

Supplementary Tables and Figures

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eTable 1. Subsequent neoplasm diagnoses (and number of affected individuals) by primary childhood cancer diagnosis.

Childhood Cancer Diagnosis	Subsequent neoplasm	All types	Leukemia			Lymphoma			Central nervous system			
			ALL	AML	Other	Hodgkin lymphoma	Non-Hodgkin lymphoma	Other	Gliial	Medulloblastoma/ Primitive neuroectodermal tumor	Meningioma (benign and malignant)	Other
Acute lymphoblastic leukemia		782 (410)	1 (1)	12 (12)	2 (2)	2 (2)	3 (3)	1 (1)	38 (37)	3 (3)	120 (104)	3 (3)
Acute myeloblastic leukemia		79 (40)	1 (1)	0	0	0	0	0	1 (1)	1 (1)	2 (2)	0
Other leukemia		50 (19)	1 (1)	0	0	0	0	0	2 (2)	0	2 (2)	0
Astrocytoma		171 (114)	1 (1)	1 (1)	1 (1)	2 (2)	1 (1)	0	17 (17)	1 (1)	39 (34)	2 (2)
Medulloblastoma/ Primitive neuroectodermal tumor		167 (83)	0	2 (2)	0	0	1 (1)	0	9 (8)	0	41 (33)	0
Other central nervous system		43 (27)	0	0	0	0	0	0	2 (2)	0	12 (11)	0
Hodgkin lymphoma		1228 (515)	1 (1)	9 (9)	4 (4)	1 (1)	20 (16)	0	3 (3)	1 (1)	4 (4)	4 (4)
Non-Hodgkin lymphoma		163 (101)	3 (3)	3 (3)	1 (1)	4 (4)	3 (3)	0	5 (5)	0	8 (8)	0
Wilms		86 (57)	2 (2)	0	0	1 (1)	0	0	0	1 (1)	0	0
Neuroblastoma		69 (61)	1 (1)	2 (2)	0	1 (1)	2 (2)	0	1 (1)	0	4 (4)	0
Rhabdomyosarcoma		109 (82)	1 (1)	0	0	1 (1)	0	0	2 (2)	0	6 (5)	2 (2)
Ewing sarcoma		72 (57)	1 (1)	2 (2)	0	0	0	0	0	0	1 (1)	0
Osteosarcoma		93 (70)	1 (1)	2 (2)	0	0	2 (2)	0	2 (2)	0	1 (1)	0
Other bone		3 (3)	0	0	0	0	0	0	0	0	0	0
TOTAL		3115 (1639)	14 (14)	33 (33)	8 (8)	12 (12)	32 (28)	1 (1)	82 (80)	7 (7)	240 (209)	11 (11)

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eTable 1 (continued). Subsequent neoplasm diagnoses (and number of affected individuals) by primary childhood cancer diagnosis.

Subsequent neoplasm Childhood Cancer Diagnosis	Solid organ				Other cancers	Skin	
	Breast	Bone	Soft tissue sarcoma	Thyroid		Melanoma	Non-melanoma skin cancer
Acute lymphoblastic leukemia	14 (14)	6 (6)	5 (5)	31 (31)	32 (31)	8 (8)	501 (183)
Acute myeloblastic leukemia	5 (5)	0	3 (3)	7 (7)	5 (5)	0	54 (19)
Other leukemia	1 (1)	0	0	9 (9)	6 (6)	2 (2)	27 (6)
Astrocytoma	5 (4)	3 (3)	5 (5)	3 (3)	13 (13)	7 (6)	70 (33)
Medulloblastoma/ Primitive neuroectodermal tumor	0	1 (1)	4 (3)	16 (16)	6 (6)	0	87 (25)
Other central nervous system	0	1 (1)	2 (2)	6 (6)	3 (3)	1 (1)	16 (5)
Hodgkin lymphoma	142 (124)	9 (9)	25 (25)	64 (64)	58 (58)	12 (12)	871 (256)
Non-Hodgkin lymphoma	10 (10)	3 (3)	3 (3)	13 (13)	19 (18)	5 (4)	83 (35)
Wilms	6 (6)	5 (5)	7 (7)	6 (6)	11 (11)	2 (2)	45 (19)
Neuroblastoma	2 (2)	2 (2)	4 (4)	14 (14)	19 (19)	0	17 (12)
Rhabdomyosarcoma	9 (9)	10 (10)	20 (20)	8 (8)	11 (11)	4 (4)	35 (20)
Ewing sarcoma	15 (13)	9 (9)	3 (3)	6 (6)	7 (7)	4 (4)	24 (13)
Osteosarcoma	22 (17)	0	7 (6)	9 (9)	16 (16)	6 (6)	25 (18)
Other bone	0	0	0	2 (2)	0	0	1 (1)
TOTAL	231 (205)	49 (49)	88 (86)	194 (194)	206 (204)	51 (49)	1856 (645)

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17 **eTable 2. Observed and expected subsequent malignant neoplasms, standardized incidence ratios and median time to occurrence, by**
 18 **decade of diagnosis.**

