Memphis
June, 2013

* Includes Neurology and Reproductive WGs

- **Chuck Sklar (Chair)**
    - **Lisa Diller**
    - **Eric Chow**
    - **Dan Green**
    - **Kevin Oeffinger (Chair-elect)**
    - **Roger Packer**

- Congenital anomalies in offspring, **Signorello (JCO)**
- Risk factors for obesity, **Green (JCO)**
- Fracture risk, **Wilson (Cancer)**
- Differential effects of radiotherapy on growth/endocrine function in leukemia, **Chow (Pediatr Blood Cancer)**
- Radiation, atherosclerotic risk factors and stroke risk, **Mueller (Int J Radiat Oncol Biol Phys)**
- Infertility, infertility treatment, and achievement of pregnancy in female survivors, **Barton (Lancet Oncology)**
- Modifiable CVRF and major cardiac events, **Armstrong (JCO)**
- Cyclophosphamide equivalent dose as an approach for quantifying alkylating agent exposure, **Green (Pediatr Blood Cancer)**

Differential Effects of Radiotherapy on Growth and Endocrine Function Among Acute Leukemia Survivors: A Childhood Cancer Survivor Study Report

Eric J. Chow, MD, MPH,[1,2]* Wei Liu, PhD,[3] Kumar Srivastava, PhD,[3] Wendy M. Leisenring, ScD,[2]
Robert J. Hayashi, MD,[4] Charles A. Sklar, MD,[5] Marilyn Stovall, PhD,[6]
Leslie L. Robison, PhD,[7] and K. Scott Baker, MD, MS[1,2]

TABLE II. Height (z-score) and Risk of Short Stature (z-score < -1.96) among Leukemia Survivors

Radiotherapy	No. analyzed[a]	Mean z-score (SD)	No. short stature (%)	OR[b]	(95% CI)
CRT/TBI					
None	983	0.02 (1.16)	37 (3.8)	1.0	(ref)
CRT only	1872	−0.64 (1.12)	189 (10.1)	2.9	(2.0, 4.2)
TBI only	55	−1.00 (1.70)	13 (23.6)	8.0	(3.7, 17.4)[c]
CRT+TBI	35	−1.36 (1.30)	11 (31.4)	10.6	(4.5, 25.3)[c]
SRT					
None	2672	−0.36 (1.18)	196 (7.3)	1.0	(ref)
Any	273	−1.15 (1.15)	54 (19.8)	2.8	(1.9–4.0)

TABLE II. Height (z-score) and Risk of Short Stature (z-score < -1.96) among Leukemia Survivors

Radiotherapy	No. analyzed[a]	Mean z-score (SD)	No. short stature (%)	OR[b]	(95% CI)
CRT/TBI					
None	983	0.02 (1.16)	37 (3.8)	1.0	(ref)
CRT only	1872	−0.64 (1.12)	189 (10.1)	2.9	(2.0, 4.2)
TBI only	55	−1.00 (1.70)	13 (23.6)	8.0	(3.7, 17.4)[c]
CRT+TBI	35	−1.36 (1.30)	11 (31.4)	10.6	(4.5, 25.3)[c]
SRT					
None	2672	−0.36 (1.18)	196 (7.3)	1.0	(ref)
Any	273	−1.15 (1.15)	54 (19.8)	2.8	(1.9–4.0)

TABLE II. Height (z-score) and Risk of Short Stature (z-score < −1.96) among Leukemia Survivors

Radiotherapy	No. analyzed[a]	Mean z-score (SD)	No. short stature (%)	OR[b]	(95% CI)
CRT/TBI					
None	983	0.02 (1.16)	37 (3.8)	1.0	(ref)
CRT only	1872	−0.64 (1.12)	189 (10.1)	2.9	(2.0, 4.2)
TBI only	55	−1.00 (1.70)	13 (23.6)	8.0	(3.7, 17.4)[c]
CRT+TBI	35	−1.36 (1.30)	11 (31.4)	10.6	(4.5, 25.3)[c]
SRT					
None	2672	−0.36 (1.18)	196 (7.3)	1.0	(ref)
Any	273	−1.15 (1.15)	54 (19.8)	2.8	(1.9–4.0)

TABLE II. Height (z-score) and Risk of Short Stature (z-score < −1.96) among Leukemia Survivors

Radiotherapy	No. analyzed[a]	Mean z-score (SD)	No. short stature (%)	OR[b]	(95% CI)
CRT/TBI					
None	983	0.02 (1.16)	37 (3.8)	1.0	(ref)
CRT only	1872	−0.64 (1.12)	189 (10.1)	2.9	(2.0, 4.2)
TBI only	55	−1.00 (1.70)	13 (23.6)	8.0	(3.7, 17.4)[c]
CRT+TBI	35	−1.36 (1.30)	11 (31.4)	10.6	(4.5, 25.3)[c]
SRT					
None	2672	−0.36 (1.18)	196 (7.3)	1.0	(ref)
Any	273	−1.15 (1.15)	54 (19.8)	2.8	(1.9–4.0)

TABLE IV. Prevalence and Odds of Hypothyroidism and Reproductive Outcomes among Leukemia Survivors

Radiotherapy	Hypothyroid No. analyzed[a]	No. affected (%)	OR[b]	(95% CI)	Ever pregnant No. analyzed	No. affected (%)	OR[b]	(95% CI)	Live birth No. affected (%)[c]	OR[b]	(95% CI)
CRT/TBI											
None	1198	48 (4.0)	1.0	(ref)	1200	527 (43.9)	1.0	(ref)	451 (37.6)	1.0	(ref)
CRT only	2127	145 (6.8)	1.6	(1.1, 2.3)	2143	773 (36.1)	0.5	(0.5–0.6)	666 (31.1)	0.6	(0.5–0.7)
TBI only	70	16 (22.9)	6.8	(3.4, 13.5)[d]	73	8 (11.0)	0.1	(0.04–0.2)[d]	5 (6.9)	0.07	(0.03–0.18)[d]
CRT+TBI	47	14 (29.8)	10.9	(5.3, 22.3)[d]	51	2 (3.9)	0.03	(0.01–0.14)[d,e]	0	0	—
SRT											
None	3148	180 (5.7)	1.0	(ref)	3160	1222 (38.7)	1.0	(ref)	1048 (33.2)	1.0	(ref)
Any	294	43 (14.6)	2.6	(1.7–3.8)	307	88(28.7)	0.5	(0.3–0.6)	74 (24.1)	0.5	(0.3–0.6)

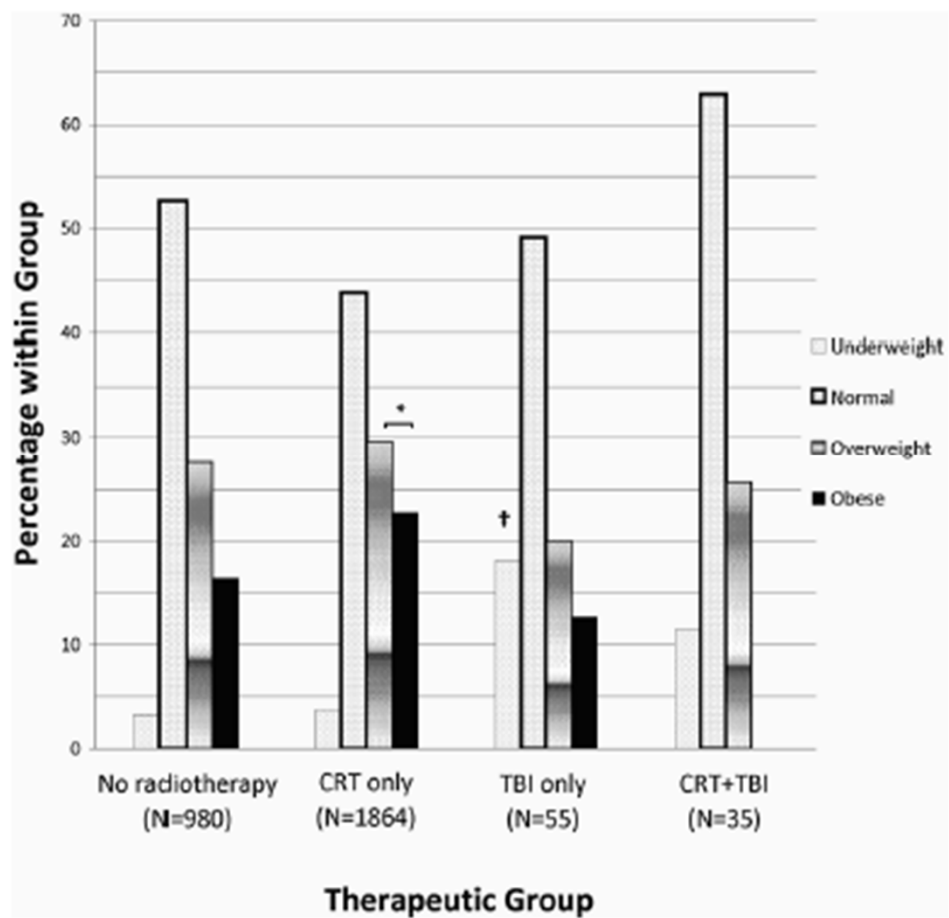**TABLE IV. Prevalence and Odds of Hypothyroidism and Reproductive Outcomes among Leukemia Survivors**

