

Guidelines for Cancer Survivorship Care

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Director, Institute for Cancer Outcomes and Research

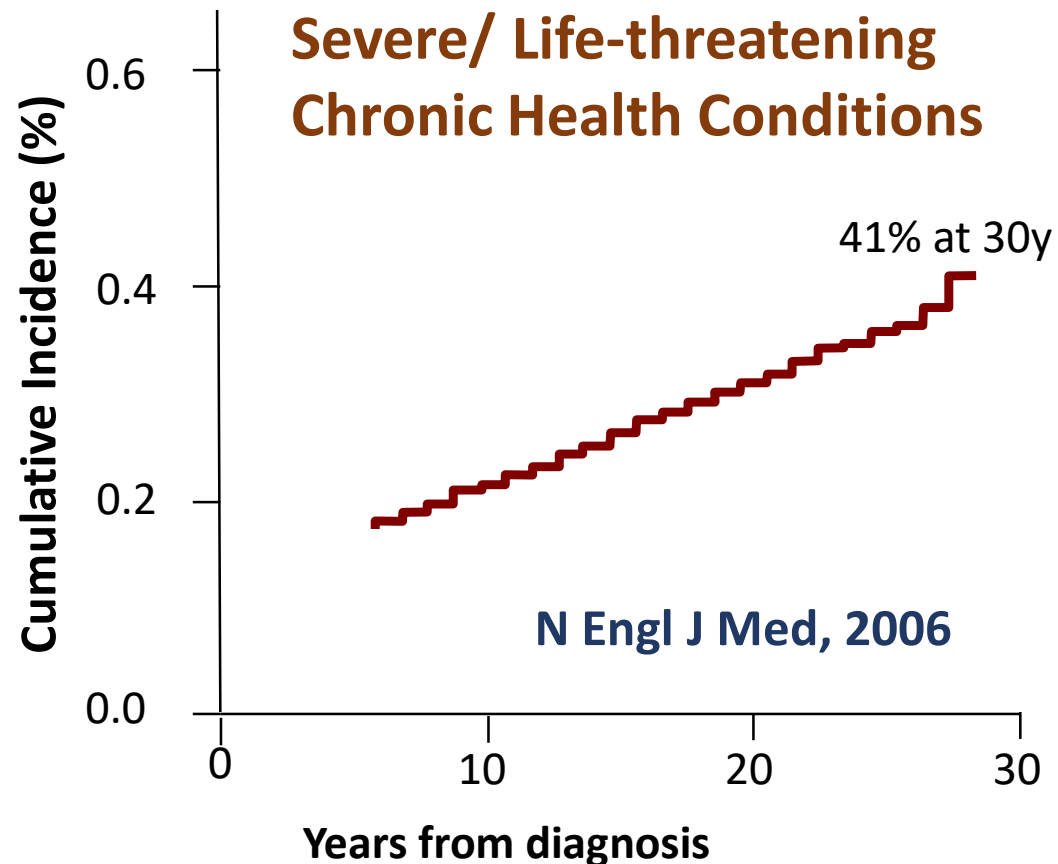
University of Alabama School of Medicine



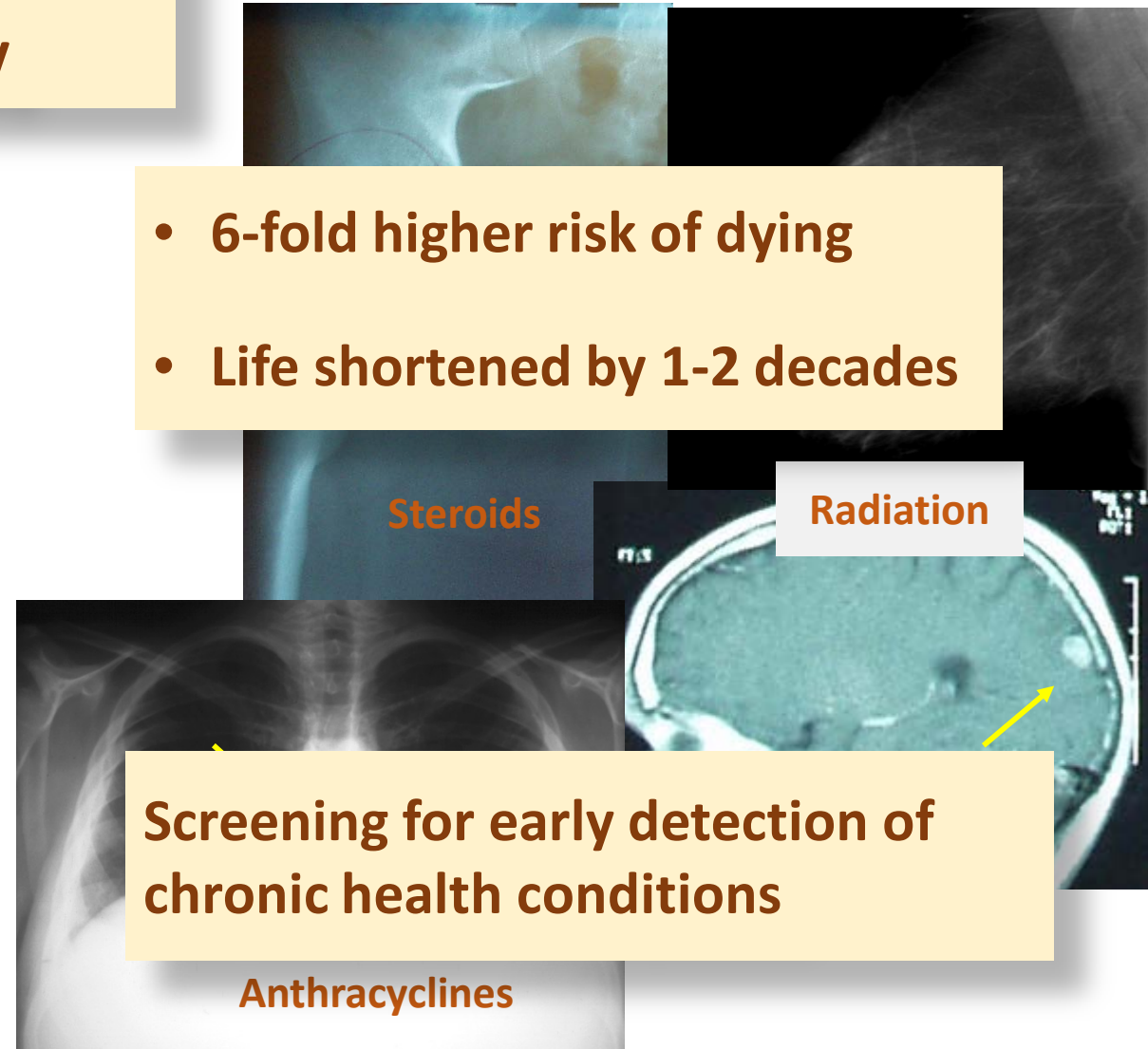
Institute for Cancer Outcomes and Survivorship

Why Long-Term Follow-Up?

