Supplemental Table 1. List of grade 3-4 chronic conditions included in the CCSS categorization matrix, stratified by organ system. Grade 5 conditions are deaths, so no further definition provided.

Chronic Condition	Grade 3 Definition	Grade 4 Definition
Cardiovascular		
Coronary artery disease	Myocardial infarction, angina, or coronary heart disease not requiring cardiac catheterization but on anti-anginal medication	Myocardial infarction requiring cardiac catheterization, angioplasty, or coronary artery bypass graft
Heart failure	Congestive heart failure, requiring medication	Heart transplant
Arrhythmia	Arrhythmia, requiring pacemaker	Ventricular fibrillation/flutter
Valvular heart disease	Not applicable	Heart valve replacement
Stroke	Occlusion of cerebral arteries	Stroke/cerebrovascular accident
Pericardial disease	Pericardial disease requiring surgical intervention	Not applicable
Other cardiac conditions	Thromboangiitis obliterans (Buerger disease) Hypotension, unspecified Other chronic pulmonary heart disease	Not applicable
Thromboembolic disease	Blood clot in head, lung, arm, leg, or pelvis, not otherwise specified	Pulmonary embolism and infarction Embolism and thrombosis of unspecified artery
Other vascular conditions	Aorta-subclavian-carotid bypass Other (peripheral) vascular shunt or bypass Other repair of aneurysm Repair of arteriovenous fistula	Other excision of vessels, aorta, abdominal (aorta)
Hypertension	Hypertensive chronic kidney disease Hypertensive heart disease	Not applicable
Endocrine		
Thyroid nodules	Thyroid nodules, requiring surgery	Not applicable
Diabetes	Diabetes, requiring insulin	Not applicable
Gonadal dysfunction	Postablative ovarian failure or testicular hypofunction Premature menopause, onset <40 years of age Female infertility Azoospermia	Not applicable
Other hormone conditions	Panhypopituitarism Diabetes insipidus Corticoadrenal hormone insufficiency Glucocorticoid deficiency	Not applicable
Pulmonary		

Chronic Condition	Grade 3 Definition	Grade 4 Definition
Emphysema	Emphysema, requiring medication	Not applicable
Pulmonary fibrosis	Requiring oxygen therapy	Not applicable
Other respiratory conditions	Primary pulmonary hypertension	Chronic respiratory failure Respiratory arrest Respirator dependency status
Musculoskeletal		
Amputation	Total ostectomy, femur Disarticulation of elbow Amputation through humerus, upper arm amputation Disarticulation of shoulder Interthoracoscapular amputation, forequarter amputation Disarticulation of knee Amputation above knee, amputation of leg through femur, amputation of thigh Disarticulation of hip Abdominopelvic amputation, hemipelvectomy, hindquarter amputation Lower leg or ankle reattachment, reattachment of leg not otherwise specified Traumatic amputation of arm and hand, unilateral, at or above elbow Upper limb amputation Lower limb amputation	Not applicable
Joint replacement	Major joint replacement	Not applicable
Neurologic		
Balance	Problems with balance or ability to manipulate objects, severe	Problems with balance or ability to manipulate objects, disabling
Paralysis	Disorders of accessory (11th) nerve	Hemiplegia; quadriplegia
Other neurologic conditions	Intracranial ventricular shunt or anastomosis Ventricular shunt to abdominal cavity or organs Irrigation and exploration of ventricular shunt Replacement of ventricular shunt Multiple sclerosis Difficulty in walking	Coma
Gastrointestinal		
Hepatitis	Cirrhosis	Liver transplant

Chronic Condition	Grade 3 Definition	Grade 4 Definition
Intestinal obstruction	Surgery for intestinal obstruction	Not applicable
Hearing		
Loss of hearing	Hearing loss, requiring a hearing aid Deafness in one ear not completely corrected by hearing aid	Deafness in both ears not completely corrected by hearing aid
Renal		
Renal failure	Not applicable	Dialysis or kidney transplant
Urinary incontinence	Neurogenic bladder	Not applicable
Other renal conditions	Nephrotic syndrome with unspecified pathologic lesion in kidney	Rupture of bladder, nontraumatic
Vision and eye		
Cataracts	Cataracts, requiring surgery	Not applicable
Blindness	Legally blind in only one eye	Legally blind in both eyes or loss of an eye
Secondary neoplasms		
	Thyroid carcinoma Benign meningiomas requiring resection Lobular cancer in situ of the breast	Invasive malignancies Ductal carcinoma in situ of the breast

Supplemental Methods: Grading the Severity of Chronic Health Conditions

In 2000, Oeffinger et al introduced the concept of using the Common Toxicity Criteria (CTCv2) to grade late effects of cancer therapy.[1] At that time, there was not a commonly used tool that was widely accepted for grading the severity of chronic health conditions following cancer therapy, or what are commonly referred to as late effects. Instead, most studies simply reported prevalence or incidence rates of a specific condition, without regard to the level of seriousness of the condition. The CTC was originally created by leaders in the Cancer Therapy Evaluation Program (CTEP) at the National Cancer Institute (NCI) as a tool to measure acute toxicity of cancer therapy.

In 1998, when the NCI released CTCv2, the Radiation Therapy Oncology Group (RTOG) / European Organization for Research and Treatment of Cancer (EORTC) Late Radiation Morbidity Scoring Scheme was incorporated into the instrument.[2] As noted in the CTCv2 manual, adverse events (toxicity) could be graded by level of severity:

Grade 0 = no adverse event or within normal limits
Grade 1 = mild adverse event
Grade 2 = moderate adverse event
Grade 3 = severe and undesirable adverse event
Grade 4 = life-threatening or disabling adverse event
Grade 5 = death related to adverse event

An important distinction was made between grade 1-2 conditions and grade 3-4 conditions, with the latter requiring a major intervention or substantially altering the activities of daily living (ADL). This tool was then incorporated into all new NCI-sponsored protocols and its use became ubiquitous among the oncology community.

As noted by Oeffinger et al,[1] "although CTCv2 was not developed specifically for use in grading late effects, the majority of late effects can be scored easily for the various organ systems or the appendixed Late Radiation Morbidity Scoring Scheme." Many late outcomes following cancer therapy were listed in CTCv2, including left ventricular dysfunction and hypothyroidism. Other conditions could be adapted to this scoring system, such as chronic hepatitis C. This work was presented at the 1999 Annual Cancer Survivorship: Research Challenges and Opportunities for the New Millennium Conference sponsored by the NCI.

Subsequently, the NCI created a multi-disciplinary group to help develop version 3, with a name change to the Common Terminology Criteria for Adverse Events (CTCAEv3). An overarching goal of CTCAEv3 was to provide a tool that provided a framework to grade acute and long-term toxicity for cancer patients / survivors, regardless of age at cancer diagnosis. Using this new rubric, Oeffinger et al graded the severity of 137 chronic health conditions among 10,397 childhood cancer survivors and 3034 siblings participating in the Childhood Cancer Survivor Study (CCSS). Many of the chronic conditions were self-reported. The exceptions were second or subsequent neoplasms, which were confirmed by pathology report or medical records, or fatal conditions, that were determined by linkage to the National Death Index. Thus, as described by the authors, to avoid overestimating the severity of outcomes, an algorithm was used that incorporated self-reported medications (e.g., antihypertensives, estrogen replacement, etc), surgical interventions (e.g., angioplasty, kidney transplant, etc.), or life-sustaining interventions

(e.g., home oxygen therapy). The majority of conditions were captured from specific questions, such as "Have you ever been told by a doctor or other health care professional that you have, or have had … a myocardial infarction (heart attack)" with response options including 'no', 'yes', 'non sure', and 'if yes, age at first occurrence'. In each of the organ systems, participants were also asked if they had 'any other problems' and a text box was provided. A trained nosologist assigned an ICD9 code for each condition. Then, a team of 9 clinicians / researchers adjudicated the inclusion/exclusion of each condition and the severity assigned for chronic health conditions. If there was not enough information to distinguish between grades, the lower score was selected. For instance, due to the lack of information, the severity of cognitive dysfunction was not well captured and so were usually graded = 1 (mild); the results substantially underestimated the severity of this important outcome among survivors of CNS tumors. This was intentional, as a goal of the authors, as stated above, was to avoid overestimating the burden of morbidity among this population. The full grading schema was provided in Appendix E of the *New England Journal of Medicine* publication.[3]

The following year, investigators from the Netherlands reported the late outcomes among 1362 long-term survivors treated at Emma Children's Hospital over a 30-year period.[4] With respect to grading the severity of late outcomes, Geenen et al also used CTCAEv3 and independently arrived at a scoring schema that was essentially the same as that of the CCSS investigators. Also of note, while 94.3% of the Dutch cohort had a medical evaluation, their findings largely mirrored those of the CCSS that depended upon self-reported outcomes.[5]

In 2009, NCI released CTCAEv4 with a subsequent minor update CTCAEv4.03.[6] The number of adverse events and the level of detail to score the events was expanded in these new versions. As highlighted in the manual, the grades for events followed these general guidelines:

Grade 1 = Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.
Grade 2 = Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL.
Grade 3 = Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL.
Grade 4 = Life-threatening consequences; urgent intervention indicated.
Grade 5 = Death related to adverse event.