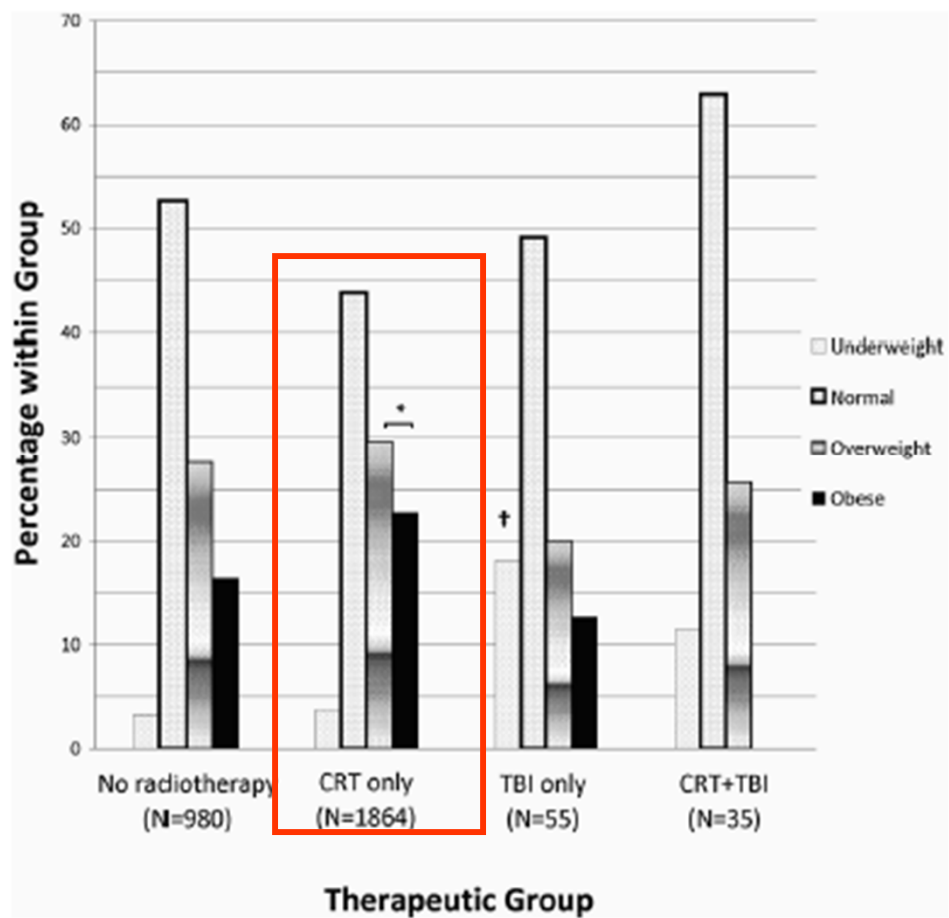| Radiotherapy	No. analyzed[a]	Hypothyroid No. affected (%)	OR[b]	(95% CI)	No. analyzed	Ever pregnant No. affected (%)	OR[b]	(95% CI)	Live birth No. affected (%)[c]	OR[b]	(95% CI)
CRT/TBI											
None	1198	48 (4.0)	1.0	(ref)	1200	527 (43.9)	1.0	(ref)	451 (37.6)	1.0	(ref)
CRT only	2127	145 (6.8)	1.6	(1.1, 2.3)	2143	773 (36.1)	0.5	(0.5–0.6)	666 (31.1)	0.6	(0.5–0.7)
TBI only	70	16 (22.9)	6.8	(3.4, 13.5)[d]	73	8 (11.0)	0.1	(0.04–0.2)[d]	5 (6.9)	0.07	(0.03–0.18)[d]
CRT+TBI	47	14 (29.8)	10.9	(5.3, 22.3)[d]	51	2 (3.9)	0.03	(0.01–0.14)[d,e]	0	0	—
SRT											
None	3148	180 (5.7)	1.0	(ref)	3160	1222 (38.7)	1.0	(ref)	1048 (33.2)	1.0	(ref)
Any	294	43 (14.6)	2.6	(1.7–3.8)	307	88 (28.7)	0.5	(0.3–0.6)	74 (24.1)	0.5	(0.3–0.6)

TABLE IV. Prevalence and Odds of Hypothyroidism and Reproductive Outcomes among Leukemia Survivors

Radiotherapy	Hypothyroid				Ever pregnant				Live birth			
	No. analyzed[a]	No. affected (%)	OR[b]	(95% CI)	No. analyzed	No. affected (%)	OR[b]	(95% CI)	No. affected (%)[c]	OR[b]	(95% CI)
CRT/TBI											
None	1198	48 (4.0)	1.0	(ref)	1200	527 (43.9)	1.0	(ref)	451 (37.6)	1.0	(ref)
CRT only	2127	145 (6.8)	1.6	(1.1, 2.3)	2143	773 (36.1)	0.5	(0.5–0.6)	666 (31.1)	0.6	(0.5–0.7)
TBI only	70	16 (22.9)	6.8	(3.4, 13.5)[d]	73	8 (11.0)	0.1	(0.04–0.2)[d]	5 (6.9)	0.07	(0.03–0.18)[d]
CRT+TBI	47	14 (29.8)	10.9	(5.3, 22.3)[d]	51	2 (3.9)	0.03	(0.01–0.14)[d,e]	0	0	—
SRT											
None	3148	180 (5.7)	1.0	(ref)	3160	1222 (38.7)	1.0	(ref)	1048 (33.2)	1.0	(ref)
Any	294	43 (14.6)	2.6	(1.7–3.8)	307	88 (28.7)	0.5	(0.3–0.6)	74 (24.1)	0.5	(0.3–0.6)

TABLE IV. Prevalence and Odds of Hypothyroidism and Reproductive Outcomes among Leukemia Survivors
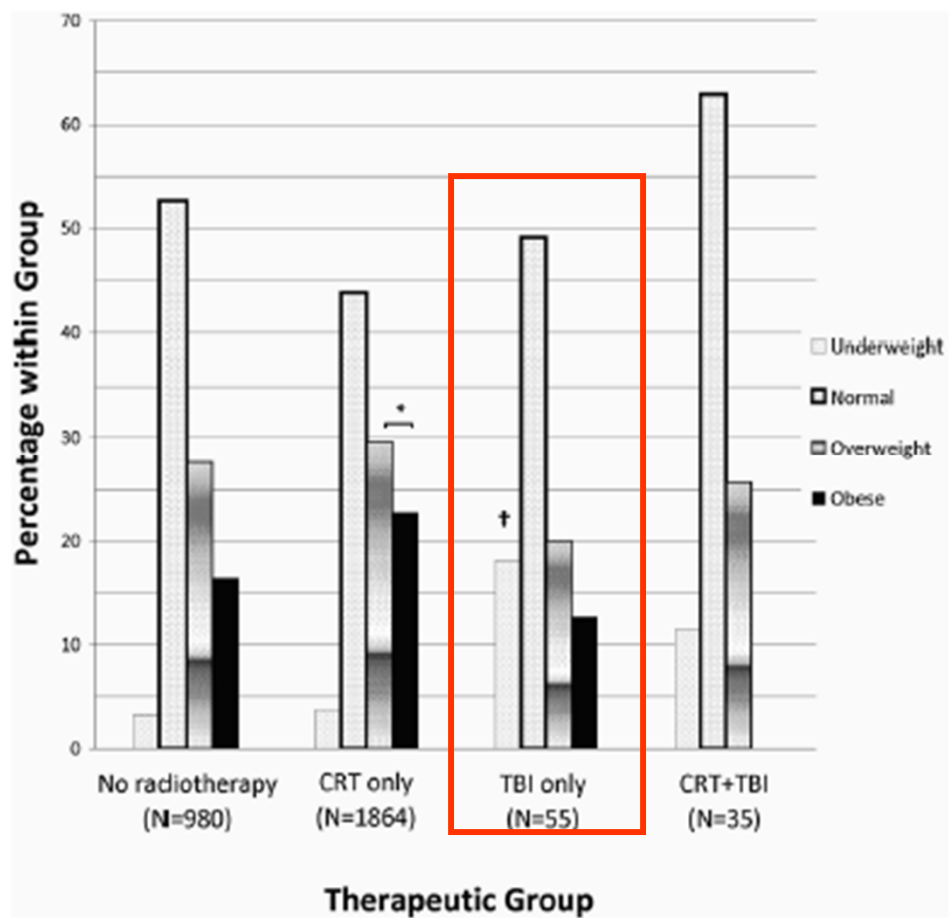
Radiotherapy	Hypothyroid				Ever pregnant				Live birth		
	No. analyzed[a]	No. affected (%)	OR[b]	(95% CI)	No. analyzed	No. affected (%)	OR[b]	(95% CI)	No. affected (%)[c]	OR[b]	(95% CI)
CRT/TBI											
None	1198	48 (4.0)	1.0	(ref)	1200	527 (43.9)	1.0	(ref)	451 (37.6)	1.0	(ref)
CRT only	2127	145 (6.8)	1.6	(1.1, 2.3)	2143	773 (36.1)	0.5	(0.5–0.6)	666 (31.1)	0.6	(0.5–0.7)
TBI only	70	16 (22.9)	6.8	(3.4, 13.5)[d]	73	8 (11.0)	0.1	(0.04–0.2)[d]	5 (6.9)	0.07	(0.03–0.18)[f]
CRT+TBI	47	14 (29.8)	10.9	(5.3, 22.3)[d]	51	2 (3.9)	0.03	(0.01–0.14)[d,e]	0	0	—
SRT											
None	3148	180 (5.7)	1.0	(ref)	3160	1222 (38.7)	1.0	(ref)	1048 (33.2)	1.0	(ref)
Any	294	43 (14.6)	2.6	(1.7–3.8)	307	88 (28.7)	0.5	(0.3–0.6)	74 (24.1)	0.5	(0.3–0.6)