Long-term survival is an expected outcome for most children diagnosed with cancer today



- 6-fold higher risk of dying
- Life shortened by 1-2 decades



Surveillance for long-term complications

Guiding principles

- Poor outcome
- Early detection associated with reduced morbidity

Determine if **screening**

- Magnitude of risk exceeds general population

Determine if **screening should differ** from that of general population

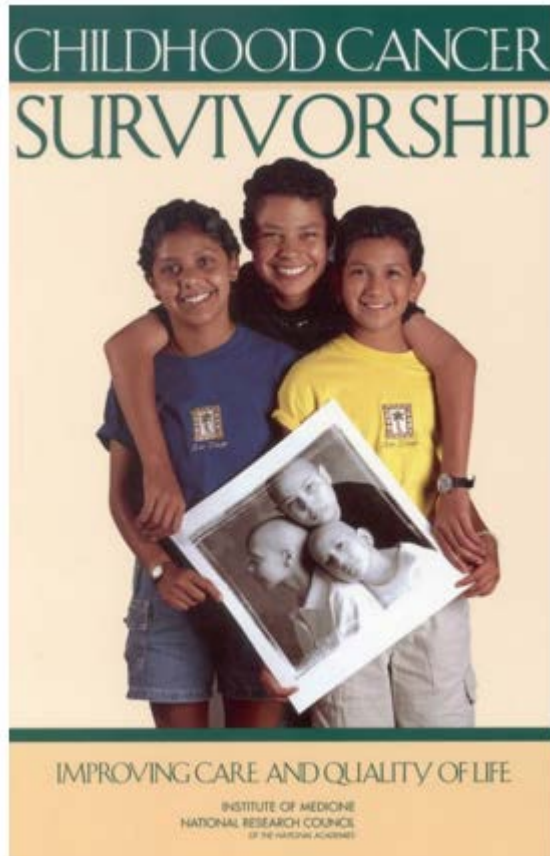
- Benefit of screening derives from **detection** of the complication **earlier** than would otherwise happen, with a **better prognosis** and chance for cure.
- Time c/w gen population (if applicable)

Determine **when** the screening should be initiated and **for how long**

- Sub-population at highest risk

Direct **high intensity of screening** for those “at risk”

The IOM Directive (January 2002)...



“Use the wealth of talent and experience within the Children’s Oncology Group to develop standardized health maintenance guidelines for childhood cancer survivors”

Melissa Hudson MD Wendy Landier PNP

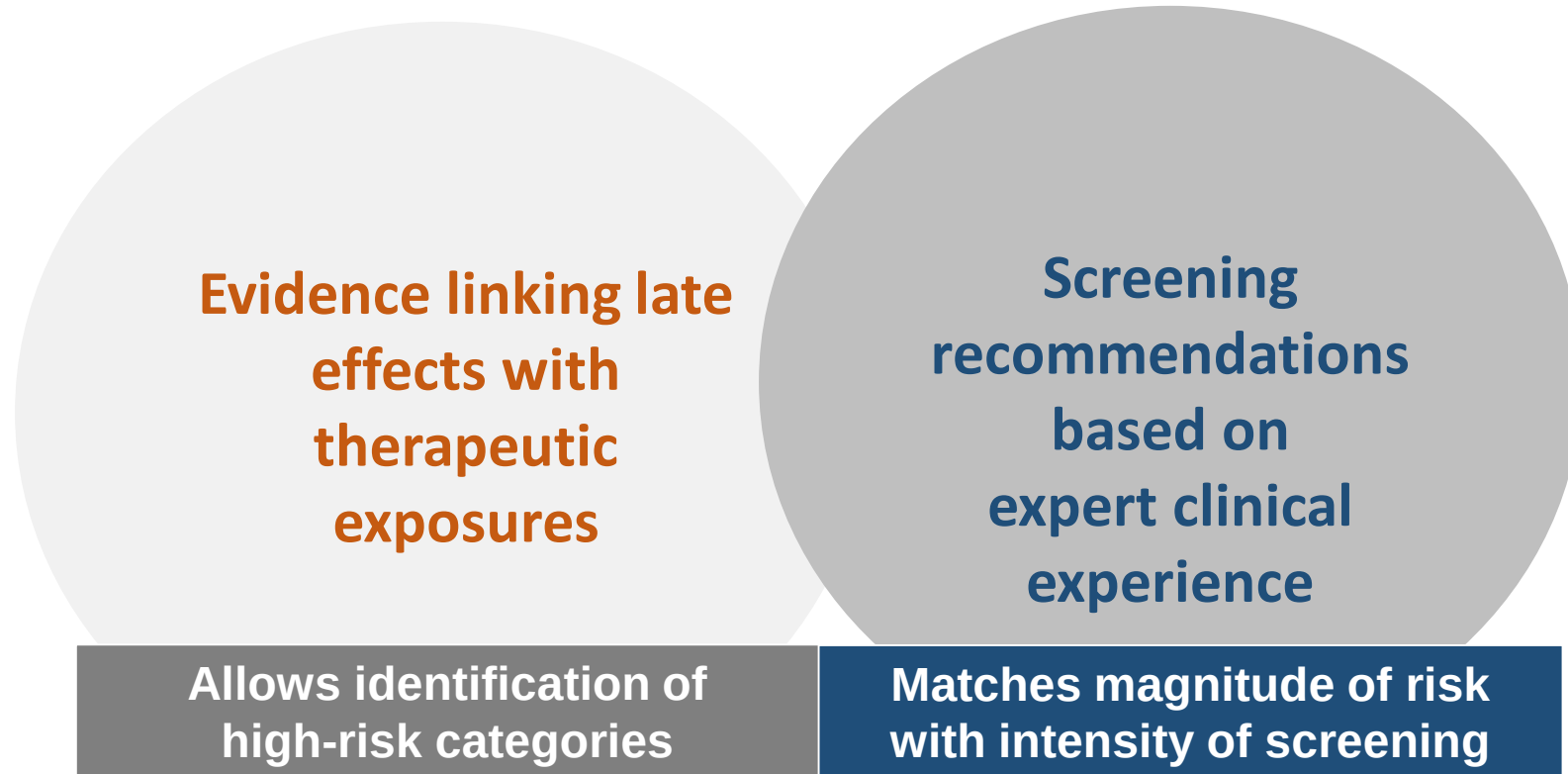
Debra Eshelman PNP Kathy Forte PNP

Teresa Sweeney PNP Allison Hester PNP

Joan Darling PhD

Smita Bhatia - Late Effects Committee Chair

Evidence-Based Guidelines: A Hybrid Model



Design Decisions

- Exposure-based
- Modular
- NOT designed to provide disease follow-up
- Grounded in clinical experience of experts

COG LTFU Guidelines

Guideline Development Process

- Use of iterative feedback loops
- Modified NCCN guideline process
- Integration of available literature with expert opinion

Review panel (N=62)