Software to convert from CTCAEv3 to CTCAEv4 (and CTCAEv4.03) was provided by the NCI. Investigators from the CCSS used this software and updated their scoring matrix. This updated matrix was then used to grade the severity of outcomes among 14,359 long-term survivors in the CCSS and to report on the aging of the cohort.

In 2017, Hudson et al expanded on this effort of using CTCAEv4.03 and modified the scoring schema for long-term survivors seen for a medical evaluation.[7] Figure 2 in this paper provided the details for scoring of all conditions observed in the St. Jude Lifetime Cohort Study. Also in 2017, Oeffinger assisted investigators from the British CCSS in grading the severity of adverse outcomes of 14,836 long-term survivors of childhood cancer.[8] Then, a risk stratification tool, based upon treatment exposures, was applied to a subgroup of 2844 survivors of acute
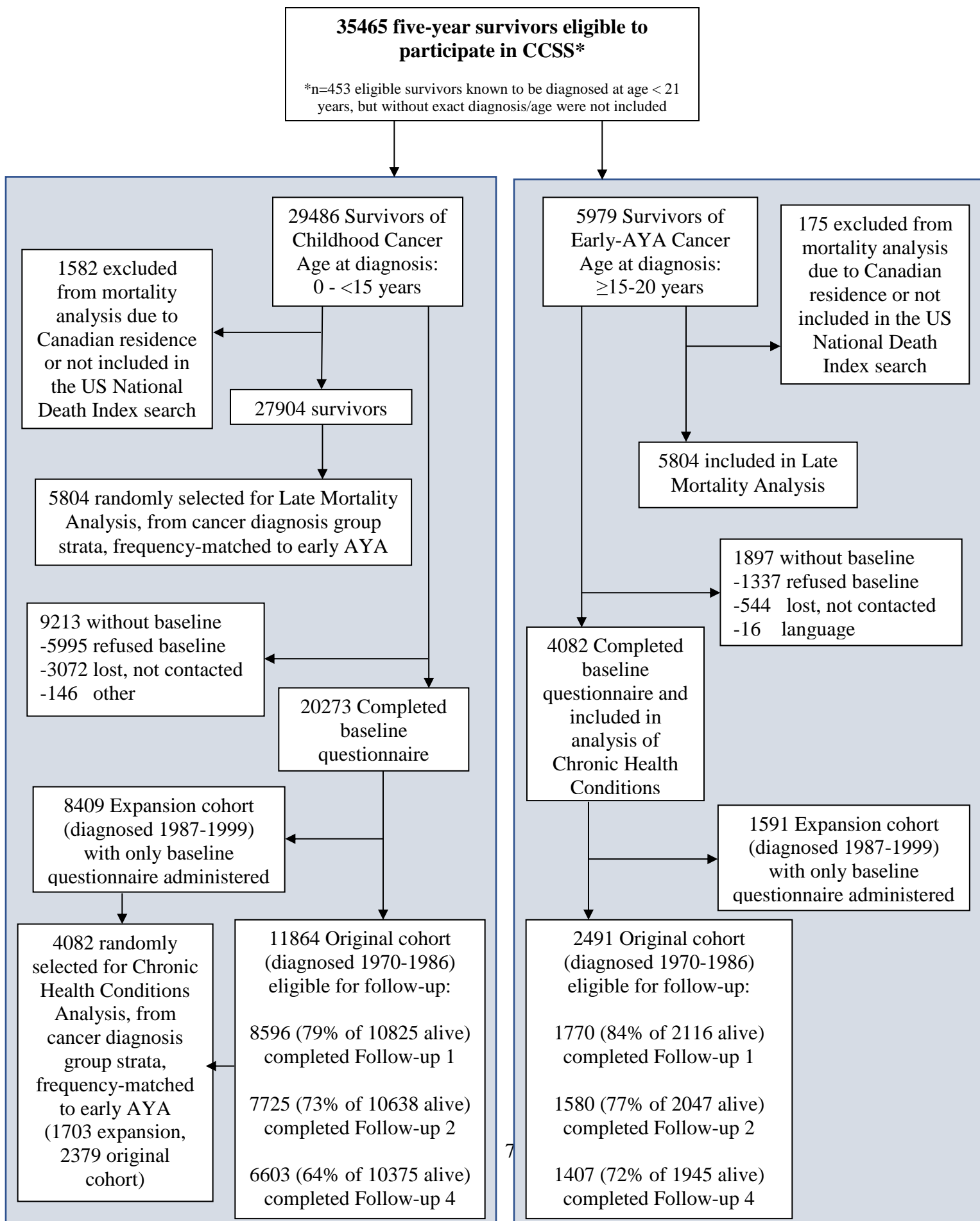
lymphoblastic leukemia and was determined to have strong discriminatory characteristics in predicting long-term outcomes.

With each new CCSS survey conducted among the cohort, the CCSS Chronic Condition Matrix has been updated. Prior to the current study by Gibson et al, a 9-person multi-disciplinary team led by Oeffinger reviewed and adjudicated all conditions graded and scored for the 23,601 long-term survivors diagnosed over a three-decade period and 5,051 siblings. The focus on this paper is on grade 3-5 conditions; the scoring matrix for these conditions is provided in Supplemental Table 1.

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Supplemental Figure 1. Consort diagram of 5-year survivors of adolescent and early young adult cancer and matched cohort of survivors diagnosed in childhood in the Childhood Cancer Survivors Study.

35465 five-year survivors eligible to participate in CCSS*

*n=453 eligible survivors known to be diagnosed at age < 21 years, but without exact diagnosis/age were not included

29486 Survivors of Childhood Cancer
Age at diagnosis:
0 - <15 years

5979 Survivors of Early-AYA Cancer
Age at diagnosis:
≥15-20 years

175 excluded from mortality analysis due to Canadian residence or not included in the US National Death Index search

1582 excluded from mortality analysis due to Canadian residence or not included in the US National Death Index search

27904 survivors

5804 included in Late Mortality Analysis

5804 randomly selected for Late Mortality Analysis, from cancer diagnosis group strata, frequency-matched to early AYA

1897 without baseline
-1337 refused baseline
-544 lost, not contacted
-16 language

9213 without baseline
-5995 refused baseline
-3072 lost, not contacted
-146 other

4082 Completed baseline questionnaire and included in analysis of Chronic Health Conditions

20273 Completed baseline questionnaire

8409 Expansion cohort (diagnosed 1987-1999) with only baseline questionnaire administered

1591 Expansion cohort (diagnosed 1987-1999) with only baseline questionnaire administered

4082 randomly selected for Chronic Health Conditions Analysis, from cancer diagnosis group strata, frequency-matched to early AYA (1703 expansion, 2379 original cohort)

11864 Original cohort (diagnosed 1970-1986) eligible for follow-up:

8596 (79% of 10825 alive) completed Follow-up 1

7725 (73% of 10638 alive) completed Follow-up 2

6603 (64% of 10375 alive) completed Follow-up 4

2491 Original cohort (diagnosed 1970-1986) eligible for follow-up:

1770 (84% of 2116 alive) completed Follow-up 1

1580 (77% of 2047 alive) completed Follow-up 2

1407 (72% of 1945 alive) completed Follow-up 4

7

Supplemental Figure 2. Distribution of the number of early-AYA and childhood cancer survivors by A) maximum attained ages and B) years since diagnosis.

Supplemental Table 2. Standardized mortality ratios and frequency of death among survivors of early-AYA and matched childhood cancer.

