Nuove raccomandazioni sulla gestione dei «Cancer Survivors»

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Torino, 21 giugno 2016

Cancer survivors: molte definizioni

VOLUME 31 · NUMBER 4 · FEBRUARY 1 2013

JOURNAL OF CLINICAL ONCOLOGY

COMMENTS AND CONTROVERSIES

Cancer Survivorship: Why Labels Matter

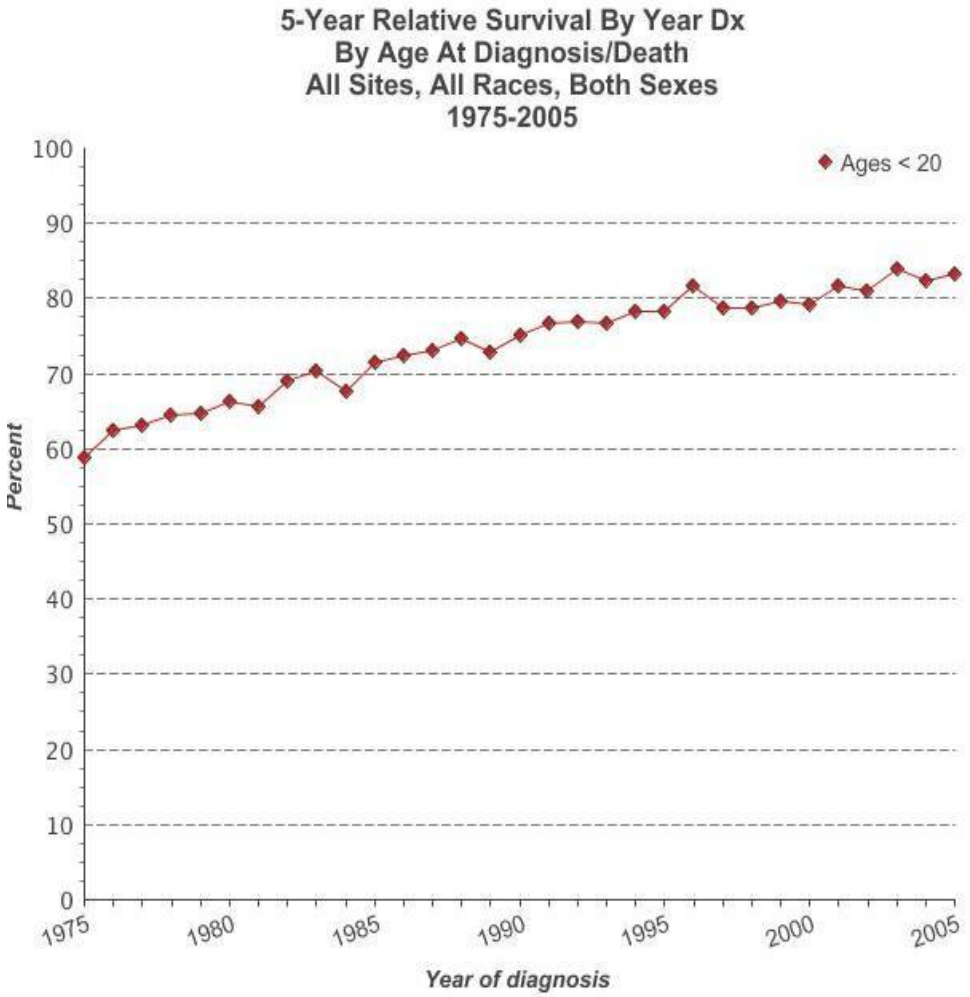
Kirsten Bell and Svetlana Ristovski-Slijepcevic, *University of British Columbia, Vancouver, British Columbia, Canada*

*The concept of cancer survivorship has been **widely debated** over the past few decades. In biomedical usage, the term survivor has a distinct clinical meaning, referring to individuals who have had a life-threatening disease but have remained **disease free for a minimum of 5 years.***

Background

• Nel corso degli ultimi 40 anni le percentuali di guarigione sono notevolmente aumentate ed oggi la maggior parte dei bambini e degli adolescenti a cui viene diagnosticata una neoplasia "guarisce" e diventa un ***childhood cancer survivors*** **(CCS).**

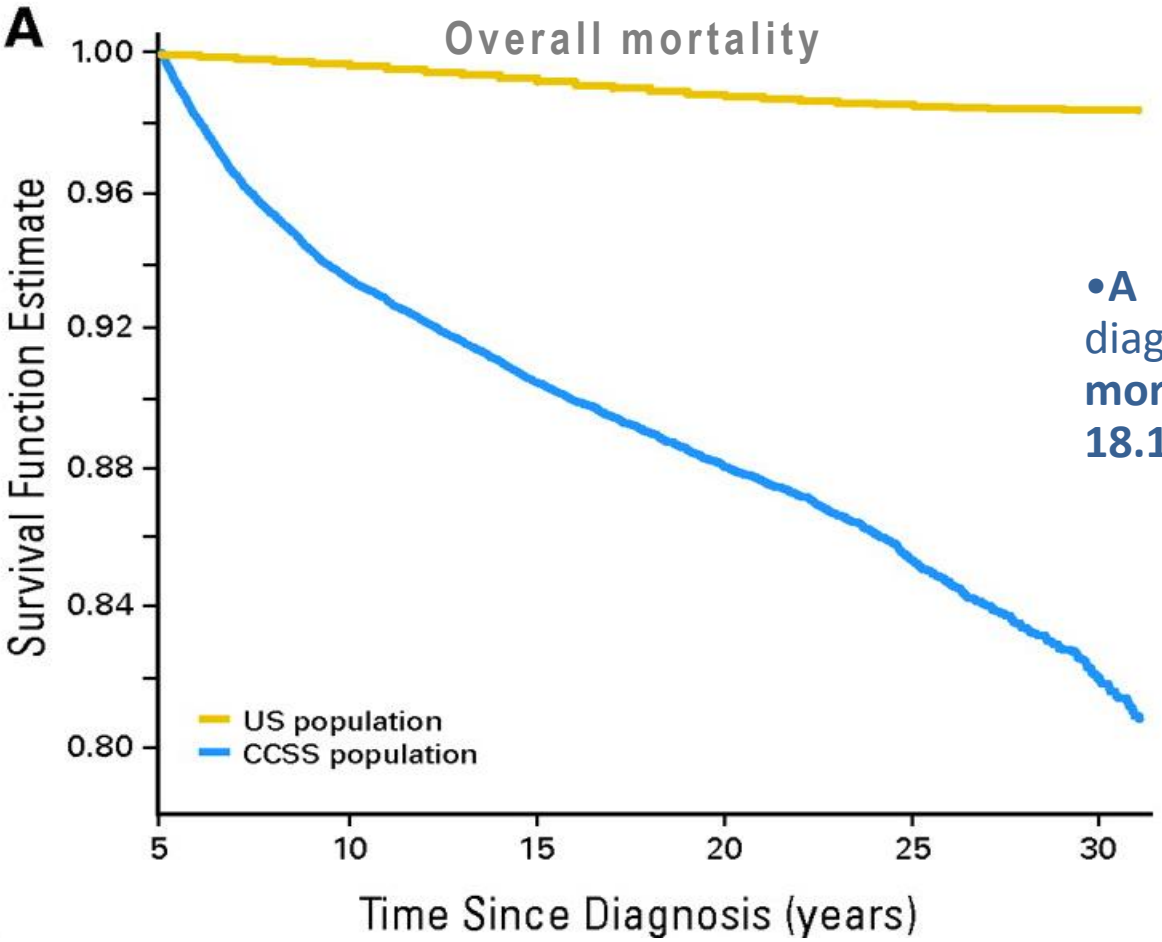
• Attualmente 1/450 adulti fra 20 e 45 anni è "guarito" da una neoplasia dell'età evolutiva, e si stima che nell'anno 2020 il rapporto sarà 1/350.



SEER Cancer Statistics, NCI

Background

Il concetto di "guarigione" fa riferimento alla guarigione dal tumore primitivo, indipendentemente da ogni **eventuale rischio o presenza di alterazioni patologiche riferibili a tossicità tardiva delle cure**.



- **A 30 anni di distanza** dalla diagnosi di tumore pediatrico, la **mortalità cumulativa globale è 18.1%** (95% CI, 17.3 to 18.9)

Armstrong et al., JCO, 2009

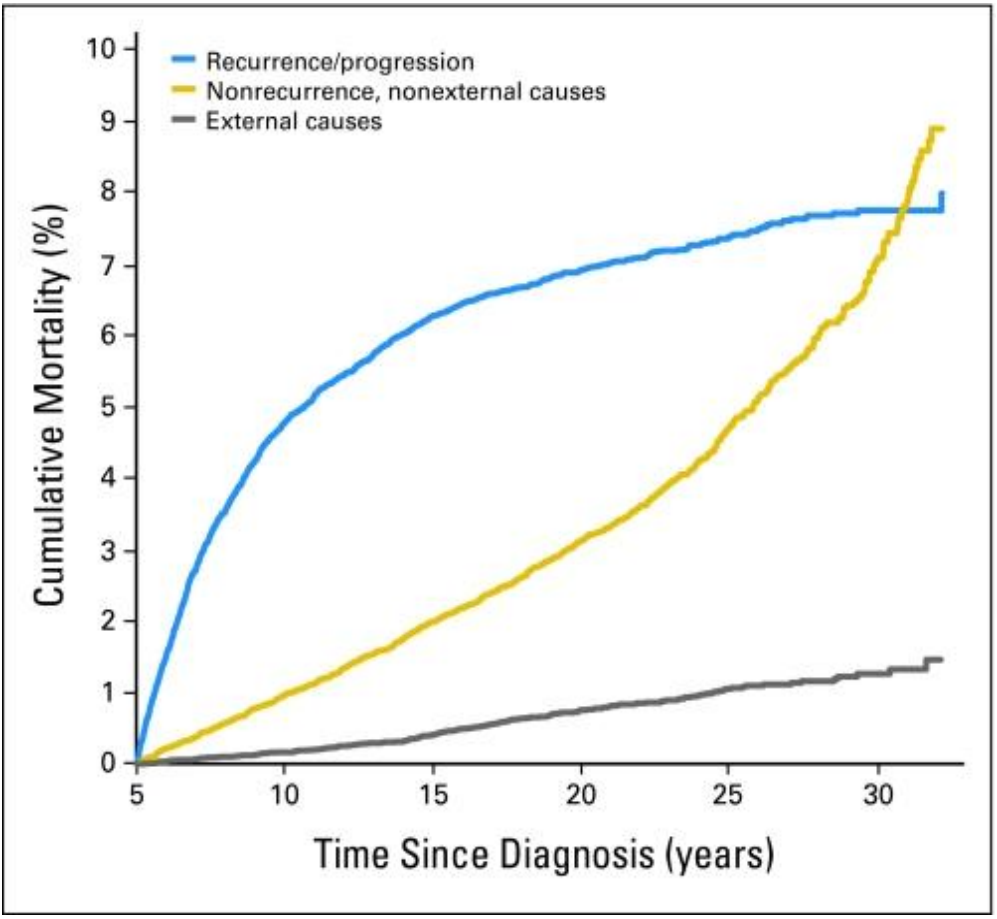
VOLUME 27 · NUMBER 14 · MAY 10 2009

JOURNAL OF CLINICAL ONCOLOGY

REVIEW ARTICLE

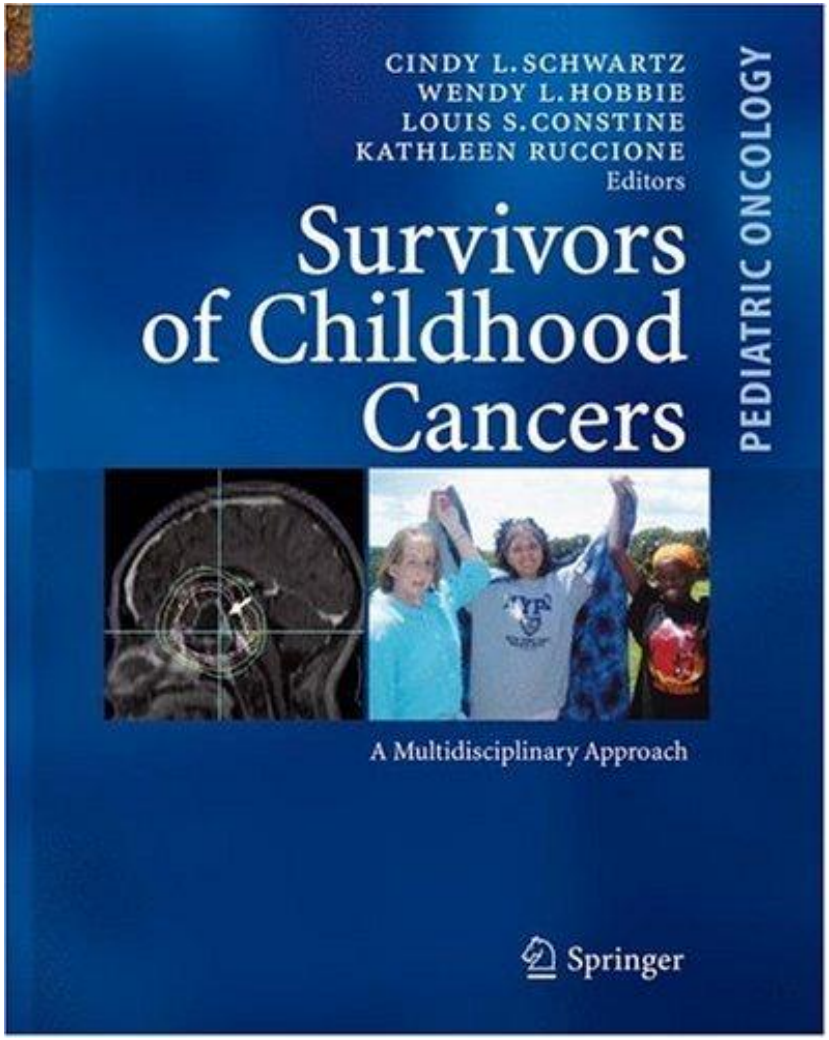
Late Mortality Among 5-Year Survivors of Childhood Cancer: A Summary From the Childhood Cancer Survivor Study

Gregory T. Armstrong, Qi Liu, Yutaka Yasui, Joseph P. Neglia, Wendy Leisenring, Leslie L. Robison, and Ann C. Mertens

