76° CONGRESSO NAZIONALE
PROSSIMITÀ E ORGANIZZAZIONE DELLE CURE:
LA MEDICINA GENERALE DI DOMANI TRA DEMOGRAFIA E CRONICITÀ

PERCORSI SIMPeSV PER UN AMBULATORIO DEGLI STILI DI VITA

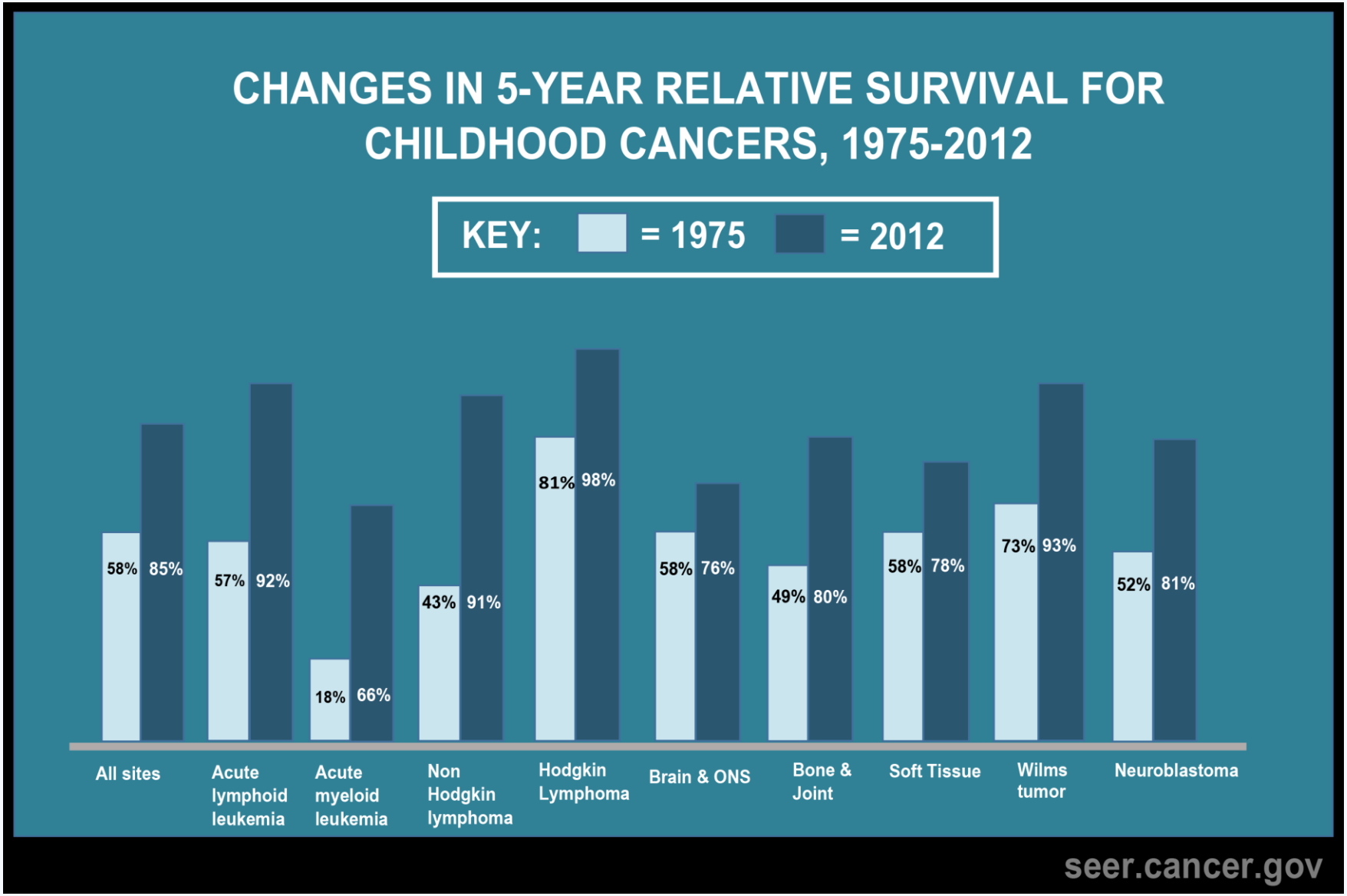
I pazienti guariti da un tumore dell'adulto: una popolazione in crescita

Enrico Brignardello

Unità di Transizione per Neoplasie Curate in Età Pediatrica

7- 12 OTTOBRE 2019 - Tanka Village - Villasimius (CA)

