**Table A1: Grade 3-5 chronic health conditions reported by survivors after study entry within each organ system\***

|  |  |
| --- | --- |
| **CTCAE Grade 3-5 Conditions** | **Survivors Affected (n)** |
| **Neurologic**  Paralysis/severe paralysis  Severe/disabling problems with balance/ability to manipulate objects  Severe problems with learning or memory  Neurologic death  Mental retardation/disabling problem with memory/learning  Other neurologic conditions | 83  17  11  11  9  5 |
| **Auditory**  Hearing loss requiring a hearing aid  Deafness in both ears not corrected by a hearing aid | 100  10 |
| **Visual**  Legally blind in one eye  Legally blind in both eyes or loss of an eye  Other visual conditions | 24  9  7 |
| **Stroke**  Stroke/cerebrovascular accident  Stroke/cerebrovascular accident resulting in death | 78  2 |
| **Cardiac**  Cardiovascular condition (not including stroke) resulting in death  Heart attack/angina/coronary heart disease  Other cardiac conditions | 7  6  8 |
| **Subsequent Neoplasm‡**  CNS tumor  CNS tumor resulting in death  Astrocytoma/Glioblastoma not resulting in death  Meningioma not resulting in death  Other CNS tumor not resulting in death  Non-CNS tumors  Sarcoma  Leukemia/lymphoma  Breast cancer  Melanoma or other malignant skin neoplasm  Other non-CNS subsequent neoplasm | 13  10  6  3  8  7  5  5  11 |
| **Endocrine**  Ovarian failure  Diabetes mellitus requiring insulin  Diabetes insipidus  Other endocrine conditions | 30  6  5  8 |

Abbreviations: CTCAE, Common Terminology Criteria for Adverse Events; CNS, central nervous system

\*Definition of CTCAE grading: Grade 3 severe/disabling; Grade 4 life-threatening; Grade 5 death

Conditions affecting less than 5 survivors were labeled as other. Chronic conditions that developed in organ systems not highlighted are not included.

‡CNS tumors not resulting in death were divided by type of tumor. Tumor type was not available for those who died of CNS tumors. For other tumor types, non-lethal and lethal tumors are reported together.

**Table A2: Cumulative incidence of grade 3-5 chronic health conditions at 25 years after cohort entry in survivors of pediatric astrocytoma and siblingsa**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Siblings** | **All Survivors** | **Survivors: XRT** | **Survivors: No XRT** |
| **Organ Systems** | **Cumulative Incidence (%)**  **(95% CI)** | **Cumulative Incidence (%)**  **(95% CI)** | **Cumulative Incidence (%)**  **(95% CI)** | **Cumulative Incidence (%)**  **(95% CI)** |
| **All Organ Systems**  **Neurologic**  **Auditory**  **Visual**  **Stroke**  **Cardiac**  **Subsequent Neoplasm**  **Endocrine** | 8.7 (7.8-9.7)  1.4 (1.0-1.8)  1.3 (0.9-1.7)  1.7 (1.3-2.1)  0.2 (0.1-0.4)  0.6 (0.4-1.0)  0.7 (0.4-1.0)  1.9 (1.5-2.4) | 56.7 (53.3-60.1)  25.8 (23.0-28.6)  16.6 (14.1-19.4)  19.3 (17.0-21.7)  12.8 (10.2-15.6)  7.6 (6.1-9.3)  7.2 (5.2-9.5)  5.9 (4.6-7.4) | 69.4 (64.9-73.3)  33.6 (29.5-37.7)  24.2 (20.3-28.3)  22.1 (118.9-25.4)  18.4 (14.3-23.0)  10.0 (7.8-12.5)  9.8 (7.0-13.3)  7.6 (5.6-9.8) | 32.1 (27.0-37.3)  13.5 (10.2-17.1)  3.3 (1.8-5.6)  13.6 (10.3-17.2)  4.4 (2.5-7.0)  4.1 (2.4-6.6)  2.8 (1.0-6.3)  2.4 (1.1-4.6) |

Abbreviations: CI, confidence interval; XRT, radiation exposure

aDeath from a condition other than a chronic health condition was a competing risk factor

