: 12 (17.4%) • Diagnosed after cancer: 40 (58%) • Diagnosed time unknown: 17 (24.6%) (Table 2) Of which 14.5% inattentive type, 13% hyperactive/impulsive type, 10.1% combined type, 62.3% not specified Among participants without ADHD diagnoses (n = 459), 103 (19.5%) had at least one symptom related to ADHD documented in the medical record. Of that group, 83 (15.7%) had symptoms of inattention, 14 (2.7%) hyperactivity, and 43 (8.1%) impulsivity. Of those with ADHD-related symptoms without ADHD diagnoses, 17 (26.6%) were on ADHD medication. When combining those with documented ADHD diagnoses and those with ADHD-related symptoms without ADHD diagnoses, 172 (32.6%) participants experienced ADHD-related symptoms. This ADHD prevalence rate of 13.1% was significantly higher (p = 0.002) than the highest cited estimated prevalence of 9.4% in the general population[1] While some survivors may have had premorbid ADHD, this study suggests an increased risk above and beyond the risk in the general population, particularly in children with brain tumors at younger ages and with supratentorial tumors.--> no multivariate analysis (t-test, chi-square and logistic regression (univariate)). (p. 308)	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☐Yes/☒no/ ☐unclear **Remarks:** Only univariate testing

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Burghardt et al. **Prevalence of mental distress among adult survivors of childhood cancer in Germany – compared to the general population. 2019**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **Diagnosed from 1980-1990** **Years of follow-up:** **≥ 5 years after end of treatment, Median: 28.1yrs (range:23-36) since dx.** **Country:** **Germany** **Study center:** **University Medical Center Mainz** **Measurement tool:** **Cardiovascular examination with clinical phenotyping, self-report questionnaires and computer assisted personal interviews.** **Specifically:** **PHQ-8 (major depression)** **One question for suicidal ideation.** **GAD-2 (general anxiety)** **Brief PHQ panic module (panic).** **Mini-Spin (Social anxiety)** **PHQ-15 (severity of symptoms, burden).** **Jenkins sleep scale (sleep disorder).**	**Sample size:** 951 (55% male) **Diagnoses: %, N** Leukemias: 43.5% (414) Lymphomas 9.9% (94) CNS tumors 12.8% (122) Neuroblastoma 7.6% (72) Retinoblastoma 1.1% (10) Renal tumors 8.1% (77) Hepatic tumors 0.7% (7) Bone tumors 5.3% (50) Soft tissue sarcoma 7.5% (71) Germ cell tumors 2.7% (26) Carcinoma 0.7% (7) Others 0.1% (1) **Age at diagnosis:** Median: 5.0 (range: 0-15) <1 yrs 9.5 (90) 1-<4 yrs 30.8% (293) 4-<8 yrs 27.7% (263) 8-<11 yrs 13.5% (128) 11-<15 yrs 18.6% (177) **Age at study:** Median: 34.2 (range: 24-49) 20-29 yrs: 23.9% (227) 30-39 yrs: 58.4% (555) 40-49 yrs: 17.8% (169) **Controls:** German Household Panel from three years: 2006: n=569 (57.1% female) social phobia, generalized anxiety, panic; 2008: n=1130 (52.8% female) Somatic stress, depression, suicidality 2010: n=1054 (54.1% female) sleep disorders.	None reported	**Risk: Prevalence** Survivors: Somatic distress (18%), sleep disturbances (11%), social anxiety (9%), and **depression (9%).** CCS reported **suicidal ideation** and **generalized anxiety in 8%** of cases and **panic** in 7% of cases. Survivors: 32% reported some form of **clinically relevant distress ("any distress");** these were 24% of male and 41% of female survivors. "Any distress": Definition: occurrence of at least one of the mental conditions (depression, somatic distress, suicidal ideation, generalized anxiety, panic, social anxiety, or sleep disturbances) "Any distress" was only available for the CVSS sample Controls: social anxiety (5%), sleep disturbances (5%), and depression (4%), somatic distress (3%). Controls: suicidal ideation 6% and generalized anxiety 3%, panic 3%). **Comparison CCS (1) with controls (0): OR [95%CI]** Depression: 4.69 [2.70, 8.16] Somatic distress: 20.89 [11.68, 37.36] Suicidal ideation: 2.22 [1.38, 3.57] Generalized anxiety: 7.66 [3.41, 17.22] Panic: 4.36 [1.88, 10.09] Social anxiety: 2.75 [1.40, 5.42] Sleep disorders: 2.32 [1.14, 4.73] For all, except for Social anxiety: ($P < 0.001$)	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?

Crochet et al. **Posttraumatic stress as a contributor to behavioral health outcomes and healthcare utilization in adult Survivors of Childhood Cancer: A report From the Childhood Cancer Survivor Study. 2019**

Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: ☐ **Cross-sectional study** ☐ **Case-control study** ☒ **Cohort study** ☐ **Qualitative study (→ exclude!)** ☐ **Systematic/narrative review (→ exclude!)** ☐ **RCT** ☐ **Other: (specify!)** **Treatment era:** **Diagnosed from 1970-1986** **Years of follow-up:** **Not stated; survival at least 5y from diagnosis** **Country: US & Canada** **Study center: Multicenter, 27 institutions (CCSS)** **Measurement tool:** • **Post-traumatic stress scale: Intrusion, Avoidance, Hypervigilance, cut-off ≥13 for caseness** • **Brief Symptom Inventory-18: depression, anxiety, somatization; clinical cut-off of being in the top 10th percentile** • **Questions on healthcare utilization.** • **Short Form-36:** • **CCSS Neurocognitive Questionnaire**	**Sample size:** N=6844 N_{wo}=5227 without PTSS; N_w=832 with PTSS **Mixed Diagnoses: w/o PTSS; w/ PTSS** CNS tumor: n=610 (10.4 %); n=117 (11.8%) Sarcoma: n=1072 (18.3%); n=191 (19.2%) Lymphoma: n=1285 (22.0%); n=204 (20.5%) Solid tumor: n=945 (16.2%); n=133 (13.4%) Leukemia n=1937 (33.1%); n=350 (35.2%) **Age at diagnosis:** Mean age at diagnosis: 7.6 years (SD 5.8) **Age at study:** Mean age at follow-up: 34.9 years (SD 7.5) **Controls:** None	Without PTSS N_{wo}=5227 / With PTSS N_w=832 Anthracycline dose > 0 m = 290.1 (IQR = 174.9, 348.8) / m = 292.3 (197.7, 397.4) Anthracyclines in the 1st 5 years n = 2113 (36.1%) / n = 369 (37.1%) Alkylating agents dose > 0 m = 6600.0 (IQR = 3589.2, 11525.0) / m = 6958.3 (IQR = 3264.4, 12415.5) Alkylating agents in the 1st 5 years n = 2708 (46.3%) / n = 470 (47.2%) Methotrexate IV dose > 0 m = 3540.7 (IQR = 400.9, 15891.7) / m = 3963.1 (IQR = 474.2, 21038.7) Methotrexate IV in the 1st 5 years n = 1024 (17.5%) / n = 180 (18.1%) Methotrexate IT dose > 0 m = 123.5 (IQR = 69.2, 222.2) / m = 125.8 (IQR = 75.0, 221.7) Methotrexate IT in the 1st 5 years n = 1771 (30.3%) / n = 309 (31.1%) Cranial radiation dose > 0 m = 200.0 (IQR = 20.0, 2400.0) / m = 1800.0 (IQR = 20.0, 2400.0) Cranial radiation n = 3478 (59.5%) / n = 641(64.4%) m= median IQR=interquartile range	**Risk:** <u>Prevalence of PTSS:</u> 14.5%, N=995 <u>Prevalence of clinical levels of global emotional distress (BSI-18):</u> 4.4% of survivors without PTSS (N_{wo}=5227 x 0.044 → n=230 survivors with distress) 44.4% of survivors with PTSS (N_w=832 x 0.444 → n=369 survivors with distress) n=230+369 → 599 survivors with distress (9.9%) <u>Prevalence of clinical levels of depression (BSI-18):</u> 6.2% of survivors without PTSS (N_{wo}=5227 x 0.062 → n=324 survivors with depression) 44.9% of survivors with PTSS (N_w=832 x 0.449 → n=374 survivors with depression) n=324+374 → 698 survivors with depression (11.5%) <u>Prevalence of clinical levels of anxiety (BSI-18):</u> 3.5% of survivors without PTSS (N_{wo}=5227 x 0.035 → n=183 survivors with anxiety) 32.3% of survivors with PTSS (N_w=832 x 0.323 → n=269 survivors with anxiety) n=183+269 → 452 survivors with anxiety (7.5%)	**Quality assessment:** 1. Is the study group representative? ☐Yes/☐no/ ☒unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1a. What is the risk for suffering from mental health disorders/symptoms in childhood, adolescent and young adult cancer (CAYA) survivors?				
Tonorezos et al. **Impact of Exercise on Psychological Burden in Adult Survivors of Childhood Cancer: A report From the Childhood Cancer Survivor Study. 2019**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☐ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **Diagnosed from 1970-1986** **Years of follow-up:** **Not stated; survival at least 5y from diagnosis** **Country:** **US & Canada** **Study center: Multicenter, 26 institutions (CCSS)** **Measurement tool:** • **Vigorous exercise assessed with a question. Calculated using frequency and duration, weighted energy expenditure and transformed into metabolic equivalent units (MET) and expressed as MET-hours per week. And then combined into Levels.** • **Brief Symptom Inventory-18: depression, anxiety, somatization; prevalence of clinically significant symptoms was defined as a T-score ≥63**	**Sample size:** N=6199 **Mixed Diagnoses:** Leukemia n=1857 (30.0%) CNS n=766 (12.4%) Hodgkin lymphoma n=1001 (16.1%) Non-Hodgkin lymphoma n=576 (9.3%) Kidney, Wilms n=438 (7.1%) Neuroblastoma n=249 (4.0%) Soft-tissue sarcoma n=628 (10.1%) **Age at diagnosis:** Median [range] 10.0 years [0.0 21.0] **Age at study:** Mean [range] 34.0 years [22.0-54.0] **Controls:** n.a.	**Chemotherapy** Any chemotherapy n=4376 (78.0%) Alkylating dose: CED, mg/m2 None n=2747 (53.3%) >0 to <4000 n=482 (9.4%) 4000-8000 n=587 (11.4%) ≥8000 n=1334 (25.9%) Anthracycline dose, mg/m2 None n=3470 (64.5%) >0 to <250 n=685 (12.7%) ≥250 n=1226 (22.8%) **Radiation therapy** Any radiation therapy n=4032 (68.1%) Chest, Gy n=1571 (28.5%) Chest direct dose None n=1650 (51.4%) <20 n=226 (7.0%) 20 to <30 n=398 (12.4%) 30 to <40 n=510 (15.9%) 40 to <50 n=363 (11.3%) ≥50 n=65 (2.0%) Brain or head, Gy n=2048 (37.1%) All head direct dose None n=1650 (44.7%) <20 n=39 (1.1%) 20 to <30 n=1191 (32.3%) 30 to <40 n=114 (3.1%)	**Risk:** At a median follow-up of 7.8 years (range, 0.1- 10.4 years), the prevalence of depression was 11.4% (95% CI, 10.6%-12.3%), the prevalence of anxiety was 7.4% (95% CI, 6.7%-8.2%)	**Quality assessment:** 1. Is the study group representative? ☐Yes/☒no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

		40 to <50 n=143 (3.9%) ≥50 n=551 (14.9%)		

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?				
Prasad et al. **Psychosocial and Neurocognitive Outcomes in Adult Survivors of Adolescent and Early Young Adult Cancer: A Report From the Childhood Cancer Survivor Study. 2015**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☐ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1970-1986** **Years of follow-up:** **At least 5 years from diagnosis at the time of recruitment** **Country:** **US** **Study center:** **Multi-institutional (CCSS)** **Measurement tool:** **BSI-18: T score ≥ 63 classified as having emotional distress**	**Sample size:** N=6192 survivors (n=2589 AeYA (11-21y), n=3603 Non-AeYA (<11)) **Diagnoses:** Leukemia n=2458 (39.7%) CNS malignancies n=902 (14.6%) Hodgkin lymphoma n=980 (15.8%) Non-Hodgkin lymphoma n=553 (8.9%) Soft tissue sarcoma n=656 (10.6%) Osteosarcoma/Ewing n=643 (10.4%) **Age at diagnosis:** AeYA: 11-21 years (48.5% 11-14 years; 51.5% 15-21 years) Non-AeYA: 0-10 years (62.1% <6 years, 37.9% 6-10 years) **Age at study:** 15-39 years AeYAs: 15-19 years: n=0 20-24 years: n=0 25-29 years: n=62 30-34 years: n=568 ≥35 years: n=1959 **Controls:** 390 siblings	**AeYA** *Overall treatment* Surgery only n=204 (7.9%) Chemotherapy n=540 (20.9%) Radiotherapy n=494 (19.1%) Chemotherapy and radiotherapy n= 540 (20.9%) *Chemotherapy:* Antimetabolites n=959 (37.0%) Corticosteroids n=1055 (40.8%) *CNS irradiation:* None n=825 (31.9%) Indirect n=966 (37.3%) Direct < 20 Gy n=274 (10.6%) Direct ≥ 20 Gy n=405 (15.6%) **Non-AeYA:** *Overall treatment:* Surgery only n=211 (5.9%) Chemo n=903 (25.1%) Radio n=332 (9.2%) Chemo and Radio: n=1920 (53.3%) *Chemo:* Antimetabolites n=2249 (62.4%) Corticosteroids n=2232 (62.0%) *CNS irradiation:* None n=1226 (34.0%) Indirect n=424 (11.8%) Direct < 20 Gy n=648 (18.0%) Direct ≥ 20Gy n=1108 (30.8%)	**Risk factors from multivariable logistic regression, stratified by diagnostic groups (CNS tumors/leukemia and Lymphomas/sarcomas).** <u>Somatization:</u> CNS tumors and leukemia survivors (n=3360): • Age at diagnosis, years: 11-21 (Ref. ≤10 years) OR=1.18 (95%CI:0.93-1.51) • Sex: Female (Ref. Male) OR=1.74 (95%CI:1.41-2.16) • Current age, chemotherapy, cranial irradiation, second malignant neoplasm (SMN) or recurrence are variables that were not selected to contribute to the model using Akaike Information Criterion Lymphomas and sarcomas (n=2832): • Age at diagnosis, years: 11-21 (Ref. ≤10 years) OR=0.97 (95%CI:0.77-1.22) • Current age: variable that was not selected to contribute to the model using Akaike Information Criterion • Chemotherapy: Antimetabolites (Ref. unclear!) OR=0.74 (95%CI:0.57-0.95) • Chemotherapy: Corticosteroids (Ref. unclear!) OR=1.32 (95%CI:1.16-2.48) • SMN or recurrence: Yes (Ref. No) OR=1.70 (95%CI:1.16-2.48) • Sex: Female (Ref. Male) OR=1.47 (95%CI:1.18-1.84) <u>Depression:</u> CNS tumors and leukemia survivors: • Age at diagnosis, years: 11-21 (Ref. ≤10 years) OR=1.11 (95%CI:0.87-1.42) • Chemotherapy: Antimetabolites (Ref. unclear!) OR=0.72 (95%CI:0.58-0.90) • Current age, chemotherapy (corticosteroids), cranial irradiation, SMN or recurrence, and sex are variables that were not selected to contribute to the model using Akaike Information Criterion Lymphomas and sarcomas: • Age at diagnosis, years: 11-21 (Ref. ≤10 years) OR=0.75 (95%CI:0.59-0.97) • Current age, chemotherapy, SMN or recurrence, and sex are variables that were not selected to contribute to the model using Akaike Information Criterion <u>Anxiety:</u> CNS tumors and leukemia survivors: • Age at diagnosis, years: 11-21 (Ref. ≤10 years) OR=1.44 (95%CI:0.97-2.13) • Current age (per year): OR=0.98 (95%CI:0.95-1.00) • Chemotherapy, cranial irradiation, SMN or recurrence, and sex are variables that were not selected to contribute to the model using Akaike Information Criterion	**Quality assessment:** 1. Is the study group representative? ☐Yes/☒no/ ☐unclear <75% of original FU2 survey participated 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear >75% of participants completed main outcomes 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:** Several variables were not selected to contribute to the models using Akaike Information Criterion, limiting information about non-significant variables.

			Lymphomas and sarcomas: • Age at diagnosis, years: 11-21 (Ref. ≤10 years) OR=0.73 (95%CI:0.54-0.98) • Chemotherapy: Corticosteroids (Ref. unclear!) OR=1.48 (95%CI:1.11-1.99) • Current age, chemotherapy (antimetabolites), SMN or recurrence, and sex are variables that were not selected to contribute to the model using Akaike Information Criterion	

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?				
Hudson et al. **Age-dependent changes in health status in the Childhood Cancer Survivor cohort. 2015**				
Study Design Treatment era Years of follow-up	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment Remarks**
Study Design: ☐ **Cross-sectional study** ☐ **Case-control study** ☒ **Cohort study** ☐ **Qualitative study (→ exclude!)** ☐ **Systematic/narrative review (→ exclude!)** ☐ **RCT** ☐ **Other: (specify!)** **Treatment era:** **1970-1986** **Years of follow-up:** **Mean 22.4 years since diagnosis (Range 6-39 years)** **Country:** **USA** **Study center:** **26 centers in US & Canada (CCSS)** **Measurement tool:** **<u>"Poor" or "Adverse" Mental Health:</u> BSI-18: T score > 63 on Global Severity Index or any of the Depression, Anxiety, or Somatization subscales classified as having "poor" or "adverse" mental health** **<u>Cancer-related Anxiety:</u> 1 item; Dichotomized as**	**Sample size:** 22,568 survivors **Diagnoses:** **L**eukemia 30.4% CNS malignancies 12.4% Hodgkin lymphoma 17.1% Non-Hodgkin lymphoma 9.1% Wilms tumor 6.7% Neuroblastoma 4.1% Soft tissue sarcoma 9.6% Bone malignancy 10.6% **Age at diagnosis:** M=9.5 years (SD= 5.6 yrs) Range: 0-20 yrs **Age at study:** 18-48 yrs at baseline survey **Controls:** 7,504 siblings	Anthracyclines: 26.9% Alkylators: 52.0% Brain radiation: None 66.9% 3-23.9 Gy 9.2% 24.0-29.9 Gy 11.4% 30+ Gy 11.1% Chest radiation: None 71.6% 6.2-23.9 Gy 7.4% 24.0-37.9 Gy 11.4% 38+ Gy 9.6% Abdominal radiation: None 74.2% 1.4-23.9 Gy 7.0% 24.0-34.9 Gy 8.6% 35+ Gy 10.2% Crainotomy 10.1% Thoracotomy 4.4% Nephrectomy 5.8% Cystectomy 0.7% Lower extremity amputation 4.8% Upper extremity amputation 0.5%	**Risk factors for "Poor" or "Adverse" Mental Health (BSI>63) from 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, craniotomy, and within-person correlation) Prevalence Ratio (PR) (95% CI) Age at interview, age at diagnosis, anthracyclines, cranial radiation, chest radiation, abdominal radiation, thoracotomy, nephrectomy, cystectomy, lower extremity amputation and upper extremity amputation were not included in the multivariable model. <u>*Demographic risk factors:*</u> • Female sex (Ref. Male): 1.16 (1.05 to 1.29) • Nonwhite race/ethnicity (Ref. White): 1.10 (0.93 to 1.29) • Income <$20,000/yr (Ref. ≥$20,000/yr): 1.84 (1.65 to 2.05) • No high school graduate (Ref. High school graduate): 1.43 (1.19 to 1.73) <u>*Clinical risk factors:*</u> • BMI <18.5kg/m^2 (Ref. BMI 18.5-24.9kg/m^2): 1.12 (0.92 to 1.38) • BMI 25.0-29.9kg/m^2 (Ref. BMI 18.5-24.9kg/m^2): 1.08 (0.97 to 1.20) • BMI ≥30kg/m^2 (Ref. BMI 18.5-24.9kg/m^2): 1.24 (1.10 to 1.41) • Smoking: Former (Ref. Never): 1.53 (1.33 to 1.75) • Smoking: Current (Ref. Never): 1.92 (1.71 to 2.16) • Meets CDC guidelines for physical activity: No (Ref. Yes) 1.26 (1.15 to 1.38) • Any chronic condition, grade 3-4 (Ref. no chronic condition): 1.78 (1.63 to 1.95)* • One chronic condition, grade 3-4 (Ref. no chronic condition): 1.53 (1.38 to 1.69)* • Two chronic conditions, grade 3-4 (Ref. no chronic condition): 2.63 (2.32 to 2.98)* • Second malignancy (Ref. No organ-specific chronic condition): 1.22 (1.01 to 1.46)* • Vision/hearing/speech chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): 1.47 (1.26 to 1.70)* • Endocrine chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): 1.41 (1.23 to 1.62)* • Respiratory chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): 2.63 (1.83 to 3.78)* • Cardiac chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): 1.72 (1.47 to 2.03)* • Gastrointestinal chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): 1.29 (1.04 to 1.61)* • Renal chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): 1.55 (1.02 to 2.35)* • Musculoskeletal chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): 1.05 (0.89 to 1.25)*	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear >75% participated in they surveys 2. Is the follow-up adequate? ☐Yes/☒no/ ☐unclear <75% of participants responded to T3 survey (5982/9711) 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:** All generalized estimating equations were adjusted for other host- and treatment-related risk factors with a reported PR and for within-person correlation. Variables with P<0.10 were retained using backward selection criteria.

"Yes" (medium, a lot, very many, or extreme fears or anxiety related to cancer/treatment) versus "No" (no or small amount of fears or anxiety related to cancer/treatment			• Neurologic chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): 2.13 (1.81 to 2.52)* • Other hematologic chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): 1.30 (1.04 to 1.63)* *Treatment risk factors:* • Alkylating agents: Yes (Ref. No) 1.19 (1.08 to 1.32) • Craniotomy: Yes (Ref. No) 1.23 (1.05 to 1.44) **Risk factors for cancer-related anxiety from 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, thoracotomy, nephrectomy, and within-person correlation) Prevalence Ratio (PR) (95% CI) Race/ethnicity, age at interview, age at diagnosis, BMI, cranial radiation, chest radiation, craniotomy, cystectomy, lower extremity amputation, upper extremity amputation were not included in the multivariable model. *Demographic risk factors:* • Female sex (Ref. Male): 1.73 (1.55 to 1.94) • Income <$20,000/yr (Ref. ≥$20,000/yr): 1.51 (1.33 to 1.72) • No high school graduate (Ref. High school graduate): 1.23 (0.99 to 1.51) *Clinical risk factors:* • Smoking: Former (Ref. Never):1.24 (1.06 to 1.45) • Smoking: Current (Ref. Never): 1.25 (1.09 to 1.44) • Meets CDC guidelines for physical activity: No (Ref. Yes) 1.10 (0.99 to 1.22) • Any chronic condition, grade 3-4 (Ref. no chronic condition): 1.56 (1.42 to 1.72)* • One chronic condition, grade 3-4 (Ref. no chronic condition): 1.41 (1.26 to 1.57)* • Two chronic conditions, grade 3-4 (Ref. no chronic condition): 2.03 (1.76 to 2.34)* • Second malignancy (Ref. No organ-specific chronic condition): 1.70 (1.41 to 2.05)* • Vision/hearing/speech chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): 1.15 (0.97 to 1.37)* • Endocrine chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): 1.24 (1.06 to 1.46)* • Respiratory chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): 2.14 (1.44 to 3.17)* • Cardiac chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): 1.23 (1.01 to 1.50)* • Gastrointestinal chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): 1.48 (1.17 to 1.87)* • Renal chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): 0.98 (0.55 to 1.75)* • Musculoskeletal chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): 1.10 (0.91 to 1.32)* • Neurologic chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): 1.59 (1.33 to 1.92)* • Other hematologic chronic condition, grade 3-4 (Ref. No organ-specific chronic condition): 1.21 (0.95 to 1.55)* *Treatment risk factors:* • Anthracyclines (Ref. No anthracyclines): 1.14 (1.00 to 1.29)	

			• Alkylating agents (Ref. No alkylating agents): 1.20 (1.06 to 1.36) • Thoracotomy (Ref. No thoracotomy): 1.32 (1.05 to 1.67) • Nephrectomy (Ref. No nephrectomy): 0.79 (0.61 to 1.03) • Abdominal radiation: 1.4-23.9 Gy (Ref. None): 0.96 (0.75 to 1.22) • Abdominal radiation: 24.0-34.9 Gy (Ref. None): 1.11 (0.90 to 1.37) • Abdominal radiation: 35.0+ Gy (Ref. None): 1.34 (1.12 to 1.60) * from a separate model: generalized estimating equation, adjusted for sex, race/ethnicity, age at questionnaire administration, age at diagnosis, body mass index, smoking status, physical activity level, and within-person correlation	

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?				
Oancea et al. **Emotional distress among adult survivors of childhood cancer. 2014**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/ narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **Not specified** **Years of follow-up:** **≥ 10 years after diagnosis** **18+ years at study enrollment** **Country:** **USA** **Study center:** **St Jude Children's Research Hospital, St. Jude Lifetime Cohort Study** **Measurement tool:** **BSI-18: T-score≥63 clinically relevant distress**	**Sample size:** N=1863 **Diagnoses:** Leukemia 41% Other diagnoses not specified, survivors of childhood cancer **Age at diagnosis:** Median age 7 years **Age at study:** Median age 32 years (Interquartile range 26-38 years) **Controls:** NA	Not specified	**Clinical risk factors for GSI≥63 (BSI-18) from 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) • Learning or memory problems: Severe or disabling problem (Ref. No problem) OR=5.79 (95%CI:2.14-15.72) • Learning or memory problems: Moderate problem (Ref. No problem) OR=3.27 (95%CI:2.17-4.93) • Learning or memory problems: Mild problem (Ref. No problem) OR=2.26 (95%CI:1.52-3.36) **Demographic risk factors for GSI≥63 (BSI-18):** • Gender: n.s. in univariable analysis, therefore not included in the model. • 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) • Employment: Unable to work due to illness or disability (Ref. Caring for home or family (not seeking paid work), or student, or retired, or 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 (not seeking paid work), or student, or retired, or working part- or full-time) OR=1.20 (95%CI:0.82-1.77) • Health insurance: None (Ref. Canadian resident, or through spouse's or parent's policy, or through place of employment, or through self-purchased policy) OR=1.60 (95%CI:1.11-2.32) • Health insurance: Through Medicare or Medicaid or other public assistance programs, or military dependent/veteran's benefits (CHAMPUS) (Ref. Canadian resident, or through spouse's or parent's policy, or through place of employment, or through self-purchased policy) OR=1.07 (95%CI:0.67-1.71) • Age at clinical evaluation (continuous): OR=1.036 (95%CI:1.017-1.055) **Treatment-related risk factors for GSI≥63 (BSI-18):** n.a. **Clinical risk factors for Anxiety≥63 (BSI-18) from 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=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) • Learning or memory problems: Severe or disabling problem (Ref. No problem) OR=2.78 (95%CI:1.01-7.70)	**Quality assessment:** 1. Is the study group representative? ☐Yes/☒no/ ☐unclear <75% of eligible participated (n=1863/4129) 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

			• Learning or memory problems: Moderate problem (Ref. No problem) OR=2.29 (95%CI:1.48-3.54) • Learning or memory problems: Mild problem (Ref. No problem) OR=1.49 (95%CI:0.96-2.33) **Demographic risk factors for Anxiety≥63 (BSI-18):** • Gender: n.s. in univariable analysis, therefore not included in the model. • 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) • Employment: Unable to work due to illness or disability (Ref. Caring for home or family (not seeking paid work), or student, or retired, or 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), or student, or retired, or working part- or full-time) OR=1.41 (95%CI:0.94-2.11) • Health insurance: None (Ref. Canadian resident, or through spouse's or parent's policy, or through place of employment, or 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 (CHAMPUS) (Ref. Canadian resident, or through spouse's or parent's policy, or through place of employment, or through self-purchased policy) OR=0.85 (95%CI:0.52-1.42) • Age at clinical evaluation (continuous): OR=1.021 (95%CI:1.001-1.041) **Treatment-related risk factors for Anxiety≥63 (BSI-18):** n.a. **Clinical risk factors for Depression≥63 (BSI-18) from multivariable logistic regression** (adjusted for sex, 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=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) • Learning or memory problems: Severe or disabling problem (Ref. No problem) OR=9.73 (95%CI:3.71-25.56) • Learning or memory problems: Moderate problem (Ref. No problem) OR=4.00 (95%CI:2.71-5.91) • Learning or memory problems: Mild problem (Ref. No problem) OR=1.86 (95%CI:1.24-2.78) **Demographic risk factors for Depression≥63 (BSI-18):** • Gender: Male (Ref. female) OR=1.56 (95%CI:1.17-2.09) • 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) • Employment: Unable to work due to illness or disability (Ref. Caring for home or family (not seeking paid work), or student, or retired, or 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), or student, or retired, or working part- or full-time) OR=1.39 (95%CI:0.96-2.02) • Health insurance: None (Ref. Canadian resident, or through spouse's or parent's policy, or through place of employment, or 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 (CHAMPUS) (Ref. Canadian resident, or through spouse's or parent's policy, or through place of employment, or through self-purchased policy) OR=1.01 (95%CI:0.64-1.60)	

			• Age at clinical evaluation (continuous): OR=1.027 (95%CI:1.008-1.045) **Treatment-related risk factors for <u>Depression</u>≥63 (BSI-18):** n.a. **Clinical risk factors for <u>Somatization</u>≥63 (BSI-18) from multivariable logistic regression** (adjusted for sex, 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=27.67 (95%CI:9.49-80.65) • Cancer-related pain: A lot of pain (Ref. No pain) OR=16.91 (95%CI:9.94-28.79) • Cancer-related pain: Medium amount of pain (Ref. No pain) OR=5.13 (95%CI:3.41-7.69) • Cancer-related pain: Small amount of pain (Ref. No pain) OR=2.57 (95%CI:1.78-3.71) • Learning or memory problems: Severe or disabling problem (Ref. No problem) OR=6.29 (95%CI:2.14-18.53) • Learning or memory problems: Moderate problem (Ref. No problem) OR=2.07 (95%CI:1.35-3.17) • Learning or memory problems: Mild problem (Ref. No problem) OR=2.57 (95%CI:1.75-3.77) **Demographic risk factors for <u>Somatization</u>≥63 (BSI-18):** • Gender: Male (Ref. female) OR=0.91 (95%CI:0.57-1.43) • Education: Did not graduate high school (Ref. College graduate or post-graduate level) OR=2.21 (95%CI:1.30-3.74) • Education: Completed high school/GED or received training after high school (Ref. College graduate or post-graduate level) OR=1.90 (95%CI:1.26-2.86) • Education: Some college (Ref. College graduate or post-graduate level) OR=1.56 (95%CI:1.05-2.32) • Employment: Unable to work due to illness or disability (Ref. Caring for home or family (not seeking paid work), or student, or retired, or working part- or full-time) OR=1.26 (95%CI:0.68-2.34) • 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), or student, or retired, or working part- or full-time) OR=1.10 (95%CI:0.75-1.61) • Health insurance: None (Ref. Canadian resident, or through spouse's or parent's policy, or through place of employment, or through self-purchased policy) OR=1.43 (95%CI:0.98-2.09) • Health insurance: Through Medicare or Medicaid or other public assistance programs, or military dependent/veteran's benefits (CHAMPUS) (Ref. Canadian resident, or through spouse's or parent's policy, or through place of employment, or through self-purchased policy) OR=1.56 (95%CI:1.02-2.44) • Age at clinical evaluation (continuous): OR=1.032 (95%CI:1.014-1.051) **Treatment-related risk factors for <u>Somatization</u>≥63 (BSI-18):** n.a.	

