Supplementary Appendix

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Supplementary Methods

Details about the cohort

The Childhood Cancer Survivor Study (CCSS) was established in the early 1990s for the purpose of investigating late effects in five-year survivors of childhood cancer diagnosed in 1970-1986. It was designed as a multicenter, hospital-based, retrospective cohort study with longitudinal follow-up and initially included a consortium of 26 pediatric oncology centers in North America. It has since expanded to include five-year survivors diagnosed in 1987-1999, now involving 31 centers. Because the goal of CCSS is to serve as a resource for investigating a wide range of late effects, rare and common, the strategy of the CCSS study design was to maximize the quality and quantity of data. The cohort, therefore, tried to recruit all eligible survivors and maximize the sample size of the CCSS cohort available for investigation. The only exception was the under-sampling of ALL survivors in the Expansion Cohort (diagnosed 1987-1999): ALL was the dominant diagnosis and, given a fixed budget, it was decided that under-sampling ALL and inclusion of all the other diagnosis groups would maximize the study power for many investigations of interest. The CCSS identified and recruited all survivors meeting eligibility criteria at participating institutions. Cancer diagnosis and treatment information was abstracted from participating institutions using a standardized medical records abstraction form by individual abstracters who were centrally trained. Eligible participants were contacted to complete baseline and subsequent follow-up questionnaires which included self-reported demographic, education, and socioeconomic factors as well as chronic health conditions and medical events. Next of kin were contacted and asked to complete the baseline questionnaire for eligible participants known to have died after achieving five-year survival. Information on sex (used as a biologic factor in our analyses) was collected in the medical record abstraction (from treating institutions). Information on race and ethnicity was collected as a self-reported variable on surveys to participants. As race and ethnicity information was not included in the medical records abstraction for the original cohort (diagnosed 1970-1986), eligible non-participants from this group do not have data on race/ethnicity. Additional methodologic details of the cohort are available in two previous reports cited here.[1,2]

Details about Lifestyle Components and Score

The healthy behavior score included in this analysis is modeled after similar scores used in other population level mortality analyses that assessed the impact of lifestyle or health behaviors on death. Li Y et al. utilized NHANES (National Health and Nutrition Examination Survey) data to estimate the distribution of a five point lifestyle score including ever smoking, heavy alcohol use, unhealthy BMI, poor diet quality and low physical activity each as a binary (0 or 1) score and evaluated associations with mortality.[3] Similar studies using various components of these 5 indicators (or surrogates of) have also been conducted to determine the association of lifestyle factors with mortality in the US (Behrens G et al. using a 4 point score of waist circumference, diet quality, physical activity and smoking)[4] and internationally in the United Kingdom (Khaw KT et al. using smoking, physical activity, alcohol use and diet)[5] and a multinational global cohort (Yusuf S et al. using tobacco use, alcohol, diet, physical activity and sodium intake.)[6] As the CCSS does not collect information on diet quality, we chose to use a 4-point score using BMI in addition to smoking, alcohol use, and physical activity.

As stated in the manuscript, lifestyle factors including smoking, alcohol use, physical activity, and unhealthy weight, were assigned a score of 0 (unhealthy) or 1 (healthy) and combined to create a lifestyle score ranging from 0-4 for each survey time-point. We defined unhealthy as: ever smoked more than 100 cigarettes, heavy or risky drinking (>7 drinks/week or >3 drinks/day for women, >14 drinks/week or >4 drinks/day for men; consistent with the definition of heavy alcohol use from the National Institute of Alcohol Abuse and Alcoholism), body mass index <18·5 (underweight) or ≥30 (obese) kg/m2, and sedentary (0-3 MET-h/week of activity). For low physical activity (3-6 MET-h/week) a score of 0·5 was assigned.[7] The lifestyle score was categorized as unhealthy (0-2), moderately healthy (2·5-3), and healthy (3·5-4).

The choice to use a cut-point for "ever smoker" of 100 cigarettes smoked in an individual's lifetime is based on the definition of a former/current smoker from the US National Health Interview Survey being "An adult who has smoked 100 cigarettes in his or her lifetime (but has quit smoking/and who currently smokes)" at the time of interview. The National Health Interview Survey and National Health and Nutrition Examination Survey both ask this question to participants and, for those answering yes, collect additional information related to smoking history. The 100 cigarette criterion has been used since tobacco-related questions were introduced to the NHIS in 1965.[8] Similarly, the CCSS surveys ask "Have you smoked at least 100 cigarettes in your entire life?" with additional

questions for those answering "yes", questionnaires available at https://ccss.stjude.org/tools-documents/questionnaires/. By these definitions and widely used survey questions, we defined an individual who has "ever smoked" as one who responded yes to this survey question.

In this analysis, obesity (BMI ≥ 30 mg/m^2) and not overweight (BMI 25-<30 kg/m^2) was categorized as unhealthy. Repeated mortality studies across populations in the US and Europe have identified a U-shaped or J-shaped curve when plotting the relationship between BMI and future risk of death with the nadir of this curve typically at the upper limits of the healthy weight range (BMI 23-25 kg/m^2). Given the multiple time-points included in this analysis, should overweight progress to obesity it would be recognized as unhealthy in the analysis. And, should overweight contribute to the development of traditional cardiovascular risk factors, they would be accounted for in the analysis. However, we did not feel justified in including overweight at a single timepoint as an "unhealthy" factor because, when looking specifically at future mortality risk in the general population, it is not clear that BMI in the 25-29·9 range alone would confer any greater risk than those in the lower ranges of "normal" weight (18·5-22 for example). Our data were consistent with this trend given that standardized mortality rates (SMR) for all-cause and health-related mortality by BMI categories in table S9 are similar for healthy weight (BMI 18·5-<25 kg/m^2) and overweight (BMI 25-<30 kg/m^2) survivors. In fact, many SMRs for overweight are lower than those for healthy weight. Although we suspect there are cardiometabolic complications associated with overweight in survivors that do increase risk for future comorbidities and likely death, the CVRFs included in the analysis may account for many of these adiposity-related comorbidities.

These factors were collected at the baseline and with each follow-up survey and a score for each participant at each time-point (0-4) was generated and included in the model as a time-varying covariate. For the 20,051 survivors included in the modifiable risk analysis (participating in at least one survey at age 18 or older) there was an average of 2·1 surveys (range 1 – 4 surveys) completed per survivor with 7209, 6420, 3102, and 3320 survivors completing 1, 2, 3, and 4 surveys, respectively. To decrease missingness of lifestyle components, we first used carry-forward; if a survivor previously reported being a non-smoker at one time point and omitted a response at a subsequent time point we assumed the response at the second time point was equal to that at the previous time point for the individual. Second, for individuals without prior surveys and with at least two non-missing lifestyle items we used the mean score of the non-missing items for the individual surveyed to replace missing values.

Details about Statistical Analysis

Piecewise exponential models were selected for mortality analyses given their ability to provide estimates of absolute rates over time. Piecewise exponential models have been widely-used since late 1970s.[9-11] They approximate models of Cox regression by modeling the baseline hazard of proportional hazards models parametrically with piecewise exponential hazards in the form of a step function[12] or other flexible parametric forms (e.g., restricted cubic splines), the latter being a type of "flexible parametric survival models" and the approach we took. Piecewise-exponential models assume proportional mortality rates in association with covariates. All regression analyses were adjusted for sex, age at diagnosis, attained age during follow-up and race/ethnicity, while modifiable risk analyses further included treatment exposures, educational attainment, income, and insurance status. All sociodemographic covariates were categorized (categories shown in Table 1 and Table S8). Attained age in integer values and each of the treatment variables (cranial irradiation dose, chest irradiation dose, anthracycline dose, alkylator dose) were modeled using a restricted cubic spline to avoid a strict proportionality assumption for continuous variables. Specifically, we modelled the integer values of attained age with a restricted cubic spline with 5 knots selected by the general strategy suggested by Stone and Koo[13] at 22, 30, 35, 40 and 50 for regression on lifestyle factors (Table 2 and S11, using participants ≥18 years of age) and at 15, 25, 35, 45, and 55 for regression on mortality and associations with the treatment exposures with knots also determined by the strategy of Stone and Koo (Table S5 and S6): thus, within each integer value of age, the hazard is constant but the hazard changes over integer values of attained age according to a flexible restricted cubic spline. An exception to the use of restricted cubic splines for the treatment variables was when we assessed the association of treatment variables with overall and cause-specific mortality: in these models, we assumed a constant per-unit-dose association and targeted its estimation for the multiple treatment variables simultaneously. Regarding the time interval used in analyses, we split each subject's follow-up time into short segments (i.e., each subject's single year follow-up is split into up to four segments at the points when the integer values of calendar year, age, or year from cancer diagnosis changed) so that, within each segment, all time variables (the calendar year, age, and year from cancer diagnosis) are constant. The piecewise exponential hazards allow these segmentations because of its memoryless property.

Figure S1. Study population.

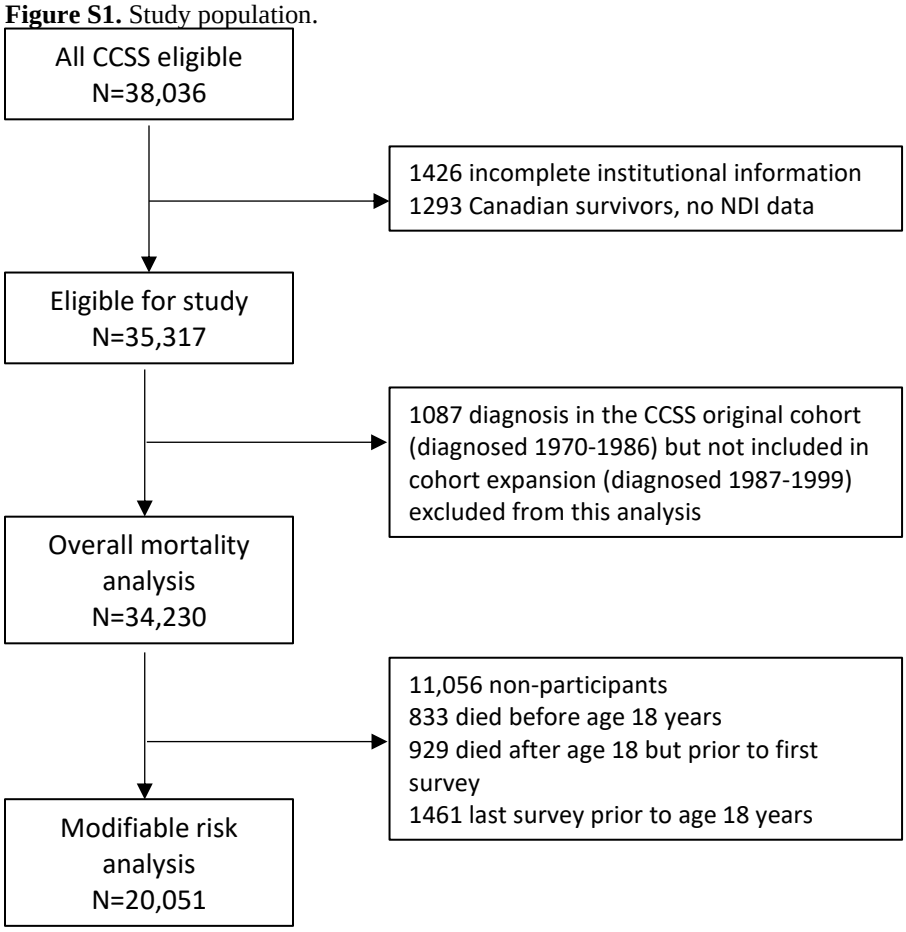


Figure S2. Directed acyclic graph of the assumed associations between potentially modifiable lifestyle and cardiovascular risk factors and death with shared risk factors of sociodemographic characteristics and cancer treatment.

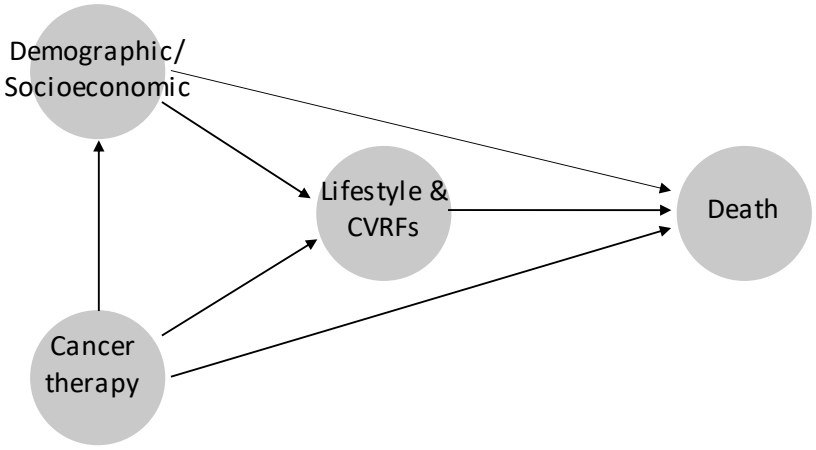
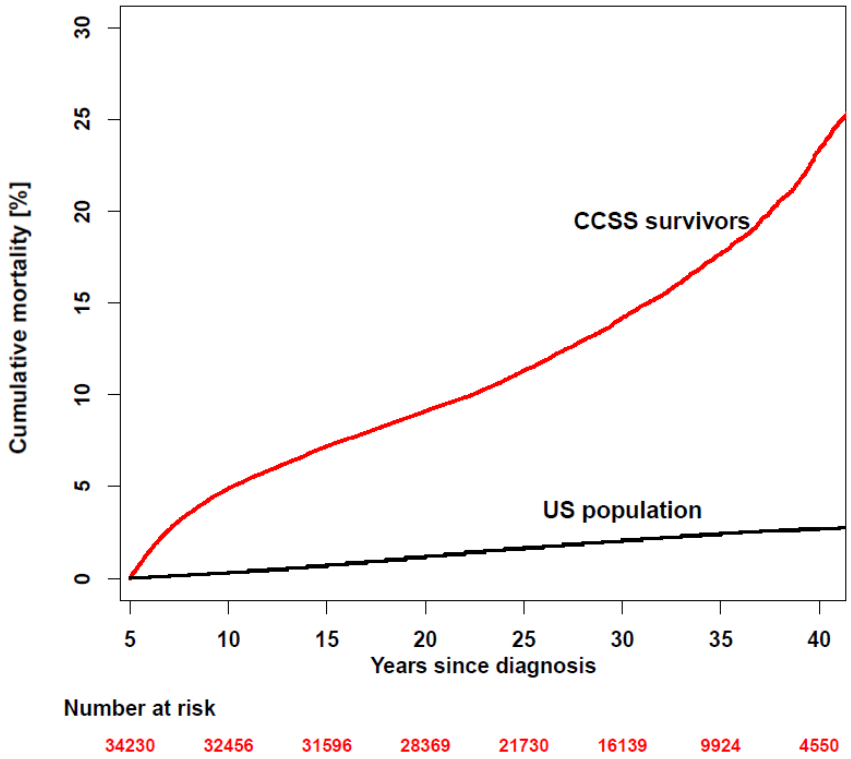


Figure S3. Cumulative late mortality among five-year survivors of childhood cancer shown as (a) all-cause cumulative mortality compared to the US population and (b) among five-year survivors diagnosed in the 1970s (black), 1980s (blue) and 1990s (red) by cause-of-death as recurrence or progression of primary cancer, health-related and external/accidental causes of death.

a)



b)

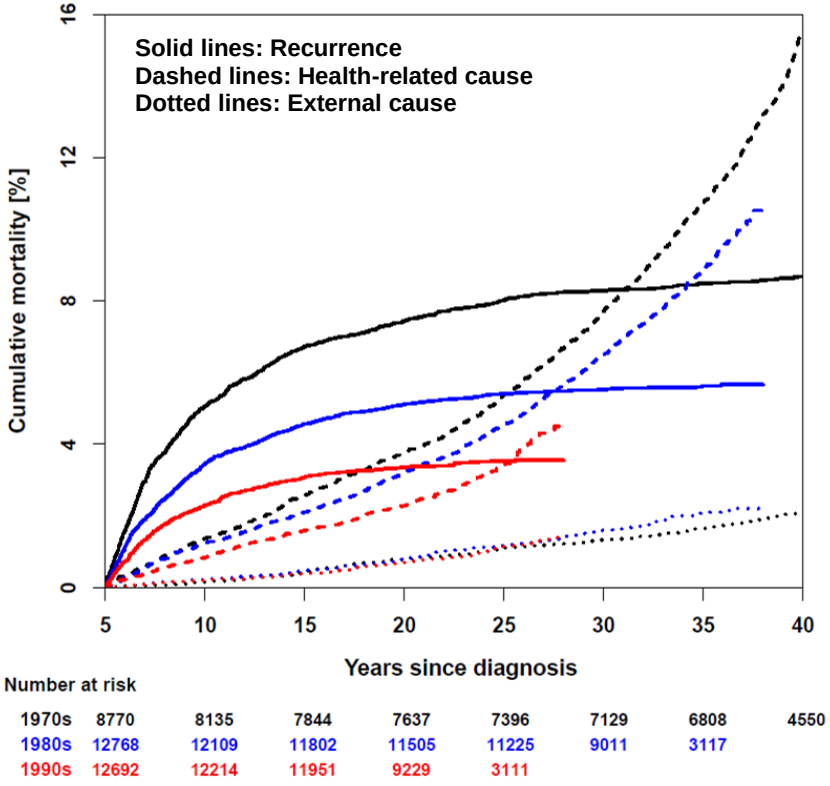


Figure S4. Cumulative mortality conditioned on survival from diagnosis in five-year periods (a, b, c) overall and (d, e, f) by sex as (a, d) all-cause, (b, e) recurrence or progression of primary cancer, and (c, f) health-related causes of death.

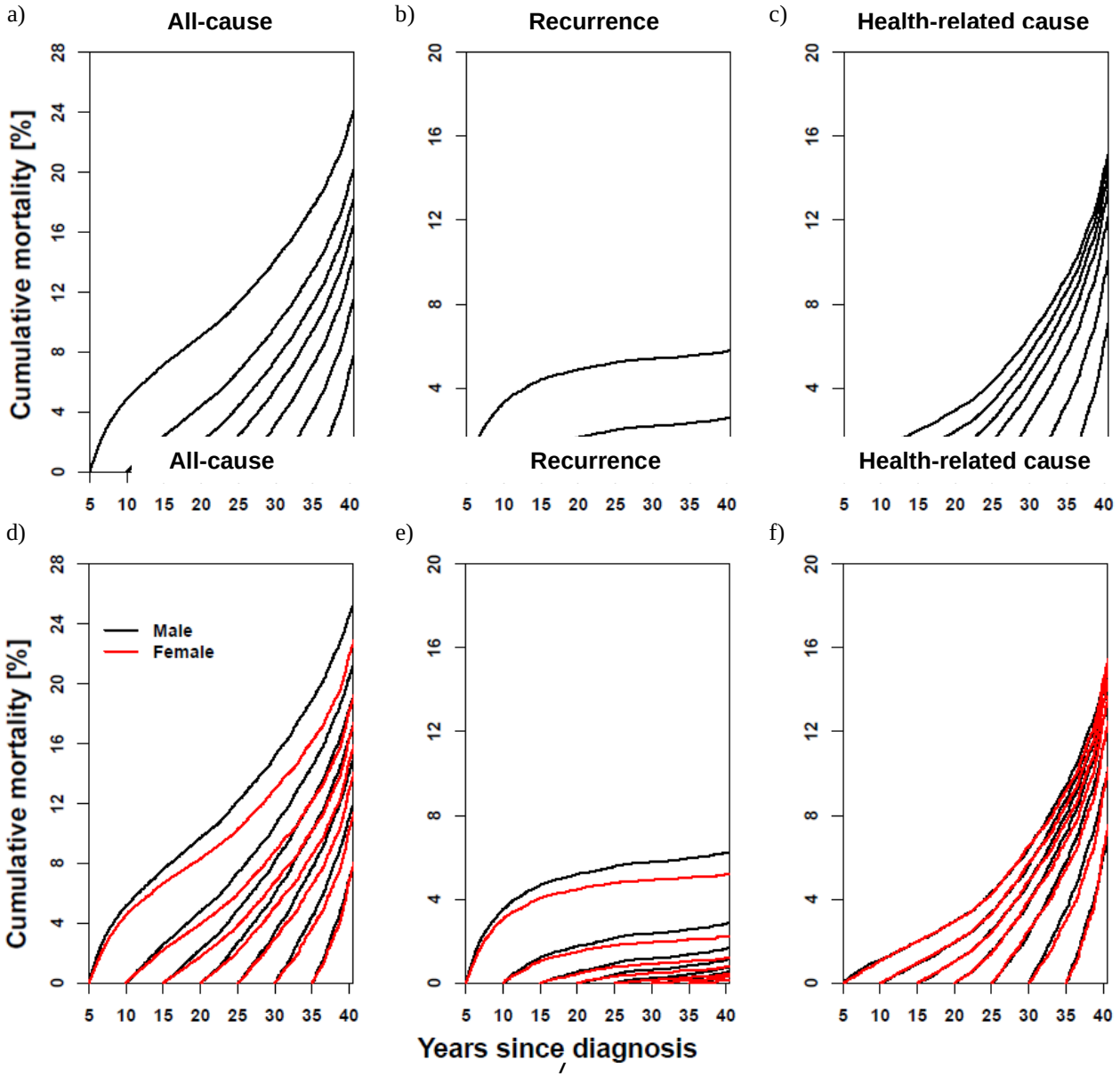


Figure S5. All-cause cumulative mortality by diagnosis among five-year survivors of (a) hematologic malignancies and (b) solid tumors and brain tumors.