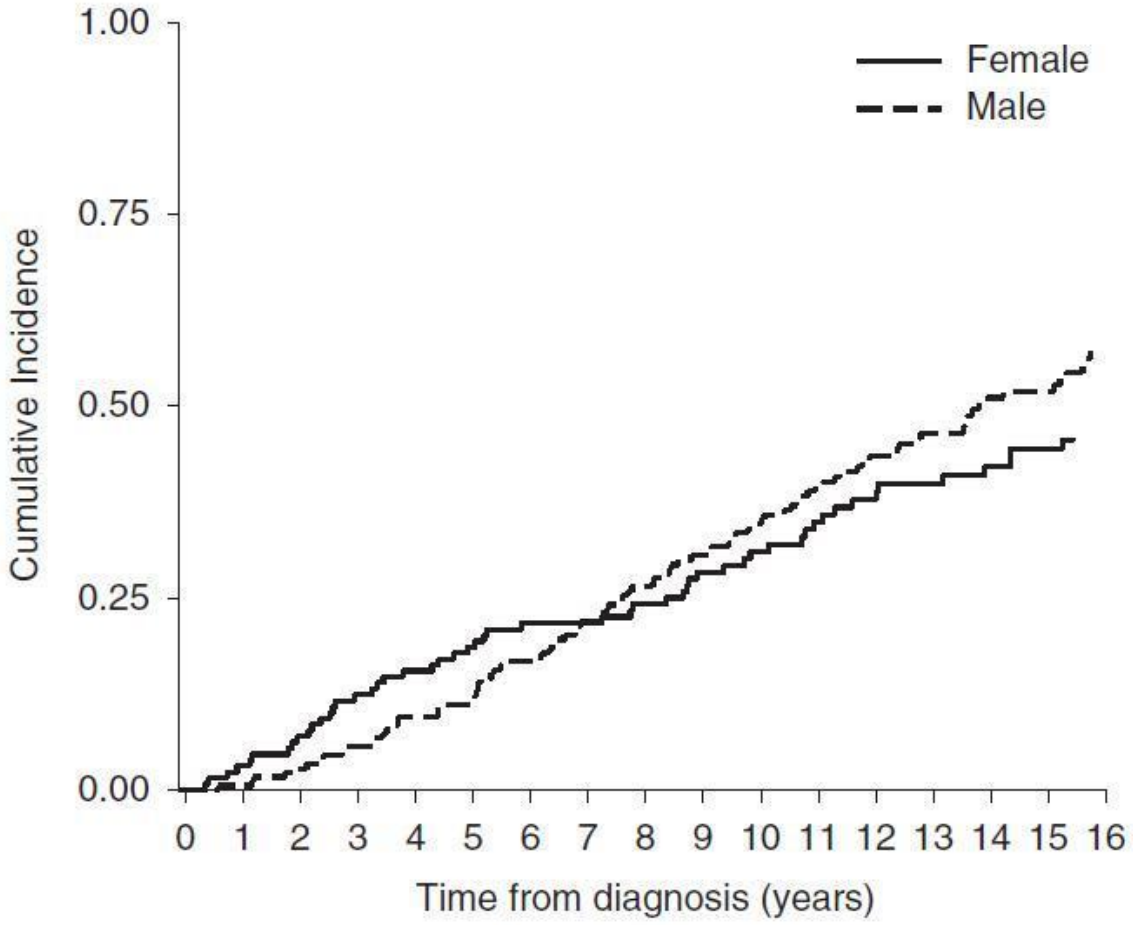


- With time mortality attributable to recurrence or progression of primary disease is decreasing, with **increases in rates of mortality attributable to late effects** of anticancer treatments.
- **Subsequent neoplasms** (SMR, 15.2; 95% CI, 13.9 to 16.6) and **cardiac death** (SMR, 7.0; 95% CI, 5.9 to 8.2) are the most common cause of death.

Tossicità tardive delle terapie oncologiche



Bisogno sanitario nuovo ed emergente, che pone ai clinici problematiche inedite delle quali sempre più i Servizi Sanitari dovranno occuparsi e che per la sua natura e la sua complessità necessita di un approccio multidisciplinare.



Cumulative incidence of any endocrine disorders after diagnosis by gender.

Brignardello et al., Eur J Endocrinol 2013

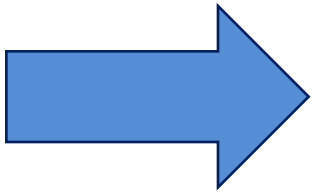
Modelli di follow-up

- Prosecuzione del monitoraggio in ambiente pediatrico
- “Transizione” al medico di medicina generale
- “Transizione” a centri specializzati, nell’ambito della medicina dell’adulto

S.S.D. Unità di Transizione per Neoplasie Curate in Età Pediatrica

Requisiti per essere avviati alla "transizione":

- **Pregressa neoplasia dell'età evolutiva**
- **Età > 18 anni**
- **Off-therapy > 5 anni**



Non necessaria la presenza di *late effects*

S.S.D. Unità di Transizione per Neoplasie Curate in Età Pediatrica

468 pazienti (M 271; F 197)

Età alla diagnosi:

10,1 7.4 (media SD)

0,3 – 18,9 (range)

Età attuale:

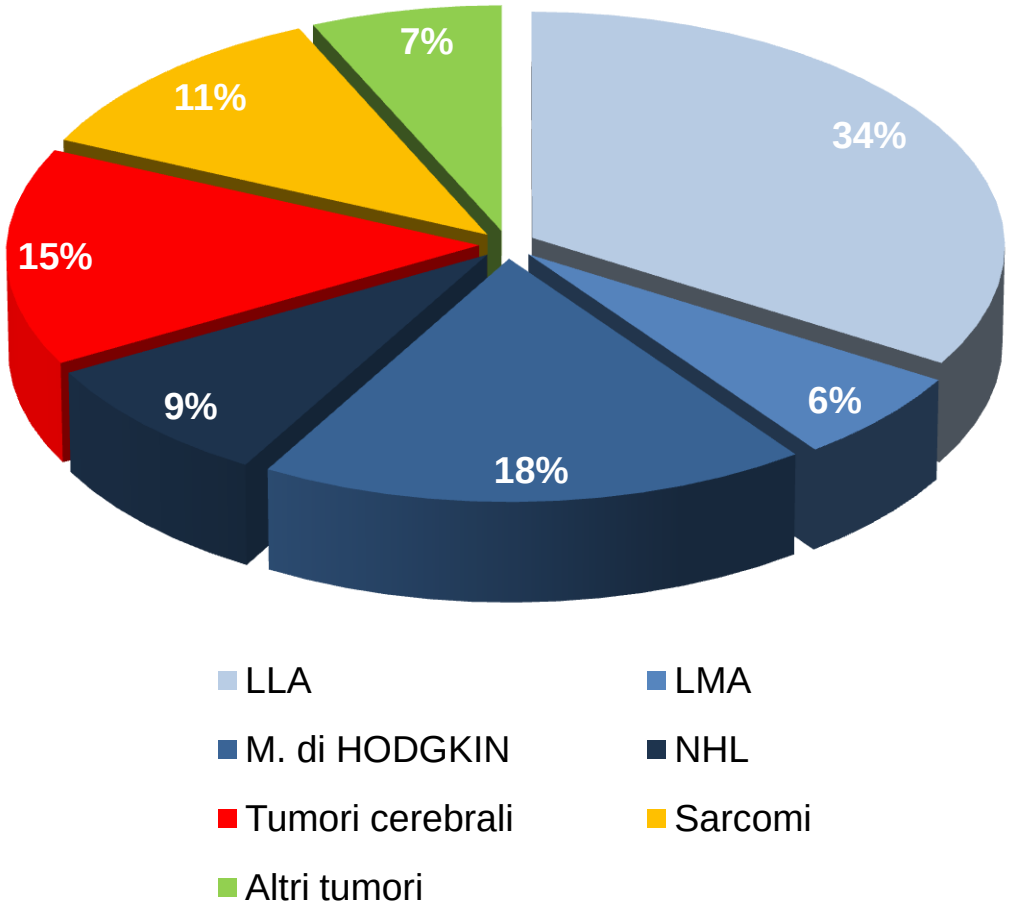
24,9 7,5 (media SD)

18,1 – 51,7 (range)

Durata follow-up:

16,4 9,5 (media SD)

5,1 – 47,4 (range)



Il follow-up a lungo termine

- Il modello organizzativo prevede la **presa in carico "globale e continuativa"** del paziente (secondo il modello della Rete Oncologica).

- **Personalizzazione del follow-up** (esami strumentali e di laboratorio, cadenza delle visite di controllo) **in funzione della stratificazione del rischio** (diagnosi oncologica e pregressi trattamenti antitumorali).

Children's Oncology Group

Long-Term Follow-Up Guidelines

for Survivors of Childhood, Adolescent, and Young Adult Cancer

Version 4.0 – October 2013

www.survivorshipguidelines.org

CHILDREN'S ONCOLOGY GROUP

The world's childhood cancer experts

CureSearch for Children's Oncology Group

Patient-Specific Guideline Identification Tool

(Applicable Guideline Sections indicated in Bold/Red; M = Male; F = Female)

Name:	Sex: M/F	Date of Birth:

Cancer Diagnosis: _____	Date of Diagnosis: _____	End Therapy Date: _____
☑ Sections 1 & 2 applicable to all patients	Prior to 1972: ☐ Section 3 Prior to 1993: ☐ Section 4 1977 - 1985: ☐ Section 5	LTFU guidelines are applicable to patients who are ≥2 years following completion of cancer therapy

CHEMOTHERAPY: ☐ Yes ☐ No If yes: ☑ Section 6 and applicable guidelines for specific chemotherapy agents below

Chemotherapy Agent (✓ if patient received)		Applicable guideline sections
Asparaginase		Section 34
Bleomycin		Section 29
Busulfan		Sections 7 M/F, 8, 9, 10
Carboplatin – all doses		Sections 7 M/F, 8, 15, 16, 17
– myeloablative dose		See also: Section 14 Note: Myeloablative dose = conditioning for HCT
Carmustine		Sections 7 M/F, 8, 9
Chlorambucil		Sections 7 M/F, 8
Cisplatin		Sections 7 M/F, 8, 14, 15, 16, 17
Cyclophosphamide		Sections 7 M/F, 8, 11, 12
Cytarabine: SQ, IT, IO, low-dose IV		Section 20 Note: Low-dose IV = all single doses < 1000 mg/m²
Cytarabine: High-dose IV		Sections 18, 19 Note: High-dose IV = any single dose ≥1000 mg/m²
Dacarbazine		Sections 7 M/F, 8
Dactinomycin		Section 30
Daunorubicin Cumulative dose: _____ mg/m² Age at first dose: _____		Sections 27, 28
Dexamethasone		Sections 31, 32, 33
Doxorubicin Cumulative dose: _____ mg/m² Age at first dose: _____		Sections 27, 28
Epirubicin* Cumulative dose: _____ mg/m² Age at first dose: _____		Sections 27, 28 Cumulative dose x 0.67 = _____ mg/m² = doxorubicin/daunorubicin isotoxic dose
Etoposide (VP-16)		Section 37
Idarubicin* Cumulative dose: _____ mg/m² Age at first dose: _____		Sections 27, 28 Cumulative dose x 5 = _____ mg/m² = doxorubicin/daunorubicin isotoxic dose
Ifosfamide		Sections 7 M/F, 8, 11, 13
Lomustine		Sections 7 M/F, 8, 9
Mechlorethamine		Sections 7 M/F, 8
Melphalan		Sections 7 M/F, 8
Mercaptopurine (6-MP)		Section 21

*Use formulas below to convert to doxorubicin/daunorubicin isotoxic equivalents prior to calculating total cumulative anthracycline dose:
Epirubicin - multiply total dose x 0.67 **Idarubicin** - multiply total dose x 5 **Mitoxantrone** - multiply total dose x 3.5
Note: There is a paucity of literature to support isotoxic dose conversion; however, the above conversion factors may be used for convenience

Il follow-up a lungo termine

- *Personale (medico, infermieristico, amministrativo) "dedicato"*
- Creazione di percorsi facilitati per questa tipologia di pazienti
- Creazione di specifici raccordi funzionali con i servizi

Specialisti dedicati

- Oncologo
- Ematologo
- Internista
- Endocrinologo
- Cardiologo
- Pneumologo
- Neurologo
- Algologo
- Urologo
- Radioterapista
- Ginecologo
- Dermatologo
- Radiologo
- Psico-oncologo
- Chirurgo

Treatment of hematologic malignancies is increasingly complex. Issues relating to pathology, transplantation, and various new therapies require oncologists and hematologists to stay abreast of breakthrough advances. In addition, targeted therapies and oral treatments bring the latest benefits to patients. These activities focus on the new approaches that have been incorporated into patient management, including the use of drugs, biologics, and diagnostics.

The NCCN 10th Annual Congress: Hematologic Malignancies™ took place October 16 – 17, 2015 in San Francisco, CA.

Recorded Presentations from this meeting include:

- **The NCCN Value Initiative: Using NCCN Evidence Blocks™ in Clinical Decisions**
- **Optimizing Small Molecular Inhibitor Therapy for Chronic Lymphocytic Leukemia**
- **Evolving Therapies for Follicular Lymphoma**
- **Management of HIV-associated Non-Hodgkin's Lymphomas**
- **Evolving Targeted Management of Acute Myeloid Leukemia**
- **Management of Myelodysplastic Syndromes**
- **Management of Acute Lymphoblastic Leukemia**
- **Survivorship Issues: Late Effects of Curative Therapy in Lymphoma Survivors**
- **Advances in Waldenström's Macroglobulinemia**
- **Management of Multiple Myeloma**
- **Bone Health in Patients with Multiple Myeloma**
- **Diagnosis and Management of Castleman Disease**
- **Targeted Therapies for Relapsed or Refractory Classical Hodgkin Lymphoma**
- **PET-Guided Treatment Approach for Advanced Stage Classical Hodgkin Lymphoma**

- **Patient Case Studies & Panel Discussions:**
  - **Amyloidosis, POEMS Syndrome, Plasmacytoma**
  - **Double-hit Lymphoma, T-cell Lymphoma, Mantle Cell Lymphoma**
  - **Myeloproliferative Disorders, Elderly Myelofibrosis, Hemophagocytic Syndromes**

CONFERENZA DI CONSENSO

DALLA PRATICA DEL **FOLLOW UP** ALLA CULTURA DI **SURVIVORSHIP CARE**

Presidenti della conferenza: Carmine Pinto, Gianmauro Numico

ROMA • 10 -11 SETTEMBRE 2015

6. **La sorveglianza dopo la diagnosi e il trattamento per una neoplasia non ha solo il significato di anticipazione diagnostica della recidiva ma deve riguardare tutte le condizioni che influiscono sulla qualità della vita.**

   L'esame clinico periodico è ritenuto rilevante perché consente di raccogliere i sintomi o i segni indicativi di recidiva o di nuova malattia e indirizzare l'eventuale successivo iter diagnostico. Ha inoltre altre importanti funzioni:

