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Second Tumors Working Group

Williamsburg, VA
June 2012

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Second Tumors Working Group
Group Membership

- **Joseph Neglia – Minnesota (chair)**
- **Sue Hammond – Nationwide Children's**
- **Greg Armstrong – St. Jude**
- **Smita Bhatia – City of Hope**
- **Tara Henderson – U Chicago**
- **Marilyn Stovall – MD Anderson**
- **Peter Inskip – NCI**

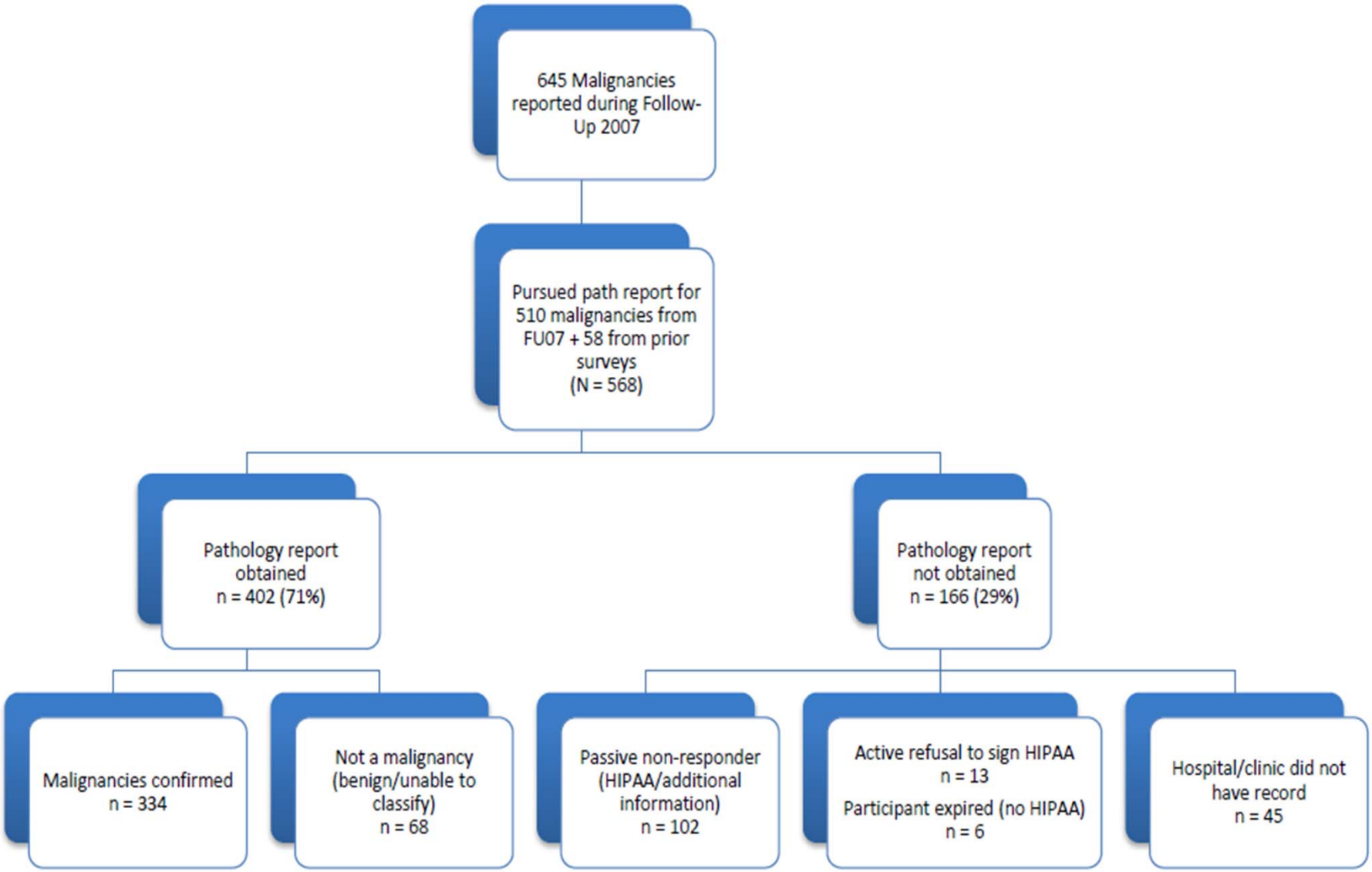
- **Aaron McDonald – St. Jude**

Distribution of Biologic Material Available for Subsequent Neoplasm Cases

SMN	Total case reported	Total with path reports	# with host tissue			Host tissue (any kind) and MRAF data	Total with MRAF data	Total with SMN tissue	Number of Cases with Tissue Type			
			Buccal cells	Oragene	Blood				H&E Slides	Unstained Slides	Scrolls	Blocks
Breast	222	206	116	87	107	140	211	63	34	49	38	16
Meningioma*	210	186	126	102	103	142	191	39	10	29	13	13
Other CNS	78	70	23	17	18	27	74	21	8	19	5	2
Thyroid	157	144	81	63	76	106	150	32	18	28	17	7
Sarcoma	87	79	33	21	23	39	78	11	6	10	7	2
Leukemia	51	35	14	8	9	15	44	7	3	6	3	0
Bone	54	46	14	4	11	16	45	7	3	5	2	1
Melanoma	55	39	24	18	23	31	53	9	4	9	3	0
Lymphoma	45	41	18	16	18	25	42	8	2	6	4	1
Renal Cell	26	26	15	14	12	17	24	0	0	0	0	0
Other Carcinoma	114	109	48	31	38	56	112	31	18	26	14	7
NMSC*	1,295	1,147	832	658	311	906	1,219	2	2	1	1	0
All Other	64	41	18	16	13	21	51	9	5	9	4	1
TOTALS	*2,458*	*2,169*	*1,362*	*1,055*	*762*	*1,541*	*2,294*	*239*	*113*	*197*	*111*	*50*

As of 1/2012

New Neoplasms from 2007 Follow Up



Report Date 5/2012

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Second Tumors Working Group