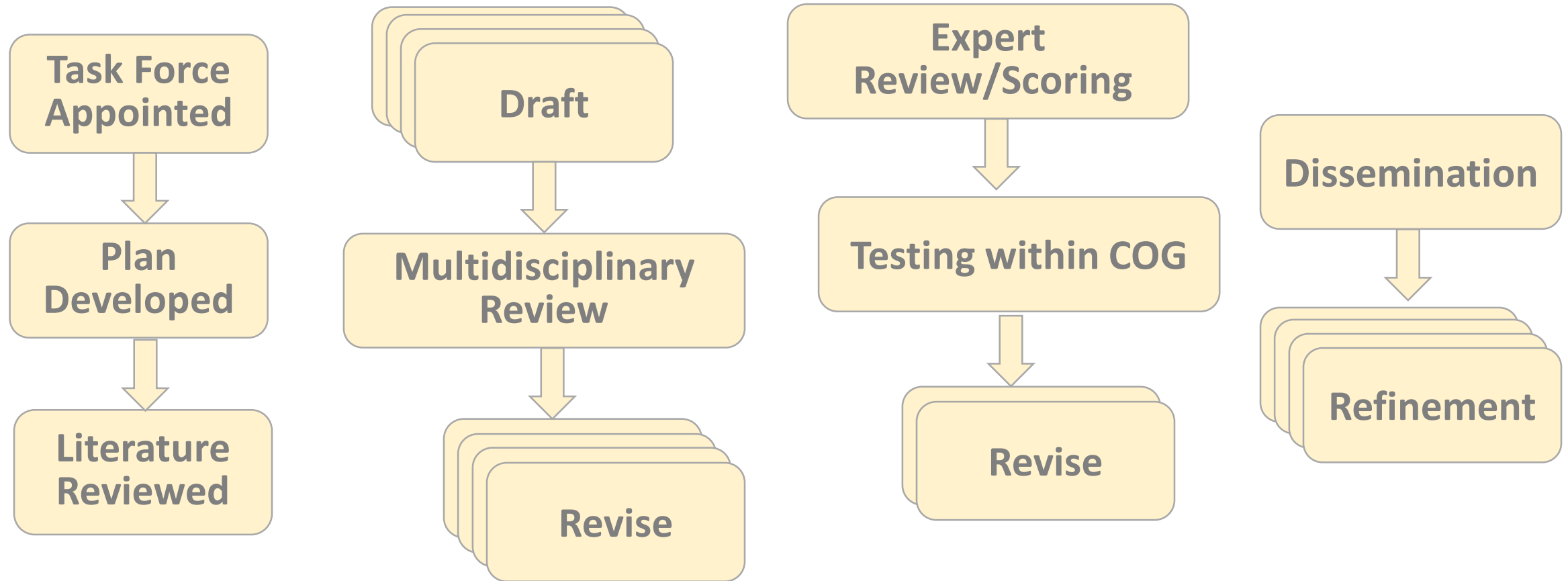
- Physicians (N=29)
- Patient advocates (N=15)
- Nurses (N=13)
- Other healthcare professionals (N=5)

Key Content Areas

- Therapeutic exposures
- Potential late effects
- Risk factors/highest risk
- Periodic evaluations
- Cancer screening
- References

Scoring

Guideline Development Process



Scoring: Modified NCCN “Categories of Consensus”

Initial Release (March 2003)



Late Effects Screening Guidelines

Version 1.0 - March 2003

- 112 Sections
- 118 Pages
- 6 Health Links



Childhood Cancer Survivor Long-Term Follow-Up Guidelines

Version 1.1 - September 2003

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SPECIAL ARTICLE

From the Division of Pediatrics, City of Hope Comprehensive Cancer Center, Duarte, Department of Pediatric Hematology-Oncology, Stanford University Medical Center, Stanford; Division of Hematology-Oncology, Department of Pediatrics, USC Keck School of Medicine and Children's Hospital Los Angeles, CA; Center for Cancer and Blood Disorders, Children's Medical Center; Department of Family Practice and Community Medicine, University of Texas Southwestern Medical School, Dallas, TX; Division of Pediatric Oncology, AFAC Cancer Center and Blood Disorders Service, Children's Healthcare of Atlanta, Atlanta, GA; Department of Hematology-Oncology, St. Jude Children's Research Hospital, Memphis, TN; Children's Oncology Group Patient Advocacy

Development of Risk-Based Guidelines for Pediatric Cancer Survivors: The Children's Oncology Group Long-Term Follow-Up Guidelines From the Children's Oncology Group Late Effects Committee and Nursing Discipline

Wendy Landier, Smita Bhatia, Debra A. Edelman, Katherine J. Forte, Teresa Sweeney, Allison L. Hester, Joan Darling, F. Daniel Armstrong, Julie Blatt, Louis S. Constine, Carolyn R. Freeman, Debra L. Friedman, Daniel M. Green, Neyssa Marina, Anna T. Meadows, Joseph P. Neglia, Kevin C. Offinger, Leslie L. Robison, Kathleen S. Ruccione, Charles A. Sklar, and Melissa M. Hudson

CureSearch

Children's Oncology Group

Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers

Version 1.2 - March 2004

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Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Couns Further Considerations
41	PLANT ALKALOIDS Vincristine Vincorline	Peripheral sensory or motor neuropathy Areflexia Weakness Foot drop Parosmia Info Link - Acute toxicities most commonly occur and usually improve or resolve prior to patients entering long-term follow-up. - Neuropathy can persist after treatment and is typically not life threatening.	Treatment Factors Combined with platinum chemotherapy, granulocyte or leukine Medical Conditions Anorexia Severe weight loss	Medical Conditions Cherol-More-Both disease	HISTORY Areflexia Weakness Foot drop Parosmia Dysarthria Yearly until 2 to 3 years after therapy, monitor yearly if symptoms persist PHYSICAL Neurologic exam Yearly until 2 to 3 years after therapy monitor yearly if symptoms persist	Health Links Peripheral Neuropathy Considerations for Further Testing Physical therapy referral for patients with neuropathy. Physical therapy and occupational assessment of hand function. Consider anticholinergic effective for neuropathic and antidiabetic. SYSTEM = PM SCORE = 1A

Periodic Evaluation	Health Concerns Further Consider
HISTORY Areflexia Weakness Foot drop Parosmia Osmophobia Yearly until 2 to 3 years after therapy, monitor yearly if symptoms persist.	Health Links Peripheral Neuropathy Considerations for Further Testing Physical therapy referral for patients with neuropathy. Physical therapy and social assessment of household function. Consider anticonvulsant/analgesics for neuropathic and amitriptyline.
PHYSICAL Neurologic exam Yearly until 2 to 3 years after therapy, monitor yearly if symptoms persist.	SYSTEM = PN SCORE = JA

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors
III Health	Chest (Thorax) Extended Mastectomy Mastectomy Mediastinal Whole lung Hepatic Inverted Y Left Flank/Hemithorax Left upper quadrant Parascapular Renal Right Flank/Hemithorax Right lower quadrant Spleen (partial) Spleen (entire) Whole abdomen Spine (thoracic) Spine (sacral) Subtotal Laminectomy	Coronary toxicity Congestive heart failure Cardiomyopathy Pericarditis Pericardial fibrosis Valvular disease Myocardial infarction Atherosclerosis Atherosclerotic heart disease	Host Factors Younger age at irradiation Family history of dyslipidemia Coronary artery disease Treatment Factors Radiation dose > 20 Gy to chest TBI Combined with radiochemotherapy (e.g., doxorubicin, dacarbazine) Combined with other cardiotoxic chemotherapy - Anthracyclines - Cyclophosphamide conditioning for SCT - Asparaginase Medical Conditions Hypertension Obesity Dyslipidemia Diabetes mellitus Congenital heart disease Fibrotic disease Health Behaviors	Host Factors Black/African descent Younger than age 5 years at treatment Treatment Factors Anteriorly-weighted radiation fields Lack of subcardinal shielding Dose > 20 Gy in patients who have received anthracyclines Doses > 40 Gy in patients who have not received anthracyclines Longer time since treatment

