

# **SUPPLEMENTAL MATERIAL**

**TABLE S1. Characteristics and physiologic measurements of childhood cancer survivors at high cardiovascular disease risk by original cancer diagnosis.**

Characteristics and measurements*	Acute lymphoblastic leukemia N=146	Other leukemia N=50	Bone cancer / sarcoma N=86	Central nervous system N=59	Hodgkin lymphoma N=95	Non-Hodgkin lymphoma N=47	Kidney N=55	Neuroblastoma N=33
Female sex (%)	79 (54.1%)	35 (70.0%)	54 (62.8%)	28 (47.5%)	47 (49.5%)	22 (46.8%)	38 (69.1%)	22 (66.7%)
White non-Hispanic race/ethnicity (%)	122 (83.6%)	42 (84.0%)	72 (83.7%)	53 (89.8%)	78 (82.1%)	43 (91.5%)	48 (87.3%)	28 (84.8%)
Median current age, y (range)	38.3 (21.5-62.5)	35.6 (21.6-59.4)	40.3 (20.1-59.4)	34.5 (23.8-55.2)	42.9 (26.9-65.0)	38.1 (27.4-58.3)	33.4 (22.1-56.2)	31.7 (20.4-42.4)
Median cancer diagnosis age, y (range)	4.9 (0.2-19.7)	6.8 (0.1-17.3)	13.5 (0.2-20.1)	8.8 (0.5-16.2)	14.2 (3.4-20.8)	9.8 (1.4-18.6)	3.7 (0.5-17.3)	0.9 (0.0-17.6)
Chest radiation exposure (%)	32 (22.1%)	16 (32.0%)	17 (20.0%)	59 (100.0%)	73 (76.8%)	9 (19.1%)	23 (42.6%)	16 (48.5%)
History of hypertension (%)	37 (25.3%)	17 (34.0%)	25 (29.1%)	14 (23.7%)	27 (28.4%)	12 (25.5%)	12 (21.8%)	9 (27.3%)
Currently on medications	24 (64.9%)	10 (58.8%)	20 (80.0%)	9 (64.3%)	21 (77.8%)	9 (75.0%)	7 (58.3%)	3 (33.3%)
History of dyslipidemia (%)	53 (36.3%)	18 (36.0%)	32 (37.2%)	23 (39.0%)	34 (35.8%)	11 (23.4%)	14 (25.5%)	6 (18.2%)
Currently on medications	23 (43.4%)	8 (44.4%)	11 (34.4%)	9 (39.1%)	19 (55.9%)	4 (36.4%)	3 (21.4%)	3 (50.0%)
History of diabetes (%)	14 (9.6%)	6 (12.0%)	7 (8.1%)	2 (3.4%)	7 (7.4%)	5 (10.6%)	7 (12.7%)	4 (12.1%)
Currently on medications	10 (71.4%)	4 (66.7%)	5 (71.4%)	2 (100.0%)	6 (85.7%)	3 (60.0%)	4 (57.1%)	3 (75.0%)
Lifestyle factors (%)								
Physically active <sup>†</sup>	110 (75.3%)	34 (68.0%)	56 (65.1%)	36 (61.0%)	63 (66.3%)	32 (68.1%)	39 (70.9%)	20 (60.6%)
≥5 cups daily fruits/vegetables	31 (21.2%)	8 (16.0%)	12 (14.0%)	11 (18.6%)	21 (22.1%)	11 (23.4%)	21 (38.2%)	5 (15.2%)
Current smoking/tobacco use	15 (10.3%)	6 (12.0%)	4 (4.7%)	4 (6.8%)	10 (10.5%)	1 (2.1%)	6 (10.9%)	2 (6.1%)