Radiation, Atherosclerotic Risk Factors, and Stroke Risk in Survivors of Pediatric Cancer: A Report From the Childhood Cancer Survivor Study

Sabine Mueller, MD, PhD,* Heather J. Fullerton, MD, MAS,† Kayla Stratton, MS,§ Wendy Leisenring, ScD,§ Rita E. Weathers, MS,‖ Marilyn Stovall, PhD,‖ Gregory T. Armstrong, MD,¶ Robert E. Goldsby, MD,‡ Roger J. Packer, MD,# Charles A. Sklar, MD,** Daniel C. Bowers, MD,†† Leslie L. Robison, PhD,¶ and Kevin R. Krull, PhD¶

Table 3 Multivariate hazard ratio of first late-occurring stroke* in pediatric cancer survivors followed by the CCSS (n=14,186)

Characteristic	Model I[†]		Model II[†]	
	HR (95% CI)	P	HR (95% CI)	P
Age at diagnosis (y)				
0-4 vs 15-20	0.8 (0.5-1.3)	.35	0.8 (0.5-1.3)	.38
5-9 vs 15-20	0.9 (0.6-1.4)	.65	0.9 (0.6-1.4)	.73
10-14 vs 15-20	0.8 (0.6-1.3)	.39	0.8 (0.6-1.2)	.38
Male vs female	1.0 (0.8-1.4)	.78	1.0 (0.8-1.4)	.76
Max CRT dose				
50+ Gy vs none				<.0001
30-49 Gy vs none				<.0001
1.5-29 Gy vs none				.01
Indirect radiation vs none				.41
Known stroke risk factor				
HTN vs none				
Diabetes vs none				.21
Recurrence vs none	2.1 (1.5-2.9)	<.0001	2.1 (1.5- 2.9)	<.0001
Race				
Black non-Hispanic vs white non-Hispanic	1.7 (0.9-3.2)	.10	n/a	
Other race/ethnicity vs White non-Hispanic	1.3 (0.9-1.9)	.17	n/a	
White, HTN vs white, no HTN	n/a		3.8 (2.7-5.5)	<.0001
Black, HTN vs white, no HTN	n/a		15.9 (6.9-36.6)	<.0001
Black, no HTN vs white, no HTN	n/a		1.0 (0.4-2.5)	.95
Other race, HTN vs white, no HTN	n/a		4.1 (1.8-9.5)	<.001
Other race, no HTN vs white, no HTN	n/a		1.4 (0.9-2.1)	.14

229 Late-Occurring Strokes

RR 7.8 (95% CI 4.7-13.0)

Table 3 Multivariate hazard ratio of first late-occurring stroke* in pediatric cancer survivors followed by the CCSS (n=14,186)

Characteristic	Model I[†] HR (95% CI)	P	Model II[†] HR (95% CI)	P
Age at diagnosis (y)				
0-4 vs 15-20	0.8 (0.5-1.3)	.35	0.8 (0.5-1.3)	.38
5-9 vs 15-20	0.9 (0.6-1.4)	.65	0.9 (0.6-1.4)	.73
10-14 vs 15-20	0.8 (0.6-1.3)	.39	0.8 (0.6-1.2)	.38
Male vs female	1.0 (0.8-1.4)	.78	1.0 (0.8-1.4)	.76
Max CRT dose				
50+ Gy vs none	11.0 (7.4-16.5)	<.0001	11.0 (7.4-16.5)	<.0001
30-49 Gy vs none	5.9 (3.5-9.9)	<.0001	5.9 (3.5-9.9)	<.0001
1.5-29 Gy vs none	1.8 (1.2-2.8)	.01	1.8 (1.1-2.8)	.01
Indirect radiation vs none	1.2 (0.8-1.8)	.48	1.2 (0.8-1.8)	.41
Known stroke risk factor				
HTN vs none	4.0 (2.8-5.5)	<.0001	n/a	
Diabetes vs none	1.5 (0.8-2.6)	.17	1.4 (0.8-2.5)	.21
Recurrence vs none	2.1 (1.5-2.9)	<.0001	2.1 (1.5- 2.9)	<.0001
Race				
Black non-Hispanic vs white non-Hispanic	1.7 (0.9-3.2)	.10	n/a	
Other race/ethnicity vs White non-Hispanic	1.3 (0.9-1.9)	.17	n/a	
White, HTN vs white, no HTN	n/a		3.8 (2.7-5.5)	<.0001
Black, HTN vs white, no HTN	n/a		15.9 (6.9-36.6)	<.0001
Black, no HTN vs white, no HTN	n/a		1.0 (0.4-2.5)	.95
Other race, HTN vs white, no HTN	n/a		4.1 (1.8-9.5)	<.001
Other race, no HTN vs white, no HTN	n/a		1.4 (0.9-2.1)	.14

Table 3 Multivariate hazard ratio of first late-occurring stroke* in pediatric cancer survivors followed by the CCSS (n=14,186)