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?				
Brinkman, Zhang et al. **Suicide ideation and associated mortality in adult survivors of childhood cancer. 2014**				
Study Design Treatment era Years of follow-up	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment Remarks**
Study Design: **☐ Cross-sectional study** **☐ Case-control study** **☒ Cohort study including longitudinal assessment (3 time-points)** **☐ Qualitative study (→ exclude!)** **☐ Systematic/ narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1970-1986** **Years of follow-up:** **1992-2010** **Country:** **USA** **Study center:** **Multi-site (CCSS)** **Measurement tool:** **BSI-18: single item assessing suicidal ideation (SI)**	**Sample size:** N=7708 survivors **Diagnoses:** Leukemia, CNS tumor, Hodgkin disease, Non-Hodgkin lymphoma, wilms tumor, neuroblastoma, soft tissue sarcoma, osteosarcoma **Age at diagnosis:** ≤21 years **Age at study:** ≥ 18 years at baseline survey, mean age (SD) was 25.1 (7.4) years- 26.3 (7.3) years, depending on suicidal ideation status (3 groups) **Controls:** N=2776 randomly selected sibling controls	All treatment data were reported according to suicidal ideation status (3 groups, therefor 3 values are reported in each category Chemotherapy Yes 72.2- 76.9% No 17.4- 19.3% (not explained why this did not add up to 100%) Radiation None: 27.4-30.1% Noncranial: 24.3-29.5% CRT ≤20 Gy: 10.3-13.2% CRT ≥20 Gy: 18.9-27.4%	Suicidal ideation (SI) was ascertained at 3 separate time points over the follow-up period. Risk of Suicidal ideation was analyzed as 1) Late Report (none at baseline but reported at one of two later time points) and as 2) Recurrent (SI at least 2 of the 3 timepoints). All covariates were measured at baseline. OR are expressed with 95th CI in parentheses () Best fitting multivariable models selected using minimum Akaike information criterion. **<u>Clincal risk factors for late-report SI, from multivariable logistic regression</u>** (adjusted for age at diagnosis, physical health status, seizure, pain, chronic health conditions, and depression): • Physical health status: Fair/Poor (Ref. ≥good): OR=1.88 (95%CI:1.29-5.74) • Seizure: Yes (Ref. No) OR=2.04 (95%CI:1.32-3.16) • 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) • 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) • Depression: Yes (Ref. No) OR=2.95 (95%CI:2.10-4.14) **<u>Demographic risk factors for late-report SI, from multivariable logistic regression</u>** (adjusted for age at diagnosis, physical health status, seizure, pain, chronic health conditions, and depression): • Age at diagnosis (continuous): OR=0.98 (95%CI:0.96-1.00) **<u>Clincal risk factors for recurrent SI, from multivariable logistic regression</u>** (adjusted for age at study, marital status, health insurance, physical health status, seizure, pain, and depression): • Physical health status: Fair/Poor (Ref. ≥good): OR 1.87 (95%CI:1.20-2.91) • Seizure: Yes (Ref. No) OR=2.25 (95%CI:1.29-3.93) • 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) • Depression: Yes (Ref. No) OR=9.12 (95%CI:6.32-13.2) **<u>Demographic risk factors for recurrent SI, from multivariable logistic regression</u>** (adjusted for age at study, marital status, health insurance, physical health status, seizure, pain, and depression): • Age at baseline (continuous): OR=1.04 (95%CI:1.00-1.07) • 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) • Health insurance: Yes (Ref. No) OR=0.51 (95%CI:0.33-0.78) **<u>Treatment-related risk factors:</u>** not tested in the multivariable model	**Quality assessment:** 1. Is the study group representative? ☐Yes/☐no/ ☒unclear Unclear how many were eligible. 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear >75% of baseline participants responded to T3 assessment 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?				
Van der Geest et al. **Emotional distress in 652 Dutch very long-term survivors of childhood cancer, using the hospital anxiety and depression scale (HADS). 2013**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **2001-2009** **Years of follow-up:** **Median follow-up time: 15 years, Range: 5-42yrs** **Country:** **Netherlands** **Study center:** **Erasmus MC-Sophia Children's Hospital** **Measurement tool:** **<u>Emotional Distress:</u> Hospital Anxiety and Depression Scale (HADS) total score, clinical cutoff <u>≥</u> 15**	**Sample size:** 652 survivors of childhood cancer **Diagnoses:** ALL (n= 203, 31%) Renal tumor (n= 84, 13%) Non-Hodgkin Lymphoma (n= 73, 11%) Sarcoma (n= 71, 11%, included Rhabdomyosarcoma, Ewing sarcoma, osteosarcoma) Hodgkin lymphoma (n= 51, 8%) Neuroblastoma (n= 48, 7%) Brain tumor (n= 34, 5%) AML (n= 22, 4%) various tumor (n= 66, 10%; included Langerhans cell histiocytosis, germ cell tumors, other rare tumors) **Age at diagnosis:** Median: 6 years, Range: 0-18 yrs **Age at study:** Median: 23 yrs, Range: 15-46 yrs **Controls:** 440 Dutch participants Mean age: 51 years, Range: 17-89 yrs	**Radiotherapy type (Y/N):** Global CNS radiotherapy (n= 77, 12%) focal brain radiotherapy (n= 21, 3%) limbs (n= 6, 1%) abdomen (n= 41, 6%) total body irradiation (n= 9, 1%) SCT – allogenous (Y/N): n= 20, 3% Limb amputation or rotation plastic (Y/N): n= 11, 2%	**Risk factors for increased emotional distress (HADS score) from multivariable linear regression analysis** (adjusted for sex, age at study, age at diagnosis, duration of treatment, global CNS irradiation, educational achievement): **Clinical risk factors:** Disease-related variables were not independently associated with HADS score. Non-significant variables were: age at diagnosis (y) β=0.07, p=0.14 **Demographic risk factors:** High educational achievement (β=-1.28, p<0.01) was significantly associated with a lower HADS score and older age at study time (β=0.08, p=0.03) with higher HADS scores. Non-significant variables were: Sex (m vs f, β=0.58, p=0.18), low educational achievement β=0.44, p=0.53. **Treatment-related risk factors:** In univariable regression, survivors that received global central nervous system irradiation had significantly higher HADS scores than controls and other survivors (8.3±6.6, p=0.05). However, the HADS scores of brain tumor survivors who received focal tumor irradiation was not sign. different from the controls (7.1±5.7, p=0.85). Specific chemotherapeutic agents did not have any effect compared to controls. Survivors with a limb amputation, total body irradiation or limb irradiation were not significantly different from controls. In multivariate regression treatment-related variables were not independently associated with HADS score: duration of treatment (y, β=0.03, p=0.78, global CNS irradiation (yes vs. no, β=0.63, p=0.40)	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?				
Brinkman, Liptak et al. **Suicide ideation in pediatric and adult survivors of childhood brain tumors. 2013**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☒ Other: (specify!) Retrospective medical record view and semi-structured clinical interviews** **Treatment era:** **n.a.** **Years of follow-up:** **n.a** **Country:** **United States of America** **Study center:** **Neuro-oncology outcomes program at Dana Farber Cancer Institute and Children's Hospital Boston.** **Measurement tool: Medical record view and semi-structured clinical interviews based on criteria set forth by DSM IV-TR and included assessment of depression, anxiety, behavior and social functioning**	**Sample size:** 319 Survivors of pediatric brain tumors. **Diagnoses:** Pediatric brain tumor: most common = low-grade glioma n=162 (50.8%), embryonal tumor n=64 (20.1%) Craniopharyngioma n=23, (7.2%) Germ cell tumor n=28, (8.8%) Ependymoma n=14, (4.4%) Other n=28 (8.8%) **Age at diagnosis:** Mean = 10 years before study (SD = 5.0) Approx. 40% were ≥10 years from diagnosis. **Age at study:** Mean = 18 years (SD = 5.0), range 10-35 years **Controls:** n.a.	Surgery only (observation) n=99 (31%) Surgery + radiation n=95 (29.8%) surgery, radiation + chemotherapy n=84 (26.3%) other n=41 (12.9%)	**Risk factors for suicide ideation from multivariable logistic regression analysis** (adjusted for sex, age, depression history, psychoactive medication, age at diagnosis, surgery only treatment, and seizures): • Sex: Female (Ref. Male) OR=1.6 (95%CI:0.7-3.8) • Current age: OR=1.1 (95%CI:0.99-1.2) • History of depression: Yes (Ref. No) OR=20.5 (95%CI:4.2-101.1) • Psychoactive medication use: Yes (Ref. No) OR=4.5 (95%CI:1.8-11.2) • Age at diagnosis: OR=1.1 (95%CI:0.97-1.2) • Observation or surgery only treatment: Yes (Ref. No) OR=3.7 (95%CI:1.5-9.1) • History of seizures: Yes (Ref. No) OR=3.6 (95%CI:1.1-11.1)	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?				
Kim et al. **Psychological distress in adolescent and young adult survivors of childhood cancer in Korea. 2013**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **Not reported; recruited for the study June – November 2010** **Years of follow-up:** **Time from diagnosis M=11.99 years (SD=5.91 years), range 2 to 29 years** **Country:** **Korea** **Study center:** **Multiple hospital sites in Korea (exact N unknown)** **Measurement tool:** **Brief Symptom Inventory (BSI-18)** **T-score ≥63 used to identify survivors with emotional distress: anxiety, depression, somatization, global severity index (GSI)**	**Sample size:** 223 survivors of childhood cancer **Diagnoses:** Hematological cancers 157 (71.7%) Solid or soft tissue tumors 32 (14.6%) Central nervous system or brain tumors 30 (13.7%) **Age at diagnosis:** 0-18 years of age, M=9.91, SD=4.39 **Age at study:** 15-38 years, M=21.92, SD=4.69 **Controls:** n/a	Not reported	**Risk factors for psychological distress from multivariable logistic regression (adjusted for age, economic status, and time since diagnosis):** Time since diagnosis: <10 years reference 10-14: OR 0.36, 95%CI: 0.12-1.09, p=0.071 15-19: OR 1.36, 95%CI: 0.50-3.67, p=0.544 >20 years: OR 3.67, 95%CI: 1.05-12.88, p=0.042 Age: Adolescents 15-18 years reference Emerging adults 19-25: OR 2.64 (95%CI: 0.83-8.39, p=0.1 Young adults 26-39: OR 2.82 (95%CI: 0.63-12.60, p=0.176) Economic status: Stable reference Unstable OR 2.58, 95%CI: 1.20-5.54, p=0.016	**Quality assessment:** 1. Is the study group representative? ☐Yes/☐no/ ☒unclear 2. Is the follow-up adequate? ☐Yes/☐no/ ☒unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:** Employed a convenience sample so unlikely a representative sample of survivors in Korea. Limited generalizability. Analyses were not adjusted for relevant treatment exposures. No comparison group with other non-cancer Koreans of the same age. US normative data and cut-off scores used for the BSI.

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?				
***Gianinazzi et al.* Adolescent survivors of childhood cancer: are they vulnerable for psychological distress? 2013**				
Study Design Treatment era Years of follow-up	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1976-2003** **Years of follow-up:** **Time since diagnosis:** **M= 12.2 years (SD=4.0)** **Country:** **Switzerland** **Study center:** **Swiss Childhood Cancer Registry** **Measurement tool:** **BSI-18**	**Sample size:** N=407 **Diagnoses:** Leukemias- 33% Lymphomas- 13% CNS tumors- 17% Neuroblastomas- 6% Retinoblastomas- 3% Renal tumors- 10% Hepatic tumors- 1% Bone tumors- 3% Soft tissue sarcomas- 5% Germ cell tumors- 3% Langerhans cell hystiocytosis- 5% Other- 1% **Age at diagnosis:** M= 5.7 years (SD= 3.9) **Age at study:** M = 17.9 years (SD = 1.5) Range: 16.0-19.9 years **Controls:** Three comparison groups: • N=93 healthy German adolescents • N=56 German adolescent psychotherapy patients • N=102 siblings of survivors	Chemotherapy with or without surgery- 53% Radiation with or without chemotherapy/surgery - 26% BMT- 7% Surgery only- 14%	**Risk factors for elevated psychological distress (BSI GSI T-score≥57) from multivariable logistic regression** (adjusted for age at study, sex, parents' education, perceived parents' support, diagnosis, treatment, late effects, and time since diagnosis) • Age at study, years: 18-19 (Ref. 16-17) OR=1.41 (95%CI:0.69-2.89, p=0.343) • **Female (Ref. Male) OR=3.59 (95%CI:1.71-7.52, p=0.001)** • Parents' education: Secondary, tertiary (Ref. Compulsory, primary) OR=1.30 (95%CI:0.52-3.27, p=0.574) • **Perceived parents' support: Low (Ref. High) OR=7.24 (95%CI:2.82-18.56, p<0.001)** • 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) • 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) • **Late effects: Psychological problems (Ref. No late effects) OR=14.89 (95%CI:4.72-46.99, p<0.001)** • **Late effects: Somatic problems (Ref. No late effects) OR=6.98 (95%CI:3.07-15.91, p<0.001)** **Risk factors for elevated depression scores (BSI Depression subscale T-score≥57) from multivariable logistic regression** (adjusted for age at study, sex, parents' education, perceived parents' support, diagnosis, treatment, late effects, and time since diagnosis) • Age at study, years: 18-19 (Ref. 16-17) OR=1.01 (95%CI:0.53-1.89, p=0.992) • Female (Ref. Male) OR=1.59 (95%CI:0.86-2.98, p=0.143) • Parents' education: Secondary, tertiary (Ref. Compulsory, primary) OR=1.47 (95%CI:0.66-3.28, p=0.346) • **Perceived parents' support: Low (Ref. High) OR=12.54 (95%CI:5.34-29.47, p<0.001)** • 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) • 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) • **Late effects: Psychological problems (Ref. No late effects) OR=13.08 (95%CI:4.34-39.34, p<0.001)** • **Late effects: Somatic problems (Ref. No late effects) OR=4.23 (95%CI:2.01-8.95, p<0.001)**	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/☐unclear **Remarks:**

			Risk factors for elevated somatization scores (BSI Somatization subscale T-score≥57) from multivariable logistic regression (adjusted for age at study, sex, parents' education, perceived parents' support, diagnosis, treatment, late effects, and time since diagnosis) • Age at study, years: 18-19 (Ref. 16-17) OR=0.94 (95%CI:0.43-2.06, p=0.881) • **Female (Ref. Male) OR=6.09 (95%CI:2.66-13.94, p<0.001)** • Parents' education: Secondary, tertiary (Ref. Compulsory, primary) OR=1.85 (95%CI:0.75-4.59, p=0.184) • Perceived parents' support: Low (Ref. High) OR=1.51 (95%CI:0.48-4.74, p=0.478) • Diagnosis: CNS tumors (Ref. Leukemia, lymphoma) OR=0.73 (95%CI:0.22-2.43, p=0.251) • Diagnosis: Other (Ref. Leukemia, lymphoma) OR=1.42 (95%CI:0.64-3.18, p=0.251) • Treatment: Surgery (Ref. Chemotherapy) OR=1.01 (95%CI:0.55-2.87, p=0.505) • Treatment: Radiotherapy (Ref. Chemotherapy) OR=0.99 (95%CI:0.40-2.46, p=0.505) • Treatment: Bone marrow transplantation (Ref. Chemotherapy) OR=3.19 (95%CI:0.89-11.33, p=0.505) • **Time since diagnosis, years: 10-14 (Ref. 0-9) OR=3.27 (95%CI:1.15-9.29, p=0.145)** • **Time since diagnosis, years: ≥15 (Ref. 0-9) OR=4.16 (95%CI:1.41-12.26, p=0.145)** • Late effects: Psychological problems (Ref. No late effects) OR=3.54 (95%CI:0.94-13.30, p<0.001) • **Late effects: Somatic problems (Ref. No late effects) OR=4.97 (95%CI:2.26-10.94, p<0.001)** **Risk factors for elevated anxiety scores (BSI Anxiety subscale T-score≥57) from multivariable logistic regression** (adjusted for age at study, sex, parents' education, perceived parents' support, diagnosis, treatment, late effects, and time since diagnosis) • Age at study, years: 18-19 (Ref. 16-17) OR=1.17 (95%CI:0.58-2.39, p=0.659) • **Female (Ref. Male) OR=3.01 (95%CI:1.45-6.24, p=0.003)** • Parents' education: Secondary, tertiary (Ref. Compulsory, primary) OR=0.88 (95%CI:0.33-2.36, p=0.807) • Perceived parents' support: Low (Ref. High) OR=1.91 (95%CI:0.68-5.40, p=0.220) • 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) • 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) • **Late effects: Psychological problems (Ref. No late effects) OR=9.56 (95%CI:2.96-30.91, p<0.001)** • **Late effects: Somatic problems (Ref. No late effects) OR=4.06 (95%CI:1.84-8.97, p<0.001)**	

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?				
Marina et al. **Changes in health status among aging survivors of pediatric upper and lower extremity sarcoma: a report from the childhood cancer survivor study. 2013**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☐ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **January 1, 1970 – December 31, 1986** **Years of follow-up:** **Not reported,** **Between 5 and 29 years at baseline and 20 and more than 35 years at 2007er assessment** **Country:** **U.S.** **Study center:** **Survivors of 26 participating institutions (CCSS)** **Measurement tool:** **Brief Symptom Inventory (BSI-18): If participants scored ≥63 in any of the subscales or GSI, they were classified as reporting poor mental health.** **Anxiety: "Do you currently have anxiety/fears as a result of your cancer or its treatment?" Participants who endorsed medium, a lot, or very much anxiety/fear were classified as having anxiety.**	**Sample size:** 1094 extremity sarcoma survivors who participated in the baseline questionnaire; 813 survivors who participated in the 2003; and 712 who participated in the 2007 questionnaire (see Figure 1 for details). Among this group of survivors, 661 (60.4%) participated in all three questionnaires. **Diagnoses:** Extremity sarcoma survivors (Osteosarcoma (49.0%), soft tissue sarcoma (32.0%), Ewing sarcoma (16.3%), and other bone tumors (2.7%)) **Age at diagnosis:** median age at diagnosis was 13 years (range, 0–20), **Age at study:** median age at study entry 18 years (range, 5–25) median age at questionnaire completion 33 years (range, 10–53) (different information due to repeated measurment) **Controls:** n.a.	Data on treatment is only extracted for overall sarcoma group (in manuscript they grouped it into upper and lower extremity): **Chemotherapy treatment** Anthracyclines in 64.4% of all sarcoma survivors Alkylating agents in 57.1% Platinum in 18.9% Vincristine in 59.4% **Radiotherapy** Chest radiation in 9.3% Abdominal radiation in 1.2% Limb radiation in 20.6% Thoracotomy in 87.7% **Surgery** Limb surgery: Above knew amputation in 34.8% Below knee amputation in 4.0% Arm amputation in 3.6% Limb sparing in 19.4% No surgery 38.2%	**Risk factors for poor mental health from generalized linear models (adjusted for tumor location, age at questionnaire, sex, race, tumor type, and age at diagnosis):** • Tumor location: Lower Extremity (Ref. Upper) RR=0.87 (95%CI:0.71-1.08) • 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) • Female (Ref. Male) RR=0.96 (95%CI:0.81-1.15) • Race: Non-white (Ref. White) RR=1.07 (95%CI:0.80-1.41) • 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) **Risk factors for poor mental health from generalized linear models (adjusted for tumor location, age at diagnosis):** • **Abdominal Radiation: Any (Ref. None) RR=2.24 (95%CI:1.25-4.02)** **Risk factors for anxiety from generalized linear models (adjusted for tumor location, age at questionnaire, sex, race, tumor type, and age at diagnosis):** • Tumor location: Lower Extremity (Ref. Upper) RR=0.93 (95%CI:0.57-1.50) • 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) • **Female (Ref. Male) RR=1.73 (95%CI:1.08-2.77)** • Race: Non-white (Ref. White) RR=0.96 (95%CI:0.47-1.97) • **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)	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/☐unclear **Remarks:**

			• Tumor Type: Other bone (Ref. Soft tissue sarcoma) RR=1.37 (95%CI:0.32-5.93) **Risk factors for anxiety from generalized linear models (adjusted for abdominal radiation, limb radiation, tumor location, and 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)**	

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?				
Kinahan et al. **Scarring, disfigurement, and quality of life in long-term survivors of childhood cancer: a report from the Childhood Cancer Survivor study. 2012**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/ narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era: Started treatment between January 1, 1970, and December 31, 1986** **Years of follow-up: M=16.1 yrs (SD=4.9) for diagnosis to baseline data; additional M=7.7 yrs (SD=1.2) from baseline to BSI-18 data** **Country: US** **US** **Study center: Childhood Cancer Survivor Study (CCSS)** **Measurement tool:**	**Sample size:** 14,358 survivors **Diagnoses:** Leukemia- 33.6% CNS- 13.1% Hodgkin's lymphoma- 13.4% Non-Hodgkin's lymphoma- 7.5% Kidney tumor- 8.7% Neuroblastoma- 6.6% Soft tissue sarcoma- 8.7% Bone tumor- 8.3% **Age at diagnosis:** Range: 0-21 yrs 0-4 yrs- 40.1% 5-9 yrs- 22.3% 10-14 yrs- 20.3% 15-21 yrs- 17.3% **Age at study:** Range: 5-49 yrs at baseline 5-20 yrs- 36.5% 20-29 yrs- 41.0% 30-39 yrs- 20.2% 40-49 yrs- 2.3% **Controls:** 4,023 siblings	<u>Surgery & chemotherapy</u> No surgery (chemotherapy only)- 18.4% Surgery, no chemotherapy- 19.1% Surgery, with chemotherapy- 62.5% <u>Surgeries</u> Surgery on limb(s)- 7.7% Surgery on head or neck- 8.1% Surgery on trunk of body- 16.6% <u>Cranial radiation, Gy</u> None- 33.8% Scatter only- 31.1% Direct, < 20- 11.6% Direct, 20-36- 12.1% Direct, > 36- 11.4%	**<u>Risk factors for psychological distress (BSI-18: Global Status Index) from generalized estimating equations</u>** **Clinical risk factors:** • 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)** • 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) • 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) **Demographic risk factors:** • 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) • Sex: Female (Ref. Male) OR=1.16 (95%CI:1.00-1.34, p=0.06) • Race: Black (Ref. White) OR=1.03 (95%CI:0.67-1.60, p=0.88) • Race: Other/mixed (Ref. White) OR=1.01 (95%CI:0.69-1.46, p=0.98) • **College graduate: Yes (Ref. No) OR=0.64 (95%CI:0.54-0.75, p<0.001)** • **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)** **Treatment-related risk factors:** • 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) • **Surgery: Yes (Ref. No) OR=1.35 (95%CI:1.14-1.60, p<0.001)** **<u>Risk factors for psychological distress (Somatization subscale) from generalized estimating equations</u>** **Clinical risk factors:** • **Head/neck scarring or disfigurement: Yes (male) (Ref. No) OR=1.51 (95%CI:1.19-1.91, p<0.001)** Yes (female) (Ref. No) OR=1.07 (95%CI:0.89-1.29, p=0.46) • **Arm/leg scarring or disfigurement: Yes (Ref. No) OR=1.23 (95%CI:1.05-1.43, p=0.01)** • **Chest/abdomen scarring or disfigurement: Yes (Ref. No) OR=1.18 (95%CI:1.02-1.36, p=0.02)**	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☒Yes/☐no/ ☐n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

Brief Symptom Inventory–18 (BSI-18)			• **Persistent hair loss: Yes (Ref. No) OR=1.42 (95%CI:1.18-1.71, p<0.001)** • Age at diagnosis: 5-9 years (Ref. 0-4 years) OR=1.12 (95%CI:0.93-1.34, p=0.23) • Age at diagnosis: 10-21 years (Ref. 0-4 years) OR=1.11 (95%CI:0.90-1.39, p=0.33) • Recurrence: Yes (Ref. No) OR=1.09 (95%CI:0.91-1.32, p=0.35) • Second malignant neoplasm: Yes (Ref. No) OR=1.24 (95%CI:0.97-1.57, p=0.08) **Demographic risk factors:** • Age at study: 30-39 years (Ref. <30 years) OR=0.95 (95%CI:0.78-1.15, p=0.60) • Age at study: ≥40 years (Ref. <30 years) OR=1.03 (95%CI:0.79-1.34, p=0.85) • Sex: Female (Ref. Male) 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 • Race: Black (Ref. White) OR=1.09 (95%CI:0.75-1.57, p=0.66) • Race: Other/mixed (Ref. White) OR=0.86 (95%CI:0.61-1.20, p=0.36) • **College graduate: Yes (Ref. No) OR=0.63 (95%CI:0.55-0.73, p<0.001)** • **Marital status: Divorced, separated, widowed, or no longer living as married (Ref. Married/living as married) OR=1.48 (95%CI:1.23-1.79, p<0.001)** • Marital status: Never married or lived as married (Ref. Married/living as married) OR=1.10 (95%CI:0.94-1.30, p=0.24) **Treatment-related risk factors:** • Cranial radiation: Scatter exposure only (Ref. None) OR=1.11 (95%CI:0.94-1.31, p=0.23) • Cranial radiation: Direct, ≤20 Gy (Ref. None) OR=1.21 (95%CI:0.96-1.52, p=0.10) • Cranial radiation: Direct, 20-36 Gy (Ref. None) OR=1.18 (95%CI:0.94-1.49, p=0.14) • Cranial radiation: Direct, ≥36 Gy (Ref. None) OR=1.03 (95%CI:0.80-1.34, p=0.82) • **Surgery: Yes (Ref. No) OR=1.34 (95%CI:1.16-1.55, p<0.001)** **Risk factors for psychological distress (Anxiety subscale) from generalized estimating equations** **Clinical risk factors:** • 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)** • Age at diagnosis: 5-9 years (Ref. 0-4 years) OR=0.96 (95%CI:0.74-1.23, p=0.73) • Age at diagnosis: 10-21 years (Ref. 0-4 years) OR=1.08 (95%CI:0.81-1.45, p=0.60) • 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) **Demographic risk factors:** • 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) • Sex: Female (Ref. Male) OR=0.98 (95%CI:0.82-1.17, p=0.84) • Race: Black (Ref. White) OR=1.04 (95%CI:0.61-1.77, p=0.88)	

