Chronic Disease Working Group

CCSS Investigator Meeting 2017

Kevin Oeffinger

Duke Cancer Institute


Maine
New York
New Hampshire
Massachusetts
Connecticut
Pennsylvania
New Jersey
Delaware
Maryland
Virginia
North Carolina
South Carolina
Georgia
Florida


Duke University
Duke Forest
Teaching and Research Laboratory
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CCSS
An NCI-Funded Resource

Chronic Disease Working Group Core

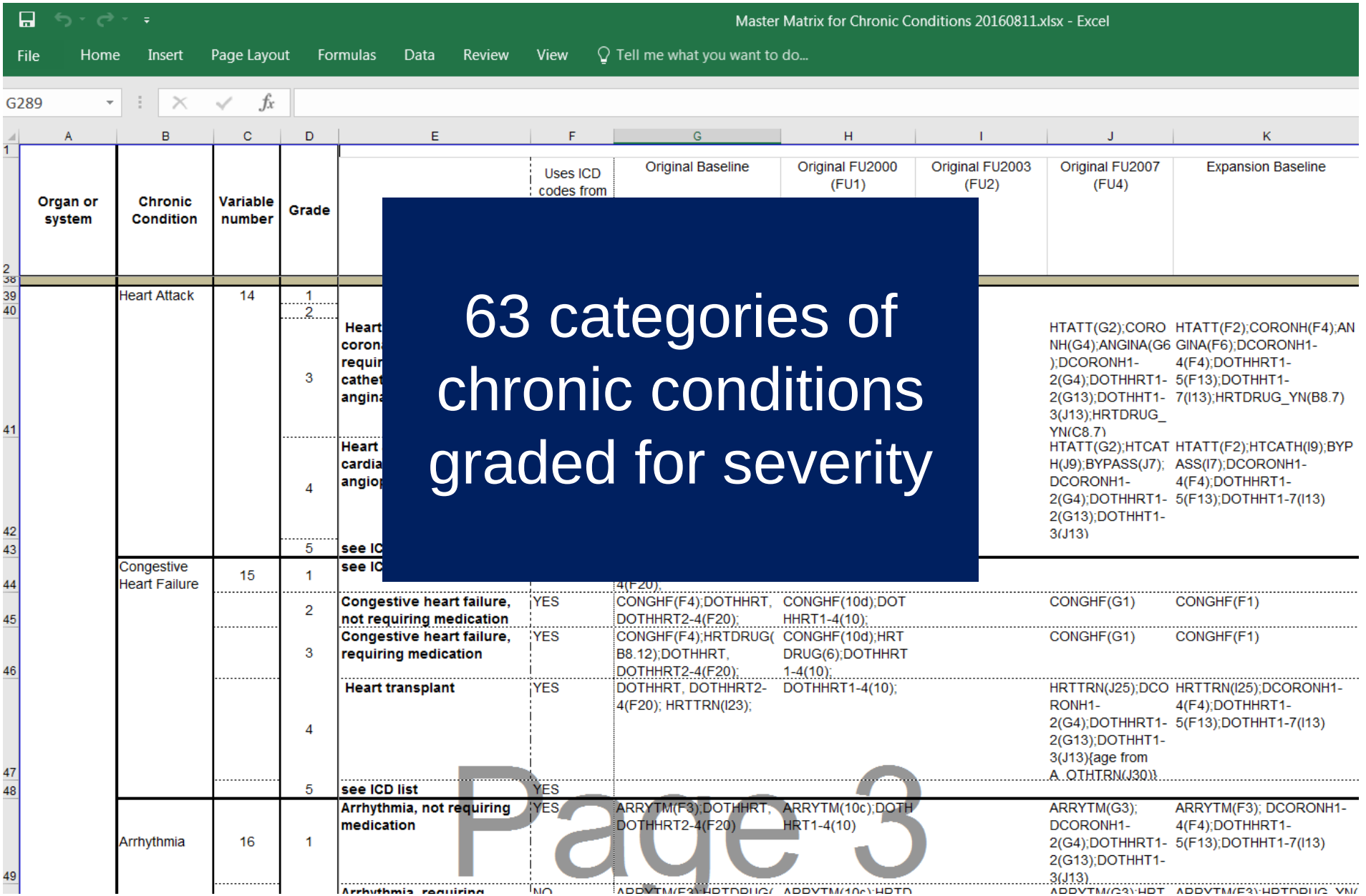
Individual	Expertise
Kevin Oeffinger	Primary care
Eric Chow (co-chair)	Pediatric oncology
Charles (Chuck) Sklar (Ex-officio)	Pediatric endocrinology
Melissa Hudson	Pediatric oncology
Louis (Sandy) Constine	Radiation oncology
Todd Gibson	Epidemiology, CCSS Project Dir
Christopher Weldon	Surgery
Daniel Mulrooney	Pediatric oncology
Emily Tonorezos	Primary care
Sogol (Goli) Mostoufi-Moab	Pediatric endocrinology / oncology
Elizabeth (Beth) Wells	Pediatric neuro-oncology
Rebecca Howell	Radiation physics / dosimetry
Kayla Stratton	Biostatistician
Wendy Leisenring	Lead biostatistician

Chronic condition categories	Therapeutic exposures	Cancer groups
Vision	Radiation	ALL
Hearing	Body areas	AML
Speech	Dosimetry	Other leukemia
Endocrine	Volume	Medulloblastoma
Respiratory	Chemotherapy	Other CNS
Cardiovascular	Yes/no	Hodgkin lymphoma
Gastrointestinal	Cumulative dose	NHL
Renal	CED	Neuroblastoma
Musculoskeletal	Dox-equivalent	Wilms tumor
Neurologic	Combinations	Soft tissue sarcoma
Other hematologic	Surgery	Osteosarcoma
Infection		Ewing sarcoma

Common Terminology Criteria for Adverse Events

- Original NEJM analysis: 114 conditions
- Aging / expansion cohort: significant increase in the number of conditions
- Universal need for standardized grading that is generalizable, transparent, and can be refined
- CTCAE task force: Sklar, Hudson, Nathan, Armstrong, Chow, Tonorezos, Mostoufi-Moab, Wells, Gibson, Smith, Barnea, Stratton, Leisenring

Master Matrix for Chronic Conditions – by Condition



Organ or system	Chronic Condition	Variable number	Grade		Uses ICD codes from	Original Baseline	Original FU2000 (FU1)	Original FU2003 (FU2)	Original FU2007 (FU4)	Expansion Baseline
	Heart Attack	14	1							
			2							
			3	**Heart coron requir cathet angina**					HTATT(G2);CORONH(G4);ANGINA(G6);DCORONH1-2(G4);DOTHHRT1-2(G13);DOTHHT1-3(J13);HRTDRUG_YN(C8.7)	HTATT(F2);CORONH(F4);ANGINA(F6);DCORONH1-4(F4);DOTHHRT1-5(F13);DOTHHT1-7(I13);HRTDRUG_YN(B8.7)
			4	**Heart cardia angiop**					HTATT(G2);HTCATH(J9);BYPASS(J7);DCORONH1-2(G4);DOTHHRT1-2(G13);DOTHHT1-3(J13)	HTATT(F2);HTCATH(I9);BYPASS(I7);DCORONH1-4(F4);DOTHHRT1-5(F13);DOTHHT1-7(I13)
			5	**see IC**						
	Congestive Heart Failure	15	1	**see IC**		4(F20);				
			2	**Congestive heart failure, not requiring medication**	YES	CONGHF(F4);DOTHHRT, DOTHHRT2-4(F20);	CONGHF(10d);DOTHHRT1-4(10);		CONGHF(G1)	CONGHF(F1)
			3	**Congestive heart failure, requiring medication**	YES	CONGHF(F4);HRTDRUG(B8.12);DOTHHRT, DOTHHRT2-4(F20);	CONGHF(10d);HRTDRUG(6);DOTHHRT1-4(10);		CONGHF(G1)	CONGHF(F1)
			4	**Heart transplant**	YES	DOTHHRT, DOTHHRT2-4(F20); HRTTRN(I23);	DOTHHRT1-4(10);		HRTTRN(J25);DCORONH1-2(G4);DOTHHRT1-2(G13);DOTHHT1-3(J13){age from A_OTHTRN(J30)}	HRTTRN(I25);DCORONH1-4(F4);DOTHHRT1-5(F13);DOTHHT1-7(I13)
			5	**see ICD list**	YES					
	Arrhythmia	16	1	**Arrhythmia, not requiring medication**	YES	ARRYTM(F3);DOTHHRT, DOTHHRT2-4(F20)	ARRYTM(10c);DOTHHRT1-4(10)		ARRYTM(G3); DCORONH1-2(G4);DOTHHRT1-2(G13);DOTHHT1-3(J13)	ARRYTM(F3); DCORONH1-4(F4);DOTHHRT1-5(F13);DOTHHT1-7(I13)
				Arrhythmia, requiring	NO	ARRYTM(F3);HRTDRUG(	ARRYTM(10c);HRTD		ARRYTM(G3);HRT	ARRYTM(F3);HRTDRUG_YN(