Healthcare utilization (%)								
Health insurance coverage	133 (91.1%)	45 (90.0%)	85 (98.8%)	57 (96.6%)	85 (89.5%)	43 (91.5%)	53 (96.4%)	32 (97.0%)
Routine check-up within 1-2 years <sup>‡</sup>	127 (87.0%)	44 (88.0%)	79 (91.9%)	57 (96.6%)	87 (91.6%)	40 (85.1%)	52 (94.5%)	31 (93.9%)
History of survivorship clinic attendance	70 (51.5%)	28 (62.2%)	42 (51.2%)	23 (43.4%)	32 (36.8%)	24 (53.3%)	26 (50.0%)	17 (56.7%)
BMI, kg/m <sup>2</sup>	28.3 (6.4)	26.1 (5.7)	26.3 (5.7)	27.1 (7.1)	27.6 (5.7)	27.8 (6.9)	26.7 (5.3)	29.4 (9.6)
No. overweight 25-29 kg/m <sup>2</sup> (%)	44 (30.1%)	12 (24.0%)	37 (43.0%)	18 (30.5%)	30 (31.6%)	16 (34.0%)	15 (27.3%)	6 (18.2%)
No. obese ≥30 kg/m <sup>2</sup> (%)	50 (34.2%)	13 (26.0%)	13 (15.1%)	13 (22.0%)	30 (31.6%)	13 (27.7%)	16 (29.1%)	12 (36.4%)
Waist circumference, cm	90.8 (16.6)	87.0 (14.0)	88.7 (16.6)	88.4 (15.3)	91.3 (13.9)	88.8 (16.7)	82.3 (11.5)	91.9 (17.3)
No. with central adiposity (%) <sup>§</sup>	57 (39.0%)	16 (32.0%)	23 (26.7%)	21 (35.6%)	30 (31.6%)	13 (27.7%)	9 (16.4%)	13 (39.4%)
Systolic blood pressure, mmHg	113.8 (14.2)	111.0 (8.0)	112.3 (12.3)	114.0 (12.4)	115.4 (13.5)	113.7 (11.2)	112.0 (11.7)	115.3 (13.0)
Diastolic blood pressure, mmHg	73.9 (9.4)	73.4 (7.2)	74.0 (8.7)	72.8 (9.6)	73.3 (8.8)	73.7 (9.2)	73.4 (8.4)	73.2 (9.0)
Total cholesterol, mg/dL	184.0 (40.3)	190.9 (38.5)	192.3 (44.9)	202.8 (49.4)	189.5 (35.7)	185.0 (36.9)	178.3 (33.3)	172.9 (29.0)
High density lipoprotein, mg/dL	49.9 (15.0)	52.1 (15.2)	54.7 (19.4)	48.7 (16.6)	56.0 (19.8)	54.1 (20.8)	52.9 (14.2)	48.5 (9.3)
Low density lipoprotein, mg/dL	101.2 (31.8)	109.8 (34.6)	106.5 (36.3)	119.2 (40.4)	106.1 (30.6)	104.3 (31.3)	99.2 (27.8)	99.9 (23.2)
Triglyceride, mg/dL	162.8 (127.4)	151.9 (109.9)	162.8 (111.8)	181.8 (162.2)	147.4 (140.5)	152.6(164.6)	135.8 (74.2)	123.0 (59.1)
Blood glucose, mg/dL	87.7 (29.3)	92.2 (21.7)	92.5 (28.8)	88.9 (26.1)	93.9 (39.7)	92.4(20.5)	88.1 (24.6)	92.2 (31.6)
Hemoglobin A1c%	5.6 (1.1)	5.6 (0.8)	5.5 (0.7)	5.5 (0.5)	5.8 (1.0)	5.5 (0.8)	5.6 (0.6)	5.6 (0.6)