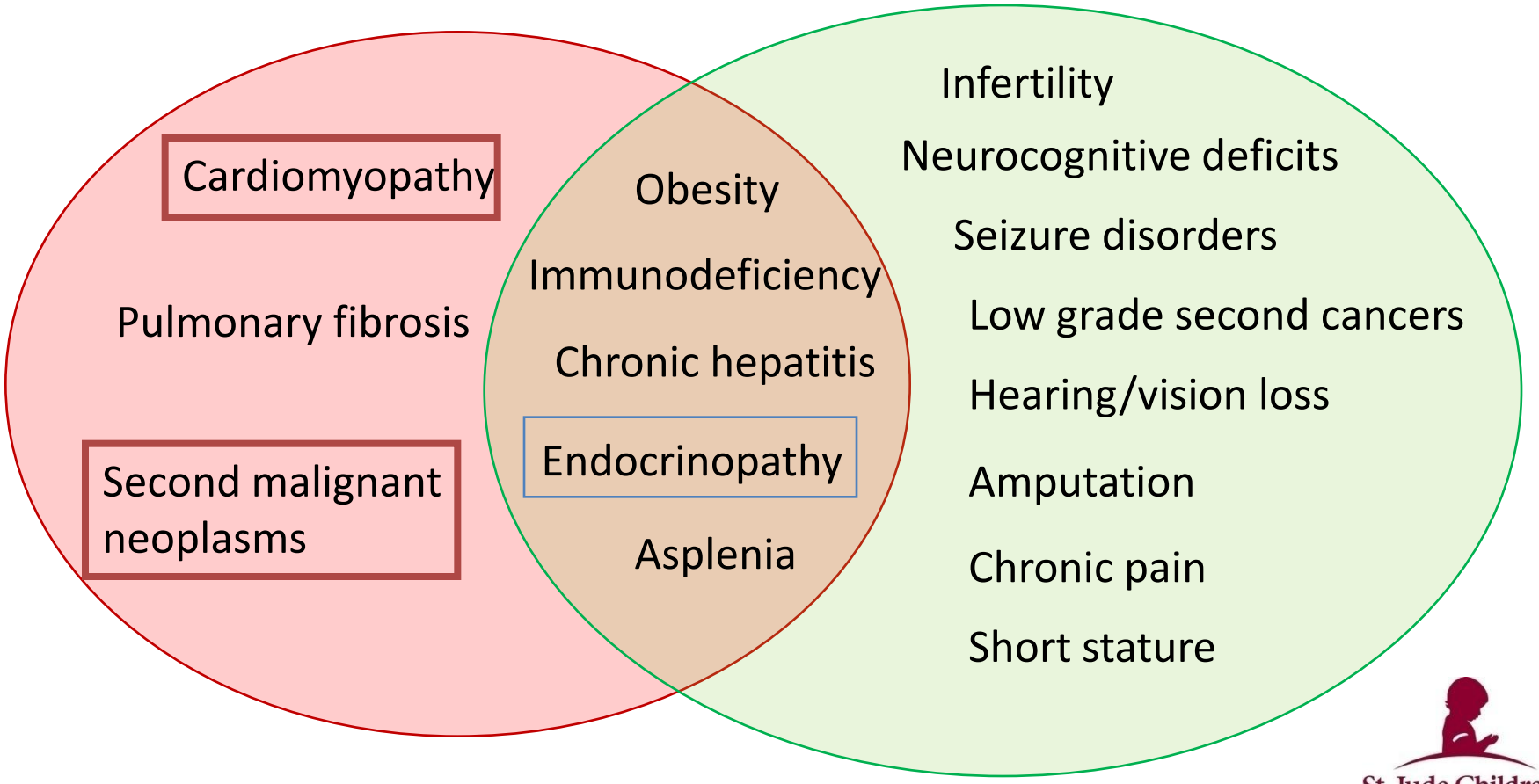
A. *Tossicità e secondi tumori*: per la maggior parte delle condizioni la sorveglianza clinica è l'unica procedura raccomandata. E' possibile che in alcuni setting sia consigliabile una sorveglianza clinico-strumentale specifica. L'informazione circa le possibili conseguenze nocive dei trattamenti dovrebbe sempre precedere l'applicazione dei trattamenti stessi e andrebbe in ogni caso ripresa e precisata durante la storia clinica del paziente.

B. *Comorbidità*: prendere in considerazione il contesto clinico rappresentato da patologie associate e da condizioni di disagio psico-sociale.

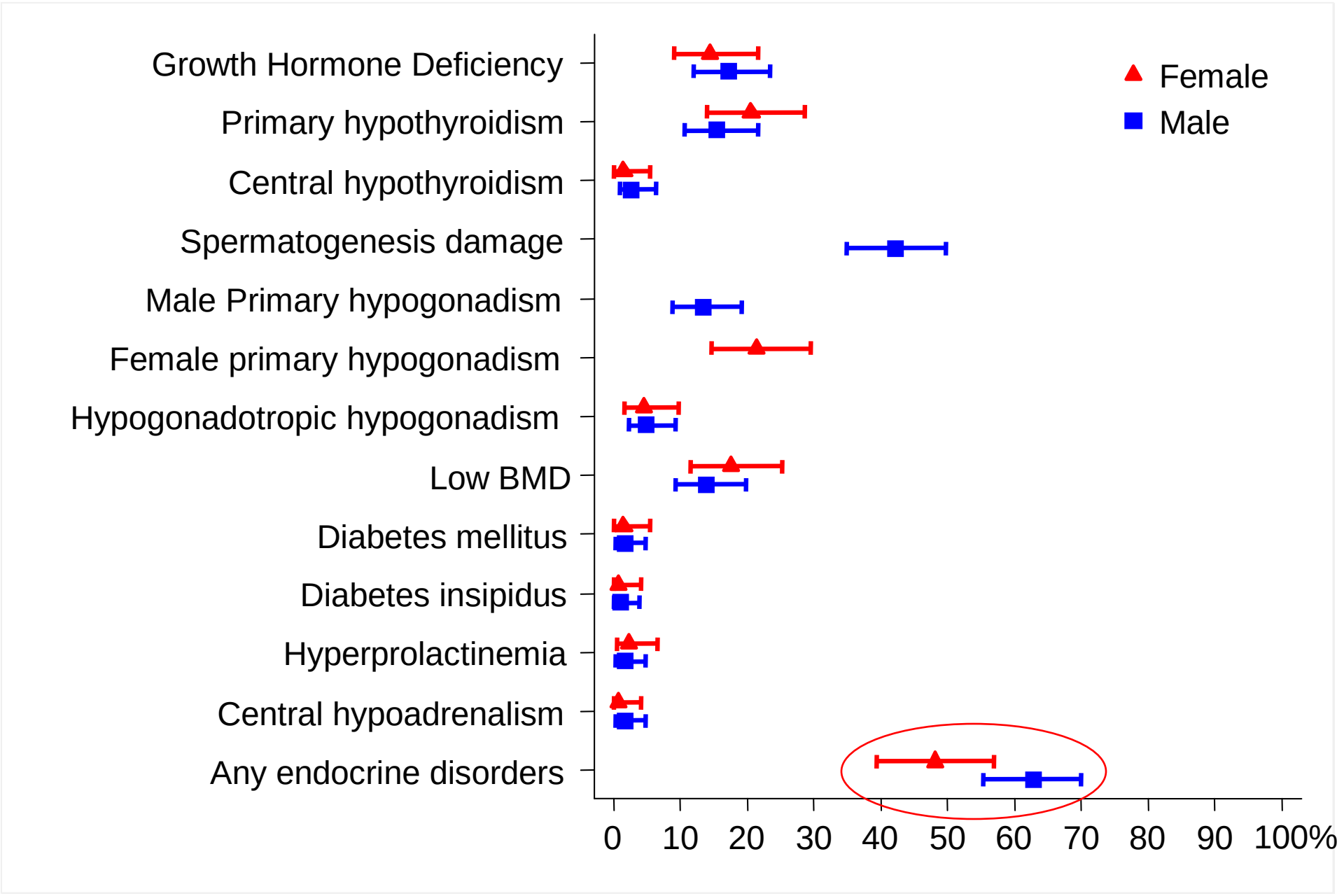
C. *Promozione della salute*: le visite di follow up rappresentano una importante occasione per offrire indicazioni relative ai cambiamenti dello stile di vita che possono influire positivamente sulla prognosi e danno l'opportunità di monitorare l'adesione alle indicazioni stesse. Per favorire l'adozione e il mantenimento nel tempo di buone nuove abitudini, oltre all'intervento di counselling, è consigliabile progettare percorsi educazionali atti ad offrire indicazioni pratiche per la realizzazione dei cambiamenti desiderati.

Spectrum of Physical Late Effects

Life Threatening → Life Altering



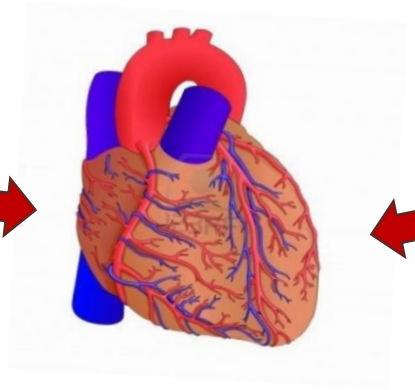
St. Jude Children's Research Hospital
ALSAC • Danny Thomas, Founder
Finding cures. Saving children.



Brignardello et al., Eur J Endocrinol 2013

Cardiac risk

Radiotherapy



Anthracyclines

Antracicline: incidenza

Review and Meta-Analysis of Incidence and Clinical Predictors of Anthracycline Cardiotoxicity

-18 studi inclusi pubblicati fra il 1979 e il 2011.

- **49.017** pazienti complessivi (48% trattati con antracicline), di cui 23.764 trattati per tumore della mammella.

- Dopo un follow-up mediano di 9 anni, l'incidenza di **cardiopatie subcliniche** era del **17.9%,** quella di **cardiopatie conclamate** del **6.3%**.

Lotrionte et al, Am J Cardiol 2013

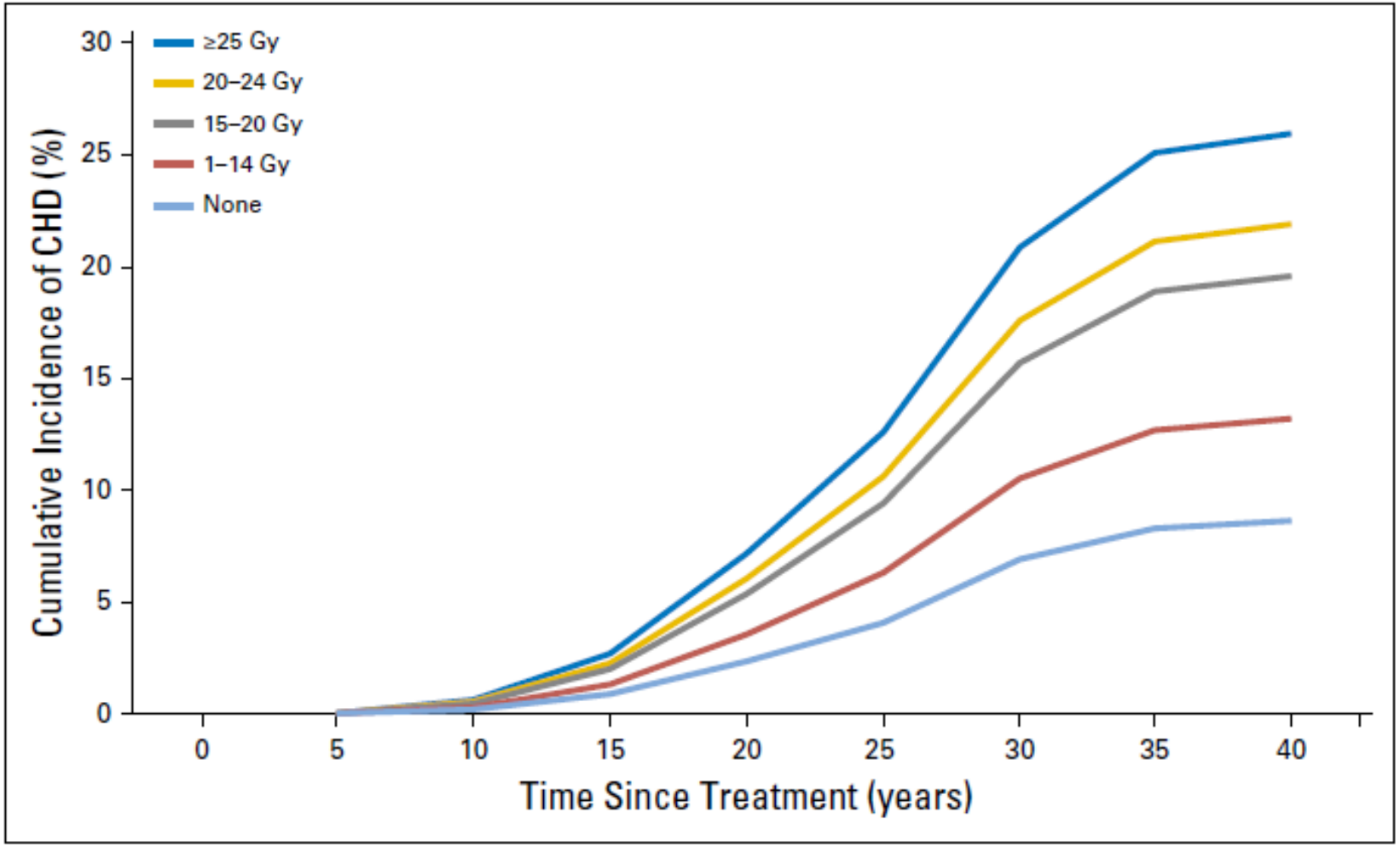
VOLUME 34 · NUMBER 3 · JANUARY 20, 2016

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Radiation Dose-Response Relationship for Risk of Coronary Heart Disease in Survivors of Hodgkin Lymphoma

Frederika A. van Nimwegen, Michael Schaapveld, David J. Cutter, Cècile P.M. Janus, Augustinus D.G. Krol, Michael Hauptmann, Karen Kooijman, Judith Roesink, Richard van der Maazen, Sarah C. Darby, Berthe M.P. Aleman, and Flora E. van Leeuwen