**Table A3: Treatment-related risk factors for development of grade 3-5 chronic conditions in 5-year astrocytoma survivorsa**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Any Chronic Condition  HR (95% CI) | Neurologic  HR (95% CI) | Auditory  HR (95% CI) | Visual  HR (95% CI) |
| Age at diagnosis  0-4 years  5-9 years  10-20 years |  |  |  | **3.7 (1.2-11.2)**  1.9 (0.5-6.8)  Referent |
| Chemotherapy  No  Yes | Referent  **2.5 (1.7-3.6)** | Referent  **2.5 (1.4-4.4)** | Referent  1.6 (1.0-2.6) | Referent  **3.7 (1.6-8.4)** |
| Cranial Radiation Dose  None  0-49 Gy  ≥50 Gy | Referent  **2.3 (1.3-4.1)**  **3.1 (2.1-4.7)** | Referent  1.8 (0.7-4.3)  **1.9 (1.1-3.6)** | Referent  **3.3 (1.2-8.6)**  **7.3 (3.6-14.9)** |  |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Stroke  HR (95% CI) | Cardiac  HR (95% CI) | Subsequent Malignancy  HR (95% CI) | Endocrine  HR (95% CI) |
| Age at diagnosis  0-4 years  5-9 years  10-20 years |  | **0.2 (0.0-0.7)**  **0.1 (0.0-1.0)**  Referent |  |  |
| Chemotherapy  No  Yes | Referent  **2.4 (1.4-4.2)** | Referent  **5.3 (1.7-16.3)** |  | Referent  1.6 (0.7-3.6) |
| Cranial Radiation Dose  None  18-49 Gy  ≥50 Gy | Referent  2.3 (0.8-6.1)  **3.6 (1.8-7.3)** |  | Referent  2.5 (0.8-7.9)  **4.5 (2.0-10.3)** | Referent  1.9 (0.5-6.6)  **2.9 (1.2-6.9)** |

Abbreviations: HR, hazard ratio; CI, confidence interval; Gy, Gray

Bold values reach significance level of p≤0.05

aVariables were only included in multivariate models if univariate analysis reached a significance level of p<0.1. Multivariate models were adjusted for sex and race and accounted for time in cohort in the time scale.

**Table A4: Percentages of adverse health status outcomes in adult 5-year survivors of pediatric astrocytoma and siblings based on age**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Poor General  Health  % | Poor Mental  Health  % | Functional Impairment  % | Activity  Limitation  % | Cancer-related Paina  % | Cancer-related Anxietya  % |
| Survivors  18-24 years  25-29 years  30-34 years  35-39 years  40+ years | 15.5  16.8  16.5  17.6  21.5 | 20.9  21.8  20.0  20.4  21.8 | 35.4  34.3  30.4  35.9  30.8 | 17.4  19.5  20.4  23.9  22.7 | 12.1  14.5  9.8  13.3  16.5 | 11.9  11.7  11.7  12.8  12.4 |
| Survivors: XRT  18-24 years  25-29 years  30-34 years  35-39 years  40+ years | 19.3  22.9  17.9  21.9  29.2 | 21.2  24.9  23.2  22.7  25.9 | 47.5  42.8  40.3  45.3  40.3 | 21.6  23.9  27.1  32.6  28.6 | 15.6  16.7  11.6  14.1  21.3 | 14.0  15.6  14.8  14.9  17.0 |
| Survivors: No XRT  18-24 years  25-29 years  30-34 years  35-39 years  40+ years | 10.3  10.1  11.5  6.7  9.8 | 22.6  19.0  14.7  18.9  18.4 | 19.7  20.3  14.0  18.1  13.9 | 12.3  11.3  9.3  7.7  13.9 | 8.0  10.9  6.2  12.4  9.5 | 11.3  8.0  7.4  9.5  6.3 |
| Siblings  18-24 years  25-29 years  30-34 years  35-39 years  40+ years | 4.5  3.9  5.3  7.0  7.4 | 13.4  10.7  9.9  10.3  10.4 | 2.9  2.8  3.8  4.5  5.4 | 4.3  5.0  5.4  6.1  9.0 | N/A  N/A  N/A  N/A  N/A | N/A  N/A  N/A  N/A  N/A |

Abbreviations: N/A, not applicable; XRT, radiation exposure

aSurvivors only