Master Matrix for Chronic Conditions – Using ICD codes

	A	B	C	D	E	F
1	**Organ system**	**Variable #**	**Chronic Condition**	**Grade**	**ICD 9/10 code with label**	**ICD code**
336	Cardiovascular	14	Heart Attack	4	00.66 Percutaneous transluminal coronary angioplasty [PTCA] or coronary atherectomy Balloon angioplasty of coronary artery Coronary atherectomy Percutaneous coronary angioplasty NOS PTCA NOS Code also any: injection or infusion of thrombolytic agent (99.10) insertion of coronary artery stent(s) (36.06-36.07) intracoronary artery thrombolytic infusion (36.04) number of vascular stents inserted (00.45-00.48) number of vessels treated (00.40-00.43) procedure on vessel bifurcation (00.44) SuperSaturated oxygen therapy (00.49)	0.66
337	Cardiovascular	14	Heart Attack		ry angioplasty NOS Code also any: f vessels treated (00.40-00.43) pen angioplasty (36.03) that by coronary atherectomy (00.66)	36.09
338	Cardiovascular	14	Heart Attack		t otherwise specified Direct r vein graft coronary with catheter ent, prosthesis, or vein graft rt revascularization NOS	36.1
339	Cardiovascular	14	Heart Attack			410
340	Cardiovascular	14	Heart Attack			410.8
341	Cardiovascular	14	Heart Attack			410.9
342	Cardiovascular	14	Heart Attack		sode of care unspecified	410.9
343	Cardiovascular	14	Heart Attack			411
344	Cardiovascular	14	Heart Attack			411.1
345	Cardiovascular	14	Heart Attack			411.8
346	Cardiovascular	14	Heart Attack	3	411.81 Acute coronary occlusion without myocardial infarction	411.81
347	Cardiovascular	14	Heart Attack	3	412. Old myocardial infarction	412
348	Cardiovascular	14	Heart Attack	3	413.1	413.1
349	Cardiovascular	14	Heart Attack	3	413.9 Other and unspecified angina pectoris	413.9
350	Cardiovascular	14	Heart Attack	5	414.: oth chr ischemic hrt dis	414
351	Cardiovascular	14	Heart Attack	3	414.0: coronary atherosclerosis	414
352	Cardiovascular	14	Heart Attack	5	414.0: coronary atherosclerosis	414
353	Cardiovascular	14	Heart Attack	3	414.00 Coronary atherosclerosis of unspecified type of vessel, native or graft	414
354	Cardiovascular	14	Heart Attack	4	414.05 Coronary atherosclerosis of unspecified bypass graft	414.05

1086 individual ICD9-10 codes included

Cumulative burden of cardiovascular morbidity in paediatric, adolescent, and young adult survivors of Hodgkin's lymphoma: an analysis from the St Jude Lifetime Cohort Study

Nickhill Bhakta, Qi Liu, Frederick Yeo, Malek Baassiri, Matthew J Ehrhardt, Deo K Srivastava, Monika L Metzger, Matthew J Krasin, Kirsten K Ness, Melissa M Hudson, Yutaka Yasui, Leslie L Robison

Summary

Background The magnitude of cardiovascular morbidity in paediatric, adolescent, and young adult survivors of Hodgkin's lymphoma is not known. Using medically ascertained data, we applied the cumulative burden metric to compare chronic cardiovascular health conditions in survivors of Hodgkin's lymphoma and general population controls.

Lancet Oncol 2016; 17: 1325–34
Published Online
July 25, 2016
http://dx.doi.org/10.1016/S1470-2045(16)30215-7

Conditions categorized as:

- Chronic, non-recurrent conditions (eg, hypercholesterolemia)
- Single, recurrent conditions (eg, thrombus)
- Chronic, recurrent (cardiomyopathy, surgical intervention)

Largely based upon in-person, detailed examination with the opportunity to clarify on sequence of events.

Cumulative burden of cardiovascular morbidity in paediatric, adolescent, and young adult survivors of Hodgkin's lymphoma: an analysis from the St Jude Lifetime Cohort Study

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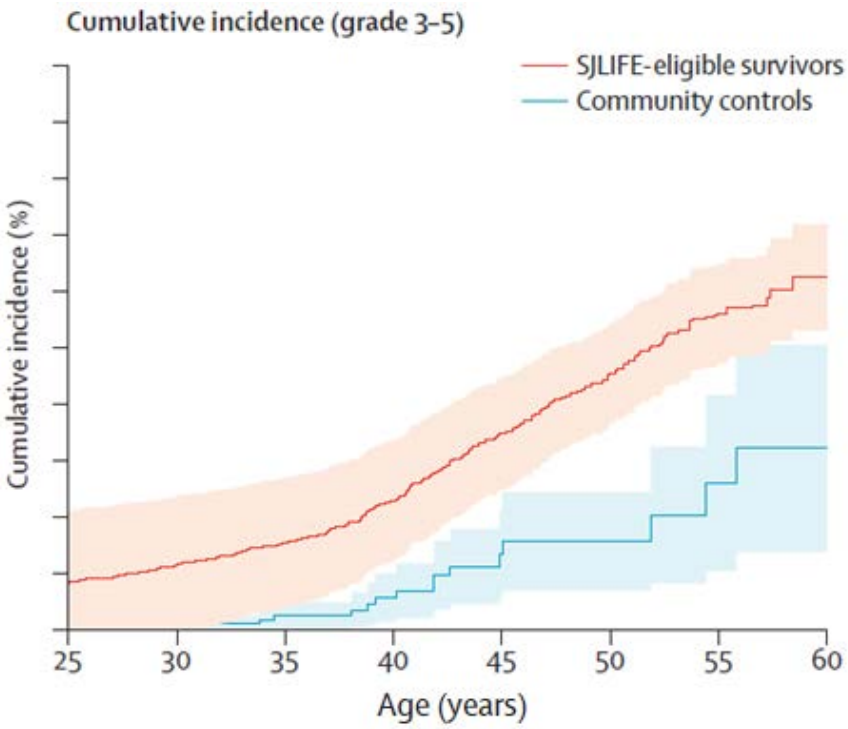
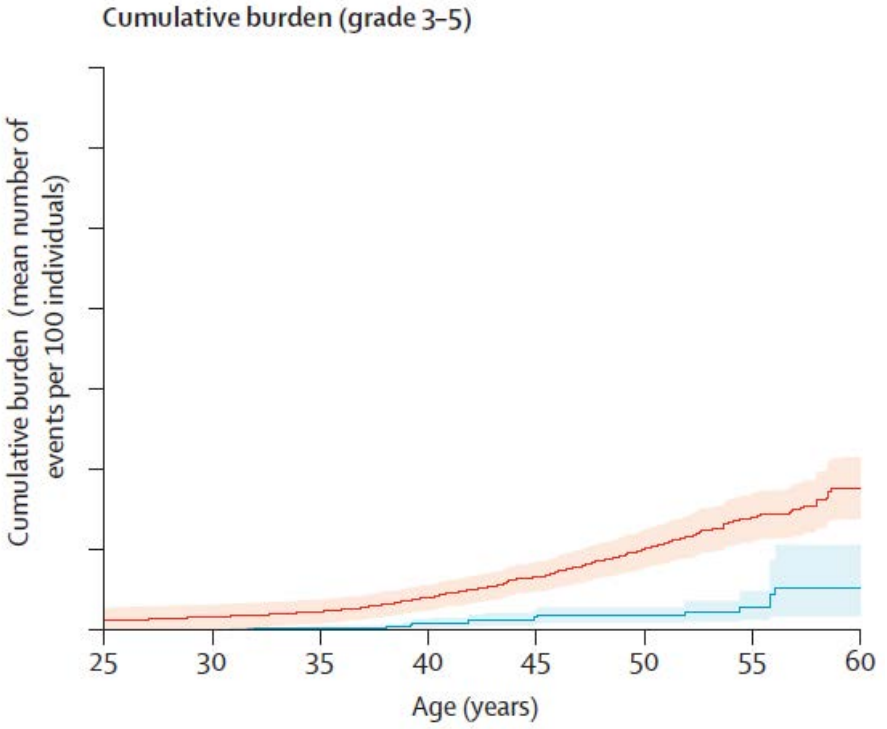
Background The magnitude of cardiovascular morbidity in paediatric, adolescent, and young adult survivors of Hodgkin's lymphoma is not known. Using medically ascertained data, we applied the cumulative burden metric to compare chronic cardiovascular health conditions in survivors of Hodgkin's lymphoma and general population controls.