\* Mean value (standard deviation) unless otherwise noted

<sup>†</sup> Reporting ≥150 minutes of moderate activity/week or ≥75 minutes of vigorous activity/week, or equivalent mixture of both

<sup>‡</sup> Defined as having had a check-up by a physician, physician assistant, or nurse practitioner within 1-2 years

<sup>§</sup> Males ≥102 cm or females ≥88 cm

**TABLE S2. Demographic and clinical characteristics of participating versus non-participating cancer survivors recruited from the Childhood Cancer Survivor Study (CCSS) cohort.**

Characteristic (%)	Participants		Non-participants N=825	Overall CCSS cohort* N=24,730
	All consented N=766	Complete data N=571		
Female sex	428 (55.9%)	325 (56.9%)	365 (44.2%)	11,544 (46.7%)
White non-Hispanic race/ethnicity	641 (83.7%)	486 (85.1%)	669 (81.1%)	20,233 (81.8%)
Median current age, years (range)	37.3 (20.1-65.0)	37.7 (20.1-65.0)	37.7 (19.7-64.9)	40.8 (19.1-69.5)
Median age at cancer diagnosis, years (range)	8.6 (0.01-20.9)	8.3 (0.01-20.8)	7.3 (0.00-20.7)	6.8 (0.0-21.0)
Cancer diagnosis				
Bone cancer / sarcoma	116 (15.1%)	86 (15.1%)	136 (16.5%)	3684 (14.9%)
Central nervous system	69 (9.0%)	59 (10.3%)	80 (9.7%)	4173 (16.9%)
Kidney	80 (10.4%)	55 (9.6%)	72 (8.7%)	2233 (9.0%)
Leukemia	251 (32.8%)	196 (34.3%)	255 (30.9%)	7699 (31.1%)
Lymphoma	205 (26.7%)	142 (24.9%)	215 (26.0%)	5077 (20.5%)
Neuroblastoma	45 (5.9%)	33 (5.8%)	67 (8.1%)	1864 (7.5%)
Anthracycline exposure	601 (78.9%)	441 (77.4%)	638 (78.1%)	10856 (48.1%)
Chest radiation exposure	315 (41.4%)	245 (43.1%)	329 (40.1%)	5430 (24.6%)
History of hypertension requiring medications <sup>†</sup>	107 (14.0%)	79 (13.8%)	85 (10.3%)	2990 (12.1%)
History of dyslipidemia requiring medications <sup>†</sup>	85 (11.1%)	70 (12.3%)	78 (9.5%)	2108 (8.5%)
History of diabetes requiring medications <sup>†</sup>	29 (3.8%)	23 (4.0%)	33 (4.0%)	1061 (4.3%)
History of tobacco use <sup>†</sup>	252 (32.9%)	175 (30.6%)	280 (33.9%)	7958 (32.2%)

\* Not known to be deceased as of January 1, 2019

<sup>†</sup> Based on responses to prior Childhood Cancer Survivor Study questionnaires

**TABLE S3. Physiologic measurements of childhood cancer survivors (CCSS) at high cardiovascular risk compared with the general population (NHANES), stratified by cardiovascular disease risk factor underdiagnosis and undertreatment status.**

Outcomes*	No underdiagnosis or undertreatment			Any underdiagnosis			Any undertreatment		
	CCSS N=323 <sup>†</sup>	NHANES N=218 <sup>†</sup>	P-value <sup>‡</sup>	CCSS N=155 <sup>†</sup>	NHANES N=90 <sup>†</sup>	P-value <sup>‡</sup>	CCSS N=120 <sup>†</sup>	NHANES N=48 <sup>†</sup>	P-value <sup>‡</sup>
BMI, kg/m <sup>2</sup>	26.2 (6.0)	28.2 (7.2)	0.01	28.8 (6.9)	30.7 (6.7)	0.02	29.4 (6.4)	31.7 (7.0)	0.14
No. overweight 25-29 kg/m <sup>2</sup> (%)	91 (28.2%)	52 (23.9%)	0.02	61 (39.4%)	33 (36.7%)	0.06	36 (30.0%)	11 (22.9%)	0.35
No. obese ≥30 kg/m <sup>2</sup> (%)	72 (22.3%)	75 (34.4%)		49 (31.6%)	40 (44.4%)		50 (41.7%)	28 (58.3%)	
Waist circumference, cm	85.7 (14.8)	95.8 (17.0)	<0.001	93.1 (15.3)	103.8(15.2)	<0.001	94.6 (15.4)	107.7 (15.4)	<0.001
No. with central adiposity (%) <sup>§</sup>	90 (27.9%)	109 (50.0%)	<0.001	56 (36.1%)	54 (60.0%)	<0.001	50 (41.7%)	34 (70.8%)	0.001
Systolic blood pressure, mmHg	109.7 (10.2)	112.3 (9.1)	0.001	118.7 (11.9)	126.0 (13.8)	<0.001	118.9 (15.2)	131.5 (17.8)	<0.001
Diastolic blood pressure, mmHg	70.6 (7.0)	66.9 (8.9)	<0.001	79.4 (8.4)	74.6 (12.7)	<0.001	75.9 (10.3)	78.3(11.2)	0.26
Total cholesterol, mg/dL	177.5 (30.4)	176.7 (32.7)	0.73	198.7 (46.7)	216.0 (45.1)	0.01	211.0 (50.7)	226.5 (39.6)	0.02
High density lipoprotein, mg/dL	56.9 (16.5)	58.9 (17.4)	0.10	48.9 (18.1)	45.2(10.4)	0.07	42.3 (10.5)	49.7(13.2)	<0.001
Low density lipoprotein, mg/dL	99.6 (25.7)	101.1 (27.8)	0.41	112.2 (36.7)	135.5 (40.6)	<0.001	119.1 (46.0)	145.0 (35.5)	<0.001
Triglyceride, mg/dL	106.0 (50.7)	76.8 (35.5)	<0.001	201.0 (156.1)	173.5 (78.0)	0.15	265.1 (174.7)	166.0 (74.0)	0.001
Blood glucose, mg/dL	85.4 (16.7)	97.7 (10.5)	<0.001	91.7 (36.7)	109.4 (42.4)	0.001	108.2 (45.1)	118.9 (36.8)	0.054
Hemoglobin A1c%	5.4 (0.4)	5.2 (0.4)	<0.001	5.6 (0.81)	5.6 (1.2)	0.54	6.3 (1.50)	5.9 (1.1)	0.24