Subsequent malignant neoplasm	Overall Cohort				1970-79			
	Observed ^a	Expected	SIR (95% CI)	Median time to occurrence, y (IQR)	Observed ^a	Expected	SIR (95% CI)	Median time to occurrence, y (IQR)
All	1086.7	201.4	5.4 (5.1 - 5.7)	17.1 (11.2 - 22.8)	523.0	99.2	5.3 (4.8 - 5.7)	21.7 (14.6 - 26.7)
Leukemia	64.0	11.5	5.5 (4.3 - 7.1)	9.0 (6.2 - 14.2)	15.0	4.0	3.7 (2.1 - 6.1)	8.9 (7.5 - 24.7)
Acute lymphoblastic leukemia	14.0	5.1	2.7 (1.5 - 4.6)	13.3 (6.6 - 20.0)	4.0	1.5	2.7 (0.7 - 6.8)	26.1 (13.8 - 31.1)
Acute myeloblastic leukemia	36.7	3.6	10.3 (7.2 - 14.2)	7.8 (6.2 - 13.4)	7.0	1.4	5.2 (2.1 - 10.6)	8.1 (7.1 - 12.5)
Other	10.3	2.5	4.2 (2.0 - 7.6)	14.1 (5.8 - 14.1)	1.0	1.0	1.0 (0.0 - 5.5)	14.2 (14.2 - 14.2)
Lymphoma	45.0	28.5	1.6 (1.2 - 2.1)	17.9 (12.7 - 25.1)	24.0	12.0	2.0 (1.3 - 3.0)	24.3 (16.2 - 28.5)
Central nervous system	131.8	12.1	10.8 (9.1 - 12.9)	10.9 (7.8 - 15.2)	41.0	4.3	9.6 (6.9 - 13.0)	18.3 (12.1 - 24.6)
Glial	103.9	9.4	11.0 (9.0 - 13.4)	9.4 (7.4 - 13.2)	27.0	3.5	7.7 (5.1 - 11.2)	14.0 (10.2 - 23.9)
Medulloblastoma	9.6	1.2	8.3 (3.9 - 15.5)	9.2 (8.8 - 13.8)	3.0	0.3	9.9 (2.0 - 29.0)	14.6 (9.4 - 24.2)
Breast	231.0	25.0	9.2 (8.1 - 10.5)	21.5 (17.1 - 26.4)	159.0	16.9	9.4 (8.0 - 11.0)	24.1 (19.3 - 27.7)
Bone	49.2	4.1	12.0 (8.9 - 15.9)	10.0 (8.2 - 12.9)	23.0	1.2	18.4 (11.7 - 27.7)	11.0 (8.5 - 17.9)
Osteosarcoma	39.2	2.0	19.7 (14.0 - 26.9)	9.8 (8.2 - 12.7)	18.0	0.5	33.5 (19.8 - 52.9)	10.6 (8.5 - 12.4)
Ewing sarcoma	3.0	1.0	2.9 (0.6 - 8.4)	14.7 (11.9 - 16.3)	1.0	0.3	3.4 (0.0 - 18.8)	16.3 (16.3 - 16.3)
Other bone	6.0	1.0	6.2 (2.3 - 13.5)	12.1 (9.8 - 23.2)	3.0	0.4	7.8 (1.6 - 22.7)	23.2 (12.4 - 26.7)
Soft tissue sarcoma	88.2	12.4	7.1 (5.7 - 8.8)	15.2 (10.6 - 20.7)	43.0	6.0	7.2 (5.2 - 9.7)	17.1 (11.2 - 26.6)
Thyroid	204.8	19.6	10.5 (9.1 - 12.0)	18.7 (13.8 - 22.2)	84.0	8.1	10.3 (8.2 - 12.8)	20.1 (15.4 - 25.7)
Melanoma	56.3	21.7	2.6 (2.0 - 3.4)	18.3 (13.2 - 22.1)	26.0	10.3	2.5 (1.6 - 3.7)	22.1 (14.7 - 27.0)
All Others	195.5	66.5	2.9 (2.5 - 3.4)	16.3 (10.2 - 23.8)	95.0	36.3	2.6 (2.1 - 3.2)	21.4 (14.7 - 26.9)

19 ^a Analyses, including reported percentages and means/medians, were weighted to account for undersampling of acute lymphoblastic leukemia (ALL)
 20 survivors (1987-1999), with a weight of 1.21 for ALL age 0 or 11-20 years at diagnosis, and a weight of 3.63 for those aged 1-10 years.
 21 Abbreviations: IQR, interquartile range; SIR, standardized incidence ratio.
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eTable 2 (continued). Observed and expected subsequent malignant neoplasms, standardized incidence ratios and median time to occurrence, by decade of diagnosis.

	1980-89				1990-99			
	Observed ^a	Expected	SIR (95% CI)	Median time to occurrence, y (IQR)	Observed ^a	Expected	SIR (95% CI)	Median time to occurrence, y (IQR)
Subsequent malignant neoplasm								
All	391.0	68.7	5.7 (5.1 - 6.3)	16.1 (9.9 - 20.5)	172.7	33.5	5.2 (4.4 - 6.0)	11.1 (8.3 - 14.7)
Leukemia	28.6	4.4	6.5 (4.4 - 9.4)	7.1 (6.1 - 15.0)	20.3	3.1	6.5 (4.0 - 10.0)	9.0 (6.1 - 14.1)
Acute lymphoblastic leukemia	9.0	1.9	4.7 (2.1 - 8.9)	10.5 (6.3 - 15.0)	1.0	1.7	0.6 (0.0 - 3.3)	14.1 (14.1 - 14.1)
Acute myeloblastic leukemia	17.6	1.4	12.6 (7.4 - 20.1)	6.9 (6.0 - 14.5)	12.1	0.8	14.8 (7.7 - 25.8)	9.0 (6.2 - 13.4)
Other	2.0	0.9	2.2 (0.2 - 7.9)	13.8 (5.1 - 22.4)	7.3	0.5	13.5 (5.5 - 27.5)	9.9 (5.8 - 14.1)
Lymphoma	15.0	10.6	1.4 (0.8 - 2.3)	14.4 (12.5 - 20.2)	6.0	5.9	1.0 (0.4 - 2.2)	9.2 (6.8 - 13.0)
Central nervous system	54.6	4.7	11.5 (8.7 - 15.0)	9.2 (6.2 - 12.9)	36.2	3.1	11.6 (8.1 - 16.0)	8.3 (7.4 - 12.2)
Glial	44.0	3.6	12.1 (8.8 - 16.2)	9.2 (6.2 - 12.0)	33.0	2.3	14.4 (9.9 - 20.2)	8.3 (7.4 - 12.2)
Medulloblastoma	6.6	0.5	13.5 (5.3 - 28.4)	8.8 (8.8 - 9.2)	0.0	0.4	0.0 (. - 10.1)	
Breast	60.0	6.5	9.2 (7.0 - 11.8)	19.2 (15.9 - 21.7)	12.0	1.5	7.8 (4.0 - 13.6)	12.9 (8.7 - 17.1)
Bone	21.0	1.6	12.8 (7.9 - 19.6)	9.5 (8.2 - 12.7)	5.2	1.2	4.3 (1.4 - 10.0)	10.5 (9.0 - 11.7)
Osteosarcoma	17.0	0.8	20.9 (12.1 - 33.4)	9.2 (8.2 - 12.7)	4.2	0.6	6.6 (1.9 - 16.6)	9.0 (7.6 - 10.5)
Ewing sarcoma	2.0	0.4	4.8 (0.5 - 17.3)	13.3 (11.9 - 14.7)	0.0	0.3	0.0 (. - 11.0)	
Other bone	2.0	0.4	5.3 (0.6 - 19.1)	8.1 (6.4 - 9.8)	1.0	0.2	4.8 (0.1 - 26.9)	11.7 (11.7 - 11.7)
Soft tissue sarcoma	32.2	4.3	7.6 (5.2 - 10.7)	16.0 (9.6 - 20.6)	13.0	2.1	6.1 (3.2 - 10.4)	11.2 (10.1 - 13.3)
Thyroid	83.3	7.5	11.2 (8.9 - 13.8)	19.7 (15.9 - 21.6)	37.5	4.0	9.4 (6.6 - 12.9)	13.0 (10.7 - 17.4)
Melanoma	16.0	7.9	2.0 (1.2 - 3.3)	18.8 (14.1 - 21.9)	14.3	3.5	4.0 (2.2 - 6.7)	12.1 (11.0 - 15.9)
All Others	74.3	21.2	3.5 (2.8 - 4.4)	14.4 (8.3 - 20.7)	26.3	9.0	2.9 (1.9 - 4.3)	8.9 (8.3 - 15.7)