Cumulative Burden in CCSS

- Limitations:
  - Self-report vs in-person examination
  - Unable to distinguish between two separate events (eg, two different episodes of thrombus)
- Adaptations:
  - Count each individual type of cancer
  - No adjustment with other chronic conditions
  - Caveats

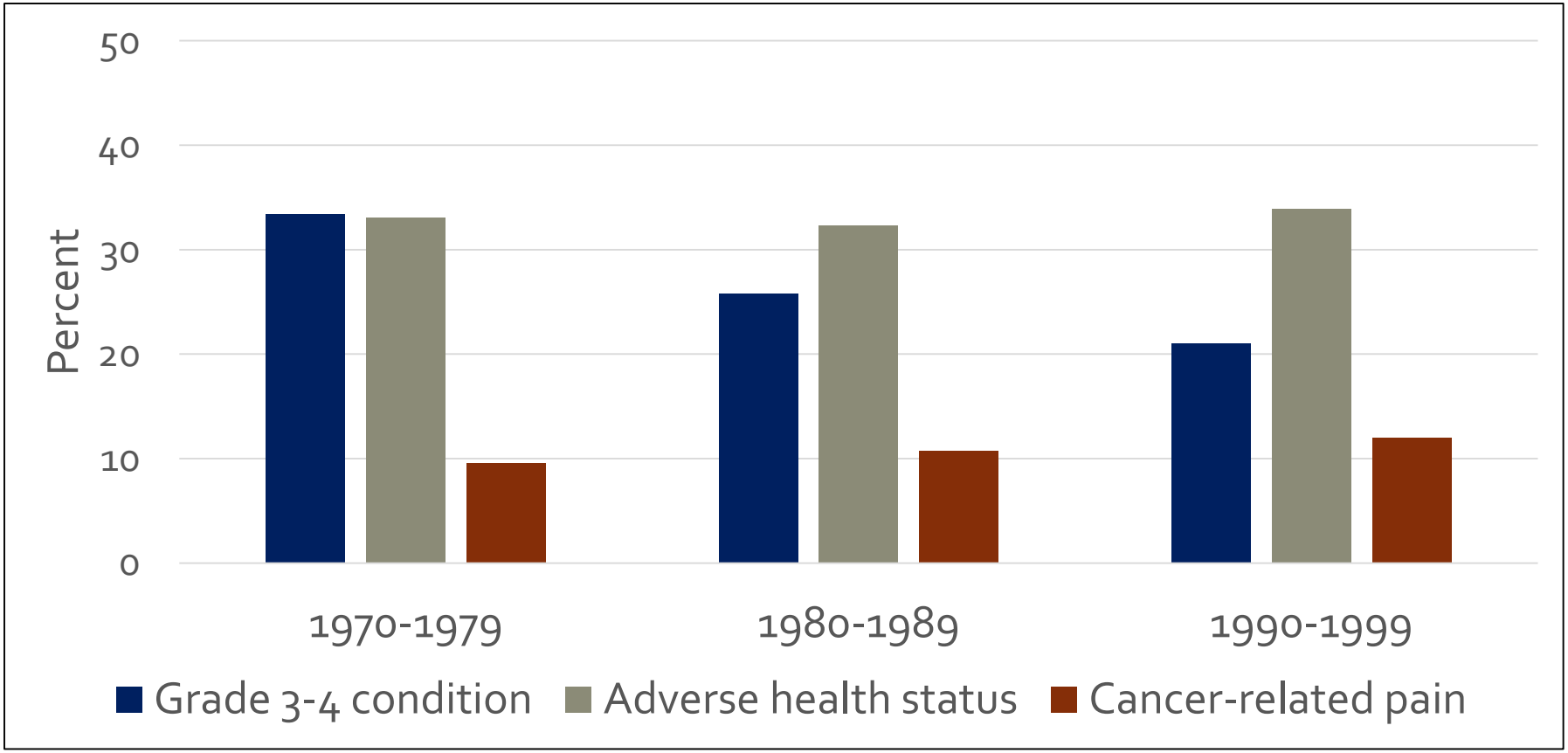
Selected Publications 2015-2016

1. Overall estimates of chronic conditions and how they influence health status
2. By condition or outcome
3. By organ system
4. By (special) cancer types
5. Chronic conditions as a consequence of a benign neoplasm
6. How chronic conditions influence psychosocial issues
7. Chronic conditions and utility-based, health-related quality of life

Annals of Internal Medicine ORIGINAL RESEARCH

Effect of Temporal Changes in Therapeutic Exposure on Self-reported Health Status in Childhood Cancer Survivors

Kirsten K. Ness, PhD*; Melissa M. Hudson, MD*; Kendra E. Jones, MS; Wendy Leisenring, ScD; Yutaka Yasui, PhD; Yan Chen, MS; Marilyn Stovall, PhD; Todd M. Gibson, PhD; Daniel M. Green, MD; Joseph P. Neglia, MD; Tara O. Henderson, MD; Jacqueline Casillas, MD; Jennifer S. Ford, PhD; Karen E. Effinger, MD, MS; Kevin R. Krull, PhD; Gregory T. Armstrong, MD, MSCE; Leslie L. Robison, PhD; Kevin C. Oeffinger, MD†; and Paul C. Nathan, MD†

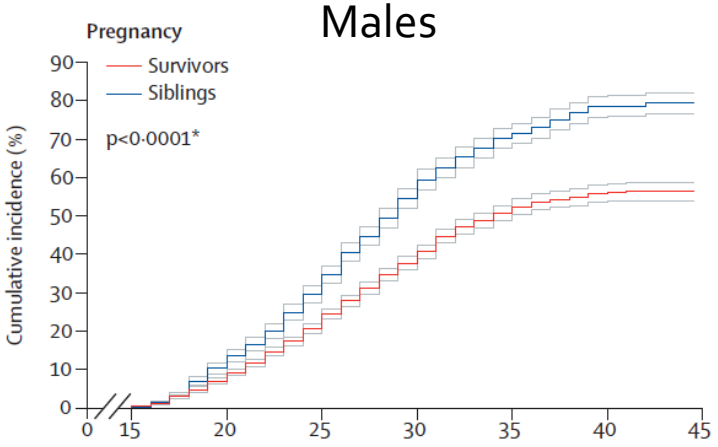


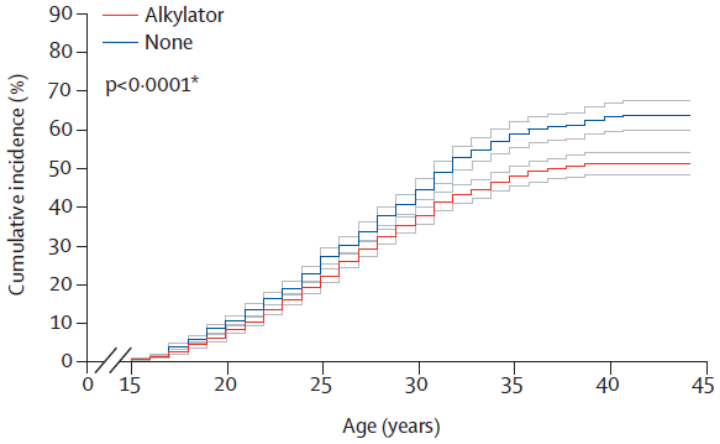
Pregnancy after chemotherapy in male and female survivors of childhood cancer treated between 1970 and 1999: a report from the Childhood Cancer Survivor Study cohort

Eric J Chow, Kayla L Stratton, Wendy M Leisenring, Kevin C Oeffinger, Charles A Sklar, Sarah S Donaldson, Jill P Ginsberg, Lisa B Kenney, Jennifer M Levine, Leslie L Robison, Margarett Shnorhavorian, Marilyn Stovall, Gregory T Armstrong, Daniel M Green