	Periodic Evaluation	Health Counseling/ Further Considerations
HISTORY	SORE DOE Orthopnea Chest pain Polydipsia If under 25 yrs: abdominal symptoms (nausea, vomiting) Noisy	Health Needs Heart Health Cardiovascular Risk Factors Diet and Physical Activity Dental Health
Info Link	• S1 surfaced intolerance is uncommon in patients younger than 25 years old. • Abdominal symptoms (nausea, stress) may be observed more frequently than discomfort, dyspnea, or chest pain to urge patients.	Counseling Counsel patients with prolonged QTc interval about use of medications that may further prolong the QTc interval (e.g., tricyclic anti-depressants, antiarrhythmics, macrolide antibiotics, neuroleptics). Counsel regarding maintaining appropriate weight, blood pressure and heart healthy diet. Counsel regarding endocarditis prophylaxis if at highest risk. Note: The AHA use lends their recommendation regarding endocarditis prophylaxis only to patients with cardiac conditions who are at the highest risk of adverse outcome, which includes, but is not limited to the following box categories: (1) prosthetic heart valves, (2) previous history of infective endocarditis, (3) certain patients with congenital heart disease, and (4) valvulopathy following cardiac transplantation. Survivors diagnosed with heart valve disorders should discuss the need for endocarditis prophylaxis with their cardiologist. See Wilson et al., (2007) for specifics. Counsel regarding appropriate exercise. Aerobic exercise is generally safe and should be encouraged to meet patients' interest in aerobic activities (e.g., heavy weight lifting, swimming) should generally be avoided. High repetition
PHYSICAL	Cardiac murmur S3, S4 Increased P2 sound Pericardial rales Rales Wheezes Extremity edema/distribution	

(cont)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
110	Humanized Anti-CD 19 Transplant (ACT)	Renal toxicity Gastrointestinal injury Tubular injury Hypertension	Treatment Factors Chronic cyclosporine use	Risk Factors Older age at transplant Treatment Factors TBI Medical Conditions	PHYSICAL Blood pressure Urinary SCREENING	Health Links Kidney Health Cardiovascular Risk Factors Considerations for Further Testing and Interventions

Sec #	Therapeutic Agent(s)	Potential Side Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations
120	Amputation	Amputation-related complications Impaired circulation Functional and activity limitations Residual limb integrity problems Phantom pain Neuropathic pain Musculoskeletal pain Increased energy expenditure Impaired quality of life and functional status Psychological readjustment	Real Factors Obesity Smoking Diabetes Treatment Factors Site of amputation Nerve management → Tense flexor amputation → Tense distal amputation → Tense distal amputation	Health Status Obesity Diabetes Poor residual limb healing	HEALTH STATUS Phantom pain Functional and activity limitations Numb PHYSICAL Residual limb integrity Numb SCALING Pain Prosthetic evaluation Every 6 months with sensory control Numb	Health Status Amputation Counseling General regarding end checks, signs of poor prosthetic fit, residual limb and prosthetic hygiene, physical fitness and importance of maintaining a healthy weight and lifestyle. Considerations for Further Testing and Interventions Prosthetic fittings consultation to ensure good fit, strength, physical status with or without pain or gait training with a new prosthetic, and by non-physiological pain management. Therapeutic interventions are needed to assist with activities of daily living. Physiotherapeutic work consultation to assist with residual difficulties related to body image, integration, prosthetic, gait, employment, education and depression. Documented counseling/teaching to identify residual limb and not produce excessive functional limitations.

Periodic Evaluation	Health Counseling/ Further Considerations
HISTORY Phantom pain Functional and activity limitations Stable	Health Links Amputation
PHYSICAL Residual limb integrity Stable	Counseling Continued regarding skin checks, signs of pain, prosthetic fit, residual limb and prosthetic hygiene, physical fitness and importance of maintaining a healthy weight and lifestyle.
SCHEMATA	Considerations for Further Testing and Intervention Physical therapy interventions to maintain good strength and good training with a new prosthetic and the non-pharmacological pain management. Supplemental therapies (counseling) are needed to assist with activities of daily living. Psychological/social work consultation to assist with emotional difficulties related to body image, acceptance, prosthetic, phantom limb, amputation, insurance and disposition. Additional counseling/therapy to identify residual limb and prosthetic/functional limitations.
Prosthetic evaluation Every 6 months with sensitivity studies. Good quality	
SYSTEM = Musculoskeletal SCORE = 1	

Sec #	Organ	Population Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling/ Further Considerations	action
130	Colonial	High fat/diet, less diet Age > 50 years Obesity	Reduction with potential impact in the colon/rectum (see Factor 90) excretion: 1.30 (a) to the following	REFERENCE AT STANDARD RISK (ACS Recommendations) SCREENING	Health Links Colonel Cancer	circle water

Periodic Evaluation	Health Counseling/ Further Considerations	Revision
ACSI Assessment (tab)	Health Links Colonial Cancer	Health counsel update

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Healthy living after treatment for childhood cancer

Anthracyclines

Anthracyclines are one type of chemotherapy used to treat many childhood cancers. Included in the anthracycline group are doxorubicin (Adriamycin®), daunorubicin (daunomycin, Cerubidine®), idarubicin (Idamycin®), mitoxantrone (Novantrone®), and epirubicin. The use of anthracyclines has resulted in significant improvement in survival for children and adolescents with cancer, but it has also sometimes led to problems with the heart that may not become apparent until many years after treatment is completed. It is therefore important for each childhood cancer survivor who has received anthracyclines to continue to have regular medical check-ups so that if a problem with the heart develops, it can be detected and treated early.

The heart is a large muscle that is divided into four chambers and is designed to pump blood throughout the body. The upper chambers are called "atria" and the lower chambers are called "ventricles." The blood returning from the body enters the right atrium, is squeezed into the right ventricle, and then is pumped into the blood vessels in the lungs. It is here that the oxygen we breathe is transferred into the many small blood vessels in the lungs. The oxygen-rich blood returns to the left atrium and is then squeezed into the left ventricle, the largest and most powerful of the chambers. The left ventricle contracts to circulate the blood to the entire body.