Recent Publications

- Nathan et al: Screening and surveillance for second malignant neoplasms in adult survivors of childhood cancer: A Report from the Childhood Cancer Survivor Study Ann Int Med 2010
- Best et al: Variants at 6q21 implicated PRDM1in the etiology of therapy-induced second malignancies after Hodgkin lymphoma. Nature Medicine 2011
- Nottage et al: Long-term Risk for Secondary Leukemia after Treatment for Childhood Cancer: A Report from the Childhood Cancer Survivor Study. Blood 2011

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Second Tumors Working Group
Recent Publications

- Armstrong et al: Occurrence of multiple subsequent neoplasms in long-term survivors of childhood cancer: A Report from the Childhood Cancer Survivor Study. J Clin Oncol 2011
- Viega et al: Chemotherapy and Thyroid Cancer Risk: A Report from the Childhood Cancer Survivor Study. Ca Epidemiol Biomarkers Prev 2011
- Henderson et al: Secondary Gastrointestinal Malignancies in Childhood Cancer Survivors: A Childhood Cancer Survivor Study Report. Ann Int Med 2012
- Inskip et al: Risk of Salivary Gland Cancer Following Childhood Cancer: A Report From the Childhood Cancer Survivor Study International Journal of Radiation Oncology Biology Physics

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Second Tumors Working Group
Activities

December 2010 Meeting in Memphis

- Internal audit of selected cases
- Semantics of Second Neoplasm coding
- Processes for adjudication of SMNs without path reports
- ICDO 3 transition
- Global database audit
- Creation of SMN SOP

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Second Tumors Working Group
Active AOIs to Concept