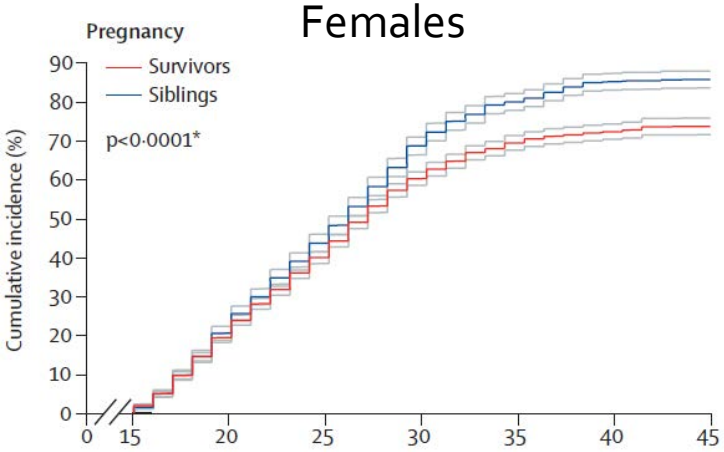
Lancet Oncol 2016; 17: 567–76

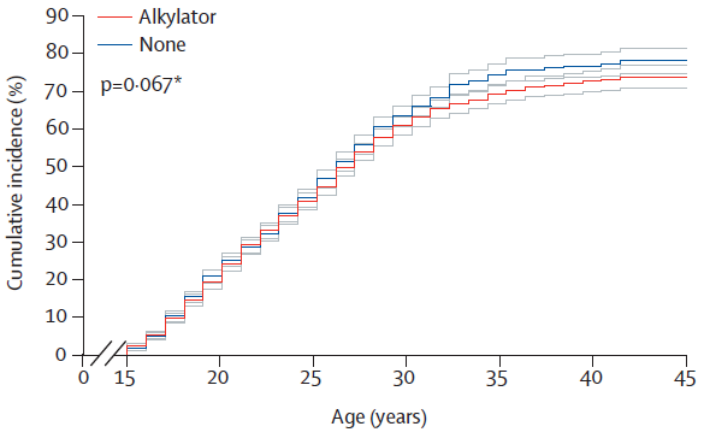
Males





Females



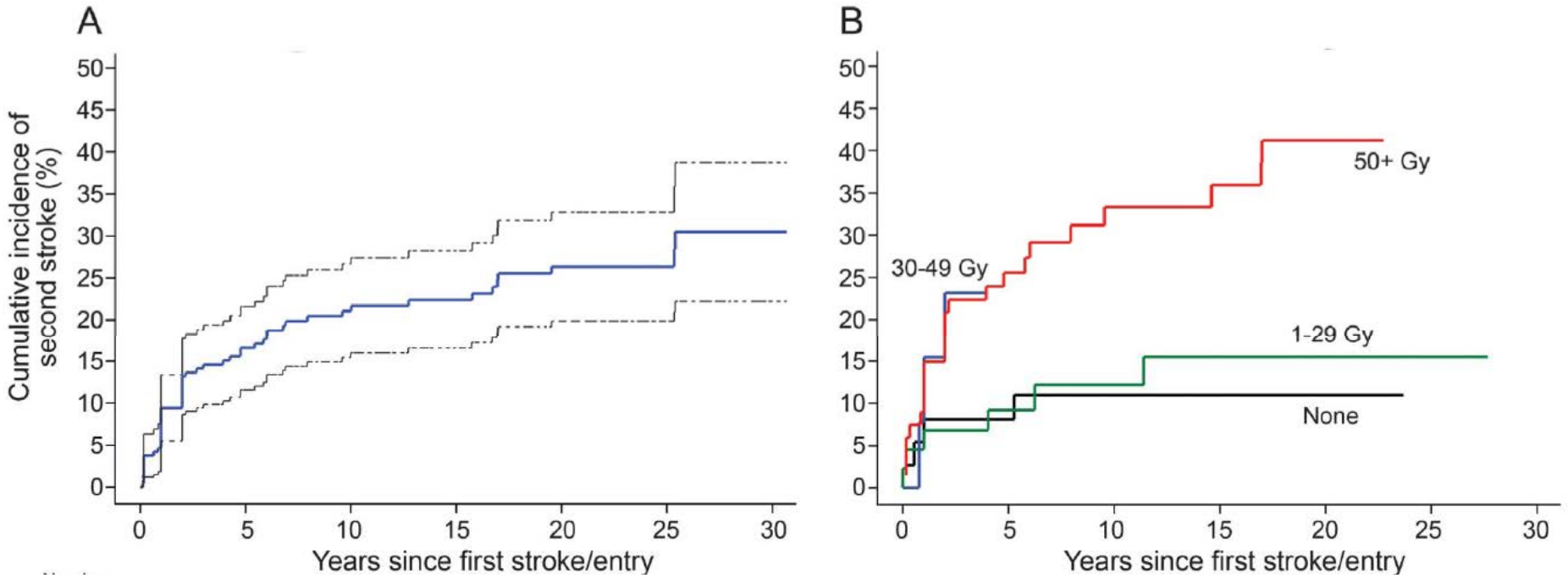


Recurrent stroke in childhood cancer survivors

Neurology 85 September 22, 2015

Heather J. Fullerton, MD, MAS
Kayla Stratton, MS
Sabine Mueller, MD, PhD
Wendy W. Leisenring,

Figure 1 Cumulative incidence of recurrent stroke in childhood cancer survivors



Recurrent stroke in childhood cancer survivors

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Characteristics	Recurrence (n = 52), n (%)	No recurrence (n = 161), n (%)	HR (95% CI)	*p* Value
First stroke symptom duration >24 h	40 (77)	96 (60)	1.9 (1.0-3.6)	0.057
Presentation with hemiparesis	30 (58)	111 (69)	0.6 (0.3-1.0)	0.064
Stroke risk factors[b]				
Narrowing of blood vessels to brain	4 (8)	9 (6)	1.3 (0.5-3.6)	0.62
Moyamoya	5 (10)	5 (3)	2.6 (1.0-6.5)	0.044
Hypertension	24 (46)	48 (30)	3.3 (1.9-5.7)	<0.0001
Diabetes mellitus	5 (10)	12 (7)	2.3 (0.9-5.7)	0.08
Smoking (ever)	7 (13)	43 (27)	0.7 (0.3-1.6)	0.45

THE JOURNAL OF
SEXUAL MEDICINE

ONCOLOGY

Erectile Dysfunction in Male Survivors of Childhood Cancer—A Report From the Childhood Cancer Survivor Study

Chad W. M. Ritenour, MD,[1] Kristy D. Seidel, MS,[2] Wendy Leisenring, ScD,[2,3] Ann C. Mertens, PhD,[4,5] Karen Wasilewski-Masker, MD,[4,5] Margarett Shnorhavorian, MD,[6] Charles A. Sklar, MD,[7] John A. Whitton, MS,[2] Marilyn Stovall, PhD,[8] Louis S. Constine, MD,[9] Gregory T. Armstrong, MD, MSCE,[10] Leslie L. Robison, PhD,[10] and Lillian R. Meacham, MD[4,5]

Table 3. Multivariable comparison summary of survivors and siblings for ED and treatment of ED

Outcome measurement	Frequency (% yes)	Unadjusted relative risk (95% CI)	Adjusted relative risk (95% CI)*
ED			
Survivors	143/1,166 (12)	2.90 (1.50–5.60)	2.63 (1.40–4.97)
Siblings	9/213 (4)	1.00 (referent)	1.00 (referent)
Self-reported treatment for ED			
Survivors	88/1,474 (6)	2.59 (1.14–5.86)	2.73 (1.26–5.94)
Siblings	6/260 (2)	1.00 (referent)	1.00 (referent)

ED = erectile dysfunction; IIEF-EF = International Index of Erectile Function erectile function domain.
*Adjusted for age at time of completing the Male Health Questionnaire, general health level, physical activity, at least grade 3 cardiac condition, hypertension requiring medication, diabetes, depression and other major psychiatric illness, prostate disease, and current use of exogenous testosterone.

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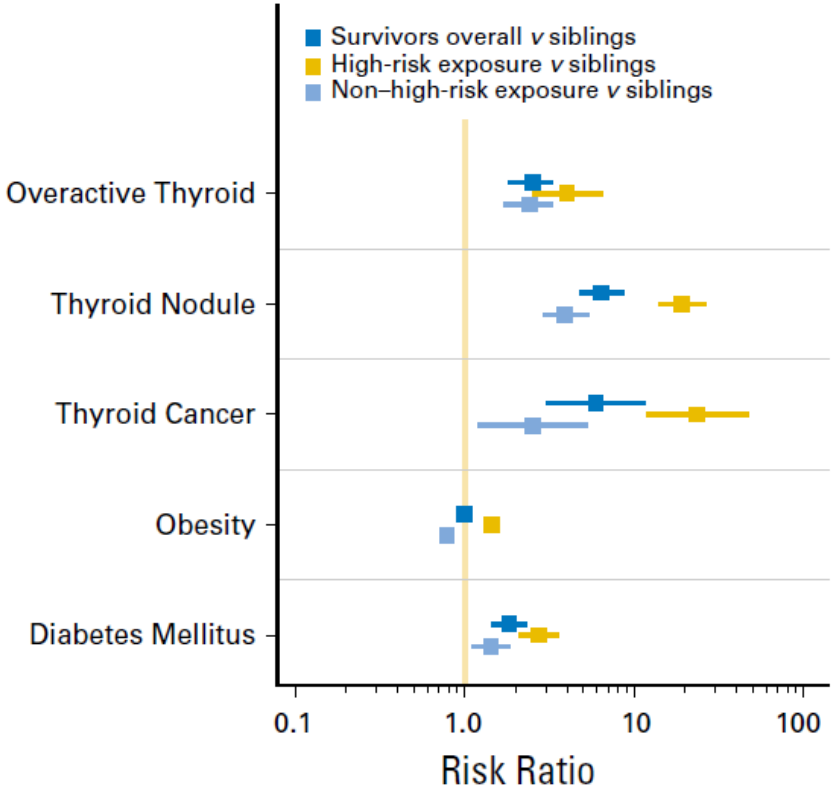
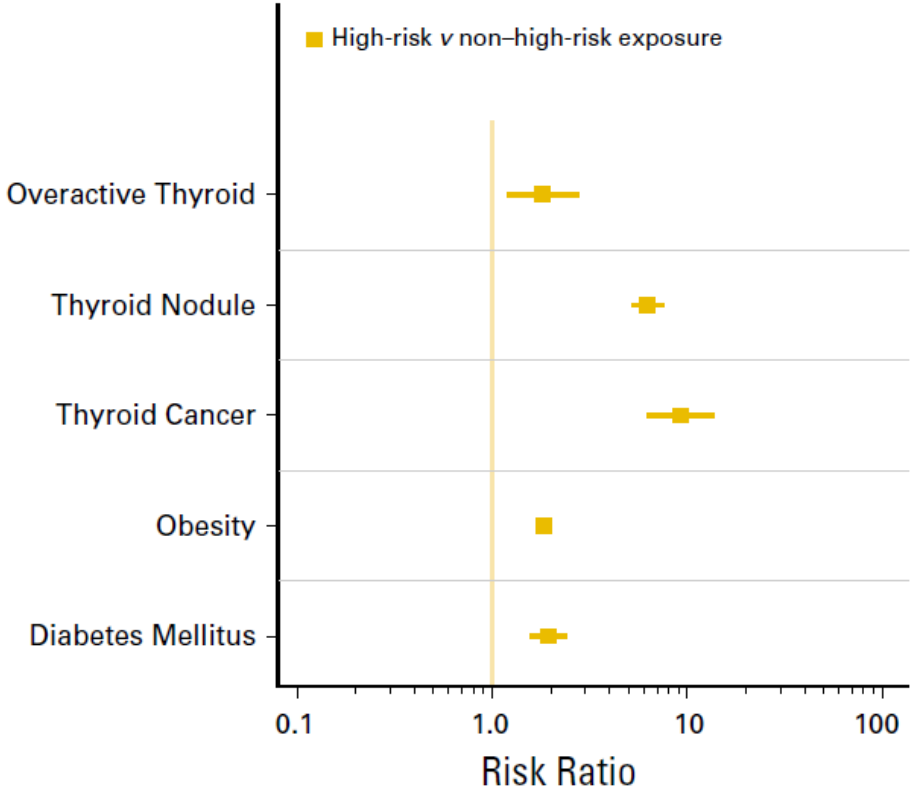
JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Endocrine Abnormalities in Aging Survivors of Childhood Cancer: A Report From the Childhood Cancer Survivor Study