Cause of death	Group	Level	early-AYA				Childhood				
			# deaths	# expected	Rate / 1000 PY	SMR (95% CI)	# deaths	# expected	Rate/ 1000 PY	SMR (95% CI)	p-value
All causes	Among all patients		1357	231·9	11·5	5·9(5·5-6·2)	963	155·7	7·5	6·2(5·8-6·6)	0·22
	Sex	Male	791	163·0	12·2	4·9(4·5-5·2)	563	115·3	7·6	4·9(4·5-5·3)	0·91
		Female	566	68·9	10·7	8·2(7.5-9.0)	400	40·5	7·5	9·9(8·9-11·0)	0·0084
	Survival after diagnosis, y	05-9	462	33·7	16·5	13·7(12.5-15.0)	269	20·2	8·9	13·3(11·6-15·2)	0·70
		10-19	383	68·6	7·9	5·6(5.1-6.2)	311	54·3	5·8	5·7(5·1-6·4)	0·75
		20-29	292	74·1	9·7	3·9(3.5-4.4)	206	47·0	6·5	4·4(3·8-5·0)	0·26
		30+	219	55·5	19·6	3·9(3.5-4.5)	177	34·2	14·4	5·2(4·5-6·0)	0·0072
	Current age, y	05-19	NA	NA	NA		266	20·6	7·3	12·9(11·3-14·8)	NA
		20-29	569	51·1	13·6	11·1(10.2-12.1)	296	56·2	6·0	5·3(4·7-5·9)	<0·0001
		30-39	336	69·4	7·7	4·8(4.3-5.4)	205	44·0	7·0	4·7(4·1-5·3)	0·66
		40+	452	111·4	14·0	4·1(3.7-4.5)	196	34·9	15·8	5·6(4·9-6·5)	<0·001
	5-9 y after diagnosis, current age 5-19		NA	NA	NA	NA	202	11·8	9·0	17·1(14·6-20·0)	NA
	10-19 y after diagnosis, current age 5-19		NA	NA	NA	NA	64	8·8	4·6	7·3(5·6-9·5)	NA
	5-9 y after diagnosis, current age 20-39		462	33·7	16·5	13·7(12·5-15·0)	66	8·4	8·5	7·9(6·2-10·1)	<0·0001
	10-19 y after diagnosis, current age 20-39		382	68·2	7·9	5·6(5·1-6·2)	248	45·5	6·3	5·4(4·8-6·2)	0·72
	20+ y after diagnosis, current age 20-39		60	18·6	6·6	3·2(2·5-4·2)	187	46·3	5·9	4·0(3·5-4·7)	0·14
	10-19 y after diagnosis, current age 40+		1	0·4	5·1	2·5(0·3-17·3)	0	NA	NA	NA	NA
	20+ y after diagnosis, current age 40+		451	111·0	14·1	4·1(3·7-4·5)	196	34·9	15·8	5·6(4·9-6·5)	0·00017
Subsequent malignant neoplasm	Among all patients		323	41·5	2·7	7·8(7.0-8.7)	221	18·6	1·7	11·9(10·4-13·6)	<0·0001

9

Cause of death	Group	Level	# deaths	# expected	Rate / 1000 PY	SMR (95% CI)	# deaths	# expected	Rate/ 1000 PY	SMR (95% CI)	p-value
						early-AYA				**Childhood**	
	Sex	Male	153	22·4	2·4	6·8(5.8-8.0)	116	10·3	1·6	11·3(9·4-13·5)	<0·0001
		Female	170	19·1	3·2	8·9(7.7-10.4)	105	8·3	2·0	12·6(10·4-15·4)	0·0056
	Survival after diagnosis, y	05-9	45	2·4	1·6	18·6(13.9-24.9)	41	1·3	1·4	31·8(23·4-43·2)	0·013
		10-19	74	7·9	1·5	9·4(7.5-11.8)	73	3·8	1·4	19·2(15·2-24·2)	<0·0001
		20-29	113	15·2	3·8	7·4(6.2-8.9)	44	6·0	1·4	7·4(5·5-9·9)	0·95
		30+	91	16·0	8·2	5.7(4·6-7·0)	63	7·5	5·1	8·4(6·5-10·7)	0·019
	Current age, y	05-19	NA	NA	NA	NA	39	1·4	1·1	29·1(21·2-39·9)	NA
		20-29	62	4·0	1·5	15·7(12·2-20·1)	61	3·8	1·2	16·0(12·5-20·6)	0·90
		30-39	77	9·4	1·8	8·2(6·5-10·2)	56	5·6	1·9	9·9(7·6-12·9)	0·29
		40+	184	28·1	5·7	6·5(5·7-7·6)	65	7·8	5·2	8·3(6·5-10·6)	0·097
	5-9 y after diagnosis, current age 5-19		NA	NA	NA	NA	27	0·8	1·2	32·0(22·0-46·7)	NA
	10-19 y after diagnosis, current age 5-19		NA	NA	NA	NA	12	0·5	0·9	24·2(13·7-42·6)	NA
	5-9 y after diagnosis, current age 20-39		45	2·4	1·6	18·6(13·9-24·9)	14	0·4	1·8	31·4(18·6-53·0)	0·086
	10-19 y after diagnosis, current age 20-39		74	7·8	1·5	9·5(7·5-11·9)	61	3·3	1·5	18·5(14·3-23·8)	0·00012
	20+ y after diagnosis, current age 20-39		20	3·1	2·2	6·4(4·1-9·9)	42	5·7	1·3	7·4(5·4-10·0)	0·60
	20+ y after diagnosis, current age 40+		184	28·1	5·7	6·6(5·7-7·6)	65	7·8	5·2	8·3(6·5-10·6)	0·10
Cardiac causes	Among all patients		141	32·3	1·2	4·4(3·7-5·2)	101	14·8	0·8	6·8(5·6-8·3)	<0·001
	Sex	Male	91	24·0	1·4	3·8(3·1-4·7)	60	11·0	0·8	5·5(4·2-7·0)	0·030
		Female	50	8·3	0·9	6·0(4·6-7·9)	41	3·8	0·8	10·7(7·9-14·5)	0·0060
	Survival after diagnosis, y	05-9	12	1·6	0·4	7·6(4·3-13·4)	7	0·6	0·2	12·0(5·7-25·1)	0·34
		10-19	49	6·4	1·0	7·7(5·8-10·2)	18	2·7	0·3	6·7(4·2-10·6)	0·62

Cause of death	Group	Level	early-AYA				Childhood				
			# deaths	# expected	Rate / 1000 PY	SMR (95% CI)	# deaths	# expected	Rate/ 1000 PY	SMR (95% CI)	p-value
		20-29	41	12·7	1·4	3·2(2·4-4·4)	32	5·3	1·0	6·0(4·2-8·5)	0·0085
		30+	39	11·6	3·5	3·4(2·5-4·6)	44	6·2	3·6	7·1(5·3-9·5)	<0·001
	Current age, y	05-19	NA	NA	NA		11	0·6	0·3	19·6(10·9-35·4)	NA
		20-29	24	2·8	0·6	8·7(5·8-13·0)	11	2·8	0·2	3·9(2·2-7·0)	0·027
		30-39	42	7·9	1·0	5·3(3·9-7·2)	31	5·1	1·1	6·1(4·3-8·7)	0·55
		40+	75	21·6	2·3	3·5(2·8-4·3)	48	6·4	3·9	7·5(5·7-10·0)	<0·0001
	5-9 years post dx, age 5-19		NA	NA	NA	NA	7	0·3	0·3	21·7(10·4-45·6)	NA
	10-19 years post dx, age 5-19		NA	NA	NA	NA	4	0·2	0·3	16·7(6·3-44·5)	NA
	5-9 years post dx, age 20-39		12	1·6	0·4	7·6(4·3-13·4)	0	0·3	0·0	NA	NA
	10-19 years post dx, age 20-39		49	6·3	1·0	7·8(5·9-10·3)	14	2·4	0·4	5·7(3·4-9·7)	0·32
	20+ years post dx, age 20-39		5	2·8	0·5	1·8(0·7-4·3)	28	5·2	0·9	5·4(3·7-7·8)	0·024
	20+ years post dx, age 40+		75	21·6	2·3	3·5(2·8-4·4)	48	6·4	3·9	7·5(5·7-10·0)	<0·0001
Pulmonary causes	Among all patients		58	7·9	0·5	7·4(5·7-9·5)	42	4·1	0·3	10·3(7·6-14·0)	0·095
	Sex	Male	36	4·7	0·6	7·8(5·6-10·8)	23	2·5	0·3	9·4(6·2-14·1)	0·48
		Female	22	3·3	0·4	6·8(4·5-10·3)	19	1·6	0·4	11·8(7·5-18·6)	0·078
	Survival after diagnosis, y	05-9	10	0·7	0·4	15·6(8·4-29·1)	6	0·4	0·2	15·2(6·8-33·9)	0·96
		10-19	18	1·7	0·4	10·5(6·6-16·7)	12	1·1	0·2	11·2(6·3-19·7)	0·88
		20-29	11	2·6	0·4	4·3(2·4-7·7)	13	1·2	0·4	10·6(6·2-18·3)	0·026
		30+	19	3·0	1·7	6·4(4·1-10·0)	11	1·4	0·9	8·0(4·4-14·5)	0·55
	Current age, y	05-19	NA	NA	NA	NA	10	0·4	0·3	24·0(12·9-44·6)	NA
		20-29	17	1·1	0·4	16·4(10·2-26·3)	9	1·1	0·2	8·3(4·3-15·9)	0·099
		30-39	13	1·9	0·3	7·1(4·1-12·2)	7	1·2	0·2	6·0(2·9-12·7)	0·74
		40+	28	5·0	0·9	5·6(3·9-8·1)	16	1·4	1·3	11·4(7·0-18·7)	0·023
Other medical causes$	Among all patients		188	67·2	1·6	2·8(2·4-3·2)	141	36·9	1·1	3·8(3·2-4·6)	0·0073
	Sex	Male	101	45·6	1·6	2·2(1·8-2·7)	81	24·9	1·1	3·3(2·6-4·2)	0·014