			• Race: Other/mixed (Ref. White) OR=1.02 (95%CI:0.67-1.57, p=0.91) • **College graduate: Yes (Ref. No) OR=0.71 (95%CI:0.59-0.86, p<0.001)** • Marital status: Divorced, separated, widowed, or no longer living as married (Ref. Married/living as married) 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 • Marital status: Never married or lived as married (Ref. Married/living as married) 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 **Treatment-related risk factors:** • **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) • Surgery: Yes (Ref. No) OR=1.18 (95%CI:0.97-1.44, p=0.10) **<u>Risk factors for psychological distress (Depression subscale) from generalized estimating equations</u>** **Clinical risk factors:** • **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)** • 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) • 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) **Demographic risk factors:** • 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) • Sex: Female (Ref. Male) 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 • Race: Black (Ref. White) OR=0.86 (95%CI:0.55-1.34, p=0.50) • Race: Other/mixed (Ref. White) OR=1.10 (95%CI:0.80-1.51, p=0.57) • **College graduate: Yes (Ref. No) OR=0.79 (95%CI:0.68-0.92, p<0.01)** • Marital status: Divorced, separated, widowed, or no longer living as married (Ref. Married/living as married) 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 • Marital status: Never married or lived as married (Ref. Married/living as married) 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 **Treatment-related risk factors:** • **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) • **Surgery: Yes (Ref. No) OR=1.24 (95%CI:1.06-1.45, p=0.01)**	

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?				
Zebrack et al. **The perceived impact of cancer on quality of life for post-treatment survivors of childhood cancer. 2011**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1968-2005** **Years of follow-up:** **n.a.** **Country:** **US** **Study center:** **3 childhood cancer centers** **Measurement tool:** **Brief Symptom Inventory (BSI-18)**	**Sample size:** 621 survivors of childhood cancer **Diagnoses:** Hematological (n= 379, 61.0%), brain tumor (n= 79, 12.7%), solid tumors/soft tissue tumors/other (n= 163, 26.2%; included germ cell tumors, retinoblastoma, neuroblastoma, and other tumors not specified) **Age at diagnosis:** M = 11.1 yrs, SD = 5.5 yrs Range: 0-21 yrs **Age at study:** M = 26.9 yrs, SD = 5.5 Range: 18-39 yrs **Controls:** n.a.	No information provided	**Global Distress (BSI-18 GSI)** Multivariate hierarchical regression standardized beta coefficients presented. **Clinical risk factors:** *Significant:* Health problems (1 = yes, present): 0.077, *p* <0.05 Impact of cancer – negative: 0.443, *p* <0.001 Impact of cancer – positive: -0.253, *p* <0.001 *Non-significant:* Cancer type (1 = brain tumor): 0.024 Cancer type (1 = solid tumor): -0.018 **Demographic risk factors:** *Significant:* Employment status (1 = employed): -0.075, *p* <0.05 Education (1 = some college): 0.097, *p* <0.05 Marital/relationship status (1 = yes): -0.115, *p* <0.01 *Non-significant:* Gender (1 = male): 0.065 Education (1 = having college degree): 0.062 Income (1 ≥ $25,000): -0.053 Age at diagnosis: 0.022 Years since diagnosis: -0.019 **Treatment-related risk factors:** n.a.	**Quality assessment:** 1. Is the study group representative? ☐Yes/☒no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:** Only 29.3% of those eligible participated in the study

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?				
Stuber et al. **Prevalence and predictors of posttraumatic stress disorder in adult survivors of childhood cancer. 2010**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: ☒ Cross-sectional study ☐ Case-control study ☐ Cohort study ☐ Qualitative study (→ exclude!) ☐ Systematic/narrative review (→ exclude!) ☐ RCT ☐ Other: (specify!) Treatment era: 1970-1986 Years of follow-up: Years since dx: 15-19 years (27.1%); 20-24 years (35.8%) 25-29 years (25.5%); 30-34 years (11.6%) Country: USA Study center: Various in USA and Canada (CCSS) Measurement tool: Posttraumatic stress response Diagnostic Scale (PDS): PTSD coded as dichotomous categorical variable: yes/no Brief Symptom Inventory-18 (BSI-18) T-score ≥ 63 considered as clinically significant distress on the global stress index (GSI) or subscales of depression, anxiety, or somatization	**Sample size:** 6542 survivors of childhood cancer **Diagnoses:** Bone cancer (9.2%), Central Nervous System Malignancies (10.5%), Hodgkin Lymphoma (14.2%), Kidney-Wilms (9.6%), Leukemia (33.4%), Non-Hodgkin Lymphoma (7.7%), Neuroblastoma (6.2%), Soft tissue sarcoma (9.2%) **Age at diagnosis:** Mean age = 8.2 yrs, SD = 5.87 yrs Range: 0-20 yrs **Age at study:** Mean age = 31.85 yrs, SD = 7.55 yrs Range: 18-53 yrs **Controls:** 368 siblings Mean age = 33.44 yrs, SD = 8.2 yrs Range: 18-54	Chemotherapy Y/N • None (20.3%) • Anthracycline/ Alkylating (59.8%) • Other drugs (19.9%) Radiation Therapy (RT) Y/N • RT to brain (29.6%) • RT, but not brain (33.5%) • RT site unknown (2.9%) • No RT (34.0%)	**Clinical risk factors:** Risk of PTSD as compared to siblings (from logistic regression models adjusted for age at interview, gender, race and intrafamily correlation): Significant enhanced risk for all diagnostic groups > 2 fold • Bone cancer: OR=3.57 (95%CI:1.56 - 8.21), p<0.01 • CNS: OR=3.64 (95%CI:1.54 - 8.63), p<0.01 • Hodgkin Lymphoma: OR=4.64 (95%CI:1.91 - 11.26), p<0.001 • Wilms: OR=2.41 (95%CI:1.04 - 5.55), p=0.04 • Leukemia: OR=3.84 (95%CI:1.74 - 8.46), p<0.01 • Non-Hodgkin Lymphoma: OR=4.08 (95%CI:1.74 - 9.54), p<0.01 • Neuroblastoma: OR=2.89 (95%CI:1.01 - 8.31), p=0.05 • Soft tissue sarcoma: OR=3.24 (95%CI:1.42 - 7.41), p<0.01 **Demographic and treatment-related risk factors:** Risk of PTSD as compared to other survivors (from multivariable logistic regression models, adjusted for sex an race, age at interview, education, employment, personal income, marital status, radiation and age at diagnosis, chemotherapy, SMN, and 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 • 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 • Education: ≤High school graduate (Ref. ≥College graduate): OR=1.51 (95%CI:1.16 – 1.98), p<0.01 • Education: Some college: OR=1.12 (95%CI:0.90 – 1.39), p=0.32 • Employment: Unemployed (Ref. employed): OR=2.01 (95%CI:1.62 - 2.51), p<0.0001 • 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 • 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 Radiation stratified by age at diagnosis: • 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	**Quality assessment:** 1. Is the study group representative? ☒ Yes/☐ no/ ☐ unclear 2. Is the follow-up adequate? ☒ Yes/☐ no/ ☐ unclear 3. Are the outcome assessors blinded? ☐ Yes/ ☐ no/ ☒ n.a./ ☐ unclear 4. Are the analyses adjusted for important confounding factors? ☒ Yes/☐ no/ ☐ unclear **Remarks:** Controlled for demographic and treatment variables

RAND Health Status Survey, Short Form-36 (RAND SF-36) T-score ≤ 40 considered clinically impaired Diagnostic Criterion F for PTSD Met if BSI-18 GSI ≥ 63, two subscale scores ≥ 63 or SF-36 score ≤ 40 indicating functional limitations caused by emotional stress			○ RT other site (Ref. No RT): OR=1.09 (95%CI:0.67 – 1.77), p=0.74 • 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 • 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	

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?				
Michel et al. **Psychological distress in adult survivors of childhood cancer: the Swiss Childhood Cancer Survivor study. 2010**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1976-2003** **Years of follow-up:** **Time since diagnosis** ***M*= 19.5 yrs (SD=6.5 yrs)** **Range: 5.8 - 37.9 yrs** **5-14 yrs = 26.3%** **15-19 yrs =26.6%** **20-24 yrs =26.1%** **≥25 yrs = 20.9%** **Country:** **Switzerland** **Study center:** **Swiss Childhood Cancer Registry (SCCR)** **Measurement tool:** **Brief symptom Inventory (53 items, T-scores ≥63)**	**Sample size:** 1076 responders to invitation to participate 987 with valid BSI 623 non-responders to invitation **Diagnoses:** Leukemia (36.9%), lymphoma (21.5%), CNS tumor (11.7%), neuroblastoma (3.2%), retinoblastoma (1.9%), renal tumor (5.3%), hepatic tumor (0.5%), malignant bone tumor (5.3%), soft tissue sarcoma (5.3%), germ cell tumor (2.7%), carcinamo (1%), other malignancy (0.3%) or Langerhans cell histiocytosis (4.3%) **Age at diagnosis:** *M*=8.4 yrs (SD=4.7 yrs) Range: 0.0 - 16.0 yrs **Age at study:** *M*=27.9 yrs (SD=6.0 yrs) Range: 20.0 - 49.1 yrs 20-24.9 yrs = 38.0% 25-29.9 yrs = 29.7% ≥30 yrs = 32.3% **Controls:** Population Norms for BSI	Surgerly only (8.8%) Chemotherapy (49.6%) Radiotherapy (40.7%) Bone marrow transplantation (4%)	**Clinical, demographic and treatment-related risk factors:** Multivariable logistic regression for psychological distress caseness (GSI of BSI T≥ 63), adjusted for sex, current age, siblings, immigration status, age at diagnosis, and late effects Education level, employment status, income, time since diagnosis, diagnosis, treatment, bone marrow transplantation, relapse were not significant in univariable logistic regression and therefore not included in the multivariable model. • Sex: female (Ref. male): OR=1.79 (95%CI:1.22-2.64), p=0.003 • 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) • Siblings: No (Ref. Yes): OR=2.53 (95%CI:1.48-4.32), p=0.001 • Immigration status: Immigrant (Ref. Native Swiss): OR=2.11 (95%CI:1.05-4.26), p=0.037 • 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 • Late effects: Somatic problems only (Ref. No late effects): OR=2.00 (95%CI:1.29-3.11), p=0.002 • Late effects: Psychological problems (may include somatic problems) (Ref. No late effects): OR=6.74 (95%CI:4.06-11.17), p<0.001	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?				
Recklitis, Diller et al. **Suicide ideation in adult survivors of childhood cancer: a report from the Childhood Cancer Survivor Study. 2010**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/ narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1.1.1970-31.12.1986** **Years of follow-up:** **≥5 years from diagnosis** **Country:** **US** **Study center:** **Multicenter (CCSS), check appendix** **Measurement tool:** **BSI-18, specifically item 9: Suicidal ideation (SI)**	**Sample size:** N: 9126 (4312 female, 4814 male) **Diagnoses:** Leukemia: 2681 (29.4%) Hodgkins Lymphoma: 1645 (18.0%) CNS: 1136 (12.5%) Bone: 991 (10.9%) Sarcoma: 88 (9.7) NHL 842 (9.2%) Wilms tumor 584 (6.4%) Neuroblastoma 360 (3.9%) **Age at diagnosis:** <3 years: 820 (9.0%) 3-6 years: 2043 (22.4%) 7-10 years: 1764 (19.3%) 11-17: 3509 (10.9%) **Age at study:** 18-24 years: 3566 (39.1%) 25-29 years: 2501 (27.5%) 30-34 years: 1859 (20.4%) ≥ 35 years: 1200 (13.2%) **Controls:** Siblings: 2968 (1585 female, 4814 male)	Surgery only: 578 (7.3%) RT only: 23 (0.3%) Chemo only: 307 (3.9%) Chemo and RT: 910 (11.5%) Chemo and surgery: 1310 (16.6%) RT and surgery: 1143 (14.5%) Chemo and RT and surgery 3632 (46.0%)	**Risk factors for suicidal ideation from hierarchical logistic regression analysis (adjusted for sex, age at study, diagnosis, age at diagnosis, depression score, physical health, no. of chronic conditions, cancer pain, and no. of hospital admissions)** • Sex: Female (Ref. Male): OR=1.2 (95%CI:1.0-1.4, p≥0.05) • 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) • 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)** • **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)** • **BSI-Depression score ≥63 (Ref. <63): OR=16.4 (95%CI:13.7-19.7, p<0.001)** • **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) • 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) • **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)** • 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)	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?

Zeltzer et al. **Psychosocial outcomes and health-related quality of life in adult childhood cancer survivors: a report from the childhood cancer survivor study. 2008**

Study Design Treatment era Years of follow-up	Participants	Treatment	Main outcomes	Quality assessment Remarks
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1970-1986** **Years of follow-up:** **Mean survival time = 23 years (range: 15-34)** **Country:** **USA and Canada** **Study center:** **Multi-centre 26 sites (CCSS)** **Measurement tool:** **BSI-18: T-scores ≥ 63 classified as poor outcome on depression (dep), anxiety (anx) and somatisation (som) subscales, or Global Severity Index (GSI)** **SF-36: 1 SD below mean (T-score ≤ 40) on mental health subscale (MH) or mental component**	**Sample size:** 7147 survivors **Diagnoses:** Acute lymphoblastic leukemia(ALL): n=2090, 29.2% Acute myeloid leukemia (AML): n=170, 2.4% Other leukemia: n=146, 2.0% Astrocytomas: n=548, 7.7% Medulloblastoma, PNET: n=195, 2.7% Other CNS tumors: n=143, 2.0% Hodgkins disease (HD): n=955, 13.4 % Non-Hodgkins lymphoma (NHL: n=533, 7.5% Wilm's tumor: n=671, 9.4% Neuroblastoma: n=448, 6.3% Soft tissue sarcoma: n=631, 8.8% Ewing's sarcoma: n=194, 2.7% Osteosarcoma: n=395, 5.5% Other bone: n=28, 0.4% **Age at diagnosis:** Median age at diagnosis: 7 yrs 0-3 yrs: n=2211, 30.9% 4-9 yrs: n=2137, 29.9% 10-14 yrs: n=1497, 20.9% 15-20 yrs: n=1302, 18.2%	**Chemotherapy:** Yes: n=5326, 74.5% No: n=1411, 19.7% Medical record unavailable: n=410, 5.7% **Radiation** Cranial: n=2057, 28.8% Other than cranial: n=2415, 33.8% None: n=2265, 31.7% Medical record unavailable: n=410, 5.7%	**Clinical risk factors:** No clinical risk factors analyzed. **Demographic risk factors for psychological distress from multiple variable logistic regression** (in survivors, risk for poor outcome on BSI subscales or GSI) Odds ratios and 95% confidence intervals presented as OR (CI) **Sex** Male: Reference / Reference / Reference / Reference Female: 1.3 (1.1-1.5) / 1.7 (1.4-2.0) / 1.7 (1.4-1.9) / 1.5 (1.3-1.8) **Age at second follow-up** 18-24: Reference / Reference / Reference / Reference 25-34: 1.0 (0.8-1.2) / 0.8 (0.6-1.0) / 1.1 (0.9-1.3) / 0.9 (0.7-1.1) 35+: 1.3 (1.0-1.6) / 0.9 (0.6-1.1) / 1.2 (0.9-1.5) / 1.1 (0.9-1.5) **Race/ ethnicity** White: Reference / Reference / Reference / Reference Black: 0.7 (0.4-1.1) / 1.0 (0.6-1.6) / 1.1 (0.7-1.7) / 1.0 (0.7-1.6) Hispanic: 1.2 (0.8-1.7) / 1.3 (0.9-2.0) / 1.5 (1.1-2.1) / 1.4 (1.0-2.0) Other: 1.1 (0.7-1.7) / 0.8 (0.4-1.4) / 0.6 (0.4-1.1) / 0.8 (0.5-1.4) **Educational attainment** < high school: 1.2 (0.9-1.8) / 1.6 (1.1-2.3) / 1.6 (1.2-2.3) / 1.6 (1.1-2.2) High school grad: 1.2 (1.0-1.4) / 1.2 (1.0-1.4) / 1.4 (1.2-1.6) / 1.3 (1.1-1.5) College grad: Reference / Reference / Reference / Reference **Marital status** Single: 1.9 (1.6-2.3) / 1.1 (0.9-1.4) / 0.8 (0.7-1.0) / 1.3 (1.1-1.6) Married/ living as: Reference / Reference / Reference / Reference Divorced/ separated: 2.2 (1.7-2.9) / 1.6 (1.1-2.1) / 1.2 (0.9-1.6) / 1.7 (1.2-2.2) **Employment** Employed/ caring for home: Reference / Reference / Reference / Reference Student: 1.0 (0.7-1.4) / 1.0 (0.6-1.5) / 0.9 (0.6-1.3) / 1.0 (0.7-1.5) Looking for work/ unable to work: 2.5 (2.0-3.0) / 2.5 (2.0-3.1) / 3.4 (2.8-4.1) / 3.1 (2.5-3.7) **Annual income** $20,000+: Reference / Reference / Reference / Reference < $20,000: 1.8 (1.5-2.2) / 1.6 (1.3-2.0) / 1.7 (1.4-2.1) / 1.8 (1.5-2.3) **Health Insurance** Yes: Reference / Reference / Reference / Reference No: 1.3 (1.0-1.7) / 1.3 (1.0-1.7) / 1.3 (1.0-1.4) / 1.3 (1.1-1.7)	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/☐unclear 3. Are the outcome assessors blinded? ☒Yes/☐no/☐n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/☐unclear **Remarks:** BSI scores not transposed to DSM-IV; e.g. Matcham et al. (2016) suggests SF-36 MH and MCS can predict DSM-IV diagnoses at a similar cut-off

summary scale (MCS) classified as poor	**Age at study:** Median age: 32 yrs 18-24 yrs: n=1482, 20.7% 25-34 yrs: n=3169, 44.3% 35+ yrs: n=2496, 34.9% **Controls:** 388 siblings of survivors from random sample of sibling pool Siblings median age: 33 yrs 18-24 yrs: n=61, 15.7% 25-34 yrs: n=157, 40.5% 35+ yrs: n=170, 43.8%		**Major med condition** Yes No **Treatment-related risk factors for psychological distress from multiple variable logistic regression** (in survivors, risk for poor outcome on BSI subscales or GSI, adjusted for sex) Odds ratios and 95% confidence intervals presented as OR (CI)	1.2 (1.0-1.4) Reference	1.2 (1.0-1.6) Reference	1.3 (1.1-1.6) Reference	1.2 (1.0-1.4) Reference	

	Depression	Anxiety	Somatization	GSI
Age at diagnosis (y)				
0-3	1.0 (0.8-1.2)	1.1 (0.8-1.4)	0.8 (0.6-0.9)	1.1 (0.8-1.4)
4-9	1.0 (0.8-1.2)	1.1 (0.8-1.5)	0.9 (0.7-1.1)	1.1 (0.9-1.4)
10-14	0.9 (0.7-1.1)	0.9 (0.7-1.2)	1.0 (0.8-1.2)	1.0 (0.8-1.3)
15-20	Reference	Reference	Reference	Reference
Survival time (y)				
<20	1.0 (0.8-1.3)	1.1 (0.8-1.6)	0.8 (0.7-1.1)	0.9 (0.7-1.2)
20-24	0.9 (0.7-1.2)	1.0 (0.8-1.4)	0.8 (0.6-1.0)	0.7 (0.6-1.0)
25-29	1.0 (0.7-1.2)	1.0 (0.7-1.3)	0.9 (0.7-1.1)	0.9 (0.7-1.1)
30+	Reference	Reference	Reference	Reference
Surgery				
Yes	1.1 (0.9-1.4)	1.1 (0.8-1.4)	1.0 (0.8-1.2)	1.2 (0.9-1.5)
No	Reference	Reference	Reference	Reference
Chemotherapy				
Yes	1.0 (0.8-1.2)	1.2 (0.9-1.5)	1.1 (0.9-1.4)	1.1 (0.9-1.4)
No	Reference	Reference	Reference	Reference
Radiation				
Cranial	1.2 (1.0-1.5)	0.9 (0.7-1.1)	1.1 (1.0-1.4)	1.0 (0.8-1.2)
Other than cranial	0.9 (0.7-1.1)	0.9 (0.7-1.1)	1.3 (1.1-1.5)	1.0 (0.8-1.2)
None	Reference	Reference	Reference	Reference

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?				
Schultz et al. **Behavioral and social outcomes in adolescent survivors of childhood cancer: a report from the childhood cancer survivor study. 2007**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1.1.1970-31.12.1986** **Years of follow-up:** **≥ 5 years post diagnosis, mean 11.5 years from diagnosis** **Country:** **USA** **Study center:** **26 institutions in USA & Canada (CCSS)** **Measurement tool:** **Behavior Problem Index (BPI):** **clinically significant was ≥1.3 SD above comparison sibling group's mean score in each domain: depression/anxiety, headstrong, peer conflict/social withdrawal, attention deficit, antisocial and social competence.**	**Sample size:** 2979 survivors **Diagnoses:** leukemia (n= 1345, 45.2%), CNS cancer (n= 376, 12.6%), Hodgkin's disease (n= 39, 1.3%), non-Hodgkin's lymphoma (n= 132, 4.4%), Wilms' tumor (n= 474, 15.9%), neuroblastoma (n= 382, 12.8%), soft tissue sarcoma (n= 200, 6.7%), bone cancer (n= 31, 1.0%) **Age at diagnosis: yrs(SD)** Mean (M): 3.2 (2.9) Range: 0-9.9 **Age at study:** M = 14.8 (1.6) Range: 12-17 **Controls:** 649 siblings M = 14.9 (1.6) Range: 12-17	Overall treatment Surgery only: n= 215 (7.2%) Chemotherapy: n= 1015 (34.1%) Radiation: n= 206 (6.9%) Chemotherapy & radiation: n= 1236 (41.5%) No surgery, chemotherapy, or radiation: n= 5 (0.2%) Unknown: n= 9 (0.3%) CNS treatment Neither IT Mtx or cranial radiation: n= 1369 (46.0%) IT Mtx: n= 739 (24.8%) Cranial radiation: n= 232 (7.8%) Both IT Mtx and cranial radiation: n= 639 (21.4%) Disfigurement: Head/neck/scalp/eye: n = 663 (22.3%) Limb: n = 392 (13.2%) Chest or abdomen: n = 1122 (37.7%)	For all below, % in clinically significant range, risk ratio (RR), and 99% CI presented in comparison to reference group with 1.0 RR, adjusted for sex, current age group, age at diagnosis, race/ethnicity, annual household income, disfigurement and treatment (Table 5) **Depression/Anxiety** Clinical risk factors: n.a. Demographic risk factors: *Sex* Male: 16.1%; RR = 1.0 Female: 19.4%; RR = 1.2; 99% CI, 1.0 to 1.5 *Current age group* 12-14 years: 16.5%; RR = 1.1; 99% CI, 0.9 to 1.4 15-17 years: 18.5%; RR = 1.0 *Age at diagnosis* <2 years: 19.1%; RR = 1.0; 99% CI, 0.7 to 1.4 2-4 years: 16.1%; RR = 0.8; 99% CI, 0.6 to 1.1 5-9 years: 20.0%; RR = 1.0 *Race/ethnicity* White: 17.2%; RR = 1.0 Black: 19.8%; RR = 1.3; 99% CI, 0.8 to 1.9 Hispanic: 21.8%; RR = 1.2; 99% CI, 0.8 to 1.9 Other: 17.4%; RR = 1.0; 99% CI, 0.6 to 1.7 *Household income ($/year)* < 20,000: 23.6%; RR = 1.3; 99% CI, 1.0 to 1.9 20,000-60,000: 16.6%; RR = 1.0; 99% CI, 0.7 to 1.3 60,000+: 16.8%; RR = 1.0 Treatment-related risk factors: *CNS treatment:* Neither IT Mtx or cranial radiation: 15.0%; RR = 1.0 IT Mtx: 15.4%; RR = 1.3; 99% CI, 1.0 to 1.7 Cranial radiation: 26.3%; RR = 1.7; 99% CI, 1.2 to 2.6 Both IT Mtx and cranial radiation: 22.8%; RR = 1.8; 99% CI, 1.3 to 2.4 *Disfigurement:* Head/neck/scalp/eye *Yes:* 22.9%; RR = 1.2; 99% CI, 0.9 to 1.6 *No:* 16.1%; RR = 1.0 Limb	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/☐unclear **Remarks:**

			Yes: 22.4%; RR = 1.2; 99% CI, 0.9 to 1.6 *No:* 16.9%; RR = 1.0 Chest or abdomen *Yes:* 19.6%; RR = 1.3; 99% CI, 1.0 to 1.6 *No:* 16.5%; RR = 1.0 **Headstrong** Clinical risk factors:n.a. Demographic risk factors: *Sex* Male: 15.6%; RR = 1.0 Female: 13.4%; RR = 0.9; 99% CI, 0.7 to 1.1 *Current age group* 12-14 years: 14.2%; RR = 1.1; 99% CI, 0.8 to 1.3 15-17 years: 14.9%; RR = 1.0 *Age at diagnosis* <2 years: 14.5%; RR = 0.9; 99% CI, 0.6 to 1.4 2-4 years: 14.2%; RR = 0.9; 99% CI, 0.6 to 1.2 5-9 years: 15.9%; RR = 1.0 *Race/ethnicity* White: 14%; RR = 1.0 Black: 18.7%; RR = 1.2; 99% CI, 0.7 to 1.9 Hispanic: 17.6%; RR = 1.1; 99% CI, 0.7 to 1.9 Other: 14.5%; RR = 1.1; 99% CI, 0.6 to 2.0 *Household income ($/year)* < 20,000: 20.4%; RR = 1.8; 99% CI, 1.2 to 2.7 20,000-60,000: 14.8%; RR = 1.4; 99% CI, 1.0 to 1.9 60,000 +: 10.8%; RR = 1.0 Treatment-related risk factors: *CNS treatment:* Neither IT Mtx or cranial radiation: 14%; RR = 1.0 IT Mtx: 15%; RR = 1.2; 99% CI, 0.8 to 1.7 Cranial radiation: 14.2%; RR = 1.1; 99% CI, 0.7 to 1.8 Both IT Mtx and cranial radiation: 15.3%; RR = 1.2; 99% CI, 0.8 to 1.7 *Disfigurement:* Head/neck/scalp/eye *Yes:* 14.9%; RR = 1.1; 99% CI, 0.7 to 1.4 *No:* 14.5%; RR = 1.0 Limb *Yes:* 16.6%; RR = 1.1; 99% CI, 0.8 to 1.6 *No:* 14.3%; RR = 1.0 Chest or abdomen *Yes:* 15.9%; RR = 1.2; 99% CI, 0.9 to 1.6 *No:* 13.8%; RR = 1.0 **Attention Deficit**	

			Clinical risk factors:n.a. Demographic risk factors: *Sex* Male: 22.0%; RR = 1.0 Female: 19.1%; RR = 0.9; 99% CI, 0.7 to 1.1 *Current age group* 12-14 years: 20.9%; RR = 1.0; 99% CI, 0.8 to 1.2 15-17 years: 20.4%; RR = 1.0 *Age at diagnosis* <2 years: 22.1%; RR = 1.1; 99% CI, 0.8 to 1.6 2-4 years: 19.8%; RR = 0.9; 99% CI, 0.7 to 1.3 5-9 years: 20.8%; RR = 1.0 *Race/ethnicity* White: 19.9%; RR = 1.0 Black: 25.1%; RR = 1.2; 99% CI, 0.2 to 1.9 Hispanic: 23.5%; RR = 1.1; 99% CI, 0.7 to 1.7 Other: 23.9%; RR = 1.2; 99% CI, 0.8 to 2.0 *Household income ($/year)* < 20,000: 28.1%; RR = 1.7; 99% CI, 1.2 to 2.3 20,000-60,000: 21.2%; RR = 1.3; 99% CI, 1.1 to 1.7 60,000 +: 16.1%; RR = 1.0 Treatment-related risk factors: *CNS treatment:* Neither IT Mtx or cranial radiation: 17.7%; RR = 1.0 IT Mtx: 19.2%; RR = 1.3; 99% CI, 1.0 to 1.8 Cranial radiation: 29.7%; RR = 1.8; 99% CI, 1.2 to 2.6 Both IT Mtx and cranial radiation: 25.4%; RR = 1.6; 99% CI, 1.2 to 2.2 *Disfigurement:* Head/neck/scalp/eye *Yes:* 24.6%; RR = 1.1; 99% CI, 0.8 to 1.4 *No:* 19.5%; RR = 1.0 Limb *Yes:* 24.5%; RR = 1.1; 99% CI, 0.8 to 1.5 *No:* 20.1%; RR = 1.0 Chest or abdomen *Yes:* 22.6%; RR = 1.3; 99% CI, 1.0 to 1.6 *No:* 19.4%; RR = 1.0 **Peer conflict/social withdrawal** Clinical risk factors: n.a. Demographic risk factors: *Sex* Male: 16.3%; RR = 1.0 Female: 12.2%; RR = 0.8; 99% CI, 0.6 to 1.0 *Current age group* 12-14 years: 14.0%; RR = 1.0; 99% CI, 0.8 to 1.3	