Sogol Mostoufi-Moab, Kristy Seidel, Wendy M. Leisenring, Gregory T. Armstrong, Kevin C. Oeffinger, Marilyn Stovall, Lillian R. Meacham, Daniel M. Green, Rita Weathers, Jill P. Ginsberg, Leslie L. Robison, and Charles A. Sklar

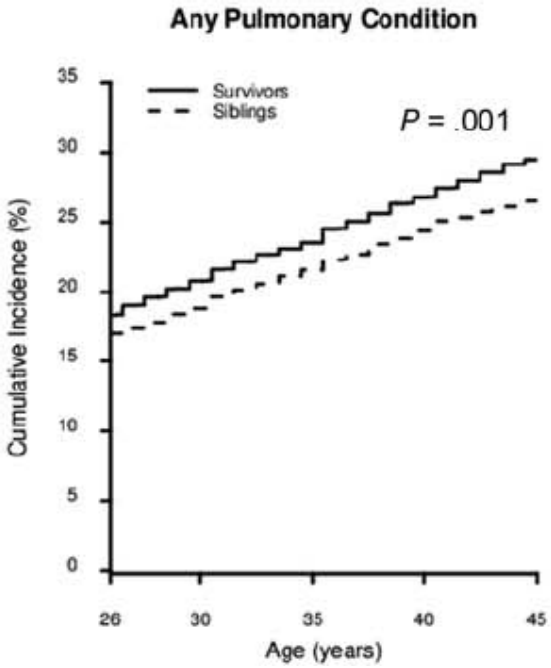


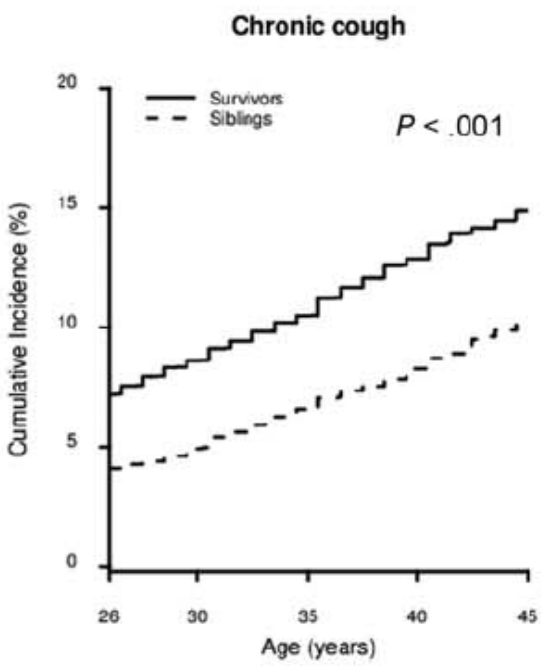


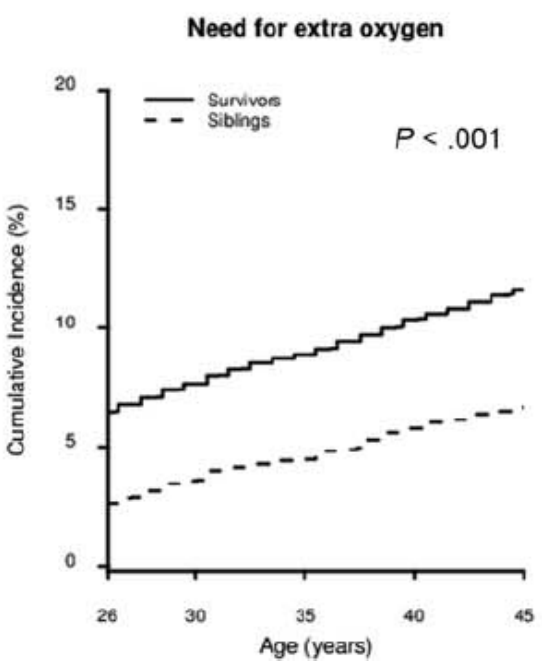
Risk and Impact of Pulmonary Complications in Survivors of Childhood Cancer: A Report From the Childhood Cancer Survivor Study

Cancer December 1, 2016

Andrew C. Dietz, MD, MSCR[1]; Yan Chen, MMath[2]; Yutaka Yasui, PhD[3]; Kirsten K. Ness, PhD[3]; James S. Hagood, MD[4]; Eric J. Chow, MD, MPH[5]; Marilyn Stovall, PhD[6]; Joseph P. Neglia, MD, MPH[7]; Kevin C. Oeffinger, MD[8]; Ann C. Mertens, PhD[9]; Leslie L. Robison, PhD[3]; Gregory T. Armstrong, MD, MSCE[3]; and Daniel A. Mulrooney, MD, MS[3]

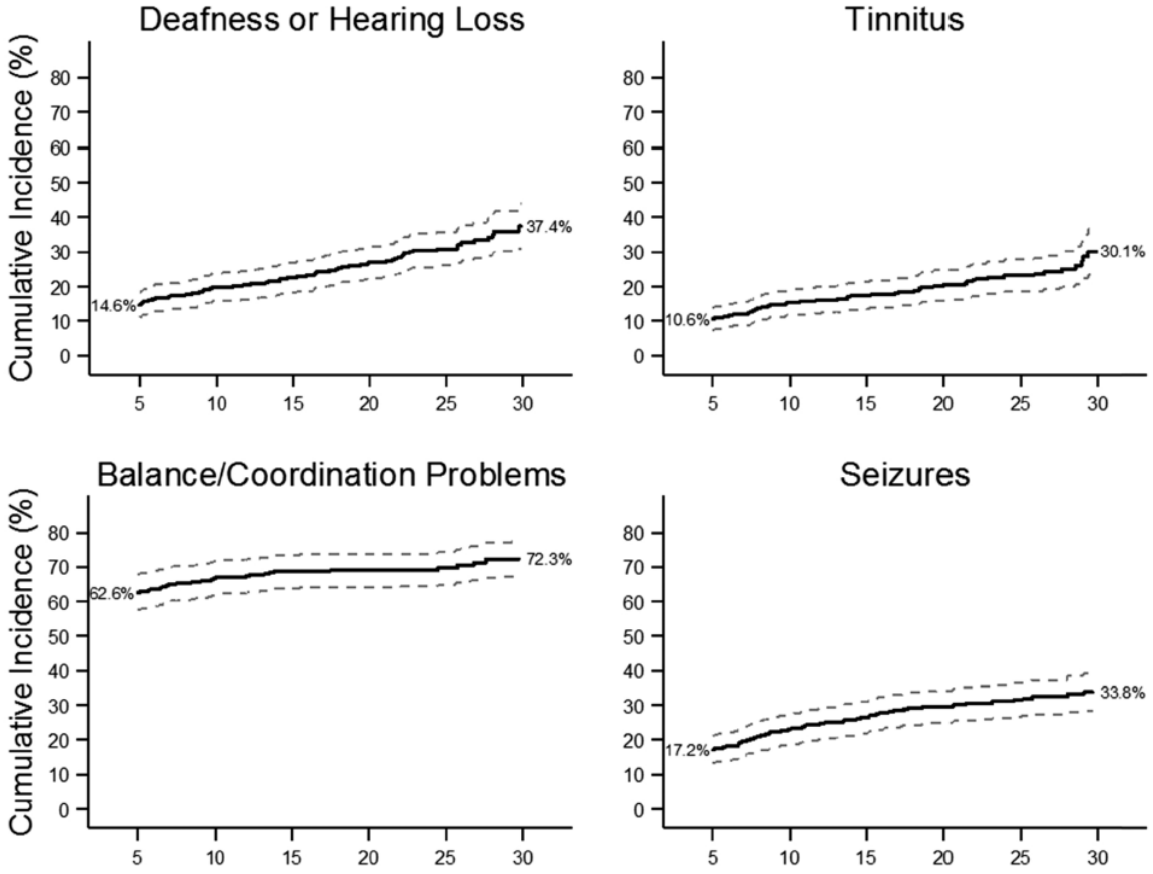






Long-term neurologic health and psychosocial function of adult survivors of childhood medulloblastoma/PNET: a report from the Childhood Cancer Survivor Study