Cause of death	Group	Level	early-AYA				Childhood				p-value
			# deaths	# expected	Rate / 1000 PY	SMR (95% CI)	# deaths	# expected	Rate/ 1000 PY	SMR (95% CI)	
		Female	87	21·5	1·7	4·1(3·3-5·0)	60	12·0	1·1	5·0(3·9-6·4)	0·22
	Survival after diagnosis, y	05-9	26	6·7	0·9	3·9(2·6-5·7)	14	2·8	0·5	5·0(3·0-8·5)	0·44
		10-19	63	20·1	1·3	3·1(2·5-4·0)	34	10·8	0·6	3·1(2·1-4·6)	0·96
		20-29	56	23·5	1·9	2·4(1·8-3·1)	57	13·0	1·8	4·4(3·3-5·8)	0·0021
		30+	43	16·8	3·9	2·6(1·9-3·5)	37	10·3	3·0	3·6(2·6-5·0)	0·13
	Current age, y	05-19	NA	NA	NA	NA	15	2·8	0·4	5·4(3·3-9·0)	NA
		20-29	36	11·5	0·9	3·2(2·3-4·4)	39	11·0	0·8	3·6(2·4-5·2)	0·64
		30-39	65	21·4	1·5	3·0(2·4-3·9)	46	12·5	1·6	3·7(2·8-4·9)	0·33
		40+	87	34·3	2·7	2·5(2·1-3·1)	41	10·6	3·3	3·9(2·8-5·2)	0·027
Nonrecurrent, Health-related cause	Among all patients		711	149·0	6·0	4·8(4·4-5·1)	506	74·4	4·0	6·8(6·2-7·4)	<0·0001
	Sex	Male	381	96·8	5·9	3·9(3·6-4·4)	280	48·6	3·8	5·8(5·1-6·5)	<0·0001
		Female	330	52·2	6·3	6·3(5·7-7·1)	225	25·8	4·2	8·7(7·7-10·0)	<0·001
	Survival after diagnosis, y	05-9	94	11·4	3·4	8·2(6·7-10·1)	68	5·1	2·3	13·5(10·6-17·1)	0·0019
		10-19	204	36·1	4·2	5·7(4·9-6·5)	137	18·4	2·6	7·4(6·2-8·8)	0·016
		20-29	221	54·1	7·4	4·1(3·6-4·7)	146	25·6	4·6	5·7(4·8-6·7)	0·0023
		30+	192	47·4	17·2	4·1(3·5-4·7)	155	25·4	12·6	6·1(5·2-7·1)	<0·001
	Current age, y	05-19	NA	NA	NA	NA	75	5·1	2·1	14·8(11·8-18·6)	NA
		20-29	140	19·3	3·3	7·3(6·1-8·6)	120	18·7	2·4	6·4(5·3-7·8)	0·35
		30-39	197	40·6	4·5	4·9(4·2-5·6)	140	24·4	4·8	5·7(4·8-6·8)	0·14
		40+	374	89·1	11·6	4·2(3·8-4·6)	170	26·2	13·7	6·5(5·6-7·5)	<0·0001
	5-9 y after diagnosis, current age 5-19		NA	NA	NA	NA	49	3·1	2·2	15·9(12·0-21·1)	NA
	10-19 y after diagnosis, current age 5-19		NA	NA	NA	NA	26	2·0	1·9	13·1(8·9-19·2)	NA

| Cause of death | Group | Level | early-AYA | | | | Childhood | | | | |
			# deaths	# expected	Rate / 1000 PY	SMR (95% CI)	# deaths	# expected	Rate/ 1000 PY	SMR (95% CI)	p-value
	5-9 y after diagnosis, current age 20-39		94	11·4	3·4	8·2(6·7-10·1)	19	2·0	2·4	9·6(6·1-15·1)	0·53
	10-19 y after diagnosis, current age 20-39		203	35·8	4·2	5·7(4·9-6·5)	110	16·4	2·8	6·7(5·5-8·2)	0·16
	20+ y after diagnosis, current age 20-39		40	12·6	4·4	3·2(2·3-4·3)	131	24·8	4·1	5·3(4·4-6·3)	0·0054
	10-19 y after diagnosis, current age 40+		1	0·3	5·1	3·5(0·5-24·9)	NA	NA	NA	NA	NA
	20+ y after diagnosis, current age 40+		373	88·8	11·6	4·2(3·8-4·7)	170	26·2	13·7	6·5(5·6-7·5)	<0·0001
External causes	Among all patients		91	82·9	0·8	1·1(0·9-1·3)	95	81·3	0·7	1·2(0·9-1·5)	0·65
	Sex	Male	75	66·3	1·1	1·1(0·9-1·4)	67	66·6	0·9	1·0(0·8-1·3)	0·50
		Female	16	16·7	0·3	1·0(0·6-1·6)	29	14·7	0·5	1·9(1·3-3·0)	0·032
	Survival after diagnosis, y	05-9	24	22·3	0·9	1·1(0·7-1·6)	13	15·2	0·4	0·9(0·5-1·5)	0·49
		10-19	28	32·5	0·6	0·9(0·6-1·3)	49	35·9	0·9	1·4(1·0-1·9)	0·076
		20-29	24	20·1	0·8	1·2(0·8-1·8)	22	21·5	0·7	1·0(0·7-1·6)	0·60
		30+	14	8·1	1·3	1·7(1·0-2·9)	11	8·8	0·9	1·3(0·7-2·3)	0·43
	Current age, y	05-19	NA	NA	NA	NA	16	15·5	0·4	1·0(0·5-1·9)	NA
		20-29	31	31·8	0·7	1·0(0·7-1·4)	45	37·5	0·9	1·2(0·9-1·6)	0·44
		30-39	29	28·8	0·7	1·0(0·7-1·5)	24	19·6	0·8	1·2(0·8-1·8)	0·50
		40+	30	22·3	0·9	1·3(0·9-1·9)	11	8·7	0·9	1·3(0·7-2·3)	0·86
Recurrence/progression of primary cancer	Among all patients		492	NA	NA		325	NA	NA		NA
	Sex	Female	193	NA	NA		132	NA	NA		NA
		Male	298	NA	NA		193	NA	NA		NA
	Survival after diagnosis, y	05-9	313	NA	NA		175	NA	NA		NA
		10-19	130	NA	NA		110	NA	NA		NA