^a Analyses, including reported percentages and means/medians, were weighted to account for undersampling of acute lymphoblastic leukemia (ALL) survivors (1987-1999), with a weight of 1.21 for ALL age 0 or 11-20 years at diagnosis, and a weight of 3.63 for those aged 1-10 years. Abbreviations: IQR, interquartile range; SIR, standardized incidence ratio.

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34 **eTable 3. Cumulative incidence at 15 years, SIR, and absolute excess risk per 1000 person years for subsequent malignant neoplasms,**
 35 **for each childhood cancer diagnosis, by decade of diagnosis.**

Childhood cancer diagnosis	Overall cohort			1970-79			1980-89			1990-99		
	SIR (95% CI)	Absolute Excess Risk (95% CI)	Cumulative Incidence (%) (95% CI)	SIR (95% CI)	Absolute Excess Risk (95% CI)	Cumulative Incidence (%) (95% CI)	SIR (95% CI)	Absolute Excess Risk (95% CI)	Cumulative Incidence (%) (95% CI)	SIR (95% CI)	Absolute Excess Risk (95% CI)	Cumulative Incidence (%) (95% CI)
All diagnoses	5.4 (5.1 - 5.7)	2.1 (2.0 - 2.3)	1.7 (1.5 - 1.8)	5.3 (4.8 - 5.7)	3.0 (2.7 - 3.4)	2.1 (1.7 - 2.4)	5.7 (5.1 - 6.3)	2.0 (1.7 - 2.2)	1.7 (1.5 - 2.0)	5.2 (4.4 - 6.0)	1.2 (1.0 - 1.5)	1.3 (1.1 - 1.5)
Hodgkin lymphoma	7.7 (6.9 - 8.6)	6.1 (5.4 - 6.9)	3.6 (3.0 - 4.3)	7.9 (6.9 - 9.0)	8.0 (6.8 - 9.3)	4.8 (3.6 - 6.1)	7.9 (6.4 - 9.6)	5.1 (4.0 - 6.4)	3.1 (2.0 - 4.1)	6.1 (4.1 - 8.7)	2.8 (1.7 - 4.2)	2.6 (1.4 - 3.7)
Non-Hodgkin lymphoma	4.2 (3.3 - 5.3)	1.8 (1.3 - 2.4)	1.2 (0.7 - 1.7)	3.8 (2.6 - 5.4)	2.1 (1.2 - 3.4)	0.9 (0.0 - 1.7)	5.1 (3.5 - 7.3)	2.1 (1.3 - 3.1)	1.5 (0.6 - 2.3)	3.5 (1.7 - 6.4)	0.9 (0.3 - 2.0)	1.1 (0.4 - 1.9)
Rhabdomyosarcoma	7.5 (5.9 - 9.5)	3.0 (2.3 - 4.0)	2.6 (1.7 - 3.5)	7.2 (5.1 - 9.9)	3.8 (2.5 - 5.4)	2.7 (1.1 - 4.4)	9.3 (6.1 - 13.6)	3.2 (2.0 - 4.9)	3.2 (1.6 - 4.9)	4.6 (1.5 - 10.7)	1.0 (0.1 - 2.8)	1.8 (0.2 - 3.4)
Neuroblastoma	6.3 (4.7 - 8.4)	1.4 (1.0 - 1.9)	1.0 (0.6 - 1.5)	5.4 (3.3 - 8.3)	1.6 (0.8 - 2.6)	1.4 (0.3 - 2.4)	9.1 (5.8 - 13.7)	1.8 (1.1 - 2.9)	1.4 (0.5 - 2.3)	3.8 (1.2 - 9.0)	0.5 (0.0 - 1.4)	0.5 (0.0 - 1.0)
Kidney tumor	3.7 (2.7 - 5.0)	0.8 (0.5 - 1.3)	0.8 (0.4 - 1.2)	4.0 (2.5 - 6.1)	1.3 (0.7 - 2.2)	1.3 (0.3 - 2.3)	3.8 (2.1 - 6.3)	0.8 (0.3 - 1.4)	0.8 (0.2 - 1.4)	2.5 (0.7 - 6.3)	0.3 (0 - 1.0)	0.3 (0.0 - 0.8)
Acute lymphoblastic leukemia	4.3 (3.7 - 4.9)	1.2 (1.0 - 1.4)	1.4 (1.1 - 1.6)	3.5 (2.7 - 4.3)	1.4 (1.0 - 1.9)	1.1 (0.6 - 1.6)	4.6 (3.7 - 5.6)	1.2 (0.9 - 1.6)	1.7 (1.3 - 2.2)	5.3 (4.0 - 6.9)	1.1 (0.7 - 1.5)	1.1 (0.8 - 1.4)
Acute myeloblastic leukemia	4.1 (2.6 - 6.1)	1.4 (0.7 - 2.3)	0.8 (0.2 - 1.4)	4.8 (2.3 - 8.8)	2.8 (1.0 - 5.8)	0.8 (0.0 - 2.3)	3.9 (1.8 - 7.5)	1.3 (0.3 - 2.8)	1.2 (0.0 - 2.4)	3.1 (0.8 - 7.9)	0.6 (0 - 2.1)	0.5 (0.0 - 1.2)
Other leukemia	10.9 (6.7 - 16.7)	4.7 (2.7 - 7.4)	2.4 (0.7 - 4.2)	12.4 (5.9 - 22.8)	6.8 (2.9 - 12.9)	4.1 (0.0 - 8.5)	10.9 (4.4 - 22.4)	4.3 (1.5 - 9.4)	1.0 (0.0 - 2.8)	8.4 (2.3 - 21.6)	2.8 (0.5 - 7.7)	2.7 (0.0 - 5.8)
Bone cancer	4.9 (4.1 - 5.9)	3.0 (2.4 - 3.8)	2.5 (1.8 - 3.2)	4.5 (3.4 - 5.8)	3.5 (2.4 - 4.9)	2.8 (1.5 - 4.2)	5.1 (3.7 - 7.0)	2.8 (1.8 - 4.0)	2.3 (1.2 - 3.4)	6.4 (3.8 - 9.9)	2.5 (1.3 - 4.1)	2.4 (1.1 - 3.6)
Ewing	6.7 (4.9 - 8.9)	3.8 (2.6 - 5.3)	3.1 (1.8 - 4.4)	6.6 (4.2 - 9.9)	4.8 (2.7 - 7.6)	3.9 (1.3 - 6.6)	8.0 (4.9 - 12.3)	4.3 (2.4 - 6.9)	3.3 (1.2 - 5.5)	4.1 (1.1 - 10.5)	1.3 (0.0 - 4.0)	1.9 (0.1 - 3.7)
Osteosarcoma	4.2 (3.2 - 5.3)	2.6 (1.8 - 3.5)	2.1 (1.3 - 2.9)	3.7 (2.6 - 5.2)	2.9 (1.7 - 4.6)	2.2 (0.7 - 3.7)	3.9 (2.4 - 5.9)	2.0 (1.0 - 3.5)	1.7 (0.5 - 2.9)	7.1 (3.8 - 12.2)	3.0 (1.3 - 5.4)	2.3 (0.7 - 3.9)
Central nervous system cancer	4.4 (3.6 - 5.3)	1.5 (1.2 - 1.9)	1.3 (1.0 - 1.7)	3.3 (2.3 - 4.6)	1.6 (0.9 - 2.4)	1.1 (0.6 - 1.6)	4.8 (3.5 - 6.4)	1.6 (1.0 - 2.2)	1.1 (0.6 - 1.6)	5.6 (3.9 - 7.8)	1.4 (0.9 - 2.1)	1.5 (1.0 - 2.1)