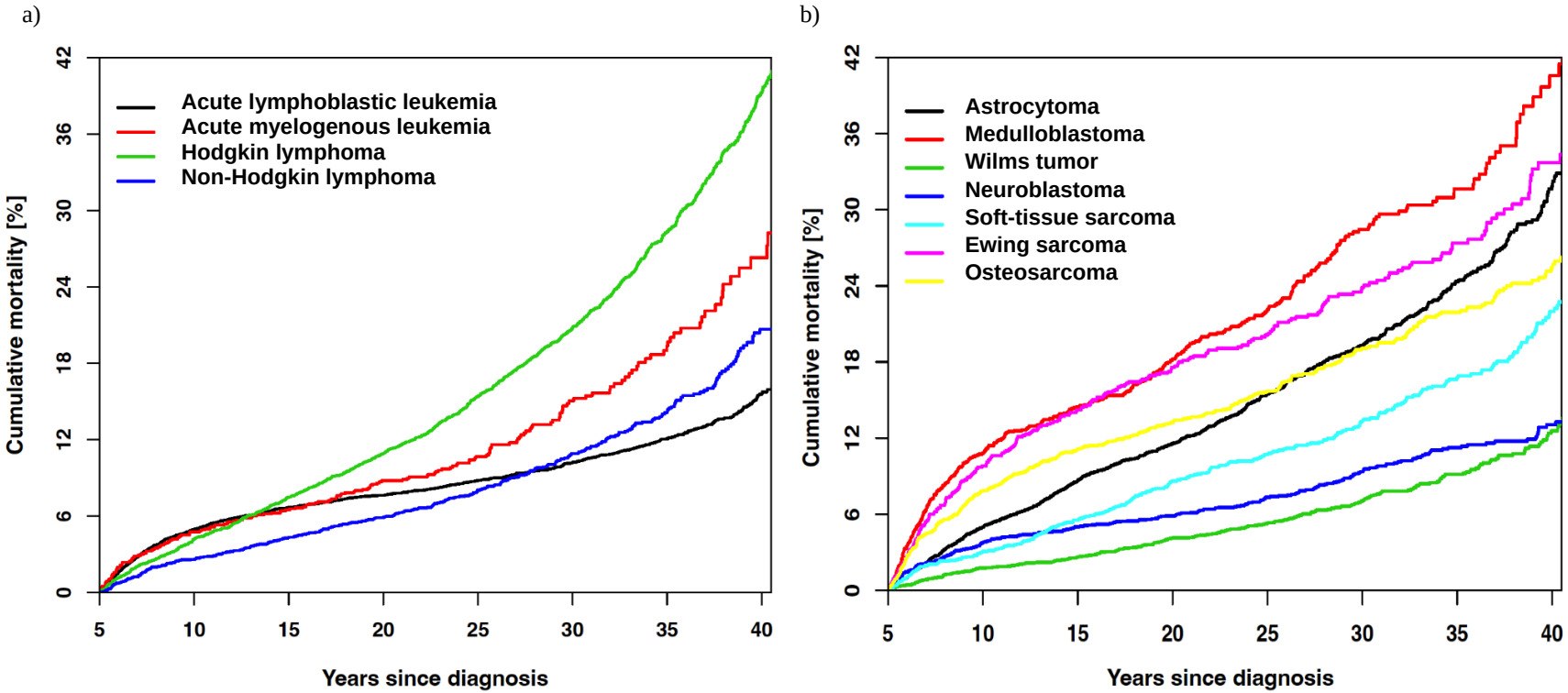
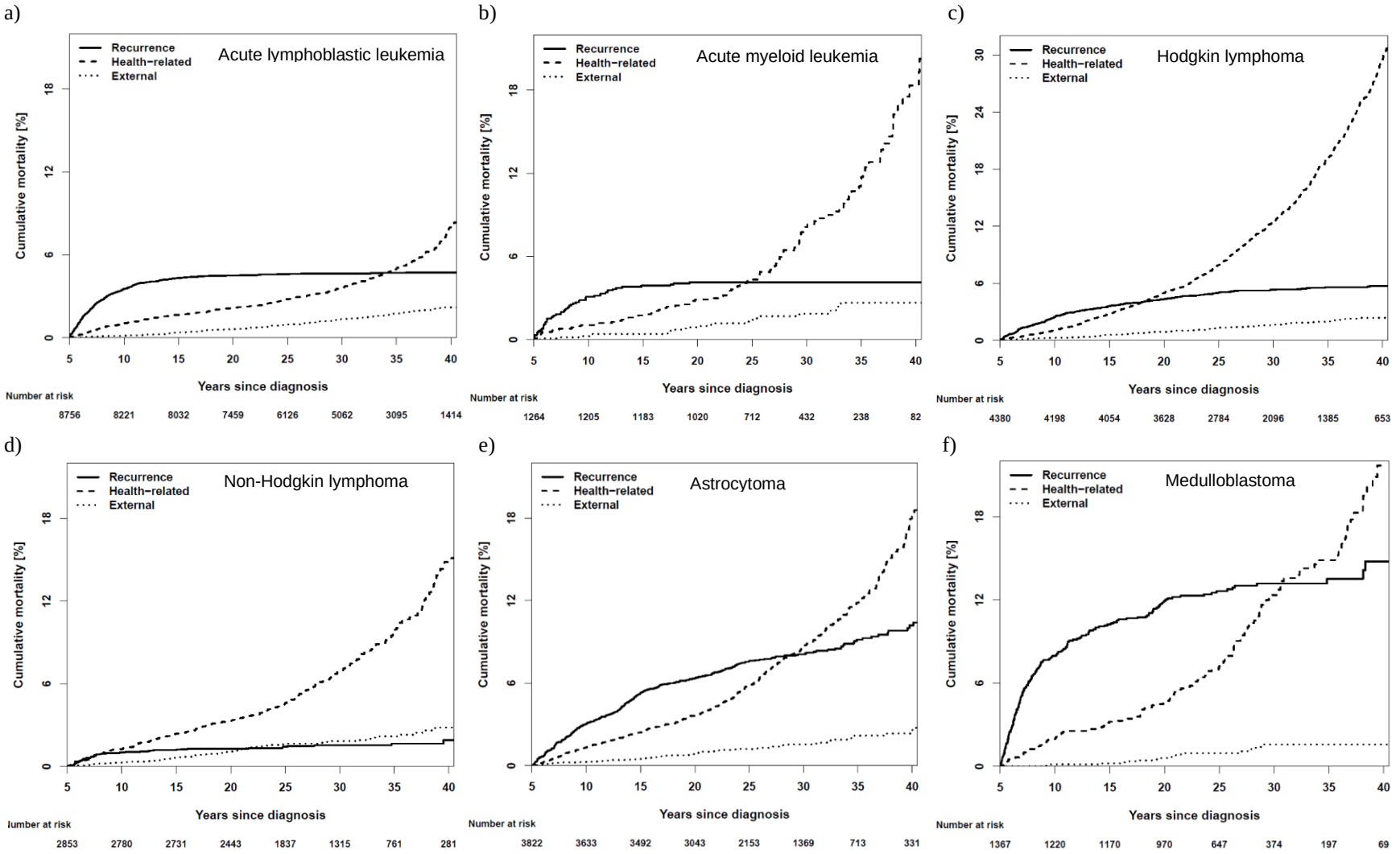
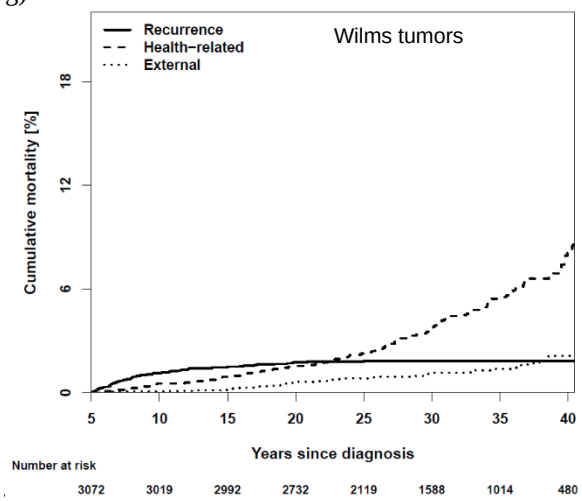


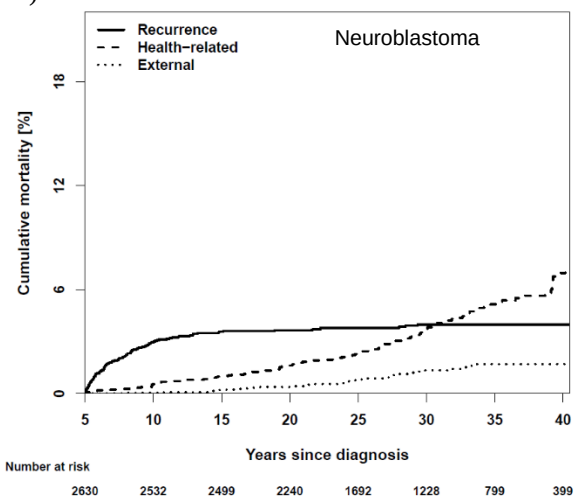
Figure S6. Cause-specific mortality by diagnosis as recurrence/progression of primary cancer, health-related and external/accidental cause among five-year survivors of (a) acute lymphoblastic leukemia, (b) acute myeloid leukemia, (c) Hodgkin lymphoma, (d) non-Hodgkin lymphoma, (e) astrocytoma, (f) medulloblastoma, (g) Wilms tumor, (h) neuroblastoma, (i) soft tissue sarcoma, (j) osteosarcoma, and (k) Ewing sarcoma.



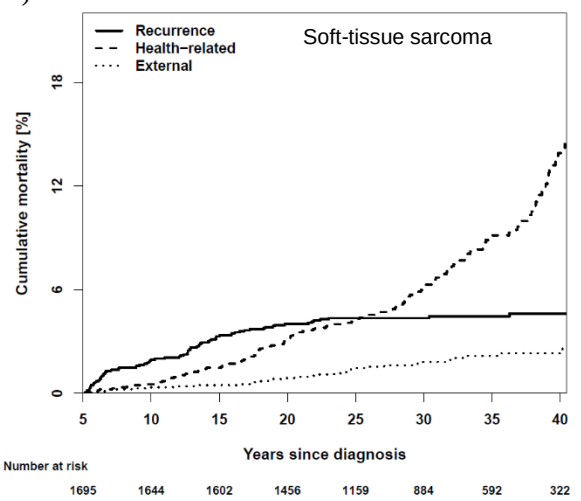
g)


Recurrence
Health−related
External
Wilms tumors
Cumulative mortality [%]
0
6
12
18
5
10
15
20
25
30
35
40
Years since diagnosis
Number at risk
3072 3019 2992 2732 2119 1588 1014 480

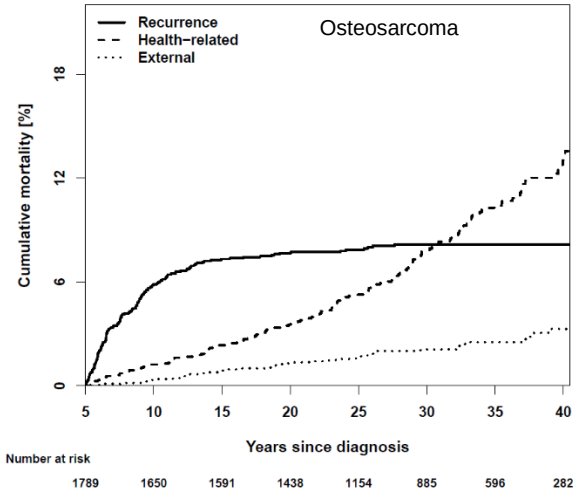
h)


Recurrence
Health−related
External
Neuroblastoma
Cumulative mortality [%]
0
6
12
18
5
10
15
20
25
30
35
40
Years since diagnosis
Number at risk
2630 2532 2499 2240 1692 1228 799 399

i)


Recurrence
Health−related
External
Soft-tissue sarcoma
Cumulative mortality [%]
0
6
12
18
5
10
15
20
25
30
35
40
Years since diagnosis
Number at risk
1695 1644 1602 1456 1159 884 592 322

j)


Recurrence
Health−related
External
Osteosarcoma
Cumulative mortality [%]
0
6
12
18
5
10
15
20
25
30
35
40
Years since diagnosis
Number at risk
1789 1650 1591 1438 1154 885 596 282

k)

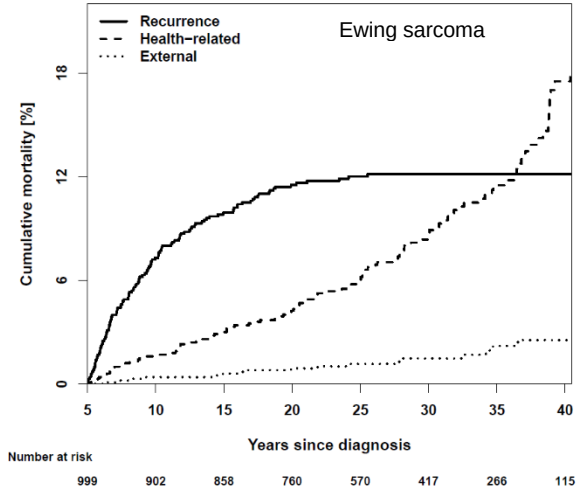
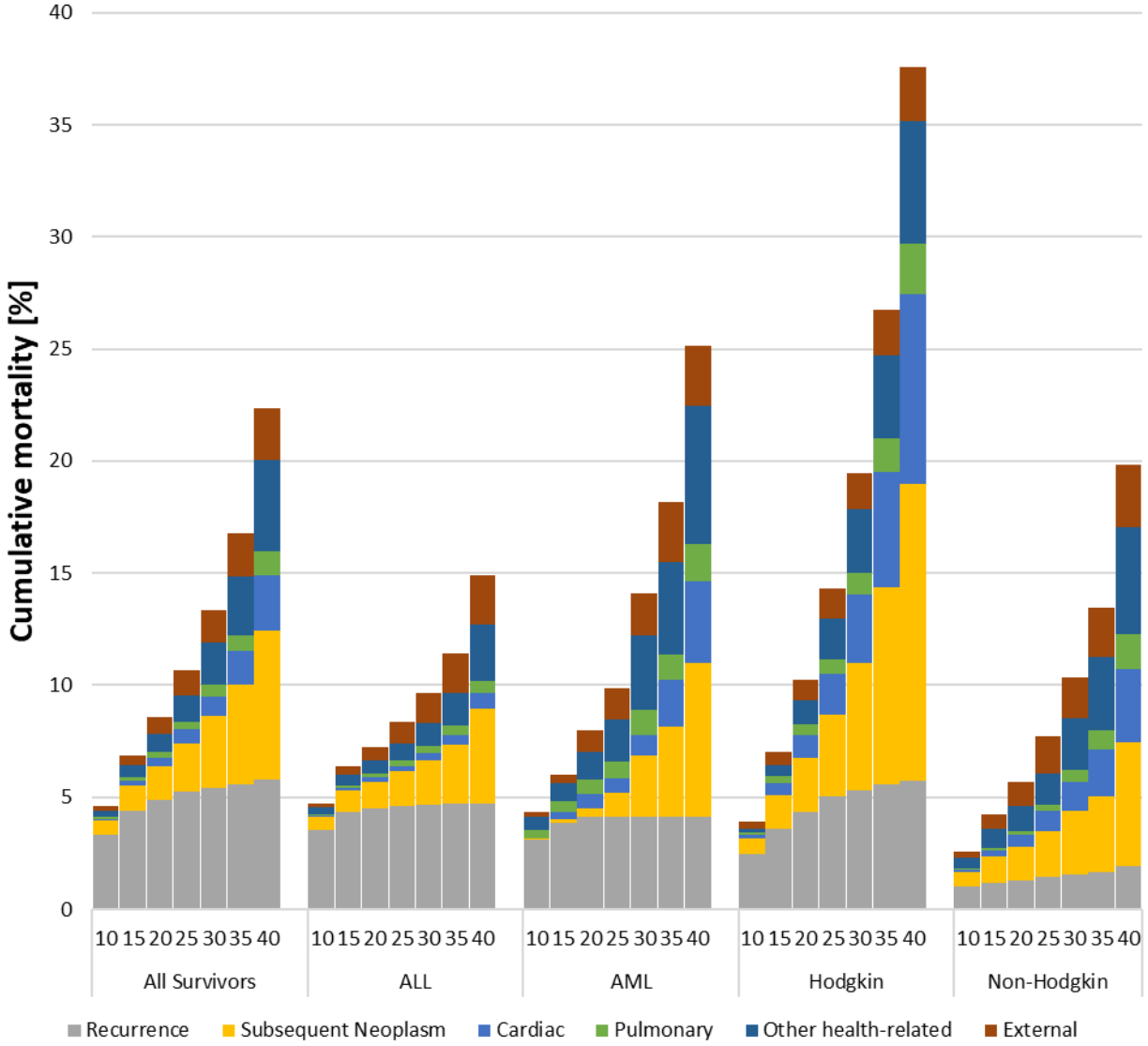

Recurrence
Health−related
External
Ewing sarcoma
Cumulative mortality [%]
0
6
12
18
5
10
15
20
25
30
35
40
Years since diagnosis
Number at risk
999 902 858 760 570 417 266 115

Figure S7. Cause specific mortality by survival time overall and by diagnosis as (a) hematologic malignancies and (b) solid tumors for six causes of death (recurrence/progression of primary cancer, specific health-related causes of death: subsequent neoplasm, cardiac, pulmonary, and other health-related causes, and external/accidental causes).

a)



b)