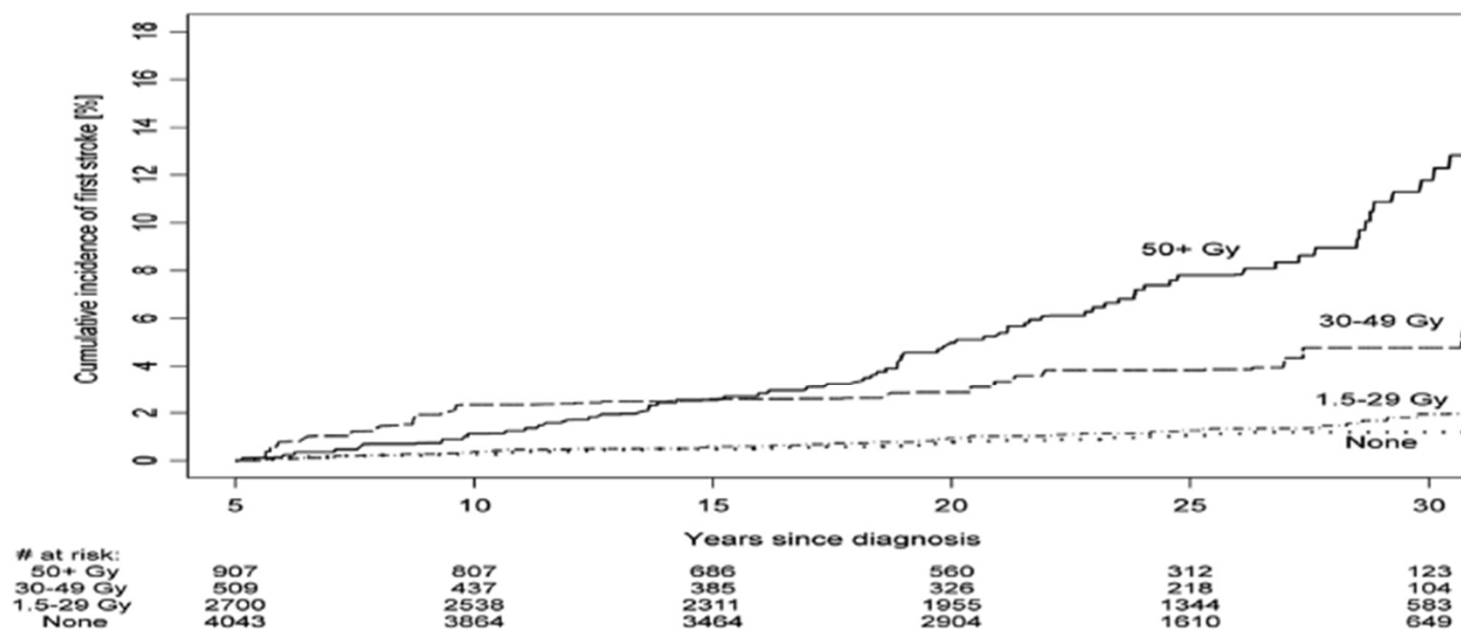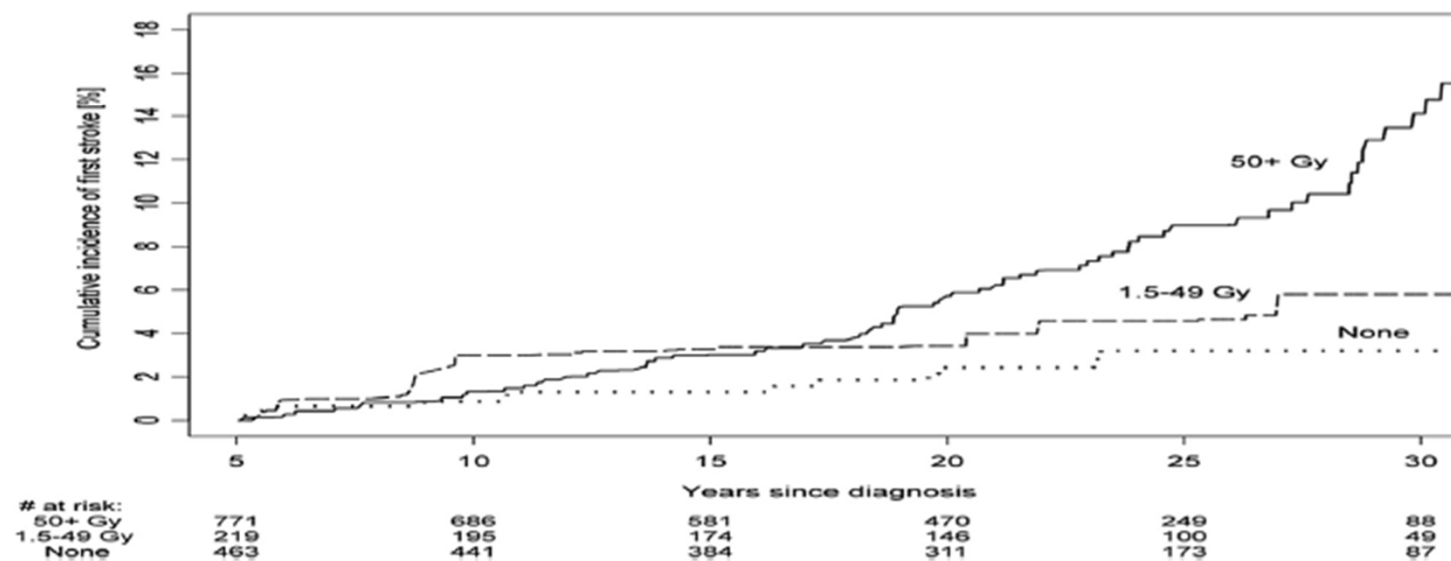| Characteristic	Model I†		Model II†	
	HR (95% CI)	P	HR (95% CI)	P
Age at diagnosis (y)				
0-4 vs 15-20	0.8 (0.5-1.3)	.35	0.8 (0.5-1.3)	.38
5-9 vs 15-20	0.9 (0.6-1.4)	.65	0.9 (0.6-1.4)	.73
10-14 vs 15-20	0.8 (0.6-1.3)	.39	0.8 (0.6-1.2)	.38
Male vs female	1.0 (0.8-1.4)	.78	1.0 (0.8-1.4)	.76
Max CRT dose				
50+ Gy vs none	11.0 (7.4-16.5)	<.0001	11.0 (7.4-16.5)	<.0001
30-49 Gy vs none	5.9 (3.5-9.9)	<.0001	5.9 (3.5-9.9)	<.0001
1.5-29 Gy vs none	1.8 (1.2-2.8)	.01	1.8 (1.1-2.8)	.01
Indirect radiation vs none	1.2 (0.8-1.8)	.48	1.2 (0.8-1.8)	.41
Known stroke risk factor				
HTN vs none	4.0 (2.8-5.5)	<.0001	n/a	
Diabetes vs none	1.5 (0.8-2.6)	.17	1.4 (0.8-2.5)	.21
Recurrence vs none	2.1 (1.5-2.9)	<.0001	2.1 (1.5- 2.9)	<.0001
Race				
Black non-Hispanic vs white non-Hispanic	1.7 (0.9-3.2)	.10	n/a	
Other race/ethnicity vs White non-Hispanic	1.3 (0.9-1.9)	.17	n/a	
White, HTN vs white, no HTN	n/a		3.8 (2.7-5.5)	<.0001
Black, HTN vs white, no HTN	n/a		15.9 (6.9-36.6)	<.0001
Black, no HTN vs white, no HTN	n/a		1.0 (0.4-2.5)	.95
Other race, HTN vs white, no HTN	n/a		4.1 (1.8-9.5)	<.001
Other race, no HTN vs white, no HTN	n/a		1.4 (0.9-2.1)	.14

Table 3   Multivariate hazard ratio of first late-occurring stroke* in pediatric cancer survivors followed by the CCSS (n=14,186)

Characteristic	Model I[†] HR (95% CI)	P	Model II[†] HR (95% CI)	P
Age at diagnosis (y)				
0-4 vs 15-20	0.8 (0.5-1.3)	.35	0.8 (0.5-1.3)	.38
5-9 vs 15-20	0.9 (0.6-1.4)	.65	0.9 (0.6-1.4)	.73
10-14 vs 15-20	0.8 (0.6-1.3)	.39	0.8 (0.6-1.2)	.38
Male vs female	1.0 (0.8-1.4)	.78	1.0 (0.8-1.4)	.76
Max CRT dose				
50+ Gy vs none	11.0 (7.4-16.5)	<.0001	11.0 (7.4-16.5)	<.0001
30-49 Gy vs none	5.9 (3.5-9.9)	<.0001	5.9 (3.5-9.9)	<.0001
1.5-29 Gy vs none	1.8 (1.2-2.8)	.01	1.8 (1.1-2.8)	.01
Indirect radiation vs none	1.2 (0.8-1.8)	.48	1.2 (0.8-1.8)	.41
Known stroke risk factor				
HTN vs none	4.0 (2.8-5.5)	<.0001	n/a	
Diabetes vs none	1.5 (0.8-2.6)	.17	1.4 (0.8-2.5)	.21
Recurrence vs none	2.1 (1.5-2.9)	<.0001	2.1 (1.5- 2.9)	<.0001
Race				
Black non-Hispanic vs white non-Hispanic	1.7 (0.9-3.2)	.10	n/a	
Other race/ethnicity vs White non-Hispanic	1.3 (0.9-1.9)	.17	n/a	
White, HTN vs white, no HTN	n/a		3.8 (2.7-5.5)	<.0001
Black, HTN vs white, no HTN	n/a		15.9 (6.9-36.6)	<.0001
Black, no HTN vs white, no HTN	n/a		1.0 (0.4-2.5)	.95
Other race, HTN vs white, no HTN	n/a		4.1 (1.8-9.5)	<.001
Other race, no HTN vs white, no HTN	n/a		1.4 (0.9-2.1)	.14

(A) All Survivors

Cumulative incidence of first stroke [%]

50+ Gy

30-49 Gy

1.5-29 Gy

None

Years since diagnosis

# at risk:					
50+ Gy	907	807	686	560	312	123
30-49 Gy	509	437	385	326	218	104
1.5-29 Gy	2700	2538	2311	1955	1344	583
None	4043	3864	3464	2904	1610	649

(B) CNS Tumor Survivors

Cumulative incidence of first stroke [%]

50+ Gy

1.5-49 Gy

None

Years since diagnosis

# at risk:					
50+ Gy	771	686	581	470	249	88
1.5-49 Gy	219	195	174	146	100	49
None	463	441	384	311	173	87

Modifiable Risk Factors and Major Cardiac Events Among Adult Survivors of Childhood Cancer

A Report from the Childhood Cancer Survivor Study

Greg Armstrong, Kevin Oeffinger, Yan Chen, Toana Kawashima, Charles Sklar, Daniel Mulrooney, Eric Chow, William Border, JB Durand, Ann Mertens, Marilyn Stovall, Wendy Leisenring, Yutaka Yasui, Leslie Robison, Lillian Meacham

St. Jude Children's
Research Hospital
ALSAC • Danny Thomas, Founder
Finding cures. Saving children.