36 Abbreviations: CI, confidence interval; SIR, standardized incidence ratio.

37 **eTable 4. Observed and expected numbers of malignant events, by attained age and decade of diagnosis, as included in Figure 2.**

Attained age	Observed ^a			Expected, based on SEER			SIR		
	1970s	1980s	1990s	1970s	1980s	1990s	1970s	1980s	1990s
10-19	17.6	14.1	13.9	1.7	1.7	1.7	10.6 (8.1 - 13.5)	8.2 (6.6 - 10.2)	8.0 (6.3 - 9.9)
20-29	25.0	21.3	16.2	4.5	4.5	4.6	5.6 (4.7 - 6.6)	4.7 (4.0 - 5.6)	3.5 (2.7 - 4.6)
30-29	56.5	48.8	30.3	10.5	10.2	9.8	5.4 (4.7 - 6.2)	4.8 (3.9 - 5.8)	3.1 (1.8 - 5.0)

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39 ^a Analyses, including reported percentages and means/medians, were weighted to account for undersampling of acute lymphoblastic leukemia (ALL) survivors
 40 (1987-1999), with a weight of 1.21 for ALL age 0 or 11-20 years at diagnosis, and a weight of 3.63 for those aged 1-10 years.

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43 **eTable 5. Standardized incidence ratios of subsequent malignant neoplasms by decade of diagnosis and by attained age groups among**
 44 **Hodgkin lymphoma survivors.**

	1970-79	1980-89	1990-99	P
Attained age, years				
10-19	21.9 (10.0 - 41.7)	8.0 (1.6 - 23.4)	17.3 (5.6 - 40.3)	0.53
20-29	10.7 (7.7 - 14.4)	6.8 (4.4 - 10.0)	5.5 (3.2 - 9.0)	0.016
30-39	10.2 (8.2 - 12.5)	8.4 (6.3 - 11.0)	5.2 (2.4 - 9.8)	0.038

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47 eTable 6. Source data^a for multivariable model presented in Table 2.

Variable	N	Person years	Number of events			
			Subsequent neoplasm	Subsequent malignant neoplasm	Meningioma	Non-melanoma skin cancer
Sex						
Male	9898	156681	1094	296	80	718
Female	8884	144311	1368	491	112	765
Age at diagnosis						
0-4	7688	125506	549	187	95	267
5-9	4258	67784	387	143	57	187
10-14	3931	61861	602	213	25	364
15+	2905	45841	924	244	15	665
Year of diagnosis						
1970-74	1685	43402	782	199	53	530
1975-79	2797	61502	810	197	69	544
1980-84	3928	67636	490	181	37	272
1985-89	3525	55036	220	103	17	100
1990-94	3239	42824	106	67	10	29
1995-99	3608	30592	54	40	6	8
Maximum radiation treatment dose to any body region (Gy)						
None	8728	127682	242	160	6	76
0.1-10	262	4080	36	14	4	18
10.1-20	2737	45195	277	93	26	158
20.1-30	2416	45605	451	131	70	250
30.1-40	1296	24754	582	151	10	421
40.1-50	1507	26863	622	149	28	445
50+	1836	26813	252	89	48	115
History of splenectomy (yes/no)						
Yes	1107	22467	792	177	2	613
No	17675	278525	1670	610	190	870
Cyclophosphamide equivalent dose (mg/m ²)						
None	9139	153887	1178	321	126	731
1-3999	2421	35854	178	76	11	91
4000-7999	2479	36934	301	115	17	169
8000+	4743	74316	805	275	38	492
Anthracycline (mg/m ²)						
None	10039	174654	1742	473	152	1117
0-100	1276	17453	80	27	9	44
101-300	4553	62099	386	149	16	221
>300	2914	46787	254	138	15	101

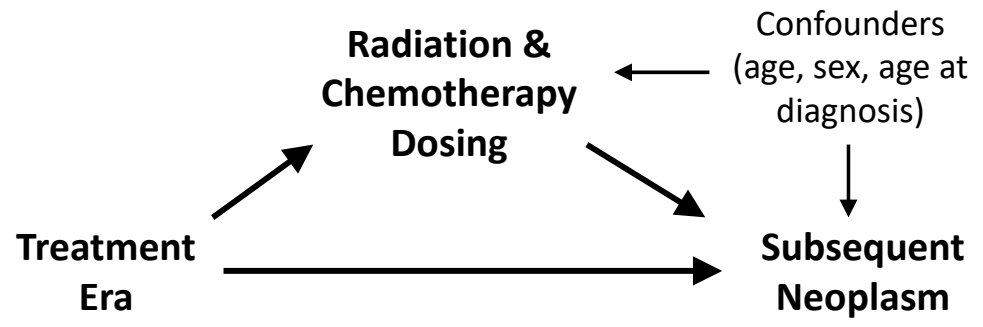
48 **eTable 6 (continued). Source data^a for multivariable model presented in Table 2.**