			15-17 years: 14.7%; RR = 1.0 *Age at diagnosis* <2 years: 16.2%; RR = 1.1; 99% CI, 0.8 to 1.7 2-4 years: 13.0%; RR = 0.8; 99% CI, 0.6 to 1.2 5-9 years: 15.5%; RR = 1.0 *Race/ethnicity* White: 13.2%; RR = 1.0 Black: 23.0%; RR = 1.5; 99% CI, 1.0 to 2.3 Hispanic: 20.0%; RR = 1.3; 99% CI, 0.8 to 2.1 Other: 16.7%; RR = 1.3; 99% CI, 0.7 to 2.3 *Household income ($/year)* < 20,000: 22.7%; RR = 2.1; 99% CI, 1.4 to 3.2 20,000-60,000: 14.0%; RR = 1.4; 99% CI, 1.0 to 2.0 60,000 +: 9,9%; RR = 1.0 Treatment-related risk factors: *CNS treatment:* Neither IT Mtx or cranial radiation: 14.0%; RR = 1.0 IT Mtx: 15.4%; RR = 1.3; 99% CI, 0.9 to 1.8 Cranial radiation: 13.4%; RR = 1.1; 99% CI, 0.6 to 1.9 Both IT Mtx and cranial radiation: 14.4%; RR = 1.1; 99% CI, 0.8 to 1.6 *Disfigurement:* Head/neck/scalp/eye *Yes:* 13.7%; RR = 0.9; 99% CI, 0.7 to 1.3 *No:* 14.6%; RR = 1.0 Limb *Yes:* 15.3%; RR = 1.1; 99% CI, 0.7 to 1.5 *No:* 14.3%; RR = 1.0 Chest or abdomen *Yes:* 14.4%; RR = 1.0; 99% CI, 0.8 to 1.4 *No:* 14.4%; RR = 1.0 **Antisocial** Clinical risk factors: n.a. Demographic risk factors: *Sex* Male: 21.8%; RR = 1.0 Female: 23.9%; RR = 1.1; 99% CI, 0,9 to 1.3 *Current age group* 12-14 years: 22.7%; RR = 1.0; 99% CI, 0.8 to 1.3 15-17 years: 22.8%; RR = 1.0 *Age at diagnosis* <2 years: 24.5%; RR = 1.1; 99% CI, 0.8 to 1.6 2-4 years: 21.9%; RR = 1.0; 99% CI, 0.7 to 1.3 5-9 years: 22.7%; RR = 1.0 *Race/ethnicity* White: 22.7%; RR = 1.0 Black: 23.5%; RR = 1.0; 99% CI, 0.7 to 1.6	

			Hispanic: 24.1%; RR = 1.0; 99% CI, 0.7 to 1.6 Other: 20.3%; RR = 0.9; 99% CI, 0.6 to 1.5 *Household income ($/year)* < 20,000: 29.5%; RR = 1.5; 99% CI, 1.1 to 2.2 20,000-60,000: 22.7%; RR = 1.1; 99% CI, 0.9 to 1.4 60,000 +: 20.1%; RR = 1.0 Treatment-related risk factors: *CNS treatment:* Neither IT Mtx or cranial radiation: 18.8%; RR = 1.0 IT Mtx: 18.5%; RR = 1.1; 99% CI, 0.8 to 1.5 Cranial radiation: 42.7%; RR =2.2; 99% CI, 1.6 to 3.1 Both IT Mtx and cranial radiation: 28.8%; RR = 1.6; 99% CI, 1.2 to 2.1 *Disfigurement:* Head/neck/scalp/eye *Yes:* 29.3%; RR = 1.1; 99% CI, 0.9 to 1.5 *No:* 20.9%; RR = 1.0 Limb *Yes:* 26.8%; RR = 1.1; 99% CI, 0.8 to 1.5 *No:* 22.1%; RR = 1.0 Chest or abdomen *Yes:* 22.7%; RR = 1.1; 99% CI, 0.8 to 1.3 *No:* 22.8%; RR = 1.0 **Social competence** Clinical risk factors: n.a. Demographic risk factors: *Sex* Male: 18.8%; RR = 1.0 Female: 20.9%; RR = 1.1; 99% CI, 0,9 to 1.4 *Current age group* 12-14 years: 20.9%; RR = 0.9; 99% CI, 0.7 to 1.1 15-17 years: 19.0%; RR = 1.0 *Age at diagnosis* <2 years: 19.0%; RR = 1.0; 99% CI, 0.7 to 1.5 2-4 years: 20.2%; RR = 1.0; 99% CI, 0.7 to 1.3 5-9 years: 19.9%; RR = 1.0 *Race/ethnicity* White: 20.1%; RR = 1.0 Black: 16.6%; RR = 0.9; 99% CI, 0.6 to 1.5 Hispanic: 24.1%; RR = 1.2; 99% CI, 0.8 to 1.8 Other: 13.8%; RR = 0.7; 99% CI, 0.4 to 1.1 *Household income ($/year)* < 20,000: 22.0%; RR = 1.3; 99% CI, 0.9 to 1.8 20,000-60,000: 20.9%; RR = 1.2; 99% CI, 0.9 to 1.6 60,000 +: 17.4%; RR = 1.0	

			Treatment-related risk factors: *CNS treatment:* Neither IT Mtx or cranial radiation: 14.7%; RR = 1.0 IT Mtx: 19.0%; RR = 1.4; 99% CI, 1.0 to 1.8 Cranial radiation: 36.0%; RR =2.3; 99% CI, 1.6 to 3.3 Both IT Mtx and cranial radiation: 26.0%; RR = 1.8; 99% CI, 1.4 to 2.5 *Disfigurement:* Head/neck/scalp/eye *Yes:* 25.5%; RR = 1.2; 99% CI, 0.9 to 1.5 *No:* 18.2%; RR = 1.0 Limb *Yes:* 22.2%; RR = 1.1; 99% CI, 0.8 to 1.5 *No:* 19.4%; RR = 1.0 Chest or abdomen *Yes:* 19.1%; RR = 1.1; 99% CI, 0.8 to 1.3 *No:* 20.2%; RR = 1.0	

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?				
Schrag et al. **Stress-related mental disorders in childhood cancer survivors. 2008**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: ☐ **Cross-sectional study** ☐ **Case-control study** ☒ **Cohort study** ☐ **Qualitative study (→ exclude!)** ☐ **Systematic/narrative review (→ exclude!)** ☐ **RCT** ☐ **Other: (specify!)** **Treatment era:** **n.a.** **Years of follow-up:** **"at least one year of survival", more detailed information not available** **Country:** **USA** **Study center:** **South Carolina division of the Department of Health and Human Services; South Carolina Central Cancer Registry** **Measurement tool:** **n.a.**	**Sample size:** N=390, 170 (43.59%) female, 219 (56.15%) male **Diagnoses:** Hematologic n=180 Bone or joint n=21 Brain, CNS, eye, or orbital n=72 Other tissues n=117 **Age at diagnosis:** 0-5 years: n=175 6-11 years: n=116 12-15 years: n=99 **Age at study:** 0-5 years: n=175 (44.87%) 6-11 years: n=118 (30.26%) 12-15 years: n=97 (24.87) **Controls:** Children with no history of malignancy (n=1329)	Chemotherapy only n=140 Any radiation, no BMT n=87 BMT n=13 None in Medicaid records n=150	Risk factors for SRMD from multivariable Cox Proportional Hazards Models (adjusted for diagnosis, 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) • **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) • 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)** • **Previous mental disorder diagnosis (Ref. None) HR=2.83 (95%CI:1.02-7.84)**	**Quality assessment:** 1. Is the study group representative? ☐Yes/☐no/ ☒unclear 2. Is the follow-up adequate? ☐Yes/☐no/ ☒unclear 3. Are the outcome assessors blinded? ☐Yes/☒no/ ☐n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?

Langeveld et al. **Posttraumatic stress symptoms in adult survivors of childhood cancer. 2004**

Study Design Treatment era Years of follow-up	Participants	Treatment	Main outcomes	Quality assessment Remarks
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **5-33 years ago** **Years of follow-up:** **33 years ago** **Country:** **The Netherlands** **Study center:** **Academic medical centre** **Measurement tool:** **Impact of Events Scale (IES)** • **Subscales of intrusion and avoidance** • **15 items** **Score of 8-25=”moderate’, 26+=”severe”**	**Sample size:** 500 **Diagnoses:** Leukemia or Non-Hodgkins lymphoma without CRT: n = 136, 27% Leukemia or Non-Hodgkins lymphoma with CRT: n = 105, 21% Solid tumor: n = 214, 45% Brain/CNS tumor: n = 45, 9% **Age at diagnosis:** Median = 8 years Range: 0-19 **Age at study:** Mean = 24 years, SD = 5.1 Range: 16-49 **Controls:** none	Chemotherapy (with or without surgery): n = 226, 45% Radiation therapy (with or without surgery): n = 40, 8% Combination therapy (chemotherapy and radiation with or without surgery): n = 234, 47%	**Clinical risk factors for posttraumatic stress from 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): Severe late effects/health problems (β=0.15), leukemia/non-Hodgkin’s lymphoma without cranial radiation therapy (beta=-0.012) **Demographic risk factors:** Female gender strongest predictor (β=0.23), Lower education (β=0.15), Employment (β=-0.20 student/homemaker, β=-0.17 employed) **Treatment-related risk factors:** None were statistically significant Sex (female) 0.23** Age at follow-up (years) -0.35 Marital status (married) 0.05 Educational level (higher level) -0.15* *Employment status*[b] Student/homemaker -0.20* Employed -0.17* Age at diagnosis (years) 0.35 *Diagnosis*[c] Leukemia/non-Hodgkins lymphoma with CRT -0.12* Solid tumor -0.07 Brain/CNS tumor -0.07 Duration of treatment (months) 0.06 Years since completion of therapy 0.35 Late effects/health problems 0.15* *Treatment*[d] Radiation therapy (with or without surgery) -0.04 Combination therapy (with or without surgery) -0.00 **Total R^{2a}** 13% IES, Impact of Event Scale; CRT, cranial radiation therapy; CNS, central nervous system. [a]R is the percentage of the total variation of the dependent variable score that is explained by the independent variables together.; [b]Reference group.unemployment.; [c]Reference group.leukemia/non-Hodgkins lymphoma without CRT.; [d]Reference group.chemotherapy (with or without surgery).; *Statistically significant differences (P<0.05).; **Statistically significant differences (P<0.001).	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/☐unclear **Remarks:**

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?				
Zebrack et al. **Psychological outcomes in long-term survivors of childhood brain cancer: a report from the childhood cancer survivor study. 2004**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **Year of diagnosis** **1970-1973: n=177 (16.1%)** **1974-1978: n=335 (30.4%)** **1979-1986: n=589 (53.5%)** **Years of follow-up:** **Not stated; survival at least 5y from diagnosis** **Country:** **USA + Canada** **Study center:** **Multicenter 25 institutions (CCSS)** **Measurement tool:** **BSI-18: main outcome was T-score ≥ 63 for GSI or any 2 of 3 sub-scales, classified as positive risk for psychological distress** **Subscales: depression, somatization and anxiety**	**Sample size:** 1101 survivors of childhood brain cancer, 507 (46%) female, 594 (54%) male **Diagnoses:** Astrocytoma/glial cell: n=714 (64.9%) PNET / Medulloblastoma: n=202 (18.3%) Other CNS: 185 (16.8%) **Age at diagnosis:** 0-4: n=186 (16.9%) 5-11: n=508 (46.1%) 12-20: n=407 (37.0%) **Age at study:** Mean 26.5y SD 5.5y Range 18-44y **Controls:** 2817 siblings of childhood cancer survivors Controls age at study Mean 29.4y SD 7.2y Range 18-56y	Chemotherapy: yes: n= 205 (21.1%) Chemotherapy: no: n=766 (78.9%) Missings: n=127 Radiotherapy • Max brain radiation dose: - 0-29 Gy: n=313 (35.1%) - 30-49 Gy: n=112 (12.6%) - ≥ 50 Gy: n=467 (52.3%) • Localisation: - Localised: n=289 5(1.6%) - Whole brain: n=280 (48.4%) - missings: n=314	**GSI: Clinical and treatment-related risk factors** from generalized linear mixed modeling, adjusted for sex, income, self-rated health, major medical condition, brain radiation dosage, age, income&health (higher LS mean indicates more problems)**:** Ethnicity, education, marital status, employment status, and income&ethnicity were not statistically significant in univariable analysis and not included in the multivariable model (no effect measures given) • **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** • **Major medical condition: Yes: LS mean 11.24 (SE 0.64), compared to No: LS mean 9.30 (SE 0.63), p=0.007** • 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 **GSI: Demographic risk factors** from generalized linear mixed modeling, adjusted for sex, income, self-rated health, major medical condition, brain radiation dosage, age, income&health (higher LS mean indicates more problems)**:** Ethnicity, education, marital status, employment status, and income&ethnicity were not statistically significant in univariable analysis and not included in the multivariable model (no effect measures given) • **Sex: Female: LS mean 11.00 (SE 0.62), compared to male: LS mean 9.53 (SE 0.62), p=0.023** • **Income $US: <20,000: LS mean 12.31 (SE 0.79), ≥20,000+: LS mean 8.23 (SE 0.65), p<0.001** • Age: LS mean -0.114 (SE 0.06), p=0.057 • **Income $US, 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** **Depression: Clinical and treatment-related risk factors** from generalized linear mixed modeling, adjusted for sex, education, marital status, self-rated health (higher LS mean indicates more problems)**:** Ethnicity, income, employment status, major medical condition, brain radiation dosage, age, income&ethnicity, income&health were not statistically significant in univariable analysis and not included in the multivariable model (no effect measures given) • **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** **Depression: Demographic risk factors** from generalized linear mixed modeling, adjusted for sex, education, marital status, self-rated health (higher LS mean indicates more problems)**:**	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☒Yes/☐no/ ☐n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:** Positive risk on BSI-18 was not transposed to DSM-IV criteria 180/1281 (14%) eliminated from analyses because of incomplete data, may have been more impaired

			Ethnicity, income, employment status, major medical condition, brain radiation dosage, age, income&ethnicity, income&health were not statistically significant in univariable analysis and not included in the multivariable model (no effect measures given) • Sex: Female: LS mean 3.98 (SE 0.26), compared to male: LS mean 3.66 (SE 0.26), p=0.215 • **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** • **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** **Somatic distress: Clinical and treatment-related risk factors** from generalized linear mixed modeling, adjusted for sex, employment status, self-rated health, major medical condition, and age (higher LS mean indicates more problems)**:** Ethnicity, income, education, marital status, brain radiation dosage, income&ethnicity, and income&health were not statistically significant in univariable analysis and not included in the multivariable model (no effect measures given) • **Self-rated health: Poor or fair: LS mean 3.03 (SE 0.02), compared to good/very good/excellent: LS mean 1.56 (SE 0.10), p<0.001** • **Major medical condition: Yes: LS mean 2.64 (SE 0.15), compared to No: LS mean 1.95 (SE 0.14), p<0.001** **Somatic distress: Demographic risk factors** from generalized linear mixed modeling, adjusted for sex, employment status, self-rated health, major medical condition, and age (higher LS mean indicates more problems)**:** Ethnicity, income, education, marital status, brain radiation dosage, income&ethnicity, and income&health were not statistically significant in univariable analysis and not included in the multivariable model (no effect measures given) • **Sex: Female: LS mean 2.60 (SE 0.14), compared to male: LS mean 1.99 (SE 0.14), p<0.001** • **Employment status: Not employed in last year: LS mean 2.49 (SE 0.17), compared to currently employed: LS mean 2.11 (SE 0.14), p=0.047** • **Age: LS mean -0.029 (SE 0.04), p=0.042** **Anxiety: Clinical and treatment-related risk factors** from generalized linear mixed modeling, adjusted for ethnicity, income, employment status, self-rated health, brain radiation dosage, income&ethnicity, and income&health (higher LS mean indicates more problems)**:** Sex, education, marital status, major medical condition, and age were not statistically significant in univariable analysis and not included in the multivariable model (no effect measures given) • **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** • 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 **Anxiety: Demographic risk factors** from generalized linear mixed modeling, adjusted for ethnicity, income, employment status, self-rated health, brain radiation dosage, income&ethnicity, and income&health (higher LS mean indicates more problems)**:** Sex, education, marital status, major medical condition, and age were not statistically significant in univariable analysis and not included in the multivariable model (no effect measures given)	

			• **Ethnicity: Non-white: LS mean 4.04 (SE 0.44), compared to white: LS mean 2.85 (SE 0.20), p=0.007** • **Income $US: <20,000: LS mean 4.50 (SE 0.39), ≥20,000+: LS mean 2.10 (SE 0.33), p<0.001** • 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 • **Income $US 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 $US, 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**	

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?

Glover et al. **Impact of CNS treatment on mood in adult survivors of childhood leukemia: a report from the Children's Cancer Group. 2003**

Study Design Treatment era Years of follow-up

Study Design:
☒ Cross-sectional study
☐ Case-control study
☐ Cohort study
☐ Qualitative study (→ exclude!)
☐ Systematic/narrative review (→ exclude!)
☐ RCT
☐ Other: (specify!)

Treatment era:
1970-1986

Years of follow-up:
Not reported

Country:
USA

Study center:
23 institutions participating in the Children's Cancer Group (CCG)
Measurement tool: Profile of mood scale (POMS)
Measure of mood states (tension/anxiety, depression, anger, confusion, vigor, fatigue) where higher scores indicated greater mood disturbance.

Total Mood Disturbance (TMD) scores greater than 33 labeled as mood-disturbed and lower than 33, as healthy

Participants

Sample size: 555

Diagnoses:
ALL leukemia

Age at diagnosis:
Not reported

Age at study:
18-33 years

Controls: n.a.

Treatment

ALL therapy in CCG trials

Including cranial radiation, methotrexate for many participants

1. No/ Low MTX (< 83 mg) & CRT (< 21 Gy)- 23.6%

2. High MTX (> 83 mg) & No/Low CRT- 33.7%

3. High CRT (> 21 Gy) & No/Low MTX- 32.3%

4. High CRT & MTX- 10.5%

Main outcomes

Risk factors for elevated POM Total Mood Disturbance (TMD) Score (≥33) from multivariable logistic regression (adjusted for age at diagnosis, treatment, level of education, ethnicity, sex, special education, influence of cancer on employment, self-reported health, age at interview, relapse, and mother's highest level of education)

Clinical risk factors:
- Survivors who reported fair (OR=3.7, P=0.04) or poor (OR=4.7, P<0.001) health were at higher risk than those reporting excellent heath.
- Those reporting that cancer impacted their ability to work were at higher risk (OR=3.3, P<0.001).

Demographic risk factors:
- Preadolescent age at diagnosis (<12.5 years) was associated with significantly higher risk (OR=3.7, P<0.001).
- Non-white ethnicity was associated with significantly higher risk (OR=1.7, P=0.01).
- White female (OR=3.1, P=0.006) and non-white male (OR=3.8, P=0.004) survivors had higher risks as compared to white males.
- Special education history was associated with higher risk in HS dropouts (OR=48.2, P<0.001) and female survivors (OR=6.0, P=0.003).

Treatment-related risk factors:
- High Dose CRT associated with decrease risk in college educated survivors (OR=0.4, P=0.02).
- High dose MTX associated with decreased risk in HS drop-outs (OR=0.1, P=0.03).

Logistic regression model for prediction of mood disturbance

Treatment Variable	Relative Odds	95% CI	*p*
Age at dx (y): Older than 12.5	1.0		
Age at dx (y): Younger than 12.5	3.7	2.0 to 6.6	<0.001
Treatment: No-low	1.0		
Treatment: High MTX	0.4	0.2 to 1.2	0.11
Treatment: High CRT	0.4	0.2 to 1.2	0.10
Treatment: High both	1.7	0.4 to 6.8	0.45
Treatment X, highest education			
Some college: No-low	1.0		
Some college: High MTX	0.6	0.3 to 1.4	0.26
Some college: High CRT	0.4	0.2 to 0.9	0.02
Some college: High both	0.7	0.2 to 2.0	0.46
HS graduate: No-low	1.0		
HS graduate: High MTX	2.6	0.9 to 7.9	0.09
HS graduate: High CRT	2.5	0.9 to 6.5	0.07
HS graduate: High both	1.8	0.5 to 7.2	0.39
Dropout: No-low	1.0		
Dropout: High MTX	0.1	0.0 to 0.8	0.03

Quality assessment Remarks

Quality assessment:
1. Is the study group representative?
☒Yes/☐no/☐unclear
2. Is the follow-up adequate?
☐Yes/☐no/☒unclear
3. Are the outcome assessors blinded?
☐Yes/☐no/☒n.a./☐unclear
Are the analyses adjusted for important confounding factors?
☒Yes/☐no/☐unclear

Remarks:

Model retains nonsignificant covariates of age at interview, relapse (yes or no), and mother's highest level of education

Dropout: High CRT	0.1	0.0 to 1.3	0.07
Dropout: High both	4.1	0.1 to 171	0.47
Demographics			
Highest education: Some college	1.0		
Highest education: High school graduate	1.63	0.6 to 4.8	0.37
Highest education: Dropout	2.87	0.6 to 13.1	0.17
Ethnicity: White	1.0		
Ethnicity: Minority	1.7	0.1 to 3.2	0.01
Sex X, ethnicity			
White			
Male	1.0		
Female	3.1	1.4 to 6.8	0.006
Nonwhite			
Male	3.8	1.6 to 9.2	0.004
Female	2.3	0.7 to 7.2	0.15
Sex X, special education			
Male	1.0		
No special education	1.1	0.3 to 4.1	0.94
Yes special education	1.0		
Female			
No special education	6.0	2.8 to 20.0	0.003
Yes special education	1.0		
Special education X, highest education			
Some college			
No special education	1.0		
Yes special education	0.2	0.0 to 1.4	0.11
High school graduate			
No special education	1.0		
Yes special education	1.6	0.6 to 4.0	0.35
Dropout			
No special education	1.0		
Yes special education	48.2	5.1 to 457	<0.001
Perceptions			
Has cancer limited your ability to work?			
No	1.0		
Yes	3.3	1.8 to 5.8	<0.001
Self-reported health: Excellent	1.00		
Self-reported health: Good	1.71	0 to 2.7	0.04
Self-reported health: Poor	4.7	2.2 to 10.5	<0.001

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?

Hudson et al. **Health status of adult long-term survivors of childhood cancer: a report from the Childhood Cancer Survivor Study. 2003**

Study Design Treatment era Years of follow-up

Study Design:
☒ Cross-sectional study
☐ Case-control study
☐ Cohort study
☐ Qualitative study (→ exclude!)
☐ Systematic/narrative review (→ exclude!)
☐ RCT
☐ Other: (specify!)

Treatment era:
1970-1986

Years of follow-up:
n/a

Country:
United States

Study center:
26 centres in US & Canada (CCSS)

Measurement tool:
BSI-18:
Global Severity Index; Depression, Anxiety, & Somatization subscales ; T score > 63 on any of subscales classified as having "poor" or "adverse" mental health
Cancer-related Anxiety: 1 item; Dichotomized as "Yes" (medium, a lot, very many, or extreme fears or anxiety related to cancer/treatment) versus "No" (no or small amount of fears or anxiety related to cancer/treatment

Participants

Sample size:
N=9535

Diagnoses:
Leukemia: n = 2865, 30.1%
CNS malignancies: n = 1186, 12.4%
Hodgkin disease: n = 1666, 17.5%
Non-Hodgkin lymphoma (NHL): n = 867, 9.1%
Wilms tumor: n = 636, 6.7%
Neuroblastoma: n = 403, 4.2%
Sarcoma: n = 902, 9.5%
Bone malignancy: n = 1010, 10.6%

Age at diagnosis:
M= 10.0 yrs (SD= 5.6 yrs)
Range: 0-20 yrs

Age at study:
M= 26.8 yrs (SD= 6.2 yrs)
Range: 18-48 yrs

Controls:
n/a

Treatment

Radiotherapy
- Any 5925/9535= 62.1%

Chemotherapy
- Any 6434/9535= 67.5%

Combination
- Surgery only: n = 624, 7.3%
- Radiation only: n = 23, 0.3%
- Chemo only: n = 340, 4.1%
- Chemo+radiation: n = 959, 11.6%
- Chemo+surgery: n = 1362, 16.5%
- Radiation+surgery: n = 1172, 14.2%
- Chemo+radiation+ surgery: n = 3754, 45.5%

Main outcomes

Multiple Regression Results of demographic and socioeconomic factors - OR (95% CI)
Mental health is adverse outcome (T-score <63) in any of the 3 Brief Symptom Inventory 18-item subscales (depression, somatization, or anxiety). Anxiety/fears as a result of the cancer or its treatment. Minorities included black non-Hispanic, Hispanic, and other. High school or less means some high school or high school graduate; high school + some college means high school graduate with either some college courses or other training.

Variable	Mental Health	Anxiety
Age at interview		
18-24	1.0	1.0
25-29	1.0 (0.8-1.1)	1.1 (0.9-1.2)
30-34	1.0 (0.8-1.1)	1.0 (0.8-1.2)
≥ 35	0.9 (0.8-1.1)	1.1 (0.9-1.3)
Sex		
Male	1.0	1.0
Female	1.2 (1.1-1.3)	1.6 (1.4-1.9)
Race/ethnicity		
White, non-Hispanic	1.0	1.0
Minority	0.9 (0.8-1.1)	0.9 (0.7-1.1)
Education		
High school or less	1.3 (1.1-1.5)	1.1 (1.0-1.3)
High school + some college	1.0	1.0
Household income		
<$20,000	1.8 (1.5-2.0)	1.4 (1.2-1.7)
≥$20,000	1.0	1.0
Health insurance		
No	1.4 (1.2-1.6)	1.1 (0.9-1.3)
Yes or Canadian	1.0	1.0
Cancer diagnosis		
Leukemia	1.0	1.0
CNS	1.1 (0.9-1.3)	1.0 (0.8-1.3)
Hodgkin disease	1.1 (1.0-1.4)	1.4 (1.2-1.8)
NHL	1.0 (0.8-1.3)	1.1 (0.8-1.4)
Wilms	0.8 (0.6-1.0)	0.9 (0.7-1.2)
Neuroblastoma	0.9 (0.6-1.2)	0.9 (0.6-1.2)
Sarcoma	1.0 (0.8-1.2)	1.4 (1.2-1.8)
Bone	1.0 (0.9-1.3)	1.4 (1.1-1.7)

Quality assessment Remarks

Quality assessment
1. Is the study group representative?
☒Yes/☐no/☐unclear
2. Is the follow-up adequate?
☒Yes/☐no/☐unclear
3. Are the outcome assessors blinded?
☐Yes/☐no/☒n.a./☐unclear
4. Are the analyses adjusted for important confounding factors?
☒Yes/☐no/☐unclear

Remarks:

Multiple Regression Results of demographic and socioeconomic factors - OR (95% CI) adjusted by age, sex, race, and diagnosis. Mental health is adverse outcome (T-score <63) in any of the 3 Brief Symptom Inventory 18-item subscales (depression, somatization, or anxiety). Anxiety/fears as a result of the cancer or its treatment.

Variable	Mental Health	Anxiety
Surgery		
No	1.0	1.0
Yes	1.1 (0.9-1.3)	1.2 (1.0-1.6)
Radiation therapy		
None	1.0	1.0
Head/brain	1.0 (0.8-1.2)	1.1 (0.9-1.3)
Chest/mantle	1.1 (0.9-1.3)	1.2 (0.9-1.5)
Brain/chest	1.1 (0.7-1.7)	1.2 (0.7-2.0)
Other	1.1 (0.9-1.3)	1.2 (1.0-1.5)
Chemotherapy		
None	1.0	1.0
Alkylating agent	1.2 (1.0-1.4)	1.2 (1.0-1.5)
Anthracycline	1.1 (0.8-1.5)	1.1 (0.8-1.5)
Alkylating+ Anthracycline	1.2 (1.0-1.5)	1.5 (1.2-1.9)
Other	1.0 (0.8-1.3)	1.1 (0.9-1.5)

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?				
Zebrack et al. **Psychological outcomes in long-term survivors of childhood leukemia, Hodgkin's disease, and non-Hodgkin's lymphoma: a report from the Childhood Cancer Survivor Study. 2002**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **Diagnosed 1970-1986** **Years of follow-up:** **12-16y since establishment of retrospective cohort** **Country:** **USA & Canada** **Study center:** **25 centers** **Measurement tool:** **BSI-18 'depressive symptoms' scale, transposed onto DSM-IV criteria for Major Depressive Episode**	**Sample size:** 5736 subset of CCSS survivors with leukaemia or lymphoma **Diagnoses:** Leukaemia (n=2991), Hodgkin's disease (HD): (n=1843) and Non-Hodgkin's Lymphoma (NHL): (n=902) **Age at diagnosis:** Mean=10.1 yrs, SD=5.5 Range 0-20 **Age at study:** Survivors Mean= 26.9 yrs, SD=6.2 Range: 18-48 **Controls:** 2565 siblings of survivors	Received intensive chemotherapy (includes various protocols and cumulative doses of chemothera-peutic agents, defined by disease-specific criteria): (n=1685) 36.4% Received cranial radiotherapy: (n=1725) 40.1%	**<u>Multivariate analyses of risk factors for symptomatic scores</u>** - The main risk factors in the best model for symptomatic depression included female gender, intensive chemotherapy, low household income, and low education. - The best model for symptomatic somatic distress included female gender, age, exposure to intensive chemotherapy, low household income, low education, and lack of employment. **<u>Full data of multivariate models with all survivors included</u>** **Depression** **Characteristic** — RR (95% CI) — p value **Gender** Female — 2.06 (1.53-2.76) — <0.0001 Male — 1.0 **Intensive chemo** Yes — 1.46 (1.09-1.96) — 0.01 No — 1.0 **Income** <$20000 — 2.21 (1.64-2.99) — <0.0001 $20000-60000+ — 1.0 **Education** <High school grad — 2.27 (1.39-3.70) — 0.001 High school-some college — 1.41 (1.01-1.97) — 0.04 College-postgrad — 1.0 **Somatic distress** **Characteristic** — RR (95% CI) — p value **Gender** Female — 2.13 (1.72-2.63) — <0.0001 Male — 1.0 **Age** — 1.04 (1.02-1.05) — <0.0001 **Intensive chemo** Yes — 1.30 (1.06-1.61) — 0.01 No — 1.0 **Income** <$20000 — 1.92 (1.52-2.44) — <0.0001 $20000-60000+ — 1.0 **Education** <High school grad — 2.63 (1.80-3.85) — <0.0001 High school-some college — 1.55 (1.21-1.97) — <0.001	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/☐unclear **Remarks:** DSM-IV depressive symptoms, but non-standardised cutoffs

			College-postgrad	1.0		
			Employment			
			Not employed	1.59 (1.16-2.17)	0.004	
			Employed	1.0		

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?