Date Received	Title	Author/ Institution	Secondary Working Group(s)	Date Investigator Notified	Concept to Publication Committee
10.28.10	Primary Tumor Recurrence and SMN After Pregnancy	Rokitka/Roswell Park		11.10.10	Pending
11.9.10	SMN After Diabetes Mellitus	Chang/UCSF	Chronic Disease	11.23.10	Pending
11.11.10	Breast Cancer Risk Factors	Inskip/NCI		12.7.10	Approved
11.16.10	Radiation Dose and Risk of Meningioma	Rajaraman/NCI	Epi/Biostats		
02.3.11	Renal Cell Carcinoma	Wilson/SJCRH		03.09.11	Approved
04.13.11	Gynecological Malignancies	Nathan/Sick Kids		05.03.11	Pending
04.20.11	Development and validation of an absolute risk prediction model for thyroid cancer in childhood cancer survivors	Ronckers/Netherlands	Epi/Biostats	05.03.11	Approved
04.27.11	Testicular Cancer Following Pediatric Cancer	Oeffinger/MSKCC	Chronic Disease	05.10.11	Pending

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Active AOIs to Concept

Date Received	Title	Author/ Institution	Secondary Working Group(s)	Date Investigator Notified	Concept to Publication Committee
05.03.11	Development of Radiobiologic Models of Second Cancer Risk for Childhood Cancer Patients Treated with Radiation Therapy	Hodgson/Princess Margaret	Epi/Biostats	06.02.11	Pending
05.09.11	Risk of Breast Cancer in Survivors Not Exposed to Chest Radiation	Henderson/Univ. of Chicago	Genetics	06.02.11	Approved
05.30.11	Breast Cancer Following Spinal Radiation	Moskowitz/MSKCC	Cancer Control Epi/Biostats	06.22.11	Approved
08.11.11	Subsequent neoplasms in adult survivors of childhood cancer in relation to weight and physical activity	George/NCI	Cancer Control Epi/Biostats Psychology	08.21.11	Pending
08.31.11	Lymphoma as SMN	Suh/University of Chicago		08.21.11	Pending
04.03.12	Late Second Neoplasms in Long-Term Survivors of Childhood Cancer	Turcotte/University of Minnesota	Epi/Biostats	04.26.12	Pending

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- **Second Neoplasm AOIs**
  - **Nine of Fourteen with Concepts Pending**
  - **Active follow up with holders of approved AOIs for timelines / barriers**

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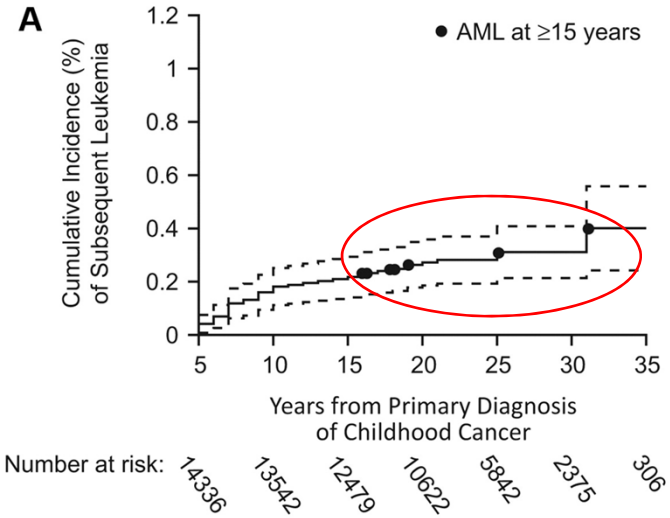
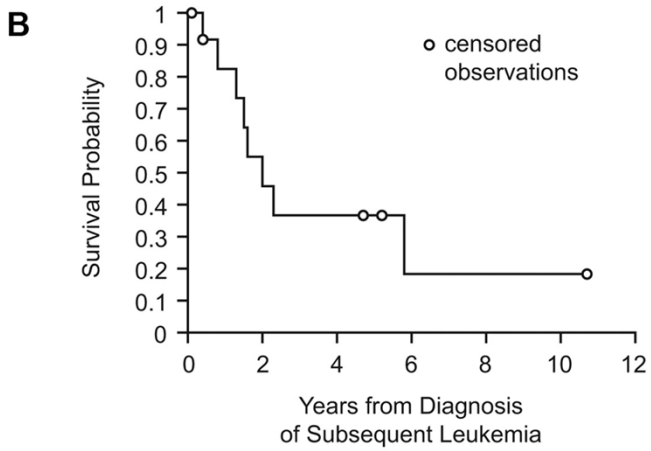
- **Selected Reports**
  - **Nottage; Late Occurring Leukemia**
  - **Armstrong; Multiple SMNs**
  - **Moskowitz; Breast Cancer Risk**

Long-Term Risk of Leukemia - Nottage et al (Blood 2011)

- Presumed that risk of secondary leukemia plateaus at 10 – 15 years form diagnosis
- Typically AML
  - Alkylator associated (changes on 5 or 7), five to 7 year latency
  - Epipodophyllotoxin associated (MLL), two to three year latency
- Recognized 13 pathologically confirmed cases of secondary leukemia after 15 years in the cohort

Long-term incidence and overall survival of subsequent leukemia.