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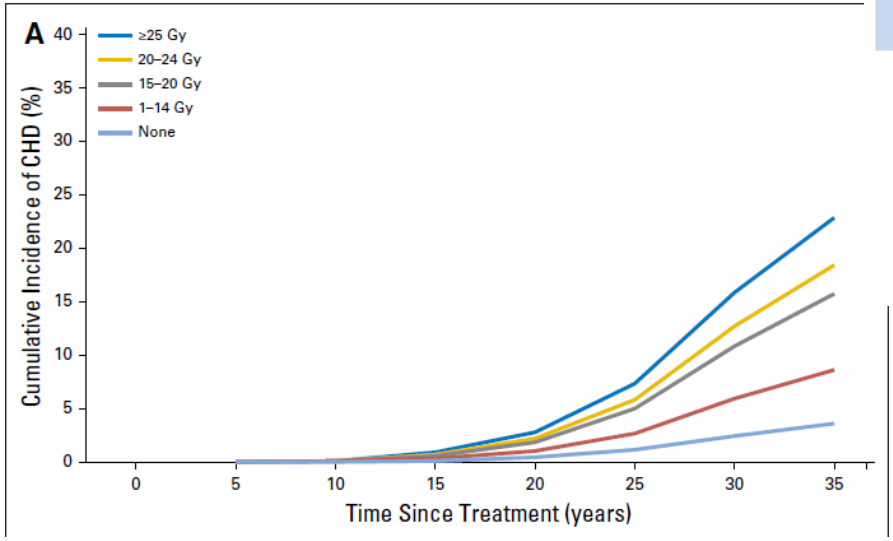
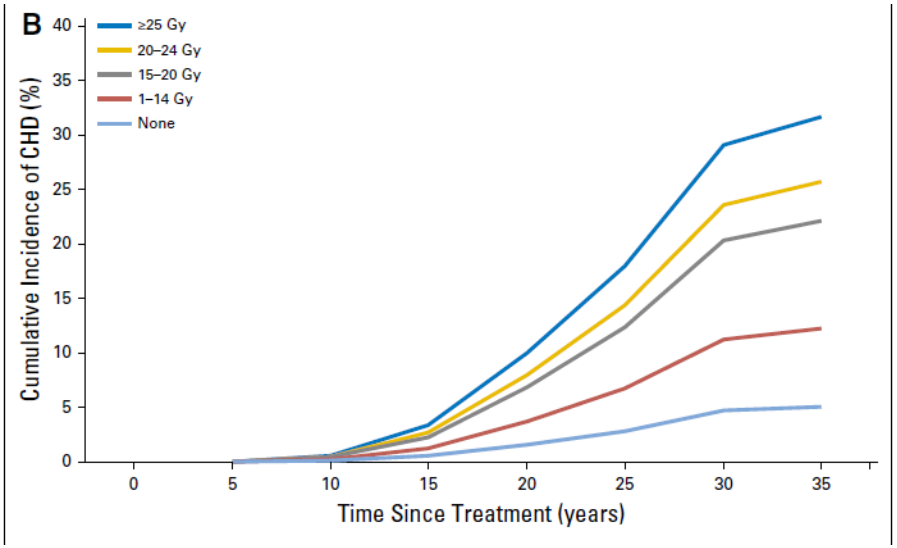
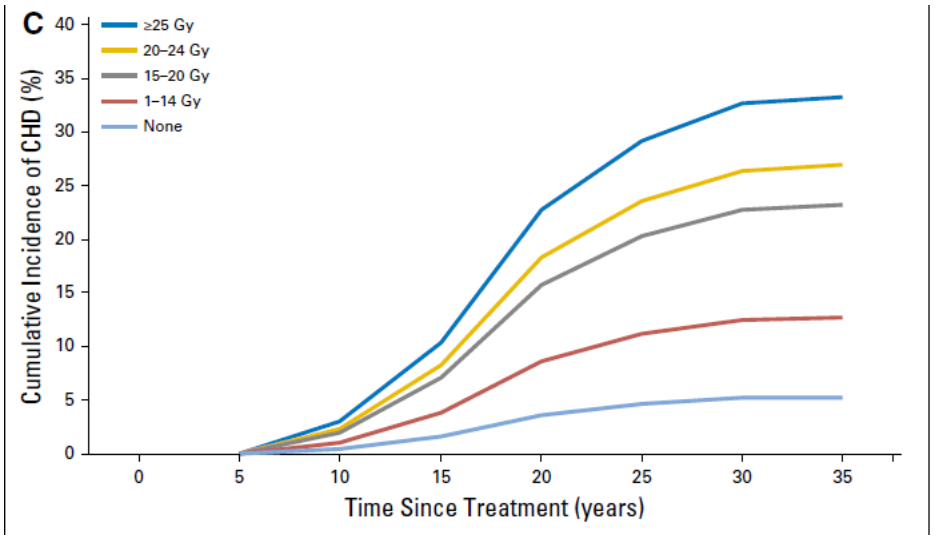
See accompanying editorial on page 208





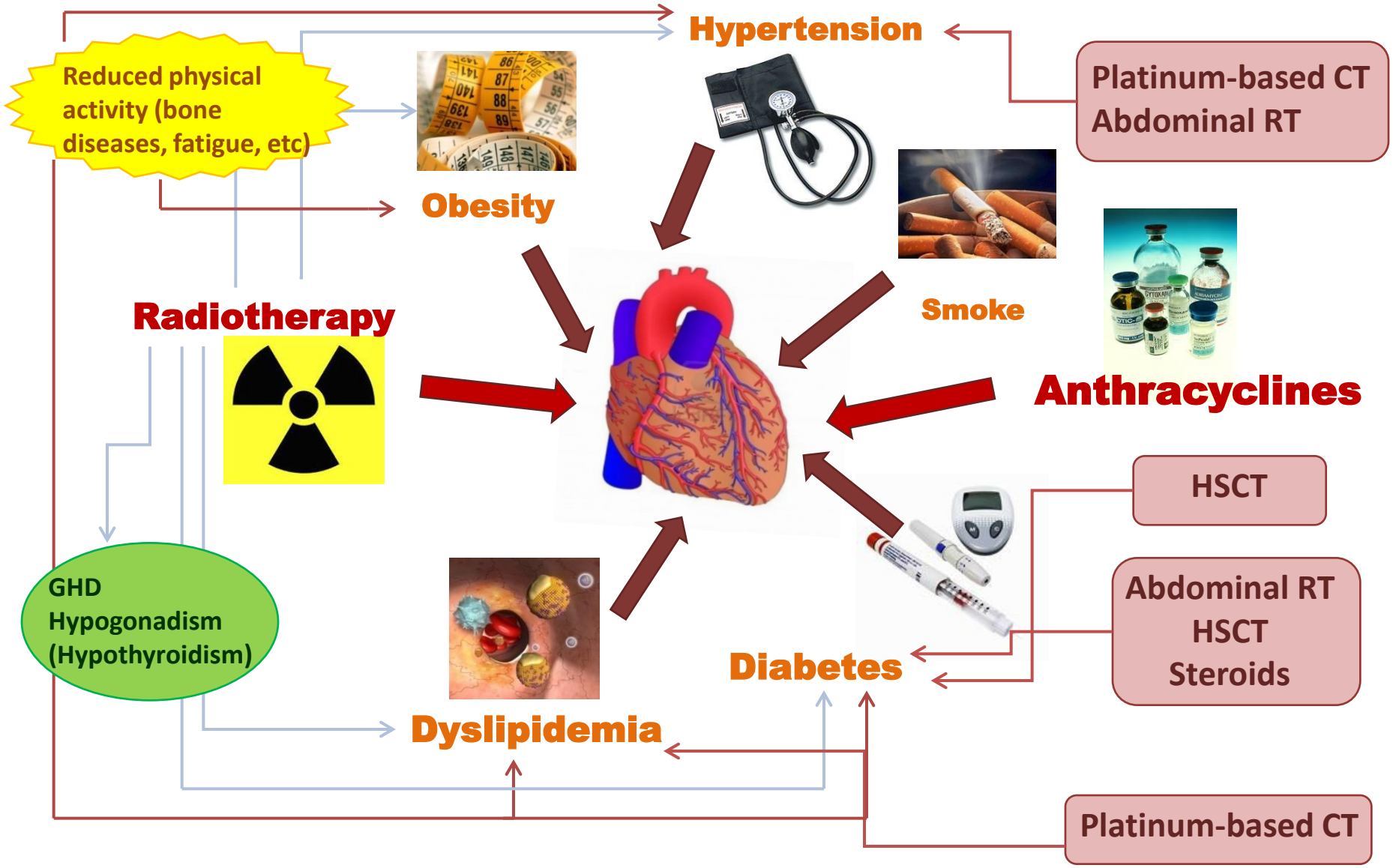


A: < 27,5 yrs

B: 27,5-36,4 yrs

C: 36,5-50,9 yrs

Cardiac risk or cardio-metabolic risk?



Cancer survivors: fattori di rischio CV

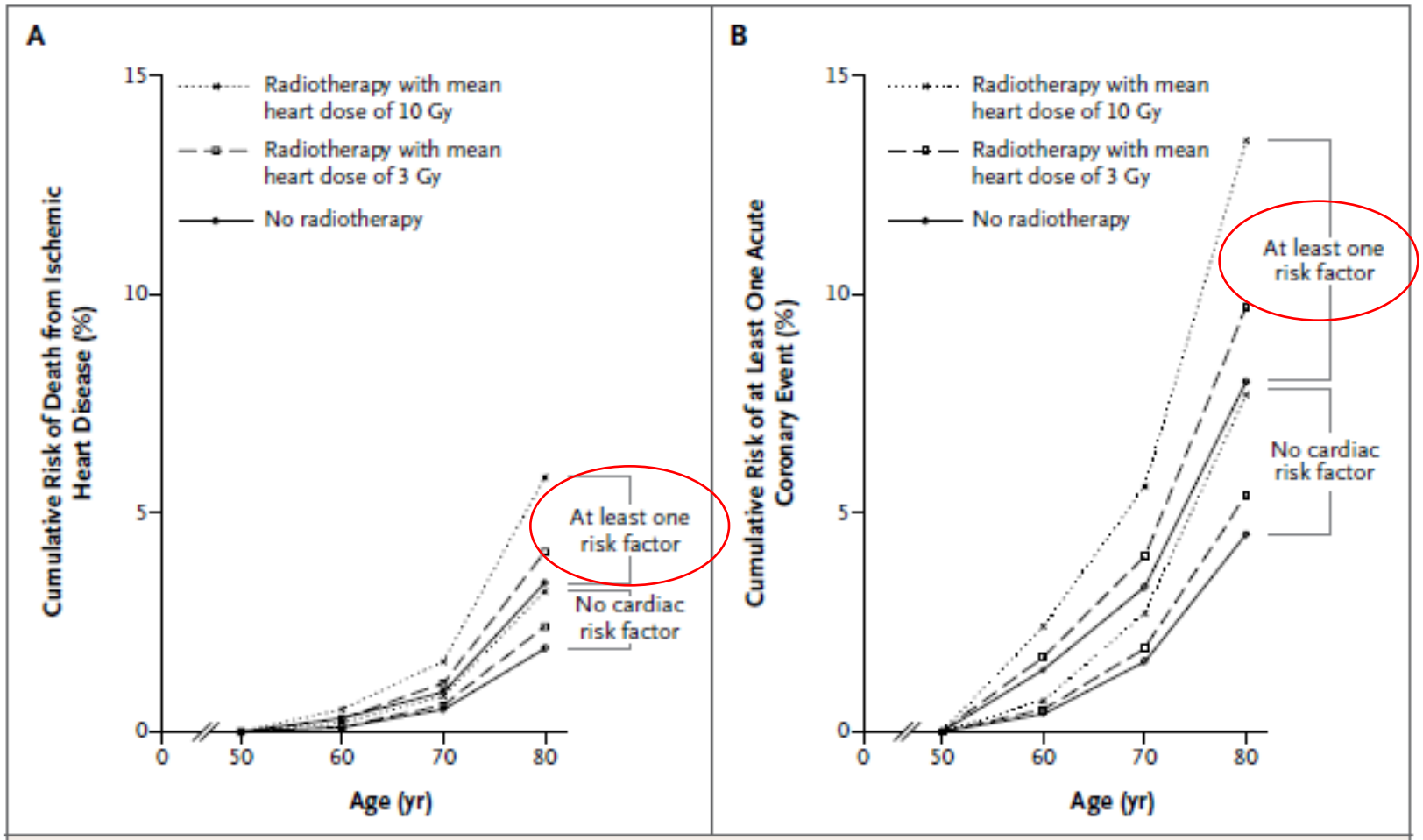
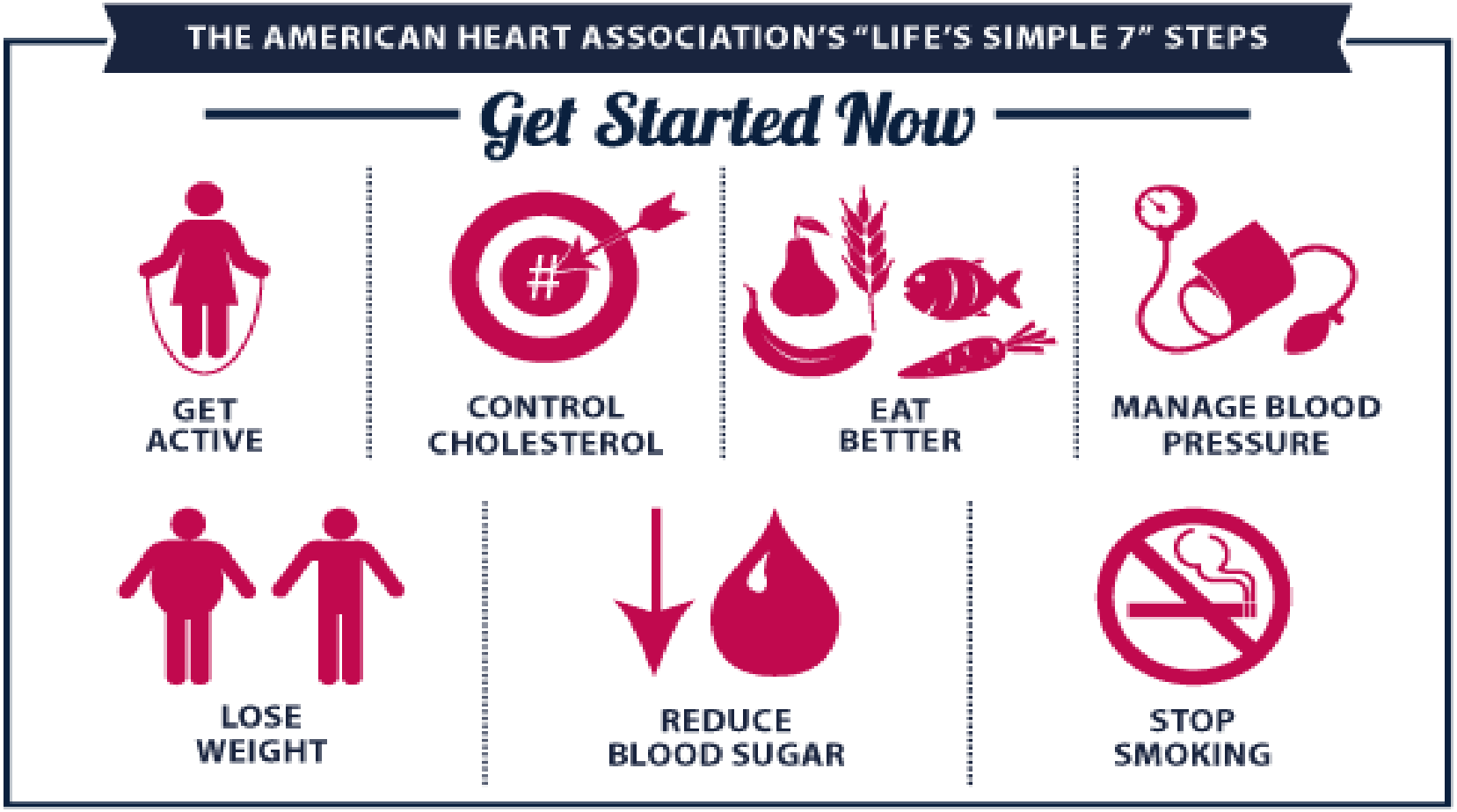


Figure 2. Cumulative Risks of Death from Ischemic Heart Disease and of at Least One Acute Coronary Event.