13

| Cause of death	Group	Level	early-AYA				Childhood				
			# deaths	# expected	Rate / 1000 PY	SMR (95% CI)	# deaths	# expected	Rate/ 1000 PY	SMR (95% CI)	p-value
		20-29	37	NA	NA		29	NA	NA		NA
		30+	11	NA	NA		10	NA	NA		NA
	Current age, y	05-19	NA	NA	NA		162	NA	NA		NA
		20-29	360	NA	NA		118	NA	NA		NA
		30-39	91	NA	NA		32	NA	NA		NA
		40+	40	NA	NA		13	NA	NA		NA
Unknown	Among all patients		63	NA	NA		37	NA	NA		NA
	Sex	Female	27	NA	NA		14	NA	NA		NA
		Male	36	NA	NA		23	NA	NA		NA
	Survival after diagnosis, y	05-9	31	NA	NA		12	NA	NA		NA
		10-19	20	NA	NA		15	NA	NA		NA
		20-29	10	NA	NA		9	NA	NA		NA
		30+	2	NA	NA		1	NA	NA		NA
	Current age, y	05-19	NA	NA	NA		13	NA	NA		NA
		20-29	37	NA	NA		13	NA	NA		NA
		30-39	18	NA	NA		9	NA	NA		NA
		40+	8	NA	NA		2	NA	NA		NA
	Primary diagnosis	Bone cancer	8	NA	NA		4	NA	NA		NA
		CNS	9	NA	NA		4	NA	NA		NA
		HL	23	NA	NA		20	NA	NA		NA
		Leukemia	13	NA	NA		6	NA	NA		NA
		NHL	4	NA	NA		1	NA	NA		NA
		Soft tissue sarcoma	6	NA	NA		2	NA	NA		NA

Abbreviations: y, year; PY, person-year; SMR, standardized mortality ratio; CI, confidence interval; CNS, central nervous system; HL, Hodgkin lymphoma; NHL, non-Hodgkin lymphoma; NA, not applicable.
*Kidney and Neuroblastoma not included due to low # of early-AYA survivors with these diagnoses.
and % include weighting, e.g. 1357 deaths after weighting.
$ Other medical causes: Nonrecurrent, health-related causes of death other than subsequent malignant neoplasms, cardiac causes, or pulmonary causes.

Supplemental Figure 3. Standardized mortality ratios for nonrecurrent, health-related cause of death in survivors of early-AYA and
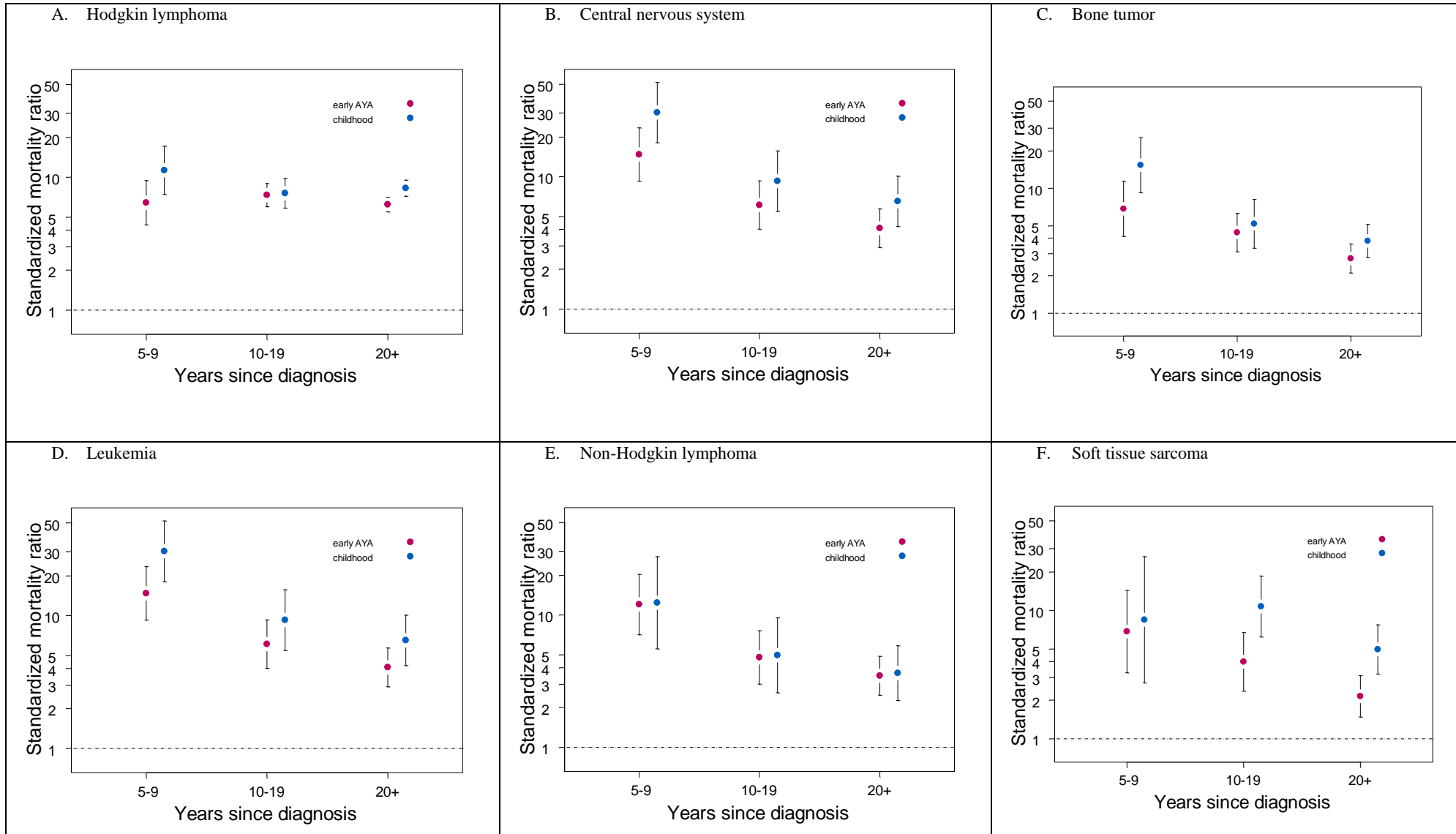
matched childhood cancer survivors as a function of time since diagnosis and by original cancer diagnosis.

Abbreviation: p, p-value comparing SMR for early-AYA and childhood cancer survivors for each time group.

Supplemental Table 3. Risk of death due to recurrence/progression of primary cancer among survivors of early-AYA cancer compared to childhood cancer survivors, by cancer diagnosis.

Diagnosis	HR (95 % CI)	p-value	# deaths-early-AYA survivors	# deaths-childhood cancer survivors
All diagnoses	1·6 (1·4-1·9)	<0·0001	492	325
Leukemia	1·9 (1·4-2·6)	0·0001	86	64
CNS	1·5 (1·0-2·1)	0·0356	72	51
Hodgkin lymphoma	2·5 (1·9-3·4)	<0·0001	152	67
NHL	1·6 (0·6-4·1)	0·3532	11	7
Soft tissue sarcoma	1·3 (0·8-2·0)	0·2255	46	35
Bone cancer	1·1 (0·8-1·4)	0·7032	109	100

-Each row represents a separate Cox model with time since diagnosis as scale, adjusted for sex, and censored at 31DEC2013.

- Abbreviations: HR, hazard ratio; CI, confidence interval; CNS, central nervous system; NHL, non-Hodgkin lymphoma.

Supplemental Table 4. Multivariate hazard ratios and 95% CI for development of organ system grade 3-5 conditions within the early-AYA survivor population following specific therapeutic exposures for the primary cancer.