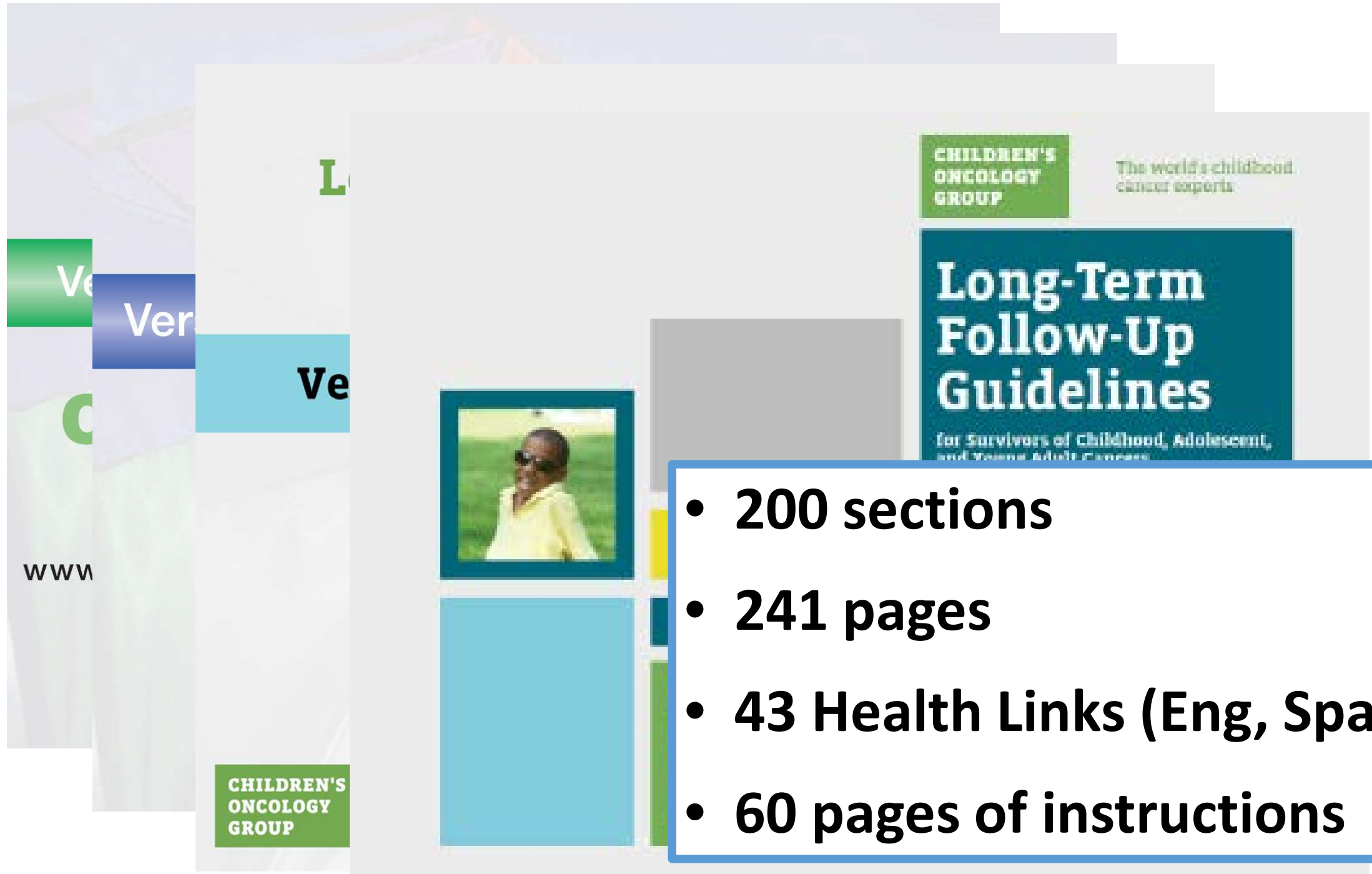
Methodology: Maintaining Currency

Core Guideline Committee

- Smita Bhatia
- Wendy Landier
- Melissa Hudson
- Sandy Constine

- Auditory/Ocular
- Cardiovascular/Pulmonary
- Endocrine/Reproductive
- GI/Oral/Dental
- HCT/Immune/Derm/ Spleen

- Musculoskeletal
- Neurocognitive/Psychosocial
- Neurologic (CNS, PNS)
- SMN/Cancer Screening
- Urinary Tract



- **200 sections**
- **241 pages**
- **43 Health Links (Eng, Span, Fr)**
- **60 pages of instructions**



International Guideline Harmonization Group

for Late Effects of Childhood Cancer



Pancare Childhood and Adolescent Cancer
Survivor Care and Follow-up Studies



Providing health care for patients with childhood cancer survivors: A survey of pediatric primary care providers

- **PCP comfort level higher when collaborating with a pediatric oncologist to provide health maintenance care for childhood cancer survivors compared with independently providing such care.**
- **~30% of PCPs were confident in their knowledge regarding immunizations for survivors.**

Cancer. 2019 Nov 1;125(21):3864-3872

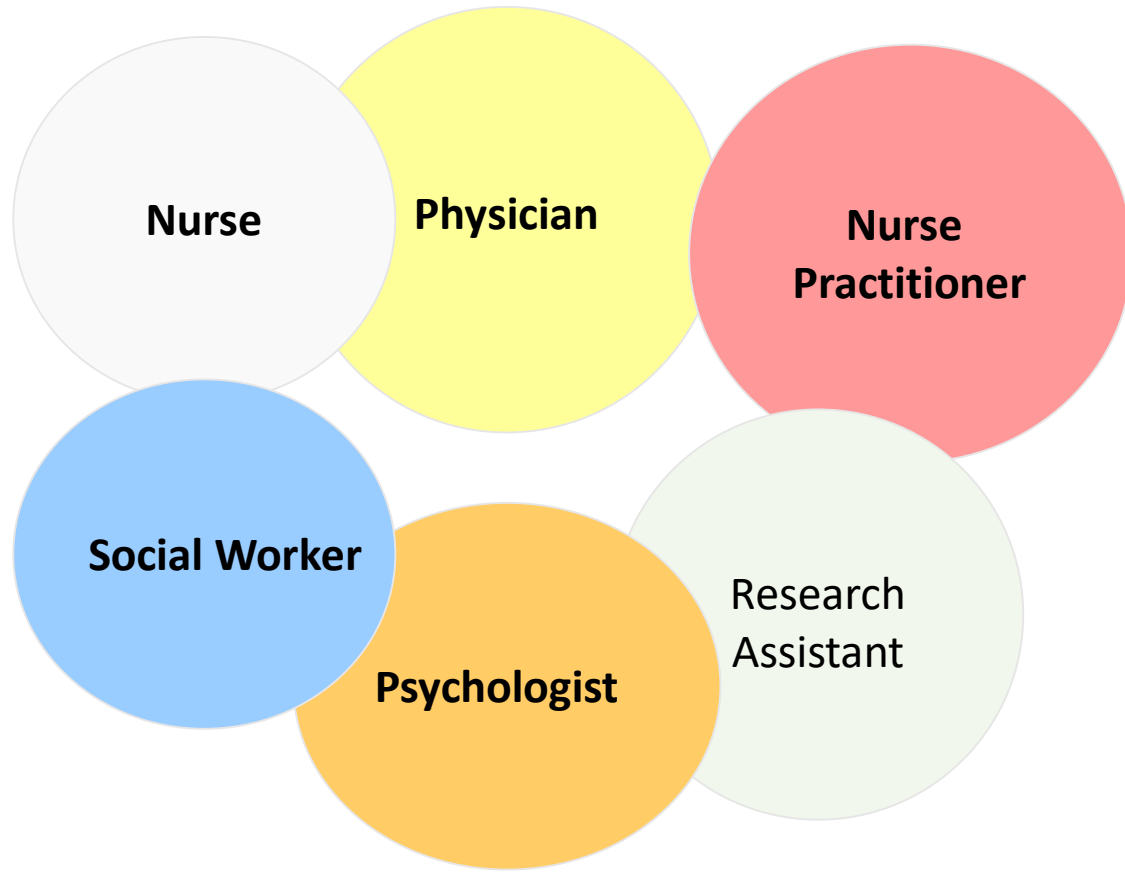
Taking on Life After Cancer (TLC) Clinic at Children's of Alabama/UAB