Darby et al, NEJM 2013



International Guideline Harmonization Group
for Late Effects of Childhood Cancer

Generally, health-care providers **are asked to educate and counsel all survivors** of childhood cancer about the importance of maintaining **a heart-healthy lifestyle** […]. Extensive studies done in non-oncology populations support the benefits of interventions to reduce modifiable risk factors […].

Armenian S et al, Lancet Oncol 2015

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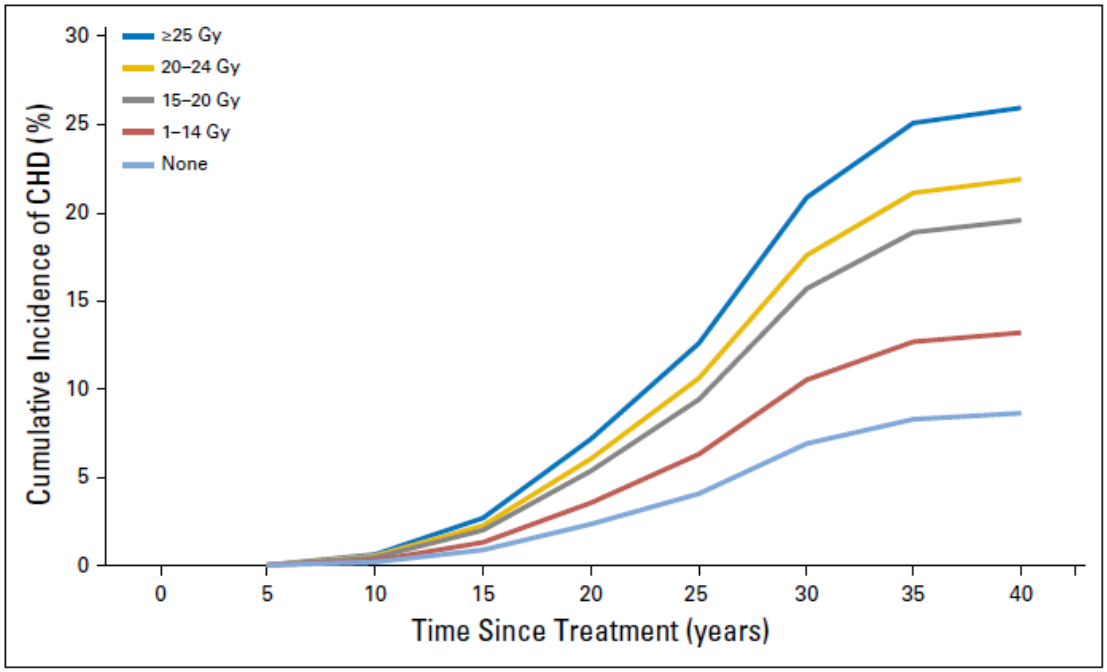


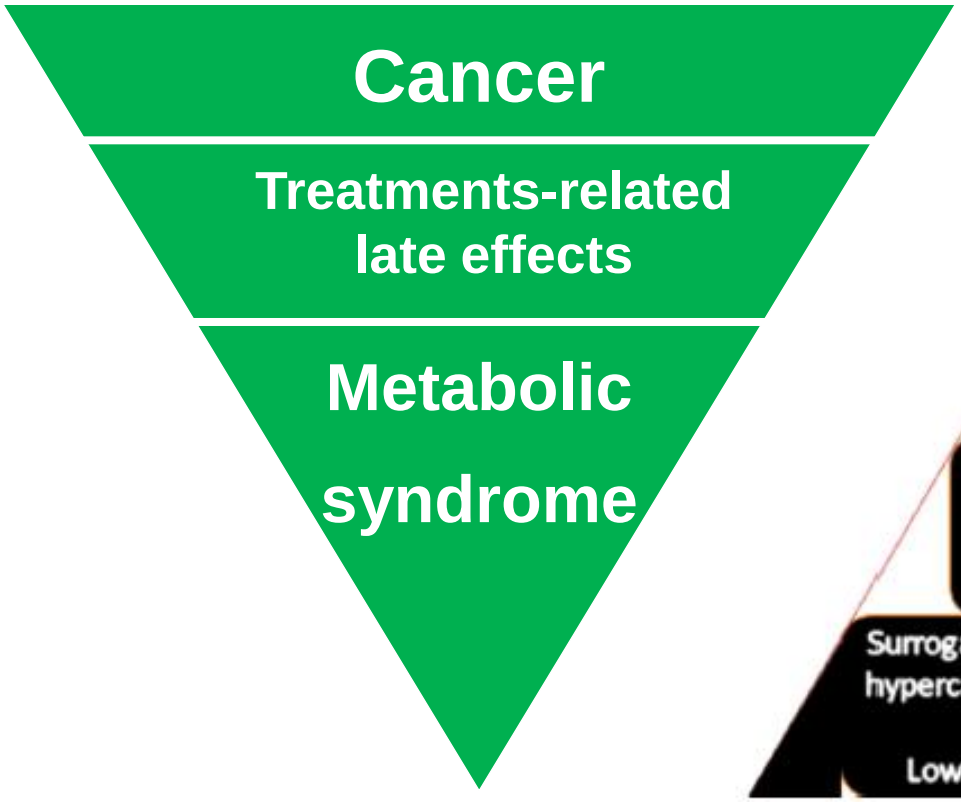
Conclusion

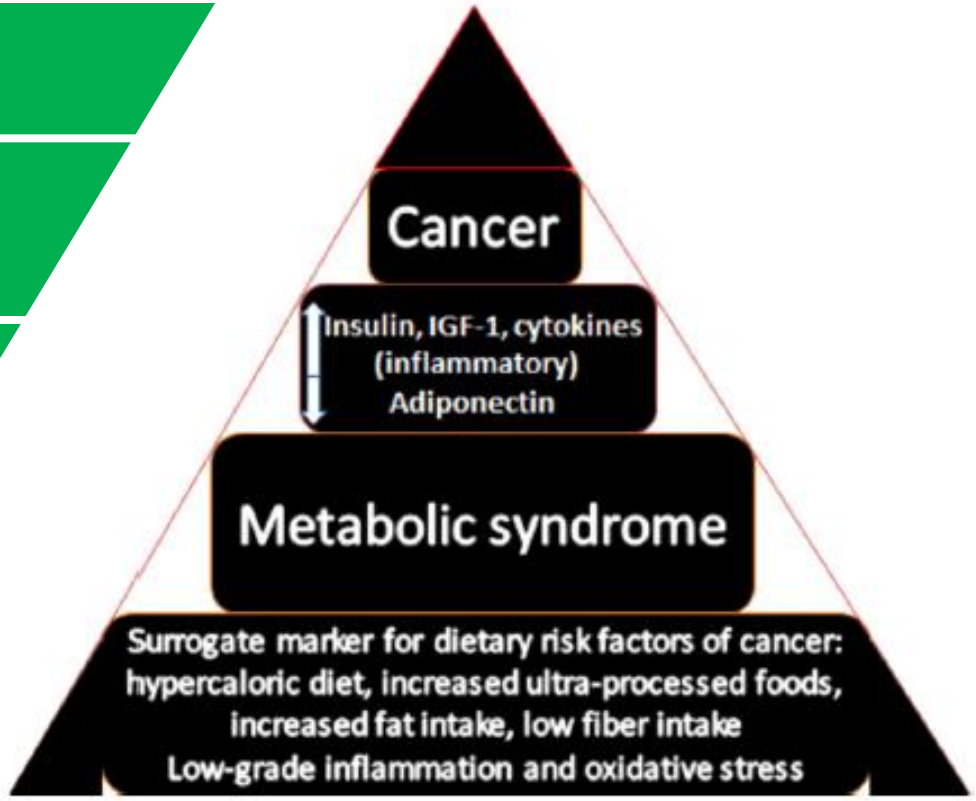
The linear radiation dose-response relationship identified can be used to predict CHD risk for future HL patients and survivors. Appropriate early management of CHD risk factors and stimulation of physical activity may reduce CHD risk in HL survivors.

J Clin Oncol 34:235-243.

"Common soil hypothesis"

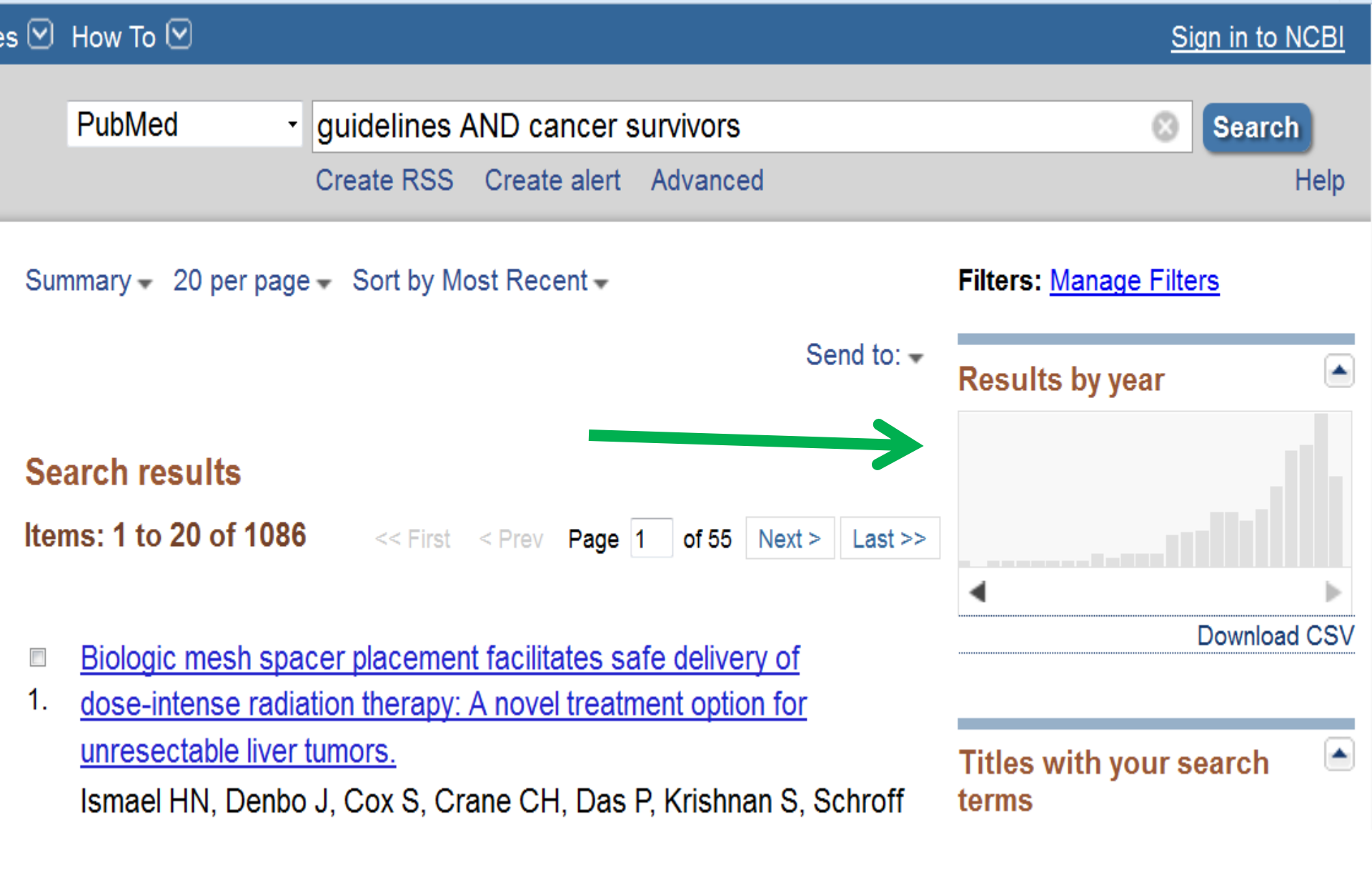
Metabolic syndrome and cancer: which direction?





Esposito K et al, Endocrine 2013

Survivorship Care & Linee Guida



AHA Scientific Statement

Long-term Cardiovascular Toxicity in Children, Adolescents, and Young Adults Who Receive Cancer Therapy: Pathophysiology, Course, Monitoring, Management, Prevention, and Research Directions

A Scientific Statement From the American Heart Association

Steven E. Lipshultz, MD, FAHA, Chair; M. Jacob Adams, MD, MPH; Steven D. Colan, MD, FAHA; Louis S. Constine, MD; Eugene H. Herman, PhD; Daphne T. Hsu, MD, FAHA; Melissa M. Hudson, MD; Leontien C. Kremer, MD, PhD; David C. Landy, PhD; Tracie L. Miller, MD; Kevin C. Oeffinger, MD; David N. Rosenthal, MD; Craig A. Sable, MD, FAHA; Stephen E. Sallan, MD; Gautam K. Singh, MD; Julia Steinberger, MD, MS, FAHA; Thomas R. Cochran, BA; James D. Wilkinson, MD, MPH; on behalf of the American Heart Association Congenital Heart Defects Committee of the Council on Cardiovascular Disease in the Young, Council on Basic Cardiovascular Sciences, Council on Cardiovascular and Stroke Nursing, Council on Cardiovascular Radiology and Intervention, Council on Clinical Cardiology, Council on Epidemiology and Prevention, and Council on Nutrition, Physical Activity and Metabolism

Endorsed by the American Academy of Pediatrics

(*Circulation*. 2013;128:1927-1995.)

The present scientific statement is not meant to be an evidence-based guideline. Specific recommendations for care have not been provided, and other initiatives are currently focused on guideline development for survivors of childhood, adolescent, and young adult cancer.

Recommendations for Cardiomyopathy Surveillance for Survivors of Childhood Cancer: A Report from the International Late Effects of Childhood Cancer Guideline Harmonization Group

Saro H. Armenian[1], Melissa M. Hudson[2], Renee L. Mulder[3], Ming Hui Chen[4], Louis S. Constine[5], Mary Dwyer[6], Paul C. Nathan[7], Wim J.E. Tissing[8], Sadhna Shankar[9], Elske Sieswerda[3], Rod Skinner[10], Julia Steinberger[11], Elvira C. van Dalen[3], Helena van der Pal[12], W. Hamish Wallace[13], Gill Levitt[14], and Leontien C.M. Kremer[3]

Abstract

Childhood cancer survivors treated with anthracycline chemotherapy or chest radiation are at an increased risk of developing congestive heart failure (CHF). In this population, CHF is well-recognized as a progressive disorder, with a variable period of asymptomatic cardiomyopathy which precedes signs and symptoms. As a result, a number of practice guidelines have been developed to facilitate detection and treatment of asymptomatic cardiomyopathy. These guidelines differ with regards to definitions of at risk populations, surveillance modality and frequency, and recommendations for interventions. These differences may hinder the effective implementation of these recommendations. We report on the results of an international collaboration to harmonize existing cardiomyopathy surveillance recommendations, using an evidence-based approach that relied on standardized definitions for outcomes of interest and transparent presentation of the quality of the evidence. The resultant recommendations were graded according to the quality of the evidence and the potential benefit gained from early detection and intervention.