Organ system	Treatment	HR (95 % CI)	p-value
SMN	Any radiation vs. none	2·2 (1·6-2·9)	<0·0001
	Anti-metabolites[1] vs. none	0·8 (0·6-1·1)	0·1847
	Platinum drugs vs. none	2·1 (1·3-3·3)	0·0019
	Plant alkaloid[2] vs. none	0·8 (0·6-1·1)	0·1453
	CED: 1 - <4000 mg/m2 vs. none	0·9 (0·5-1·5)	0·6819
	CED: 4000 - <8000 mg/m2 vs. none	1·2 (0·8-1·8)	0·4014
	CED: >/= 8000+ mg/m2 vs. none	1·6 (1·1-2·3)	0·0091
	Anthracycline: 1 - 299 mg/m2 vs. none	1·1 (0·8-1·6)	0·4012
	Anthracycline: >/= 300 mg/m2 vs. none	1·0 (0·7-1·4)	0·8294
	Female vs. male	2·4 (1·9-3·0)	<0·0001
	Hispanic or non-white race vs. white non-Hispanic	1·1 (0·8-1·5)	0·5367
Cardiac	Chest RT: 0·1 – 14·9 Gy vs. none	0·9 (0·6-1·3)	0·4793
	Chest RT: 15 – 34·9 Gy vs. none	1·8 (1·2-2·8)	0·0046
	Chest RT: >/= 35 Gy vs. none	3·3 (2·4-4·6)	<0·0001
	Bleomycin vs. none	1·3 (0·9-1·8)	0·1910
	Platinum drugs vs. none	1·4 (0·9-2·2)	0·1917
	Plant alkaloid[2] vs. none	0·8 (0·6-1·2)	0·3573
	CED: 1 - <4000 mg/m2 vs. none	1·4 (0·9-2·3)	0·1607
	CED: 4000 - <8000 mg/m2 vs. none	1·2 (0·8-1·7)	0·4610
	CED: >/=8000 mg/m2 vs. none	1·4 (1·0-2·0)	0·0896
	Anthracycline: 1 - 299 mg/m2 vs. none	1·0 (0·7-1·5)	0·9421
	Anthracycline: >/= 300 mg/m2 vs. none	1·2 (0·8-1·7)	0·3878
	Female vs. male	0·6 (0·5-0·7)	<0·0001
	Hispanic or non-white race vs. white non-Hispanic	1·1 (0·8-1·5)	0·4727
	Ever smoked vs. never	1·0 (0·8-1·2)	0·6454
Endocrine	Total body RT vs. no RT	3·3(1·4-7·8)	<0·0067
	Chest/neck RT vs. no RT	3·9(2·6-5·7)	<0·0001
	Abdominal RT vs. no RT	1·2(0·4-3·5)	0·7073
	Central Nervous System RT vs. no RT	1·6(0·8-3·0)	0·1918
	Other RT vs. no RT	1·9(1·0-3·8)	0·0629

Organ system	Treatment	HR (95 % CI)	p-value
	CED: 1-<4000 mg/m2 vs. none	1·3(0·8-2·0)	0·3521
	CED: 4000-<8000 mg/m2 vs. none	1·0(0·7-1·6)	0·8801
	CED: >/= 8000 mg/m2 vs. none	1·0(0·7-1·4)	0·9912
	Female vs. male	3·2(2·4-4·3)	<0·0001
	Hispanic or non-white race vs. white non-hispanic	1·3(0·8-1·9)	0·2609
Pulmonary	Chest RT: 0·1 – 14·9 Gy vs. none	1·1 (0·4-2·8)	0·8434
	Chest RT: 15 – 34·9 Gy vs. none	1·6 (0·4- 5·7)	0·4790
	Chest RT: >/= 35 Gy vs. none	3·1 (1·6- 6·2)	0·0013
	Carmustine (BCNU) vs. none	1·5 (0·4-5·2)	0·5179
	Bleomycin vs. none	1·2 (0·5-2·7)	0·7023
	Cyclophosphamide vs. none	1·5 (0·8-2·8)	0·1643
	Female vs. male	1·2 (0·7-2·0)	0·6064
	Hispanic or non-white race vs. white non-Hispanic	0·7 (0·3-2·1)	0·5599
	Ever smoked vs. never	0·6 (0·3-1·2)	0·1458

Abbreviations: HR, hazard ratio; CI, cumulative incidence; SMN, subsequent malignant neoplasms; CED, cyclophosphamide equivalent dose; RT, radiation therapy.
Models for each organ system adjusted for all listed treatments/demographics in addition to time since diagnosis.

[1]Anti-metabolites include Ara-A, 5-Azacytidine, Cytosine Arabinoside, 5-FU, Fludarabine, 6-Mercaptopurine, Methotrexate, 6-Thioguanine.
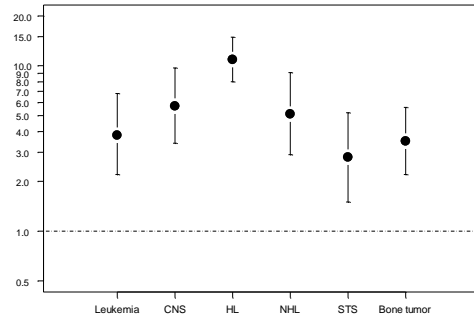[2]Plant alkaloids include Vinblastine and Vincristine.

Supplemental Figure 4: Hazard ratios and 95% CI of grade 3-5 chronic health conditions among early-AYA survivors, according to tumor type, compared to siblings. (a) All Grade 3-5 Conditions, (b) Cardiac, (c) Endocrine, and (d) Pulmonary.

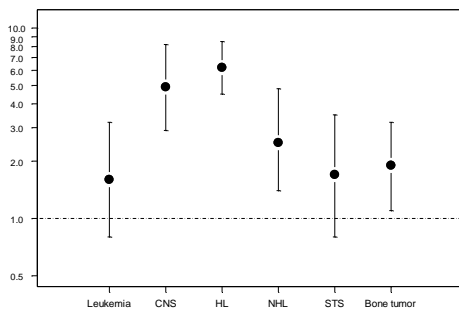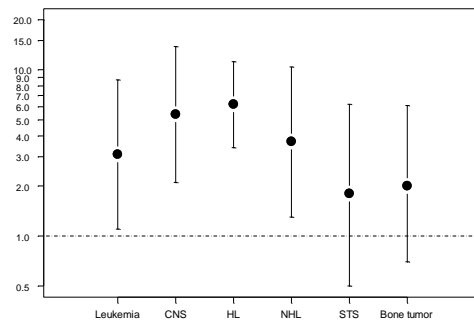**a) Grade 3-5 conditions**
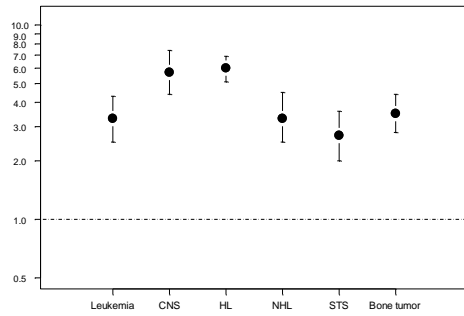
b) Cardiac

c) Endocrine

d) Pulmonary

Y-axis presented with log scale in order to have symmetric confidence intervals.

Each combination of condition with diagnosis represents the results of a separate model adjusted for sex and race.

Abbreviations: CNS, central nervous system; HL, Hodgkin lymphoma; NHL, non-Hodgkin lymphoma; STS, soft tissue sarcoma.

Supplemental Table 5. Standardized incidence ratios of Subsequent Malignant Neoplasms among survivors of early-AYA and matched childhood cancer.

Subsequent Malignant Neoplasm	Original Cancer Diagnosis	Group	Level	early-AYA				childhood				
				# observed	# expected	Rate	SIR (95% CI)	# observed	# expected	Rate	SIR (95% CI)	p-value
All SMNs	All survivors	Overall		336	70·7	5·2	4·7(4·2-5·3)	254	37·0	3·7	6·9(6·0-7·8)	<0·0001
		Current age, y	05-19	NA	NA	NA		55	4·2	2·3	13·3(9·7-18·1)	NA
			20-29	73	14·0	2·5	5·2(4·0-6·6)	83	13·4	2·8	6·2(5·0-7·7)	0·28
			30-39	143	27·6	5·5	5·2(4·4-6·2)	92	13·3	7·2	6·9(5·6-8·6)	0·04
			40+	120	29·1	11·9	4·1(3·4-5·0)	24	6·2	9·7	3·8(2·5-5·8)	0·76
		Survival after diagnosis, y	05-9	59	10·9	2·9	5·4(4·1-7·2)	63	5·3	2·9	11·9(9·0-15·8)	<0·001
			10-19	136	28·2	4·4	4·8(4·1-5·7)	103	15·0	3·1	6·9(5·6-8·4)	0·0086
			20-29	121	24·5	10·0	4·9(4·1-5·9)	76	12·7	6·1	6·0(4·7-7·5)	0·21
			30+	19	7·1	12·6	2·7(1·7-4·2)	12	3·9	6·9	3·0(1·7-5·4)	0·74
		5-9 y after diagnosis, current age 5-19		NA	NA	NA	NA	38	2·4	2·6	16·1(11·0-23·5)	NA
		10-19 y after diagnosis, current age 5-19		NA	NA	NA	NA	17	1·8	1·8	9·6(5·7-16·2)	NA
		5-9 y after diagnosis, current age 20-39		41	8·0	2·2	5·2(3·7-7·1)	9	1·8	1·8	5·1(2·7-9·8)	0·99
		10-19 y after diagnosis, current age 20-39		136	26·5	4·4	5·1(4·3-6·1)	89	12·6	3·6	7·0(5·7-8·7)	0·03
		20+ y after diagnosis, current age 20-39		38	7·1	7·1	5·4(3·8-7·4)	77	12·2	5·8	6·3(5·0-8·0)	0·43
		20+ y after diagnosis, current age 40+		120	29·0	12·0	4·1(3·5-5·0)	24	6·2	9·7	3·8(2·5-5·8)	0·75
	Bone survivors	Overall		57	12·8	4·7	4·4(3·3-6·0)	36	7·7	3·0	4·7(3·3-6·6)	0·82
	CNS survivors	Overall		17	5·9	2·7	2·9(1·8-4·6)	12	2·6	1·8	4·7(2·5-8·6)	0·22