Inclusion Parameters

- **Diagnosed at age 21 or younger**
 - No upper age limit for subsequent follow-up
- **All cancer diagnoses/therapeutic exposures**
 - In remission/off therapy for at least 2 years
- **Consultative model w/primary care collaboration and subspecialty referrals**
 - Follow-up by oncologist continues as needed for primary disease (outside of TLC clinic)

Annual, longitudinal follow-up for life

TLC Clinic – multidisciplinary approach



- Clinical/psychosocial evaluation
- Review of treatment summary
- Individualized health education
- Health promotion strategies
- History/physical exam
- Screening tests based on therapeutic exposures per COG LTFU Guidelines

TLC Clinic Management System



LIB MEDICINE Taking on life after Cancer Clinic at Children's of Alabama

Cancer Treatment Summary

PATIENT	
Name:	Jane Doe
Demographics:	Female
Location:	Little Rock, MD

CANCER TREATMENT	
Primary Diagnosis:	Wilms Tumor
Date of Initial Diagnosis:	4/15/2007
Age at:	5 years
Protocol:	COG BREN0221 Regimen (NCT01010101)

CHEMOTHERAPY	
Drug Name:	Carboplatin
Chemotherapy Regimen:	Carboplatin (AUC=6)
Frequency:	Every 2 weeks
Duration:	4 cycles
Notes:	Completed. Anticipated Side Effects (See separate report)

RADIATION	
Site/Field:	Abdomen/Pelvis
Procedure:	External Beam Radiation Therapy
Notes:	Completed. Anticipated Side Effects (See separate report)

SURGERY	
Procedure:	Partial Nephrectomy
Notes:	Completed. Anticipated Side Effects (See separate report)

ADDITIONAL COMMENTS	
ALLERGIES:	No known allergies
KNOWN COMPLICATIONS:	• Single kidney

LIB MEDICINE Taking on life after Cancer Clinic at Children's of Alabama

Health Care Recommendations Summary
Jane Doe

TOPIC	TIPS FOR HEALTHY LIVING	IMPORTANCE	HEALTH LINK
Introduction to LTFL	• Get a record of your cancer treatment, including: - type of chemotherapy	You can now think of yourself as a survivor.	Introduction to Long-Term

Health Link
Healthy living after treatment of childhood cancer

Keeping Your Single Kidney Healthy

The kidneys are vital organs responsible for filtering out waste products from the blood, controlling blood pressure, and stimulating red blood cell production. Treatment for childhood cancer sometimes requires removal of one kidney (nephrectomy). Although you can live a healthy life with only one kidney, it is important that you take steps to protect your remaining kidney in order to keep it as healthy as possible.

What follow up is recommended?

- Have a **medical check-up at least yearly**. This should include a blood pressure check and urinalysis.
- Have a **blood test for kidney function (BUN, creatinine) and electrolytes (blood salts and minerals) at your first long-term follow-up visit** (at least 2 years after completing cancer treatment). If problems are detected, follow your health care provider's recommendations.
- If you have high blood pressure, protein in the urine, or other signs of worsening kidney problems, you should have an **evaluation by a nephrologist** (kidney specialist).

What can I do to keep my kidney healthy?

- Drink plenty of water**, especially when playing sports, while out in the sun, and during hot weather.
- Call your healthcare provider immediately if you have symptoms of a urinary tract infection** (burning when you urinate, urinating more frequently than usual, and/or feeling an urgent sensation to urinate).
- Check with your healthcare provider or pharmacist before taking any new medicines** (prescription, over-the-counter, or herbal). Be sure that your healthcare provider or pharmacist is aware that you have a single kidney.

- Significant knowledge deficits exist in childhood cancer survivors regarding their treatment-related health risks
- Only 35% of at-risk survivors understand that serious health problems could result from their treatment for childhood cancer

JAMA 287:1832-39, 2002



Impact of Tailored Education on Awareness of Personal Risk for Therapy-Related Complications Among Childhood Cancer Survivors

Wendy Landier, Yanjun Chen, Golnaz Namdar, Liton Francisco, Karla Wilson, Claudia Herrera, Saro Armenian, Julie A. Wolfson, Can-Lan Sun, F. Lennie Wong, and Smita Bhatia

See accompanying editorial on page 3849

A B S T R A C T

Purpose

Survivors of childhood cancer carry a substantial burden of long-term morbidity; personal risk awareness is critical to ensure survivors' engagement in early detection/management of complications. The impact of education provided in survivorship clinics on survivors' understanding of their personal health risks is unclear.

Methods

Patients diagnosed with cancer at age 21 years or younger and at 2 or more years off therapy completed questionnaires about awareness of personal risk for therapy-related complications at T0 (first survivorship clinic visit) and at T1 to T5 (subsequent visits). After questionnaire completion at each clinic visit, survivors received education tailored to personal risk.

Results

A total of 369 survivors completed 1,248 visits (median, three visits; range, one to six visits). The median age at cancer diagnosis was 11 years (range, 0 to 21 years); the median age at T0 was 24 years (range, 5

All authors: City of Hope, Duarte, CA; and Wendy Landier, Liton Francisco, and Smita Bhatia, University of Alabama at Birmingham, Birmingham, AL.

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Supported in part through the generosity of the Lincy, Bandai, Hearst, Graham Family, Rite Aid, Altschul, and Newman's Own Foundations, and by the Sam Bottlesman Estate.

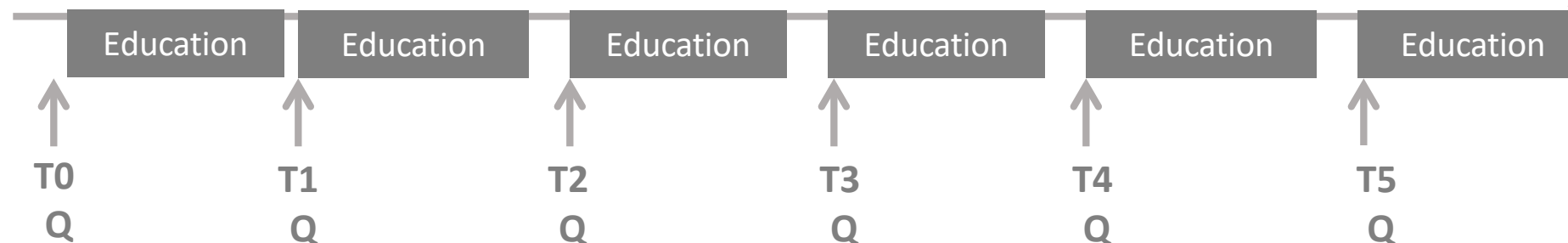
Presented in part at the European Symposium on Late Complications After Childhood Cancer, Edinburgh, United Kingdom, September 15, 2014.