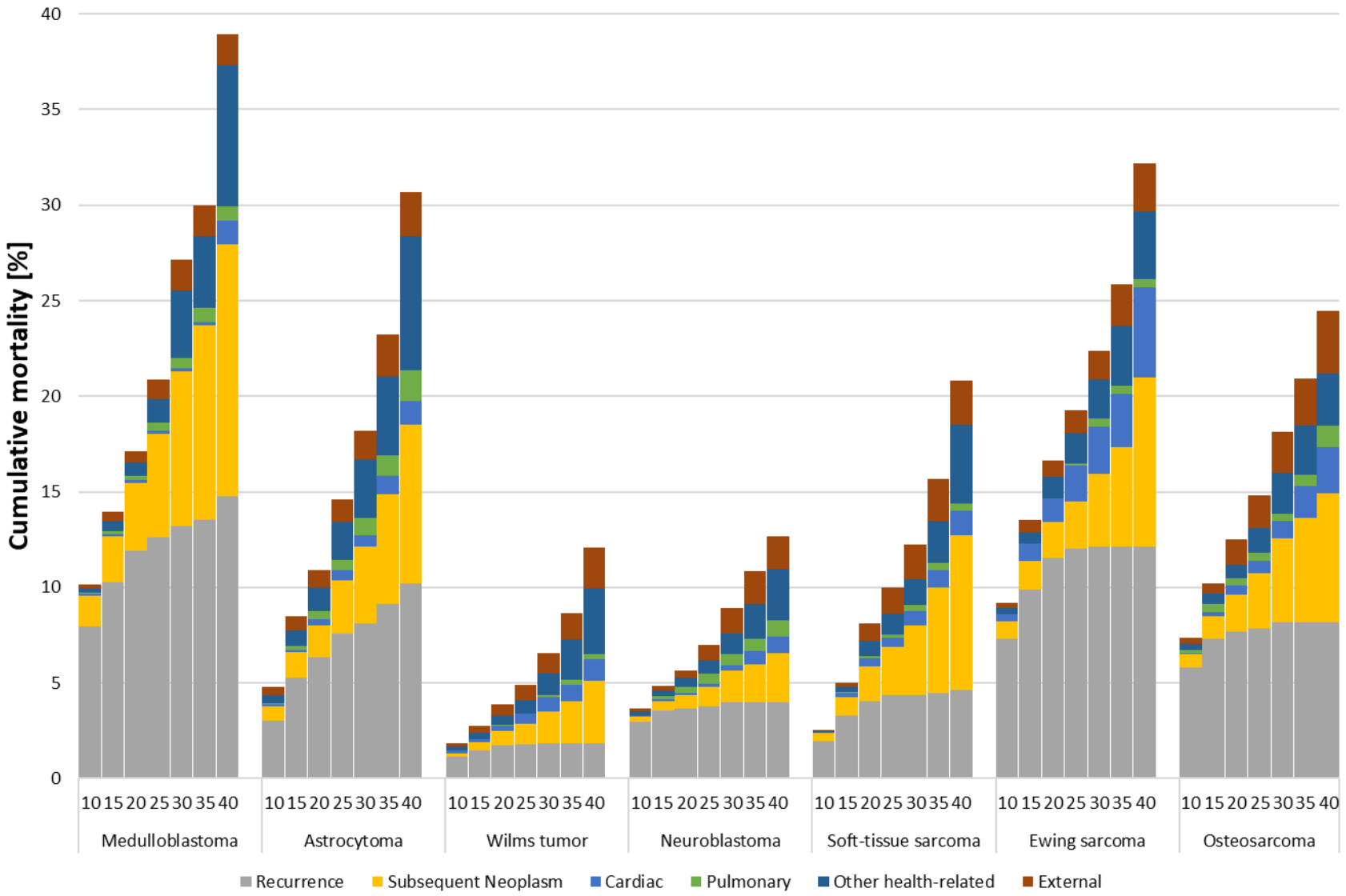
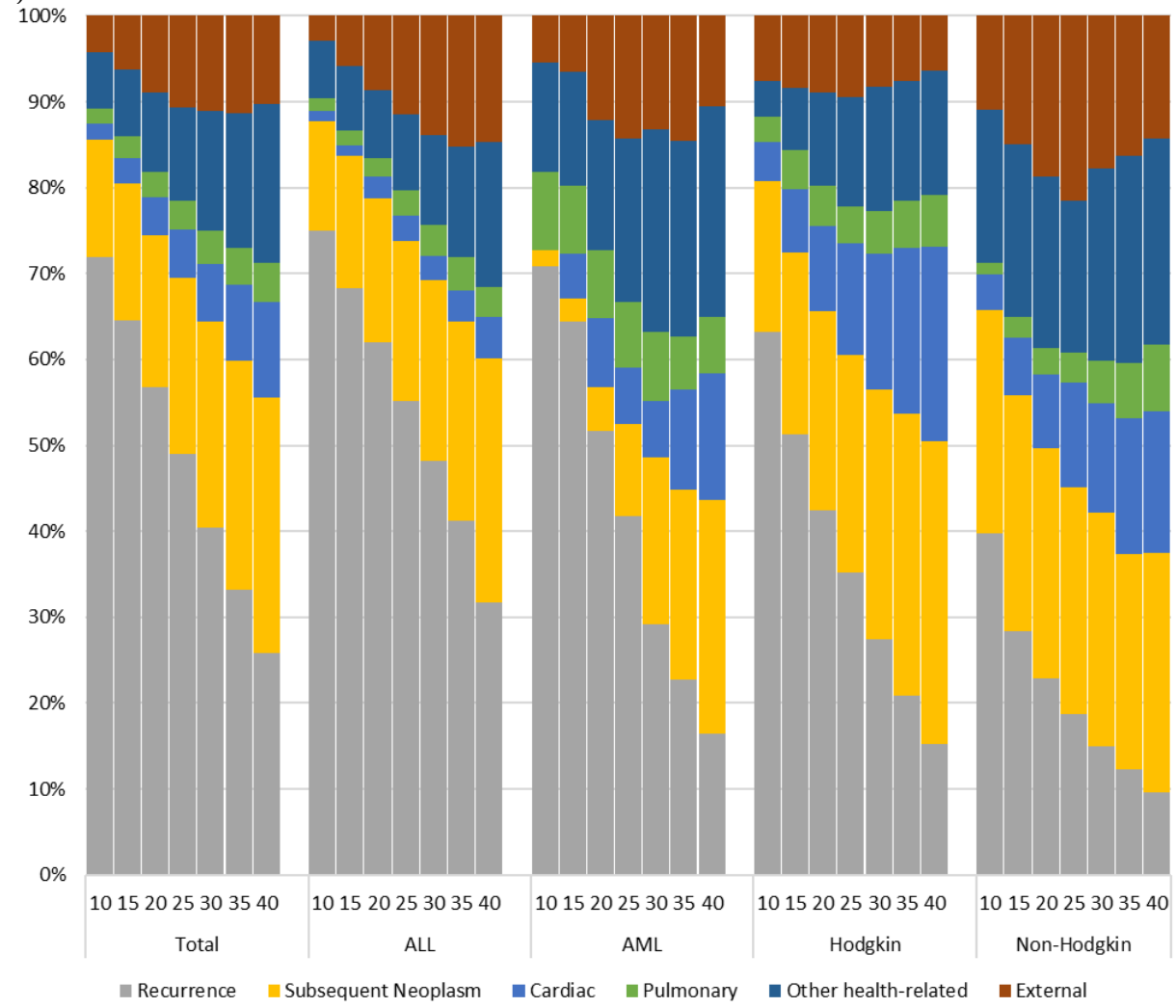

Cumulative mortality [%]
0
5
10
15
20
25
30
35
40
10 15 20 25 30 35 40
Medulloblastoma
Astrocytoma
Wilms tumor
Neuroblastoma
Soft-tissue sarcoma
Ewing sarcoma
Osteosarcoma
Recurrence
Subsequent Neoplasm
Cardiac
Pulmonary
Other health-related
External

Figure S8. Proportion of cumulative death attributable to each of six causes (recurrence/progression of primary cancer, health-related causes of death: subsequent neoplasm, cardiac, pulmonary, and other health-related causes, and external/accidental causes) by survival time (a) overall and by diagnosis as (a) hematologic malignancies and (b) solid tumors and brain tumors showed as six causes of death. *Note that each bar in the chart represents the proportion of all deaths occurring from five-years to assessed time-point by six causes.

a)



b)

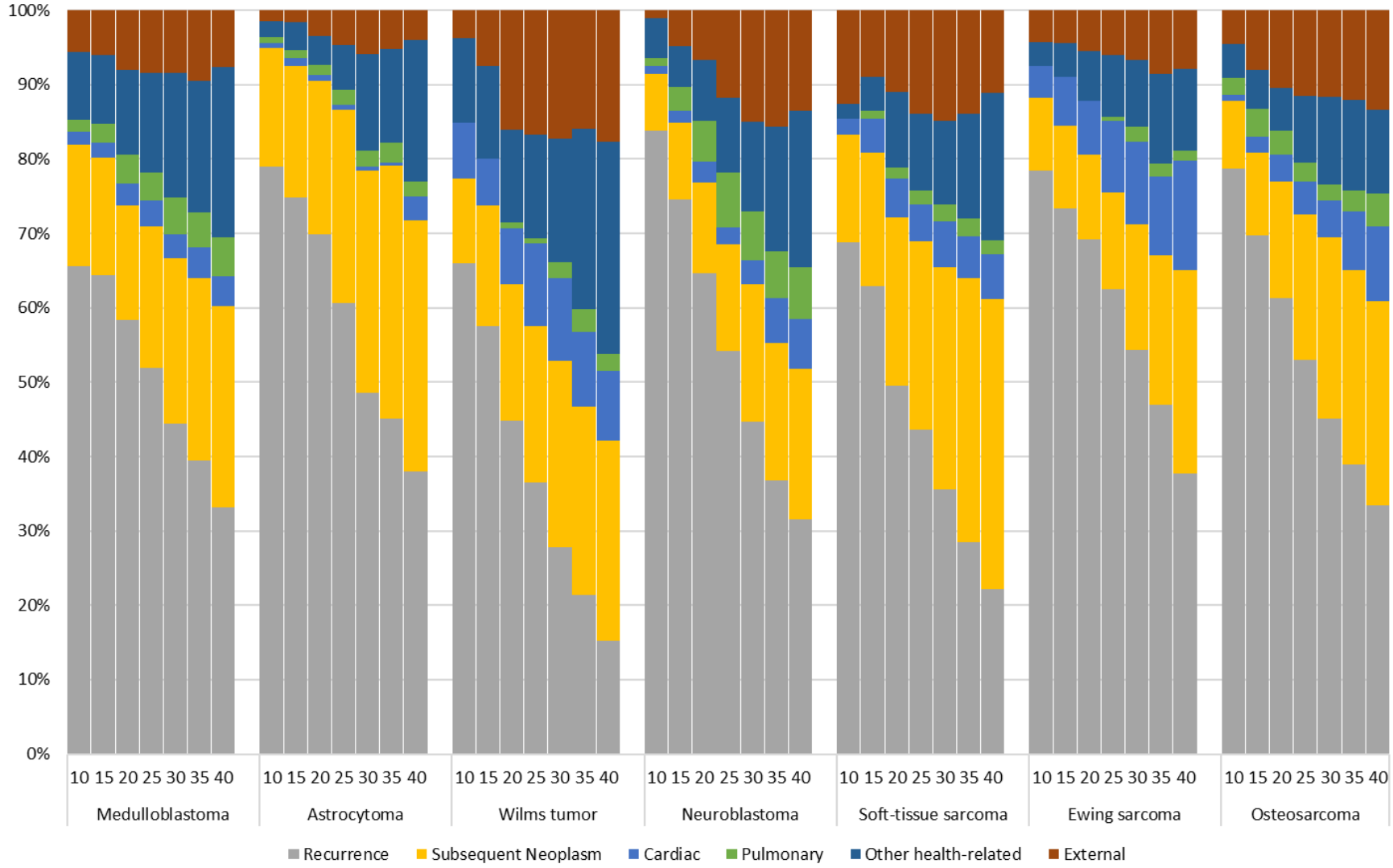

100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
10 15 20 25 30 35 40
Medulloblastoma
Astrocytoma
Wilms tumor
Neuroblastoma
Soft-tissue sarcoma
Ewing sarcoma
Osteosarcoma
Recurrence
Subsequent Neoplasm
Cardiac
Pulmonary
Other health-related
External

Figure S9. Standardized Mortality Ratios (with 95% CI) for all-cause and health-related cases of death among five-year survivors compared to the US population by time from diagnosis.

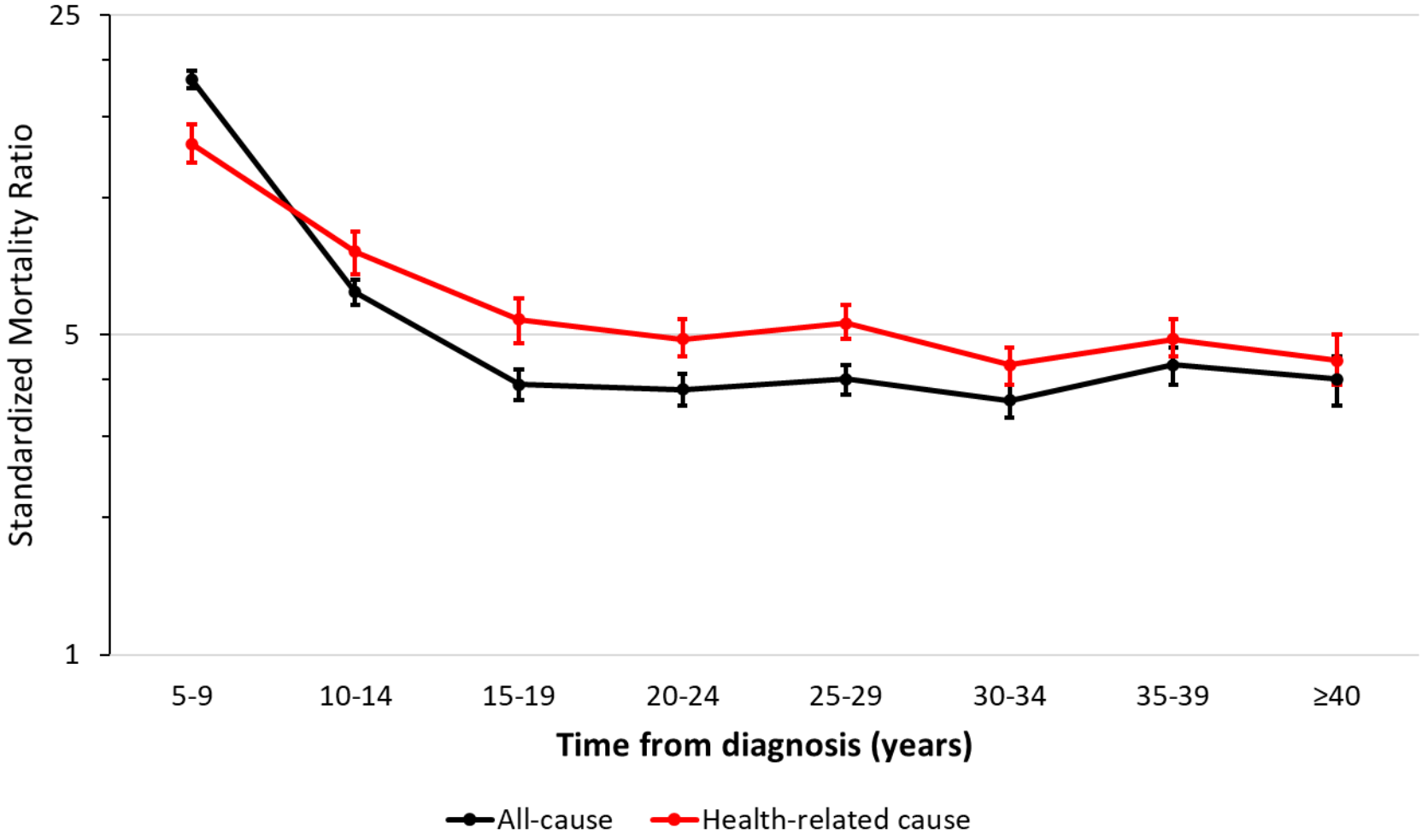


Figure S10. Absolute excess risk of death per 10,000 person-years by survival time among five-year survivors as cause-specific mortality by diagnosis.

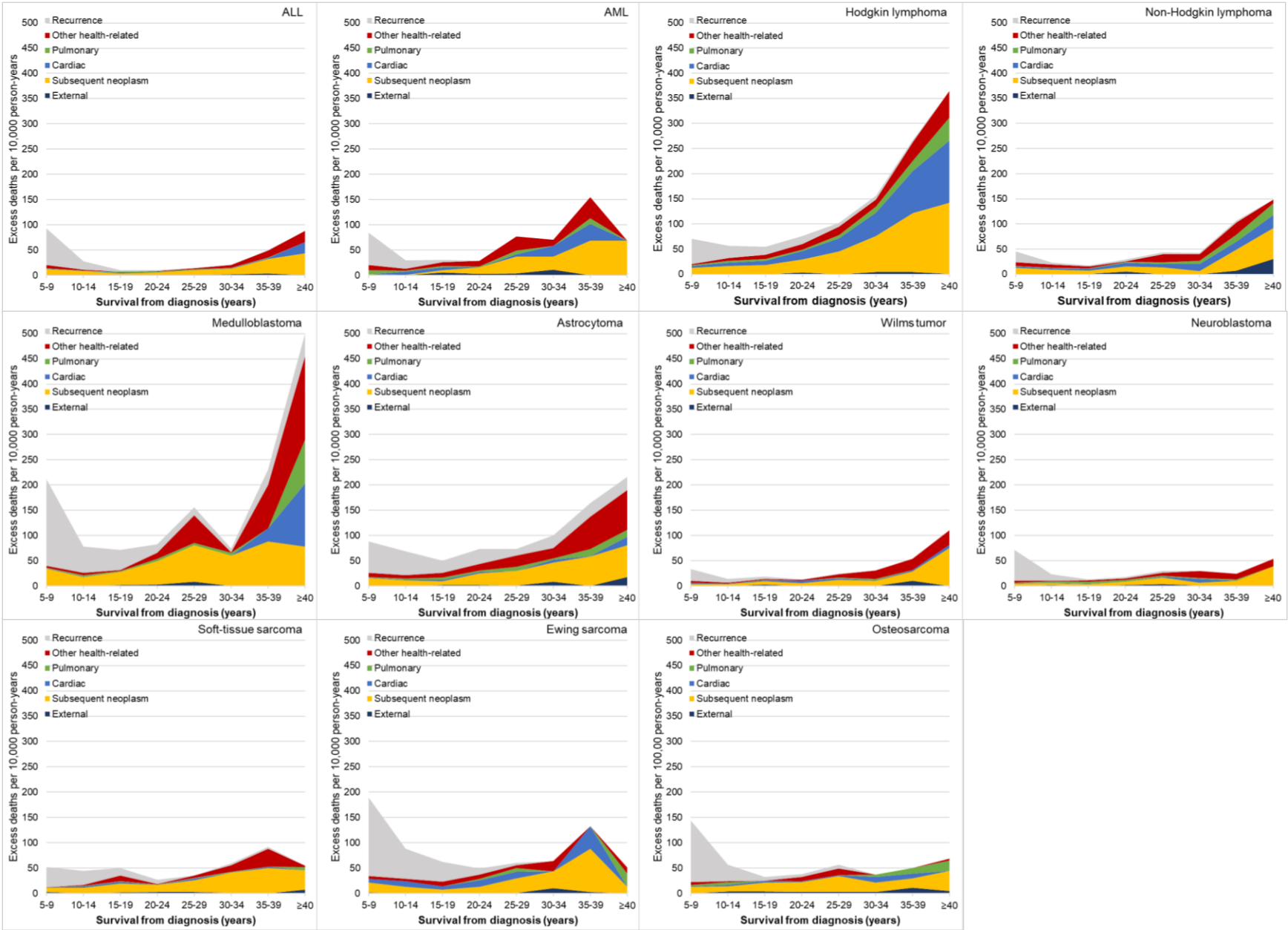
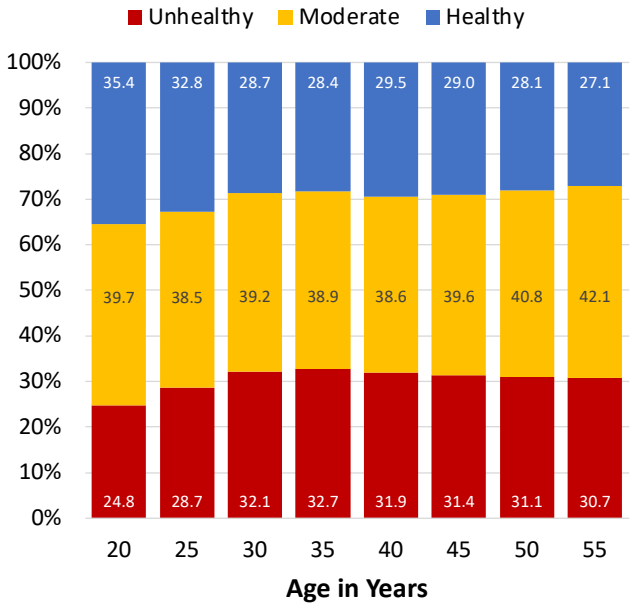


Figure S11. Distribution of lifestyle category and cumulative incidence of modifiable cardiovascular risk factors by age.

a)



b)

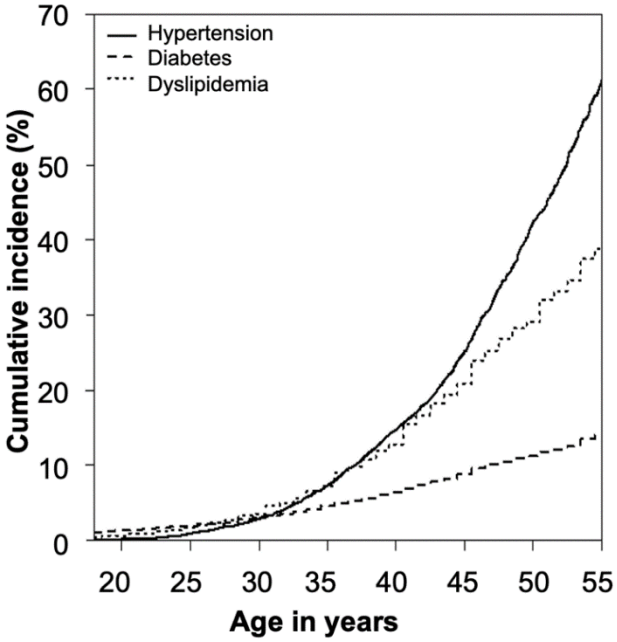


Table S1. Frequency of deaths by cause in the Childhood Cancer Survivor Study (all eligible) modified from the 113 selected causes of death according to the 9th and 10th revision of International Classification of Disease (ICD) codes from the National Center for Vital Statistics and Center for Disease Control.[1]