Department of Epidemiology and Cancer Control

A Coronary Artery Disease
P<0.001
RT
No RT
Sibling

B Valvular Disease
P<0.001
RT
No RT
Sibling

C Arrhythmia
P<0.001
RT
No RT
Sibling

D Heart Failure
P<0.001
RT + Anthracycline
Anthracycline alone
RT alone
No RT or Anthracycline
Sibling

Age (Years)
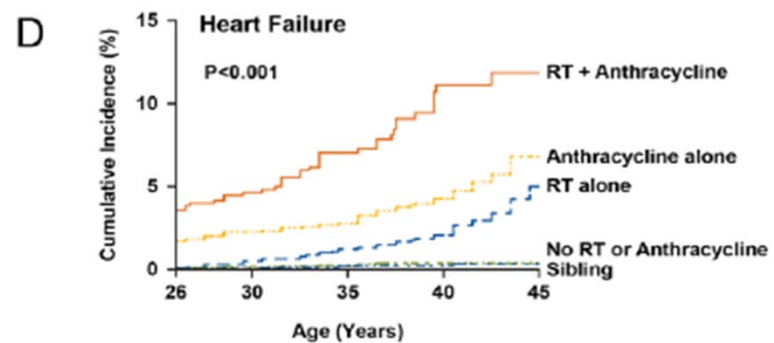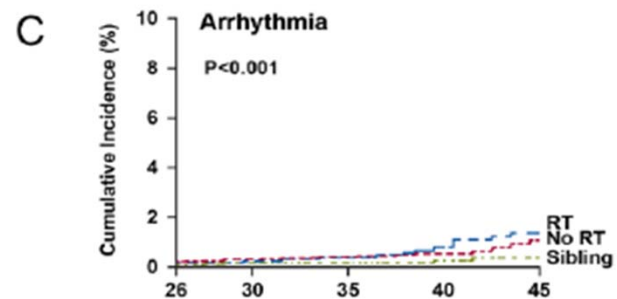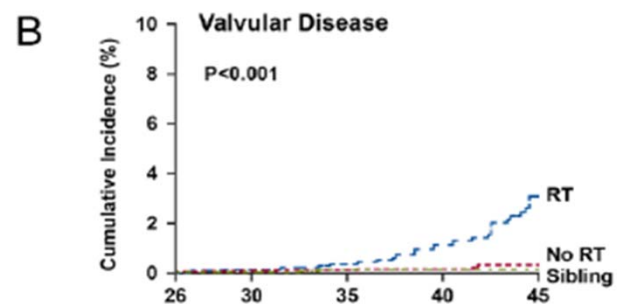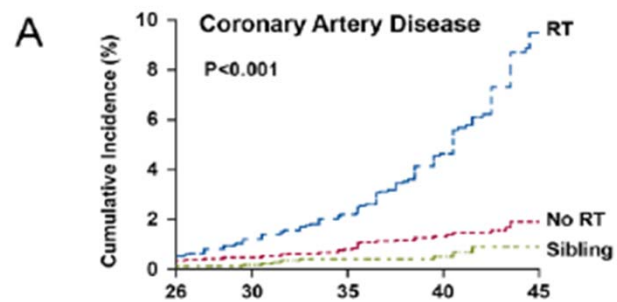
Supplemental Figure 1. Prevalence of cardiovascular risk factors with increasing age.

| Cardiovascular Risk Factor | Treatment Exposure Present | Risk Factor Present | Chest-Directed Radiotherapy | | | | | | | | Anthracycline Chemotherapy | |
| | | | Coronary Artery Disease | | Heart Failure | | Valvular Disease | | Arrhythmia | | Heart Failure | |
			RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Hypertension[†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	8.7	4.8-15.8	12.2	7.4-20.2	8.1	1.6-40.8	9.3	3.8-23.0	34.1	17.7-65.6
	Yes	No	5.3	3.2-8.7	3.2	1.9-5.2	10.1	2.9-35.6	2.9	1.2-7.0	8.3	4.4-15.6
	Yes	Yes	37.2	22.2-62.3	55.8	35.1-88.7	106.8	31.1-366.9	18.5	7.4-46.2	85.5	45.2-161.8
	Relative excess risk due to interaction**		24.2	11.8-39.7	41.4	24.1-7.8	89.6	32.6-5.0	7.3	-4.7-24.8	44.5	17.2-106.1
Dyslipidemia[†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	5.0	2.4-10.3	3.5	1.7-7.3	2.7	0.3-23.6	0.0	0.0-1.3	2.3	1.1-4.8
	Yes	No	4.6	3.0-6.9	4.3	3.0-6.1	12.3	4.7-32.1	1.8	0.9-3.6	4.3	3.0-6.2
	Yes	Yes	25.0	15.2-41.3	7.0	3.5-13.8	33.8	11.3-101.0	6.9	2.8-17.2	8.9	4.6-17.4
	Relative excess risk due to interaction**		16.4	7.9-29.8	0.1	-4.8-5.4	19.8	3.0-109.8	6.1	1.6-14.5	3.3	-2.2-10.6
Diabetes[†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	5.2	2.2-12.5	0.6	0.1-4.7	6.4	0.7-55.3	1.7	0.2-12.8	2.6	1.0-7.4
	Yes	No	5.1	3.5-7.5	3.6	2.6-5.1	14.4	5.6-37.0	2.4	1.2-4.6	4.2	3.0-6.1
	Yes	Yes	20.1	10.6-38.4	13.5	6.9-26.6	36.4	9.5-138.8	9.4	2.7-32.4	10.8	4.9-23.9
	Relative excess risk due to interaction**		10.8	0.0-28.6	10.2	2.9-22.8	16.6	-19.3-123.0	6.3	-3.8-21.4	4.9	-2.9-17.2
Obesity[†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	1.4	0.7-2.6	1.4	0.8-2.5	0.8	0.1-6.6	0.7	0.2-2.5	2.0	1.1-3.6
	Yes	No	4.6	3.1-7.0	4.1	2.8-5.9	10.4	4.0-27.3	2.0	1.0-4.0	5.0	3.3-7.4
	Yes	Yes	9.3	5.6-15.5	5.7	3.3-10.1	23.8	8.3-68.3	5.5	2.2-13.5	5.4	3.0-9.8
	Relative excess risk due to interaction**		4.3	0.9-8.7	1.3	-1.7-4.6	13.6	0.2-66.4	3.8	0.1-8.6	-0.6	-3.9-2.6
Multiple (≥2) risk factors including Hypertension[†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	7.9	4.1-15.1	5.2	2.7-9.9	7.4	1.3-41.1	1.5	0.3-6.7	8.7	4.8-15.5
	Yes	No	5.0	3.3-7.7	3.7	2.6-5.4	13.4	4.6-38.9	2.0	1.0-4.0	4.9	3.3-7.3
	Yes	Yes	39.8	23.9-66.3	26.3	15.7-43.9	80.7	25.7-253.8	11.1	4.4-27.7	24.5	13.7-43.6
	Relative excess risk due to interaction**		27.9	14.6-51.0	18.3	7.6-37.4	60.9	18.0-487.0	8.6	1.7-21.7	11.9	0.3-29.6

Cardiovascular Risk Factor	Treatment Exposure Present	Risk Factor Present	Coronary Artery Disease RR	95% CI	Heart Failure RR	95% CI	Valvular Disease RR	95% CI	Arrhythmia RR	95% CI	Heart Failure RR	95% CI
			Chest-Directed Radiotherapy								**Anthracycline Chemotherapy**	
Hypertension[†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	8.7	4.8-15.8	12.2	7.4-20.2	8.1	1.6-40.8	9.3	3.8-23.0	34.1	17.7-65.6
	Yes	No	5.3	3.2-8.7	3.2	1.9-5.2	10.1	2.9-35.6	2.9	1.2-7.0	8.3	4.4-15.6
	Yes	Yes	37.2	22.2-62.3	55.8	35.1-88.7	106.8	31.1-366.9	18.5	7.4-46.2	85.5	45.2-161.8
	Relative excess risk due to interaction**		24.2	11.8-39.7	41.4	24.1-7.8	89.6	32.6-5.0	7.3	-4.7-24.8	44.5	17.2-106.1
Dyslipidemia[†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	5.0	2.4-10.3	3.5	1.7-7.3	2.7	0.3-23.6	0.0	0.0-1.3	2.3	1.1-4.8
	Yes	No	4.6	3.0-6.9	4.3	3.0-6.1	12.3	4.7-32.1	1.8	0.9-3.6	4.3	3.0-6.2
	Yes	Yes	25.0	15.2-41.3	7.0	3.5-13.8	33.8	11.3-101.0	6.9	2.8-17.2	8.9	4.6-17.4
	Relative excess risk due to interaction**		16.4	7.9-29.8	0.1	-4.8-5.4	19.8	3.0-109.8	6.1	1.6-14.5	3.3	-2.2-10.6
Diabetes[†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	5.2	2.2-12.5	0.6	0.1-4.7	6.4	0.7-55.3	1.7	0.2-12.8	2.6	1.0-7.4
	Yes	No	5.1	3.5-7.5	3.6	2.6-5.1	14.4	5.6-37.0	2.4	1.2-4.6	4.2	3.0-6.1
	Yes	Yes	20.1	10.6-38.4	13.5	6.9-26.6	36.4	9.5-138.8	9.4	2.7-32.4	10.8	4.9-23.9
	Relative excess risk due to interaction**		10.8	0.0-28.6	10.2	2.9-22.8	16.6	-19.3-123.0	6.3	-3.8-21.4	4.9	-2.9-17.2
Obesity[†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	1.4	0.7-2.6	1.4	0.8-2.5	0.8	0.1-6.6	0.7	0.2-2.5	2.0	1.1-3.6
	Yes	No	4.6	3.1-7.0	4.1	2.8-5.9	10.4	4.0-27.3	2.0	1.0-4.0	5.0	3.3-7.4
	Yes	Yes	9.3	5.6-15.5	5.7	3.3-10.1	23.8	8.3-68.3	5.5	2.2-13.5	5.4	3.0-9.8
	Relative excess risk due to interaction**		4.3	0.9-8.7	1.3	-1.7-4.6	13.6	0.2-66.4	3.8	0.1-8.6	-0.6	-3.9-2.6
Multiple (≥2) risk factors including Hypertension[†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	7.9	4.1-15.1	5.2	2.7-9.9	7.4	1.3-41.1	1.5	0.3-6.7	8.7	4.8-15.5
	Yes	No	5.0	3.3-7.7	3.7	2.6-5.4	13.4	4.6-38.9	2.0	1.0-4.0	4.9	3.3-7.3
	Yes	Yes	39.8	23.9-66.3	26.3	15.7-43.9	80.7	25.7-253.8	11.1	4.4-27.7	24.5	13.7-43.6
	Relative excess risk due to interaction**		27.9	14.6-51.0	18.3	7.6-37.4	60.9	18.0-487.0	8.6	1.7-21.7	11.9	0.3-29.6