Lancet Oncol 2015

Recommendations for cardiomyopathy surveillance for survivors of childhood cancer: a report from the International Late Effects of Childhood Cancer Guideline Harmonization Group

International Guideline Harmonization Group

Who needs cardiomyopathy surveillance?	
Patients treated with anthracyclines	Cardiomyopathy surveillance is recommended for survivors treated with high dose (≥250 mg/m²) anthracyclines
	Cardiomyopathy surveillance is reasonable for survivors treated with moderate dose (≥100 to <250 mg/m²) anthracyclines
Patients treated with	conventional fractionation
Patients treated with anthracyclines + chest radiation	Cardiomyopathy surveillance is recommended for survivors treated with moderate to high dose anthracyclines (≥100 mg/m²) and moderate to high dose chest radiation (≥15 Gy)

Cardiomyopathy surveillance is recommended for CAYACS treated with high dose anthracyclines (>250 mg/m²), high dose chest radiation (>35 Gy) or anthracyclines + chest radiation, but is also reasonable for those treated with lower doses.

Armenian S et al, Lancet Oncol 2015

Recommendations for cardiomyopathy surveillance for survivors of childhood cancer: a report from the International Late Effects of Childhood Cancer Guideline Harmonization Group

International Guideline Harmonization Group
for Late Effects of Childhood Cancer

What surveillance modality should be used?	Echocardiography is recommended as the primary cardiomyopathy surveillance modality for assessment of left ventricular systolic function in survivors treated with anthracyclines or chest radiation
At what frequency should surveillance be performed for moderate or low risk survivors?	Cardiomyopathy surveillance is reasonable for moderate and low risk survivors to begin no later than 2 years after completion of cardiotoxic therapy, repeated at 5 years after diagnosis and continue every 5 years thereafter
	More frequent cardiomyopathy surveillance may be reasonable for moderate and low risk survivors Lifelong cardiomyopathy surveillance may be reasonable for moderate and low risk survivors

Echocardiography is recommended as the primary modality for the cardiomyophaty surveillance, to begin no later than 2 years after the completion of therapy.

The evaluation should be repeated at 5 years after diagnosis and continued every 5 years thereafter .

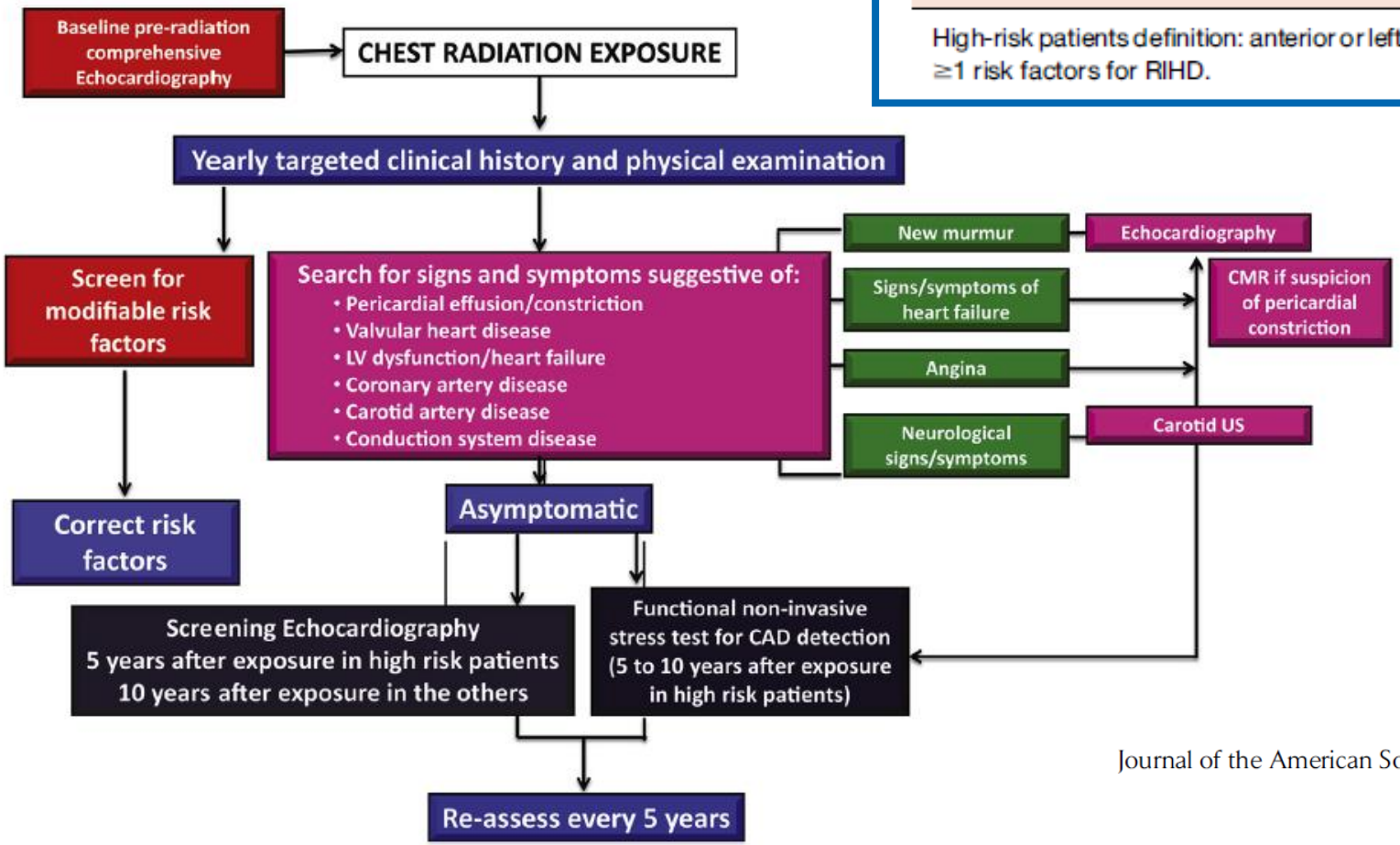
Armenian S et al, Lancet Oncol 2015

Expert Consensus for Multi-Modality Imaging Evaluation of Cardiovascular Complications of Radiotherapy in Adults: A Report from the European Association of Cardiovascular Imaging and the American Society of Echocardiography

Table 2 Risk factors of radiation-induced heart disease

Anterior or left chest irradiation location
High cumulative dose of radiation (>30 Gy)
Younger patients (<50 years)
High dose of radiation fractions (>2 Gy/day)
Presence and extent of tumour in or next to the heart
Lack of shielding
Concomitant chemotherapy (the anthracyclines considerably increase the risk)
Cardiovascular risk factors (i.e. diabetes mellitus, smoking, overweight, ≥moderate hypertension, hypercholesterolaemia)
Pre-existing cardiovascular disease

High-risk patients definition: anterior or left-side chest irradiation with ≥1 risk factors for RIHD.



Journal of the American Society of Echocardiography
September 2013

REVIEW | Annals of Internal Medicine

Systematic Review: Surveillance for Breast Cancer in Women Treated With Chest Radiation for Childhood, Adolescent, or Young Adult Cancer

Tara O. Henderson, MD, MPH; Alison Amsterdam, MD; Smita Bhatia, MD, MPH; Melissa M. Hudson, MD; Anna T. Meadows, MD; Joseph P. Neglia, MD, MPH; Lisa R. Diller, MD; Louis S. Constine, MD; Robert A. Smith, PhD; Martin C. Mahoney, MD, PhD; Elizabeth A. Morris, MD; Leslie L. Montgomery, MD; Wendy Landier, MSN, CPNP; Stephanie M. Smith, MPH; Leslie L. Robison, PhD; and Kevin C. Oeffinger, MD

Data Synthesis: **Standardized incidence ratios ranged from 13.3 to 55.5; cumulative incidence of breast cancer by age 40 to 45 years ranged from 13% to 20%.** Risk for breast cancer increased linearly with chest radiation dose. Available limited evidence suggests that the characteristics of breast cancer in these women and the outcomes after diagnosis are similar to those of women in the general population; mammography can detect breast cancer, although sensitivity is limited.

Ann Intern Med. 2010;152:444-455.

Breast Cancer Screening and Diagnosis

Version 1.2015

Increased Risk:

Prior history of breast cancer → See NCCN Guidelines for Breast Cancer - Surveillance Section

Women ≥35 y with 5-year risk of invasive breast cancer ≥1.7%[d]

OR

Women who have a lifetime risk >20% based on history of LCIS or ADH/ALH

OR

→
- Annual screening mammogram[h] + clinical breast exam[a] every 6–12 mo[l]
  - to begin at diagnosis but not less than age 30 y
- Breast awareness[g]
- Consider risk reduction strategies (See NCCN Guidelines for Breast Cancer Risk Redu

Women who have a lifetime risk >20% as defined by models that are largely dependent on family history[e] →
- Annual screening mammogram[h] + clinical breast exam[a] every 6–12 mo[l]
  - to begin 10 years prior to youngest family member but not less than age 30 y
- Breast awareness[g]
- Consider risk reduction strategies (See NCCN Guidelines for Breast Cancer Risk Redu
- Recommend annual breast MRI[l]
  - to begin 10 years prior to youngest family member but not less than age 30 y
- Referral to genetic counseling if not already done

Prior thoracic RT between the ages of 10 and 30 y

Current age <25 y →
- Annual clinical breast exam[a]
  - beginning 8–10 y after RT
- Breast awareness[g]

Current age ≥25 y →
- Annual screening mammogram[h] + clinical breast exam[a] every 6–12 mo[l]
  - Begin 8–10 y after RT
- Recommend annual breast MRI[l]
- Breast awareness[g]

Recommendations for breast cancer surveillance for female survivors of childhood, adolescent, and young adult cancer given chest radiation: a report from the International Late Effects of Childhood Cancer Guideline Harmonization Group

Renée L Mulder, Leontien C M Kremer, Melissa M Hudson, Smita Bhatia, Wendy Landier, Gill Levitt, Louis S Constine, W Hamish Wallace, Flora E van Leeuwen, Cécile M Ronckers, Tara O Henderson, Mary Dwyer, Roderick Skinner, Kevin C Oeffinger

	North American Children's Oncology Group	Dutch Childhood Oncology Group	UK Children's Cancer and Leukaemia Group	Concordant or discordant
Who needs breast cancer surveillance?				
At risk				
Chest radiation	Yes	Yes	Yes	Concordant
Chest radiation plus alkylating agents*	Not specified	Not specified	Yes	Discordant
High risk	Not specified	7–20 Gy chest radiation (excluding total body irradiation); 14–40 Gy abdominal radiation	Not specified	Discordant
Highest risk	≥20 Gy chest radiation	≥20 Gy chest radiation; ≥40 Gy abdominal radiation; total body irradiation	Not specified	Discordant
At what age should breast cancer surveillance be initiated?	25 years	25 years	25 years	Concordant

Lancet Oncol 2013; 14: e621–29

Recommendations for breast cancer surveillance for female survivors of childhood, adolescent, and young adult cancer given chest radiation: a report from the International Late Effects of Childhood Cancer Guideline Harmonization Group

Renée L Mulder, Leontien C M Kremer, Melissa M Hudson, Smita Bhatia, Wendy Landier, Gill Levitt, Louis S Constine, W Hamish Wallace, Flora E van Leeuwen, Cécile M Ronckers, Tara O Henderson, Mary Dwyer, Roderick Skinner, Kevin C Oeffinger

Panel 1: Harmonised recommendations for breast cancer surveillance for female survivors of CAYA cancer given chest radiation before age 30 years*

Who needs breast cancer surveillance?

- Strong recommendation: providers and female survivors of CAYA cancer given chest radiation should be aware of breast cancer risk
- Strong recommendation: breast cancer surveillance is recommended for those given 20 Gy or higher chest radiation
- Moderate recommendation: breast cancer surveillance is reasonable for those given 10–19 Gy chest radiation, based on clinical judgment and additional risk factors
- Weak recommendation: breast cancer surveillance might be reasonable for those given 1–9 Gy chest radiation, based on clinical judgment and additional risk factors

Lancet Oncol 2013; 14: e621–29

Recommendations for breast cancer surveillance for female survivors of childhood, adolescent, and young adult cancer given chest radiation: a report from the International Late Effects of Childhood Cancer Guideline Harmonization Group

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At what age should breast cancer surveillance be initiated?

- Strong recommendation: initiation of breast cancer surveillance is recommended at age 25 years or at least 8 years after radiation (whichever occurs last) for those given 20 Gy or higher chest radiation
- Moderate recommendation: initiation of breast cancer surveillance is reasonable at age 25 years or at least 8 years after radiation (whichever occurs last) for those given 10–19 Gy chest radiation
- Weak recommendation: initiation of breast cancer surveillance might be reasonable at age 25 years or at least 8 years after radiation (whichever occurs last) for those given 1–9 Gy chest radiation

Lancet Oncol 2013; 14: e621–29

Recommendations for breast cancer surveillance for female survivors of childhood, adolescent, and young adult cancer given chest radiation: a report from the International Late Effects of Childhood Cancer Guideline Harmonization Group

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At what frequency should breast cancer surveillance be done?

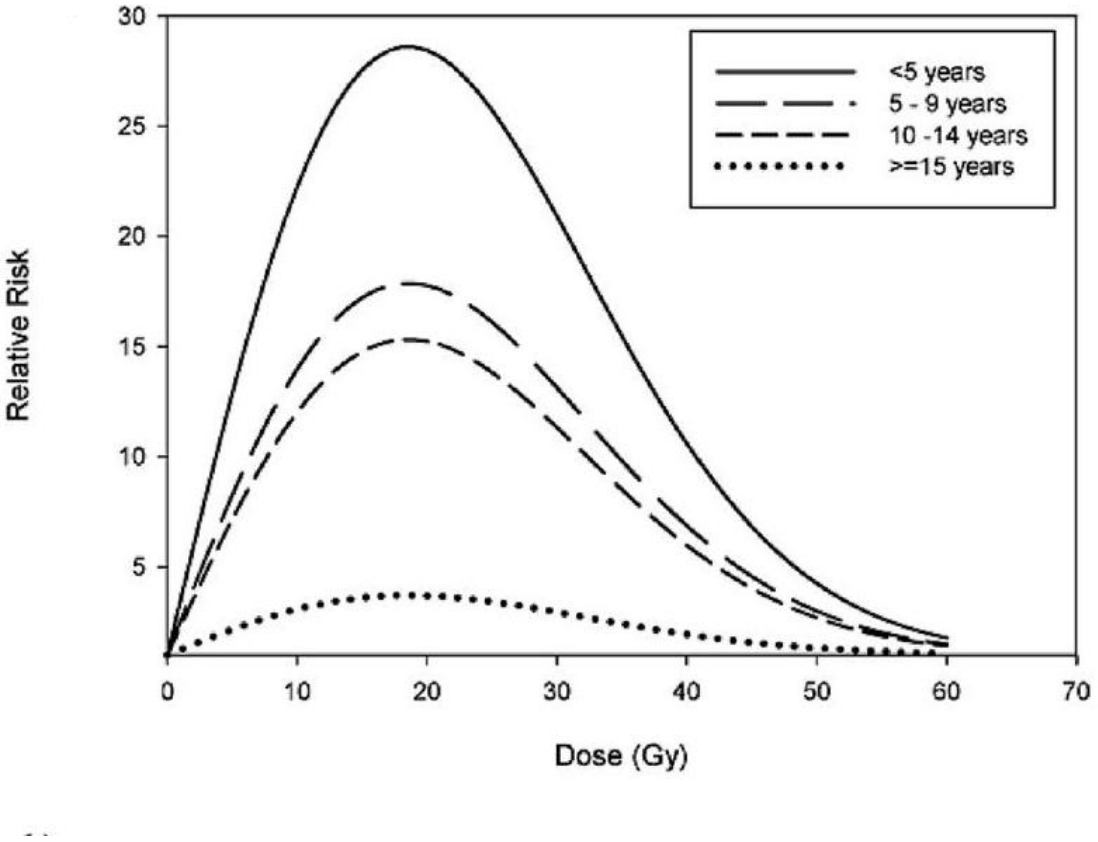
- Strong recommendation: annual breast cancer surveillance is recommended for those given 20 Gy or higher chest radiation, for at least up to age 50 years
- Moderate recommendation: annual breast cancer surveillance is reasonable for those given 10–19 Gy chest radiation, for at least up to age 50 years
- Weak recommendation: annual breast cancer surveillance might be reasonable for those given 1–9 Gy chest radiation, for at least up to age 50 years

What surveillance method should be used?

