Supplemental Methods: Methodology for linkage between CCSS and OPTN databases

Through a data-sharing agreement with OPTN, SOT and wait-list outcomes were obtained for all eligible CCSS participants through 12/31/2013. OPTN began consistently collecting transplant data in October, 1987. For the 13,318 eligible CCSS participants, the following information was sent to OPTN: First Name, Middle Name, Last Name (+ former last name, if relevant), Sex, Date of Birth, Social Security number (if available), Ages of any known heart, kidney, liver or lung transplants, Medical Record notes, date of last CCSS survey (last contact) and primary cancer diagnosis. OPTN based matching on first and last names, sex, date of birth and, if available, social security number and classified identified cases into 3 levels of certainty: (1) Denotes highly certain match; (2) Denotes potential, but unlikely match unless CCSS has extra data that matches on additional data provided by OPTN (height, weight, zip code, type of malignancy, etc); (3) Denotes a match of any of the blocking criteria, but a highly unlikely match. This analysis used only level 1 matches and additionally reviewed agreement between other available clinical data from both sources. Manual searches were carried out for any patients who selfreported a transplant that wasn't identified via the above methodology, but a match was not found. These events were excluded from this analysis, though a sensitivity analysis was carried out to evaluate the impact on results if they were included. The final number of SOTs occurring after cohort entry to the CCSS utilized in this manuscript and their method of identification are shown in the supplmental methods table below, within 3 key time intervals defined by pre-October, 1987 when OPTN began collecting transplant data and the last date of contact for the CCSS participant.

Supplemental Methods		Source of Transplant Ascertainment		
Time interval	Total Transplants	CCSS Only	Both CCSS and OPTN	OPTN Only
Prior to October, 1987	3	2	1	0
October, 1987 – End of CCSS Follow-up	67	0	54	13
After end of CCSS follow-up	33	0	0	33
Total Time	103	2	55	46

Supplemental table: Univariable hazard ratio estimates

Kidney *		Univariable	95%	
		Hazard	Confidence	
Treatment factor	Level of exposure	Ratio	Interval	p-value
Ifosfamide	No	1.0	referent	
	Yes	30.7	(9.6, 98.7)	< 0.0001
IV or IM Methotrexate	No	1.0	referent	
	Yes	0.6	(0.3, 1.2)	0.15
Kidney radiation exposure (Gy)	None	1.0	referent	
	>0 to 10	0.4	(0.2, 0.7)	0.0021
	>10 to 20	4.4	(2.3, 8.6)	<0.0001
	>20 TDI	4.0	(0.9, 16.8)	0.061
	TBI	4.4	(1.5, 12.6)	0.0061
Nephrectomy	No	1.0	referent	<0.0001
	Yes	7.1	(4.3, 11.8)	<0.0001
Age at primary cancer diagnosis	0-4	2.4	$(1 \cdot 1, 5 \cdot 4)$	0.031
(years)	5-9	1.8	(0.7, 4.3)	0.21
	10-14	0.9	(0.3, 2.5)	0.78
	15-20	1.0	referent	
Heart **				
		Univariable	95%	
TT	T 1 C	Hazard	Confidence	
Treatment factor	Level of exposure	Ratio	Interval	p-value
Cyclophosphamide (mg/m2)	None	1.0	referent	
	>0 to 10000	0.8	(0.4, 1.7)	0.60
	>10000 to 20000	2.8	(1.4, 5.6)	0.0028
	>20000	3.3	(1.3, 8.7)	0.014
Anthracyclines (mg/m2)	None	1.0	referent	
	>0 to 150	3.4	(0.9, 12.5)	0.69
	>150 to 300	2.6	(0.8, 8.5)	0.11
		10.0		
	>300 to 450	10.0	(4.4, 22.6)	< 0.0001
	>450	31.2	(4·4, 22·6) (14·3, 68·2)	
Heart radiation exposure (Gy)	>450 None	31·2 1·0	(4·4, 22·6) (14·3, 68·2) referent	<0.0001 <0.0001
Heart radiation exposure (Gy)	>450 None >0 to 10	31·2 1·0 1·9	(4·4, 22·6) (14·3, 68·2) referent (0·9, 4·1)	<0.0001 <0.0001 0.075
Heart radiation exposure (Gy)	>450 None >0 to 10 > 10 to 20	31·2 1·0 1·9 1·3	(4·4, 22·6) (14·3, 68·2) referent (0·9, 4·1) (0·4, 4·7)	<0.0001 <0.0001 0.075 0.70
Heart radiation exposure (Gy)	>450 None >0 to 10 > 10 to 20 > 20 to 30	31·2 1·0 1·9 1·3 2·6	(4·4, 22·6) (14·3, 68·2) referent (0·9, 4·1) (0·4, 4·7) (0·8, 8·4)	<0.0001 <0.0001 0.075 0.70 0.10
Heart radiation exposure (Gy)	>450 None >0 to 10 > 10 to 20	31·2 1·0 1·9 1·3	(4·4, 22·6) (14·3, 68·2) referent (0·9, 4·1) (0·4, 4·7)	<0.0001 <0.0001 0.075 0.70
Heart radiation exposure (Gy) Liver †	>450 None >0 to 10 > 10 to 20 > 20 to 30	31·2 1·0 1·9 1·3 2·6	(4·4, 22·6) (14·3, 68·2) referent (0·9, 4·1) (0·4, 4·7) (0·8, 8·4)	<0.0001 <0.0001 0.075 0.70 0.10
	>450 None >0 to 10 > 10 to 20 > 20 to 30	31·2 1·0 1·9 1·3 2·6 4·1	(4·4, 22·6) (14·3, 68·2) referent (0·9, 4·1) (0·4, 4·7) (0·8, 8·4) (1·7, 9·6)	<0.0001 <0.0001 0.075 0.70 0.10
Liver [†]	>450 None >0 to 10 > 10 to 20 > 20 to 30 > 30	31·2 1·0 1·9 1·3 2·6 4·1 Univariable Hazard	(4·4, 22·6) (14·3, 68·2) referent (0·9, 4·1) (0·4, 4·7) (0·8, 8·4) (1·7, 9·6) 95% Confidence	<0.0001 <0.0001 0.075 0.70 0.10 0.0013
Liver [†] Treatment factor	>450 None >0 to 10 > 10 to 20 > 20 to 30 > 30 Level of exposure	31·2 1·0 1·9 1·3 2·6 4·1 Univariable Hazard Ratio	(4·4, 22·6) (14·3, 68·2) referent (0·9, 4·1) (0·4, 4·7) (0·8, 8·4) (1·7, 9·6) 95% Confidence Interval	<0.0001 <0.0001 0.075 0.70 0.10
	>450 None >0 to 10 > 10 to 20 > 20 to 30 > 30 Level of exposure No	31·2 1·0 1·9 1·3 2·6 4·1 Univariable Hazard Ratio 1·0	(4·4, 22·6) (14·3, 68·2) referent (0·9, 4·1) (0·4, 4·7) (0·8, 8·4) (1·7, 9·6) 95% Confidence Interval	<0.0001 <0.0001 0.075 0.70 0.10 0.0013
Liver † Treatment factor Dactinomycin	>450 None >0 to 10 > 10 to 20 > 20 to 30 > 30 Level of exposure No Yes	31·2 1·0 1·9 1·3 2·6 4·1 Univariable Hazard Ratio 1·0 3·6	(4·4, 22·6) (14·3, 68·2) referent (0·9, 4·1) (0·4, 4·7) (0·8, 8·4) (1·7, 9·6) 95% Confidence Interval referent (1·5, 8·8)	<0.0001 <0.0001 0.075 0.70 0.10 0.0013
Liver [†] Treatment factor	>450 None >0 to 10 > 10 to 20 > 20 to 30 > 30 Level of exposure No	31·2 1·0 1·9 1·3 2·6 4·1 Univariable Hazard Ratio 1·0	(4·4, 22·6) (14·3, 68·2) referent (0·9, 4·1) (0·4, 4·7) (0·8, 8·4) (1·7, 9·6) 95% Confidence Interval	<0.0001 <0.0001 0.075 0.70 0.10 0.0013