Cardiovascular Risk Factor	Treatment Exposure Present	Risk Factor Present	Chest-Directed Radiotherapy								Anthracycline Chemotherapy	
			Coronary Artery Disease		Heart Failure		Valvular Disease		Arrhythmia		Heart Failure	
			RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Hypertension[†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	8.7	4.8-15.8	12.2	7.4-20.2	8.1	1.6-40.8	9.3	3.8-23.0	34.1	17.7-65.6
	Yes	No	5.3	3.2-8.7	3.2	1.9-5.2	10.1	2.9-35.6	2.9	1.2-7.0	8.3	4.4-15.6
	Yes	Yes	37.2	22.2-62.3	55.8	35.1-88.7	106.8	31.1-366.9	18.5	7.4-46.2	85.5	45.2-161.8
	Relative excess risk due to interaction**		24.2	11.8-39.7	41.4	24.1-7.8	89.6	32.6-5.0	7.3	-4.7-24.8	44.5	17.2-106.1
Dyslipidemia[†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	5.0	2.4-10.3	3.5	1.7-7.3	2.7	0.3-23.6	0.0	0.0-1.3	2.3	1.1-4.8
	Yes	No	4.6	3.0-6.9	4.3	3.0-6.1	12.3	4.7-32.1	1.8	0.9-3.6	4.3	3.0-6.2
	Yes	Yes	25.0	15.2-41.2	7.0	3.6-13.8	23.8	11.3-101.0	6.0	2.8-17.2	8.0	4.6-17.4
	Relative excess risk due to interaction**		16.4	7.9-29.8	0.1	-4.8-5.4	19.8	3.0-109.8	6.1	1.6-14.5	3.3	-2.2-10.6
Diabetes[†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	5.2	2.2-12.5	0.6	0.1-4.7	6.4	0.7-55.3	1.7	0.2-12.8	2.6	1.0-7.4
	Yes	No	5.1	3.5-7.5	3.6	2.6-5.1	14.4	5.6-37.0	2.4	1.2-4.6	4.2	3.0-6.1
	Yes	Yes	20.1	10.6-38.4	13.5	6.9-26.6	36.4	9.5-138.8	9.4	2.7-32.4	10.8	4.9-23.9
	Relative excess risk due to interaction**		10.8	0.0-28.6	10.2	2.9-22.8	16.6	-19.3-123.0	6.3	-3.8-21.4	4.9	-2.9-17.2
Obesity[†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	1.4	0.7-2.6	1.4	0.8-2.5	0.8	0.1-6.6	0.7	0.2-2.5	2.0	1.1-3.6
	Yes	No	4.6	3.1-7.0	4.1	2.8-5.9	10.4	4.0-27.3	2.0	1.0-4.0	5.0	3.3-7.4
	Yes	Yes	9.3	5.6-15.5	5.7	3.3-10.1	23.8	8.3-68.3	5.5	2.2-13.5	5.4	3.0-9.8
	Relative excess risk due to interaction**		4.3	0.9-8.7	1.3	-1.7-4.6	13.6	0.2-66.4	3.8	0.1-8.6	-0.6	-3.9-2.6
Multiple (≥2) risk factors including Hypertension[†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	7.9	4.1-15.1	5.2	2.7-9.9	7.4	1.3-41.1	1.5	0.3-6.7	8.7	4.8-15.5
	Yes	No	5.0	3.3-7.7	3.7	2.6-5.4	13.4	4.6-38.9	2.0	1.0-4.0	4.9	3.3-7.3
	Yes	Yes	39.8	23.9-66.3	26.3	15.7-43.9	80.7	25.7-253.8	11.1	4.4-27.7	24.5	13.7-43.6
	Relative excess risk due to interaction**		27.9	14.6-51.0	18.3	7.6-37.4	60.9	18.0-487.0	8.6	1.7-21.7	11.9	0.3-29.6

Cardiovascular Risk Factor	Treatment Exposure Present	Risk Factor Present	Chest-Directed Radiotherapy								Anthracycline Chemotherapy	
			Coronary Artery Disease		Heart Failure		Valvular Disease		Arrhythmia		Heart Failure	
			RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Hypertension[†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	8.7	4.8-15.8	12.2	7.4-20.2	8.1	1.6-40.8	9.3	3.8-23.0	34.1	17.7-65.6
	Yes	No	5.3	3.2-8.7	3.2	1.9-5.2	10.1	2.9-35.6	2.9	1.2-7.0	8.3	4.4-15.6
	Yes	Yes	37.2	22.2-62.3	55.8	35.1-88.7	106.8	31.1-366.9	18.5	7.4-46.2	85.5	45.2-161.8
	Relative excess risk due to interaction**		24.2	11.8-39.7	41.4	24.1-7.8	89.6	32.6-5.0	7.3	-4.7-24.8	44.5	17.2-106.1
Dyslipidemia[†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	5.0	2.4-10.3	3.5	1.7-7.3	2.7	0.3-23.6	0.0	0.0-1.3	2.3	1.1-4.8
	Yes	No	4.6	3.0-6.9	4.3	3.0-6.1	12.3	4.7-32.1	1.8	0.9-3.6	4.3	3.0-6.2
	Yes	Yes	25.0	15.2-41.3	7.0	3.5-13.8	33.8	11.3-101.0	6.9	2.8-17.2	8.9	4.6-17.4
	Relative excess risk due to interaction**		16.4	7.9-29.8	0.1	-4.8-5.4	19.8	3.0-109.8	6.1	1.6-14.5	3.3	-2.2-10.6
Diabetes[†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	5.2	2.2-12.5	0.6	0.1-4.7	6.4	0.7-55.3	1.7	0.2-12.8	2.6	1.0-7.4
	Yes	No	5.1	3.5-7.5	3.6	2.6-5.1	14.4	5.6-37.0	2.4	1.2-4.6	4.2	3.0-6.1
	Yes	Yes	20.1	10.6-38.4	13.5	6.9-26.6	36.4	9.5-138.8	9.4	2.7-32.4	10.8	4.9-23.9
	Relative excess risk due to interaction**		10.8	0.0-28.6	10.2	2.9-22.8	16.6	-19.3-123.0	6.3	-3.8-21.4	4.9	-2.9-17.2
Obesity[†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	1.4	0.7-2.6	1.4	0.8-2.5	0.8	0.1-6.6	0.7	0.2-2.5	2.0	1.1-3.6
	Yes	No	4.6	3.1-7.0	4.1	2.8-5.9	10.4	4.0-27.3	2.0	1.0-4.0	5.0	3.3-7.4
	Yes	Yes	9.3	5.6-15.5	5.7	3.3-10.1	23.8	8.3-68.3	5.5	2.2-13.5	5.4	3.0-9.8
	Relative excess risk due to interaction**		4.3	0.9-8.7	1.3	-1.7-4.6	13.6	0.2-66.4	3.8	0.1-8.6	-0.6	-3.9-2.6
Multiple (≥2) risk factors including Hypertension[†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	7.9	4.1-15.1	5.2	2.7-9.9	7.4	1.3-41.1	1.5	0.3-6.7	8.7	4.8-15.5
	Yes	No	5.0	3.3-7.7	3.7	2.6-5.4	13.4	4.6-38.9	2.0	1.0-4.0	4.9	3.3-7.3
	Yes	Yes	39.8	23.9-66.3	26.3	15.7-43.9	80.7	25.7-253.8	11.1	4.4-27.7	24.5	13.7-43.6
	Relative excess risk due to interaction**		27.9	14.6-51.0	18.3	7.6-37.4	60.9	18.0-487.0	8.6	1.7-21.7	11.9	0.3-29.6