Subsequent Malignant Neoplasm	Original Cancer Diagnosis	Group	Level	early-AYA				childhood				p-value
				# observed	# expected	Rate	SIR (95% CI)	# observed	# expected	Rate	SIR (95% CI)	
	HL survivors	Overall		197	28·7	8·3	6·9(6·0-7·9)	145	15·7	5·9	9·2(7·8-10·9)	0·0087
	Leukemia survivors	Overall		21	8·9	2·1	2·3(1·5-3·7)	24	4·6	1·8	5·2(3·1-8·8)	0·021
	NHL survivors	Overall		27	6·5	4·1	4·1(2·8-6·2)	13	3·1	2·0	4·2(2·4-7·4)	0·97
	STS survivors	Overall		16	7·3	2·7	2·2(1·4-3·5)	24	3·1	4·1	7·6(4·9-11·9)	<0·001
Bone tumors	All survivors	Overall		5	0·4	0·1	11·2(4·7-26·9)	18	0·7	0·3	27·4(17·2-43·5)	0·077
CNS	All survivors	Overall		11	2·3	0·2	4·9(2·7-8·9)	18	2·0	0·3	8·8(4·9-15·6)	0·17
Leukemia	All survivors	Overall		15	2·1	0·2	7·1(4·3-11·8)	11	1·9	0·2	5·8(3·2-10·4)	0·61
Lymphoma	All survivors	Overall		20	7·3	0·3	2·7(1·7-4·5)	8	5·3	0·1	1·5(0·7-3·3)	0·21
Soft tissue sarcoma	All survivors	Overall		20	4·0	0·3	5·0(3·3-7·8)	29	2·3	0·4	12·6(8·5-18·5)	0·0022
		Current age , y	05-19	NA	NA	NA	NA	11	0·3	0·5	32·4(16·2-64·5)	NA
			20-29	5	1·2	0·2	4·3(1·8-10·2)	12	1·0	0·4	11·9(6·8-21·0)	0·053
			30+	15	2·8	0·4	5·4(3·2-8·9)	6	1·0	0·4	6·2(2·8-13·8)	0·76
		Survival after diagnosis, y	05-9	6	0·8	0·3	7·8(3·5-17·3)	9	0·4	0·4	24·2(12·6-46·5)	0·031
			10-19	6	2·2	0·2	2·7(1·2-6·0)	15	1·2	0·5	12·9(7·8-21·4)	0·0011
			20+	8	1·0	0·6	8·3(4·2-16·7)	5	0·8	0·4	6·5(2·7-15·6)	0·66
		5-9 y after diagnosis, current age 5-19		NA	NA	NA	NA	4	0·2	0·3	20·6(7·7-54·9)	NA
		10-19 y after diagnosis, current age 5-19		NA	NA	NA	NA	7	0·1	0·7	48·0(19·0-121·5)	NA
		5-9 y after diagnosis, current age 20-39		4	0·6	0·2	6·2(2·3-16·4)	2	0·1	0·4	17·0(4·2-67·9)	0·24
		10-19 y after diagnosis, current age 20-39		5	2·2	0·2	2·2(0·9-5·4)	9	1·0	0·4	9·0(4·7-17·3)	0·01

| Subsequent Malignant Neoplasm | Original Cancer Diagnosis | Group | Level | early-AYA | | | | childhood | | | | p-value |
				# observed	# expected	Rate	SIR (95% CI)	# observed	# expected	Rate	SIR (95% CI)	
		20+ y after diagnosis, current age 20-39		1	0·4	0·2	2·5(0·4-17·9)	5	0·7	0·4	7·1(3·0-17·2)	0·34
		20+ y after diagnosis, current age 40+		10	0·7	1·0	14·6(7·9-27·1)	2	0·2	0·8	13·3(3·4-52·8)	0·90
Breast	All survivors, females	Overall		139	13·6	4·5	10·2(8·6-12·2)	56	4·7	1·8	11·8(8·9-15·8)	0·40
		Current age, y	05-19	NA	NA	NA	NA	1	0·01	0·1	96·2(13·5-682·8)	NA
			20-29	15	0·8	1·1	19·4(10·7-35·2)	10	0·6	0·7	17·1(9·2-31·8)	0·78
			30-39	64	5·1	5·2	12·5(9·6-16·3)	32	2·4	5·3	13·4(9·0-19·8)	0·77
			40+	60	7·7	12·1	7·8(6·0-10·1)	13	1·8	10·5	7·4(4·2-13·0)	0·87
		Survival after diagnosis, y	05-9	16	1·2	1·6	13·8(7·8-24·4)	7	0·2	0·7	29·5(14·4-60·4)	0·10
			10-19	54	4·7	3·7	11·4(8·7-15·0)	19	1·1	1·3	17·3(10·7-28·2)	0·14
			20-29	59	6·3	10·6	9·4(7·2-12·3)	22	2·4	3·9	9·2(5·9-14·2)	0·92
			30+	10	1·4	15·1	7·0(3·8-13·1)	8	1·0	9·9	7·9(3·9-15·8)	0·81
		5-9 y after diagnosis, current age 5-19		NA	NA	NA	NA	1	0·0	0·2	NA	NA
		10-19 y after diagnosis, current age 5-19		NA	NA	NA	NA	0	0·0	NA	NA	NA
		5-9 y after diagnosis, current age 20-39		5	0·4	0·6	13·1 (5·5-31·6)	0	0·0	NA	NA	NA
		10-19 y after diagnosis, current age 20-39		57	3·9	3·9	14·4(10·9-19·1)	20	0·9	1·8	22·5(13·7-36·8)	0·13
		20+ y after diagnosis, current age 20-39		17	1·6	6·7	10·8(6·6-17·7)	22	2·1	3·6	10·7(6·8-16·8)	0·98
		20+ y after diagnosis, current age 40+		60	7·6	12·1	7·8(6·1-10·2)	13	1·8	10·5	7·4(4·2-13·0)	0·86