Allison A. King, Kristy Seidel, Chongzhi Di, Wendy M. Leisenring, Stephanie Mabry Perkins, Kevin R. Krull, Charles A. Sklar, Daniel M. Green, Gregory T. Armstrong, Lonnie K. Zeltzer, Elizabeth Wells, Marilyn Stovall, Nicole J. Ullrich, Kevin C. Oeffinger, Leslie L. Robison, and Roger J. Packer



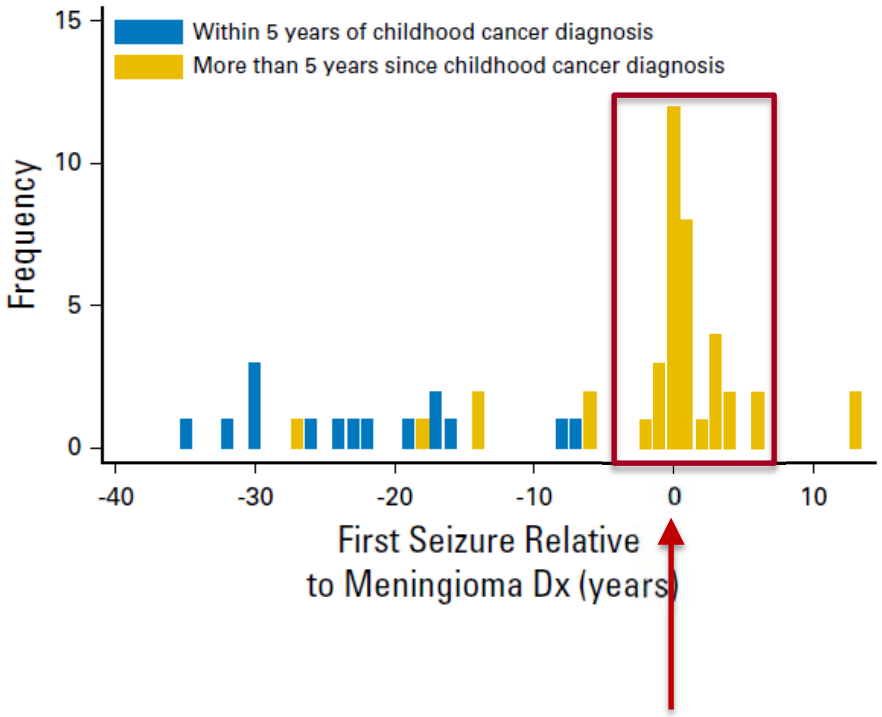
VOLUME 35 · NUMBER 14 · MAY 10, 2017

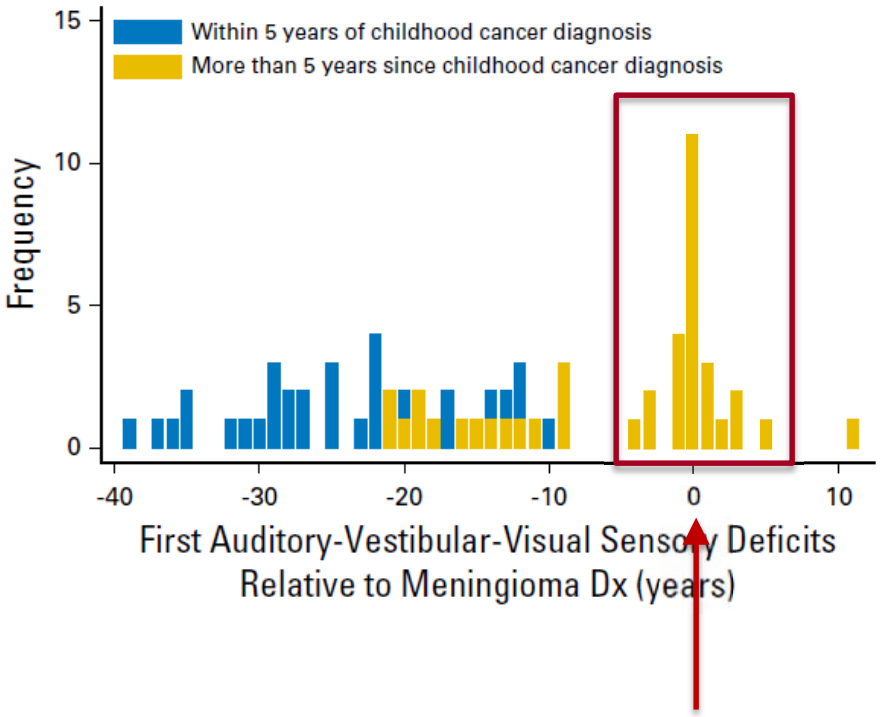
JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Morbidity and Mortality Associated With Meningioma After Cranial Radiotherapy: A Report From the Childhood Cancer Survivor Study

Daniel C. Bowers, Chaya S. Moskowitz, Joanne F. Chou, Claire M. Mazewski, Joseph P. Neglia, Gregory T. Armstrong, Wendy M. Leisenring, Leslie L. Robison, and Kevin C. Oeffinger

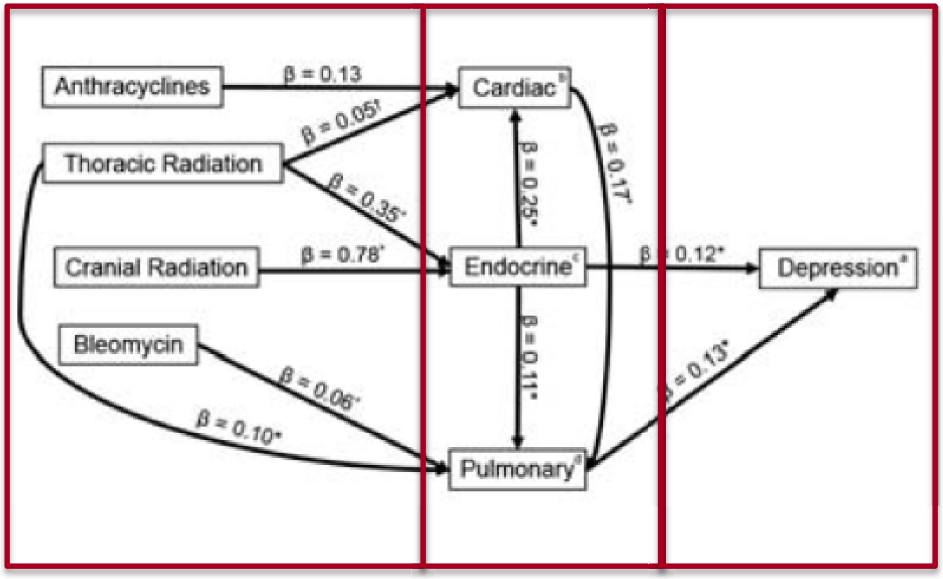


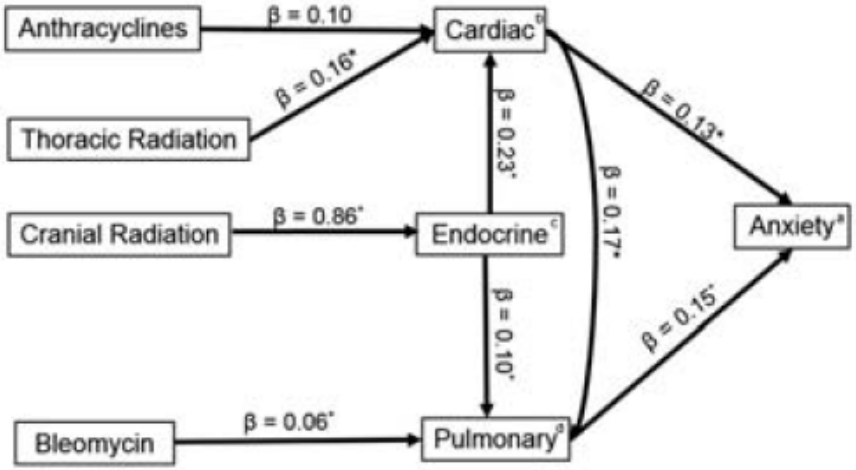


Impact of Chronic Disease on Emotional Distress in Adult Survivors of Childhood Cancer: A Report From the Childhood Cancer Survivor Study

Stefanie C. Vuotto, PhD[1]; Kevin R. Krull, PhD[1]; Chenghong Li, PhD[2]; Kevin C. Oeffinger, MD[3]; Daniel M. Green, MD[1]; Sunita K. Patel, PhD[4]; Deokumar Srivastava, PhD[2]; Marilyn Stovall, PhD[5]; Kirsten K. Ness, PhD[1]; Gregory T. Armstrong, MD, MSCE[1]; Leslie L. Robison, PhD[1]; and Tara M. Brinkman, PhD[1]