Cardiovascular Risk Factor	Treatment Exposure Present	Risk Factor Present	Chest-Directed Radiotherapy								Anthracycline Chemotherapy	
			Coronary Artery Disease		Heart Failure		Valvular Disease		Arrhythmia		Heart Failure	
			RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Hypertension[†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	8.7	4.8-15.8	12.2	7.4-20.2	8.1	1.6-40.8	9.3	3.8-23.0	34.1	17.7-65.6
	Yes	No	5.3	3.2-8.7	3.2	1.9-5.2	10.1	2.9-35.6	2.9	1.2-7.0	8.3	4.4-15.6
	Yes	Yes	37.2	22.2-62.3	55.8	35.1-88.7	106.8	31.1-366.9	18.5	7.4-46.2	85.5	45.2-161.8
	Relative excess risk due to interaction**		24.2	11.8-39.7	41.4	24.1-7.8	89.6	32.6-5.0	7.3	-4.7-24.8	44.5	17.2-106.1
Dyslipidemia[†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	5.0	2.4-10.3	3.5	1.7-7.3	2.7	0.3-23.6	0.0	0.0-1.3	2.3	1.1-4.8
	Yes	No	4.6	3.0-6.9	4.3	3.0-6.1	12.3	4.7-32.1	1.8	0.9-3.6	4.3	3.0-6.2
	Yes	Yes	25.0	15.2-41.3	7.0	3.5-13.8	33.8	11.3-101.0	6.9	2.8-17.2	8.9	4.6-17.4
	Relative excess risk due to interaction**		16.4	7.9-29.8	0.1	-4.8-5.4	19.8	3.0-109.8	6.1	1.6-14.5	3.3	-2.2-10.6
Diabetes[†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	5.2	2.2-12.5	0.6	0.1-4.7	6.4	0.7-55.3	1.7	0.2-12.8	2.6	1.0-7.4
	Yes	No	5.1	3.5-7.5	3.6	2.6-5.1	14.4	5.6-37.0	2.4	1.2-4.6	4.2	3.0-6.1
	Yes	Yes	20.1	10.6-38.4	13.5	6.9-26.6	36.4	9.5-138.8	9.4	2.7-32.4	10.8	4.9-23.9
	Relative excess risk due to interaction**		10.8	0.0-28.6	10.2	2.9-22.8	16.6	-19.3-123.0	6.3	-3.8-21.4	4.9	-2.9-17.2
Obesity[†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	1.4	0.7-2.6	1.4	0.8-2.5	0.8	0.1-6.6	0.7	0.2-2.5	2.0	1.1-3.6
	Yes	No	4.6	3.1-7.0	4.1	2.8-5.9	10.4	4.0-27.3	2.0	1.0-4.0	5.0	3.3-7.4
	Yes	Yes	9.3	5.6-15.5	5.7	3.3-10.1	25.8	8.3-68.3	5.5	2.2-13.5	5.4	3.0-9.8
	Relative excess risk due to interaction**		4.3	0.9-8.7	1.3	-1.7-4.6	13.6	0.2-66.4	3.8	0.1-8.6	-0.6	-3.9-2.6
Multiple (≥2) risk factors including Hypertension[†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	7.9	4.1-15.1	5.2	2.7-9.9	7.4	1.3-41.1	1.5	0.3-6.7	8.7	4.8-15.5
	Yes	No	5.0	3.3-7.7	3.7	2.6-5.4	13.4	4.6-38.9	2.0	1.0-4.0	4.9	3.3-7.3
	Yes	Yes	39.8	23.9-66.3	26.3	15.7-43.9	80.7	25.7-253.8	11.1	4.4-27.7	24.5	13.7-43.6
	Relative excess risk due to interaction**		27.9	14.6-51.0	18.3	7.6-37.4	60.9	18.0-487.0	8.6	1.7-21.7	11.9	0.3-29.6

Cardiovascular Risk Factor	Treatment Exposure Present	Risk Factor Present	Chest-Directed Radiotherapy								Anthracycline Chemotherapy	
			Coronary Artery Disease		Heart Failure		Valvular Disease		Arrhythmia		Heart Failure	
			RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Hypertension [†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	8.7	4.8-15.8	12.2	7.4-20.2	8.1	1.6-40.8	9.3	3.8-23.0	34.1	17.7-65.6
	Yes	No	5.3	3.2-8.7	3.2	1.9-5.2	10.1	2.9-35.6	2.9	1.2-7.0	8.3	4.4-15.6
	Yes	Yes	37.2	22.2-62.3	55.8	35.1-88.7	106.8	31.1-366.9	18.5	7.4-46.2	85.5	45.2-161.8
	Relative excess risk due to interaction**		24.2	11.8-39.7	41.4	24.1-7.8	89.6	32.6-5.0	7.3	-4.7-24.8	44.5	17.2-106.1
Dyslipidemia [†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	5.0	2.4-10.3	3.5	1.7-7.3	2.7	0.3-23.6	0.0	0.0-1.3	2.3	1.1-4.8
	Yes	No	4.6	3.0-6.9	4.3	3.0-6.1	12.3	4.7-32.1	1.8	0.9-3.6	4.3	3.0-6.2
	Yes	Yes	25.0	15.2-41.3	7.0	3.5-13.8	33.8	11.3-101.0	6.9	2.8-17.2	8.9	4.6-17.4
	Relative excess risk due to interaction**		16.4	7.9-29.8	0.1	-4.8-5.4	19.8	3.0-109.8	6.1	1.6-14.5	3.3	-2.2-10.6
Diabetes [†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	5.2	2.2-12.5	0.6	0.1-4.7	6.4	0.7-55.3	1.7	0.2-12.8	2.6	1.0-7.4
	Yes	No	5.1	3.5-7.5	3.6	2.6-5.1	14.4	5.6-37.0	2.4	1.2-4.6	4.2	3.0-6.1
	Yes	Yes	20.1	10.6-38.4	13.5	6.9-26.6	36.4	9.5-138.8	9.4	2.7-32.4	10.8	4.9-23.9
	Relative excess risk due to interaction**		10.8	0.0-28.6	10.2	2.9-22.8	16.6	-19.3-123.0	6.3	-3.8-21.4	4.9	-2.9-17.2
Obesity [†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	1.4	0.7-2.6	1.4	0.8-2.5	0.8	0.1-6.6	0.7	0.2-2.5	2.0	1.1-3.6
	Yes	No	4.6	3.1-7.0	4.1	2.8-5.9	10.4	4.0-27.3	2.0	1.0-4.0	5.0	3.3-7.4
	Yes	Yes	9.3	5.6-15.5	5.7	3.3-10.1	23.8	8.3-68.3	5.5	2.2-13.5	5.4	3.0-9.8
	Relative excess risk due to interaction**		4.3	0.9-8.7	1.3	-1.7-4.6	13.6	0.2-66.4	3.8	0.1-8.6	-0.6	-3.9-2.6
Multiple (≥2) risk factors including Hypertension [†]	No	No	1.0		1.0		1.0		1.0		1.0	
	No	Yes	7.9	4.1-15.1	5.2	2.7-9.9	7.4	1.3-41.1	1.5	0.3-6.7	8.7	4.8-15.5
	Yes	No	5.0	3.3-7.7	3.7	2.6-5.4	13.4	4.6-38.9	2.0	1.0-4.0	4.9	3.3-7.3
	Yes	Yes	39.8	23.0-66.3	26.3	15.7-43.9	80.7	25.7-253.8	11.1	4.4-27.7	24.5	13.7-43.6
	Relative excess risk due to interaction**		27.9	14.6-51.0	18.3	7.6-37.4	60.9	18.0-487.0	8.6	1.7-21.7	11.9	0.3-29.6

Risk Factors: Cardiac Mortality

Characteristic	HR (95% CI)	P-Value
Diabetes	2.2 (0.8–6.1)	0.34
Hypertension	5.6 (3.2–9.7)	<0.001
Dyslipidemia	1.7 (0.7–3.8)	0.48
Obesity	1.2 (0.6–2.3)	0.47
Multiple Risk Factors	2.4 (1.2–4.9)	0.22

Adjusting for: sex, race/ethnicity, education, household income

Risk Factors: Cardiac Mortality

Characteristic	HR (95% CI)	P-Value
Diabetes	2.2 (0.8–6.1)	0.34
Hypertension	5.6 (3.2–9.7)	<0.001
Dyslipidemia	1.7 (0.7–3.8)	0.48
Obesity	1.2 (0.6–2.3)	0.47
Multiple Risk Factors	2.4 (1.2–4.9)	0.22

Adjusting for: sex, race/ethnicity, education, household income

The Cyclophosphamide Equivalent Dose as an Approach for Quantifying Alkylating Agent Exposure. A Report from the Childhood Cancer Survivor Study

Daniel M. Green, M.D.[1]

Vikki G. Nolan, D. Sc.[2]

Pamela J. Goodman, M.S. [3]

John A. Whitton, M.S.[3]

DeoKumar Srivastava, Ph.D.[4]

Wendy M. Leisenring, Sc.D.[3]

Joseph P. Neglia, M.D., M.P.H.[5]

Charles A. Sklar, M.D.[6]

Sue C. Kaste, D.O.[7,8,9]

Melissa M. Hudson, M.D.[1,8]

Lisa R. Diller, M.D.[10]

Marilyn Stovall, Ph.D.[11]

Sarah S. Donaldson, M.D.[12]