Category	Specific Cause of Death (subcategories)	ICD-10 Code	ICD-9 Code	N sub	N
Primary cancer cause: recurrence/progression					**2009**
Second neoplasm causes					**1458**
	Oropharyngeal and gastrointestinal malignancies	C00-C25	140-157		212
	Lip, oral cavity and pharynx	C00-C14	140-149	25	
	Esophagus	C15	150	16	
	Stomach	C16	151	31	
	Small intestine	C17	152	6	
	Colon, rectum and anus	C18-C21	153-154	74	
	Liver and intrahepatic bile ducts	C22	155	31	
	Pancreas	C25	157	26	
	Gallbladder and extrahepatic bile ducts	C23-C24	156	3	
	Laryngeal, tracheal and lung malignancies	C32-C34	161-162		90
	Larynx	C32	161	2	
	Trachea, bronchus and lung	C33-C34	162	88	
	Skin cancers	C43-C44	172-173		23
	Melanoma	C43	172	19	
	Other malignancies of the skin	C44	173	4	
	Breast cancer	C50	174-175		107
	Genitourinary malignancies	C51-C58, C60-C68	179-189		69
	Cervix	C53	180	5	
	Uterus	C54-C55	179, 182	7	
	Ovary	C56	183.0	9	
	Prostate	C61	185	5	
	Kidney and renal pelvis	C64-C65	189.0, 189.1	27	
	Bladder	C67	188	11	
	Other reproductive or urinary tract	C51-C52, C57-C58, C60, C62-C63, C66, C68	181, 183.2-183.9, 184, 186-187, 189.2-189.9	5	
	CNS malignancies	C70-C72	191-192		229
	Bone, connective, and soft tissue malignancies	C40, C41, C49	170-171		145
	Hodgkin lymphoma	C81	201		36
	Non-Hodgkin lymphoma	C82-C85	200, 202		62
	Leukemia	C91-C95	204-208		116
	Benign meningioma	D32	225.2, 225.4		21
	All other specified neoplasms				167
	All other malignant neoplasms	C26–C31, C37–C39, C45–C48, C69, C73-C79, C88, C90, C96 (excl 96.9) C97	158–160, 163-165, 173, 190, 193–198, 203, 209	152	
	Other neoplasms	D010 D126 D180 D332 D361 D469	212.5 212.7 225.1	15	
	Malignant and other neoplasms NOS				181
	Malignant, NOS	C79.9, C80, C96.9	199, 202.9	15	
	Other neoplasms, NOS	D09.9, D36.9, D37-D44, D47-48	229.9, 235-237, 238.0-238.3, 238.79, 238.8, 238.9, 239	166	
Cardiac causes					**504**
	Rheumatic and other valvular heart disease	I00-I09, I34-I39	390-398, 424		62
	Hypertensive heart disease	I11, I13	402, 404		12
	Ischemic heart disease	I20-I25	410-414, 429.2, 429.7		182
	Acute myocardial infarction	I21-I22	410	61	

	Other acute and chronic ischemic heart disease	I20, I23-I25	411-414, 429.2, 429.7	121	
	Heart failure and cardiomyopathy	I42, I43, I50	425, 428		157
	Heart failure	I50	428	40	
	Cardiomyopathy	I42, I43	425	117	
	Cardiac arrhythmias	I47-I49	427 (excluding 427.5)		15
	Other specified heart disease	I26-I33, I40-I41, I44-I46, I51 (excl I51.89, I51.9)	415-423, 426, 427.5, 429 (excl 429.2, 429.7, 429.89, 429.9)		60
	Heart disease, NOS	I51.89, I51.9	429.89, 429.9		16
Pulmonary causes					**238**
	Influenza and pneumonia	J09-J18	480-487		88
	Influenza	J09-J11	487, 488	9	
	Pneumonia	J12-J18	480-486	79	
	Chronic lower respiratory disease, includes asthma and chronic obstructive lung diseases	J40-J47	490-494, 496		23
	Aspiration pneumonitis	J69	507		26
	Interstitial lung disease, includes pulmonary fibrosis	J84	515, 516		50
	Other specified respiratory diseases	J00-J06, J20-J22, J30-J39, J60-J68, J70-J83, J85-J98	034.0, 460-478, 495, 500-506, 508-514, 517-519		51
Other health-related cause					**861**
	Sepsis	A40–A41	038		68
	Viral Hepatitis	B15–B19	070		31
	HIV and other infectious causes of death	A00-A39, A42-A99, B00-B14, B20-B99	001-037, 039-069, 071-139, 771.3		79
	HIV	B20-B24	042-044	25	
	Other infectious causes of death	A00-A39, A42-A99, B00-B14, B25-B99	001-037, 039-041, 045-069, 071-139, 771.3	54	
	Diabetes mellitus	E10-E14	250		34
	Essential hypertension and assoc. kidney disease	I10, I12	401, 403		10
	Cerebrovascular disease	I60-I69	430-434, 436-438		100
	Other atherosclerotic and vascular disease	I70, I71-I78, I80-I99	440, 441-448, 451-459		31
	Chronic liver disease and cirrhosis	K70, K73, K74	571		38
	Alcoholic liver disease	K70	571.0-571.3	16	
	Other chronic liver disease and cirrhosis	K73, K74	571.4-571.9	22	
	Other diseases of the gastrointestinal system	K25-K28, K35-K38, K40-K46, K80-K82	531-534, 540-543, 550-553, 574-575		13
	Kidney failure	N17-N19	584-586		48
	Complications of pregnancy, childbirth and the peripartum	O00-O99	630-676		9
	Congenital malformations and chromosomal anomalies	Q00-Q99	740-759		49
	Other health-related causes	Residual (all known codes not otherwise specified)	Residual (all known codes not otherwise specified)		307
	Ill-defined or NOS causes	R00-R99	780-799		44
External causes					**552**
	All transportation accidents	V01-V99, Y85	E800-E848, E929.0, E929.1		181
	Falls	W00-W19	E880-E888		24
	Other accidents and sequelae	W20-W99, X00-X39, X50-X59, Y86	E890-E929 (excl E924.1, E929.0, E929.1)		54
	Accidental poisoning and exposure to noxious substance	X40-X49	E850-E868, E924.1		103
	Suicide	X60-X84, X87.0	E950-E959		101

	By firearm	X72-X74	E955.0-E955.4	61	
	By other method	X60-X71, X75-X84, X87.0	E950-E954, E955.5-E959	40	
	Homicide				39
	By firearm	X93-X95	E965.0-E965.4	26	
	By other method	X85-X92, X96-Y09, Y87.1	E960-E964, E965.5-E969	13	
	Complications of medical and surgical care	Y40-Y84, Y88	E870-E879, E930-E949		30
	Other external causes	Y10-Y36, Y87.2, Y89	E970-E978, E980-E999		20

Central nervous system (CNS); Human immunodeficiency Virus (HIV); Not otherwise specified (NOS)

Table S2. Cumulative incidence (%) of all-cause and cause-specific mortality at 20 years-40 years survival time by cancer diagnosis.

	At risk	All-cause	Recurrence/ Progression	External cause (accident/injury)	Health-related cause
		Cumulative incidence (95% CI)	Cumulative incidence (95% CI)	Cumulative incidence (95% CI)	Cumulative incidence (95% CI)
20-years from diagnosis					
All survivors	28369	9·1 (8·8 - 9·4)	4·9 (4·7 - 5·1)	0·8 (0·7 - 0·8)	2·9 (2·8 - 3·1)
Sex					
Male	15709	9·7 (9·3 - 10·1)	5·2 (4·9 - 5·5)	1·0 (0·9 - 1·1)	3·0 (2·7 - 3·2)
Female	12660	8·3 (7·9 - 8·7)	4·5 (4·2 - 4·8)	0·4 (0·3 - 0·5)	2·9 (2·7 - 3·2)
Diagnosis					
Acute lymphoblastic leukemia	7459	7·6 (7·2 - 8·1)	4·5 (4·2 - 4·8)	0·6 (0·5 - 0·8)	2·1 (1·9 - 2·4)
Acute myeloid leukemia	1020	8·8 (7·2 - 10·3)	4·1 (3·0 - 5·2)	1·0 (0·4 - 1·5)	2·9 (2·0 - 3·8)
Other leukemia	425	18·4 (15·2 - 21·6)	11·3 (8·7 - 13·9)	0·7 (0·0 - 1·4)	4·1 (2·4 - 5·7)
Astrocytoma	3043	11·6 (10·6 - 12·6)	6·3 (5·6 - 7·1)	0·9 (0·6 - 1·2)	3·7 (3·1 - 4·3)
Medulloblastoma	970	18·2 (16·2 - 20·3)	11·9 (10·2 - 13·7)	0·6 (0·2 - 1·0)	4·6 (3·5 - 5·7)
Other CNS tumors	705	13·5 (11·3 - 15·6)	8·1 (6·4 - 9·9)	0·7 (0·2 - 1·3)	4·0 (2·7 - 5·2)
Hodgkin lymphoma	3628	10·9 (10·0 - 11·8)	4·3 (3·7 - 5·0)	0·9 (0·6 - 1·2)	5·0 (4·3 - 5·6)
Non-Hodgkin lymphoma	2443	5·9 (5·0 - 6·7)	1·3 (0·9 - 1·7)	1·1 (0·7 - 1·4)	3·3 (2·6 - 4·0)
Wilms tumor	2732	4·1 (3·4 - 4·8)	1·8 (1·3 - 2·2)	0·6 (0·3 - 0·9)	1·5 (1·1 - 2·0)
Neuroblastoma	2240	5·9 (5·0 - 6·8)	3·7 (2·9 - 4·4)	0·4 (0·1 - 0·6)	1·6 (1·1 - 2·1)
Soft tissue sarcoma	1456	8·6 (7·3 - 9·9)	4·0 (3·1 - 5·0)	0·9 (0·4 - 1·3)	3·2 (2·4 - 4·1)
Ewing sarcoma	760	17·6 (15·2 - 19·9)	11·5 (9·5 - 13·5)	0·9 (0·3 - 1·5)	4·2 (3·0 - 5·5)
Osteosarcoma	1438	13·2 (11·7 - 14·8)	7·7 (6·4 - 8·9)	1·3 (0·8 - 1·8)	3·5 (2·7 - 4·4)
Other bone tumors	62	7·4 (1·7 - 13·1)	2·5 (0·0 - 5·8)	1·2 (0·0 - 3·6)	3·7 (0·0 - 7·8)
25-years from diagnosis					
All survivors	21730	11·3 (11·0 - 11·7)	5·2 (5·0 - 5·4)	1·1 (1·0 - 1·2)	4·3 (4·1 - 4·5)
Sex					
Male	11927	12·2 (11·7 - 12·6)	5·6 (5·3 - 5·9)	1·5 (1·4 - 1·7)	4·3 (4·1 - 4·6)
Female	9803	10·3 (9·8 - 10·7)	4·8 (4·5 - 5·1)	0·6 (0·5 - 0·8)	4·3 (4·0 - 4·6)
Diagnosis					
Acute lymphoblastic leukemia	6126	8·8 (8·3 - 9·3)	4·6 (4·3 - 4·9)	1·0 (0·8 - 1·1)	2·8 (2·5 - 3·1)
Acute myeloid leukemia	712	10·7 (8·9 - 12·4)	4·1 (3·0 - 5·2)	1·4 (0·7 - 2·1)	4·3 (3·1 - 5·5)
Other leukemia	319	20·7 (17·3 - 24·1)	11·3 (8·7 - 13·9)	0·9 (0·1 - 1·7)	5·9 (3·9 - 8·0)
Astrocytoma	2153	15·5 (14·3 - 16·7)	7·6 (6·7 - 8·5)	1·2 (0·9 - 1·6)	5·8 (5·0 - 6·6)
Medulloblastoma	647	22·1 (19·9 - 24·4)	12·6 (10·8 - 14·4)	1·0 (0·4 - 1·5)	7·2 (5·8 - 8·7)
Other CNS tumors	445	16·8 (14·3 - 19·3)	9·3 (7·4 - 11·2)	0·9 (0·3 - 1·5)	6·0 (4·4 - 7·6)
Hodgkin lymphoma	2784	15·4 (14·3 - 16·5)	5·0 (4·4 - 5·7)	1·4 (1·0 - 1·7)	7·9 (7·1 - 8·8)
Non-Hodgkin lymphoma	1837	8·0 (7·0 - 9·1)	1·4 (1·0 - 1·9)	1·7 (1·2 - 2·1)	4·6 (3·8 - 5·4)
Wilms tumor	2119	5·3 (4·5 - 6·1)	1·8 (1·3 - 2·3)	0·8 (0·5 - 1·2)	2·3 (1·8 - 2·9)
Neuroblastoma	1692	7·3 (6·3 - 8·4)	3·8 (3·1 - 4·5)	0·8 (0·4 - 1·2)	2·4 (1·8 - 3·0)
Soft tissue sarcoma	1159	10·7 (9·2 - 12·2)	4·4 (3·4 - 5·3)	1·4 (0·8 - 2·0)	4·2 (3·3 - 5·2)
Ewing sarcoma	570	20·1 (17·6 - 22·7)	12·0 (10·0 - 14·0)	1·2 (0·5 - 1·8)	6·1 (4·5 - 7·6)
Osteosarcoma	1154	15·7 (14·0 - 17·4)	7·9 (6·6 - 9·1)	1·7 (1·1 - 2·3)	5·3 (4·2 - 6·3)
Other bone tumors	26	12·6 (3·8 - 21·5)	2·5 (0·0 - 5·8)	1·2 (0·0 - 3·6)	8·9 (0·9 - 17·0)
30-years from diagnosis					
All survivors	16139	14·2 (13·8 - 14·6)	5·4 (5·2 - 5·6)	1·5 (1·4 - 1·6)	6·5 (6·2 - 6·8)
Sex					
Male	8797	15·2 (14·6 - 15·7)	5·8 (5·5 - 6·1)	2·0 (1·8 - 2·2)	6·4 (6·1 - 6·8)
Female	7343	13·0 (12·4 - 13·5)	4·9 (4·6 - 5·2)	0·8 (0·7 - 0·9)	6·5 (6·1 - 7·0)
Diagnosis					
Acute lymphoblastic leukemia	5062	10·2 (9·7 - 10·8)	4·6 (4·3 - 5·0)	1·3 (1·1 - 1·6)	3·6 (3·3 - 4·0)
Acute myeloid leukemia	432	15·0 (12·7 - 17·4)	4·1 (3·0 - 5·2)	1·9 (1·0 - 2·7)	8·1 (6·2 - 10·0)
Other leukemia	228	23·6 (19·9 - 27·3)	11·6 (8·9 - 14·2)	0·9 (0·1 - 1·7)	8·3 (5·7 - 10·9)
Astrocytoma	1369	19·3 (17·9 - 20·7)	8·1 (7·2 - 9·0)	1·5 (1·1 - 2·0)	8·6 (7·5 - 9·6)
Medulloblastoma	374	28·4 (25·7 - 31·2)	13·2 (11·3 - 15·0)	1·6 (0·8 - 2·4)	12·4 (10·2 - 14·5)
Other CNS tumors	260	21·1 (18·0 - 24·1)	9·5 (7·6 - 11·4)	1·4 (0·5 - 2·4)	9·5 (7·2 - 11·9)
Hodgkin lymphoma	2096	20·8 (19·4 - 22·1)	5·3 (4·6 - 6·0)	1·6 (1·2 - 2·0)	12·5 (11·4 - 13·6)
Non-Hodgkin lymphoma	1315	10·9 (9·6 - 12·2)	1·5 (1·1 - 2·0)	1·8 (1·3 - 2·4)	7·0 (5·9 - 8·0)
Wilms tumor	1588	7·0 (6·1 - 8·0)	1·8 (1·4 - 2·3)	1·1 (0·7 - 1·6)	3·6 (2·9 - 4·4)
Neuroblastoma	1228	9·3 (8·1 - 10·6)	4·0 (3·2 - 4·8)	1·3 (0·8 - 1·9)	3·6 (2·8 - 4·4)
Soft tissue sarcoma	884	13·3 (11·6 - 15·0)	4·4 (3·4 - 5·3)	1·8 (1·1 - 2·5)	6·1 (4·8 - 7·3)
Ewing sarcoma	417	23·9 (21·0 - 26·7)	12·2 (10·1 - 14·2)	1·5 (0·7 - 2·3)	8·7 (6·8 - 10·7)
Osteosarcoma	885	19·1 (17·1 - 21·0)	8·2 (6·9 - 9·5)	2·1 (1·4 - 2·8)	7·8 (6·5 - 9·2)

Other bone tumors	14	12·6 (3·8 - 21·5)	2·5 (0·0 - 5·8)	1·2 (0·0 - 3·6)	8·9 (0·9 - 17·0)
35-years from diagnosis					
All survivors	9924	17·7 (17·2 - 18·1)	5·6 (5·3 - 5·8)	1·9 (1·7 - 2·1)	9·3 (8·9 - 9·7)
Sex					
Male	5388	18·9 (18·3 - 19·6)	6·0 (5·6 - 6·3)	2·6 (2·3 - 2·8)	9·4 (8·9 - 9·9)
Female	4536	16·1 (15·5 - 16·8)	5·1 (4·7 - 5·4)	1·1 (0·9 - 1·2)	9·1 (8·6 - 9·7)
Diagnosis					
Acute lymphoblastic leukemia	3095	12·1 (11·4 - 12·7)	4·7 (4·3 - 5·0)	1·7 (1·4 - 2·0)	5·0 (4·5 - 5·5)
Acute myeloid leukemia	238	19·3 (16·3 - 22·4)	4·1 (3·0 - 5·2)	2·7 (1·4 - 3·9)	11·4 (8·8 - 14·0)
Other leukemia	141	27·6 (23·3 - 32·0)	11·6 (8·9 - 14·2)	0·9 (0·1 - 1·7)	11·9 (8·5 - 15·3)
Astrocytoma	713	24·3 (22·6 - 26·1)	9·2 (8·1 - 10·2)	2·2 (1·6 - 2·8)	11·9 (10·5 - 13·2)
Medulloblastoma	197	31·6 (28·5 - 34·8)	13·5 (11·6 - 15·5)	1·6 (0·8 - 2·4)	14·9 (12·3 - 17·4)
Other CNS tumors	130	26·4 (22·5 - 30·4)	9·8 (7·8 - 11·8)	2·2 (0·7 - 3·7)	13·8 (10·4 - 17·1)
Hodgkin lymphoma	1385	28·3 (26·7 - 30·0)	5·6 (4·9 - 6·3)	2·0 (1·5 - 2·5)	19·1 (17·7 - 20·6)
Non-Hodgkin lymphoma	761	14·1 (12·5 - 15·7)	1·7 (1·1 - 2·2)	2·2 (1·6 - 2·8)	9·6 (8·2 - 11·0)
Wilms tumor	1014	9·1 (7·9 - 10·4)	1·8 (1·4 - 2·3)	1·4 (0·9 - 1·9)	5·4 (4·4 - 6·4)
Neuroblastoma	799	11·2 (9·8 - 12·7)	4·0 (3·2 - 4·8)	1·7 (1·1 - 2·3)	5·1 (4·1 - 6·2)
Soft tissue sarcoma	592	16·8 (14·7 - 18·8)	4·5 (3·5 - 5·5)	2·2 (1·4 - 3·0)	9·0 (7·4 - 10·7)
Ewing sarcoma	266	27·4 (24·2 - 30·6)	12·2 (10·1 - 14·2)	2·2 (1·1 - 3·4)	11·5 (9·1 - 13·9)
Osteosarcoma	596	21·9 (19·8 - 24·1)	8·2 (6·9 - 9·5)	2·5 (1·7 - 3·3)	10·3 (8·6 - 11·9)
Other bone tumors	9	22·3 (2·7 - 41·9)	2·5 (0·0 - 5·8)	1·2 (0·0 - 3·6)	18·6 (0·0 - 38·0)
40-years from diagnosis					
All survivors	4550	23·3 (22·7 - 24·0)	5·8 (5·5 - 6·0)	2·3 (2·1 - 2·5)	14·3 (13·7 - 14·9)
Sex					
Male	2433	24·5 (23·6 - 25·4)	6·2 (5·9 - 6·6)	3·0 (2·7 - 3·3)	14·2 (13·4 - 15·0)
Female	2119	21·9 (20·9 - 22·9)	5·2 (4·8 - 5·5)	1·4 (1·1 - 1·7)	14·4 (13·5 - 15·3)
Diagnosis					
Acute lymphoblastic leukemia	1414	15·6 (14·6 - 16·6)	4·7 (4·4 - 5·1)	2·2 (1·8 - 2·6)	8·0 (7·1 - 8·8)
Acute myeloid leukemia	82	26·3 (21·7 - 30·9)	4·1 (3·0 - 5·2)	2·7 (1·4 - 3·9)	18·3 (14·0 - 22·7)
Other leukemia	78	28·9 (24·3 - 33·5)	11·6 (8·9 - 14·2)	0·9 (0·1 - 1·7)	13·2 (9·4 - 17·0)
Astrocytoma	331	31·8 (29·3 - 34·4)	10·2 (8·9 - 11·5)	2·3 (1·7 - 3·0)	18·2 (15·9 - 20·4)
Medulloblastoma	69	40·6 (35·5 - 45·7)	14·8 (12·2 - 17·4)	1·6 (0·8 - 2·4)	22·6 (17·9 - 27·2)
Other CNS tumors	50	37·8 (31·2 - 44·3)	11·6 (8·4 - 14·8)	4·3 (1·1 - 7·4)	21·3 (15·8 - 26·7)
Hodgkin lymphoma	653	39·2 (37·1 - 41·3)	5·7 (5·0 - 6·5)	2·4 (1·8 - 2·9)	29·4 (27·4 - 31·4)
Non-Hodgkin lymphoma	281	20·7 (18·1 - 23·2)	1·9 (1·2 - 2·6)	2·8 (1·9 - 3·7)	15·1 (12·8 - 17·4)
Wilms tumor	480	12·6 (10·8 - 14·3)	1·8 (1·4 - 2·3)	2·1 (1·4 - 2·9)	8·1 (6·6 - 9·7)
Neuroblastoma	399	13·1 (11·3 - 14·8)	4·0 (3·2 - 4·8)	1·7 (1·1 - 2·3)	7·0 (5·5 - 8·5)
Soft tissue sarcoma	322	22·0 (19·3 - 24·7)	4·6 (3·6 - 5·7)	2·3 (1·5 - 3·2)	13·9 (11·5 - 16·4)
Ewing sarcoma	115	33·7 (29·5 - 37·9)	12·2 (10·1 - 14·2)	2·5 (1·2 - 3·9)	17·5 (13·8 - 21·2)
Osteosarcoma	282	25·4 (22·8 - 28·0)	8·2 (6·9 - 9·5)	3·3 (2·2 - 4·4)	13·0 (10·9 - 15·2)
Other bone tumors	7	22·3 (2·7 - 41·9)	2·5 (0·0 - 5·8)	1·2 (0·0 - 3·6)	18·6 (0·0 - 38·0)

Table S2 continued. Cumulative incidence (%) of all-cause and cause-specific mortality at 20 years-40 years survival time by cancer diagnosis.