Subsequent Malignant Neoplasm	Original Cancer Diagnosis	Group	Level	early-AYA				childhood				
				# observed	# expected	Rate	SIR (95% CI)	# observed	# expected	Rate	SIR (95% CI)	p-value
	HL survivors, females	Overall		97	6·4	7·4	15·2(12·4-18·6)	39	2·2	3·9	17·4(12·3-24·6)	0·51
		Current age, y	05-19	NA	NA	NA	NA	0	0·002	0·0	NA	NA
			20-29	8	0·3	1·5	25·1(11·6-54·3)	6	0·2	1·2	27·1(12·3-60·1)	0·89
			30-39	46	2·2	8·7	20·8(15·2-28·3)	25	1·1	9·3	23·3(15·0-36·0)	0·68
			40+	43	3·8	17·6	11·2(8·3-15·1)	8	0·9	12·0	8·5(4·4-16·5)	0·46
		Survival after diagnosis, y	05-9	7	0·7	1·6	10·1(4·8-21·2)	3	0·2	1·0	19·0(6·2-58·8)	0·36
			10-19	39	2·3	6·3	17·0(12·3-23·6)	15	0·6	3·2	27·1(15·5-47·4)	0·16
			20-29	42	2·7	18·1	15·5(11·2-21·4)	16	1·0	8·4	15·3(9·1-25·8)	0·96
			30+	9	0·7	28·4	13·1(6·7-25·4)	5	0·5	14·7	10·4(4·2-25·3)	0·68
	Survivors of diagnosis other than HL, females	Overall		42	7·2	2·4	5·8(4·2-8·2)	17	2·5	0·8	6·8(4·1-11·4)	0·62
		Current age, y	05-19	NA	NA	NA	NA	1	0·01	0·1	119·0(16·8-845·3)	NA
			20-29	7	0·5	0·8	15·4(6·1-38·8)	4	0·4	0·5	11·0(4·1-29·4)	0·63
			30-39	18	2·9	2·5	6·2(3·7-10·2)	7	1·3	2·1	5·3(2·3-12·3)	0·76
			40+	17	3·8	6·7	4·4(2·7-7·3)	5	0·8	8·7	6·2(2·2-16·9)	0·56
		Survival after diagnosis, y	05-9	9	0·5	1·6	19·3(8·4-43·9)	4	0·1	0·6	50·2(21·0-120·4)	0·12
			10-19	15	2·5	1·8	6·1(3·7-10·0)	4	0·5	0·4	7·4(2·8-19·4)	0·74
			20-29	17	3·6	5·2	4·8(3·0-7·7)	6	1·3	1·6	4·5(2·0-10·0)	0·88
			30+	1	0·7	2·9	1·4(0·2-9·7)	3	0·5	6·5	5·7(1·9-17·3)	0·22
Thyroid	All survivors	Overall		28	5·7	0·4	4·9(3·4-7·1)	68	3·7	1·0	18·4(14·5-23·2)	<0·0001
		Current age, y	05-19	NA	NA	NA	NA	11	0·3	0·5	41·0(22·7-74·0)	NA
			20-29	6	1·6	0·2	3·7(1·7-8·3)	20	1·6	0·7	12·3(7·9-19·0)	0·010
			30-39	17	2·6	0·7	6·5(4·0-10·4)	35	1·4	2·7	24·9(17·9-34·6)	<0·0001

23

Subsequent Malignant Neoplasm	Original Cancer Diagnosis	Group	Level	early-AYA				childhood				p-value
				# observed	# expected	Rate	SIR (95% CI)	# observed	# expected	Rate	SIR (95% CI)	
			40+	5	1·5	0·5	3·3(1·4-8·0)	2	0·4	0·8	5·0(1·2-19·9)	0·64
		Survival after diagnosis, y	05-9	4	1·1	0·2	3·6(1·3-9·5)	14	0·5	0·6	30·7(18·2-51·8)	<0·001
			10-19	17	2·8	0·6	6·2(3·8-9·9)	28	1·7	0·8	16·6(11·5-24·0)	0·0012
			20-29	5	1·6	0·4	3·2(1·3-7·6)	24	1·3	1·9	18·6(12·5-27·9)	<0·001
			30+	2	0·3	1·3	7·6(1·9-30·4)	2	0·3	1·1	7·2(1·8-29·0)	0·96
		5-9 y after diagnosis, current age 5-19		NA	NA	NA	NA	9	0·1	0·6	67·6(35·2-129·8)	NA
		10-19 y after diagnosis, current age 5-19		NA	NA	NA	NA	2	0·1	0·2	14·8(3·7-59·2)	NA
		5-9 y after diagnosis, current age 20-39		4	0·9	0·2	4·5(1·7-12·0)	1	0·2	0·2	4·8(0·7-34·3)	0·95
		10-19 y after diagnosis, current age 20-39		16	2·7	0·5	6·0(3·7-9·7)	27	1·5	1·1	18·0(12·4-26·2)	<0·001
		20+ y after diagnosis, current age 20-39		3	0·7	0·6	4·6(1·5-14·2)	27	1·3	2·0	20·3(14·0-29·6)	0·01
		20+ y after diagnosis, current age 40+		5	1·5	0·5	3·4(1·4-8·1)	2	0·4	0·8	5·0(1·2-19·9)	0·64
	HL survivors	Overall		14	2·3	0·6	6·1(3·6-10·2)	50	1·5	2·0	33·9(25·8-44·6)	<0·0001
		Current age, y	05-19	NA	NA	NA	NA	8	0·1	1·5	138·7(69·6-276·4)	NA
			20-29	3	0·6	0·3	5·0(1·6-15·4)	15	0·6	1·3	25·4(15·4-42·0)	0·0099
			30-39	8	1·0	0·8	7·8(3·9-15·5)	25	0·6	4·2	40·7(27·6-59·9)	<0·0001
			40+	3	0·7	0·7	4·4(1·4-13·7)	2	0·2	1·5	9·4(2·3-37·9)	0·41
		Survival after diagnosis, y	05-9	1	0·5	0·1	2·1(0·3-14·8)	10	0·2	1·3	47·0(25·3-87·4)	0·0030
			10-19	10	1·1	0·9	9·0(4·9-16·8)	23	0·7	2·0	34·7(23·2-51·8)	<0·001
			20-29	2	0·6	0·5	3·3(0·8-13·3)	16	0·5	3·4	33·6(20·5-55·1)	0·0021
			30+	1	0·1	1·5	8·5(1·2-59·1)	1	0·1	1·3	8·2(1·1-58·4)	0·98

Subsequent Malignant Neoplasm	Original Cancer Diagnosis	Group	Level	early-AYA				childhood				
				# observed	# expected	Rate	SIR (95% CI)	# observed	# expected	Rate	SIR (95% CI)	p-value
	Survivors of diagnosis other than HL	Overall		14	3·4	0·3	4·1(2·4-6·9)	18	2·2	0·4	8·1(5·1-12·8)	0·057
		Current age, y	05-19	NA	NA	NA	NA	3	0·2	0·2	14·2(4·6-44·2)	NA
			20-29	3	1·0	0·2	3·0(1·0-9·3)	5	1·0	0·3	4·8(2·0-11·6)	0·51
			30-39	9	1·6	0·5	5·7(2·9-10·9)	10	0·8	1·5	12·7(6·8-23·5)	0·079
			40+	2	0·8	0·3	2·4(0·6-9·8)	NA	0·2	NA	NA	NA
		Survival after diagnosis, y	05-9	3	0·6	0·2	4·7(1·5-14·4)	4	0·2	0·3	16·5(6·2-43·8)	0·097
			10-19	7	1·7	0·4	4·2(2·0-8·9)	5	1·0	0·2	4·9(2·0-11·7)	0·80
			20-29	3	1·0	0·4	3·1(1·0-9·6)	8	0·8	1·0	9·9(4·9-19·7)	0·087
			30+	1	0·1	1·2	7·0(1·0-49·6)	1	0·2	1·0	6·5(0·9-46·0)	0·96

Abbreviations: SMN, Subsequent Malignant Neoplasm; y, year; SIR, standardized incidence ratio; CI, confidence interval; CNS, central nervous system; HL, Hodgkin lymphoma; NHL, non-Hodgkin lymphoma; STS, soft tissue sarcoma; NA, not applicable.

Supplemental Methods: CCSS Institutions

1) Children's Hospitals and Clinics of Minnesota, Minneapolis, MN
2) Children's Hospital of Colorado, Aurora CO
3) Children's Hospital of Los Angeles, Los Angeles, CA
4) Children's Hospital of Philadelphia, Philadelphia, PA
5) Children's Hospital of Pittsburgh, Pittsburgh, PA
6) Children's National Medical Center, Washington, DC
7) Dana Farber Cancer Institute/Children's Hospital, Boston, MA
8) Emory University/Children's Healthcare of Atlanta, Atlanta, GA
9) Mayo Clinic, Rochester, MN
10) Memorial Sloan Kettering Cancer Center, New York, NY
11) Nationwide Children's Hospital, Columbus, OH
12) Riley Hospital for Children, Indianapolis, IN
13) Roswell Park Cancer Institute, Buffalo, NY
14) St. Jude Children's Research Hospital, Memphis, TN
15) St. Louis Children's Hospital, St. Louis, MO
16) Seattle Children's Hospital, Seattle, WA
17) Stanford University School of Medicine, Palo Alto, CA
18) Texas Children's Hospital, Houston, TX
19) University of Alabama, Birmingham, AL
20) University of California Los Angeles, Los Angeles, CA
21) University of California San Francisco, San Francisco, CA
22) University of Michigan, Ann Arbor, MI
23) University of Minnesota, Minneapolis, MN
24) University of Texas MD Anderson Cancer Center, Houston, TX
25) University of Texas Southwestern Medical Center, Dallas, TX
26) Hospital for Sick Children, Toronto, Ontario, Canada
27) City of Hope National Medical Center, Duarte, CA