Variable	N	Person years	Number of events			
			Subsequent neoplasm	Subsequent malignant neoplasm	Meningioma	Non-melanoma skin cancer
Epipodophyllotoxin (mg/m ²)						
None	15538	261199	2293	707	171	1415
1-1000	874	11114	77	24	9	44
1001-4000	1611	19107	54	29	5	20
>4000	759	9572	38	27	7	4
Platinum (mg/m ²)						
None	16754	276423	2338	719	171	1448
1-400	700	9008	47	20	10	17
401-750	664	8479	46	29	5	12
>750	664	7082	31	19	6	6

49 ^aIncludes survivors with non-missing data on all treatment variables, consistent with the analysis cohort of Table 2.

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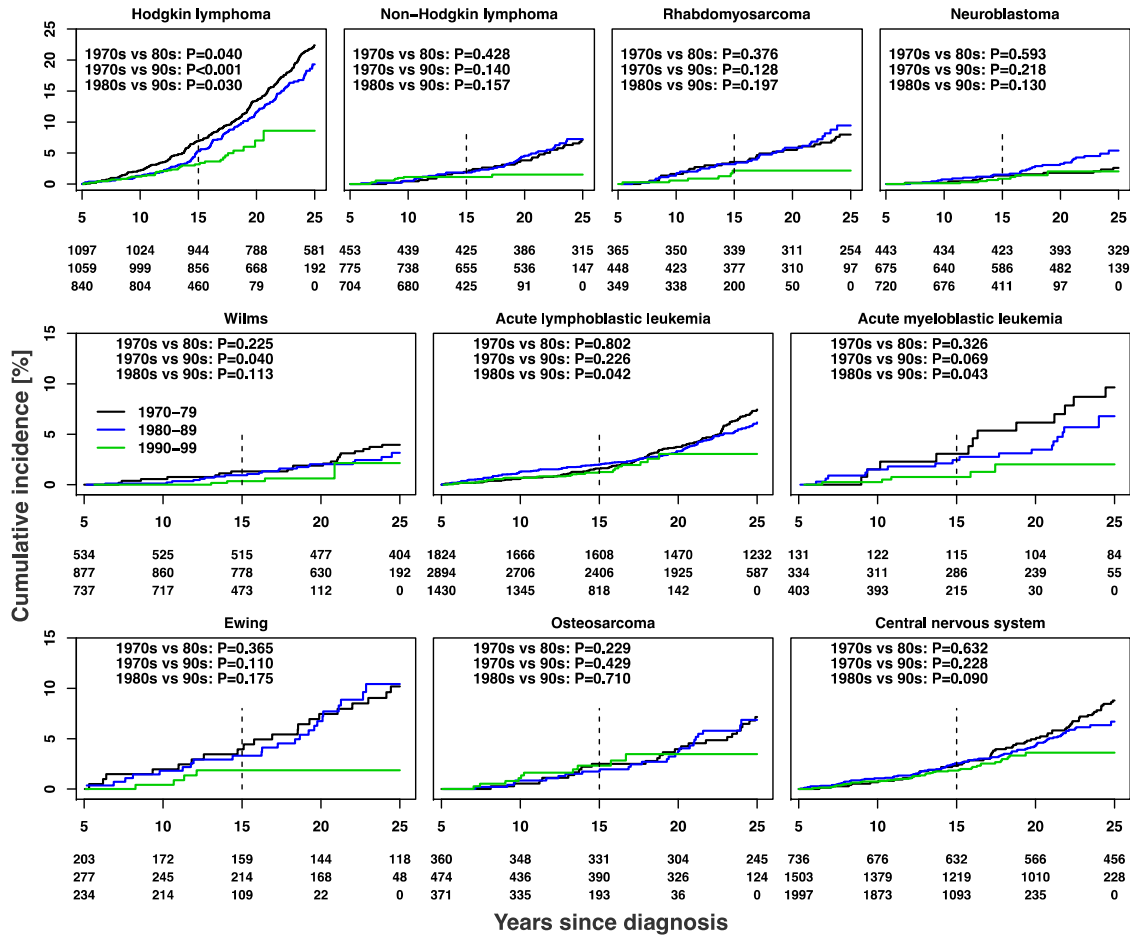
54 | eFigure 1. The causal diagram of the mediation analysis for the association of treatment era and subsequent neoplasm rates, mediated
55 | by radiation and chemotherapy dosing.



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59 eFigure 2. Cumulative incidence of subsequent neoplasms (A) and subsequent malignant neoplasms (B), by initial cancer diagnosis and
 60 decade of initial cancer diagnosis.