		Health-related causes of death			
	At risk	Subsequent neoplasm	Cardiac	Pulmonary	Other
		Cumulative incidence (95% CI)	Cumulative incidence (95% CI)	Cumulative incidence (95% CI)	Cumulative incidence (95% CI)
20-years from diagnosis					
All survivors	28369	1·5 (1·4 - 1·6)	0·4 (0·3 - 0·4)	0·3 (0·2 - 0·3)	0·8 (0·7 - 0·9)
Sex					
Male	15709	1·5 (1·3 - 1·7)	0·4 (0·3 - 0·5)	0·3 (0·2 - 0·3)	0·8 (0·7 - 0·9)
Female	12660	1·5 (1·3 - 1·7)	0·3 (0·2 - 0·4)	0·3 (0·2 - 0·3)	0·8 (0·7 - 1·0)
Diagnosis					
Acute lymphoblastic leukemia	7459	1·2 (1·0 - 1·4)	0·2 (0·1 - 0·3)	0·2 (0·1 - 0·2)	0·6 (0·4 - 0·7)
Acute myeloid leukemia	1020	0·4 (0·1 - 0·8)	0·6 (0·2 - 1·1)	0·6 (0·2 - 1·1)	1·2 (0·6 - 1·8)
Other leukemia	425	1·4 (0·4 - 2·4)	0·5 (0·0 - 1·1)	0·9 (0·1 - 1·7)	1·2 (0·3 - 2·2)
Astrocytoma	3043	1·7 (1·3 - 2·1)	0·3 (0·1 - 0·5)	0·4 (0·2 - 0·6)	1·2 (0·9 - 1·6)
Medulloblastoma	970	3·5 (2·6 - 4·5)	0·1 (0·0 - 0·3)	0·2 (0·0 - 0·5)	0·7 (0·2 - 1·1)
Other CNS tumors	705	2·7 (1·7 - 3·8)	0·0 (0·0 - 0·4)	0·1 (0·0 - 0·3)	1·2 (0·5 - 1·8)
Hodgkin lymphoma	3628	2·4 (1·9 - 2·8)	1·0 (0·7 - 1·3)	0·5 (0·3 - 0·7)	1·1 (0·8 - 1·4)
Non-Hodgkin lymphoma	2443	1·5 (1·1 - 2·0)	0·5 (0·2 - 0·7)	0·2 (0·0 - 0·3)	1·1 (0·7 - 1·5)
Wilms tumor	2732	0·7 (0·4 - 1·0)	0·3 (0·1 - 0·5)	0·0 (0·0 - 0·1)	0·5 (0·2 - 0·7)
Neuroblastoma	2240	0·7 (0·4 - 1·0)	0·2 (0·0 - 0·3)	0·3 (0·1 - 0·5)	0·5 (0·2 - 0·7)
Soft tissue sarcoma	1456	1·8 (1·2 - 2·5)	0·4 (0·1 - 0·7)	0·1 (0·0 - 0·3)	0·8 (0·4 - 1·3)
Ewing sarcoma	760	1·9 (1·1 - 2·8)	1·2 (0·5 - 1·9)	0·0 (0·0 - 0·4)	1·1 (0·5 - 1·8)
Osteosarcoma	1438	2·0 (1·3 - 2·6)	0·5 (0·1 - 0·8)	0·4 (0·1 - 0·7)	0·7 (0·3 - 1·1)
Other bone tumors	62	2·5 (0·0 - 5·8)	0·0 (0·0 - 5·3)	1·2 (0·0 - 3·6)	0·0 (0·0 - 5·3)
25-years from diagnosis					
All survivors	21730	2·2 (2·0 - 2·3)	0·6 (0·5 - 0·7)	0·4 (0·3 - 0·4)	1·2 (1·1 - 1·3)
Sex					
Male	11927	2·1 (1·9 - 2·3)	0·7 (0·6 - 0·8)	0·4 (0·3 - 0·4)	1·2 (1·0 - 1·3)
Female	9803	2·2 (2·0 - 2·5)	0·5 (0·4 - 0·6)	0·4 (0·3 - 0·4)	1·2 (1·0 - 1·3)
Diagnosis					
Acute lymphoblastic leukemia	6126	1·6 (1·3 - 1·8)	0·2 (0·2 - 0·3)	0·2 (0·2 - 0·3)	0·7 (0·6 - 0·9)
Acute myeloid leukemia	712	1·1 (0·4 - 1·7)	0·6 (0·2 - 1·1)	0·8 (0·3 - 1·3)	1·9 (1·1 - 2·7)
Other leukemia	319	2·8 (1·3 - 4·3)	0·5 (0·0 - 1·1)	1·1 (0·2 - 2·0)	1·5 (0·5 - 2·5)
Astrocytoma	2153	2·8 (2·2 - 3·3)	0·5 (0·3 - 0·7)	0·6 (0·3 - 0·8)	2·0 (1·5 - 2·4)
Medulloblastoma	647	5·4 (4·1 - 6·7)	0·1 (0·0 - 0·3)	0·4 (0·0 - 0·8)	1·3 (0·6 - 1·9)
Other CNS tumors	445	3·7 (2·5 - 5·0)	0·3 (0·0 - 0·7)	0·1 (0·0 - 0·3)	1·9 (1·0 - 2·8)
Hodgkin lymphoma	2784	3·6 (3·1 - 4·2)	1·9 (1·4 - 2·3)	0·6 (0·4 - 0·9)	1·8 (1·4 - 2·2)
Non-Hodgkin lymphoma	1837	2·0 (1·5 - 2·6)	0·9 (0·6 - 1·3)	0·3 (0·1 - 0·5)	1·4 (0·9 - 1·8)
Wilms tumor	2119	1·0 (0·7 - 1·4)	0·5 (0·3 - 0·8)	0·0 (0·0 - 0·1)	0·7 (0·4 - 1·0)
Neuroblastoma	1692	1·0 (0·6 - 1·4)	0·2 (0·0 - 0·3)	0·5 (0·2 - 0·8)	0·7 (0·4 - 1·0)
Soft tissue sarcoma	1159	2·5 (1·8 - 3·3)	0·5 (0·2 - 0·8)	0·2 (0·0 - 0·4)	1·0 (0·5 - 1·5)
Ewing sarcoma	570	2·5 (1·5 - 3·5)	1·9 (1·0 - 2·7)	0·1 (0·0 - 0·3)	1·6 (0·8 - 2·4)
Osteosarcoma	1154	2·9 (2·1 - 3·7)	0·6 (0·3 - 1·0)	0·4 (0·1 - 0·7)	1·3 (0·8 - 1·9)
Other bone tumors	26	7·7 (0·0 - 15·4)	0·0 (0·0 - 1·3)	1·2 (0·0 - 3·6)	0·0 (0·0 - 1·3)
30-years from diagnosis					
All survivors	16139	3·2 (3·0 - 3·4)	0·9 (0·8 - 1·0)	0·5 (0·4 - 0·6)	1·9 (1·7 - 2·0)
Sex					
Male	8797	3·1 (2·8 - 3·4)	1·0 (0·8 - 1·2)	0·5 (0·4 - 0·6)	1·8 (1·6 - 2·0)
Female	7343	3·3 (3·0 - 3·6)	0·8 (0·6 - 0·9)	0·5 (0·4 - 0·6)	1·9 (1·7 - 2·2)
Diagnosis					
Acute lymphoblastic leukemia	5062	2·0 (1·8 - 2·3)	0·3 (0·2 - 0·4)	0·3 (0·2 - 0·5)	1·0 (0·8 - 1·2)
Acute myeloid leukemia	432	2·7 (1·5 - 3·9)	0·9 (0·3 - 1·5)	1·1 (0·4 - 1·8)	3·3 (2·1 - 4·6)
Other leukemia	228	3·1 (1·5 - 4·7)	0·8 (0·0 - 1·6)	1·1 (0·2 - 2·0)	3·3 (1·5 - 5·0)
Astrocytoma	1369	4·0 (3·3 - 4·8)	0·6 (0·3 - 0·9)	0·9 (0·5 - 1·3)	3·0 (2·4 - 3·7)
Medulloblastoma	374	8·1 (6·4 - 9·8)	0·1 (0·0 - 0·3)	0·6 (0·1 - 1·1)	3·5 (2·2 - 4·8)
Other CNS tumors	260	5·5 (3·7 - 7·2)	0·5 (0·0 - 1·1)	0·1 (0·0 - 0·3)	3·4 (1·9 - 5·0)
Hodgkin lymphoma	2096	5·7 (4·9 - 6·4)	3·1 (2·5 - 3·7)	1·0 (0·6 - 1·3)	2·8 (2·3 - 3·4)
Non-Hodgkin lymphoma	1315	2·8 (2·1 - 3·5)	1·3 (0·8 - 1·8)	0·5 (0·2 - 0·8)	2·3 (1·7 - 2·9)
Wilms tumor	1588	1·7 (1·1 - 2·2)	0·7 (0·4 - 1·1)	0·1 (0·0 - 0·3)	1·1 (0·7 - 1·5)
Neuroblastoma	1228	1·7 (1·1 - 2·2)	0·3 (0·0 - 0·5)	0·6 (0·3 - 0·9)	1·1 (0·6 - 1·5)
Soft tissue sarcoma	884	3·7 (2·7 - 4·6)	0·8 (0·3 - 1·2)	0·3 (0·0 - 0·6)	1·4 (0·8 - 2·0)
Ewing sarcoma	417	3·8 (2·4 - 5·1)	2·5 (1·4 - 3·6)	0·4 (0·0 - 1·0)	2·0 (1·1 - 3·0)
Osteosarcoma	885	4·4 (3·4 - 5·5)	0·9 (0·4 - 1·4)	0·4 (0·1 - 0·7)	2·1 (1·4 - 2·9)

Other bone tumors	14	7·7 (0·0 - 15·4)	0·0 (0·0 - 15·4)	1·2 (0·0 - 3·6)	0·0 (0·0 - 15·4)
35-years from diagnosis					
All survivors	9924	4·5 (4·2 - 4·7)	1·5 (1·3 - 1·6)	0·7 (0·6 - 0·8)	2·6 (2·4 - 2·8)
Sex					
Male	5388	4·3 (4·0 - 4·7)	1·7 (1·4 - 1·9)	0·7 (0·6 - 0·9)	2·7 (2·4 - 3·0)
Female	4536	4·6 (4·2 - 5·0)	1·3 (1·0 - 1·5)	0·7 (0·5 - 0·9)	2·6 (2·3 - 2·9)
Diagnosis					
Acute lymphoblastic leukemia	3095	2·7 (2·3 - 3·0)	0·4 (0·3 - 0·6)	0·4 (0·3 - 0·6)	1·5 (1·2 - 1·7)
Acute myeloid leukemia	238	4·0 (2·4 - 5·7)	2·1 (0·8 - 3·4)	1·1 (0·4 - 1·8)	4·1 (2·6 - 5·6)
Other leukemia	141	3·1 (1·5 - 4·7)	1·2 (0·1 - 2·4)	1·4 (0·3 - 2·5)	6·2 (3·5 - 8·9)
Astrocytoma	713	5·7 (4·7 - 6·7)	1·0 (0·5 - 1·4)	1·1 (0·6 - 1·5)	4·1 (3·3 - 5·0)
Medulloblastoma	197	10·2 (8·0 - 12·3)	0·1 (0·0 - 0·3)	0·8 (0·2 - 1·4)	3·8 (2·4 - 5·2)
Other CNS tumors	130	7·7 (5·2 - 10·2)	0·9 (0·0 - 1·8)	0·1 (0·0 - 0·3)	5·1 (2·9 - 7·3)
Hodgkin lymphoma	1385	8·8 (7·7 - 9·8)	5·2 (4·3 - 6·0)	1·5 (1·1 - 1·9)	3·7 (3·1 - 4·4)
Non-Hodgkin lymphoma	761	3·4 (2·6 - 4·2)	2·1 (1·4 - 2·8)	0·9 (0·4 - 1·3)	3·3 (2·4 - 4·1)
Wilms tumor	1014	2·2 (1·6 - 2·8)	0·9 (0·5 - 1·2)	0·3 (0·0 - 0·5)	2·1 (1·4 - 2·8)
Neuroblastoma	799	2·0 (1·3 - 2·6)	0·7 (0·2 - 1·1)	0·7 (0·3 - 1·0)	1·8 (1·2 - 2·5)
Soft tissue sarcoma	592	5·6 (4·2 - 6·9)	0·9 (0·4 - 1·4)	0·4 (0·0 - 0·7)	2·2 (1·4 - 3·1)
Ewing sarcoma	266	5·2 (3·5 - 6·9)	2·7 (1·6 - 3·9)	0·4 (0·0 - 1·0)	3·1 (1·8 - 4·5)
Osteosarcoma	596	5·5 (4·3 - 6·7)	1·6 (0·9 - 2·4)	0·6 (0·2 - 1·0)	2·5 (1·7 - 3·4)
Other bone tumors	9	7·7 (0·0 - 15·4)	0·0 (0·0 - 19·5)	1·2 (0·0 - 3·6)	9·7 (0·0 - 27·7)
40-years from diagnosis					
All survivors	4550	6·7 (6·3 - 7·1)	2·5 (2·2 - 2·8)	1·0 (0·9 - 1·2)	4·1 (3·8 - 4·5)
Sex					
Male	2433	6·4 (5·9 - 6·9)	2·8 (2·4 - 3·2)	1·0 (0·8 - 1·2)	4·0 (3·6 - 4·5)
Female	2119	7·0 (6·4 - 7·6)	2·1 (1·7 - 2·5)	1·1 (0·8 - 1·3)	4·2 (3·7 - 4·7)
Diagnosis					
Acute lymphoblastic leukemia	1414	4·2 (3·6 - 4·9)	0·7 (0·4 - 1·0)	0·5 (0·3 - 0·7)	2·5 (2·0 - 3·0)
Acute myeloid leukemia	82	6·8 (4·1 - 9·6)	3·7 (1·4 - 6·0)	1·7 (0·4 - 2·9)	6·2 (3·7 - 8·6)
Other leukemia	78	3·9 (1·7 - 6·0)	1·2 (0·1 - 2·4)	1·4 (0·3 - 2·5)	6·7 (3·8 - 9·6)
Astrocytoma	331	8·3 (6·7 - 9·9)	1·2 (0·7 - 1·8)	1·6 (0·9 - 2·3)	7·0 (5·5 - 8·6)
Medulloblastoma	69	13·2 (10·0 - 16·3)	1·2 (0·0 - 2·8)	0·8 (0·2 - 1·4)	7·4 (4·1 - 10·6)
Other CNS tumors	50	8·4 (5·6 - 11·2)	0·9 (0·0 - 1·8)	1·5 (0·0 - 3·5)	10·5 (6·0 - 14·9)
Hodgkin lymphoma	653	13·2 (11·8 - 14·6)	8·5 (7·3 - 9·7)	2·2 (1·6 - 2·9)	5·5 (4·5 - 6·4)
Non-Hodgkin lymphoma	281	5·5 (4·1 - 6·9)	3·3 (2·1 - 4·5)	1·5 (0·7 - 2·4)	4·8 (3·5 - 6·1)
Wilms tumor	480	3·3 (2·3 - 4·2)	1·1 (0·6 - 1·7)	0·3 (0·0 - 0·5)	3·5 (2·4 - 4·5)
Neuroblastoma	399	2·6 (1·7 - 3·4)	0·9 (0·3 - 1·4)	0·9 (0·3 - 1·4)	2·7 (1·7 - 3·7)
Soft tissue sarcoma	322	8·1 (6·2 - 10·0)	1·3 (0·5 - 2·0)	0·4 (0·0 - 0·7)	4·1 (2·7 - 5·6)
Ewing sarcoma	115	8·8 (6·0 - 11·6)	4·7 (2·6 - 6·8)	0·4 (0·0 - 1·0)	3·5 (2·0 - 5·1)
Osteosarcoma	282	6·7 (5·2 - 8·3)	2·5 (1·4 - 3·5)	1·1 (0·4 - 1·8)	2·7 (1·8 - 3·6)
Other bone tumors	7	7·7 (0·0 - 15·4)	0·0 (0·0 - 20·6)	1·2 (0·0 - 3·6)	9·7 (0·0 - 27·7)

Central nervous system (CNS)

Table S3. Standardized mortality ratios and 95% confidence intervals by cause of death in all eligible survivors.

	All-cause			External cause (accident/injury)			Health-related cause		
	SMR	**95% CI**	**p-value**	**SMR**	**95% CI**	**p-value**	**SMR**	**95% CI**	**p-value**
All survivors	5·6	5·4 - 5·7	<·001	1·1	1·0 - 1·2	0·013	5·6	5·4 - 5·8	<·001
Sex									
Male	4·6	4·4 - 4·7	<·001	1·0	0·9 - 1·1	0·52	4·8	4·6 - 5·1	<·001
Female	8·0	7·7 - 8·3	<·001	1·4	1·2 - 1·7	<·001	6·9	6·5 - 7·2	<·001
Diagnosis									
Acute lymphoblastic leukemia	4·7	4·4 - 4·9	<·001	1·0	0·9 - 1·2	0·95	4·2	3·9 - 4·5	<·001
Acute myeloid leukemia	6·2	5·3 - 7·1	<·001	1·5	0·9 - 2·2	0·11	6·6	5·4 - 8·1	<·001
Other leukemia	8·7	7·3 - 10·3	<·001	0·6	0·2 - 1·5	0·41	6·5	4·8 - 8·5	<·001
Astrocytoma	7·9	7·4 - 8·5	<·001	1·3	1·0 - 1·6	0·077	7·5	6·8 - 8·3	<·001
Medulloblastoma	12·9	11·6 - 14·3	<·001	1·0	0·6 - 1·6	0·99	13·0	11·1 - 15·2	<·001
Other CNS tumors	9·1	7·9 - 10·5	<·001	1·3	0·7 - 2·2	0·32	8·4	6·8 - 10·3	<·001
Hodgkin disease	6·2	5·8 - 6·5	<·001	1·1	0·9 - 1·3	0·51	6·9	6·4 - 7·4	<·001
Non-Hodgkin lymphoma	3·4	3·1 - 3·8	<·001	1·1	0·9 - 1·5	0·40	4·5	3·9 - 5·1	<·001
Wilms tumor	3·9	3·4 - 4·4	<·001	1·0	0·7 - 1·4	0·81	5·2	4·5 - 6·1	<·001
Neuroblastoma	5·0	4·4 - 5·7	<·001	1·0	0·7 - 1·5	0·90	5·5	4·5 - 6·5	<·001
Soft tissue sarcoma	4·8	4·2 - 5·4	<·001	1·2	0·8 - 1·7	0·28	4·9	4·2 - 5·8	<·001
Ewing sarcoma	7·3	6·5 - 8·3	<·001	1·1	0·7 - 1·8	0·66	5·3	4·3 - 6·4	<·001
Osteosarcoma	4·7	4·2 - 5·2	<·001	1·5	1·1 - 2·0	0·021	3·3	2·9 - 3·9	<·001
Other bone tumors	4·4	2·0 - 8·3	<·001	1·0	0·0 - 5·8	0·99	5·5	2·0 - 11·9	0·002
Survival after diagnosis (years)									
5-9	18·1	17·3 - 18·9	<·001	1·1	0·8 - 1·3	0·66	13·1	11·9 - 14·4	<·001
10-14	6·2	5·8 - 6·6	<·001	0·9	0·7 - 1·1	0·43	7·6	6·8 - 8·4	<·001
15-19	3·9	3·6 - 4·2	<·001	1·1	0·9 - 1·3	0·43	5·4	4·8 - 6·0	<·001
20-24	3·8	3·5 - 4·1	<·001	1·2	1·0 - 1·4	0·12	4·9	4·5 - 5·4	<·001
25-29	4·0	3·7 - 4·3	<·001	1·1	0·9 - 1·4	0·25	5·3	4·9 - 5·8	<·001
30-34	3·6	3·3 - 3·9	<·001	1·3	1·0 - 1·7	0·048	4·3	3·9 - 4·7	<·001
35-39	4·3	3·9 - 4·7	<·001	1·4	1·0 - 1·9	0·064	4·9	4·5 - 5·4	<·001
≥40	4·0	3·5 - 4·5	<·001	1·3	0·7 - 2·1	0·41	4·4	3·9 - 5·0	<·001