- Strong recommendation: mammography, breast MRI, or both is recommended. Evidence is insufficient to recommend the ideal imaging method

Lancet Oncol 2013; 14: e621–29

Carcinoma tiroideo & cancer survivors



Il rischio di **carcinoma tiroideo** nei *childhood cancer survivors* aumenta con il diminuire dell' **età alla radioterapia**.

Il rischio aumenta in modo lineare fino alla **dose di 20-25 Gy**, poi si riduce (ed aumenta quello di ipotiroidismo*).*

Bhatti et al, Radiat Res 2010

Thyroid neoplasms following radiotherapy may not become evident for many years after exposure to radiation: ***therefore, all individuals at risk require lifelong follow-up.***

Ultrasound Screening for Thyroid Carcinoma in Childhood Cancer Survivors: A Case Series

Enrico Brignardello, Andrea Corrias, Giuseppe Isolato, Nicola Palestini, Luca Cordero di Montezemolo, Franca Fagioli, and Giuseppe Boccuzzi

Transition Unit for Childhood Cancer Survivors (E.B.) and Oncological Endocrinology (E.B., G.B.), San Giovanni Battista Hospital, 10126 Turin, Italy; Pediatric Endocrinology (A.C.) and Pediatric Hematology Oncology Unit (F.F.), Regina Margherita Children's Hospital, 10126 Turin, Italy; and Institute of Diagnostic and Interventional Radiology (G.I.), Department of Surgery (N.P.), Pediatric Hematology Oncology Unit (L.C.d.M.), and Department of Clinical Pathophysiology (G.B.), University of Turin, 10126 Turin, Italy

Context: Childhood cancer survivors need regular monitoring into young adulthood and beyond, because they are at risk for developing late-onset complications of cancer therapy, including second malignancies.

Objective: This study focuses on the use of thyroid ultrasound to screen for thyroid carcinoma in a population of childhood cancer survivors.

Patients: A total of 129 subjects who had received radiotherapy to the head, neck, or upper thorax for a pediatric cancer were studied in the setting of a long-term follow-up unit.

Design: Thyroid ultrasound usually began 5 yr after radiotherapy and was repeated every third year, if negative. Median follow-up time since childhood cancer diagnosis was 15.8 yr (range 6.1–34.8 yr). Solid thyroid nodules were found in 35 patients. Fine-needle aspiration was performed in 19 patients, of which 14 had nodules above 1 cm.

Main Outcome Measure: The main outcome measure was the finding of not palpable thyroid cancers.

Results: Cytological examination of specimens diagnosed papillary carcinoma in five patients who underwent surgery. The cytological diagnosis of papillary thyroid carcinoma was confirmed in all cases by histological examination. Notably, only two of these patients had palpable nodules; the other three were smaller than 1 cm and were detected only by ultrasound. However, histological examination showed nodal metastases in two of these.

Conclusions: Although ultrasound screening for thyroid cancer in the general population is not cost effective and could lead to unnecessary surgery, due to false positives, we believe that in childhood cancer survivors who received radiotherapy involving the head, neck, or upper thorax, it would be worthwhile. **(*J Clin Endocrinol Metab* 93: 4840–4843, 2008)**

European Journal of Cancer 55 (2016) 74–80

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Original Research

Ultrasound surveillance for radiation-induced thyroid carcinoma in adult survivors of childhood cancer

Enrico Brignardello [a,*], Francesco Felicetti [a], Anna Castiglione [b], Marco Gallo [c], Francesca Maletta [d], Giuseppe Isolato [e], Eleonora Biasin [f], Franca Fagioli [f], Andrea Corrias [g], Nicola Palestini [h]

Outstanding problems…

- Evidenze in continuo aggiornamento (di pari passo con l’evolvere delle terapie oncologiche)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Reduction in Late Mortality among 5-Year Survivors of Childhood Cancer

[…] we confirmed the effect of treatment regimens that have been designed to reduce the potential risk and severity of late effects. Quantitative evidence now shows that **the modification of treatment regimens to reduce radiotherapy and chemotherapy exposures, along with increased promotion of strategies for early detection of late effects and improvements in medical care for late effects of therapy, has resulted in the extension of life spans for many survivors of childhood cancer.**

Armstrong et al., N ENGL J MED 374;9 NEJM.ORG MARCH 3, 2016

NCCN Guidelines® Insights
Survivorship, Version 1.2016
Featured Updates to the NCCN Guidelines

Abstract

The NCCN Guidelines for Survivorship provide screening, evaluation, and treatment recommendations for common consequences of cancer and cancer treatment. They are intended to aid health care professionals who work with survivors of adult-onset cancer in the posttreatment period, including those in general oncology, specialty cancer survivor clinics, and primary care practices. Guidance is also provided to help promote physical activity, weight management, and proper immunizations in survivors. This article summarizes the NCCN Survivorship panel's discussions for the 2016 update of the guidelines regarding the management of anxiety, depression, posttraumatic stress disorder–related symptoms, and emotional distress in survivors.

J Natl Compr Canc Netw 2016;14(6):715–724

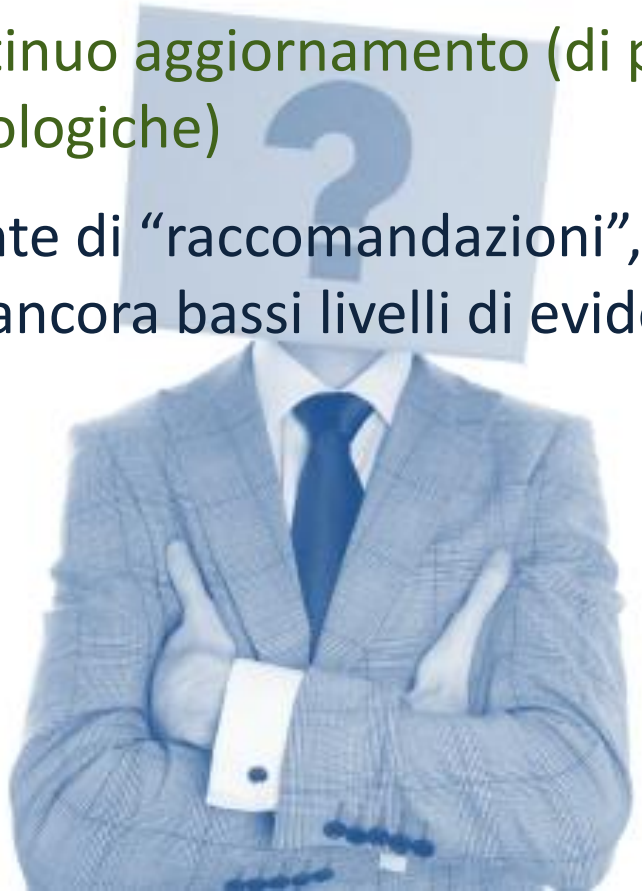
NCCN symptom specific survivorship care guidelines

- Anthracycline induced cardiac toxicity
- Anxiety and depression
- Cognitive function
- Fatigue
- Pain
- Sexual function
- Sleep disorders
- Healthy lifestyles and immunizations and infections

Outstanding problems…

- Evidenze in continuo aggiornamento (di pari passo con l'evolvere delle terapie oncologiche)

- Numero crescente di "raccomandazioni", non sempre concordanti, ma ancora bassi livelli di evidenza



American Cancer Society/American Society of Clinical Oncology Breast Cancer Survivorship Care Guideline

TABLE 6. Guideline for Assessment and Management of Physical and Psychosocial Long-Term/Late Effects

RECOMMENDATION	LEVEL OF EVIDENCE[a]
It is recommended that primary care clinicians:	
Recommendation 3.1: Body image concerns	
(a) Should assess for patient body image/appearance concerns	0 (Assessment)
(b) Should offer the option of adaptive devices (eg, breast prostheses, wigs) and/or surgery when appropriate	0 (Adaptive devices)
(c) Should refer for psychosocial care as indicated	IA (Couple-based intervention)
Recommendation 3.2: Lymphedema	
(a) Should counsel survivors on how to prevent/reduce the risk of lymphedema, including weight loss for those who are overweight or obese	0 (Prevention)
(b) Should refer patients with clinical symptoms or swelling suggestive of lymphedema to a therapist knowledgeable about the diagnosis and treatment of lymphedema, such as a physical therapist, occupational therapist, or lymphedema specialist	0 (Referral)
Recommendation 3.3: Cardiotoxicity	
(a) Should monitor lipid levels and provide cardiovascular monitoring, as indicated	0 (Monitoring)
(b) Should educate breast cancer survivors on healthy lifestyle modifications, potential cardiac risk factors, and when to report relevant symptoms (shortness of breath or fatigue) to their health care provider	I (Lifestyle modifications)
Recommendation 3.4: Cognitive impairment	
(a) Should ask patients if they are experiencing cognitive difficulties	0 (Assessment)
(b) Should assess for reversible contributing factors of cognitive impairment and optimally treat when possible	IA (Contributing factors)
(c) Should refer patient with signs of cognitive impairment for neurocognitive assessment and rehabilitation, including group cognitive training if available	IA (Group cognitive rehabilitation)

Fertility Preservation in Children, Adolescents, and Young Adults With Cancer: Quality of Clinical Practice Guidelines and Variations in Recommendations

Font-Gonzales A et al, Cancer 2016 (in press)

TABLE 2. Concordant and Discordant Guideline Areas in High-Quality Female Fertility Preservation CPGs

	Concordant[a]	% per Row	Discordant[b]	% per Row	Total
Who should be advised to receive fertility preservation?	3	27.3	8	72.7	11
What fertility preservation method should be used?	1	14.3	6	85.7	7
When should fertility preservation be discussed and initiated?	1	14.3	6	86	7
Who should be involved in the counseling and decision making regarding fertility preservation?	1	7.7	12	92.3	13
What are the ethical and logistical aspects?	0	0.0	9	100	9
Total	6	12.8	41	87.2	47

Abbreviation: CPG, clinical practice guideline.
[a] Concordant guideline areas were those that presented the same recommendation in all CPGs.
[b] Discordant guideline areas were those that did not present the same recommendation in all CPGs, those guideline areas that did not have a recommendation, or if only 1 CPG covered a guideline area.

TABLE 3. Concordant and Discordant Guideline Areas in High-Quality Male Fertility Preservation CPGs

	Concordant[a]	% per Row	Discordant[b]	% per Row	Total
Who should be advised to receive fertility preservation?	2	20.0	8	80.0	10
What fertility preservation method should be used?	1	12.5	7	87.5	8
When should fertility preservation be discussed and initiated?	1	12.5	7	87.5	8
Who should be involved in the counseling and decision making about fertility preservation?	0	0.0	13	100.0	13
What are the ethical and logistical aspects?	1	20.0	4	80.0	5
Total	5	11.4	39	88.6	44

CONCLUSIONS: Only approximately one-third of the identified CPGs were found to be of sufficient quality. Of these CPGs, the fertility preservation recommendations varied substantially, which can be a reflection of inadequate evidence for specific recommendations, thereby hindering the ability of providers to deliver high-quality care. CPGs including a transparent decision process for fertility preservation can help health care providers to deliver optimal and uniform care, thus improving the quality of life of CAYAs with cancer and cancer survivors.

International Guideline Harmonization Group

for Late Effects of Childhood Cancer

The International Late Effects of Childhood Cancer Guideline Harmonization Group, IGHG, is a worldwide endeavor initiated by several national guideline groups and the Cochrane Childhood Cancer Group in partnership with the PanCareSurFup Consortium to collaborate in guideline development.

Our main goal is to **establish a common vision and integrated strategy for the surveillance of chronic health problems and subsequent cancers in childhood, adolescent, and young adult cancer survivors.**

By international collaboration in guideline development **we aim to reduce duplication of effort, optimize the quality of care, and improve quality of life** for childhood, adolescent, and young adult cancer survivors.

We welcome all individuals who are willing to contribute to this initiative.

Topics −

- Breast cancer +
- Cardiomyopathy +
- Premature ovarian insufficiency +
- Male gonadotoxicity
- Thyroid cancer
- Central nervous system neoplasms
- Vasculopathy
- Metabolic syndrome
- Ototoxicity
- Pulmonary dysfunction
- Hypothalamic-pituitary dysfunction
- Fatigue, mental health and psychosocial problems

Surveillance Imaging in Patients in Remission From Hodgkin and Diffuse Large B-Cell Lymphoma

Chadi Nabhan, MD; Sonali M. Smith, MD; Adam S. Cifu, MD

GUIDELINE TITLE Follow-up Surveillance Imaging for Hodgkin and Diffuse Large B-Cell Lymphoma Patients in Remission Without Clinical or Radiographic Evidence of Disease

DEVELOPERS National Comprehensive Cancer Network (NCCN) and European Society of Medical Oncology (ESMO)

RELEASE DATES July 2014, May 2015, August 2015, February 2016

PRIOR VERSIONS 2011, 2012, 2014

FUNDING SOURCE For the NCCN, annual dues from member institutions; for the ESMO, the European Medical Association

TARGET POPULATION All patients with Hodgkin and diffuse large B-cell non-Hodgkin lymphomas who have completed initial therapy and are in complete remission

MAJOR RECOMMENDATIONS

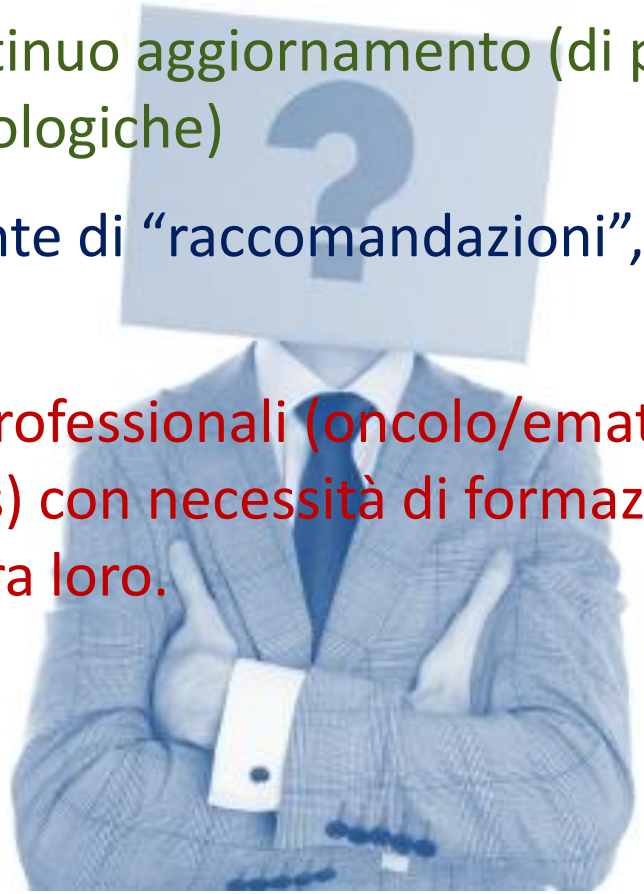
- Once remission is confirmed in patients with Hodgkin lymphoma, imaging should be done as clinically indicated. No routine screening imaging is recommended. Surveillance positron emission tomography (PET) scans are not recommended.
- Beyond 5 years, Hodgkin lymphoma patients with higher risk of lung cancer (prior radiation therapy to chest and/or prior use of alkylating agents) should undergo annual low-dose chest computed tomography (CT).
- Women with Hodgkin lymphoma and prior chest/axillary radiation should have yearly magnetic resonance imaging (MRI) or mammograms starting 8 to 10 years after therapy completion or at age 40 years, whichever comes first.
- Imaging studies should be conducted only as clinically indicated (for abnormal laboratory results, atypical examination findings, or abnormal symptoms) for diffuse large B-cell lymphoma patients in remission (NCCN) or at a very low frequency (6, 12, and 24 months) only (ESMO). Surveillance PET scans are not recommended.