- 13 path confirmed cases
- 7 cases of AML
  - 2 APL
  - 2 preceding MDS
  - No MLL changes
- 4 cases of ALL
  - 2 B lineage
  - 1 T lineage
  - 1 unidentified
- 1 T-cell large granular
- 1 Leukemia NOS

- Mean Latency 21.6 years
- Risk > 15 years from diagnosis
  - Leukemia: SIR 3.5 (1.9-6.0)
  - AML: SIR 5.3 (2.1-10.9)

- Too few cases to describe specific associations

blood
JOURNAL OF THE AMERICAN SOCIETY OF HEMATOLOGY

Nottage K et al. Blood 2011;1 17:6315-6318

Multiple Subsequent Neoplasms in the Childhood Cancer Survivor Study (CCSS) Cohort

Greg Armstrong, Wei Liu, Sue Hammond, Smita Bhatia, Joseph P. Neglia, Marilyn Stovall, Wendy Leisenring, Yutaka Yasui, Kumar Srivastava, Leslie Robison

Department of Epidemiology and Cancer Control

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Study Objective

Describe the cumulative incidence and risk factors for development of multiple subsequent neoplasms (SNs) among survivors of childhood cancer diagnosed 1970-1986.

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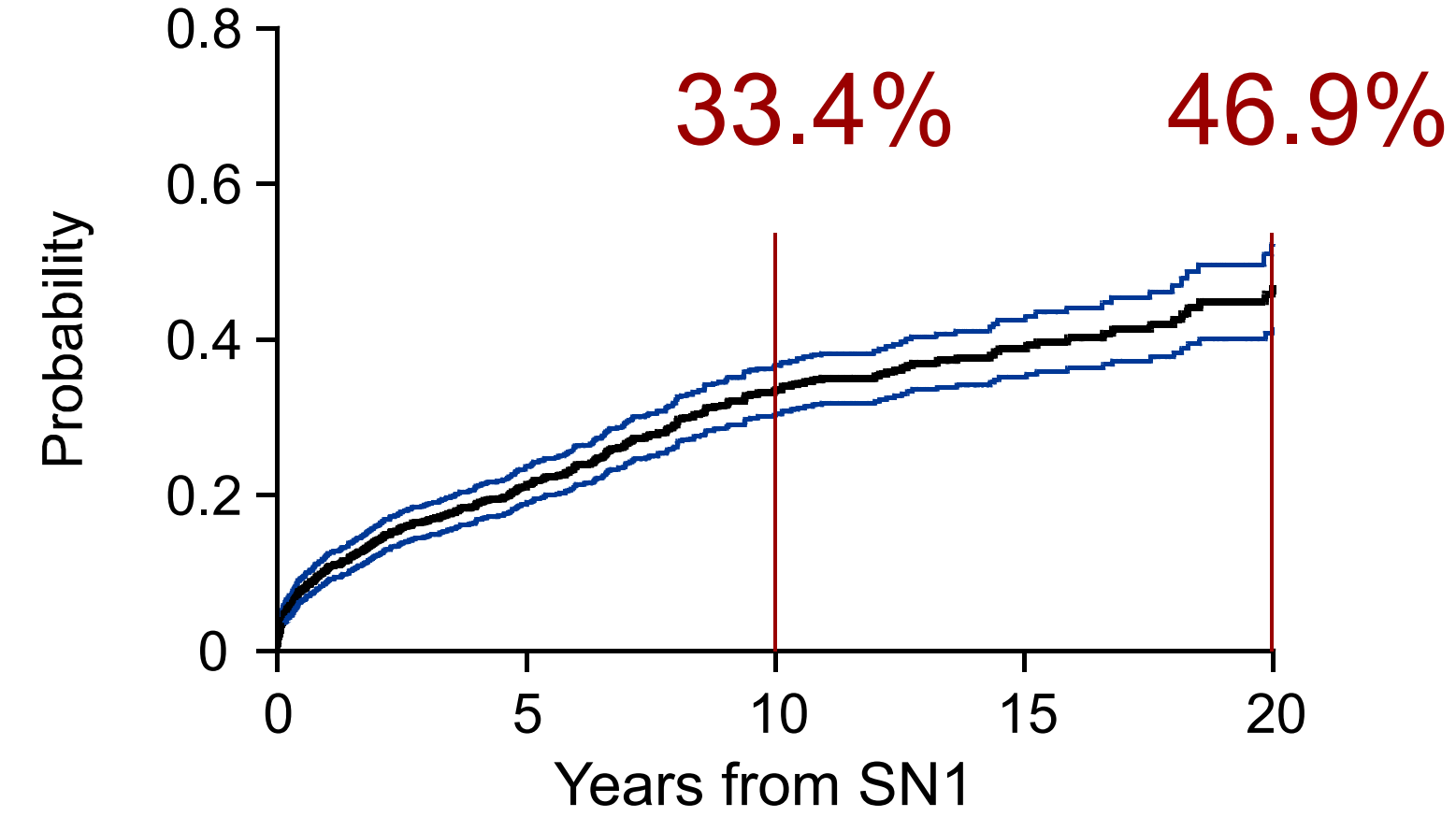
Cumulative Incidence: SN1 → SN2