	Health-related causes of death											
	Subsequent neoplasm			Cardiac			Pulmonary			Other		
	SMR	**95% CI**	**P**	**SMR**	**95% CI**	**P**	**SMR**	**95% CI**	**P**	**SMR**	**95% CI**	**P**
All survivors	10·1	9·6 - 10·6	<·001	4·3	3·9 - 4·7	<·001	7·5	6·6 - 8·4	<·001	3·3	3·1 - 3·6	<·001
Sex												
Male	9·9	9·2 - 10·6	<·001	3·6	3·2 - 4·0	<·001	7·0	5·9 - 8·3	<·001	2·8	2·6 - 3·1	<·001
Female	10·3	9·6 - 11·1	<·001	6·2	5·4 - 7·1	<·001	8·1	6·7 - 9·8	<·001	4·3	3·9 - 4·8	<·001
Diagnosis												
Acute lymphoblastic leukemia	8·9	8·0 - 10·0	<·001	2·1	1·6 - 2·7	<·001	5·2	3·8 - 6·9	<·001	2·5	2·1 - 2·9	<·001
Acute myeloid leukemia	8·5	5·9 - 11·9	<·001	5·6	3·3 - 9·0	<·001	13·5	6·9 - 23·5	<·001	5·2	3·6 - 7·1	<·001
Other leukemia	8·5	5·0 - 13·6	<·001	3·0	1·0 - 6·9	0·057	15·7	6·3 - 32·4	<·001	5·9	3·7 - 8·9	<·001
Astrocytoma	13·1	11·2 - 15·2	<·001	3·0	2·0 - 4·2	<·001	12·1	8·4 - 16·8	<·001	5·8	4·8 - 6·8	<·001
Medulloblastoma	33·6	27·4 - 40·8	<·001	2·9	1·2 - 5·9	0·025	12·3	5·6 - 23·4	<·001	6·7	4·8 - 9·1	<·001
Other CNS tumors	17·4	12·9 - 23·0	<·001	1·8	0·5 - 4·6	0·37	6·3	1·7 - 16·1	0·008	6·6	4·6 - 9·2	<·001
Hodgkin disease	10·8	9·7 - 11·9	<·001	8·7	7·6 - 9·9	<·001	9·9	7·8 - 12·5	<·001	3·1	2·6 - 3·6	<·001
Non-Hodgkin lymphoma	6·9	5·6 - 8·5	<·001	4·1	3·1 - 5·5	<·001	7·1	4·4 - 10·8	<·001	3·0	2·4 - 3·8	<·001
Wilms tumor	9·2	7·2 - 11·6	<·001	4·4	2·9 - 6·5	<·001	2·7	0·9 - 6·4	0·078	3·8	2·9 - 5·0	<·001
Neuroblastoma	9·3	6·9 - 12·4	<·001	2·9	1·4 - 5·1	0·004	11·5	6·4 - 19·0	<·001	3·7	2·7 - 5·1	<·001
Soft tissue sarcoma	11·1	8·9 - 13·7	<·001	2·2	1·2 - 3·6	0·014	3·4	1·3 - 7·5	0·018	2·9	2·1 - 3·9	<·001
Ewing sarcoma	9·2	6·8 - 12·1	<·001	6·3	4·1 - 9·2	<·001	3·6	1·0 - 9·1	0·055	2·8	1·8 - 4·1	<·001
Osteosarcoma	6·3	5·0 - 7·7	<·001	2·3	1·5 - 3·4	<·001	4·9	2·6 - 8·1	<·001	1·8	1·3 - 2·4	0·001
Other bone tumors	12·6	3·4 - 32·4	<·001	0·0	0·0 - 16·7	0·99	14·7	0·2 - 81·5	0·13	2·0	0·0 - 11·3	0·78
Survival after diagnosis (years)												
5-9	29·5	26·0 - 33·4	<·001	8·8	6·1 - 12·3	<·001	13·0	8·9 - 18·4	<·001	6·4	5·3 - 7·7	<·001
10-14	17·4	15·0 - 20·1	<·001	7·1	5·2 - 9·4	<·001	11·7	8·1 - 16·2	<·001	3·4	2·7 - 4·2	<·001
15-19	10·8	9·2 - 12·6	<·001	6·0	4·7 - 7·6	<·001	8·7	6·0 - 12·1	<·001	2·7	2·2 - 3·3	<·001
20-24	10·7	9·3 - 12·3	<·001	4·1	3·2 - 5·2	<·001	6·5	4·4 - 9·4	<·001	2·6	2·1 - 3·1	<·001
25-29	9·7	8·5 - 11·1	<·001	3·2	2·5 - 4·1	<·001	7·8	5·5 - 10·8	<·001	3·6	3·0 - 4·2	<·001
30-34	6·6	5·7 - 7·6	<·001	3·7	2·9 - 4·5	<·001	5·5	3·7 - 7·8	<·001	2·8	2·4 - 3·4	<·001
35-39	7·2	6·2 - 8·3	<·001	3·9	3·1 - 4·8	<·001	5·5	3·7 - 7·9	<·001	3·7	3·1 - 4·4	<·001
≥40	6·0	4·9 - 7·2	<·001	3·9	2·9 - 5·0	<·001	5·6	3·6 - 8·4	<·001	3·1	2·3 - 3·9	<·001

Central nervous system (CNS); standardized mortality ratio (SMR)

Table S4. Absolute Excess Risk (AER) per 10,000 person-years and 95% confidence intervals by cause of death in all eligible survivors.

	All-cause			External cause (accident/injury)			Health-related cause		
	AER	**95% CI**	**p-value**	**AER**	**95% CI**	**p-value**	**AER**	**95% CI**	**p-value**
All survivors	56	54 - 57	<·001	1	0 - 1	0·013	29	27 - 30	<·001
Sex									
Male	57	54 - 59	<·001	0	0 - 1	0·52	28	26 - 29	<·001
Female	55	52 - 57	<·001	1	1 - 2	<·001	30	28 - 32	<·001
Diagnosis									
Acute lymphoblastic leukemia	38	35 - 40	<·001	0	0 - 1	0·95	15	13 - 16	<·001
Acute myeloid leukemia	57	47 - 67	<·001	3	0 - 7	0·11	31	24 - 39	<·001
Other leukemia	98	80 - 118	<·001	0	0 - 3	0·41	35	24 - 48	<·001
Astrocytoma	81	75 - 88	<·001	2	0 - 4	0·077	38	34 - 43	<·001
Medulloblastoma	128	114 - 143	<·001	0	0 - 4	0·99	55	46 - 65	<·001
Other CNS tumors	94	80 - 110	<·001	2	0 - 7	0·32	42	33 - 53	<·001
Hodgkin disease	97	91 - 14	<·001	1	0 - 2	0·51	69	64 - 75	<·001
Non-Hodgkin lymphoma	37	32 - 43	<·001	1	0 - 3	0·40	27	23 - 32	<·001
Wilms tumor	25	21 - 30	<·001	0	0 - 2	0·81	17	13 - 20	<·001
Neuroblastoma	32	27 - 37	<·001	0	0 - 2	0·90	15	12 - 18	<·001
Soft tissue sarcoma	50	43 - 58	<·001	1	0 - 5	0·28	28	22 - 34	<·001
Ewing sarcoma	100	86 - 115	<·001	1	0 - 6	0·66	39	30 - 49	<·001
Osteosarcoma	68	60 - 78	<·001	3	0 - 7	0·021	27	22 - 34	<·001
Other bone tumors	45	13 - 97	<·001	0	0 - 30	0·99	32	7 - 77	0·002
Survival after diagnosis (years)									
5-9	95	91 - 100	<·001	0	0 - 1	0·66	21	19 - 23	<·001
10-14	41	38 - 45	<·001	0	0 - 1	0·43	17	15 - 19	<·001
15-19	31	28 - 34	<·001	1	0 - 2	0·43	17	15 - 19	<·001
20-24	36	32 - 40	<·001	1	0 - 3	0·12	24	21 - 27	<·001
25-29	48	44 - 54	<·001	1	0 - 3	0·25	40	36 - 44	<·001
30-34	59	53 - 67	<·001	2	0 - 5	0·048	50	44 - 57	<·001
35-39	102	91 - 115	<·001	3	0 - 7	0·064	94	83 - 16	<·001
≥40	138	117 - 161	<·001	2	0 - 9	0·41	131	111 - 153	<·001

	Health-related causes of death											
	Subsequent neoplasm			Cardiac			Pulmonary			Other		
	AER	**95% CI**	**P**	**AER**	**95% CI**	**P**	**AER**	**95% CI**	**P**	**AER**	**95% CI**	**P**
All survivors	15	14 - 16	<·001	4	4 - 5	<·001	2	2 - 3	<·001	7	6 - 7	<·001
Sex												
Male	15	13 - 16	<·001	4	4 - 5	<·001	2	2 - 3	<·001	6	5 - 7	<·001
Female	16	14 - 17	<·001	4	3 - 5	<·001	2	2 - 3	<·001	8	7 - 9	<·001
Diagnosis												
Acute lymphoblastic leukemia	9	8 - 10	<·001	1	1 - 2	<·001	1	1 - 2	<·001	3	3 - 4	<·001
Acute myeloid leukemia	11	7 - 16	<·001	5	2 - 9	<·001	4	2 - 7	<·001	11	7 - 16	<·001
Other leukemia	12	6 - 20	<·001	3	0 - 8	0·057	5	2 - 11	<·001	15	8 - 24	<·001
Astrocytoma	19	16 - 22	<·001	2	1 - 4	<·001	4	3 - 5	<·001	13	11 - 16	<·001
Medulloblastoma	37	30 - 45	<·001	2	0 - 4	0·025	3	1 - 6	<·001	13	9 - 18	<·001
Other CNS tumors	24	18 - 33	<·001	1	0 - 4	0·37	2	0 - 5	0·008	15	10 - 22	<·001
Hodgkin disease	33	29 - 37	<·001	20	17 - 23	<·001	6	5 - 8	<·001	11	8 - 13	<·001
Non-Hodgkin lymphoma	12	9 - 15	<·001	6	4 - 8	<·001	3	1 - 4	<·001	7	5 - 10	<·001
Wilms tumor	8	6 - 10	<·001	2	1 - 4	<·001	0	0 - 1	0·078	6	4 - 8	<·001
Neuroblastoma	7	5 - 9	<·001	1	0 - 2	0·004	2	1 - 4	<·001	5	3 - 7	<·001
Soft tissue sarcoma	19	15 - 24	<·001	2	0 - 4	0·014	1	0 - 3	0·018	6	3 - 9	<·001
Ewing sarcoma	20	14 - 27	<·001	10	6 - 16	<·001	1	0 - 4	0·055	7	3 - 13	<·001
Osteosarcoma	18	13 - 22	<·001	3	1 - 6	<·001	3	1 - 5	<·001	4	1 - 7	0·001
Other bone tumors	24	5 - 64	<·001	0	0 - 22	0·99	6	0 - 36	0·13	3	0 - 33	0·78
Survival after diagnosis (years)												
5-9	13	11 - 14	<·001	2	1 - 2	<·001	2	1 - 2	<·001	5	4 - 6	<·001
10-14	9	8 - 11	<·001	2	1 - 3	<·001	2	1 - 2	<·001	3	3 - 5	<·001
15-19	8	7 - 10	<·001	3	2 - 4	<·001	2	1 - 2	<·001	4	3 - 5	<·001
20-24	13	12 - 16	<·001	4	3 - 5	<·001	2	1 - 3	<·001	5	4 - 7	<·001
25-29	21	18 - 24	<·001	5	3 - 6	<·001	3	2 - 5	<·001	11	9 - 14	<·001
30-34	25	21 - 29	<·001	10	7 - 13	<·001	4	2 - 6	<·001	12	9 - 16	<·001
35-39	46	38 - 54	<·001	17	12 - 22	<·001	7	4 - 10	<·001	25	19 - 32	<·001
≥40	62	49 - 78	<·001	27	18 - 38	<·001	13	7 - 21	<·001	29	19 - 41	<·001

Central nervous system (CNS)

Table S5. Risk of mortality due to specific causes of death in all eligible survivors and associations with treatment exposures.

	All-cause			Recurrence/Progression			External cause (accident/injury)			Health-related cause		
	RR	**95% CI**	**p-value**	**RR**	**95% CI**	**p-value**	**RR**	**95% CI**	**p-value**	**RR**	**95% CI**	**p-value**
Treatment exposures												
Cranial radiation per 10 Gy	1·18	1·15 - 1·20	<0·001	1·22	1·17 - 1·26	<0·001	1·05	1·00 - 1·12	0·062	1·15	1·12 - 1·18	<0·001
Chest radiation per 10 Gy	1·25	1·22 - 1·27	<0·001	1·19	1·15 - 1·23	<0·001	1·09	1·02 - 1·17	0·016	1·31	1·28 - 1·34	<0·001
TBI exposure, reference to No	1·50	1·26 - 1·78	<0·001	1·50	1·13 - 1·99	0·004	1·06	0·44 - 2·54	0·89	1·64	1·28 - 2·11	<0·001
Anthracycline per 100 mg/m^2	1·08	1·05 - 1·10	<0·001	1·11	1·07 - 1·15	<0·001	1·10	1·04 - 1·17	0·001	1·06	1·03 - 1·09	<0·001
Alkylator per 5000 mg/m^2	1·06	1·04 - 1·08	<0·001	1·07	1·04 - 1·11	<0·001	0·99	0·92 - 1·06	0·71	1·06	1·03 - 1·08	<0·001
Bleomycin per 50 mg/m^2	1·02	0·95 - 1·09	0·59	1·00	0·90 - 1·12	0·98	0·91	0·72 - 1·15	0·44	1·07	0·98 - 1·18	0·14
Epipodophyllotoxin per 1000 mg/m^2	1·03	1·01 - 1·05	0·003	1·03	1·01 - 1·06	0·010	1·02	0·97 - 1·08	0·39	1·03	1·00 - 1·06	0·029
Platinum per 500 mg/m^2	1·14	1·07 - 1·20	<0·001	1·20	1·11 - 1·30	<0·001	1·06	0·84 - 1·34	0·61	1·15	1·04 - 1·26	0·004
Methotrexate per 5000 mg/m^2	1·00	1·00 - 1·01	0·028	1·00	1·00 - 1·01	<0·001	1·00	0·99 - 1·01	0·90	1·00	0·99 - 1·01	0·60

	Health-related causes											
	Subsequent neoplasm			Cardiac			Pulmonary			Other		
	RR	**95% CI**	**p-value**	**RR**	**95% CI**	**p-value**	**RR**	**95% CI**	**p-value**	**RR**	**95% CI**	**p-value**
Treatment exposures												
Cranial radiation per 10 Gy	1·18	1·14 - 1·21	<0·001	0·96	0·89 - 1·04	0·30	1·15	1·07 - 1·24	<0·001	1·18	1·14 - 1·23	<0·001
Chest radiation per 10 Gy	1·30	1·26 - 1·35	<0·001	1·50	1·42 - 1·58	<0·001	1·30	1·19 - 1·42	<0·001	1·19	1·13 - 1·26	<0·001
TBI exposure, reference to No	1·49	1·00 - 2·22	0·047	0·67	0·27 - 1·66	0·39	2·55	1·30 - 4·99	0·006	2·29	1·57 - 3·35	<0·001
Anthracycline per 100 mg/m^2	1·05	1·01 - 1·09	0·020	1·16	1·09 - 1·23	<0·001	1·07	0·97 - 1·17	0·20	1·01	0·96 - 1·07	0·61
Alkylator per 5000 mg/m^2	1·06	1·03 - 1·09	<0·001	1·05	0·98 - 1·11	0·15	1·02	0·94 - 1·12	0·58	1·06	1·02 - 1·10	0·003
Bleomycin per 50 mg/m^2	1·08	0·95 - 1·22	0·26	1·10	0·90 - 1·35	0·34	1·07	0·76 - 1·51	0·70	1·04	0·83 - 1·29	0·73
Epipodophyllotoxin per 1000 mg/m^2	1·04	1·01 - 1·07	0·011	1·02	0·95 - 1·09	0·66	1·03	0·95 - 1·12	0·41	1·01	0·95 - 1·07	0·73
Platinum per 500 mg/m^2	1·20	1·08 - 1·34	<0·001	0·97	0·67 - 1·41	0·87	0·96	0·66 - 1·40	0·84	1·14	0·97 - 1·33	0·11
Methotrexate per 5000 mg/m^2	1·00	0·99 - 1·01	0·85	0·99	0·96 - 1·01	0·31	0·99	0·96 - 1·03	0·62	1·00	0·98 - 1·02	0·70

Relative rates (RR) are adjusted for all covariates displayed and sex, age at diagnosis, race/ethnicity and attained age adjusted as cubic splines. Statistically significant associations with treatment are bolded.

Table S6. Risk of mortality and associations with treatment exposures due to specific causes of death among survivors who have survived at least 30 years from diagnosis.

	All-cause		External cause (accident/injury)		Health-related cause	
	RR	**95% CI**	**RR**	**95% CI**	**RR**	**95% CI**
Treatment exposures						
Cranial radiation per 10 Gy	1·16	1·12 - 1·20	1·12	1·01 - 1·25	1·15	1·10 - 1·19
Chest radiation per 10 Gy	1·34	1·29 - 1·38	1·15	1·00 - 1·32	1·36	1·31 - 1·42
Anthracycline per 100 mg/m^2	1·03	0·98 - 1·07	1·14	1·02 - 1·27	1·02	0·98 - 1·07
Alkylator per 5000 mg/m^2	1·04	1·01 - 1·08	0·95	0·82 - 1·10	1·05	1·01 - 1·09
Platinum per 500 mg/m^2	0·94	0·68 - 1·31	1·20	0·81 - 1·78	0·89	0·59 - 1·34
Methotrexate per 5000 mg/m^2	1·00	0·98 - 1·01	0·99	0·94 - 1·03	1·00	0·99 - 1·01

Health-related causes	Subsequent neoplasm		Cardiac		Pulmonary		Other health-related	
	RR	**95% CI**	**RR**	**95% CI**	**RR**	**95% CI**	**RR**	**95% CI**
Treatment exposures								
Cranial radiation per 10 Gy	1·15	1·09 - 1·22	0·99	0·89 - 1·09	1·11	0·95 - 1·30	1·24	1·17 - 1·32
Chest radiation per 10 Gy	1·34	1·26 - 1·42	1·60	1·48 - 1·72	1·41	1·22 - 1·62	1·21	1·12 - 1·31
Anthracycline per 100 mg/m^2	1·02	0·95 - 1·09	1·10	1·01 - 1·20	1·03	0·87 - 1·21	0·98	0·89 - 1·08
Alkylator per 5000 mg/m^2	1·07	1·03 - 1·12	1·01	0·93 - 1·10	0·99	0·84 - 1·17	1·05	0·98 - 1·13
Platinum per 500 mg/m^2	0·92	0·53 - 1·59	0·57	0·10 - 3·43	0·63	0·10 - 4·18	0·94	0·53 - 1·66
Methotrexate per 5000 mg/m^2	1·00	0·98 - 1·02	1·00	0·98 - 1·03	1·01	0·98 - 1·05	0·98	0·94 - 1·02

Relative rates (RR) are adjusted for sex, age at diagnosis, race/ethnicity as non-Hispanic white vs. other and all covariates displayed. Attained age adjusted as cubic splines.