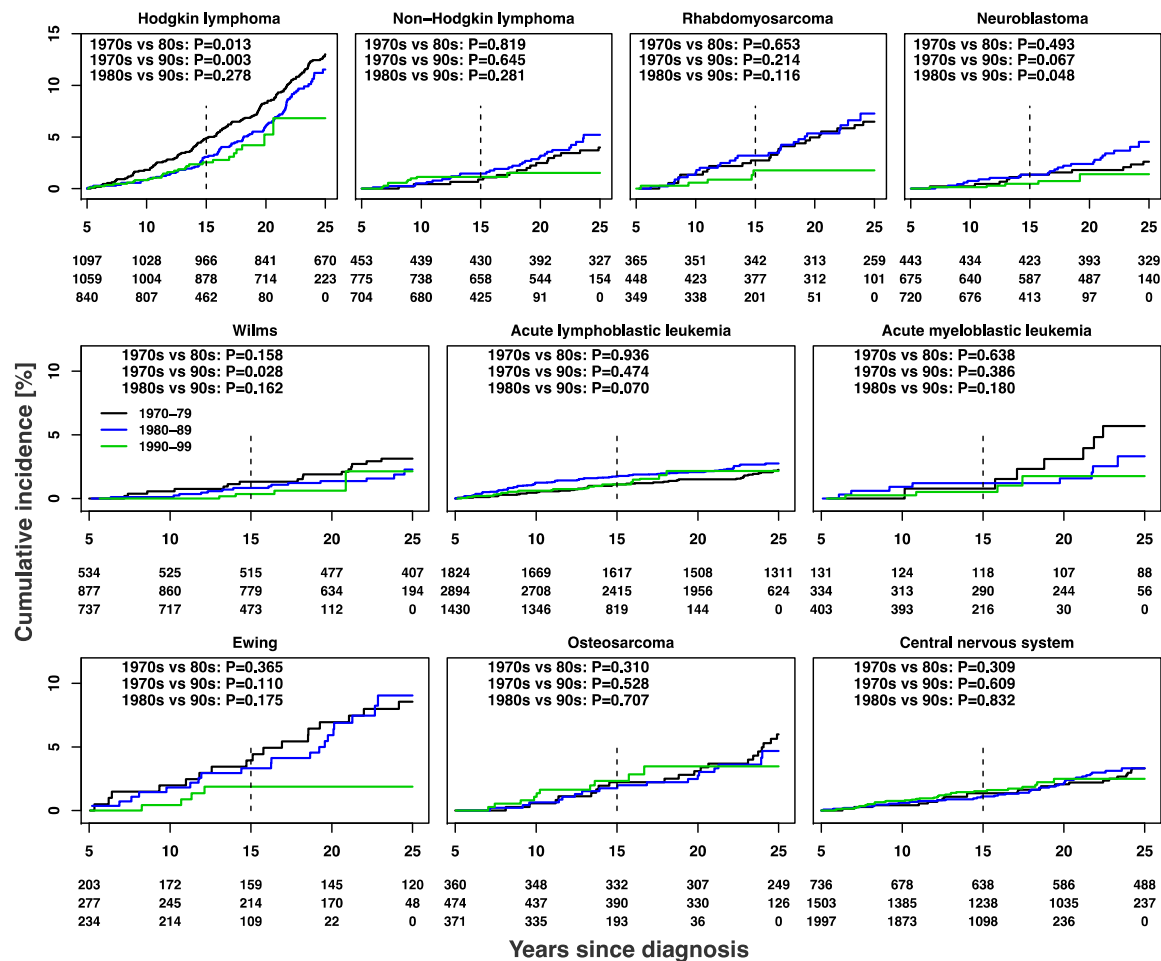
61 A.



62
 63 Permutation tests were used to assess differences between curves. Number of individuals at risk for each time point is listed below the x-axis (1970s top,
 64 1980s middle, 1990s bottom). Vertical dashed line at 15 year mark represents the time point of interest.

65 eFigure 2 (continued). Cumulative incidence of subsequent neoplasms (A) and subsequent malignant neoplasms (B), by initial cancer diagnosis and decade of initial cancer diagnosis.
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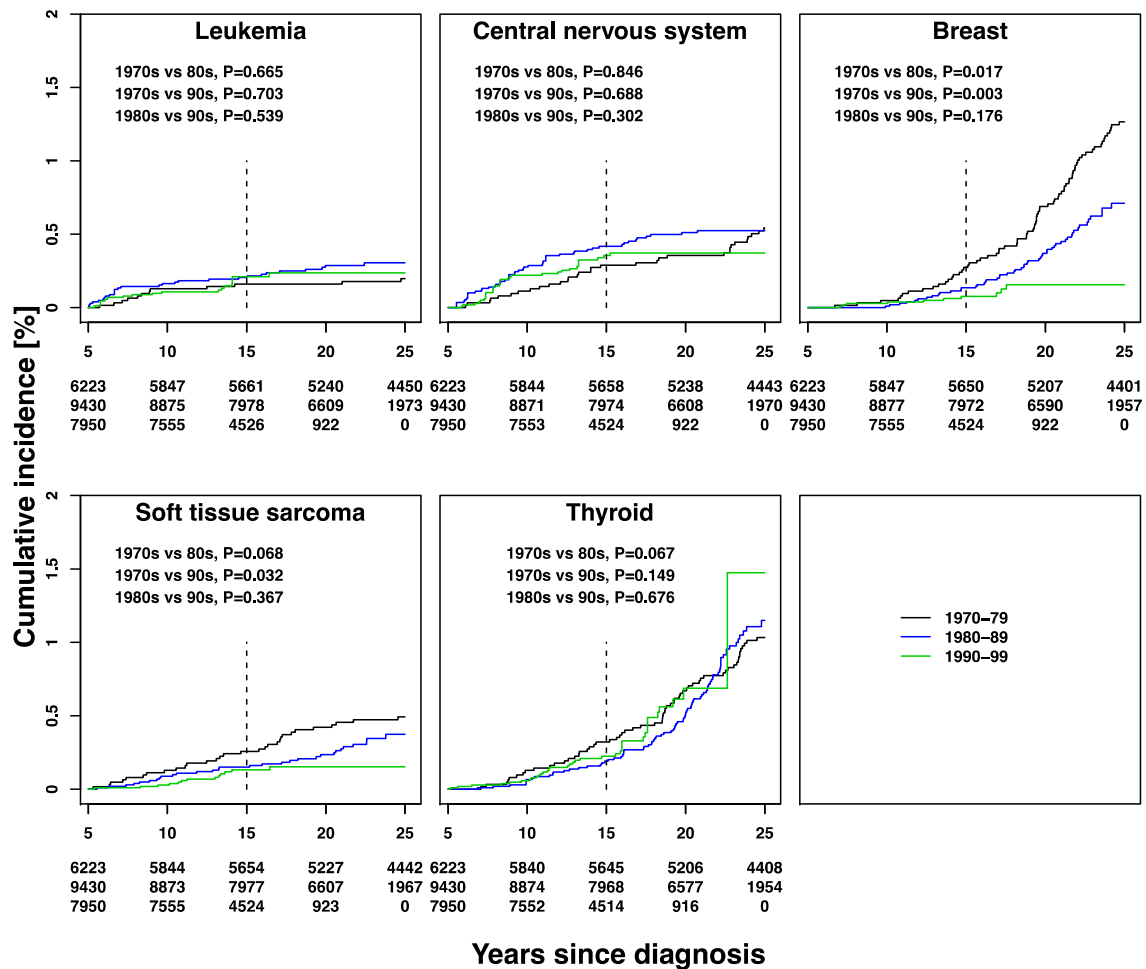
67 B.



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 69 Permutation tests were used to assess differences between curves. Number of individuals at risk for each time point is listed below the x-axis (1970s top,
 70 1980s middle, 1990s bottom). Vertical dashed line at 15 year mark represents the time point of interest.