At risk:	1377	574	219	76	21

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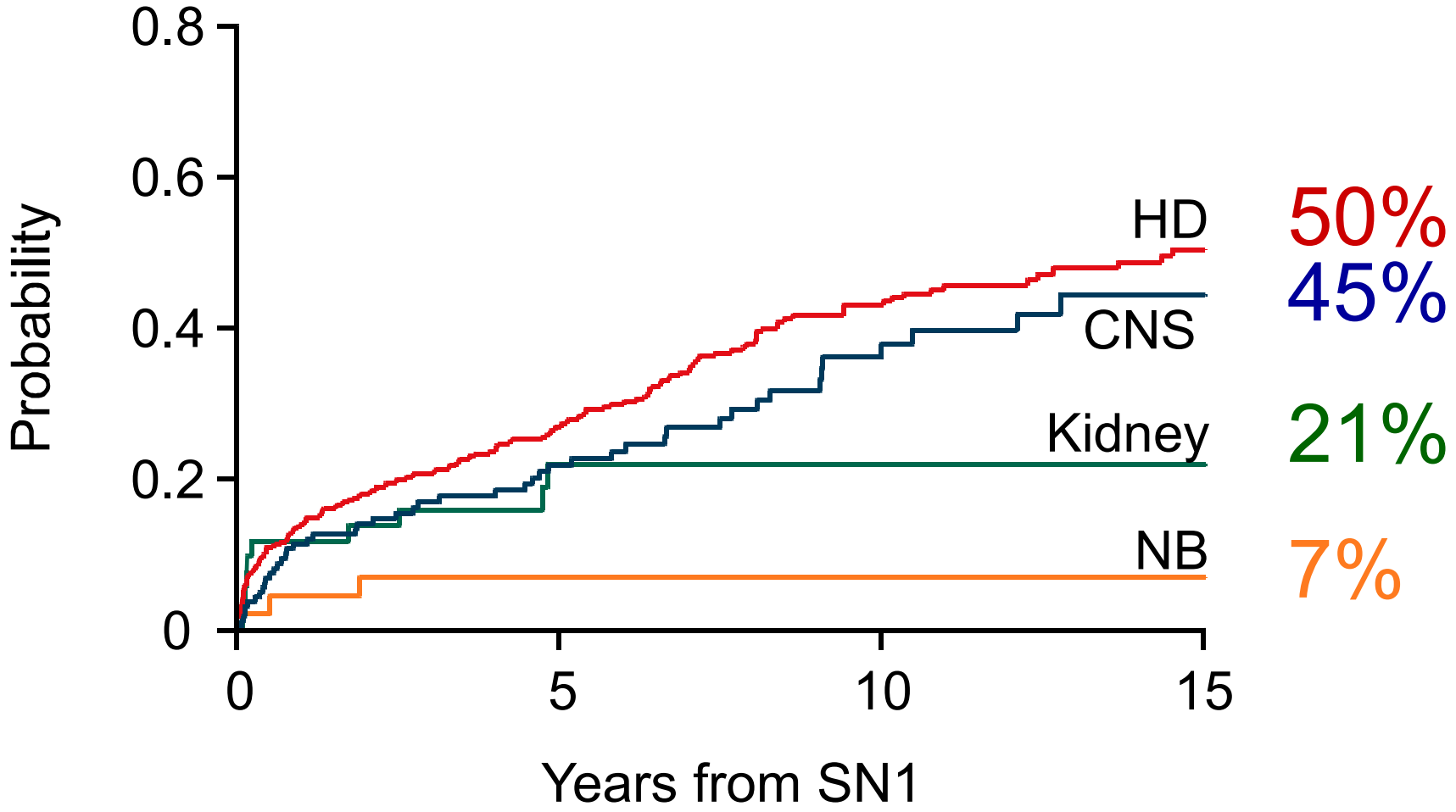