Cancer February 1, 2017





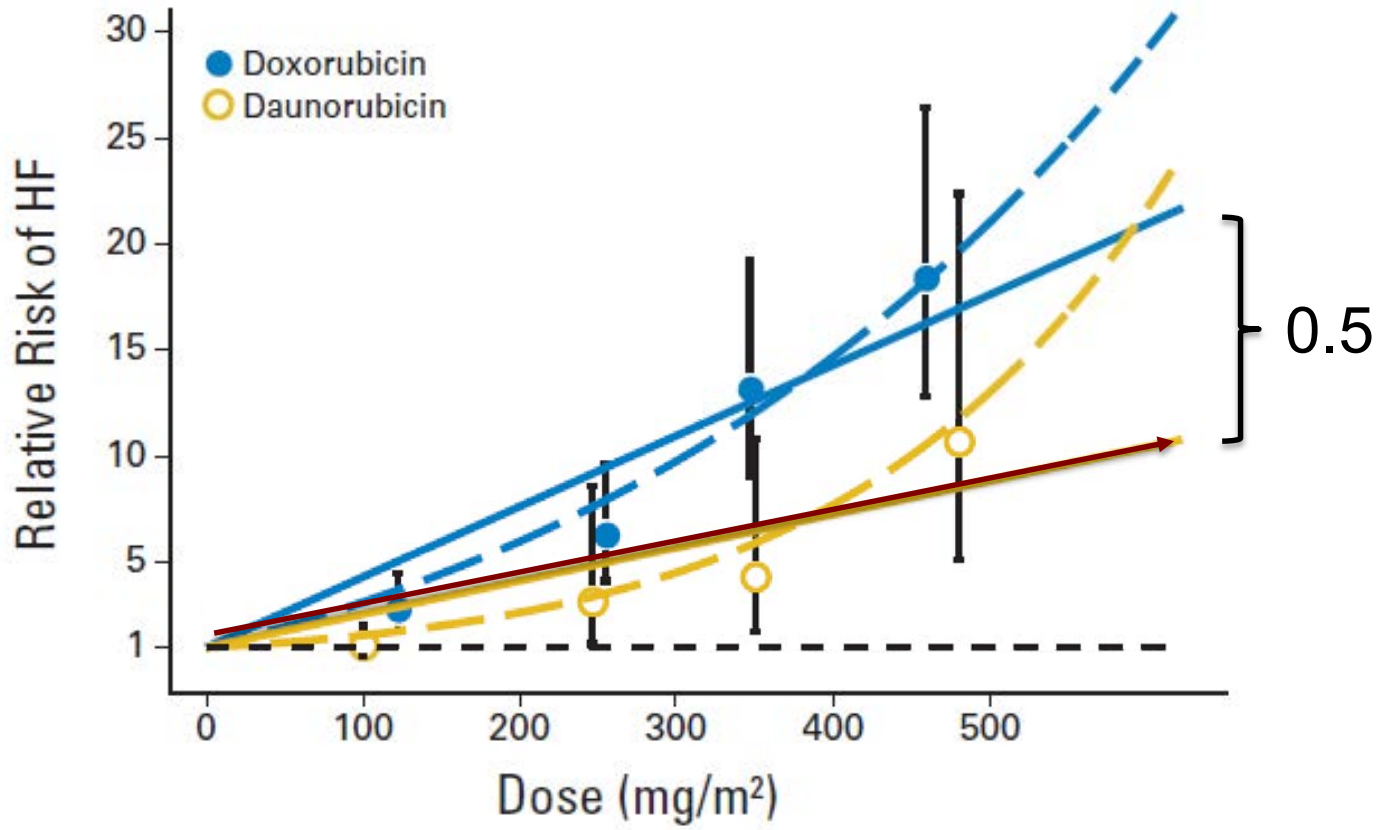
VOLUME 33 · NUMBER 32 · NOVEMBER 10 2015

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Equivalence Ratio for Daunorubicin to Doxorubicin in Relation to Late Heart Failure in Survivors of Childhood Cancer

Elizabeth A.M. Feijen, Wendy M. Leisenring, Kayla L. Stratton, Kirsten K. Ness, Helena J.H. van der Pal, Huib N. Caron, Gregory T. Armstrong, Daniel M. Green, Melissa M. Hudson, Kevin C. Oeffinger, Leslie L. Robison, Marilyn Stovall, Leontien C.M. Kremer, and Eric J. Chow



OXFORD

JNCI J Natl Cancer Inst (2016) 108(9): djw046

doi: 10.1093/jnci/djw046
First published online April 21, 2016
Brief Communication

BRIEF COMMUNICATION

Chronic Conditions and Utility-Based Health-Related Quality of Life in Adult Childhood Cancer Survivors

Jennifer M. Yeh, Janel Hanmer, Zachary J. Ward, Wendy M. Leisenring, Gregory T. Armstrong, Melissa M. Hudson, Marilyn Stovall, Leslie L. Robison, Kevin C. Oeffinger, Lisa Diller

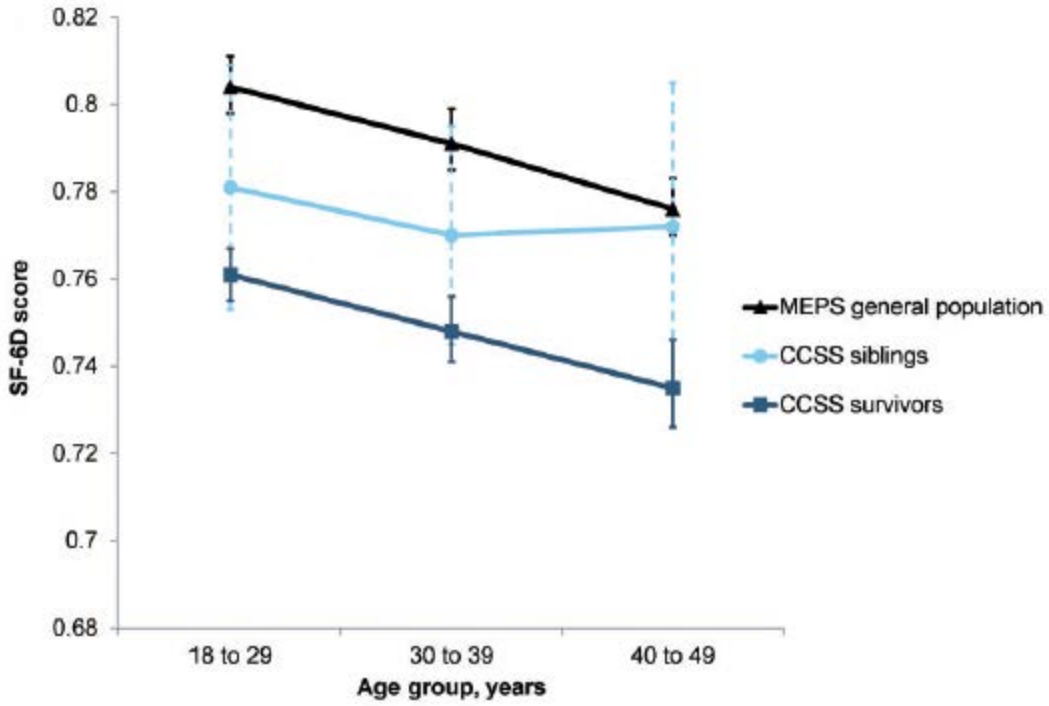


Table 2. SF-6D utility scores for CCSS survivors by number and severity of chronic conditions*

Characteristic	No.	SF-6D Mean (95% CI)	Compared with no conditions P†	Compared with no conditions Met MID‡ criteria?
No conditions	1475	0.809 (0.804 to 0.815)	Reference	Reference
No. of conditions, grades 1-4				
1	1538	0.795 (0.789 to 0.800)	<.001	No
2	1113	0.772 (0.765 to 0.779)	<.001	Yes
≥3	2979	0.735 (0.729 to 0.739)	<.001	Yes
No. of conditions, grades 3-4 only§				
1	286	0.785 (0.771 to 0.798)	<.001	No
2	518	0.725 (0.713 to 0.736)	<.001	Yes
≥3	198	0.695 (0.677 to 0.713)	<.001	Yes
Maximum severity of condition(s)‖				
Grade 1	1532	0.777 (0.771 to 0.782)	<.001	No
Grade 2	1623	0.772 (0.766 to 0.778)	<.001	Yes
Grade 3	1604	0.746 (0.739 to 0.752)	<.001	Yes
Grade 4	871	0.727 (0.718 to 0.736)	<.001	Yes

What are some of our current ongoing studies and concepts?

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Career Development Award

- Sogol (Goli) Mostoufi-Moab (2013)

  Overall risk of Chronic Endocrine Disorders in Adult Survivors of Childhood Cancer
- Danielle Novetsky Friedman (2015)

  Impact of radiation dose to the pancreas on subsequent risk of diabetes mellitus
- Adam Esbenshade (2015)

  Using the Cumulative Illness Rating Scale to characterize the burden of chronic conditions
- Miranda Fidler (2015)

  Comparison of risks for mortality and subsequent cancers in the CCSS and the BCCSS

EQUAL

Emily Tonorezos
R01CA187397

- 24-month RCT comparing the effect of a web- and telephone-based weight loss intervention (led by *Healthways at Hopkins*) to general information about weight loss and healthy living (control).
- Calculate the effect of the diet and physical activity intervention, compared to self- directed weight loss, on three key metabolic biomarkers:
  - *a. Fasting insulin*
  - *b. Leptin:adiponectin ratio*
  - *c. Small, dense LDL*

Communicating
Health
Information &
Improving Coordination with
Primary Care

Eric Chow
R01CA204378

1. Determine the prevalence of underdiagnosis and undertreatment of hypertension, dyslipidemia, and diabetes in CCSS participants at high risk of future heart disease.