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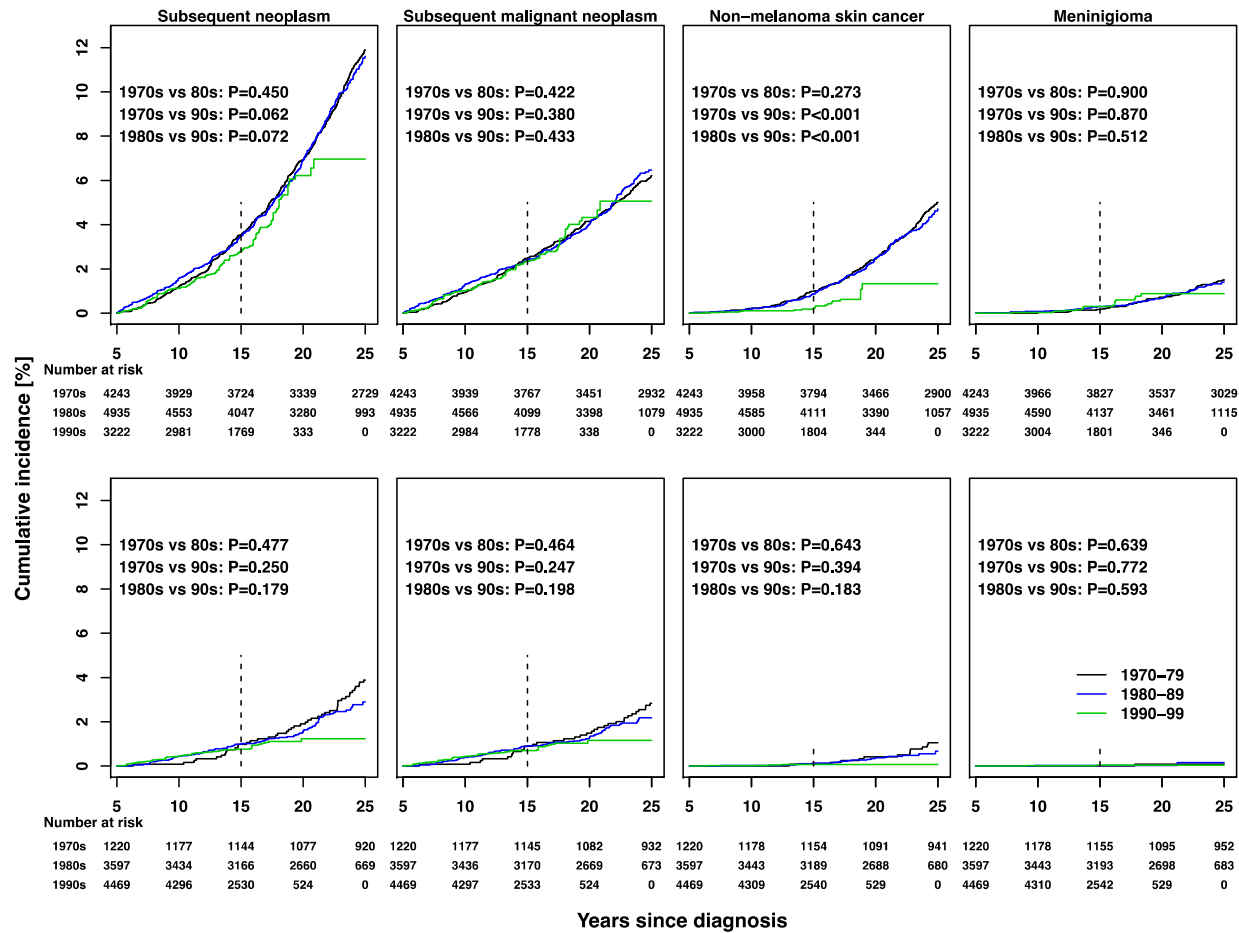
eFigure 3. Cumulative incidence of specific SMN types, by decade of initial cancer diagnosis.



Permutation tests were used to assess differences between curves. **Number of individuals at risk for each time point is listed below the x-axis (1970s top, 1980s middle, 1990s bottom).** Vertical dashed line at 15 year mark represents the time point of interest.

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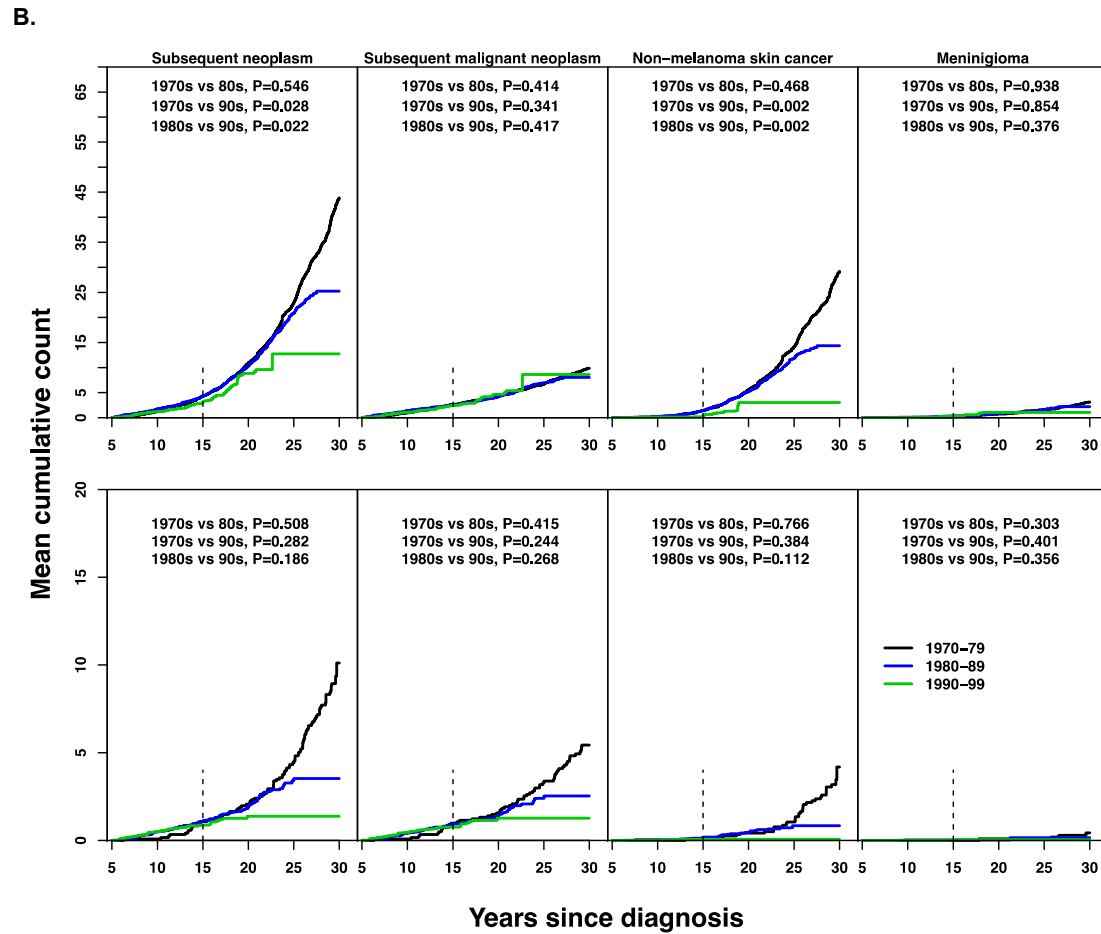
77 eFigure 4. Cumulative incidence (A) and cumulative burden (mean cumulative count per 100 survivors) (B) of subsequent neoplasms, by
 78 type, decade of initial cancer diagnosis and therapeutic radiation exposure. Radiation exposed are in the top row, unexposed are in the
 79 bottom row.
 80 A.