\* Mean value (standard deviation) unless otherwise noted

<sup>†</sup> Numbers sum to greater than 571 and 345 for CSS and NHANES, respectively, as some individuals had both at least one underdiagnosed condition and at least one undertreated condition

<sup>‡</sup> Adjusted for sex, current age, and race/ethnicity

<sup>§</sup> Males ≥102 cm or females ≥88 cm

**TABLE S4. Distribution of underdiagnosed and undertreated conditions among childhood cancer survivors.**

<b>No. under-diagnosed conditions</b>	<b>No. undertreated conditions</b>				<b>Total</b>
	<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	
0	323	79	13	1	416
1	111	26	1	0	138
2	16	0	0	0	16
3	1	0	0	0	1
<b>Total</b>	<b>451</b>	<b>105</b>	<b>14</b>	<b>1</b>	<b>571</b>

**TABLE S5. Odds of cardiovascular disease risk factor undertreatment among childhood cancer survivors, adjusted for sex, race/ethnicity, current age, chest radiotherapy, adverse lifestyle factors, body mass index, self-efficacy, and MHLC scales.**

Characteristic	Undertreatment N=120*	
	OR (95% CI)	P-value
Male vs. female (ref)	1.5 (0.9-2.5)	0.11
Other vs. non-Hispanic White (ref)	1.5 (0.9-2.5)	0.11
Current age, years <sup>†</sup>	1.4 (1.0-1.9)	0.04
Chest radiotherapy exposure vs. none (ref)	2.0 (1.2-3.4)	0.009
No. adverse lifestyle factors <sup>‡</sup>		
0	1.0 (ref)	
1	1.4 (0.7-2.8)	0.38
≥2	1.9 (0.9-4.2)	0.10
Body mass index, kg/m <sup>2</sup>		
<25	1.0 (ref)	
25-29	1.9 (1.0-3.6)	0.06
≥30	3.1 (1.7-5.8)	<.001
High vs. low health-related self-efficacy <sup>§</sup>	0.5 (0.3-1.0)	0.03
MHLC Scale <sup>  </sup>		
Internal	0.6 (0.4-0.9)	0.03
Chance	0.8 (0.6-1.2)	0.25
Powerful others	1.7 (1.2-2.5)	0.005

CI, confidence interval; MHLC, Multidimensional Health Locus of Control; OR, odds ratio; ref, referent

\* Compared with survivors without any cardiovascular disease risk factor underdiagnosis and undertreatment (n=323; referent)

<sup>†</sup> Modeled as a linear term with the following categories: 20-34, 35-39, and ≥40 years

<sup>‡</sup> Consisting of physical inactivity, low fruit/vegetable consumption, and current smoking/tobacco use

<sup>§</sup> Defined as T-score ≥50 vs. <50 (ref)

<sup>||</sup> Modeled as a linear term with risk estimates reflecting the association with a one unit increase in the scale value