Authors' disclosures of potential

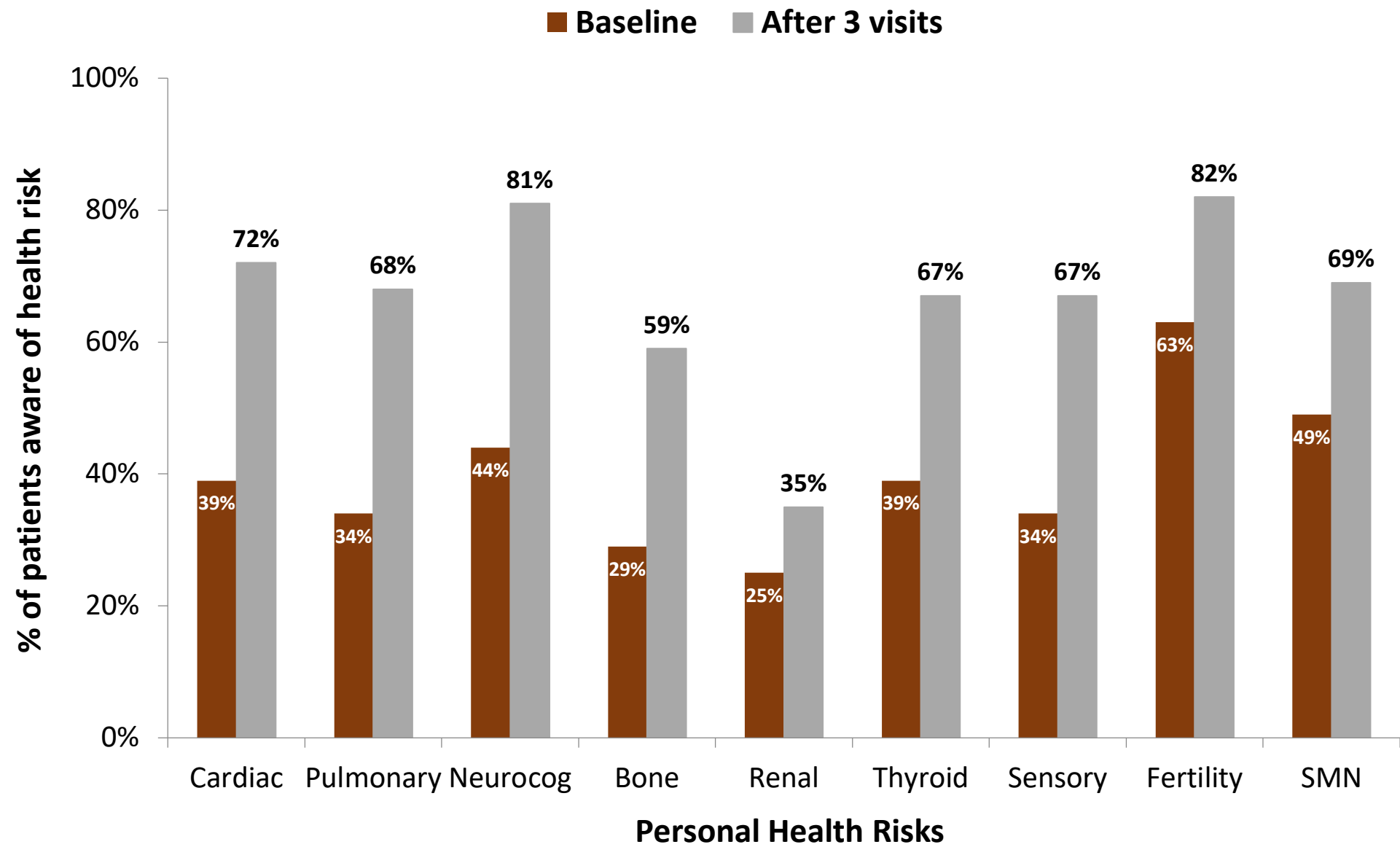
J Clin Oncol 33 (33): 3887-93, Nov 20, 2015

Health Knowledge Questionnaire

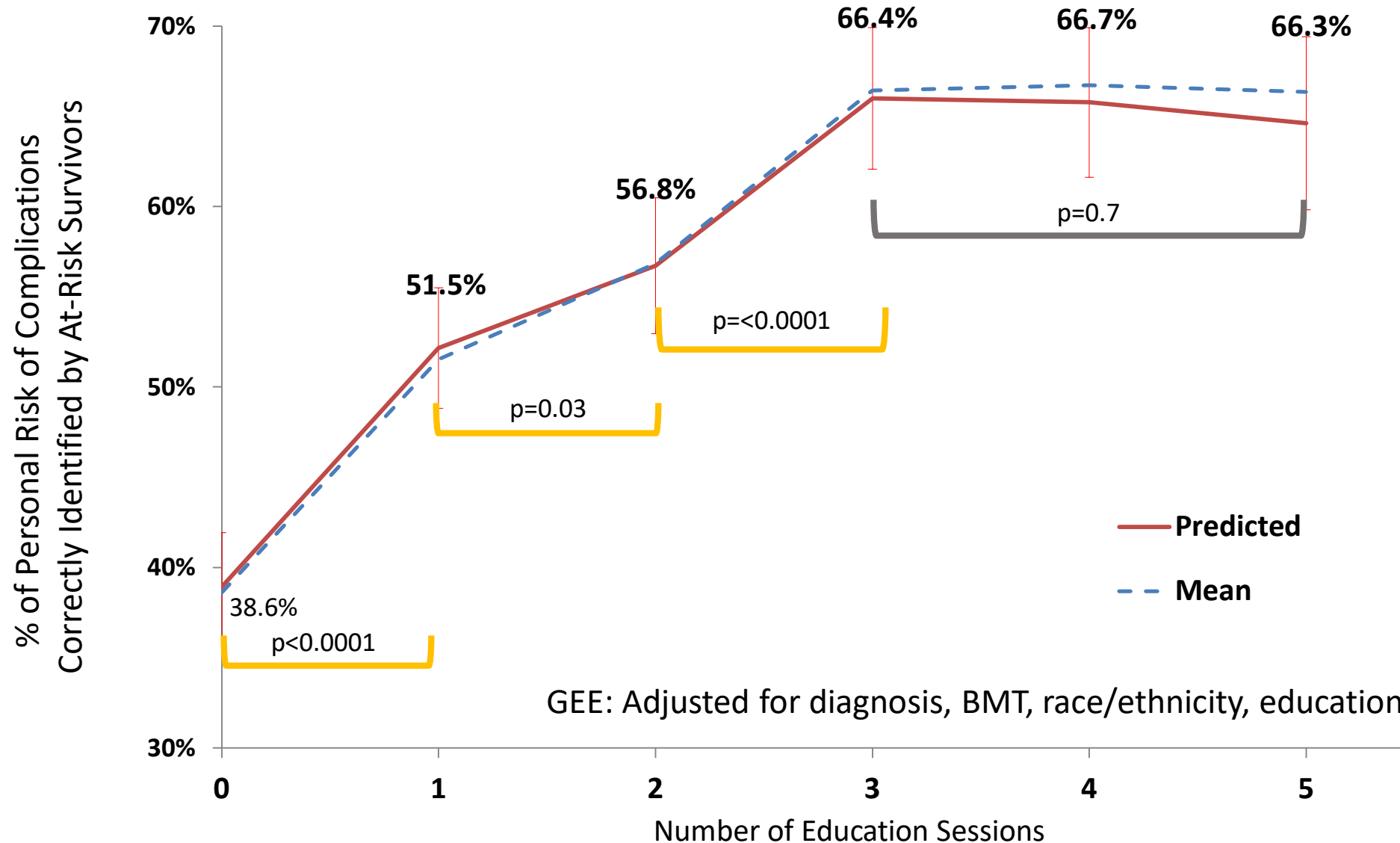
- 19 items – knowledge of treatment-related health risks
- English and Spanish



Awareness of Health Risks: At Study Entry and after 3 Education Sessions



Trajectory of Awareness of Personal Risk for Late Complications by Number of Education Sessions



Yield of Screening for Long-Term Complications Using the Children's Oncology Group Long-Term Follow-Up Guidelines

Wendy Landier, Saro H. Armenian, Jin Lee, Ola Thomas, F. Lennie Wong, Liton Francisco, Claudia Herrera, Clare Kasper, Karla D. Wilson, Meghan Zomorodi, and Smita Bhatia

Listen to the podcast by Dr Oeffinger at www.jco.org/podcasts

All authors: City of Hope, Duarte, CA.