IV or IM Methotrexate	No Yes	1·0 4·4	referent (1·8, 10·7)	0.0009
Antimetabolites (6-MP or 6-TG)	No Yes	1·0 1·2	referent $(0.5, 2.8)$	0.76
Abdominal radiation exposure (Gy)	None >0 to 20 (non TBI) > 20 (non TBI) TBI	1·0 0·3 1·1 3·6	referent (0·1, 1·2) (0·4, 3·5) (0·4, 28·9)	0·084 0·83 0·23
Sex	Male Female	1·0 0·4	referent $(0.2, 1.0)$	0.048

Lung ‡

Treatment factor	Level of exposure	Univariable Hazard Ratio	95% Confidence Interval	p-value
Carmustine	No	1.0	referent	
	Yes	9.3	(2.5, 35.1)	0.0010
IV or IM Methotrexate	No	1.0		
	Yes	1.8	(0.5, 7.1)	0.38
Lung radiation exposure (Gy)	None	1.0	referent	
	>0 to 10	1.3	(0.2, 7.2)	0.75
	> 10	5.8	(1.1, 30.0)	0.036
Age at primary cancer diagnosis	0-4 yrs old	0.8	(0.2, 3.4)	0.82
	5-9 yrs old	0.3	(0.0, 2.5)	0.24
	10-14 yrs old	0.9	(0.2, 4.3)	0.86
	15-20 yrs old	1.0	referent	
Sex	Male	1.0	referent	
	Female	2.5	(0.8, 8.1)	0.13

^{*} Other factors evaluated in univariable analysis for kidney: cyclophosphamide, cisplatin and sex ** Other factors evaluated in univariable analysis for heart: cisplatin, ifosfamide, sex and age at primary cancer diagnosis

[†] Other factors evaluated in univariable analysis for liver: age at primary cancer diagnosis

[‡] Other factors evaluated in univariable analysis for lung: cyclophosphamide, cisplatin, bleomycin