Table S7. Standardized mortality ratio comparing specific causes of death among survivors to that expected in the general US population overall. Specific causes of death are modified from the 113 selected causes of death according to the 9th and 10th revision of International Classification of Disease (ICD) codes from the National Center for Vital Statistics and Center for Disease Control.[1]

Category	Specific cause of death (subcategories)	ICD-10 Code	ICD-9 Code	SMR	95% CI
Second neoplasm causes				**10·1**	**9·6-10·6**
	Oropharyngeal and gastrointestinal malignancies	C00-C25	140-157	6·1	5·3-6·9
	Laryngeal, tracheal and lung malignancies	C32-C34	161-162	4·1	3·3-5·0
	Skin cancers	C43-C44	172-173	4·6	3·0-6·9
	Breast cancer	C50	174-175	7·0	5·8-8·5
	Genitourinary malignancies	C51-C58, C60-C68	179-189	4·1	3·2-5·2
	CNS malignancies	C70-C72	191-192	22·3	19·6-25·2
	Bone, connective, and soft tissue malignancies	C40, C41, C49	170-171	21·9	18·6-25·7
	Hodgkin lymphoma	C81	201	16·8	11·7-23·2
	Non-Hodgkin lymphoma	C82-C85	200, 202	9·8	7·6-12·5
	Leukemia	C91-C95	204-208	11·1	9·3-13·1
	Benign meningioma	D32	225·2, 225·4	123·0	76·1-188·1
	All other specified neoplasms	C26–C31, C37–C39, C45–C48, C69, C73-C79, C88, C90, C96 (excl 96·9) C97, D010, D126, D180, D332, D361, D469	158–160, 163-165, 173, 190, 193–198, 203, 209, 212·5, 212·7, 225·1	13·1	11·2-15·2
	Malignant and other neoplasms NOS	C79·9, C80, C96·9, D09·9, D36·9, D37-D44, D47-48	199, 202·9, 229·9, 235-237, 238·0-238·3, 238·79, 238·8, 238·9, 239	49·0	42·3-56·5
Cardiac causes				**4·3**	**3·9-4·7**
	Rheumatic and other valvular heart disease	I00-I09, I34-I39	390-398, 424	15·5	11·9-19·9
	Hypertensive heart disease	I11, I13	402, 404	0·9	0·5-1·6
	Ischemic heart disease	I20-I25	410-414, 429·2, 429·7	3·1	2·7-3·6
	Heart failure and cardiomyopathy	I42, I43, I50	425, 428	9·2	7·8-10·7
	Cardiac arrythmias	I47-I49	427 (excluding 427·5)	3·2	1·8-5·2
	Other specified heart disease	I26-I33, I40-I41, I44-I46, I51 (excl I51·89, I51·9)	415-423, 426, 427·5, 429 (excl 429·2, 429·7, 429·89, 429·9)	3·1	2·4-4·0
	Heart disease, NOS	I51·89, I51·9	429·89, 429·9	16·6	9·5-26·9
Pulmonary causes				**7·5**	**6·6-8·4**
	Influenza and pneumonia	J09-J18	480-488	8·5	6·9-10·4
	Chronic lower respiratory disease, includes asthma and chronic obstructive lung diseases	J40-J47	490-494, 496	1·7	1·1-2·6
	Aspiration pneumonitis	J69	507	12·4	8·1-18·2
	Interstitial lung disease, includes pulmonary fibrosis	J84	515, 516	28·0	10·8-36·8
	Other specified respiratory diseases	J00-J06, J20-J22, J30-J39, J60-J68, J70-J83, J85-J98	034·0, 460-478, 495, 500-506, 508-514, 517-519	10·9	8·2-14·3
Other health-related cause				**3·3**	**3·1-3·6**
	Sepsis	A40–A41	038	8·1	6·3-10·1
	Viral Hepatitis	B15–B19	070	6·9	4·7-9·8
	Other infectious causes of death	A00-A39, A42-A99, B00-B14, B20-B99	001-037, 039-069, 071-139, 771·3	2·3	1·9-2·8
	Diabetes mellitus	E10-E14	250	1·7	1·2-2·3
	Essential hypertension and assoc· kidney disease	I10, I12	401, 403	2·5	1·2-4·5
	Cerebrovascular disease	I60-I69	430-434, 436-438	5·1	4·2-6·2

	Other atherosclerotic and vascular disease	I70, I71-I78, I80-I99	440, 441-448, 451-459	4·2	2·9-5·9
	Chronic liver disease and cirrhosis	K70, K73, K74	571	1·6	1·1-2·2
	Other diseases of the gastrointestinal system	K25-K28, K35-K38, K40-K46, K80-K82	531-534, 540-543, 550-553, 574-575	6·3	3·3-10·8
	Kidney failure	N17-N19	584-586	6·8	5·0-9·0
	Complications of pregnancy, childbirth and the peripartum	O00-O99	630-676	2·6	1·2-4·8
	Congenital malformations and chromosomal anomalies	Q00-Q99	740-759	4·7	3·5-6·2
	Other health-related causes	Residual (all known codes not otherwise specified)	Residual (all known codes not otherwise specified)	3·4	3·0-3·8
	Ill-defined or NOS causes	R00-R99	780-799	2·1	1·5-2·8
External causes				**1·1**	**1·0-1·2**
	All transportation accidents	V01-V99, Y85	E800-E848, E929·0, E929·1	1·2	1·0-1·3
	Falls	W00-W19	E880-E888	2·9	1·9-4·4
	Other accidents and sequelae	W20-W99, X00-X39, X50-X59, Y86	E890-E929 (excl E924·1, E929·0, E929·1)	1·4	1·0-1·8
	Accidental poisoning and exposure to noxious substance	X40-X49	E850-E868, E924·1	1·3	1·1-1·5
	Suicide	X60-X84, X87·0	E950-E959	1·0	0·8-1·1
	Homicide			0·4	0·3-0·6
	Complications of medical and surgical care	Y40-Y84, Y88	E870-E879, E930-E949	21·2	14·8-29·4
	Other external causes	Y10-Y36, Y87·2, Y89	E970-E978, E980-E999	1·2	0·7-1·9

Central nervous system (CNS); Not otherwise specified (NOS)

Table S8. Demographic and diagnosis characteristics of 5-year survivors of childhood cancers who are included in modifiable risk analyses (≥18 years of age at last survey) by vital status.

	All eligible participants	Participants ≥18 years of age (N=20,051)		
	Total n (%)	Total n (%)	Alive n (%)	Dead n (%)
All survivors	34230	20,051	18138	1913
Sex				
Male	19093 (56)	10569 (53)	9512 (53)	1057 (55)
Race/ethnicity				
Non-Hispanic white	21567 (64)	16356 (80)	14746 (80)	1610 (84)
Non-Hispanic black	2116 (6)	1313 (7)	1181 (7)	132 (7)
Hispanic	2591 (9)	1629 (9)	1519 (9)	110 (6)
Other	2213 (7)	710 (4)	656 (4)	54 (3)
Unknown	5743 (15)	43 (0)	36 (0)	7 (0)
Age at diagnosis (years)				
0-4	13803 (43)	7478 (40)	7043 (42)	435 (24)
5-9	7738 (24)	4683 (25)	4285 (25)	398 (21)
10-14	7110 (19)	4490 (20)	3955 (20)	535 (28)
15-20	5579 (14)	3400 (15)	2855 (14)	545 (28)
Survival from diagnosis (years)				
5-19	5861 (17)	1781 (9)	1538 (9)	243 (13)
20-29	12231 (41)	7726 (44)	6967 (44)	759 (41)
30-39	11588 (30)	7672 (34)	6943 (33)	729 (37)
≥40	4550 (11)	2872 (13)	2690 (13)	182 (9)
Decade of diagnosis				
1970-79	8770 (22)	5143 (22)	4071 (19)	1072 (55)
1980-89	12768 (35)	7785 (37)	7102 (37)	683 (36)
1990-99	12692 (43)	7123 (41)	6965 (44)	158 (9)
Diagnosis				
Leukemia	10587 (40)	6351 (41)	5973 (43)	378 (21)
Acute lymphoblastic leukemia	8756 (36)	5339 (37)	5050 (39)	289 (16)
Acute myeloid leukemia	1264 (3)	757 (3)	695 (3)	62 (3)
Other leukemia	567 (1)	255 (1)	228 (1)	27 (1)
Hodgkin lymphoma	4380 (11)	2707 (12)	2120 (10)	587 (30)
Non-Hodgkin lymphoma	2853 (7)	1798 (8)	1659 (8)	139 (7)
CNS tumor	6144 (16)	3356 (14)	2955 (14)	401 (21)
Astrocytoma	3822 (10)	2093 (9)	1839 (9)	254 (13)
Medulloblastoma	1367 (3)	769 (3)	671 (3)	98 (5)
Other CNS	955 (2)	494 (2)	445 (2)	49 (3)
Wilms tumor	3072 (8)	1825 (8)	1742 (8)	83 (4)
Neuroblastoma	2630 (7)	1352 (6)	1287 (6)	65 (3)
Soft tissue sarcoma	1695 (4)	971 (4)	881 (4)	90 (5)
Bone tumors	2869 (7)	1691 (7)	1521 (7)	170 (9)
Ewing sarcoma	999 (3)	575 (2)	511 (2)	64 (3)
Osteosarcoma	1789 (5)	1071 (5)	967 (5)	104 (5)
Other bone tumors	81 (0)	45 (0)	43 (0)	2 (0)
Treatment exposures				
Radiation exposure				
Any radiation	18858 (55)	11125 (55)	9566 (48)	1544 (80)
Cranial radiation (Gy)[a]				
Any exposure	10183 (30)	5876 (29)	5176 (28)	687 (36)
Median dose (IQR)	24·0 (18·0 - 50·0)	24·0 (18·0 - 50·0)	24·0 (18·0 - 50·0)	45·0 (24·0 - 53·9)
Chest radiation (Gy)[a]				
Any exposure	8658 (25)	5066 (25)	4136 (21)	931 (48)
Median dose (IQR)	25·0 (15·0 - 36·0)	25·0 (15·0 - 36·0)	24·0 (15·0 - 36·0)	36·0 (24·0 - 40·9)
TBI	921 (3)	494 (2)	444(3)	51(3)
Chemotherapy				
Anthracycline (mg/m^2)[b]				
Any exposure	16365 (48)	9742 (49)	9039 (55)	683 (36)
Median dose (IQR)	159 (83 - 286)	158 (77·9 - 284·7)	154·3 (76·2 - 274·8)	247·7 (150·5 - 365·1)
Alkylating agents (mg/m^2)[c]				
Any exposure	18735 (55)	11004 (55)	9889 (56)	1079 (57)
Median dose (IQR)	7215 (3095 - 12105)	7212·0 (3123·8 - 11845·2)	7014·2 (3044·2 - 11432·3)	9761·8 (5857·1 - 14814·2)

Bleomycin (mg/m^2)				
Any exposure	2373 (7)	1443 (7)	1284 (6)	152 (8)
Median dose (IQR)	62 (41 - 103)	61·9 (41·4 - 102·4)	61·8 (41·8 - 102·1)	69·1 (39·7 - 103·9)
Epipodophyllotoxin (mg/m^2)[d]				
Any exposure	6169 (18)	3495 (17)	3315 (21)	176 (10)
Median dose (IQR)	2003 (1004 - 4458)	2098·5 (1023·7 - 4781·6)	2102·4 (1035·1 - 4722·4)	2013·4 (789·5 - 5629·9)
Platinum[e]				
Any exposure	3916 (11)	2094 (10)	1928 (9)	154 (8)
Median dose (IQR)	469 (315 - 676)	468·2 (314·3 - 661·0)	468·6 (314·4 - 666·7)	462·0 (309·8 - 632·6)
Methotrexate (mg/m^2)[f]				
Any exposure	8061 (24)	4887 (24)	4589 (30)	298 (16)
Median dose (IQR)	5921 (1506 - 21020)	5953·4 (1583·1 - 20890·5)	6125·7 (1641·4 - 20827·8)	2866·4 (563·7 - 22582·4)
Education attainment				
≤High school graduate or GED		4641 (24)	3988 (23)	653 (35)
Some college		6435 (33)	5777 (33)	658 (35)
College graduate or more		8748 (43)	8200 (44)	548 (29)
Insurance status				
Yes		17326 (86)	15679 (86)	1647 (87)
Household income, 2016 dollars				
<20,000		4141 (24)	3752 (25)	389 (23)
20-39,000		2859 (16)	2545 (15)	314 (18)
40-79,000		5202 (28)	4726 (28)	476 (27)
≥80,000		6384 (32)	5819 (32)	565 (32)
Lifestyle risk factors				
Smoking status				
Ever smoker, current or former (score = 0)		6485 (32)	5802 (32)	683 (36)
Heavy/risky drinker				
Yes (score = 0)		3790 (20)	3498 (21)	292 (17)
Body mass index				
<18·5 (score = 0)		860 (4)	705 (4)	155 (8)
18·5-24·9 (score=1)		8689 (44)	7879 (44)	810 (43)
25-<30 (score = 1)		5799 (29)	5286 (29)	513 (27)
30+ (score = 0)		4428 (23)	4026 (23)	402 (21)
Physical activity (MET-hours/week)				
0 (score = 0)		8049 (39)	7021 (37)	1028 (55)
3-6 (score = 0·5)		4174 (22)	3828 (22)	346 (19)
9-12 (score = 1)		4527 (23)	4227 (24)	300 (16)
15-21 (score = 1)		2983 (16)	2792 (17)	191 (10)
Healthy lifestyle score				
0-0·5		373 (2)	325 (2)	48 (2)
1-1·5		2338 (11)	2060 (11)	278 (14)
2		4317 (21)	3863 (21)	454 (24)
2·5		1917 (10)	1706 (10)	211 (11)
3		5832 (29)	5280 (29)	552 (29)
3·5		1725 (9)	1590 (9)	135 (7)
4		3525 (18)	3292 (19)	233 (12)
Healthy lifestyle score				
Unhealthy (0-2)		7028 (34)	6248 (34)	780 (41)
Moderate (2·5-3)		7749 (39)	6986 (39)	763 (40)
Healthy (3·5-4)		5250 (27)	4882 (28)	368 (19)
Modifiable cardiovascular risk factors				
Diabetes		955 (5)	810 (4)	145 (8)
Dyslipidemia		1974 (9)	1719 (8)	255 (13)
Hypertension		2742 (13)	2347 (12)	395 (21)
Number of cardiovascular risk factors				
None		15949 (81)	14584 (82)	1365 (71)
1		2802 (13)	2458 (13)	344 (18)
2		1031 (5)	870 (4)	161 (8)
3		269 (1)	226 (1)	43 (2)

Central nervous system (CNS); Total body irradiation (TBI)

Reported counts and percentages are based on the status of lifestyle factors and modifiable cardiovascular risk factors at the most recent survey at age ≥18 years.

The four lifestyle variables (smoking status, heavy/risky drinking, physical activity, BMI) were individually scored as unhealthy (0) or healthy (1), with the exception of physical activity of 3-6 MET-h/week being moderately healthy with a score of 0·5. Score are denoted next to each characteristic in the table. Component categories were then summed for a total lifestyle score of 0 to 4 points, categorized as unhealthy (0-2), moderately healthy (2·5-3·0) and healthy (3·5-4·0).
Analyses, including reported percentages and means/medians, were weighted to account for under-sampling of acute lymphoblastic leukemia (ALL) survivors (1987-1999).

[a] Cranial radiation and chest radiation are all excluding scatter to body site. Cranial radiation is maxTD (maximum target dose), taken as the sum of the prescribed dose for all overlapping brain fields.
Cumulative dose median and IQR are among participants who received the agent of interest·
[b] Anthracycline dose reported as doxorubicin equivalent dose where conversions are idarubicin x 3, daunorubicin x 0·5, mitoxantrone x 10 and epirubicin x 0·67.[14]
[c] Alkylator dose reported as cyclophosphamide equivalent dose conversions are ifosfamide x 0·244, procarbazine x 0·857, BCNU x 15, CCNU x 16, melphalan x 40, Thio-TEPA x 50, nitrogen mustard x 100 and Busulfan and 8·823.[15]
[d] Epipodophyllotoxin dose is the sum of teniposide and etoposide cumulative doses.
[e] Platinum dose is the sum of the cumulative carboplatin dose divided by 4 and the cisplatin dose·
[f] Methotrexate include all systemic methotrexate (IV, IM).

Table S9. Standardized mortality ratios (SMR) and 95% confidence intervals by cause of death among adult CCSS participants by modifiable risk factors.

	All-cause			External cause			Health-related cause		
	SMR	**95% CI**	**p-value**	**SMR**	**95% CI**	**p-value**	**SMR**	**95% CI**	**p-value**
Behavioral/lifestyle risk factors									
Smoking status									
Never	3·8	3·6 - 4·1	<·001	0·9	0·7 - 1·1	0·31	4·8	4·5 - 5·2	<·001
Ever	4·2	3·9 - 4·5	<·001	1·5	1·3 - 1·9	<·001	5·2	4·8 - 5·7	<·001
Heavy/risky drinker									
No	3·9	3·7 - 4·1	<·001	0·9	0·8 - 1·1	0·29	4·9	4·6 - 5·2	<·001
Yes	3·5	3·1 - 3·9	<·001	1·5	1·1 - 2·0	0·007	4·4	3·8 - 5·0	<·001
Body mass index									
<18·5	8·3	7·1 - 9·7	<·001	1·7	0·9 - 2·9	0·10	11·1	9·3 - 13·3	<·001
18·5-24·9	3·8	3·5 - 4·0	<·001	1·0	0·8 - 1·3	0·76	4·7	4·3 - 5·0	<·001
25·0-29·9	3·4	3·1 - 3·7	<·001	1·1	0·8 - 1·4	0·50	4·2	3·8 - 4·6	<·001
≥30·0	4·4	4·0 - 4·8	<·001	1·2	0·9 - 1·6	0·32	5·6	5·0 - 6·2	<·001
Physical activity (MET-hours/week)									
0	5·1	4·8 - 5·4	<·001	1·5	1·2 - 1·8	<·001	6·1	5·7 - 6·6	<·001
3-6	3·5	3·2 - 3·9	<·001	1·1	0·8 - 1·5	0·50	4·6	4·0 - 5·1	<·001
9-21	2·8	2·6 - 3·1	<·001	0·7	0·5 - 0·9	0·006	3·6	3·2 - 4·0	<·001
Healthy lifestyle score									
Unhealthy (0-2)	4·7	4·4 - 5·1	<·001	1·5	1·2 - 1·9	<·001	5·9	5·5 - 6·4	<·001
Moderate (2·5-3)	4·1	3·8 - 4·4	<·001	1·1	0·9 - 1·4	0·34	5·0	4·6 - 5·4	<·001
Healthy (3·5-4)	2·8	2·5 - 3·1	<·001	0·6	0·4 - 0·9	0·005	3·7	3·3 - 4·1	<·001
Hypertension									
Yes	5·3	4·8 - 5·9	<·001	1·2	0·7 - 1·7	0·53	6·6	5·9 - 7·3	<·001
No	3·7	3·5 - 3·9	<·001	1·1	1·0 - 1·3	0·10	4·6	4·4 - 4·9	<·001
Diabetes									
Yes	6·9	5·8 - 8·0	<·001	2·1	1·1 - 3·5	0·021	8·3	7·0 - 9·9	<·001
No	3·8	3·7 - 4·0	<·001	1·1	0·9 - 1·3	0·20	4·8	4·5 - 5·0	<·001
Dyslipidemia									
Yes	4·3	3·8 - 4·9	<·001	0·7	0·4 - 1·2	0·25	5·4	4·8 - 6·2	<·001
No	3·9	3·7 - 4·1	<·001	1·2	1·0 - 1·3	0·033	4·9	4·6 - 5·2	<·001
Modifiable cardiovascular risk factors	·			·			·		
None	3·7	3·5 - 3·9	<·001	1·1	1·0 - 1·3	0·089	4·5	4·3 - 4·8	<·001
Any 1	4·7	4·2 - 5·2	<·001	1·1	0·7 - 1·6	0·74	5·8	5·2 - 6·5	<·001
Any 2	5·5	4·8 - 6·3	<·001	1·1	0·6 - 2·0	0·79	6·8	5·9 - 7·9	<·001
Hypertension, no diabetes or dyslipidemia	5·1	4·5 - 5·9	<·001	1·2	0·7 - 1·9	0·62	6·4	5·5 - 7·4	<·001
Diabetes, no dyslipidemia or hypertension	7·0	5·3 - 9·1	<·001	3·2	1·5 - 6·1	0·004	7·4	5·2 - 10·1	<·001
Dyslipidemia, no diabetes or hypertension	3·4	2·7 - 4·1	<·001	0·1	0·0 - 0·7	0·009	4·5	3·6 - 5·5	<·001
Hypertension + Diabetes	9·4	6·7 - 12·9	<·001	0·8	0·0 - 4·3	0·99	13·0	9·2 - 18·0	<·001
Hypertension + Dyslipidemia	4·7	3·9 - 5·7	<·001	1·0	0·4 - 2·3	0·99	5·6	4·6 - 6·9	<·001
Diabetes + Dyslipidemia	5·6	3·2 - 8·9	<·001	1·3	0·0 - 6·2	0·99	7·5	4·3 - 12·1	<·001
All three conditions	5·8	4·2 - 7·8	<·001	1·6	0·3 - 4·8	0·55	7·2	5·1 - 9·8	<·001
Modifiable CVRF + lifestyle score	·			·			·		
No condition + Unhealthy lifestyle (0-2·0)	4·6	4·2 - 5·1	<·001	1·7	1·3 - 2·1	<·001	5·8	5·2 - 6·4	<·001
No condition + Moderate lifestyle (2·5-3·0)	3·8	3·5 - 4·2	<·001	1·2	1·0 - 1·5	0·29	4·5	4·1 - 5·0	<·001
No condition + Healthy lifestyle (3·5-4)	2·6	2·3 - 2·9	<·001	0·6	0·4 - 0·8	0·007	3·3	2·9 - 3·8	<·001
Hypertension unhealthy	6·3	5·1 - 7·7	<·001	1·5	0·6 - 3·1	0·29	8·2	6·6 - 10·1	<·001
Hypertension moderate	4·6	3·7 - 5·8	<·001	0·9	0·3 - 2·2	0·85	5·5	4·3 - 7·0	<·001
Hypertension healthy	4·0	2·8 - 5·6	<·001	1·1	0·2 - 3·1	0·99	4·8	3·1 - 7·0	<·001
Diabetes unhealthy	5·4	3·2 - 8·7	<·001	1·9	0·2 - 6·8	0·63	6·8	3·7 - 11·3	<·001
Diabetes moderate	9·0	5·8 - 13·1	<·001	3·0	0·7 - 8·6	0·17	8·8	5·0 - 14·2	<·001
Diabetes healthy	4·6	2·0 - 9·0	<·001	0·0	0·0 - 6·0	0·99	6·2	2·5 - 12·8	<·001
Dyslipidemia unhealthy	2·8	1·7 - 4·4	<·001	0·0	0·0 - 1·9	0·22	3·9	2·4 - 6·0	<·001
Dyslipidemia moderate	4·8	3·6 - 6·2	<·001	0·3	0·0 - 1·7	0·33	6·0	4·5 - 7·9	<·001
Dyslipidemia healthy	1·6	0·8 - 2·8	0·21	0·0	0·0 - 1·6	0·25	2·3	1·1 - 4·1	0·024
2+ conditions unhealthy	6·1	4·9 - 7·5	<·001	1·1	0·3 - 2·7	0·99	7·6	6·0 - 9·4	<·001
2+ conditions moderate	5·6	4·5 - 6·9	<·001	1·3	0·4 - 2·9	0·66	6·9	5·5 - 8·6	<·001
2+ conditions healthy	4·1	2·7 - 5·9	<·001	1·0	0·1 - 3·6	0·99	5·1	3·3 - 7·5	<·001

Table S9 continued. Standardized mortality ratios (SMR) and 95% confidence intervals by cause of death among adult CCSS participants by modifiable risk factors.