Leslie L. Robison, Ph.D.[1]

Relative Hematologic Toxicity

Cyclophosphamide	Ifosfamide	Procarbazine	Chlorambucil	BCNU	CCNU	Melphalan	Thio-TEPA	Nitrogen Mustard	Busulfan
100 mg/m2	409 mg/m2	117 mg/m2	7 mg/m2	6.7 mg/m2	6.3 mg/m2	2.5 mg/m2	2 mg/m2	1 mg/m2	11.3 mg/m2

Table IV. Rate Ratios for Non-Surgical Premature Menopause: Multiple Poisson Regression Model

Variable	CED			AAD		
	RR	95% CI	p-value	RR	95% CI	p-value
Age	1.14	1.09 to 1.20	< 0.001	1.13	1.07 to 1.19	< 0.001
Minimum ovarian dose						
Other cancers						
None	1.00			1.00		
1 to 99 cGy	2.96	0.92 to 9.50	0.069	4.25	1.18 to 15.26	0.027
≥ 100 cGy	11.68	3.59 to 38.04	< 0.001	16.77	4.55 to 61.88	< 0.001
Hodgkin lymphoma						
None	13.86	4.04 to 47.57	< 0.001	9.88	1.65 to 59.24	0.012
1 to 99 cGy	10.04	3.40 to 29.65	< 0.001	12.73	3.55 to 45.57	< 0.001
≥ 100 cGy	10.76	3.32 to 34.91	< 0.001	10.73	2.70 to 42.64	< 0.001
CED (mg/m^2)						
0	1.00					
> 0 to < 4,000	0.56	0.07 to 4.27	0.578			
≥ 4,000 to < 8,000	2.74	1.13 to 6.61	0.025			
≥ 8,000	4.19	2.18 to 8.08	< 0.001			
AAD tertile						
0				1.00		
1 to 2				2.09	0.97 to 4.51	0.060
3				4.99	2.53 to 9.84	< 0.001

Table IV. Rate Ratios for Non-Surgical Premature Menopause: Multiple Poisson Regression Model

Variable	CED			AAD		
	RR	95% CI	p-value	RR	95% CI	p-value
Age	1.14	1.09 to 1.20	< 0.001	1.13	1.07 to 1.19	< 0.001
Minimum ovarian dose						
Other cancers						
None	1.00			1.00		
1 to 99 cGy	2.96	0.92 to 9.50	0.069	4.25	1.18 to 15.26	0.027
≥ 100 cGy	11.68	3.59 to 38.04	< 0.001	16.77	4.55 to 61.88	< 0.001
Hodgkin lymphoma						
None	13.86	4.04 to 47.57	< 0.001	9.88	1.65 to 59.24	0.012
1 to 99 cGy	10.04	3.40 to 29.65	< 0.001	12.73	3.55 to 45.57	< 0.001
≥ 100 cGy	10.76	3.32 to 34.91	< 0.001	10.73	2.70 to 42.64	< 0.001
CED (mg/m²)						
0	1.00					
> 0 to < 4,000	0.56	0.07 to 4.27	0.578			
≥ 4,000 to < 8,000	2.74	1.13 to 6.61	0.025			
≥ 8,000	4.19	2.18 to 8.08	< 0.001			
AAD tertile						
0				1.00		
1 to 2				2.09	0.97 to 4.51	0.060
3				4.99	2.53 to 9.84	< 0.001

Table IV. Rate Ratios for Non-Surgical Premature Menopause: Multiple Poisson Regression Model

Variable	CED			AAD		
	RR	95% CI	p-value	RR	95% CI	p-value
Age	1.14	1.09 to 1.20	< 0.001	1.13	1.07 to 1.19	< 0.001
Minimum ovarian dose						
Other cancers						
None	1.00			1.00		
1 to 99 cGy	2.96	0.92 to 9.50	0.069	4.25	1.18 to 15.26	0.027
≥ 100 cGy	11.68	3.59 to 38.04	< 0.001	16.77	4.55 to 61.88	< 0.001
Hodgkin lymphoma						
None	13.86	4.04 to 47.57	< 0.001	9.88	1.65 to 59.24	0.012
1 to 99 cGy	10.04	3.40 to 29.65	< 0.001	12.73	3.55 to 45.57	< 0.001
≥ 100 cGy	10.76	3.32 to 34.91	< 0.001	10.73	2.70 to 42.64	< 0.001
CED (mg/m²)						
0	1.00					
> 0 to < 4,000	0.56	0.07 to 4.27	0.578			
≥ 4,000 to < 8,000	2.74	1.13 to 6.61	0.025			
≥ 8,000	4.19	2.18 to 8.08	< 0.001			
AAD tertile						
0				1.00		
1 to 2				2.09	0.97 to 4.51	0.060
3				4.99	2.53 to 9.84	< 0.001

ROC: CED vs AAD
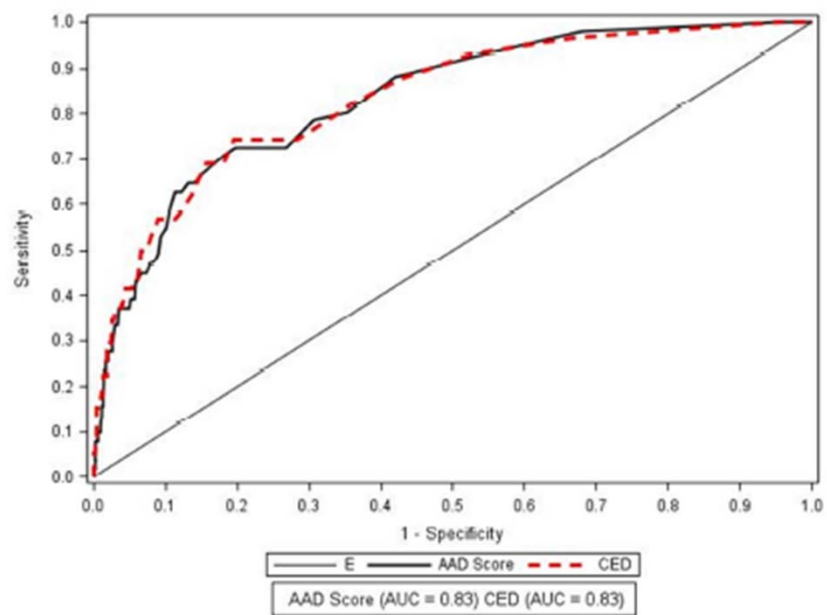
Manuscripts submitted/under review (3)

- Male infertility, **K Wasilewski-Masker**
- Aging and chronic health conditions, **G Armstrong**
- Pulmonary outcomes in CNS tumor survivors, **T Huang**
- Risk prediction models for CVD**, E Chow**

Analysis completed/Manuscript in prep (6)

- Infectious complications, **J Perkins**
- Psychosexual functioning females, **J Ford**
- Neurological sequelae in CNS tumor survivors**, E Wells**
- Long-Term GU outcomes, **M Schnorhavorian**
- GH therapy and risk of second CNS neoplasm, **B Patterson**
- Sexual health in male survivors, **C Ritenour**

Recently Approved AOIs:

Date Received	Title	Author/ Institution	Secondary Working Group(s)	Date Investigator Notified	AOI Outcome	Concept to Publication Committee
06.07.12	Longitudinal Pulmonary Complications in Survivors of Childhood Cancer	Dietz/UCSD	Epi/Biostats	07.16.12	Approved	Pending
06.07.12	Using the Cumulative Illness Rating Scale to characterize the burden of chronic conditions among childhood cancer survivors	Ness/SJCRH	Epi/Biostats	07.16.12	Approved	Pending
06.07.12	Increasing risk of chronic endocrine disorders in aging survivors of childhood cancer	Mostoufi-Moab		07.16.12	Approved	Pending
06.15.12	Medical and Psychosocial Outcomes of Survivors of AYA Cancer	Henderson/U. of Chicago	Cancer Control Psychology	07.16.12	Approved	Pending
08.20.12	Long-term Risk of Small Bowel Obstruction in Pediatric Patients with Primary Abdominal Tumors	Diller/Harvard	Epi/Biostats	08.28.12	Approved	Approved

Ancillary studies

- **<u>Active</u>**
  - **Testicular and sexual dysfunction in male survivors**, Meacham (LAF)

Home/work visits

- **Blood sampling**
- **Clinical/anthropomorphic measures**
- **Brief questionnaire**

- **Pilot/feasibility study**
  - **Fasting blood for glucose, lipids, insulin**
  - **Measure height, weight, BP waist circumference**
  - **Random sample of 200 survivors in cohort (active f/u, >/= 18, residing in US)**

Future Directions

Longitudinal outcomes using 2007 dataset

Risk modeling

Expanded Cohort

Fertility and Contemporary Chemotherapy in Male Childhood Cancer Survivors (eg, risk associated with ifosfamide, melphalan, thiotepa, busulfan)

Changes in Long-Term Outcomes in Hodgkin Lymphoma Survivors with Contemporary Risk-Adapted Therapy (eg, chronic health conditions, late mortality, health status)