2. Among those underdiagnosed / undertreated, conduct an RCT to test the effect of a remotely delivered SCP & self-management intervention on rates of undertreatment after 1-year.

3. Determine barriers among survivors & PCPs towards survivorship care that contribute to undertreatment of common modifiable CV risk factors.

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ACS Research Scholar Grant
Jennifer Yeh

Improving Cancer Screening Guidelines for Survivors of Childhood Cancer

Specific Aims

1. Develop a Childhood Cancer Survivorship Simulation Model
2. Project the lifelong magnitude and heterogeneity in disease burden associated with late-effects among childhood cancer survivors
3. Assess the comparative effectiveness of secondary cancer screening strategies to improve long-term outcomes among at-risk survivors

Contemporary Risk-Adapted Therapy for Hodgkin Lymphoma: What are the Trade-Offs?

1. Estimate all-cause and cause-specific mortality for 5+ year survivors of Hodgkin lymphoma diagnosed 1970-1999 and compare by era of therapy and by major treatment groupings.
2. Determine the incidence of chronic health conditions and compare by era of therapy and by major treatment groupings.
3. Estimate risks of chronic health conditions (any condition, grade 3-5 conditions, multiple grade 3-5 conditions) with contemporary HL therapy - use data from CCSS to create groups with similar exposures to two contemporary Children's Oncology Group (COG) protocols – AHOD 0031 and AHOD 0431.
4. Merge data with Dutch HL cohort to look more closely at treatment exposures and trade-offs (combined data almost 5,500 HL survivors).

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Oral Presentations - 2017

- **Gibson TM**, Mostoufi-Moab S, Stratton K, Barnea D, Chow EJ, Donaldson SS, Howell R, Hudson MM, Leisenring WM, Mahajan A, Nathan PC, Ness KK, Sklar CA, Tonorezos ES, Weldon CB, Wells EM, Yasui Y, Armstrong GT, Robison LL, Oeffinger KC. Temporal trends in chronic disease among survivors of childhood cancer diagnosed across three decades: a report from the Childhood Cancer Survivor Study (CCSS). American Society of Clinical Oncology; 15th International Conference on Long-Term Complications of Treatment of Children and Adolescents for Cancer.
- **Weil B**, Madenci A, Liu Q, Gibson T, Yasui Y, Neglia J, Leisenring W, Howell R, Tonorezos E, Friedman D, Tinkle C, Diller L, Armstrong GT, Oeffinger K, Weldon C. Infection related late mortality in survivors of childhood cancer with asplenia or radiation-induced hyposplenism: a report from the Childhood Cancer Survivor Study. 15th International Conference on Long-Term Complications of Treatment of Children and Adolescents for Cancer.

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Oral Presentations - 2017

- **Bates JE**, Liu Q, Yasui Y, Howell RM, Mulrooney DA, Dhakal S, Leisenring WM, Indelicato DJ, Gibson TM, Armstrong GT, Oeffinger KC, Constine LS. Age-associated vulnerability to treatment-related late cardiotoxicity: a report from the Childhood Cancer Survivor Study (CCSS). American Society of Clinical Oncology.
- **Bates JE**, Howell RM, Liu Q, Yasui Y, Mulrooney DA, Dhakal S, Leisenring WM, Indelicato DJ, Gibson TM, Armstrong GT, Oeffinger KC, Constine LS. Volumetric dose-effect analysis of late cardiotoxicity: a report from the Childhood Cancer Survivor Study (CCSS). American Society for Radiation Oncology Annual Meeting
- **Salloum R**, Chen Y, Yasui Y, Packer R, Leisenring W, Wells E, King A, Howell R, Gibson TM, Krull KR, Robison LL, Oeffinger KC, Fouladi M, Armstrong GT. Temporal trends in late-onset morbidity and mortality after medulloblastoma diagnosed across three decades: a report from the Childhood Cancer Survivor Study. American Society of Clinical Oncology.

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Oral Presentations - 2017

- **Dietz AC**, Seidel K, Leisenring WM, Mulrooney DA, Tersak JM, Glick RD, Burnweit CA, Green DM, Diller L, Oeffinger KC, Smith SA, Howell RM, Stovall M, Robison LL, Armstrong GT, Termuhlen AM. Solid organ transplant after treatment for childhood cancer: a report from the Childhood Cancer Survivor Study. 15th International Conference on Long-Term Complications of Treatment of Children and Adolescents for Cancer.
- **Tonorezos ES**, Meacham L, Chou JF, Moskowitz CS, Leisenring WM, Freidman D, Sklar CA, Dilley KJ, Hudson M, Mertens A, Armstrong GT, Robison LL, Oeffinger KC. Risk of increased mortality in underweight survivors: a report from the Childhood Cancer Survivor Study. 15th International Conference on Long-Term Complications of Treatment of Children and Adolescents for Cancer.

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Oral Presentations - 2017

- **Brooke RJ**, Chemaitilly W, Wilson CL, Krasin MJ, Li Z, Im C, Morton LM, Wu G, Wang Z, Chen W, Howell RM, Armstrong GT, Bhatia S, Chanock SJ, Zhang J, Green DM, Sklar CA, Hudson MM, Robison LL, Yasui Y. A high-risk genetic profile for premature menopause (PM) in childhood cancer survivors (CCS) exposed to gonadotoxic therapy: a report from the St. Jude Lifetime Cohort (SJLIFE) and Childhood Cancer Survivor Study (CCSS). American Society of Clinical Oncology; 15th International Conference on Long-Term Complications of Treatment of Children and Adolescents for Cancer.

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Poster Presentations - 2017

- **Madenci AL**, Weil BR, Liu Q, Gibson TM, Yasui Y, Leisenring WM, Howell RM, Tinkle C, Nekhlyudov L, Diller L, Armstrong GT, Oeffinger KC, Weldon CB. Long-term incidence of venous thromboembolism (VTE) among survivors of childhood cancer: a report from the Childhood Cancer Survivor Study. American Society of Clinical Oncology; 15th International Conference on Long-Term Complications of Treatment of Children and Adolescents for Cancer.
- **Fejien EA**, Leisenring WM, Stratton KL, Ness KK, Van der Pal HJH, van Dalen EC, Armstrong GT, Aune GJ, Green DM, Hudson MM, Loonen J, Oeffinger KC, Robison LL, Yasui Y, Kremer LC, Chow EJ. Equivalence ratios for late cardiomyopathy after doxorubicin and other anthracyclines/anthraquinones. 15th International Conference on Long-Term Complications of Treatment of Children and Adolescents for Cancer.

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Poster Presentations - 2017

- **Lupo PJ**, Brown AL, Kamdar KY, Belmont JW, Armstrong GT, Leisenring WM, Oeffinger KC, Okcu F, Robison LL, Scheurer ME, Yasui Y, Bhatia S. DNA methylation and obesity in survivors of pediatric Acute Lymphoblastic Leukemia (ALL): a report from the Childhood Cancer Survivor Study (CCSS). 15th International Conference on Long-Term Complications of Treatment of Children and Adolescents for Cancer.
- **Mueller S**, Chen Y, Yasui Y, Fullerton HJ, Howell R, Oeffinger K, Robison LL, Armstrong GT, Krull KR. Impact of stroke and stroke recurrence on late mortality as well as psychological and socioeconomic outcomes in childhood cancer survivors. Pediatric Neuro-Oncology Basic and Translational Research Conference.

List of current Applications of Intent and Concept Proposals - pages 45-51 of the CCSS booklet

Looking to the Future

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Exploitation of Expansion Cohort (1970-99)

- Increased use of Cisplatin (739 original cohort + 1,353 in expansion = 2,092 overall)
  - Hearing, renal function, cardiac disease
- Increased use of Ifosfamide (190 original cohort + 978 in expansion = 1,168 overall)
  - Renal function
- Almost 12,000 survivors exposed to anthracyclines overall
  - Heart rate variability, autonomic dysfunction

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mHealth and Chronic Disease

- Home measurement of:
  - Blood pressure
  - Heart rate, HR variability, EKH
  - Glucose, A1C, lipids
  - Pulmonary function tests
- Subcontract and combine with Examination Management Services, Inc (EMSI), used in pilot home sample, EQUAL, and CHIIP
  - Urine testing (electrolytes, creatinine, etc)
  - Other fasting labs
  - Height and weight

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GWAS and Chronic Disease

Key chronic conditions with potential interaction between genetic factors, lifestyle behaviors and treatment exposures:

- Key adverse outcomes
- Hearing
- Valvular heart disease (valve replacement)
- Pulmonary fibrosis
- Diabetes

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Observational Studies Leading to Interventions

R21 or medium-sized grants to support case-control study

- Stroke – radiation, hypertension, genetic factors
- Coronary artery disease with volumetric radiation exposure by arterial distribution to model for contemporary radiation therapy

Leading to R01-supported intervention trials

- Statin therapy (risk communication)
- Hypertension management (via mHealth approach)

Thanks
(to the many, many investigators working on chronic disease projects)

Questions?

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