Barakat et al. Families surviving childhood cancer: a comparison of posttraumatic stress symptoms with families of healthy children. 1997

Study Design Treatment era Years of follow-up	Participants	Treatment	Main outcomes	Quality assessment Remarks
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era: n.a** **Years of follow-up: n.a** **Country: USA** **Study center: Two different sites** **Measurement tool:** **Child factors** • **Impact of Event Scale (IES)- assessment of response to traumatic stress** • **Posttraumatic Stress Disorder Reaction Index – assessment of post-traumatic stress total scores are moderate (25-39) and severe (>40)** • **Assessment of Life Threat and Treatment Intensity Questionnaire (ALTTIQ) – assessed past life threat from cancer** • **Revised Children's Manifest Anxiety Scale (RCMAS)- assessed child trait anxiety** • **Trauma Symptom Checklist for Children (TSC) – assessed posttraumatic stress, dissociation, and anger**	**Sample size:** 309 survivors, 309 mothers, 213 fathers **Diagnoses:** ALL 38% Wilms tumor 10% Sarcoma 9% Acute nonlymphoblastic leukemia 8% Lymphoma 8% Hodgkins disease 6% Other cancers 21% including neuroblastoma and retinoblastoma **Age at diagnosis:** Mean = 5.83 years, range 1-17 years. **Age at study:** Range 8-20 years Mean = 13.53 years (SD=3.37) **Controls:** 219 healthy children, 211 mothers, and 114 fathers.	Treatment intensity was rated on a 3-point scale from mild (e.g., surgery only) to severe (e.g., bone marrow transplant) by a pediatric oncologist.	**Risk factors for posttraumatic stress symptoms (as measured by Reaction Index scores) from multivariable regressions** For children the full model was significant $F(13,199)=8.45$, $R^2=0.37$, $p<0.001$. Only past perceived life threat $F = 43.89$, $p= 0.001$ on the ALTTIQ made a significant independent contribution. Greater past perceived life threat was related to more PTSS. **Factors contributing to child post-traumatic stress symptoms-full model** **Predictor** / **B** / **SEB** / **β** / **P** **Child demographics** Age: -0.18 / 0.40 / -0.05 / ns Gender-male: 0.00 / / / ns Gender-female: 2.64 / 1.34 / 0.12 / ns Race-White: 0.00 / / / ns Race-Black: 9.47 / 4.83 / 0.12 / ns Race-Hispanic: -0.27 / 2.60 / -0.01 / ns Race-Asian: 6.75 / 4.29 / 0.09 / ns **Cancer treatment factors** Treatment intensity: 1.03 / 1.06 / 0.06 / ns Years off treatment: -0.01 / 0.03 / -0.03 / ns Child age at diagnosis: 0.80 / 0.37 / 0.28 / ns Past perceived life threat: 2.99 / 0.45 / 0.41 / 0.001 **Social support and resources** Mother total support network: -0.05 / 0.17 / -0.02 / ns Mother family cohesion: -0.25 / 1.09 / -0.02 / ns Mother family satisfaction: -0.60 / 1.05 / -0.04 / ns Mother family adaptability: 1.01 / 1.04 / 0.06 / ns	**Quality assessment:** 1. Is the study group representative? ☐Yes/☐no/ ☒unclear 2. Is the follow-up adequate? ☐Yes/☐no/ ☒unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:** 56% response rate for participants who were cancer survivors and 39% for healthy controls

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?				
De Laage et al. **Screening for psychological distress in very long-term adult survivors of childhood cancer. 2016**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **n.a.** **Years of follow-up:** **Mean time since the diagnosis 31.5 years (SD = 9.1 years; range: 8.8–56.1 years)** **Country:** **France** **Study center:** **Long-Term Follow-up Clinic (LTFUC) for childhood cancer survivors at Institut Gustave-Roussy and Institut Curie** **Measurement tool:** • **Brief Symptom Inventory-18 (BSI-18): gender-specific cutoff score to identify patients who experience clinically significant distress: male score ≥10, female score ≥13** • **Impact of Event Scale (IES): score between 8 and 25 to consider that a person is at risk for developing PTSD and a score of 26 or more to indicate that a person is unable to cope with the impact of the event and needs professional help**	**Sample size:** N=348 **Diagnoses:** Hodgkin: n=45 Sarcoma: n=93 Nephroblastoma: n=59 Neuroblastoma: n=50 LNH: 36 CNS tumor: n=33 Others: n=32 **Age at diagnosis:** Mean age at cancer diagnosis 7 years (SD = 5.1 years; range: 0.0–18.0 years) **Age at study:** Mean 38.5 years (SD = 8.5 years; range: 18.1–65.8 years) **Controls:** French norm population using the Mental Health in General Population (MHGP) database derived from a representative national survey of the French adult population (N = 36,105)	Surgery: n=284 Chemotherapy n=313 Radiation n=235	**Risk factors from multivariable logistic regression (non-significant variables removed after running univariable logistic regression):** BSI-18: • Sex: Male (Ref. Female) OR=0.82 (95%CI:0.51-1.32; p=0.28) • **Self-reported late effects: Yes (Ref. No) OR=2.23 (95%CI:1.30-3.8; p=0.003)** • Marital status: Couple (Ref. Single) OR=0.59 (95%CI:0.33-1.03; p=0.006) Impact of Event Scale: • **Sex: Male (Ref. Female) OR=0.48 (95%CI:0.25-0.90; p=0.01)** • Self-reported late effects: Yes (Ref. No) OR=2.05 (95%CI:0.95-4.43; p=0.07) • **Marital status: Couple (Ref. Single) OR=0.51 (95%CI:0.26-0.97; p=0.02)**	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/☐unclear **Remarks:**

• **Mini-International Neuropsychiatric Interview (MINI): MINI data of the survivors were compared with the French norm population using the Mental Health in General Population (MHGP) database derived from a representative national survey of the French adult population (N = 36,105)**				

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?			
Brinkman et al. **Alcohol consumption behaviors and neurocognitive dysfunction and emotional distress in adult survivors of childhood cancer: A report from the Childhood Cancer Survivor Study. 2019**			
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**
Study Design: **☐ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1970-1986** **Years of follow-up:** **≥ 5years** **Three timepoints: Baseline, Follow-up 2, Follow-up 4** **Country:** **USA and Canada** **Study center:** **Multi-site (CCSS)** **Measurement tool:** • **BSI-18: T-score of ≥63 defined as distress** • **Posttraumatic Stress Diagnostic Scale (PDS): at least one re-experiencing symptom, at least three avoidance symptoms and at**	**Sample size:** N=4484 survivors **Diagnoses:** Leukemia 1353 (30.2%) CNS tumor 453 (10.1%) Hodgkin lymphoma 874 (19.5%) Non-Hodgkin lymphoma 382 (8.5%) Wilms tumor 290 (6.5%) Neuroblastoma 165 (3.7%) Soft tissue sarcoma 456 (10.2%) Bone tumors 511 (11.4%) **Age at diagnosis:** <21 years Mean 10.5 years (SD 5.6) **Age at study:** >18 years at baseline Baseline: Mean 27.2 years (SD 6.2) Follow-up 2: Mean 34.8 years (SD 6.1) Follow-up 4: Mean 39.5 years (SD 6.0) **Controls:**	Radiation: None n=1240 (29.9%) Non-cranial n=1435 (34.6%) ≤20Gy Cranial n=523 (12.6%) >20Gy Cranial n=946 (22.8%) Intravenous Methotrexate: Yes n=791 (19.1%) No n=3359 (80.9%) No. of intrathecal injections: None n=2819 (66.7%) 1 n=1052 (24.9%) ≥2 n=355 (8.4%)	**Clincal risk factors** for the different outcomes from Poisson regression modeling with robust error variance+: **Depression** • **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) • **Physical health: Poor, fair (Ref. good, very good, excellent) RR=2.6 (95%CI:2.1-3.2; P≤0.01)** • **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)** **Anxiety** • **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) • **Physical health: Poor, fair (Ref. good, very good, excellent) RR=3.2 (95%CI:3.4-4.3; P≤0.01)** • **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)** **Posttraumatic Stress** • 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) • **Physical health: Poor, fair (Ref. good, very good, excellent) RR=1.9 (95%CI:1.6-2.2; P≤0.01)** • **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)** **Demographic risk factors** for the different outcomes from Poisson regression modeling with robust error variance+: **Depression** • Sex: Female (Ref. Male) RR=0.8 (95%CI:0.6-0.9) **Anxiety** • Sex: Female (Ref. Male) RR=0.8 (95%CI:0.6-1.0) **Posttraumatic Stress** • Sex: Female (Ref. Male) RR=1.2 (95%CI:1.1-1.4) **Treatment-related risk factors** for the different outcomes from Poisson regression modeling with robust error variance+ **Depression** • 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) **Anxiety** • Radiation: Non-cranial (Ref. None) RR=0.8 (0.6-1.1) • Radiation: CRT≤20Gy (Ref. None) RR=0.7 (0.5-1.1)	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☐Yes/☒no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:** Unclear whether this data is from Baseline survey, Follow-up 2 or Follow-up 4. CRT=cranial radiation therapy *from a separate model, adjusted for sex, physical health, radiation, race, age at diagnosis, age at follow-up, educational attainment, and employment status

least two arousal symptoms, with or without functional impairment was defined as positive endorsement of PTSS	N=1651 siblings		• Radiation: CRT>20Gy (Ref. None) RR=0.7 (0.5-1.0) **Posttraumatic Stress** • 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) [+]adjusted for heavy/risky drinking, sex, physical health, radiation, race, age at diagnosis, age at follow-up, educational attainment, and employment status	

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?

***Zheng et al.* Long-Term Psychological and Educational Outcomes for Survivors of Neuroblastoma: A Report from the Childhood Cancer Survivor Study. 2018**

Study Design Treatment era Years of follow-up	Participants	Treatment	Main outcomes	Quality assessment Remarks
Study Design: ☐ **Cross-sectional study** ☐ **Case-control study** ☒ **Cohort study** ☐ **Qualitative study (→ exclude!)** ☐ **Systematic/narrative review (→ exclude!)** ☐ **RCT** ☐ **Other: (specify!)** **Treatment era:** **1970-1999** **Years of follow-up:** **≥5 years from diagnosis** **Country:** **USA and Canada** **Study center:** **Multi-site (CCSS)** **Measurement tool:**	**Sample size:** N=859 **Diagnoses:** Neuroblastoma n=859 **Age at diagnosis:** <1 years: n=534 (62.2%) 1-1.99 years: n=184 (21.4%) 2-4.99 years: n=123 (14.3%) ≥5 years: n=18 (2.1%) **Age at study:** <18 years at baseline survey: 8-11 years: n=157 (18.3%) 12-13 years: n=206 (24.0%) 14-15 years: n=250 (29.1%)	Surgery only n=259 (32.8%) Surgery and chemotherapy n=292 (37.0%) Surgery and radiation n=59 (7.5%) Surgery, chemotherapy, and radiation n=163 (20.6%) None/other combinations n=17 (2.1%)	Risk factors for the different outcomes from log-binomial models**:** **Anxiety/Depression** Model 1 adjusted for age at diagnosis, age at evaluation, sex, and annual household income**:** • Male (Ref. Female) not significant • Age at diagnosis: <1 year (Ref. ≥1 year) not significant • Annual household income: Unknown (Ref. ≥$60,000) PR=0.89 (95%CI:0.4-1.73) • Annual household income: <$20,000 (Ref. ≥$60,000) PR=1.45 (95%CI:0.9-2.33) • Annual household income: $20,000-$39,999 (Ref. ≥$60,000) PR=1.32 (95%CI:0.87-2.04) • Annual household income: $40,000-$59,999 (Ref. ≥$60,000) PR=0.85 (95%CI:0.57-1.29) Model 2[a] 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 • Interaction between age at diagnosis and platinum agent: <1yearXyes (Ref. <1yearXno) not significant • Interaction between age at diagnosis and platinum agent: ≥1yearXyes (Ref. ≥1yearXno) not significant • Interaction between age at diagnosis and anthracycline: <1yearXyes (Ref. <1yearXno) not significant • Interaction between age at diagnosis and anthracycline: ≥1yearXyes (Ref. ≥1yearXno) not significant Model 3[b] adjusted for age at diagnosis, age at evaluation, sex, and annual household income**:** • **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 • Interaction between age at diagnosis and peripheral neuropathy: <1yearXyes (Ref. <1yearXno) not significant • Interaction between age at diagnosis and peripheral neuropathy: ≥1yearXyes (Ref. ≥1yearXno) not significant	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☐n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:** [a]The following were also examined but were N/S: retinoic acid, vincristine, chest/neck radiation, alkylating agents, platinum agents, interaction of age at diagnosis with sex, and

• **Behavior Problem Index (BPI), parent reported: higher scores indicate worse behavioral symptoms; impairment defined as beyond the highest 10th percentile of age-matched siblings controls**	16-17 years: n=246 (28.6%) **Controls:** N=872 siblings		**Headstrong Behavior** Model 1 adjusted for age at diagnosis, age at evaluation, sex, and annual household income**:** • Male (Ref. Female) not significant • Age at diagnosis: <1 year (Ref. ≥1 year) not significant • Annual household income: Unknown (Ref. ≥$60,000) PR=1.46 (95%CI:0.74-2.69) • Annual household income: <$20,000 (Ref. ≥$60,000) PR=1.43 (95%CI:0.84-2.41) • **Annual household income: $20,000-$39,999 (Ref. ≥$60,000) PR=1.72 (95%CI:1.12-2.72)** • Annual household income: $40,000-$59,999 (Ref. ≥$60,000) PR=1.02 (95%CI:0.67-1.61) Model 2[a] 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 • Interaction between age at diagnosis and platinum agent: <1yearXyes (Ref. <1yearXno) not significant • Interaction between age at diagnosis and platinum agent: ≥1yearXyes (Ref. ≥1yearXno) not significant • Interaction between age at diagnosis and anthracycline: <1yearXyes (Ref. <1yearXno) PR=1.28 (95%CI:0.90-1.82) • **Interaction between age at diagnosis and anthracycline: ≥1yearXyes (Ref. ≥1yearXno) PR=0.55 (95%CI:0.32-0.95; p=0.03)** Model 3[b] adjusted for age at diagnosis, age at evaluation, sex, and 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)** • Interaction between age at diagnosis and peripheral neuropathy: <1yearXyes (Ref. <1yearXno) not significant • Interaction between age at diagnosis and peripheral neuropathy: ≥1yearXyes (Ref. ≥1yearXno) not significant **Antisocial Behavior** Model 1 adjusted for age at diagnosis, age at evaluation, sex, and annual household income**:** • Male (Ref. Female) not significant • Age at diagnosis: <1 year (Ref. ≥1 year) not significant • Annual household income: Unknown (Ref. ≥$60,000) not significant • Annual household income: <$20,000 (Ref. ≥$60,000) not significant • Annual household income: $20,000-$39,999 (Ref. ≥$60,000) not significant • Annual household income: $40,000-$59,999 (Ref. ≥$60,000) not significant Model 2[a] 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)** • Interaction between age at diagnosis and platinum agent: <1yearXyes (Ref. <1yearXno) PR=0.97 (95%CI:0.62-1.53; p=0.90)	interaction of age at diagnosis with each of the treatment factors. [b]The following were also examined but were N/S: grade≥2 cardiac disease, grade≥2 renal disease, hearing loss, body mass index, physical fitness–limiting daily activities exceeding 3 months, interaction of age at diagnosis with sex, and interaction of age at diagnosis with each of the chronic conditions

			• **Interaction between age at diagnosis and platinum agent: ≥1yearXyes (Ref. ≥1yearXno) PR=0.41 (95%CI:0.20-0.81; p=0.01)** • Interaction between age at diagnosis and anthracycline: <1yearXyes (Ref. <1yearXno) not significant • Interaction between age at diagnosis and anthracycline: ≥1yearXyes (Ref. ≥1yearXno) not significant Model 3[b] adjusted for age at diagnosis, age at evaluation, sex, and 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)** • Interaction between age at diagnosis and peripheral neuropathy: <1yearXyes (Ref. <1yearXno) not significant • Interaction between age at diagnosis and peripheral neuropathy: ≥1yearXyes (Ref. ≥1yearXno) not significant	

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?				
Allen et al. **Posttraumatic stress-related psychological functioning in adult survivors of childhood cancer. 2018**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☐ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **n.a.** **Years of follow-up:** **Mean 24.1 years (SD 8.2 years); range 10.2-48.3 years** **Country:** **USA** **Study center:** **St. Jude Lifetime Cohort; St. Jude Children's Research Hospital** **Measurement tool:** • **PTSD Checklist-Civilian (PCL-C): cut-off ≥44 was used for caseness** • **BSI-18: cut-off ≥63 was used for caseness**	**Sample size:** N=2969 **Diagnoses:** Leukemia n=1108 (37.3%) Lymphoma n=612 (20.6%) CNS tumors n=293 (9.9%) Neuroblastoma n=193 (6.5%) Osteosarcoma/Ewing sarcoma n=203 (6.8%) Wilms tumor n=126 (4.2%) Retinoblastoma n=88 (3.0%) Rhabdomyosarcoma n=97 (3.3%) Other solid tumors (e.g., germ cell tumor, melanoma) n=238 (8.0%) Other n=11 (0.4%) **Age at diagnosis:** Mean 8.4 years (SD 5.6 years); range 0-21.8 years **Age at study:** Mean 32.5 years (SD 8.5); range 18.3-63.8 years **Controls:**	Chemotherapy n=2547 (85.8%) Radiation therapy n=1784 (60.1%) Surgery n=1365 (46.0%) Bone marrow transplant n=127 (4.3%)	Risk factors for post-traumatic stress disorder from multiple linear regression (adjusting for GSI Total Score, Worry total score, perceived stress scale (PSS), diagnosis, age at diagnosis, sex, and education): • **GSI T-Score (1 unit): β=0.67, p<0.001** • **Worry total score (1 unit): β=0.10, p=0.001** • **PSS (1 unit): β=0.76, p<0.0001** • **Diagnosis: CNS tumor vs. other β=-1.15, p=0.022** • Diagnosis: Leukemia/lymphoma vs. other β=0.12, p=0.69 • Age at diagnosis (1 year): β=0.02, p=0.47 • **Sex: Female vs. male β=1.64, p<0.0001** • **Education: < college graduate vs. ≥college graduate β=0.90, p=0.002** "Scores on the PCL-C were associated with gender (females with more distress), education (less than college with more distress), and diagnostic category (CNS tumor with less distress). Higher scores on the other distress measures (GSI, Worry Scale, PSS) were also associated with higher PCL-C scores"	**Quality assessment:** 1. Is the study group representative? ☐Yes/☒no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?

Anestin et al. **Psychological risk in long-term survivors of childhood acute lymphoblastic leukemia and its association with functional health status: A PETALE cohort study. 2018**

Study Design Treatment era Years of follow-up

Study Design:
☒ Cross-sectional study
☐ Case-control study
☐ Cohort study
☐ Qualitative study (→ exclude!)
☐ Systematic/narrative review (→ exclude!)
☐ RCT
☐ Other: (specify!)

Treatment era:
87-01, 91-01, 95-01, 2000-01, 2005-01

Years of follow-up:
≥5 years postdiagnosis
Mean 15.7 years (SD 5.1 years)

Country:
Canada; PETALE cohort

Study center:
Sainte-Justine University Health Center, Laval University Health Center

Measurement tool:
- **Adolescents: Beck Youth Inventories for Anxiety and Depression (BYI-AD): standardized T scores, significant anxiety T score ≥55 (BYI-A), and significant depression T score ≥55 (BYI-D)**
- **Young adults: Beck Anxiety Inventory (BAI), Beck Depression Inventory II (BDI-II): significant anxiety scores ≥8 (BAI), and significant depression scores ≥14 (BDI-II)**
- **Distress thermometer: cut-off for psychological distress≥4**

Participants

Sample size:
Total N=287:
n=105 adolescent survivors
n=182 adult survivors

Diagnoses:
Acute lymphoblastic leukemia

Age at diagnosis:
<19 years
Mean 6.2 years (SD 4.5 years)

Age at study:
Mean 21.9 years (SD 6 years)

Controls:
None

Treatment

Radiotherapy:
Yes n=161 (56.1%)
No n=126 (43.9%)

Main outcomes

Risk factors for significant levels of anxiety, depression and distress from multivariable binary logistic regression adjusted for sex, age, age at diagnosis, and treatment risk status:

Adolescents:

	Anxiety (*n* = 94)			**Depression (*n* = 94)**			**Distress (*n* = 96)**		
	OR	**95%CI**	**Pvalue**	**OR**	**95%CIb**	**Pvalue**	**OR**	**95%CI**	**Pvalue**
Mobility	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Friendship	0.95	0.75–12.11	0.970	N/A	N/A	N/A	0.71	0.05–2.11	0.803
Appearance	2.72	0.75–9.85	0.128	N/A	N/A	N/A	2.81	0.96–8.23	0.059
School	4.88	1.07–22.31	0.041	0.64	0.08–5.01	0.673	1.17	0.25–5.37	0.842
Vision	0.60	0.17–2.06	0.410	0.68	0.15–3.03	0.613	0.25	0.17–1.58	0.524
Hearing	10.70	2.43–47.11	**0.002**	18.29	2.97–112.84	**0.002**	1.88	0.48–7.34	0.366
Breathing	4.04	1.11–14.75	0.035	9.62	1.87–49.46	**0.007**	1.82	0.61–5.45	0.284
Sleeping	10.27	2.39–44.03	**0.002**	3.94	0.84–18.52	0.083	5.07	1.70–15.17	**0.004**
Eating	11.09	0.87–141.56	0.064	6.66	0.45–98.82	0.168	1.14	0.91–14.26	0.919
Speech	4.43	1.40–14.06	0.011	2.84	0.73–10.99	0.131	1.19	0.43–3.28	0.734
Excretion	11.42	2.36–55.21	**0.002**	8.20	1.58–42.42	0.012	1.56	0.41–5.95	0.517
Mental function	15.55	3.43–70.47	**<0.0001**	19.71	3.98–97.54	**<0.0001**	13.48	3.62–50.28	**<0.0001**
Discomfort/symptoms	2.19	0.68–7.03	0.187	2.34	0.61–8.96	0.214	3.45	1.28–9.31	0.014
Vitality/fatigue	2.53	0.79–8.10	0.117	7.35	1.40–38.74	0.019	3.32	1.21–9.09	0.019
16D total score	1.36	1.16–1.60	**<0.0001**	1.32	1.13–1.60	**<0.0001**	1.17	1.07–1.30	**0.003**

Adults:

	Anxiety (*n*=142)			**Depression (*n*=142)**			**Distress (*n*=156)**		
	OR	**95%CI**	**Pvalue**	**OR**	**95%CI**	**Pvalue**	**OR**	**95%CI**	**Pvalue**
Mobility	5.61	1.53–20.51	**0.009**	3.24	0.81–12.87	0.095	1.56	0.36–6.85	0.556
Vision	3.49	1.00–12.16	0.050	4.88	1.34–17.71	0.016	0.57	0.07–4.9	0.605
Hearing	3.05	0.99–9.42	0.052	1.78	0.49–6.44	0.378	1.33	0.32–5.57	0.690
Breathing	1.86	0.85–4.09	0.121	1.38	0.57–3.35	0.480	1.69	0.71–4.0	0.237
Sleeping	2.26	1.02–4.98	0.043	3.91	1.48–10.31	**0.006**	3.88	1.49–10.14	**0.006**
Eating	N/A	N/A	N/A						
Speech	4.82	1.91–12.20	**0.001**	2.66	0.98–7.16	0.054	2.47	0.92–6.62	0.072
Excretion	3.79	1.56–9.19	**0.003**	4.48	1.68–11.95	**0.003**	1.03	0.36–2.96	0.964
Usual activities	6.68	2.36–18.95	**<0.0001**	18.21	5.43–61.05	**<0.0001**	3.58	1.15–11.14	0.027
Mental function	4.23	1.84–9.73	**0.001**	6.65	2.58–17.14	**<0.0001**	5.13	2.04–12.91	**0.001**
Discomfort/symptoms	8.18	3.27–20.45	**<0.0001**	7.44	2.63–21.07	**<0.0001**	2.68	1.11–6.47	0.029
Vitality/fatigue	8.49	3.44–20.97	**<0.0001**	13.28	4.09–43.11	**<0.0001**	3.92	1.59–9.71	**0.003**
Sexual activity	6.22	2.40–16.27	**<0.0001**	6.76	2.39–19.12	**<0.0001**	2.91	1.04–8.15	0.043
15D total score	1.18	1.10–1.25	**<0.0001**	1.19	1.11–1.28	**<0.0001**	1.10	1.04–1.17	**0.001**

Quality assessment Remarks

Quality assessment:
1. Is the study group representative?
☒Yes/☐no/☐unclear
2. Is the follow-up adequate?
☒Yes/☐no/☐unclear
3. Are the outcome assessors blinded?
☐Yes/☐no/☒n.a./☐unclear
4. Are the analyses adjusted for important confounding factors?
☒Yes/☐no/☐unclear

Remarks:

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?				
Vuotto et al. **Impact of Chronic Disease on Emotional Distress in Adult Survivors of Childhood Cancer: A Report From the Childhood Cancer Survivor Study. 2017**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☐ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1970-1986** **Years of follow-up:** **Time since diagnosis, years: mean 23.2 (SD 4.5), median 23 (IQR 19-27)** **Country:** **USA and Canada** **Study center:** **Multi-site (CCSS)** **Measurement tool:** • **Brief Symptom Inventory 18: elevated distress defined as a T-score ≥63** • **Post-traumatic Stress Diagnostic Scale (PDS): positive endorsement of PTSS was defined as at least 1**	**Sample size:** N=5021 **Diagnoses:** Leukemia n=1697 (33.8%) CNS tumor n=499 (9.9%) Hodgkin lymphoma n=720 (14.3%) Non-Hodgkin lymphoma n=377 (7.5%) Wilms tumor n=473 (9.4%) Neuroblastoma n=316 (6.3%) Soft tissue sarcoma n=470 (9.4%) Bone cancer n=469 (9.3%) **Age at diagnosis:** Age at diagnosis, years: mean 8.3 (SD 5.9), median 7.0 (IQR 3-13) **Age at study:** Age at Follow-up 2, years: mean 32.0 (SD 7.6), median 32 (IQR 26-37) **Controls:** n.a.	**Surgery (n= (%))** CNS 550 (11.0) Respiratory system 417 (8.3) Cardiovascular system 50 (1.0) Other surgery 2750 (54.8) None 1208 (24.1) **Radiotherapy (n= (%))** Cranial 1451 (29.0) Thoracic 1035 (20.7) Abdominal 963 (19.2) Pelvic 713 (14.2) Other radiotherapy 421 (8.4) None 1750 (34.9) **Chemotherapy (n= (%))** IT methotrexate or cytarabine (any) 1851 (36.9) 1 injection 1274 (25.4) 2 injections 525 (10.5) ≥3 injections 52 (1.0) Corticosteroids (yes/no) 2425 (48.3) IV methotrexate 940 (18.7)	Risk factors for emotional distress from log-binomial multivariable regression (only variables with significant direct effects in structural equation modeling were included): Depression[a]: • 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) Anxiety[b]: • 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) Posttraumatic Stress: • 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) [a]adjusted for sex [b]adjusted for time since diagnosis	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☐Yes/☒no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

reexperiencing symptom, at least 3 avoidance symptoms, and at least 2 arousal symptoms		Bleomycin (yes/no) 260 (5.4) Anthracyclines 1777 (36.7)		