Outstanding problems…

- Evidenze in continuo aggiornamento (di pari passo con l'evolvere delle terapie oncologiche)

- Numero crescente di "raccomandazioni", ma ancora bassi livelli di evidenza

- Diverse figure professionali (oncolo/ematologo, **MMG**, Late effects physicians) con necessità di formazione specifica e coordinamento fra loro.



The role of the GP in follow-up cancer care: a systematic literature review

Judith A. Meiklejohn[1] · Alexander Mimery[2] · Jennifer H. Martin[3,4] · Ross Bailie[5] · Gail Garvey[6] · Euan T. Walpole[7,8,9] · Jon Adams[10] · Daniel Williamson[11] · Patricia C. Valery[1,12]

J Cancer Surviv
DOI 10.1007/s11764-016-0545-4
Published online: 02 May 2016

… **GPs and patients across the included studies supported a greater GP role in follow-up cancer care**. This included greater support for **care coordination, screening, diagnosis and management of physical and psychological effects of cancer and its treatment**, symptom and pain relief, health promotion, palliative care and continuing normal general health care provision.

Conclusion While there are variations in guidelines and practice of follow-up cancer care in the primary health care sector, GPs and patients across the reviewed studies supported a greater role by the GP.

Implications for Cancer Survivors: **Greater GP role in cancer care could improve the quality of patient care for cancer survivors**. **Better communication between the tertiary sector and GP across the cancer phases would enable clear delineation of roles.**

American Cancer Society/American Society of Clinical Oncology Breast Cancer Survivorship Care Guideline

Carolyn D. Runowicz, MD[1]; Corinne R. Leach, PhD, MS, MPH[2]*; N. Lynn Henry, MD, PhD[3]; Karen S. Henry, MSN, ARNP, FNP-BC, AOCNP[4]; Heather T. Mackey, RN, MSN, ANP, AOCN[5]; Rebecca L. Cowens-Alvarado, MPH[6]; Rachel S. Cannady, BS[7]; Mandi L. Pratt-Chapman, MA[8]; Stephen B. Edge, MD, FACS[9]; Linda A. Jacobs, PhD, RN[10]; Arti Hurria, MD[11]; Lawrence B. Marks, MD[12]; Samuel J. LaMonte, MD[13]; Ellen Warner, MD, FRCPC, FACP, MSc[14]; Gary H. Lyman, MD, MPH, FASCO, FACP[15]; Patricia A. Ganz, MD[16]

TABLE 8. Care Coordination Guideline

CA CANCER J CLIN 2016;66:43–73

RECOMMENDATION	LEVEL OF EVIDENCE[a]
It is recommended that primary care clinicians:	
Recommendation 5.1: Survivorship care plan	
Should consult with the cancer treatment team and obtain a treatment summary and survivorship care plan	0, III
Recommendation 5.2: Communication with oncology team	
Should maintain communication with the oncology team throughout your patient's diagnosis, treatment, and posttreatment care to ensure care is evidence-based and well-coordinated	0

The purpose of the American Cancer Society/American Society of Clinical Oncology Breast Cancer Survivorship Care Guideline is to **provide recommendations to assist primary care and other clinicians** in the care of female adult survivors of breast cancer.

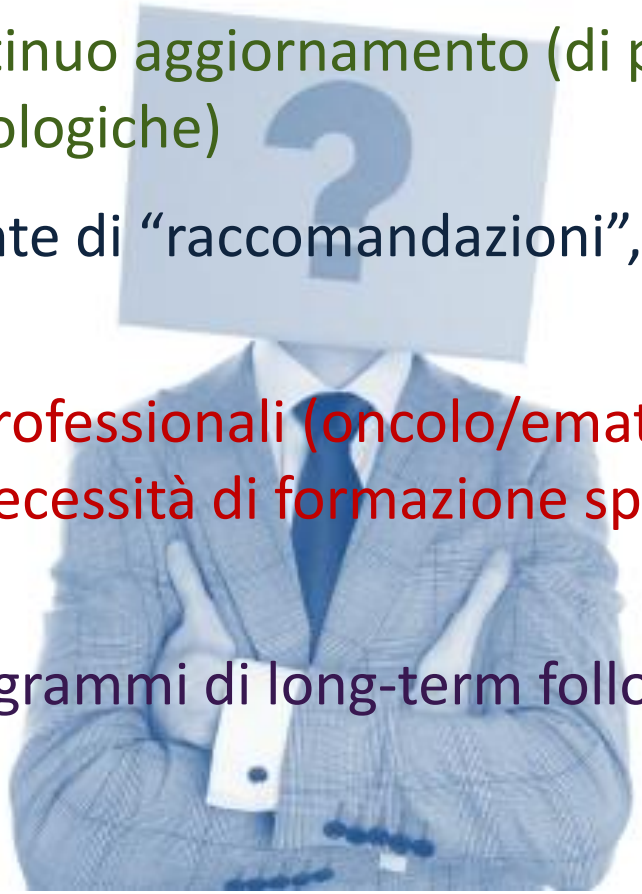
Outstanding problems…

- Evidenze in continuo aggiornamento (di pari passo con l'evolvere delle terapie oncologiche)

- Numero crescente di "raccomandazioni", ma ancora bassi livelli di evidenza

- Diverse figure professionali (oncolo/ematologo, **MMG**, LTFU physicians) con necessità di formazione specifica e coordinamento fra loro.

- Aderenza ai programmi di long-term follow-up



Survivorship care plans and adherence to lifestyle recommendations among breast cancer survivors

J Cancer Surviv
DOI 10.1007/s11764-016-0541-8

Heather Greenlee[1,2] · Christine L. Sardo Molmenti[1,2] · Katherine D. Crew[1,2,3] · Danielle Awad[2] · Kevin Kalinsky[2,3] · Lois Brafman[2] · Deborah Fuentes[2] · Zaixing Shi[1] · Wei-Yann Tsai[2,4] · Alfred I. Neugut[1,2,3] · Dawn L. Hershman[1,2,3]

Conclusions The intervention changed lifestyle behaviors and knowledge in the short-term, but the benefits did not persist. *Implications for Cancer Survivors* Culturally competent long-term behavioral interventions should be tested beyond the survivorship care plan to facilitate long-term behavior change among breast cancer survivors.

Adherence to cancer screening guidelines in Australian survivors of allogeneic blood and marrow transplantation (BMT)

Gemma Dyer[1,2], Stephen R. Larsen[3], Nicole Gilroy[2], Lisa Brice[4], Matt Greenwood[1,4,5], Mark Hertzberg[6], Masura Kabir[7], Louisa Brown[8], Megan Hogg[9], Gillian Huang[9], John Moore[10], David Gottlieb[9], John Kwan[9], Jeff Tan[10], Christopher Ward[1,4,5] & Ian Kerridge[1,4,5]

Older BMT survivors and those >2 years post transplant were more likely to undergo cancer screening. Improved quality of life was associated with screening for skin, breast, and cervical cancer. Fear of cancer recurrence negatively impacted on cervical screening. **For those who had not undergone screening, the majority reported not being advised to do so by their treatment team.**

Outstanding problems…

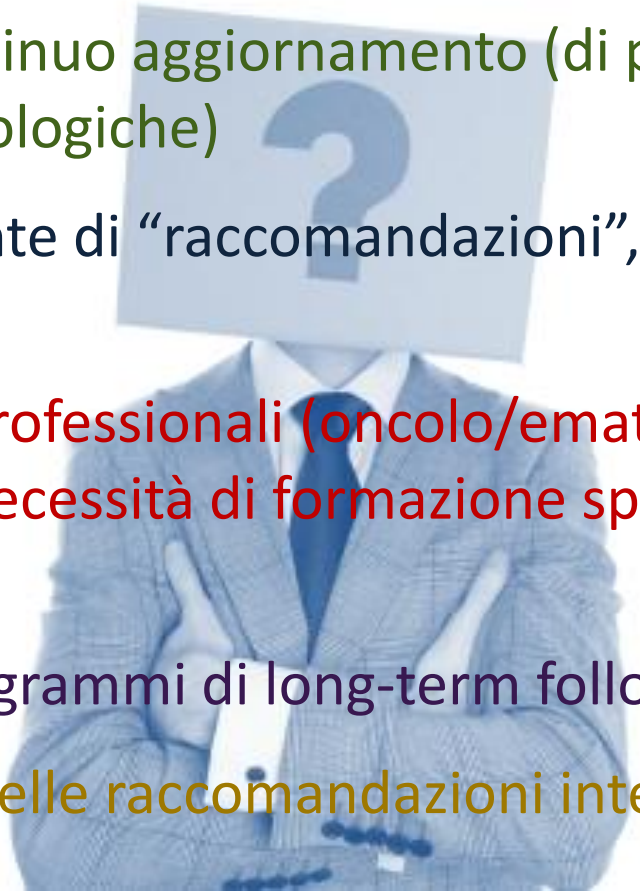
- Evidenze in continuo aggiornamento (di pari passo con l'evolvere delle terapie oncologiche)

- Numero crescente di "raccomandazioni", ma ancora bassi livelli di evidenza

- Diverse figure professionali (oncolo/ematologo, **MMG**, LTFU physicians) con necessità di formazione specifica e coordinamento fra loro.

- Aderenza ai programmi di long-term follow-up

- Adeguamento delle raccomandazioni internazionali alla pratica clinica locale



Valutazione cardiovascolare in pazienti con tumore

Coordinatore: Mauro Giorgi

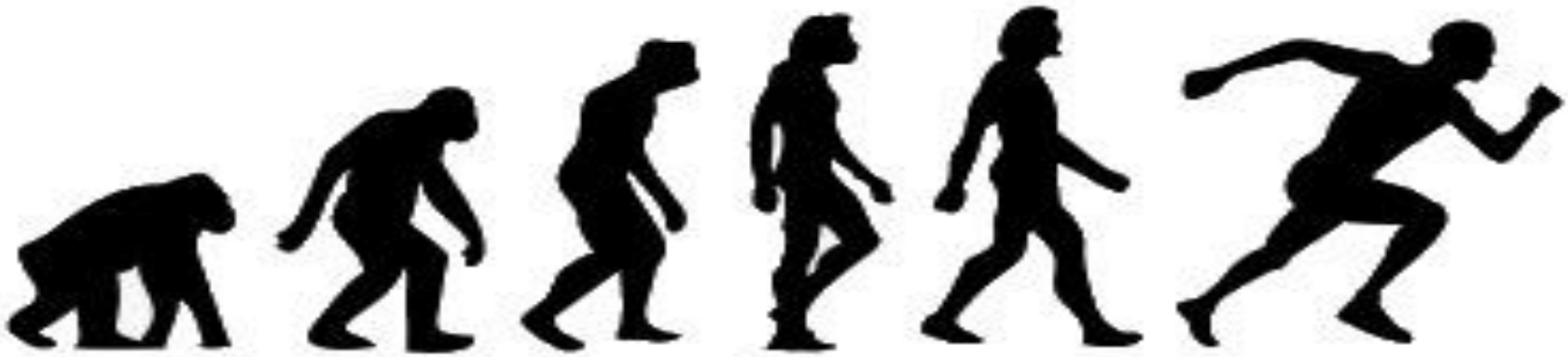
Partecipanti: Anselmino Monica, Barisone Andrea, Barolo Stefano, Bertola Benedetta, Bianco Matteo, Bonzano Alessandro, Borletto Franco, Brero Lidia Maria Teresa, Brignardello Enrico, Carrieri Luisella, Chiappella Annalisa, Ciorba Angelica, Coletti Moia Elena, Costante Annamaria, Demicheli Gloria, Destefanis Paola, De Vecchi Simona, Dogliani Sarah, Facilissimo Ivan, Fava Antonella, Ferrando Maria Luisa, Forno Davide, Gardiol Silvia, Giglio Tos Giovanna, Giorgi Mauro, Lario Chiara Valentina, Levis Mario, Luciano Alessia, Lusardi Paola, Marrara Federica, Mistrangelo Marinella, Pagliaro Maria, Parrini Iris, Pelloni Elisa, Piovano Pier Luigi, Ponzetti Agostino, Pregno Patrizia, Rebuffo Ezio Maria, Rossi Lidia, Sciscioli Tiziana, Solario Cristina, Vaccarino Antonella

A.O.U. CITTA' DELLA SALUTE E DELLA SCIENZA DI TORINO

G.I.C. TOSSICITA' TARDIVE DELLE TERAPIE ONCOLOGICHE
(Referente: Dr. Enrico Brignardello)

RACCOMANDAZIONI PER IL MONITORAGGIO A LUNGO TERMINE DEI PAZIENTI PRECEDENTEMENTE CURATI PER LINFOMA DI HODGKIN

Le presenti raccomandazioni sono applicabili al paziente precedentemente curato per linfoma di Hodgkin, off-therapy ed in remissione completa di malattia da almeno 5 anni.



TO BE CONTINUED...

G.d.L. MONITORAGGIO CLINICO A LUNGO TERMINE DEL PAZIENTE ONCOLOGICO: TOSSICITA' DELLE TERAPIE ANTITUMORALI

rete oncologica
PIEMONTE | VALLE D'AOSTA
si prende cura di te