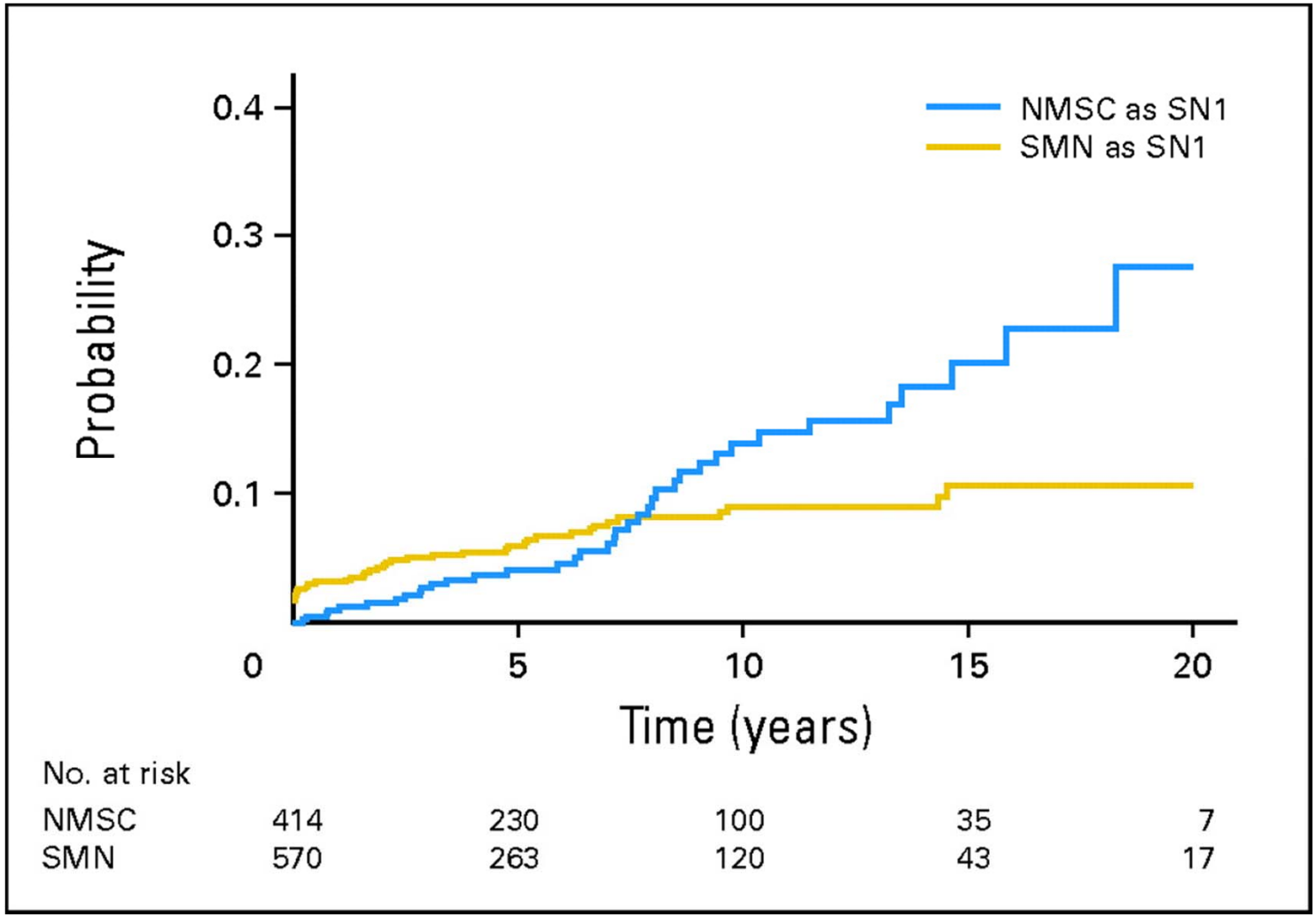
Cumulative Incidence: SN1 → SN2 By Primary Diagnosis