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?			
Korhonen et al. **Suicides and Deaths Linked to Risky Health Behavior in Childhood Cancer Patients: A Nordic Population-Based Register Study. 2019**			
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treat-ment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☐ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1971-2009** **Years of follow-up:** **Time since diagnosis:** **Median follow-up was 9.4 years (range: 0-42.0 years)** **Country:** **Denmark, Finland and Sweden: SALiCCS cohort** **Study center:** **n.a.** **Measurement tool:** • **Causes of death classified according to the International Classification of Diseases (ICD, different versions used)**	**Sample size:** N=29'285 **Diagnoses (n= (%)):** Leukemia 7409 (25) Lymphoma 3958 (14 CNS tumors 6616 (23) Neuroblastoma and other peripheral cell tumors 1415 (5) Retinoblastoma 482 (2) Renal tumors 1202 (4) Hepatic tumors 277 (1) Malignant bone tumors 1426 (5) Soft-tissue sarcomas 1741 (6) Germ cell, trophoblastic, and other gonadal neoplasms 1774 (6) Other malignant epithelial neoplasms 2596 (9) Other and unspecified malignant neoplasms 389 (1) **Age at diagnosis (n= (%)):** <20 years Birth to 4 years: 9341 (32) 5-9 years 5327 (18) 10-14 years 5694 (19) 15-19 years 8923 (31) **Age at study:** Median age at the end of follow-up was 19.0 years (range: birth to 59.1 years) **Controls:** N=146'282 population-based comparison subjects (1:5 ratio) identified from national	n.a.	Risk factors for suicide from Poisson regression, adjusting for country, sex, attained age, and diagnostic period. • Sex: Male, Survivors (Ref. Comparisons) RR=1.30 (95%CI:0.93-1.82) • Sex: Female, Survivors (Ref. Comparisons) RR=1.61 (95%CI:0.91-2.88) • Sex: No statistical difference by sex was found (p=0.47, 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) • Age at diagnosis: Birth to 4 years, Survivors (Ref. Comparisons) RR=1.43 (95%CI:0.68-3.02) • Age at diagnosis: 5-9 years, Survivors (Ref. Comparisons) RR=1.10 (95%CI:0.44-2.79) • Age at diagnosis: 10-14 years, Survivors (Ref. Comparisons) RR=0.97 (95%CI:0.50-1.86) • **Age at diagnosis: 15-19 years, Survivors (Ref. Comparisons) RR=1.61 (95%CI:1.09-2.39)** • Age at diagnosis: No statistical difference by age at diagnosis was found (p=0.50, from likelihood ratio test) • Cancer site: Leukemia, Survivors (Ref. Comparisons) RR=0.84 (95%CI:0.34-2.08) • Cancer site: Lymphoma, Survivors (Ref. Comparisons) RR=1.43 (95%CI:0.75-2.74) • Cancer site: CNS, Survivors (Ref. Comparisons) RR=1.22 (95%CI:0.60-2.45) • Cancer site: Other, Survivors (Ref. Comparisons) RR=1.56 (95%CI:1.04-2.34) • Cancer site: No statistical difference by cancer site was found (p=0.62, from likelihood ratio test) • **Time period of diagnosis: 1971-1979, Survivors (Ref. Comparisons) RR=1.56 (95%CI:1.00-2.43)** • Time period of diagnosis: 1980-1989, Survivors (Ref. Comparisons) RR=1.04 (95%CI:0.60-1.82) • **Time period of diagnosis: 1990-1999, Survivors (Ref. Comparisons) RR=1.79 (95%CI:1.01-3.18)** • Time period of diagnosis: 2000-2009, Survivors (Ref. Comparisons) RR=0.72 (95%CI:0.17-3.14) • Time period of diagnosis: No statistical difference by time period of diagnosis was found (p=0.40, from likelihood ratio test) • 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) • 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)	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:** Follow-up began at the date of cancer diagnosis for cases and from the equivalent age for matched population comparisons and ended at death, emigration, or the end of follow-up (December 31, 2008, for Denmark and Sweden and December 31, 2012, for Finland), whichever occurred first.

	population registries, matched by birth month and year, sex, and country. The median age at the end of follow-up was 27.4 years (range: birth to 58.8 years) for population comparisons			

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?				
Nathan et al. **Adverse Mental Health Outcomes in a Population-Based Cohort of Survivors of Childhood Cancer. 2018**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: ☐ **Cross-sectional study** ☐ **Case-control study** ☒ **Cohort study** ☐ **Qualitative study (→ exclude!)** ☐ **Systematic/narrative review (→ exclude!)** ☐ **RCT** ☐ **Other: (specify!)** **Treatment era (n= (%)):** **1987-1993: 1520 (36.9)** **1994-2001: 2003 (48.7)** **2002-2008: 594 (14.4)** **Years of follow-up:** **≥5 years since the latest of diagnosis, relapse, or subsequent malignant neoplasm** **Country:** **Canada** **Study center:** **Pediatric Oncology Group of Ontario's Networked Information System (Ontario's 5 pediatric cancer centers)** **Measurement tool:** • **A mental health visit was defined as a visit to a family physician, psychiatrist, or emergency department (ED) or a hospitalization.** • **A severe mental health event was defined as an ED visit, hospitalization, or suicide.**	**Sample size:** N=4117 **Diagnoses (n= (%)):** Acute lymphoblastic leukemia 1087 (26.4) Other leukemias 189 (4.6) Hodgkin lymphoma 386 (9.4) Other lymphomas 307 (7.5) Central nervous system tumors 808 (19.6) Neuroblastoma 144 (3.5) Retinoblastoma 92 (2.2) Renal tumors 240 (5.8) Hepatic tumors 39 (0.9) Bone tumors 202 (4.9) Soft tissue sarcomas 256 (6.2) Germ cell tumors 164 (4.0) Other epithelial tumors 170 (4.1) Unspecified malignancies 33 (0.9) **Age at diagnosis (n= (%)):** 0-4 years: 1347 (32.7) 5-9 years: 1052 (25.6) 10-14 years: 1181 (28.7) 15-18 years: 537 (13.0) **Age at study:** n.a.	Hematopoietic stem cell transplantation No n=3854 (93.6%) Autologous n=114 (2.8%) Allogenic n=149 (3.6%) Surgery No n=1868 (45.4%) Yes n=2249 (54.6%) Chemotherapy No n=1031 (25.0%) Yes n=3021 (73.4%) Unknown n=65 (1.6%) Cranial radiation No n=3230 (78.5%) Yes n=887 (21.5%) High-dose methotrexate No n=3229 (78.4%) Yes n=823 (20.0%) Unknown n=65 (1.6%)	Risk factors for **mental healthcare visit** from Andersen-Gill recurrent event multivariable regression models (adjusting for sex, income, age at diagnosis, diagnosis, and HSCT) Relapse or SMN, CNS radiation, ITR, surgery, chemotherapy, high-dose methotrexate, corticosteroids, treatment era, and cyclophosphamide equivalent dose not statistically significant in univariable model and therefore not included in the final model. • **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) • Income quintile: 5 (Ref. 1) RR=1.31 (95%CI:0.90-1.92; p=0.165) • 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) • 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) 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) Relapse or SMN, ITR, Surgery, Chemotherapy, Corticosteroids, treatment era, HSCT, and cyclophosphamide equivalent dose not statistically significant in univariable model and therefore not included in the final model: • 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)	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/☐unclear **Remarks:** During the study period, survivors and controls were followed for a median [range], 7.5 years [1.0-21.9]; vs. controls 7.5 years [1.0-21.9] Total person-years of follow-up survivors: 35,027, controls: 172,409

• **International Statistical Classification of Diseases-10th Revision and Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition codes was used to classify ED visits and hospitalizations into the diagnostic subcategories: substance abuse, psychotic disorders, mood/affective disorders, anxiety disorders, and selected disorders of adult personality and behavior**	**Controls:** N=20269 controls from the general population, matched by birth year and month, sex, and residential location	Corticosteroid No n=2367 (57.5%) Yes n=1685 (40.9%) Unknown n=65 (1.6%)	• 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)** • **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) • 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) • **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)	

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?				
Ranft et al. **Quality of Survivorship in a Rare Disease: Clinicofunctional Outcome and Physical Activity in an Observational Cohort Study of 618 Long-Term Survivors of Ewing Sarcoma. 2017**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: ☐ **Cross-sectional study** ☐ **Case-control study** ☒ **Cohort study** ☐ **Qualitative study (→ exclude!)** ☐ **Systematic/narrative review (→ exclude!)** ☐ **RCT** ☐ **Other: (specify!)** **Treatment era** **1980-1985** **1986-1991** **1992-1998** **1999-2009** **Years of follow-up** **3-4.9 years: n=35 (5.7%)** **5-9.9 years: n=191 (30.9%)** **10-19.9 years: n=248 (40.1%)** **≥20 years: n=144 (23.3%)** **Country** **Germany** **Study center** **N.a.** **Measurement tool** **Brief Symptom Inventory**	**Sample size** N=618 **Diagnosis** Ewing sarcoma **Age at diagnosis** 0-9.9 years: n=142 (23.0%) 10-17.9 years: n=291 (47.1%) 18-29.9 years: n=131 (21.2%) ≥30 years: n=54 (8.7%) **Age at study** Median age at study 29 years 0-9.9 years: n=5 (0.8%) 10-17.9 years: n=63 (10.2%) 18-29.9 years: n=272 (44.0%) ≥30 years: n=278 (45.0%) **Controls** N=316 controls, recruited through survivors; median age at study 30 years	Local treatment None n=2 (0.3%) Surgery n=174 (28.2%) Radiotherapy n=96 (15.5%) Surgery + Radiotherapy n=346 (56.0%) High-dose chemotherapy No n=555 (89.8%) Yes n=63 (10.2%)	**Risk factors for depression** from multivariable binary logistic regression (not specified what variables were adjusted for): • Trial: CESS 86 (Ref. CESS 81) OR= 1.02 (95%CI:0.41 to 2.53) • Trial: EICESS 92 (Ref. CESS 81) OR= 1.49 (95%CI:0.64 to 3.51) • Trial: EURO-EWING 99 (Ref. CESS 81) OR= 1.32 (95%CI:0.55 to 3.15) • **Sex: Female (Ref. Male) OR= 1.71 (**95%CI:**1.20 to 2.45)** • 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) • Risk group: Pulmonary metastases (Ref. localized disease) OR= 1.27 (95%CI:0.69 to 2.33) • Risk group: Extrapulmonary metastases (Ref. localized disease) OR= 1.75 (95%CI:0.81 to 3.79) • Site: Axial (Ref. Pelvis) OR= 0.65 (95%CI:0.39 to 1.08) • Site: Lower extremity (Ref. Pelvis) OR= 0.89 (95%CI:0.53 to 1.48) • Site: Upper extremity (Ref. Pelvis) OR= 0.69 (95%CI:0.35 to 1.38) • 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) • High-dose chemotherapy: Yes (Ref. No) OR= 1.12 (95%CI:0.58 to 2.15) Risk factors for anxiety from multivariable binary logistic regression (not specified what variables were adjusted for): • Trial: CESS 86 (Ref. CESS 81) OR= 0.58 (95%CI:0.26 to 1.29) • Trial: EICESS 92 (Ref. CESS 81) OR= 0.79 (95%CI:0.37 to 1.68) • Trial: EURO-EWING 99 (Ref. CESS 81) OR= 0.60 (95%CI:0.28 to 1.31) • **Sex: Female (Ref. Male) OR= 1.49 (**95%CI:**1.06 to 2.09)** • 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) • Risk group: Pulmonary metastases (Ref. localized disease) OR= 1.13 (95%CI:0.63 to 2.01) • Risk group: Extrapulmonary metastases (Ref. localized disease) OR= 1.17 (95%CI:0.54 to 2.53) • Site: Axial (Ref. Pelvis) OR= 1.01 (95%CI:0.63 to 1.63) • Site: Lower extremity (Ref. Pelvis) OR= 0.80 (95%CI:0.49 to 1.31) • Site: Upper extremity (Ref. Pelvis) OR= 0.45 (95%CI:0.22 to 0.91) • 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) • High-dose chemotherapy: Yes (Ref. No) OR= 1.43 (95%CI:0.76 to 2.67)	**Quality assessment:** 1. Is the study group representative? ☐Yes/☒no/ ☐unclear 2. Is the follow-up adequate? ☐Yes/☐no/ ☒n.a./☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?			
Burghardt et al. **Prevalence of mental distress among adult survivors of childhood cancer in Germany – compared to the general population. 2019**			
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **Diagnosed from 1980-1990** **Years of follow-up:** **≥ 5 years after end of treatment, Median: 28.1yrs (range:23-36)** **Country:** **Germany** **Study center:** **University Medical Center Mainz** **Measurement tool:** **Cardiovascular examination with clinical phenotyping, self-report questionnaires and computer assisted personal interviews.** **Specifically:** **PHQ-8 (major depression)** **One question for suicidal ideation.** **GAD-2 (general anxiety)** **Brief PHQ panic module (panic).** **Mini-Spin (Social anxiety)** **PHQ-15 (severity of symptoms, burden).**	**Sample size:** 951 (55% male) **Diagnoses: %, N** Leukemias: 43.5% (414) Lymphomas 9.9% (94) CNS tumors 12.8% (122) Neuroblastoma 7.6% (72) Retinoblastoma 1.1% (10) Renal tumors 8.1% (77) Hepatic tumors 0.7% (7) Bone tumors 5.3% (50) Soft tissue sarcoma 7.5% (71) Germ cell tumors 2.7% (26) Carcinoma 0.7% (7) Others 0.1% (1) **Age at diagnosis:** Median: 4.4 (range: 0-15) <1 yrs 9.5 (90) 1-<4 yrs 30.8% (293) 4-<8 yrs 27.7% (263) 8-<11 yrs 13.5% (128) 11-<15 yrs 18.6% (177) **Age at study:** Median: 34.2 (range: 24-49) 20-29 yrs: 23.9% (227) 30-39 yrs: 58.4% (555) 40-49 yrs: 17.8% (169) **Controls:** German Household Panel from three years: 2006: n=569 (57.1% female) social phobia, generalized anxiety, panic; 2008: n=1130 (52.8% female) Somatic stress, depression, suicidality	None reported	Risk factors for **depression** from multivariable logistic regression[a] (OR [95%CI]) • Sex: Female (Ref. Male) OR=1.23 [0.69, 2.18] • **Age (continuous): OR=0.92 [0.87, 0.97]** • Marital status: Married (Ref. Not married) OR=1.21 [0.62, 2.36] • **Education: Low (Ref. High) OR=2.33 [1.08, 5.02]** • Education: Middle (Ref. High) OR=1.84 [0.97, 3.48] • Income in 100 Euros per month (continuous): OR=0.98 [0.96, 1.00] • Unemployed (Ref. Employed) OR=2.63 [0.88, 7.88] Risk factors for **suicidal ideation** from multivariable logistic regression[a] • Sex: Female (Ref. Male) OR=1.15 [0.65, 2.03] • Age (continuous): OR=0.99 [0.94, 1.04] • **Marital status: Married (Ref. Not married) OR=0.37 [0.17, 0.82]** • Education: Low (Ref. High) OR=1.41 [0.61, 3.26] • Education: Middle (Ref. High) OR=1.72 [0.92, 3.23] • Income in 100 Euros per month (continuous): OR=0.99 [0.97, 1.01] • **Unemployed (Ref. Employed) OR=3.26 [1.17, 9.14]** Risk factors for **generalized anxiety** from multivariable logistic regression[a] • Sex: Female (Ref. Male) OR=1.11 [0.63, 1.96] • Age (continuous): OR=0.96 [0.91, 1.01] • Marital status: Married (Ref. Not married) OR=0.73 [0.37, 1.43] • **Education: Low (Ref. High) OR=2.68 [1.25, 5.73]** • **Education: Middle (Ref. High) OR=2.36 [1.25, 4.45]** • Income in 100 Euros per month (continuous): OR=0.99 [0.98, 1.01] • **Unemployed (Ref. Employed) OR=4.57 [1.68, 12.37]** Risk factors for **social anxiety** from multivariable logistic regression[a] • Sex: Female (Ref. Male) OR=1.17 [0.70, 1.95] • Age (continuous): OR=0.98 [0.93, 1.03] • Marital status: Married (Ref. Not married) OR=0.58 [0.31, 1.07] • Education: Low (Ref. High) OR=1.34 [0.63, 2.85] • Education: Middle (Ref. High) OR=1.32 [0.74, 2.37] • Income in 100 Euros per month (continuous): OR=1.00 [0.99, 1.01] • Unemployed (Ref. Employed) OR=1.35 [0.38, 4.79] Risk factors for **panic** from multivariable logistic regression[a] • **Sex: Female (Ref. Male) OR=1.97 [1.09, 3.58]**	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:** [a]adjusting for sex, age, marital status, education, income in 100€, and employment

Jenkins sleep scale (sleep disorder).	2010: n=1054 (54.1% female) sleep disorders.		• Age (continuous): OR=0.97 [0.91, 1.02] • Marital status: Married (Ref. Not married) OR=1.33 [0.67, 2.64] • Education: Low (Ref. High) OR=1.58 [0.71, 3.53] • Education: Middle (Ref. High) OR=0.85 [0.42, 1.72] • Income in 100 Euros per month (continuous): OR=0.98 [0.96, 1.01] • **Unemployed (Ref. Employed) OR=3.39 [1.14, 10.10]**	

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?				
Crochet et al. **Posttraumatic stress as a contributor to behavioral health outcomes and healthcare utilization in adult Survivors of Childhood Cancer: A report From the Childhood Cancer Survivor Study. 2019**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☐ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era: Diagnosed from 1970-1986** **Years of follow-up: Not stated; survival at least 5y from diagnosis** **Country: US & Canada** **Study center: Multicenter, 27 institutions (CCSS)** **Measurement tool:** • **Post-traumatic stress scale: Intrusion, Avoidance, Hypervigilance, cut-off ≥13 for caseness** • **Brief Symptom Inventory-18: depression, anxiety, somatization;**	**Sample size:** N=6844 N_{wo}=5227 without PTSS; N_w=832 with PTSS **Mixed Diagnoses: w/o PTSS; w/ PTSS** CNS tumor: n=610 (10.4 %); n=117 (11.8%) Sarcoma: n=1072 (18.3%); n=191 (19.2%) Lymphoma: n=1285 (22.0%); n=204 (20.5%) Solid tumor: n=945 (16.2%); n=133 (13.4%) Leukemia n=1937 (33.1%); n=350 (35.2%) **Age at diagnosis:** Mean age at diagnosis: 7.6 years (SD 5.8) **Age at study:** Mean age at follow-up: 34.9 years (SD 7.5) **Controls:** None	Without PTSS N_{wo}=5227 / With PTSS N_w=832 Anthracycline dose > 0 m = 290.1 (IQR = 174.9, 348.8) / m = 292.3 (197.7, 397.4) Anthracyclines in the 1st 5 years n = 2113 (36.1%) / n = 369 (37.1%) Alkylating agents dose > 0 m = 6600.0 (IQR = 3589.2, 11525.0) / m = 6958.3 (IQR = 3264.4, 12415.5) Alkylating agents in the 1st 5 years n = 2708 (46.3%) / n = 470 (47.2%) Methotrexate IV dose > 0 m = 3540.7 (IQR = 400.9, 15891.7) / m = 3963.1 (IQR = 474.2, 21038.7) Methotrexate IV in the 1st 5 years n = 1024 (17.5%) / n = 180 (18.1%) Methotrexate IT dose > 0 m = 123.5 (IQR = 69.2, 222.2) / m = 125.8 (IQR = 75.0, 221.7) Methotrexate IT in the 1st 5 years n = 1771 (30.3%) / n = 309 (31.1%) Cranial radiation dose > 0 m = 200.0 (IQR = 20.0, 2400.0) / m = 1800.0 (IQR = 20.0, 2400.0) Cranial radiation n = 3478 (59.5%) / n = 641(64.4%) m= median IQR=interquartile range	Risk factors for high emotional distress from 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; n=4798 survivors included in analysis): • **PTSS: Yes (Ref. No) RR=8.58 (95%CI:7.13–10.32; p<0.001*)** • 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) • **Cranial radiation: Per 10 Gy (continuous): RR=0.94 (95%CI:0.90–0.9; p= 0.022)** • Years since diagnosis: Per year (continuous): RR=0.99 (95%CI:0.97–1.01; p= 0.54) • Age at evaluation: Per year (continuous): RR=1.01 (95%CI:0.99–1.02; p= 0.23) • 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) • Sex: Female RR=1.03 (95%CI:0.88–1.20; p= 0.75) • Race/ethnicity: Black/Hispanic/Other RR=1.02 (95%CI:0.82–1.27; p= 0.85) • **Employment status: Unemployed RR=1.85 (95%CI:1.54–2.22; p < 0.001*)** • **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)** • **Marital status: Single or separated RR=1.29 (95%CI:1.08–1.53; p= 0.005*)**	**Quality assessment:** 1. Is the study group representative? ☐Yes/☐no/ ☒unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

clinical cut-off of being in the top 10th percentile				

1b. What are the key clinical/demographic and treatment-related risk factors for developing mental health disorders/symptoms in CAYA survivors?				
Tonorezos et al. **Impact of Exercise on Psychological Burden in Adult Survivors of Childhood Cancer: A report From the Childhood Cancer Survivor Study. 2019**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: ☐ **Cross-sectional study** ☐ **Case-control study** ☒ **Cohort study** ☐ **Qualitative study (→ exclude!)** ☐ **Systematic/narrative review (→ exclude!)** ☐ **RCT** ☐ **Other: (specify!)** **Treatment era:** **Diagnosed from 1970-1986** **Years of follow-up:** **Not stated; survival at least 5y from diagnosis** **Country:** **US & Canada** **Study center: Multicenter, 26 institutions (CCSS)** **Measurement tool:** • **Vigorous exercise assessed with a question. Calculated using frequency and duration, weighted energy expenditure and transformed into metabolic equivalent units (MET) and expressed as MET-hours per week. And then combined into Levels.** **Brief Symptom Inventory-18: depression, anxiety,**	**Sample size:** N=6199 **Mixed Diagnoses:** Leukemia n=1857 (30.0%) CNS n=766 (12.4%) Hodgkin lymphoma n=1001 (16.1%) Non-Hodgkin lymphoma n=576 (9.3%) Kidney, Wilms n=438 (7.1%) Neuroblastoma n=249 (4.0%) Soft-tissue sarcoma n=628 (10.1%) **Age at diagnosis:** Median [range] 10.0 years [0.0 21.0] **Age at study:** Mean [range] 34.0 years [22.0-54.0] **Controls:** n.a.	**Chemotherapy** Any chemotherapy n=4376 (78.0%) Alkylating dose: CED, mg/m2 None n=2747 (53.3%) >0 to <4000 n=482 (9.4%) 4000-8000 n=587 (11.4%) ≥8000 n=1334 (25.9%) Anthracycline dose, mg/m2 None n=3470 (64.5%) >0 to <250 n=685 (12.7%) ≥250 n=1226 (22.8%) **Radiation therapy** Any radiation therapy n=4032 (68.1%) Chest, Gy n=1571 (28.5%) Chest direct dose None n=1650 (51.4%) <20 n=226 (7.0%) 20 to <30 n=398 (12.4%) 30 to <40 n=510 (15.9%) 40 to <50 n=363 (11.3%) ≥50 n=65 (2.0%) Brain or head, Gy n=2048 (37.1%) All head direct dose None n=1650 (44.7%) <20 n=39 (1.1%) 20 to <30 n=1191 (32.3%) 30 to <40 n=114 (3.1%) 40 to <50 n=143 (3.9%) ≥50 n=551 (14.9%)	**Clinical risk factors for depression** from log-binomial regression (adjusted for age at diagnosis, sex, race, cancer diagnosis, alkylating exposure, anthracycline exposure, chest radiation exposure, and brain or head radiation exposure; and age, smoking status, education, and cardiovascular disease risk factor profile at FU2003, and anxiety, depression, somatization and cancer pain at the baseline, any major physical conditions at baseline, and any interim major physical 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) **Clinical risk factors for anxiety** from log-binomial regression (adjusted for age at diagnosis, sex, race, cancer diagnosis, alkylating exposure, anthracycline exposure, chest radiation exposure, and brain or head radiation exposure; and age, smoking status, education, and cardiovascular disease risk factor profile at FU2003, and anxiety, depression, somatization and cancer pain at the baseline, any major physical conditions at baseline, and any interim major physical 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)	**Quality assessment:** 1. Is the study group representative? ☐Yes/☒no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

somatization; prevalence of clinically significant symptoms was defined as a T-score ≥63				

2. Does the risk of developing poor mental health change over time in CAYA survivors?				
Brinkman, Zhu et al. **Longitudinal patterns of psychological distress in adult survivors of childhood cancer. 2013**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Treatment**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☐ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1970-1986** **Years of follow-up:** **1994-2010** **Country:** **USA and Canada** **Study center:** **Multi-site (CCSS)** **Measurement tool:** **BSI-18, with score of ≥63 classified a clinical level of emotional distress, transposed into outcome classes**	**Sample size:** 4569 survivors **Diagnoses:** **BSI=3** Leukemia 1534 (29.6%) CNS tumor 526 (11.5%) Hodgkin lymphoma 882 (19.3%) Non-Hodgkin lymphoma 394 (8.6%) Wilms tumor 278 (6.1%) Neuroblastoma 163 (3.6%) Soft tissue sarcoma 460 (10.1%) Osteosarcoma 512 (11.2%) **BSI 1-3** Leukemia 1473 (30.1%) CNS tumor 655 (13.4%) Hodgkin lymphoma 780 (16.0%) Non-Hodgkin lymphoma 468 (9.6%) Wilms tumor 349 (7.1%) Neuroblastoma 224 (4.6%) Soft tissue sarcoma 442 (9.0%) Osteosarcoma 499 (10.2%) **Age at diagnosis:** ≤ 21 years Mean 10.0 years (SD 5.6) Range 0-20 years **Age at study:** >18 years At baseline survey, mean 27.4 years (SD 6.0) **Controls:** none	**Radiation therapy** **BSI=3** None 1203 (28.5%) Non-cranial 1463 (34.7%) Cranial ≤20 Gy 523 (12.4%) Cranial > 20 Gy 1032 (24.5%) **BSI1-3** None 1095 (28.4%) Non-cranial 1257 (32.6%) Cranial ≤20 Gy 507 (13.1%) Cranial > 20 Gy 1000 (25.9%)	Survivors completed evaluations at baseline (≥ 1994), follow-up 2 (2003-2005) and follow-up 3 (2007-2010), which included the BSI-18. Based on these, they were assigned at analysis to one of 4 classes, according to trajectory of BSI-18 scores at the three timepoints (see remarks): **Class 1**: few/no symptoms at all timepoints ; **Class 2**: elevated symptoms at baseline that decreased over time; **Class 3**: few/no symptoms at baseline that increased with time; **Class 4**: elevated symptoms at baseline that persisted with time **Change in risk over time:** BSI-18 Anxiety: Class 1 (persistently few/no symptoms): 68.4% Class 2 (decreased with time): 15.2% Class 3 (increased with time): 11.8 % Class 4 (persistently elevated): 4.8% BSI-18 depression: Class 1 (persistently few/no symptoms): 65.8% Class 2 (decreased with time): 15.1% Class 3 (increased with time): 10.2 % Class 4 (persistently elevated): 8.9% BSI-18 Somatization: Class 1 (persistently few/no symptoms): 68.2% Class 2 (decreased with time): 11.6% Class 3 (increased with time): 13.0 % Class 4 (persistently elevated): 7.2%	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:** Longitudinal latent class analysis (LPA), a submodel of structural equation modeling (SEM), used to assign the grouping variable (class membership) derived from observed data, using the best-fitting model.