81
 82 Permutation tests were used to assess differences between curves. Number of individuals at risk for each time point is listed below the x-axis (1970s top,
 83 1980s middle, 1990s bottom). Vertical dashed line at 15 year mark represents the time point of interest.

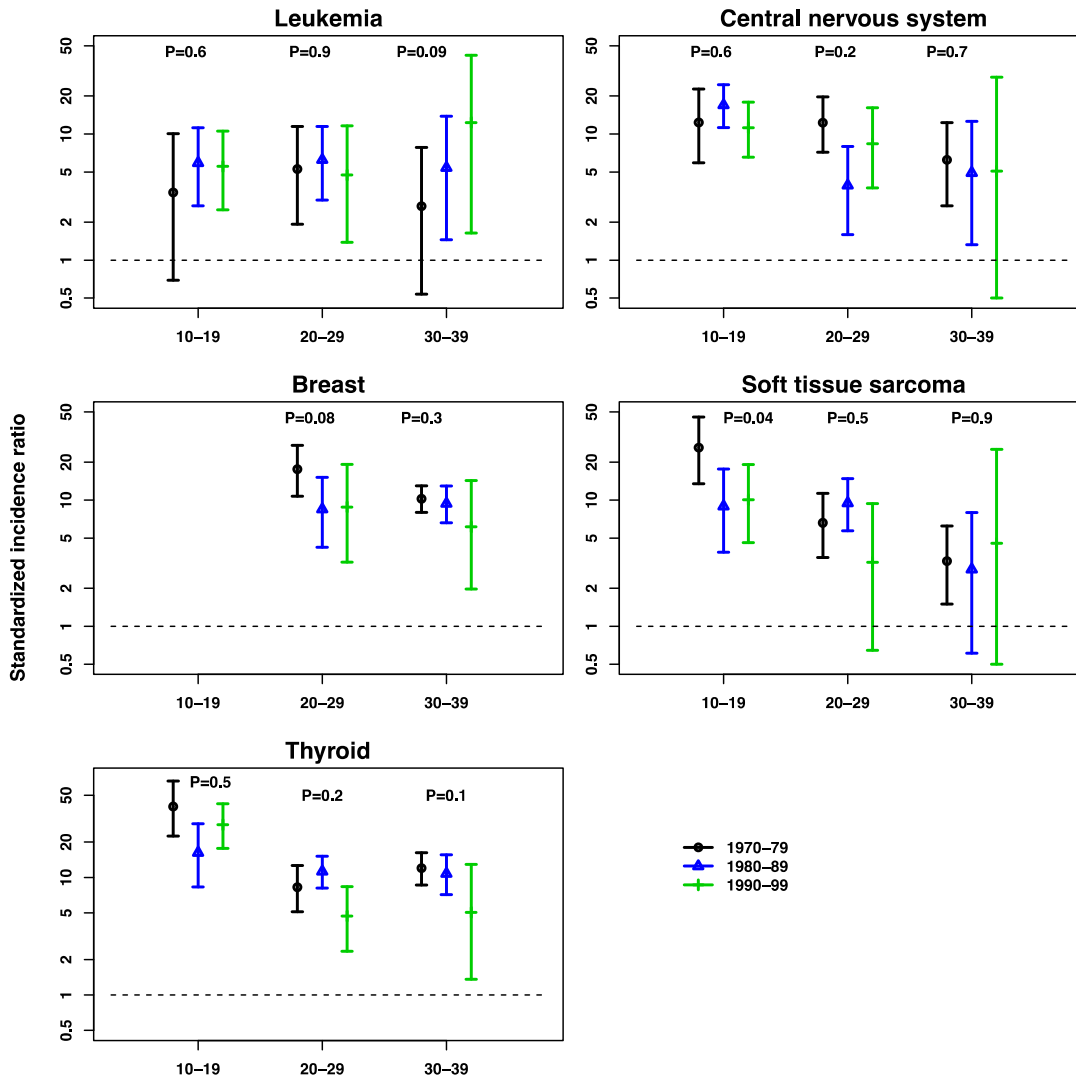
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eFigure 4 (continued). Cumulative incidence (A) and cumulative burden (mean cumulative count per 100 survivors) (B) of subsequent neoplasms, by type, decade of initial cancer diagnosis and therapeutic radiation exposure. Radiation exposed are in the top row, unexposed are in the bottom row.



90
91 Permutation tests were used to assess differences between curves. Vertical dashed line at 15 year mark represents the time point of interest.

Figure 5. Standardized incidence ratios for select subsequent malignant neoplasm diagnoses, by attained age and decade of diagnosis. Vertical bars represent 95% confidence intervals.



Standardized incidence ratio (SIR) = observed number of events/expected number of events. SIRs calculated using age-sex-calendar-year-specific U.S. cancer incidence rates from the Surveillance, Epidemiology, and End Results program to determine expected numbers of events. Analyses were weighted to account for undersampling of acute lymphoblastic leukemia (ALL) survivors (1987-1999), with a weight of 1.21 for ALL age 0 or 11-20 years at diagnosis, and a weight of 3.63 for those aged 1-10 years.

The number of individuals from each decade of diagnosis contributing data for each attained age are as follows: 1970s, 10-19 years 5,072; 20-29 years 5,810; 30-39 years 4,809; 1980s, 10-19 years 7,932; 20-29 years 8,283; 30-39 years 3,901; 1990s, 10-19 years 6,622; 20-29 years 5,517; 30-39 years 1,534.