Cumulative incidence of a subsequent malignant neoplasm among radiotherapy-exposed patients after nonmelanoma skin cancer (NMSC) as first subsequent neoplasm (SN; blue line) and subsequent malignant neoplasm (SMN) as SN1 (gold line).



Armstrong G T et al. JCO 2011;29:3056-3064

JOURNAL OF CLINICAL ONCOLOGY

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Conclusions

Multiple SNs are common in long-term survivors and most common after Hodgkin lymphoma (50% at 15 years)

Increased risk associated with RT exposure, older age at SN1 and female sex

New insights into the risk of breast cancer in childhood cancer survivors treated with chest radiation:

A report from the Childhood Cancer Survivor Study and the Women's Environmental Cancer and Radiation Epidemiology Study

Chaya S. Moskowitz, Ph.D.
Associate Member
Department of Epidemiology and Biostatistics

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Purpose

- Based on substantially extended period of follow-up, estimate breast cancer risk in childhood cancer survivors treated with chest radiation
- Contrast risk with breast cancer risk in other known high risk population
  - Carriers of a *BRCA1* or *BRCA2* mutation
- Study subpopulations of childhood cancer survivors

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Methods

- Childhood cancer survivors (CCSS)
  - Cumulative incidence estimated non-parametrically
  - Competing risk of death
  - Standardized incidence ratios (SIRs) estimated using age-, sex-, and calendar-year-specific incidence rates from the general US population

- *BRCA1* and *BRCA2* mutation carriers
  - Cumulative incidence estimated using kin-cohort method
  - WECARE study (Women's Environmental Cancer and Radiation Epi)

- US population
  - From Surveillance, Epidemiology, and End Results (SEER) Program
  - Population incidence estimated using age-specific rates
  - Weighted to account for the calendar year in which members of the CCSS cohort were at risk of breast cancer

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Conclusions

- **Come to tomorrow's session**

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Second Tumors Working Group
Short Term Priorites

- **Short Term**
  - **Assure the quality of the CCSS SMN data set: Audit of all SMNs this summer**
  - **Reconcile the availability of biologic specimens across sites**
  - **ICDO 3 Migration**
  - **Outline the high priority analyses for the CCSS II cohort**

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Second Tumors Working Group
Short Term Priorites

- **Long Term**
  - **Assure the consistency of the CCSS SMN data set through rigorous use of SOPs**
  - **Build further links between biology and epidemiology**
  - **Link to GWAS Analysis**
  - **CCSS I and II comparisons**
  - **“Screen-able” Cancers**

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Second Tumors Working Group
Short Term Priorites

- **Long Term**
  - **Pooled analysis of secondary brain tumors**
    - **CCSS/European Childhood Cancer Survivors**
    - **Radiation for benign conditions**
    - **Pediatric CT scan recipients**
    - **Atomic bomb survivors**
  - **Influence of Lifestyle on site-specific SMN risk**