Submitted April 9, 2012; accepted August 22, 2012; published online ahead of print at www.jco.org on October 22, 2012.

Supported in part by Grant No. P30 CA033572 from the National Institutes of Health; and by the Lincy, Bandai, Hearst, Graham Family, Rite Aid, Altschul, and Newman's Own Foundations; and by the Sam Bottelman Estate.

Presented in part at the European Symposium on Late Complications

ABSTRACT

Purpose

The Children's Oncology Group Long-Term Follow-Up (COG-LTFU) Guidelines use consensus-based recommendations for exposure-driven, risk-based screening for early detection of long-term complications in childhood cancer survivors. However, the yield from these recommendations is not known.

Methods

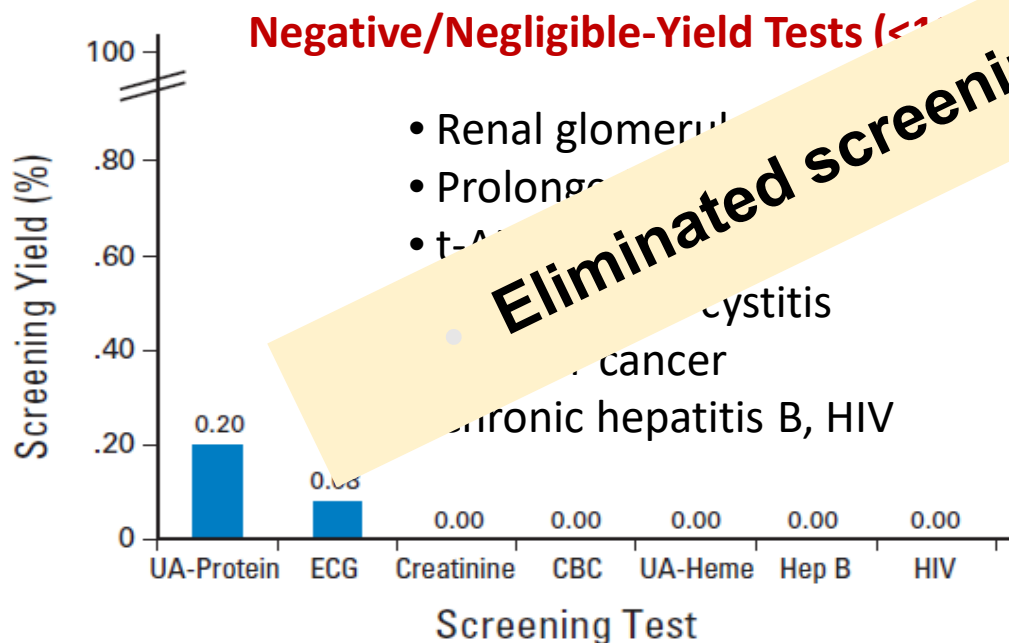
Survivors underwent COG-LTFU Guideline-directed screening. Yield was classified as negligible/negative (< 1%), intermediate ($\geq 1\%$ to < 10%), or high ($\geq 10\%$). For long-term complications with high yield, logistic regression was used to identify subgroups more likely to screen positive.

Results

Of 5,062 screenings recommended for cohort over 1,188 annual evaluations, 5062 screenings recommended for cohort over 1,188 annual evaluations

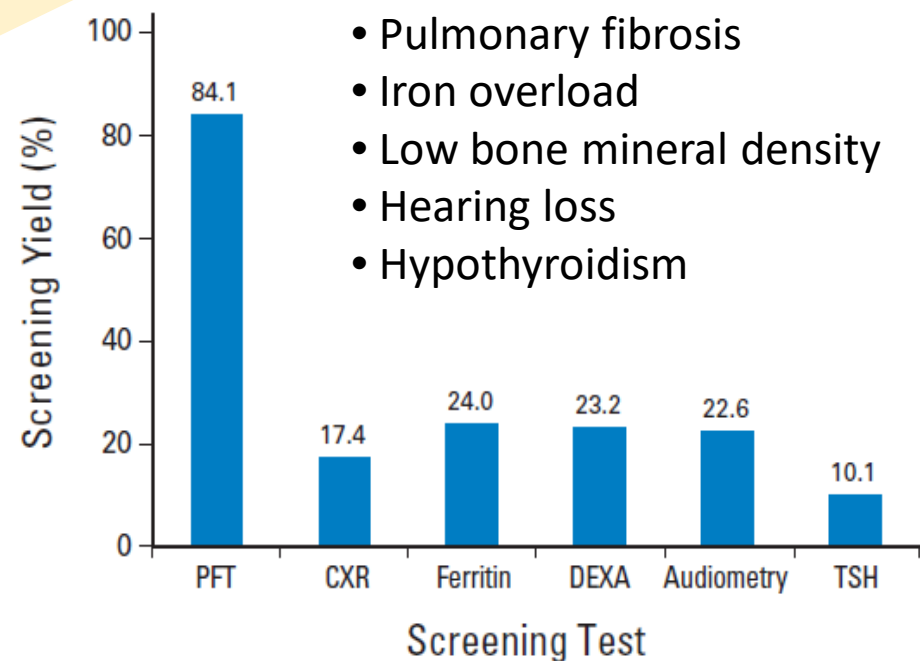
5062 screenings recommended for cohort over 1,188 annual evaluations

J Clin Oncol 30 (35): 4401-08, Dec 10, 2012



- Renal glomerulopathy
- Prolonged QTc interval
- t-Amino aciduria
- Interstitial cystitis
- Second primary cancer
- Chronic hepatitis B, HIV

Eliminated screening for low-yield tests



- Pulmonary dysfunction
- Pulmonary fibrosis
- Iron overload
- Low bone mineral density
- Hearing loss
- Hypothyroidism

Next steps...

Provide risk-stratified personalized care to cancer survivors

**“pediatric oncology...
has a culture of self-examination and improvement.”**

Joseph Simone, MD

... recommendations more uniform and
recognizable to clinicians

- Make the Guidelines more user-friendly
- Facilitate broader uptake/application of the Guidelines

Guidelines for Survivors of Adult-onset Cancer

Fertility Preservation in Patients With Cancer: **ASCO** Clinical Practice Guideline Update.

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Loprinzi CL, Lacchetti C, Bleeker J, Cavaletti G, Chauhan C, Hertz R, Kellen M, Levine A, Luthra M, Paice JA, Schneider BP, Lavoie Smith EM, Smith ML, Smith TJ, 1

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J Clin Oncol. 2017 Mar 10;35(8):893-911. doi: 10.1200/JCO.2016.70.5400. Epub 2016 Dec 5. PMID: 27918725