	Subsequent neoplasm			Cardiac			Pulmonary			Other		
	SMR	**95% CI**	**P**	**SMR**	**95% CI**	**P**	**SMR**	**95% CI**	**P**	**SMR**	**95% CI**	**P**
Behavioral/lifestyle risk factors												
Smoking status												
Never	8·9	8·1 - 9·7	<·001	3·7	3·1 - 4·3	<·001	5·7	4·4 - 7·3	<·001	2·8	2·4 - 3·1	<·001
Ever	7·8	6·8 - 8·8	<·001	4·6	3·8 - 5·5	<·001	7·0	5·0 - 9·5	<·001	3·6	3·1 - 4·2	<·001
Heavy/risky drinker												
No	8·4	7·7 - 9·1	<·001	3·9	3·4 - 4·4	<·001	6·2	4·9 - 7·6	<·001	3·0	2·7 - 3·4	<·001
Yes	7·7	6·3 - 9·3	<·001	3·9	2·9 - 5·3	<·001	6·0	3·5 - 9·6	<·001	2·5	1·9 - 3·2	<·001
Body mass index	·			·			·			·		
<18·5	14·1	10·3 - 18·9	<·001	8·8	5·3 - 13·7	<·001	25·0	14·3 - 40·7	<·001	8·5	6·1 - 11·5	<·001
18·5-24·9	8·2	7·3 - 9·1	<·001	3·8	3·1 - 4·6	<·001	6·6	4·9 - 8·7	<·001	2·6	2·2 - 3·0	<·001
25·0-29·9	8·1	7·0 - 9·2	<·001	3·2	2·5 - 4·1	<·001	4·4	2·8 - 6·5	<·001	2·2	1·8 - 2·7	<·001
≥30·0	8·3	7·0 - 9·8	<·001	5·1	4·0 - 6·5	<·001	4·9	2·9 - 7·9	<·001	4·2	3·4 - 5·1	<·001
Physical activity (MET-hours/week)												
0	9·6	8·6 - 10·6	<·001	4·8	4·0 - 5·7	<·001	8·6	6·7 - 10·9	<·001	4·1	3·6 - 4·7	<·001
3-6	8·7	7·3 - 10·2	<·001	4·2	3·2 - 5·4	<·001	4·5	2·5 - 7·4	<·001	2·3	1·8 - 2·9	<·001
9-12 or 15-21	6·4	5·5 - 7·4	<·001	2·9	2·3 - 3·7	<·001	3·9	2·5 - 5·9	<·001	2·2	1·8 - 2·7	<·001
Healthy lifestyle score												
Unhealthy (0-2)	9·0	7·9 - 10·1	<·001	5·0	4·2 - 6·0	<·001	7·5	5·5 - 10·0	<·001	4·2	3·6 - 4·8	<·001
Moderate (2·5-3)	8·4	7·4 - 9·4	<·001	3·9	3·2 - 4·8	<·001	6·5	4·7 - 8·7	<·001	3·1	2·6 - 3·6	<·001
Healthy (3·5-4)	8·0	6·8 - 9·3	<·001	2·7	2·0 - 3·6	<·001	3·9	2·3 - 6·3	<·001	1·6	1·2 - 2·0	0·002
Hypertension												
Yes	8·6	7·2 - 10·1	<·001	5·9	4·6 - 7·4	<·001	7·5	4·8 - 11·1	<·001	5·4	4·4 - 6·5	<·001
No	8·5	7·8 - 9·2	<·001	3·6	3·1 - 4·1	<·001	5·9	4·7 - 7·3	<·001	2·6	2·3 - 2·9	<·001
Diabetes												
Yes	9·5	6·9 - 12·7	<·001	8·3	5·6 - 11·8	<·001	10·8	5·2 - 19·9	<·001	7·2	5·2 - 9·6	<·001
No	8·4	7·8 - 9·1	<·001	3·8	3·3 - 4·3	<·001	5·9	4·8 - 7·2	<·001	2·9	2·6 - 3·2	<·001
Dyslipidemia												
Yes	8·9	7·4 - 10·7	<·001	4·6	3·4 - 6·0	<·001	5·8	3·2 - 9·5	<·001	3·3	2·5 - 4·3	<·001
No	8·4	7·7 - 9·1	<·001	3·9	3·4 - 4·5	<·001	6·3	5·1 - 7·7	<·001	3·0	2·7 - 3·4	<·001
Modifiable cardiovascular risk factors	·			·			·			·		
None	8·5	7·8 - 9·2	<·001	3·4	2·9 - 4·0	<·001	5·9	4·6 - 7·4	<·001	2·5	2·2 - 2·9	<·001
Any 1	8·0	6·6 - 9·6	<·001	5·1	3·9 - 6·6	<·001	6·5	4·0 - 10·1	<·001	4·5	3·6 - 5·5	<·001
Any 2	9·3	7·3 - 11·6	<·001	6·1	4·4 - 8·2	<·001	7·8	4·1 - 13·3	<·001	5·3	4·0 - 6·9	<·001
Hypertension, no diabetes or dyslipidemia	7·9	6·1 - 10·1	<·001	5·8	4·1 - 8·0	<·001	7·2	3·7 - 12·6	<·001	5·5	4·2 - 7·0	<·001
Diabetes, no dyslipidemia or hypertension	7·4	3·7 - 13·3	<·001	8·2	3·8 - 15·6	<·001	6·8	0·8 - 24·6	0·071	7·0	3·9 - 11·4	<·001
Dyslipidemia, no diabetes or hypertension	8·3	6·1 - 11·1	<·001	3·4	1·9 - 5·6	<·001	5·5	2·0 - 11·9	0·002	2·2	1·2 - 3·5	0·008
Hypertension + Diabetes	8·5	3·4 - 17·6	<·001	12·1	5·2 - 23·9	<·001	24·5	6·6 - 62·7	<·001	15·1	8·9 - 24·0	<·001
Hypertension + Dyslipidemia	8·5	6·2 - 11·5	<·001	4·7	2·9 - 7·3	<·001	4·8	1·5 - 11·2	0·009	4·1	2·7 - 5·9	<·001
Diabetes + Dyslipidemia	9·4	3·4 - 20·6	<·001	7·8	2·1 - 20·0	0·004	7·7	0·1 - 42·7	0·24	5·7	1·8 - 13·4	0·004
All three conditions	11·7	7·2 - 18·1	<·001	6·6	3·0 - 12·6	<·001	8·9	1·8 - 25·9	0·010	3·7	1·6 - 7·3	0·004
Modifiable CVRF + lifestyle score	·			·			·			·		
No condition + Unhealthy lifestyle (0-2·0)	9·3	7·9 - 10·7	<·001	4·9	3·9 - 6·2	<·001	8·1	5·5 - 11·4	<·001	3·7	3·1 - 4·5	<·001
No condition + Moderate lifestyle (2·5-3·0)	8·6	7·5 - 9·9	<·001	3·0	2·2 - 3·8	<·001	5·7	3·8 - 8·2	<·001	2·7	2·2 - 3·2	<·001
No condition + Healthy lifestyle (3·5-4)	7·5	6·3 - 8·9	<·001	2·6	1·8 - 3·5	<·001	4·0	2·2 - 6·6	<·001	1·2	0·8 - 1·6	0·36
Hypertension unhealthy	10·1	6·9 - 14·2	<·001	7·4	4·4 - 11·6	<·001	7·8	2·5 - 18·3	0·002	7·4	5·0 - 10·4	<·001
Hypertension moderate	6·1	3·8 - 9·2	<·001	6·0	3·5 - 9·6	<·001	8·3	3·0 - 18·2	<·001	4·4	2·8 - 6·7	<·001
Hypertension healthy	7·7	4·0 - 13·4	<·001	2·4	0·5 - 7·1	0·22	3·2	0·0 - 17·9	0·50	4·2	2·0 - 7·8	<·001
Diabetes unhealthy	6·5	1·7 - 16·6	0·009	6·5	1·3 - 19·1	0·026	8·2	0·1 - 45·7	0·24	6·9	2·6 - 14·9	<·001
Diabetes moderate	7·6	2·1 - 19·5	0·004	10·3	2·8 - 26·4	0·001	9·6	0·1 - 53·3	0·19	8·7	3·5 - 17·9	<·001
Diabetes healthy	8·9	1·8 - 26·1	0·008	8·1	0·9 - 29·1	0·047	0·0	0·0 - 55·1	0·99	4·2	0·5 - 15·1	0·15
Dyslipidemia unhealthy	5·8	2·6 - 11·0	<·001	4·1	1·3 - 9·6	0·027	3·1	0·0 - 17·5	0·60	2·5	0·8 - 5·7	0·17

Dyslipidemia moderate	11·4	7·6 - 16·4	<·001	4·4	2·0 - 8·4	<·001	9·8	3·2 - 22·9	<·001	2·4	1·0 - 4·7	0·041
Dyslipidemia healthy	5·3	2·1 - 10·9	<·001	0·8	0·0 - 4·6	0·69	0·0	0·0 - 13·7	0·99	1·5	0·3 - 4·4	0·52
2+ conditions unhealthy	8·8	6·0 - 12·6	<·001	6·2	3·6 - 10·0	<·001	10·2	4·1 - 21·1	<·001	7·0	4·7 - 10·0	<·001
2+ conditions moderate	9·7	6·7 - 13·6	<·001	6·8	4·1 - 10·7	<·001	7·1	2·3 - 16·5	0·001	4·7	2·9 - 7·2	<·001
2+ conditions healthy	9·2	4·9 - 15·7	<·001	4·0	1·3 - 9·4	0·014	3·5	0·0 - 19·7	0·47	3·0	1·1 - 6·6	0·025

Cardiovascular risk factor (CVRF)

Mortality analyses exclude Canadian participants as National Death Index data is limited to U.S. participants

Table S10. Absolute excess risk (AER) of health-related death per 10,000 person years by healthy lifestyle score and then by number of modifiable cardiovascular risk factors (CVRF).

		All health-related causes			Specific health-related cause										
					Subsequent neoplasm			Cardiac			Pulmonary			Other		
		AER	95% CI	P	AER	95% CI	P	AER	95% CI	P	AER	95% CI	P	AER	95% CI	P
Subset	Survival after diagnosis (years)															
Unhealthy (0-2)	6-14	16	4 - 38	0·002	14	4 - 33	<·001	2	0 - 16	0·39	3	0 - 16	0·15	0	0 - 8	0·91
	15-19	21	13 - 31	<·001	10	5 - 18	<·001	4	1 - 9	0·002	1	0 - 5	0·094	6	2 - 13	0·002
	20-24	31	23 - 40	<·001	15	10 - 21	<·001	5	2 - 9	<·001	3	1 - 6	<·001	8	4 - 14	<·001
	25-29	52	42 - 64	<·001	25	18 - 33	<·001	9	5 - 15	<·001	3	1 - 7	<·001	15	10 - 22	<·001
	30-34	74	59 - 90	<·001	32	23 - 42	<·001	15	9 - 23	<·001	7	3 - 12	<·001	20	13 - 29	<·001
	35-39	136	110 - 164	<·001	55	40 - 74	<·001	28	17 - 42	<·001	10	4 - 19	<·001	43	29 - 61	<·001
	≥40	191	144 - 246	<·001	102	70 - 143	<·001	32	14 - 58	<·001	14	3 - 33	0·002	43	21 - 74	<·001
Moderate (2·5-3)	6-14	18	7 - 35	<·001	15	6 - 30	<·001	1	0 - 10	0·54	2	0 - 11	0·22	0	0 - 9	0·99
	15-19	19	12 - 27	<·001	7	4 - 13	<·001	5	2 - 10	<·001	1	0 - 4	0·026	5	2 - 10	<·001
	20-24	25	19 - 32	<·001	15	11 - 21	<·001	3	1 - 6	<·001	2	1 - 5	<·001	4	1 - 8	0·001
	25-29	44	35 - 54	<·001	23	17 - 30	<·001	6	3 - 11	<·001	4	2 - 7	<·001	12	7 - 17	<·001
	30-34	53	41 - 67	<·001	30	22 - 40	<·001	8	3 - 14	<·001	3	1 - 8	0·002	12	6 - 20	<·001
	35-39	104	82 - 130	<·001	54	39 - 72	<·001	17	8 - 29	<·001	7	2 - 16	<·001	26	15 - 40	<·001
	≥40	162	117 - 216	<·001	63	37 - 99	<·001	40	19 - 70	<·001	18	5 - 39	<·001	41	19 - 73	<·001
Healthy (3·5-4)	6-14	7	0 - 21	<·001	1	0 - 11	0·63	4	0 - 15	0·063	2	0 - 12	0·20	0	0 - 10	0·99
	15-19	16	9 - 24	<·001	8	4 - 14	<·001	5	2 - 9	<·001	1	0 - 4	0·12	2	0 - 6	0·21
	20-24	15	9 - 22	<·001	14	9 - 20	<·001	2	0 - 6	0·020	0	0 - 2	0·99	0	0 - 1	0·29
	25-29	33	24 - 44	<·001	25	18 - 34	<·001	2	0 - 6	0·20	2	0 - 6	0·004	4	0 - 9	0·031
	30-34	36	23 - 52	<·001	23	14 - 35	<·001	7	2 - 16	0·003	3	0 - 9	0·029	3	0 - 11	0·38
	35-39	79	53 - 111	<·001	45	27 - 69	<·001	11	2 - 27	0·010	4	0 - 16	0·088	18	5 - 36	0·001
	≥40	39	5 - 90	<·001	34	9 - 77	0·002	0	0 - 19	0·90	3	0 - 26	0·81	7	0 - 39	0·57
No CVRF	6-14	13	7 - 22	<·001	10	5 - 17	<·001	2	0 - 7	0·077	2	0 - 7	0·006	0	0 - 4	0·96
	15-19	17	13 - 22	<·001	8	6 - 12	<·001	4	2 - 6	<·001	1	0 - 2	0·011	4	2 - 7	<·001
	20-24	21	17 - 25	<·001	14	11 - 17	<·001	3	1 - 5	<·001	1	0 - 2	0·003	3	1 - 5	<·001
	25-29	38	32 - 44	<·001	23	19 - 28	<·001	4	2 - 7	<·001	4	2 - 6	<·001	7	4 - 10	<·001
	30-34	45	37 - 54	<·001	25	20 - 32	<·001	7	4 - 11	<·001	4	2 - 7	<·001	8	4 - 13	<·001
	35-39	90	74 - 107	<·001	44	33 - 56	<·001	15	9 - 24	<·001	4	1 - 9	0·001	27	18 - 37	<·001
	≥40	118	87 - 154	<·001	63	42 - 89	<·001	22	10 - 41	<·001	15	6 - 29	<·001	18	5 - 36	0·002
1 CVRF	6-14	7	0 - 56	0·16	0	0 - 39	0·99	10	0 - 60	0·12	0	0 - 40	0·99	0	0 - 38	0·99
	15-19	29	13 - 54	<·001	7	1 - 23	0·025	9	2 - 26	0·002	2	0 - 14	0·21	10	1 - 28	0·011
	20-24	42	27 - 62	<·001	22	12 - 36	<·001	8	2 - 18	<·001	5	1 - 14	<·001	8	1 - 18	0·015
	25-29	64	46 - 85	<·001	26	15 - 40	<·001	12	5 - 23	<·001	0	0 - 4	0·99	27	16 - 42	<·001
	30-34	82	59 - 109	<·001	34	20 - 52	<·001	22	11 - 37	<·001	5	1 - 14	0·012	22	10 - 37	<·001
	35-39	137	101 - 179	<·001	67	43 - 97	<·001	16	4 - 35	0·002	19	8 - 37	<·001	35	17 - 60	<·001
	≥40	195	131 - 276	<·001	81	42 - 136	<·001	43	15 - 87	<·001	7	0 - 35	0·26	64	29 - 116	<·001

2+ CVRF	6-14	88	0 - 505	0·17	91	0 - 508	0·018	0	0 - 337	0·99	0	0 - 337	0·99	0	0 - 335	0·99
	15-19	46	8 - 127	0·006	25	2 - 92	0·009	12	0 - 71	0·17	13	0 - 72	0·046	0	0 - 45	0·99
	20-24	52	24 - 96	<·001	17	3 - 46	0·002	07	0 - 32	0·13	14	2 - 41	<·001	15	1 - 44	0·025
	25-29	95	62 - 137	<·001	34	16 - 62	<·001	22	7 - 46	<·001	6	0 - 22	0·045	34	15 - 62	<·001
	30-34	122	83 - 171	<·001	54	30 - 89	<·001	23	8 - 49	<·001	5	0 - 22	0·112	39	18 - 70	<·001
	35-39	203	146 - 273	<·001	85	50 - 132	<·001	58	30 - 99	<·001	10	0 - 34	0·030	50	23 - 90	<·001
	≥40	207	130 - 308	<·001	104	53 - 178	<·001	26	1 - 76	0·037	12	0 - 50	0·15	66	25 - 130	<·001

Cardiovascular risk factor (CVRF)

Table S11. Relative rate of health-related late mortality and association with modifiable lifestyle and cardiovascular risk factors among CCSS participants who completed at least one survey at age ≥18 years, including interaction between dyslipidemia and other cardiovascular risk factors.

	Health-related cause			Subsequent neoplasm			Cardiac			Pulmonary			Other		
	RR	**95% CI**	**p-value**	**RR**	**95% CI**	**p-value**	**RR**	**95% CI**	**p-value**	**RR**	**95% CI**	**p-value**	**RR**	**95% CI**	**p-value**
Healthy lifestyle score															
Unhealthy (0-2)	**Ref**			**Ref**			**Ref**			**Ref**			**Ref**		
Moderate (2·5-3)	0·9	0·8 - 1·0	0·031	0·9	0·7 - 1·1	0·25	0·9	0·7 - 1·2	0·43	0·8	0·5 - 1·4	0·47	0·8	0·6 - 1·0	0·11
Healthy (3·5-4)	0·8	0·7 - 0·9	0·002	0·9	0·8 - 1·2	0·57	0·8	0·5 - 1·2	0·25	0·6	0·3 - 1·1	0·093	0·5	0·3 - 0·7	<·001
Cardiovascular risk factors															
Hypertension No vs. Yes	0·7	0·6 - 0·8	<·001	0·9	0·7 - 1·1	0·44	0·7	0·5 - 1·0	0·024	0·7	0·4 - 1·1	0·13	0·4	0·3 - 0·6	<·001
Diabetes No vs. Yes	0·6	0·5 - 0·8	<·001	1·0	0·7 - 1·6	0·87	0·4	0·3 - 0·7	<·001	0·6	0·3 - 1·5	0·29	0·4	0·3 - 0·6	<·001
Dyslipidemia Yes with 2 other CVRFs vs. No	0·6	0·4 - 0·9	0·012	1·4	0·7 - 2·7	0·28	0·4	0·2 - 1·0	0·042	0·5	0·1 - 2·1	0·32	0·2	0·1 - 0·6	<·001
Dyslipidemia Yes with <2 other CVRFs vs No	0·9	0·7 - 1·0	0·16	1·0	0·8 - 1·3	0·80	0·9	0·6 - 1·3	0·59	0·5	0·3 - 1·1	0·083	0·8	0·6 - 1·1	0·24

Relative rates are adjusted for treatment exposures: cranial irradiation dose, chest irradiation dose, anthracycline dose, and alkylating agent dose, and sociodemographic factors including: age at diagnosis, race/ethnicity, sex, and attained age, education, income, and insurance status.

Lifestyle factors, including smoking status, alcohol use, physical activity, and unhealthy weight, were assigned a score of 0 (unhealthy) to 1 (healthy) and combined to create a lifestyle score ranging from 0-4 which was further categorized as unhealthy (0-2), moderately healthy (2·5-3), and healthy (3·5-4).

Covariates presented in the table (lifestyle category and chronic conditions) and socioeconomic factors (education, income, insurance) factors were included in the model as time-dependent variables.

Due to interaction with other CVRF (hypertension and diabetes), dyslipidemia is reported in this model as dyslipidemia with 2 other CVRFs (yes vs no) which is dyslipidemia in the presence of both hypertension and diabetes and then dyslipidemia with <2 other CVRFs (yes vs no) which is all others with dyslipidemia including dyslipidemia without hypertension or diabetes and dyslipidemia with either hypertension or diabetes (but not both).

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