2. Does the risk of developing poor mental health change over time in CAYA survivors?

Brinkman et al. **Alcohol consumption behaviors and neurocognitive dysfunction and emotional distress in adult survivors of childhood cancer: A report from the Childhood Cancer Survivor Study. 2019**

Study Design Treatment era Years of follow-up	Participants	Treatment	Main outcomes	Quality assessment Remarks
Study Design: **☐ Cross-sectional study** **☐ Case-control study** **☒ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1970-1986** **Years of follow-up:** **≥ 5years** **Three timepoints: Baseline, Follow-up 2, Follow-up 4** **Country:** **USA and Canada** **Study center:** **Multi-site (CCSS)** **Measurement tool:** • **BSI-18: T-score of ≥63 defined as distress** **Posttraumatic Stress Diagnostic Scale (PDS): at least one re-experiencing symptom, at least three avoidance symptoms and at least**	**Sample size:** N=4484 survivors **Diagnoses:** Leukemia 1353 (30.2%) CNS tumor 453 (10.1%) Hodgkin lymphoma 874 (19.5%) Non-Hodgkin lymphoma 382 (8.5%) Wilms tumor 290 (6.5%) Neuroblastoma 165 (3.7%) Soft tissue sarcoma 456 (10.2%) Bone tumors 511 (11.4%) **Age at diagnosis:** <21 years Mean 10.5 years (SD 5.6) **Age at study:** >18 years at baseline Baseline: Mean 27.2 years (SD 6.2) Follow-up 2: Mean 34.8 years (SD 6.1) Follow-up 4: Mean 39.5 years (SD 6.0) **Controls:** N=1651 siblings	Radiation: None n=1240 (29.9%) Non-cranial n=1435 (34.6%) ≤20Gy Cranial n=523 (12.6%) >20Gy Cranial n=946 (22.8%) Intravenous Methotrexate: Yes n=791 (19.1%) No n=3359 (80.9%) No. of intrathecal injections: None n=2819 (66.7%) 1 n=1052 (24.9%) ≥2 n=355 (8.4%)	"Thirteen percent of survivors experienced persistent or increasing distress symptoms characterized by elevated symptoms of depression, anxiety, and/or somatization compared to 7% of siblings (P<0.001)." Survivors: N, %; Siblings: n, %; p-value Persistent/increasing emotional distress Depression: 257, 6.0, 61, 3.7, <0.001 Anxiety: 160, 3.7, 43, 2.6, 0.031 Somatization: 306, 7.1, 54, 3.3, <0.001 Depression, anxiety, and/or somatization: 538, 12.5, 112, 6.8, <0.001	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☐Yes/☒no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:** Longitudinally persisting distress (T-score ≥63 at baseline, follow-up 2 and follow-up 4), and/or increasing emotional distress (non-significant distress at baseline (T-score <63) that increased at follow-up 2 or follow-up 4 for any of the three BSI subscales).

two arousal symptoms, with or without functional impairment was defined as positive endorsement of PTSS				

3. How sensitive are commonly used diagnostic tools for self-reported, parent-reported, different age groups, format and different clinical issues?				
Liptak et al. **The feasibility of psychosocial screening for adolescent and young adult brain tumor survivors: the value of self-report. 2012**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Diagnostic tool**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **Not specified** **Years of follow-up:** **Years since diagnosis** **Mean=9.4 years (SD=4.9)** **Country:** **US** **Study center:** **Dana Farber Cancer Institute**	**Sample size:** N=163 **Diagnoses:** All brain tumors including: Low grade glioma (n=86, 52.8%) Embryonal tumor (n=33, 20.2%) Ependymoma (n=14, 8.6%) Craniopharyngioma (n=8, 4.9%) Germ cell tumor (n=7, 4.3%) Choroid plexus tumor (n=3, 1.8%) High grade glioma (n=2, 1.2%) Other (n=10, 6.1%) **Age at diagnosis:** Mean=9.0 years (SD=4.9) **Age at study:** Overall Mean=18.9 years (SD=4.6) Range= 12-36 yrs Adolescent (n=84) 15.7 years (SD=1.9) Young adults (n=79): 22.8 years (SD=3.2) **Treatment:** Chemotherapy (88.1%) Radiotherapy (66.3%) Amputation (4%)	BSI-18 (ages 19-30) Beck Youth Inventory-II (ages 12-18) Versus clinical interviews Global Assessment of functioning (GAF) scale in DSM IV for global rating, ≤ 60 indicated a clinical case	**Sensitivity:** n.a. **Specificity:** n.a. **Feasibility, Acceptability, & Perceived Usefulness:** 84% of participants completed measures in ≤30mins. 98% found measures “moderately easy” or “very easy” to understand. 90% reported no distress completing the measures. 80% felt that the information that they provided on the measures was “moderately” to “very” useful in helping medical providers. Concordance between BYI-II and clinician rating was 73% of cases (n=60); Discordance between BYI-II and clinician rating was 27% (n=22). kappa=0.19, p=0.077 showed ‘low agreement’ between adolescent self-report & clinician ratings Kappas were similarly low when looking at depression and anxiety subscales: Of 22 discordant cases, 8 were cases as classified by self-report and 14 were classified by clinician assessment. No association with diagnosis (p=0.87), age at diagnosis (p=0.57) or time since diagnosis (p=0.95) 14 cases who rated themselves as clinical cases on BYI-II were not identified by clinicians, indicating that self-report might reveal some cases which are not brought up during clinical meetings. GSI, 27% (n=21) was classified as cases. 34% (n=24) reported depressive symptomatology, 25% (n=17) as cases on anxiety scale. Concordance between BSI-18 and GAF was 72% (n=55); Discordance between BSI-18 and GAF was 28% (n=21, kappa=0.34, p=0.003) indicating ‘moderate agreement’ between young adult self-report & clinician ratings Similar findings for subscales of BSI. Of 21 discordant cases, 10% (n=8) were classified by self-report and 17% (n=13) were classified by clinician assessment only. No association with diagnosis (p=0.37), age at diagnosis (p=0.44) or time since diagnosis (p=0.30)	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☐n.a./☒unclear 4. Are the analyses adjusted for important confounding factors? ☐Yes/☒no/ ☐unclear **Remarks:** Descriptive statistics

3. How sensitive are commonly used diagnostic tools for self-reported, parent-reported, different age groups, format and different clinical issues?				
Merport et al. **Does the Brief Symptom Inventory-18 case rule apply in adult survivors of childhood cancer? Comparison with the Symptom Checklist-90. 2012**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Diagnostic tool**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **n.a.** **Years of follow-up:** **Median time since diagnosis = 17 yrs** **Country:** **U.S.** **Study center:** **Dana-Farber Cancer Institute**	**Sample size:** 201 out of 244 (82.4%), for analysis n= 193 **Diagnoses:** Lymphomas 33.7%, Leukemias 31.6% Sarcomas 16.6% Neuroblastoma 6.2% Wilm's tumor 4.7% Other cancer/ malignancy 7.3%. **Age at diagnosis:** Median=11 yrs Range: 0-20 yrs **Age at study:** Median= 26 yrs Range: 18–54 yrs 88% of participants were <40 years of age; 94% of participants were <45 years age. **Treatment:** n.a.	Brief Symptom Inventory-18 (BSI-18) Three previously proposed BSI-18 case-rules were employed and compared with Symptom Checklist-90 (SCL-90) classification. Impairment was determined by having: 1) a SCL-90 GSI T-score ≥63 or 2) any two SCL-90 subscales T-score ≥63. The alternative BSI-18 case-rules included: (i) BSI-18 standard case-rule (Derogatis, 2001): Clinical case= GSI T-score ≥63 or at least two subscales with T-scores ≥63 (ii) Zabora case-rule (Zabora et al., 2001): Clinical case= GSI T-score ≥57 (iii) Recklitis case-rule (Recklitis & Rodriguez, 2007): Clinical case= GSI T-score ≥50.	Area under the receiver operating characteristics (ROC) curve (AUC) used to summarize diagnostic utility of the BSI-18. AUC was 0.922, indicating BSI-18 GSI T-scores have high diagnostic utility relative to SCL-90 case-rule. Authors attempted to find a case rule for the BSI-18 that demonstrated sensitivity ≥0.9 and specificity ≥0.75. **Sensitivity:** Standard BSI-18 Case Rule (GSI T-score≥63): 45.2% Zabora Case Rule (GSI T-score≥57): 67.7% Recklitis Case Rule (GSI T-score≥50): 87.1% **Specificity:** Standard BSI-18 Case Rule (GSI T-score≥63): 99.4%; Zabora Case Rule (GSI T-score≥57): 93.8%; Recklitis Case Rule (GSI T-score≥50): 83.3%; **Positive predictive value** Standard BSI-18 Case Rule (GSI T-score≥63): 93.3% Zabora Case Rule (GSI T-score≥57): 67.7% Recklitis Case Rule (GSI T-score≥50): 50% **Negative predictive value** Standard BSI-18 Case Rule (GSI T-score≥63): 90.4% Zabora Case Rule (GSI T-score≥57): 93.8% Recklitis Case Rule (GSI T-score≥50): 97.1% **Total predictive value** Standard BSI-18 Case Rule (GSI T-score≥63): 90.7% Zabora Case Rule (GSI T-score≥57): 98.6% Recklitis Case Rule (GSI T-score≥50): 83.9%	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☐Yes/☐no/ ☒unclear **Remarks:**

3. How sensitive are commonly used diagnostic tools for self-reported, parent-reported, different age groups, format and different clinical issues?				
Stuber et al. **Defining medical posttraumatic stress among young adult survivors in the Childhood Cancer Survivor Study. 2011**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Diagnostic tool**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1970-1986** **Years of follow-up:** **Years since dx:** **15-19 (27.1%); 20-24 (35.8%); 25-29 (25.5%); 30-34 (11.6%)** **Country:** **USA** **Study center:** **Various in USA and Canada (CCSS)** **Measurement tool:** **Posttraumatic stress response Diagnostic Scale (PDS), 17 questions based on DSM IV related diagnostic criteria; scale measures severity (occurrence) of symptoms on scale 0-3. PDS in study used in 3 ways: 1. Criteria for DSM symptoms cluster, 2. Number of 17 symptoms , 3. Severity/frequency of symptoms; Brief Symptom Inventory-18 (BSI-18) T-score ≥ 63 considered as clinically significant distress on the global stress index (GSI) or subscales of depression, anxiety, or somatization; RAND Health Status Survey, Short Form-36 (RAND SF-36) T-score ≤ 40 considered clinically impaired; Diagnostic Criterion F for PTSD attributed if BSI-18 GSI) ≥ 63, or two subscale scores ≥ 63; SF-36 ≤ 40 functional limitations caused by emotional stress; 5 different groups of survivors and siblings (combined) using different**	**Sample size:** 6542 survivors of childhood cancer **Diagnoses:** Bone cancer (9.2%), Central Nervous System Malignancies (10.5%), Hodgkin Lymphoma (14.2%), Kidney-Wilms (9.6%), Leukemia (33.4%), Non-Hodgkin Lymphoma (7.7%), Neuroblastoma (6.2%), Soft tissue sarcoma (9.2%) **Age at diagnosis:** Mean age = 8.2 yrs, SD = 5.87 yrs Range: 0-20 yrs **Age at study:** Mean age = 31.85 yrs, SD = 7.55 yrs Range: 18-53 yrs **Controls:** 368 siblings Mean age = 33.44 yrs, SD = 8.2 yrs Range: 18-54	Posttraumatic stress response Diagnostic Scale (PDS) Brief Symptom Inventory-18 (BSI-18 RAND Health Status Survey, Short Form-36 (RAND SF-36)	Receiving Operator Curves were used to analyze severity and number of symptoms as predictors. Main outcome measures: • Distress (BSI -18) or Impairment (SF-36), number of PTSD symptoms, severity of PTSD symptoms • Severity/frequency of PTSD symptoms and number of symptoms are better at discriminating between subjects with and without emotional distress using the BSI-18 (AUCs 0.84 and 0.82 respective) than those with or without functional impairment using the SF-36 (AUCs 0.74 and 0.74 respectively) • A threshold of 6 as true positive rate for severity of symptoms identifies 80% of survivors with emotional distress while identifying 27% incorrectly as having emotional distress. **Statistics for severity and number of PTSD symptoms as markers of clinical distress and functional impairment** True positive rate (TPR); False Positive Rate (FPR); Area under the curve (AUC) AUC Analyses: Marker: BSI-18 (distress) Severity of Symptoms: AUC: 0.84 (95% CI 0.82 – 0.85) Number of Symptoms: AUC: 0.82 (95% CI 0.80 – 0.84) Marker: SF-36 (impairment) Severity of Symptoms: AUC: 0.74 (95% CI 0.73 – 0.76) Number of Symptoms: AUC: 0.74 (95% CI 0.72 – 0.75) **TPR of 70%** Marker: BSI-18 Severity of Symptoms: ○ Threshold: 10 ○ FPR (95% CI): 14% (12% - 20%) Number of Symptoms: ○ Threshold: 6 ○ FPR (95% CI): 25% (15% - 22%) Marker: SF-36 Severity of Symptoms: ○ Threshold: 5 ○ FPR (95% CI): 30% (29% - 37%) Number of Symptoms: ○ Threshold: 4	**Quality assessment:** 1. Is the study group representative? ☒ Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒ Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒ n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:** Same sample population as Stuber, Meeske, Leinsenring, Stratton, Zeltzer, Dawson…Krull, 2010

<u>operational definitions of posttraumatic stress: 1.</u> Posttraumatic stress defined as meeting full symptoms and the presence of distress or functional impairment, 2. Posttraumatic stress defined as meeting full symptoms without functional impairment or significant distress, 3. Presence of partial symptoms (2 of 3) and the presence of functional impairment or distress, 4. Presence of partial symptoms (2 of 3) and the absence of functional impairment or distress, 5. Less than two clusters of symptoms			○ FPR (95% CI): 31% (30% - 40%) **<u>TPR of 80%</u>** <u>Marker: BSI-18</u> Severity of Symptoms: ○ Threshold: 6 ○ FPR (95% CI): 27% (23% - 33%) Number of Symptoms: ○ Threshold: 4 ○ FPR (95% CI): 33% (26% - 41%) <u>Marker: SF-36</u> Severity of Symptoms: ○ Threshold: 2 ○ FPR (95% CI): 52% (43% - 53%) Number of Symptoms: ○ Threshold: 2 ○ FPR (95% CI): 49% (48% - 61%) **<u>TPR of 90%</u>** <u>Marker: BSI-18</u> Severity of Symptoms: ○ Threshold: 2 ○ FPR (95% CI): 54% (45% - 65%) Number of Symptoms ○ Threshold: 1 ○ FPR (95% CI): 63% (50% - 64%) <u>Marker: SF-36</u> Severity of Symptoms: ○ Threshold: 0 ○ FPR (95% CI): 84% (83% - 85%) Number of Symptoms ○ Threshold: 0 ○ FPR (95% CI): 84% (83% - 85%) Summary: No difference exists in the predictive value of severity/frequency and number of symptoms in the accurate prediction of emotional distress or impaired function using the BSI-18 and SF-36	

3. How sensitive are commonly used diagnostic tools for self-reported, parent-reported, different age groups, format and different clinical issues?				
Maurice-Stam et al. **Measuring perceived benefit and disease-related burden in young cancer survivors: validation of the Benefit and Burden Scale for Children (BBSC) in The Netherlands. 2011**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Diagnostic tool**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☒ Other: (specify!) Including re-test** **Treatment era:** **December 2008 to February 2009** **Years of follow-up:** **time since diagnosis M=3.2 (SD=1.4); time since the end of treatment M=1.8 (SD=0.9)** **Country:** **The Netherlands** **Study center:** **Emma Children's Hospital AMC,** **VU University Hospital,** **Radboud University Nijmegen Medical Centre,** **Leiden University Medical Centre**	**Sample size:** 126 invited 77 first assessement 69 re-test assessment **Diagnoses:** leukaemia or lymphoma: 64.9%, solid tumour: 27.3%, CNS cancer: 7.8% **Age at diagnosis:** mean=10.2 years **Age at study:** Not specified **Treatment:** Chemotherapy (98.7%) Surgery (58.4%) Radiotherapy (36.4%) Some (14.3%) of the children were treated for a relapse of the cancer.	Benefit and Burden Scale for Children ((BBSC: 20-item self-report instrument for children 7+ years. The items describe potential benefit (10 items) or burden (10 items) of illness with a five-point Likert scale ranging from 1 'not at all true for me' to 5 'very true for me'. Items include affect, relationships with peers and family relationships.)) Higher scores indicate higher benefit and burden (scale range 10–50). The BBSC has shown to be reliable and valid in an American childhood cancer populationwith benefit and burden as independent constructs. The Dutch version of the BBSC was established by a forward– backward translation. Further instruments: • PedsQL - Pediatric Quality of Life Inventory (PedsQL) GenericCore Scales • STAI-C - State-Trait Anxiety Inventory for Children • CRIES - Children's Revised Impact of Event Scale • SDQ- Strengths and Difficulties Questionnaire for children aged 11–16 years	**Sensitivity:** N.a. **Specificity:** N.a. **Reliability** Good internal consistency (benefit: α=0.84; burden: α=0.72). Satisfactory test–retest reliability, measured with a mean interval of 21 days: Pearson's correlation coefficient benefit: 0.74 and burden: 0.78. Homogeneity indexes were satisfactory: mean inter-item correlation for benefit (0.34) and burden (0.22). Item-total correlation for benefit was satisfactory (0.34-0.71). Item-total correlation for burden was less satisfactory (0.08-0.50) caused by item 18 ('I worry that I will bring other people down or upset them'). Deleting item 18 yielded item–total correlation for burden (0.35-0.50). **Construct validity** Burden correlated strongly (r≥0.5; p<0.001) with 11 out of 15 psychological outcomes. Higher levels of burden were associated with lower HRQoL, higher levels of anxiety, more posttraumatic stress symptoms and more behavioural problems. Benefit did not correlate with any psychological outcome. The authors conclude that the BBSC-Dutch version demonstrated "satisfactory internal consistency, test–retest reliability and homogeneity, though the item–total correlations of the Burden scale would rise when item 18 ('I worry that I will bring other people down or upset them') would be removed. The results of our study support the construct validity of the Dutch version of the BBSC. In line with the American version of the BBSC, disease-related burden was strongly associated with almost all psychological outcomes, while benefit finding was not."	**Quality assessment:** 1. Is the study group representative? ☐Yes/☒no/ ☐unclear 2. Is the follow-up adequate? ☐Yes/☐no/ ☒unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:** Self-reported outcomes

3. How sensitive are commonly used diagnostic tools for self-reported, parent-reported, different age groups, format and different clinical issues?

Recklitis, Licht et al. **Screening adult survivors of childhood cancer with the distress thermometer: a comparison with the SCL-90-R. 2007**

Study Design Treatment era Years of follow-up

Study Design:
☒ Cross-sectional study
☐ Case-control study
☐ Cohort study
☐ Qualitative study (→ exclude!)
☐ Systematic/narrative review (→ exclude!)
☐ RCT
☐ Other: (specify!)

Treatment era:
n.a.

Years of follow-up:
Time since diagnosis = 2.6-30.3 years (median 14.9 years)

Country:
USA

Study center:
Multi-institutional study (three institutions)

Participants

Sample size:
N=119

Diagnoses:
Leukemias : n= 42, 35.3%
Lymphomas: n= 29, 24.4%
Sarcomas: n= 26, 21.8%
Other solid tumors: n= 22, 18.5%

Age at diagnosis:
Median age at diagnosis = 11.2 years (range: birth-19 years)

Age at study:
Median age = 23.5 years (range: 18-45)

Treatment:
n.a.

Diagnostic tool

Distress thermometer
The DT is a single-item, self-reported measure of psychological distress. This visual-analogue scale has scores from 0 'no distress' to 10 'extreme distress'. Using the scale, patients were asked to rate how distressed they felt in the past week.

SCL-90-R
The SCL-90-R is a 90-item self-report symptom checklist. Respondents rate items on a five-point scale reflecting their distress during the past 7 days. Scores are generated for nine symptom scales and an overall Global Severity Index (GSI). Using gender-specific normative data, scores are transformed into T-scores. Cases are defined as clinical according to the SCL-90-R standard rule with GSI T-score, or any of two subscale T-scores ≥ 63.
It was chosen as the criterion measure against which to compare the DT because of its superior reliability and extensive validation in psychiatric, medical, and oncology samples.

Main outcomes

Sensitivity:
Using the NCCN recommended cut-off score of 5, the DT identified 20 of the 36 SCL-90-R cases. **Sensitivity was 55.6%**, specificity was 80.7%.
Using the alternative cut-off score of 4, the DT identified 23 of the SCL-90-R cases; **sensitivity improved to 63.9%** and specificity dropped to 65.1%.

Specificity:
Using the NCCN recommended cut-off score of 5, the DT identified 20 of the 36 SCL-90-R cases. Sensitivity was 55.6%, **specificity was 80.7%**.
Using the alternative cut-off score of 4, the DT identified 23 of the SCL-90-R cases; sensitivity improved to 63.9% and **specificity dropped to 65.1%**.

Other psychometric properties (specify):
In the ROC analysis AUC was 0.72, indicating the DT had only fair diagnostic utility relative to the SCL-90-R.
Finally, each DT score was evaluated as a potential cut-off score by calculating its sensitivity and specificity with the SCL-90-R criterion. No cut-off score met the criteria of sensitivity ≥0.90 and specificity ≤0.75 set for this study.

Sensitivity and Specificity values of distress thermometer cut-off scores

DT	Sensitivity (%)	Specificity (%)
≥ 0	100	0
≥ 1	88.9	21.7
≥ 2	86.1	30.1
≥ 3	77.8	48.2
≥ 4	63.9	65.10
≥ 5	55.6	80.7
≥ 6	47.2	88.0
≥ 7	33.3	92.8
≥ 8	25.0	97.6
≥ 9	10.8	100
≥ 10	8.3	100

Quality assessment Remarks

Quality assessment:
1. Is the study group representative?
☐Yes/☐no/
☒unclear
2. Is the follow-up adequate?
☒Yes/☐no/
☐unclear
3. Are the outcome assessors blinded?
☐Yes/☒no/
☐n.a./☐unclear
4. Are the analyses adjusted for important confounding factors?
☒Yes/☐no/
☐unclear

Remarks:

3. How sensitive are commonly used diagnostic tools for self-reported, parent-reported, different age groups, format and different clinical issues?				
Recklitis and Rodriguez. **Screening childhood cancer survivors with the brief symptom inventory-18: classification agreement with the symptom checklist-90-revised. 2007**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Diagnostic tool**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **n.a** **Years of follow-up:** **Off treatment 2+ years** **Country:** **USA** **Study center:** **Survivorship clinic offering long-term follow-up for suvivors of CC**	**Sample size:** 221 (99 men, 122 women) Validation data with n = 208 **Diagnoses:** Lymphoma: 74 (33.5%) Leukemia: 71 (32.1%) Sarcoma: 30 (13.6%) Wilm's tumor: 17 (7.7%) Brain tumor: 5 (2.3%) Other solid tumors: 24 (10.9%) **Age at diagnosis:** Median: 11 years (range 10 months-20.5 years) **Age at study:** Median:26 years (range 18-55) **Treatment:** n.a.	BSI-18, 3 symptom scales (t-score 50, SD 10) SCL-90R, 9 symptom scales (t-score 50, SD 10) Initially: GSI t-score or any two subscale t-scores ≥ 63 = clinical case	**Sensitivity:** BSI 18 t-score ≥ 50: high at 97.5% **Specificity:** BSI 18 t-score ≥ 50: adequate at 85.21% **Other psychometric properties (specify):** Maximum sensitivity with acceptable specificity: t-score ≥50 had sensitivity of 97.47% and specificity of 85.21% -> BSI identified 77 of 79 positive SCL-90R cases, TPV=89.59%->indicated only 10% of results were incorrect <u>t-score ≥63:</u> SCL-90R identified 79 positive cases, BSI-18 identified only 33 BSI-18 Sensititvity was low at 41.78%, specificity was 100%, overall accuracy (Total predictive value, TPV) was 79.19% <u>Alternate case rule t-score ≥57</u> BSI-18 identified 66 of 79 cases, sensitivity was 83.54%, specificity was 97.89% AUC was 0.98, BSI-18 has very high diagnostic utility relative to the gold standard, the SCL-90R BSI-18 scales had acceptable internal consistency (alpha >0.80) and were highly correlated with the corresponding SCL-90-R subscales (correlations from 0.88 to 0.94).	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☐Yes/☐no/ ☐unclear ☒ N.a. **Remarks:**

3. How sensitive are commonly used diagnostic tools for self-reported, parent-reported, different age groups, format and different clinical issues?				
Recklitis, Parsons et al. **Factor structure of the brief symptom inventory--18 in adult survivors of childhood cancer: results from the childhood cancer survivor study. 2006**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Diagnostic tool**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **1.1.1970-31.12.1986** **Years of follow-up:** **Time since diagnosis:** **Median: 17 years (range 6-29)** **Country:** **USA and Canada** **Study center:** **Childhood cancer survivor study. 25 institutions USA and Canada** **Measurement tool:** **BSI-18** **Case definition: GSI T-score≥63**	**Sample size:** N=8945, 4233 (47.3%)female, 4712 (52.7%) male **Diagnoses:** Leukemias 29.4% Non-hodgkin lymphomas 18.2% Hodgin's disease 12.3% Bone tumors 11.0% Soft tissue sarcoma 9.7% Central nervous system tumors 9.2% Kidney tumors 6.3% Neuroblastomas 4.0% **Age at diagnosis:** Less than 21 years at diagnosis; n.a. in detail **Age at study:** Median of 26 years (range 18-48 years) 18-22y: 26.4% 23-26y: 24.4% 27-34y: 26% 35+y: 13.2% **Controls:** - Community norms - Adult oncology groups	Brief symptom inventory-18 (BSI-18)	**Other psychometric properties (specify):** <u>Internal consistency:</u> "Internal consistency of the three BSI subscales in the survivor sample was examined by using Cronbach's alpha. Coefficients ranged from 0.75 to 0.88, which are similar to those reported in a community sample, which ranged from 0.74 to 0.84. On the GSI, the alpha coefficient for the survivors was 0.90 compared with 0.89 as reported by Derogatis (2000)." <u>Reliability:</u> "The three- and four-factor models met the criteria for adequate fit to the data (root mean square error of approximation (RAMSEA)≤0.05; comparative fit index (CFI) and nonnormed fit index (NNFI)≥0.96), […] The three-factor model was considered preferable, as it was more parsimonious and easily interpretable and was most consistent with the intended design of the BSI-18. The three-factor model was designated as the final model and was the only model further evaluated." "Results demonstrate that the measurement properties of the BSI-18 scales in this sample of adult survivors of childhood cancer are consistent with the intended three-dimensional structure (depression, anxiety, somatization). The internal consistency reliabilities, as well as the factor structures, demonstrate that the scales can be reliably and meaningfully applied to this population."	**Quality assessment:** 1. Is the study group representative? ☐Yes/☒no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

3. How sensitive are commonly used diagnostic tools for self-reported, parent-reported, different age groups, format and different clinical issues?				
Helton et al. **Factor analysis and validity of the Conners Parent and Teacher Rating Scales in childhood cancer survivors. 2006**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Diagnostic tool**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/ narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **Not specified** **Years of follow-up:** **Years off treatment: range 1-13.6 years; mean=5.22 years, SD=0.27** **Country:** **USA** **Study center:** **Multiple, not stated**	**Sample size:** Total sample =150, but parent report on multiple measures limited to n= 90 **Diagnoses:** Acute lymphoblastic leukemia: n = 76, 50.7% Brain tumor: n = 74, 49.3% **Age at diagnosis:** unclear; 57 were diagnosed < age 4 and 93 diagnosed age 4+ **Age at study:** Mean = 11.73 years, SD = 3.23 Range: 6-18 years **Treatment:** All received CNS directed therapy	Connors parent rating scale revised; short form (CPRS-R:S) and the Connors teacher rating scale revised; (CTRS-T:S) Achenbach Child behavior checklist (CBCL)	**Other psychometric properties:** **Factor analyses:** The results of this study support the construct validity of the original factor structure of the CTRS-R:S with a sample of survivors of childhood cancer who received central nervous system treatment. Factor analysis of the CPRS-R:S suggested less than adequate fit for the original 3 factor structure, but principal components analyses yielded a 3-factor solution with factors similar to the original factor structure, suggesting that it may be adequate. **In sub-analysis of parents reporting on 90 participants on the CBCL and CPRS-R-S** CPRS-R-S scales and CBCL scales were significantly correlated. **Correlations between CPRS-R-S scales and parent-report on the CBCL** **CPRS-R-S Oppositional** • CBCL attention prob = 0.47, p <0.001 • CBCL School competency = -0.13 • CBCL Delinquent probs = 0.48, p <0.001 • CBCL Aggressive probs = 0.74, p <0.001 **CPRS-R-S Cognitive/inattention** • CBCL attention prob = 0.55, p <0.001 • CBCL School competency = -0.43, p <0.001 • CBCL Delinquent probs = 0.31, p <0.01 • CBCL Aggressive probs = 0.47, p <0.001 **CPRS-R-S Hyperactivity** • CBCL attention prob = 0.47, p <0.001 • CBCL School competency = -0.15 • CBCL Delinquent probs = 0.39, p <0.001 • CBCL Aggressive probs = 0.54, p <0.001 ADHD index • CBCL attention prob = 0.63, p <0.001 • CBCL School competency = -0.35, p <0.01 • CBCL Delinquent probs = 0.31, p <0.01 • CBCL Aggressive probs = 0.56, p <0.001 All intercorrelations between the subscales of the CPRS and the CTRS were statistically significant (p <0.05); however, the magnitudes of the correlations were modest, accounting for only 29% of shared variance among the subscales. This might suggest differences between the CPRS-R:S and CTRS-R:S in their construct validity in this population. One possible explanation may be that individual items on the CPRS-R:S and CTRS-R:S have dissimilar content for each of the subscales.	**Quality assessment:** 1. Is the study group representative? ☐Yes/☒no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☒no/ ☐n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☐Yes/☒no/ ☐unclear **Remarks:** both parent measures were completed by the parent any perhaps at the same sitting so the fact that they are correlated is not at all surprising and perhaps not all that informative

3. How sensitive are commonly used diagnostic tools for self-reported, parent-reported, different age groups, format and different clinical issues?				
Van der Geest et al. **The distress thermometer provides a simple screening tool for selecting distressed childhood cancer survivors 2018**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Diagnostic tool**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **n.a.** **Years of follow-up:** **Median 17 years (range 5-37 years)** **Country:** **The Netherlands** **Study center:** **Erasmus MC University-Sophia Children's Hospital, Rotterdam**	**Sample size:** N=286 **Diagnoses:** Haematological malignancy (n = 164) Solid tumour (n = 115) Brain tumour (n = 7) **Age at diagnosis:** Median 6 years (range 0-15 years) **Age at study:** Median 24 years (range 17-44 years) **Treatment:** n.a.	Distress thermometer: 0-10 visual analog scale; 0 "no distress" to 10 "extreme distress" Gold standard measure used: Hospital Anxiety and Depression Scale (HADS): HADS score ≥15 was used as cut-off for emotional distress	**Sensitivity & Specificity:** A score of at least three on the distress thermometer yielded optimal sensitivity of 92% and specificity of 79%. The authors conclude that "the distress thermometer may provide a useful rapid screening tool to identify distressed childhood cancer survivors who need further psychological support."	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

3. How sensitive are commonly used diagnostic tools for self-reported, parent-reported, different age groups, format and different clinical issues?				
Pépin et al. **How to interpret high levels of distress when using the Distress Thermometer in the long-term follow-up clinic? A study with Acute Lymphoblastic Leukemia survivors. 2017**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Diagnostic tool**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **n.a.** **Years of follow-up:** **n.a.** **Country:** **Canada, PETALE-PSY survivor cohort** **Study center:** **Sainte-Justine UHC and Québec UHC**	**Sample size:** N=204 n=84 children and adolescent survivors n=120 adult survivors **Diagnoses:** Acute lymphoblastic leukemia **Age at diagnosis:** Age at diagnosis was 6 years (±5 years) **Age at study:** Children and adolescent survivors: Mean age of 15±2 years (8–18 years) Adult survivors: Mean age of 26 ± 5 years (19–40 years) **Treatment:** Radiotherapy 57%	Distress thermometer: 0-10 visual analog scale; 0 “no distress” to 10 “extreme distress” Gold standard measure used: Children and adolescents: • The Beck Youth Inventories • The Positive and Negative Affect Scale for Children Adults: • Beck Depression Inventory-II • Beck Anxiety Inventory • Positive and Negative Affect Scale	**Validity:** Children and adolescent survivors: - DT scores were exclusively associated with the Negative Affect domain (β=0.523, p<.001; R2=0.273, p<.001). Adult survivors: - DT scores were 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), - Negative Affect (β=0.210, p=.045; R2=0,023, p=.045), - Not associated with depression Conclusions of the authors: - In both age groups, DT is consistently associated with symptoms of anxiety - depression domain was not associated with the thermometer rating in either of the two age groups - the use of the thermometer is supported especially if one wishes to evaluate anxiety in both age groups, and more so than depression. - Second, the absence of distress on the thermometer could be interpreted as a sign of positive affectivity or well-being, but only in adults	**Quality assessment:** 1. Is the study group representative? ☒Yes/☐no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

3. How sensitive are commonly used diagnostic tools for self-reported, parent-reported, different age groups, format and different clinical issues?				
Abate et al. **Could we use parent report as a valid proxy of child report on anxiety, depression, and distress? A systematic investigation of father–mother–child triads in children successfully treated for leukemia. 2018**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Diagnostic tool**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: ☐ **Cross-sectional study** ☐ **Case-control study** ☐ **Cohort study** ☐ **Qualitative study (→ exclude!)** ☐ **Systematic/narrative review (→ exclude!)** ☐ **RCT** ☐ **Other: (specify!)** **Treatment era:** **n.a.** **Years of follow-up:** **Mean 11.55 years (SD 2.51)** **Country:** **Canada** **Study center:** **PETALE cohort, Sainte-Justine University Health Center**	**Sample size:** N=62 survivors and both parents **Diagnoses:** Acute lymphoblastic leukemia **Age at diagnosis:** Mean 3.56 years (SD 2.19) **Age at study:** Mean 15.82 years (SD 1.92); range 9-18 years **Treatment:** Radiation therapy No radiation n=38 (61%) Radiation n=24 (39%)	Beck Youth Inventory (anxiety and depression) Distress rating scale Parents: Brief Symptom Inventory-18 for own psychological status	**Sensitivity & Specificity:** “Overall, limited agreement was found between parents’ and children's ratings of anxiety, depression, and distress. These observations were confirmed when examining parent–child agreement on measures treated with prevalidated cut-points.” “On all measures, the reports of anxiety, depression, and distress by both parents when the child reported these as present were not different than chance (median agreement 52.5%).” “We found medium differences on anxiety (d = 0.50) and depression (d = 0.66), and small differences on distress (d = 0.35) between mothers and children. Similarly, ratings indicated medium differences between fathers and children on anxiety (d = 0.60) and depression (d = 0.59), as well as negligible differences on distress (d = 0.06). Both parents had higher ratings than children on anxiety and depression but only mothers had higher ratings than children on distress.” “Parental ratings were associated with child sex, parental income, and parental psychological status once children's ratings were controlled for. Larger disagreement was thus associated with the child being female and with lower parental income for fathers’ ratings of child distress. No effect was associated with child age” “Elevated parental psychological symptoms were consistently associated with larger parent–child disagreement. Yet, these predictors only explained a small percentage of the residual variance (ΔR^2 = 0.10) that suggests that other non-measured factors were involved in disagreement.”	**Quality assessment:** 1. Is the study group representative? ☐Yes/☒no/ ☐unclear 2. Is the follow-up adequate? ☐Yes/☐no/ ☒n.a./☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:**

3a. How sensitive are commonly used diagnostic tools for self-reported, parent-reported, different age groups, format and different clinical issues?				
Yoon et al. **Development and validation of self- and caregiver-report of a distress screening tool for pediatric cancer survivors. 2019**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Diagnostic tool**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☒ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☐ Other: (specify!)** **Treatment era:** **n.a.** **Years of follow-up:** **Time since dx:** **1–4: n=18 (10.7%)** **5–9: n=81 (48.2%)** **10–15: n=59 (35.1%)** **> 15: n=7 (4.2%)** **Missing data: n=3 (1.8%)** **Country:** **Korea** **Study center:** **Long-term Follow-up Clinic of a cancer hospital in Seoul**	**Sample size:** Final DST: N=168 CCS and 162 caregivers of which 27 dyads completed the DST for test-retest reliability. **Diagnoses:** Leukemia n=70 (41.7%) Lymphoma n=13 (7.7%) Abdominal tumor n=28 (16.7%) Brain tumor n=18 (10.7%) Others n=39 (23.2%) **Age at diagnosis:** <18 years **Age at study:** Mean 14.05 years (SD 2.57) Range: 10-18 years Age (years): 10–12: n=60 (35.7%) 13–15: n=43 (25.6%) 16–18: n=65 (38.7%) **Treatment:** n.a.	Self-report and Care-giver report versions of Distress Screening Tool (DST) with six items (depression, anxiety, physical fatigue, peer relationship, academic difficulties and overall life satisfaction) experienced in the last 2 weeks, 5-point Likert scale (never-almost always) Each item and the total score of the DST self-report were compared with the Children's depression inventory (CDI), Revised Children's manifest anxiety scale (RCMAS), Distress Thermometer (DT) and Pediatric Quality of life (PedsQL) to assess validity. Item 1 (depression) was correlated with CDI and emotional subscale of the PedsQL. Item 2 (anxiety) was correlated with RCMAS and emotional subscale of the PedsQL. The DST caregiver-report version was compared with the child behavior checklist (CBCL) and the PedsQL parent-proxy report version.	"Reliability and validity of the DST were found to be acceptable." **Reliability:** Final DST: **Internal consistency** self-report (Cronbach's α=0.86) and caregiver-report (α=0.84) represented good internal consistency. **Test-retest reliability** over 2-week period for self-report (r=0.70) and caregiver report (r=0.85) both p<0.001, showing sufficient test-retest reliability. **Validity:** **Convergent validity:** Each DST self-report item and the total score were statistically significantly correlated to the respective items of the CDI, RCMAS, DT and PedsQL self-report version, all p<0.001. DST caregiver-report total score was statistically significantly correlated with CBCL and parent-proxy report of PedsQL total score, p<0.001. **Discriminant validity:** Mean DST score of the survivors with the PedsQL scores below the average range was significantly higher than that of the survivors with the PedsQL scores within the average range, on both self-report, p<0.05, and caregiver-report, p<0.001. **Cut-off scores** for DST: method: scores of the clinical population are expected to fall 1.5~2SD above the mean. No significant differences in DST scores were found among age groups, therefore, a single cutoff score was generated for both versions: ≥15 for self-report, ≥16 on caregiver-report.	**Quality assessment:** 1. Is the study group representative? ☐Yes/☐no/ ☒unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:** The rates of distressed survivors who scored above the cutoff were 10.7% for self-report and 10.1% for caregiver-report. Page 6.

4. What are the most effective interventions in the treatment of mental health disorders in CAYA survivors?				
Seitz et al. **Efficacy of an internet-based cognitive-behavioral intervention for long-term survivors of pediatric cancer: a pilot study. 2014**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Intervention**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: ☐ Cross-sectional study ☐ Case-control study ☐ Cohort study ☐ Qualitative study (→ exclude!) ☐ Systematic/narrative review (→ exclude!) ☐ RCT ☒ Other: (specify!) Single-arm pilot study Treatment era: Not specified Years of follow-up: Mean=13.8 years (SD 4.7), range 4-21 years Country: Germany Study center: University of Ulm Measurement tool: Posttraumatic stress (PTSS) response Diagnostic Scale (PDS) - Subscales: intrusions, avoidance, hyperarousal. Total symptom scores range 0-51 with total scores of <10 = mild, ≥11 = moderate symptomatology; For subjects under 18 yrs of age the child version CPSS was used Hospital Anxiety and Depression Scale (HADS)- Subscales of depression (HADS-D) and anxiety (HADS-D). Total scores of <8 on subscales is normal, ≤ is elevated and clinically relevant.	**Sample size:** N=20 **Diagnoses:** Leukemia (40%), Lymphoma (30%), CNS tumor (20%), Soft tissue sarcoma (5%), Germ cell tumor (5%) **Age at diagnosis:** Mean= 13.45 yrs, SD = 4.71 **Age at study:** Mean = 27.25 yrs, SD = 4.8 yrs Range: 20-36 yrs **Treatment:** No information provided	Onco-STEP – internet-based cognitive-behavioral intervention • 10 sessions • Completed over 5-6 weeks Two modules: 1. "Looking back": reprocessing the traumatic experience (5 sessions) a. Worst memory: (sessions 1-3) aimed at reliving painful experience b. Letter (sessions 4-5): cognitive reconstruction and transformation of dysfunctional thoughts 2. "Looking ahead": building coping strategies with cancer related fear (5 sessions) a. Worry diary & solution suitcase (2 sessions): actualization of current fears b. Worst case and action plan (3 sessions): decatastrophize, reappraise, and restructure, as well as create an action	**Differences in pre-treatment and post-treatment symptoms** Both primary outcomes improved significantly: PTSS (t=4.81, p<0.001) and anxiety (t=3.44, p=0.003). Fear of progression/relapse (t=2.14, p=0.046) and symptoms of depression (t=5.69, p<0.001) were also reduced. Pre–post effect sizes for the two primary outcomes were medium, effect was large for the change of symptoms of depression. A clinically significant reduction of PTSS and symptoms of anxiety were found in 60 % of the participants, respectively. Clinically relevant improvement in 55 % of the participants for comorbid depressive symptoms, 45% showed an improvement in the reported fear of progression/relapse of the disease. 14 survivors were followed-up 3 months after completion of intervention. A significant decrease of PTSS (F1,14=11.16, p=0.005) and anxiety (F1,14=15.40, p=0.002) was found. A significant decline for fear of progression/relapse (F1,14=11.92, p=0.004), but not for symptoms of depression was found. No significant time effects between post-treatment and 3-month follow-up for PTSS and anxiety. Fear of progression significantly declined between end of treatment and the 3-month follow-up assessment. Symptoms of depression receded to the same level as before the intervention. **PTSS** Pre-treatment: Mean=15.30 (SD 8.07) Post-treatment: Mean=10.10 (SD 8.34), p<0.001, d=0.63 60% improved, 40% steady, 0% deteriorated **HADS-A** Pre-treatment: Mean=10.10 (SD 3.70) Post-treatment: Mean=6.95 (SD 4.49, p=0.003, d=0.74 60% improved, 35% steady, 5% deteriorated **FOP-SF** Pre-treatment: Mean=35.60 (SD 7.71) Post-treatment: Mean=31.40 (SD9.69), p=0.046, d=0.48 45% improved, 40% steady, 15% deteriorated **HADS-D** Pre-treatment: Mean=7.45 (SD 3.32) Post-treatment: Mean=3.40 (SD 2.96), p<0.001, d=1.00 55% improved, 40% steady, 5% deteriorated **Three month follow-up:** N = 14 **PTSS** Pre-treatment: Mean=14.29 (SD 8.15) Post-treatment: Mean=8.86 (SD 7.92) 3-month FU: Mean=9.21 (SD 6.49), F(1, 14)=11.16, p=0.005 **HADS-A** Pre-treatment: Mean=9.71 (SD 4.23) Post-treatment: Mean=6.14 (SD 3.70) 3-month FU: Mean=6.29 (SD 4.97), F(1, 14)=15.40, p=0.002 **FOP-SF** Pre-treatment: Mean=35.57 (SD 8.60)	**Quality assessment:** 1. Is the study group representative? ☐Yes/☒no/ ☐ unclear Recruitment through newspapers and internet 2. Is the follow-up adequate? ☐ Yes/☒no/ ☐unclear 20/28 eligible completed the intervention 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./ ☐ unclear 4. Are the analyses adjusted for important confounding factors? ☐Yes/☒ no/ ☐unclear **Remarks:**

Short form of the Fear of progression of Relapse Questionnaire (FOP-SF) Assesses fear for progression/relapse of existing illness; 12 items with a total score of 60, with higher scores indicating higher fear of recurrence		plan to cope with future fears	Post-treatment: Mean=30.71 (SD 9.24) 3-month FU: Mean=29.57 (SD9.14), F(1, 14)=11.92, p=0.004 **HADS-D** Pre-treatment: Mean=7.29 (SD 3.60) Post-treatment: Mean=4.43 (SD 2.95) 3-month FU: Mean=7.86 (SD 3.96), F value not reported	

4. What are the most effective interventions in the treatment of mental health disorders in CAYA survivors?				
Poggi et al. **Psychological intervention in young brain tumor survivors: the efficacy of the cognitive behavioural approach. 2009**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Intervention**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: **☐ Cross-sectional study** **☐ Case-control study** **☐ Cohort study** **☐ Qualitative study (→ exclude!)** **☐ Systematic/narrative review (→ exclude!)** **☐ RCT** **☒ Other: (specify!)** **Intervention study** **Treatment era:** **CNS tumor treatment era not specified. CNS survivors in sample received rehabilitation services between 2001-2005.** **Years of follow-up:** **Study period lasted 1 year (baseline & 12 month follow-up assessments). No information on time since diagnosis/treatment completion.** **Country:** **Italy** **Study center:** **IRCCS Eugenio Medea** **Measurement tool:** **Child Behavior Checklist 4-18 (CBCL/4-18), t-score (m=50, SD=10) for three summary scales: total, internalizing and externalizing behavioural problem)** **Vineland Adaptive Behavioural Scales expanded form (VABS)**	**Sample size:** 40 (28 males, 12 females) Control group N=23 CBT clinical group N=17 **Diagnoses:** <u>Brain tumor survivors</u> Medulloblastoma: 10 (25%) Posterior fossa ependymoma 10 (25%) Astrocytoma: 8 (20%) Other tumors: 12 (30%) **Age at diagnosis:** Clinical group: mean 5.53, SD=3.78 Control group: mean 7.59, SD=4.08 **Age at study (first assessment):** Clinical group: M 9.58, SD=3.98 Control group: M 9.28, SD=3.21 **Treatment:** 80% neurosurgery 60% of the 80% received radiotherapy (mean age at radiotherapy start: 8.4years) Chemotherapy: 28 (70%)	Based on Cognitive Behavioral Therapy (CBT), treatment lasted from 4-8 months with 2-3 weekly individual sessions lasting 45-60min. Sessions focused on teaching: cognitive techniques (cognitive mediation and analysis, change in dysfunctional cognitive schemata), behavioral techniques (positive and negative reinforcement, extinction, response cost, token economy, contingency contract, time-out, relaxation training, modelling, shaping, prompting, fading, systematic desensitizing, relaxation training). A weekly session for parents was also planned.	**CBCL** a) First evaluation: Clinical group: Internalising 65%, Total problems 36%, Withdrawn 29% Control group: Internalising 61%, Total problems 29%, Withdrawn 23% b) Follow-up The CBT group showed significant decreases on the following from baseline to follow-up as compared changes observed in control group: withdrawn (p=0.032), somatic complaints (p=0.012), social problems (p=0.015), attention problems (p=0.004), internalizing (p=0.05), total problems (p=0.012). No significant improvements for anxiety/depression, thought problems, delinquent behavior, aggressive behavior, total externalizing problems were observed (p values not provided). **VABS** CBT group scored higher than control group at follow-up evaluation, revealing an improvement in social skills (p=0.037). No significant improvements for daily living skills, communication, or motor skills were observed (p values not provided).	**Quality assessment:** 1. Is the study group representative? ☐Yes/☒no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☐Yes/☒no/ ☐unclear **Remarks:** Risk for selection bias: only those with severe psychosocial problems were included, no random assignment

4. What are the most effective interventions in the treatment of mental health disorders in CAYA survivors?				
Barrera et al. **A group social skills intervention program for survivors of childhood brain tumors. 2009**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Intervention**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: ☐ **Cross-sectional study** ☐ **Case-control study** ☒ **Cohort study** ☐ **Qualitative study (→ exclude!)** ☐ **Systematic/ narrative review (→ exclude!)** ☐ **RCT** ☐ **Other: (specify!)** **Treatment era:** **2000-2006** **Years of follow-up:** **Time off therapy:** ***M*= 5.30 years (SD=4.12)** **Range: 0.42-15 years** **Country:** **Canada** **Study center:** **Neuro-oncology in a large pediatric center, Toronto** **Measurement tool:** **Pre-intervention, baseline, post-intervention, & 6 month follow-up. Mental health measures included the Child Behavior Checklist (CBCL), Youth Self Report (YSR), & Child Depression Inventory (CDI).**	**Sample size:** N=32 n=17 ≤12 children and n=15 >12 adolescents **Diagnoses:** Brain tumor: Medulloblastoma- 9 (28%) Astrocytoma- 6 (19%) Other- 3 (53%) **Age at diagnosis:** Mean=7.31 years **Age at study:** Mean=12.6 years **Treatment:** Surgery- 11 (34%) Radiation- 0 (0%) Chemotherapy- 1 (3%) Surgery & radiation- 2 (6%) Surgery & chemotherapy- 3 (9%) Radiation & chemotherapy- 2 (6%) Surgery, radiation, & chemotherapy- 12 (38%) No treatment- 1 (3%)	6 groups with 4-7 children: 2h group sessions once a week for 8 weeks. Supervised by a psychologist. First 6 sessions: a) Pre-activities: keep participants occupied upon arrival, provide the opportunity for informal verbal interaction b) Review: refresh the learning acquired in the previous session through discussion of homework, and re-involving any participant who might have missed the previous session; c) Mental Set Activity, the first specific activity of each session addresses the theme/social skills of that session and aims to focus participant's attention, interest, motivation and curiosity into thinking about the session's theme and social skill d) Social Skills, each skill is taught by implementing the "Tell" phase, in which the facilitator introduces skills by describing and asking questions, involves group participants, provides rationale for the importance of the skills, and outlines the specific skills steps, followed by the "Show" phase, which involves the facilitators' modeling the behavior positively and negatively by role-playing with active involvement of group participants, followed by role-playing of positive or negative behavior by participants and finally a discussion of the role-play e) Snack, 10min break f) Main Activity, designed to consolidate the social skill learned g) Homework: practice at home and school the social skill learnt in the session Seventh session: review of all previous skills both in the regular structured setting and in an unstructured setting (playground). Final session: practicing skills and preparation for graduation ceremony = describing to parents what was learnt. Skills: social initiation and friendship making; cooperation, managing teasing and bullying, conflict resolution; empathy; and assertion with self-confidence building.	Treatment fidelity: 88% adherence to session outline, 87% adherence to session themes and 83% successful engagement in the activities by participants. Parent report: Analysis of CBCL total change scores using a Bonferroni correction (n=4; p=.0125) revealed a borderline main effect for time [F(2,52)=3.29, p<.05]; however post-hoc pairwise comparisons found no significance between baseline and pre-intervention or pre- and post-intervention with a Bonferroni correction. Survivors: Internalizing: Survivors' reports of internalizing behavior on YSR revealed no significant effects except for a borderline time change [F(2,24)=3.89, p<.05]. The change was significant from baseline to pre-intervention [F(1,13)=11.25, p<.01] with survivors scores decreasing from baseline to pre-intervention. There was no significant effect from pre- to post-intervention. Depression: Survivor's scores on the CDI revealed no significant time differences. Survivors' scores at baseline were not significantly different from normative values and remained consistent across the investigation.	**Quality assessment:** 1. Is the study group representative? ☐Yes/☒no/ ☐unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☒no/ ☐n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☒Yes/☐no/ ☐unclear **Remarks:** Participants referred to social skills group due to observed deficits, social withdrawal, or bullying

4. What are the most effective interventions in the treatment of mental health disorders in CAYA survivors?

Kazak et al. **Treatment of posttraumatic stress symptoms in adolescent survivors of childhood cancer and their families: a randomized clinical trial. 2004**

Study Design / Treatment era / Years of follow-up

Study Design:
- ☐ **Cross-sectional study**
- ☐ **Case-control study**
- ☐ **Cohort study**
- ☐ **Qualitative study (→ exclude!)**
- ☐ **Systematic/narrative review (→ exclude!)**
- ☒ **RCT**
- ☐ **Other: (specify!)**

Treatment era:
unclear

Years of follow-up:
none

Country:
USA

Study center:
Children's Hospital of Philadelphia (CHOP)

Measurement tool:
- **Impact of Events Scale—Revised (IES-R) subscales**
  - **Intrusion**
  - **Avoidance**
  - **Arousal**
- **Post-Traumatic Stress Disorder Reaction Index (PTSD-RI)**
- **Revised Children's Manifest Anxiety Scale (RCMAS)**

Participants

Sample size:
150 cancer survivors, 146 mothers, and 106 fathers

Diagnoses:
Leukemias (25%), solid tumors (22%), lymphoma (21%), bone tumors (8%), and other (24%)

Age at diagnosis:
Median: 7.80 yrs
Range: 2.76–16.36

Age at study:
Median: 14.32 yrs
Range:10.80–19.28

Treatment:
Not reported

Intervention

The Surviving Cancer Competently Intervention Program (SCCIP) is a four-session, 1-day manualized intervention to reduce PTSS in adolescent survivors of childhood cancer and their families that uses a family group treatment model. The 76 families received active treatment and 74 families were part of a wait-list control group.

Session 1 – how cancer has affected me and my family

Session 2 – coping skills

Session 3 – Getting on with life- cancer, adolescents, and families

Session 4 – Pulling it all together – family health and our furure

Main outcomes

Due to meaningfully missing data, mean imputation was used to account for missing data. Five imputations were calculated and the results averaged to form the means and 95% confidence intervals (CIs) reported here; higher scores indicate greater reduction of symptoms. T-tests were performed on the mean of the imputed difference scores derived from transformed data. Survivors in the intervention group improved more on symptoms of arousal than did teen survivors in the control group, t(20) = 3.13, p <0.01.

No others significant changes were observed on IES-R Intrusion or Avoidance subscales, the Post-Traumatic Stress Disorder Reaction Index (PTSD-RI), or the Revised Children's Manifest Anxiety Scale (RCMAS) No group differences were evident for the teens (treatment $M_{difference}$ = 2.38, SD = 9.60, vs. control $M_{difference}$ =1.57, SD=9.10), t(110) = 0.46, p = 0.65

	Survivors-Intervention	**Survivors-Control Group**
	M (95% CI)	M (95% CI)
IES-R Intrusion	3.15 (1.59-4.72)	1.57 (-0.44-3.57)
IES-R Avoidance	3.33 (1.32-5.34)	4.18 (2.42-5.94)
IES-R-Arousal	3.51 (1.86-5.16)	1.35 (-0.30-3.00)
PTSD-RI	6.53 (4.11-8.96)	4.49 (1.97-7.01)
Group comparisons	*t*	*p*
IES-R Intrusion	t(140) = 1.32	0.19
IES-R Avoidance	t(145) = 0.66	0.51
IES-R-Arousal	t(143) = 2.77	0.01
PTSD-RI	t(143) = 1.21	0.23

Quality assessment / Remarks

Quality assessment:
1. Is the study group representative?
☐Yes/☐no/
☒unclear
2. Is the follow-up adequate?
☐Yes/☐no/
☒unclear
3. Are the outcome assessors blinded?
☐Yes/☐no/
☒n.a./☐unclear
4. Are the analyses adjusted for important confounding factors?
☒Yes/☐no/
☐unclear

Remarks:

Q1. Of the 330 contacted confirmed-eligible families, 150 (45%) enrolled in the study. Those declining participation were able to indicate one or more reasons for refusal: 46% (N=70) indicated that they did not want to revisit the cancer experience; 61% (N=94) cited time and scheduling difficulties. No sig differences were found between participants & nonparticipants with regard to the survivor age, time since treatment, gender, ethnicity and diagnosis.

Q2. Overall attrition is 22.67% which meets criteria- but attrition was 38% for intervention group (does not meet criteria) & 7% for waitlist control group.

4a. What are the most effective interventions in the treatment of mental health disorders in CAYA survivors?				
Cheung et al. **Efficacy of musical training on psychological outcomes and quality of life in Chinese pediatric brain tumor survivors. 2018**				
Study Design **Treatment era** **Years of follow-up**	**Participants**	**Intervention**	**Main outcomes**	**Quality assessment** **Remarks**
Study Design: ☐ **Cross-sectional study** ☐ **Case-control study** ☐ **Cohort study** ☐ **Qualitative study (→ exclude!)** ☐ **Systematic/narrative review (→ exclude!)** ☒ **RCT** ☐ **Other: (specify!)** **Treatment era:** **n.a.** **Years of follow-up:** **≥2 months after end of treatment** **IG: 53.4% of survivors were <25 months since treatment** **CG: 46.6% of survivors were <25 months since treatment** **Country:** **China** **Study center:** **Largest outpatient clinic of an acute public hospital in Hong Kong** **Measurement tool:** • **Center for Epidemiological Studies Depression Scale for Children (CES-DC), higher scores indicate a higher risk of depression; score ≥16 is indicative of a**	**Sample size:** N=60 childhood cancer survivors, randomized into Intervention Group (IG)=30 Comparison Group (CG)=30 IG: one discontinued due to relapse, CG: three dropped out, lost interest in study. Attrition rate: 6.7% **Diagnoses:** Brain tumor **Age at diagnosis:** Not reported **Age at study:** Range 7-16 years **IG**: Mean: 12.53 years, SD: 3.18 **CG**: Mean: 13.97 years, SD: 3.26 **Treatment:** **IG:** Surgery: n=10 (33.3%) RT: n=2 (6.7%) Chemotherapy: n=0 (0%) Mixed: n=18 (60%) **CG:** Surgery: n=11 (36.7%) RT: n=1 (3.3%) Chemotherapy: n=0 (0%) Mixed: n=18 (60%)	Only survivors with elevated scores on the CES-DC and on the MMSE were eligible for this study. One-to-one 45-min lesson on musical training conducted by qualified orchestral performers at the participants' homes, for 52 weeks. Participants were assigned a musical instrument to learn, based on their interest and their capabilities. Training started low-level (hitting simple notes) and ended high-level (able to play an entire song) with tests in between, which could be repeated if failed. Control group: Placebo intervention, mimicking the same amount of time and attention required by the experimental group but have no specific or a minimal effect on the dependent variables of the study. Weekly 45-min home visit for 52 weeks by research assistants. Unstructured leisure activities, such as playing card games, chess, or watching videos, movies.	Baseline measure (T1), measure at 6 (T2) and 12 months (T3). Primary measure: Depressive symptoms at 12 months, measured by the CES-DC Secondary outcomes: Self-esteem (Rosenberg Self-Esteem Scale (RSES)) and quality of life (PedsQL-4) at 12 months, TABLE 3 The results of post-hoc comparisons using the Tukey procedure for depressive symptoms, self-esteem and quality of life scores across the three periods (*N* = 60) **Depressive Symptoms, M (*SD*), *P* value** **T1: IG:** 20.60 (7.44)**; CG:** 20.43 (7.23), 0.930 **T2: IG:** 16.27 (6.24) vs CG: 21.10 (7.55), 0.009 **T3: IG:** 15.03 (5.39) vs CG: 21.47 (7.16), 0.000 "Significant between-group differences in depressive symptoms were observed at T2 and T3."	**Quality assessment:** 1. Is the study group representative? ☐Yes/☐no/ ☒unclear 2. Is the follow-up adequate? ☒Yes/☐no/ ☐unclear 3. Are the outcome assessors blinded? ☐Yes/☐no/ ☒n.a./☐unclear 4. Are the analyses adjusted for important confounding factors? ☐Yes/☒no/ ☐unclear **Remarks:**

significant level of depression. • **Modified Mini-Mental Scale (MMSE) ≥18**				