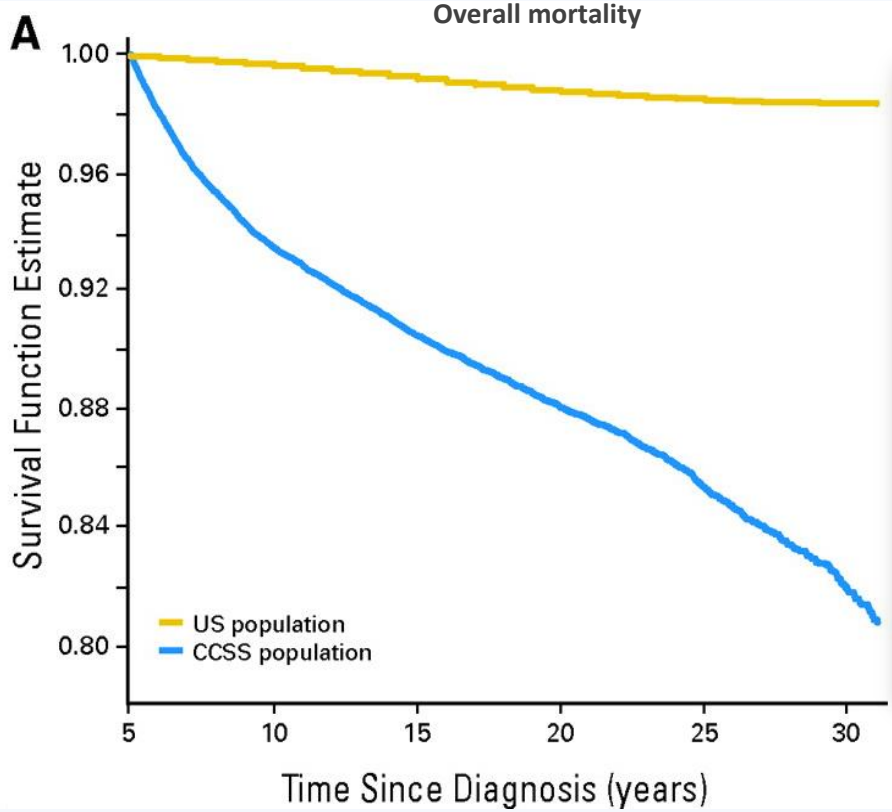
CHANGES IN 5-YEAR RELATIVE SURVIVAL FOR CHILDHOOD CANCERS, 1975-2012



seer.cancer.gov

Il prezzo del successo

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**.



I soggetti guariti da una neoplasia dell'età evolutiva risultano infatti spesso affetti da patologie inquadrabili come **complicanza cronica** dei pregressi trattamenti antitumorali.

La mortalità complessiva è 18.1% (95% CI, 17.3 to 18.9) a 30 anni dalla diagnosi di tumore pediatrico

Armstrong et al., JCO, 2009

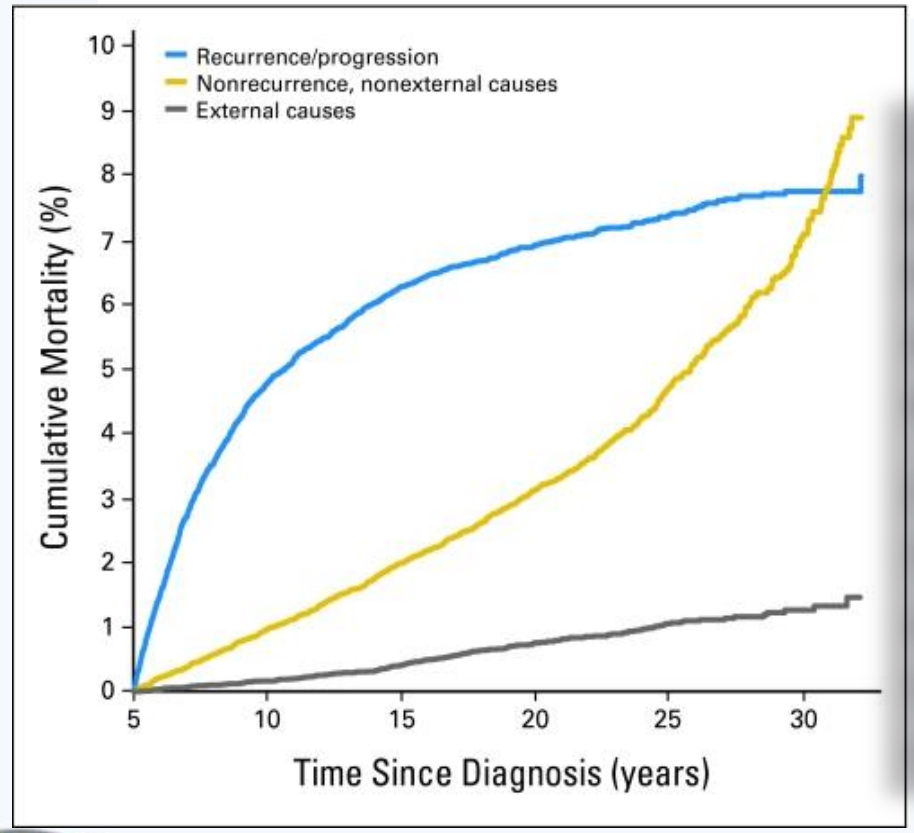
VOLUME 27 · NUMBER 14 · MAY 10 2009

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

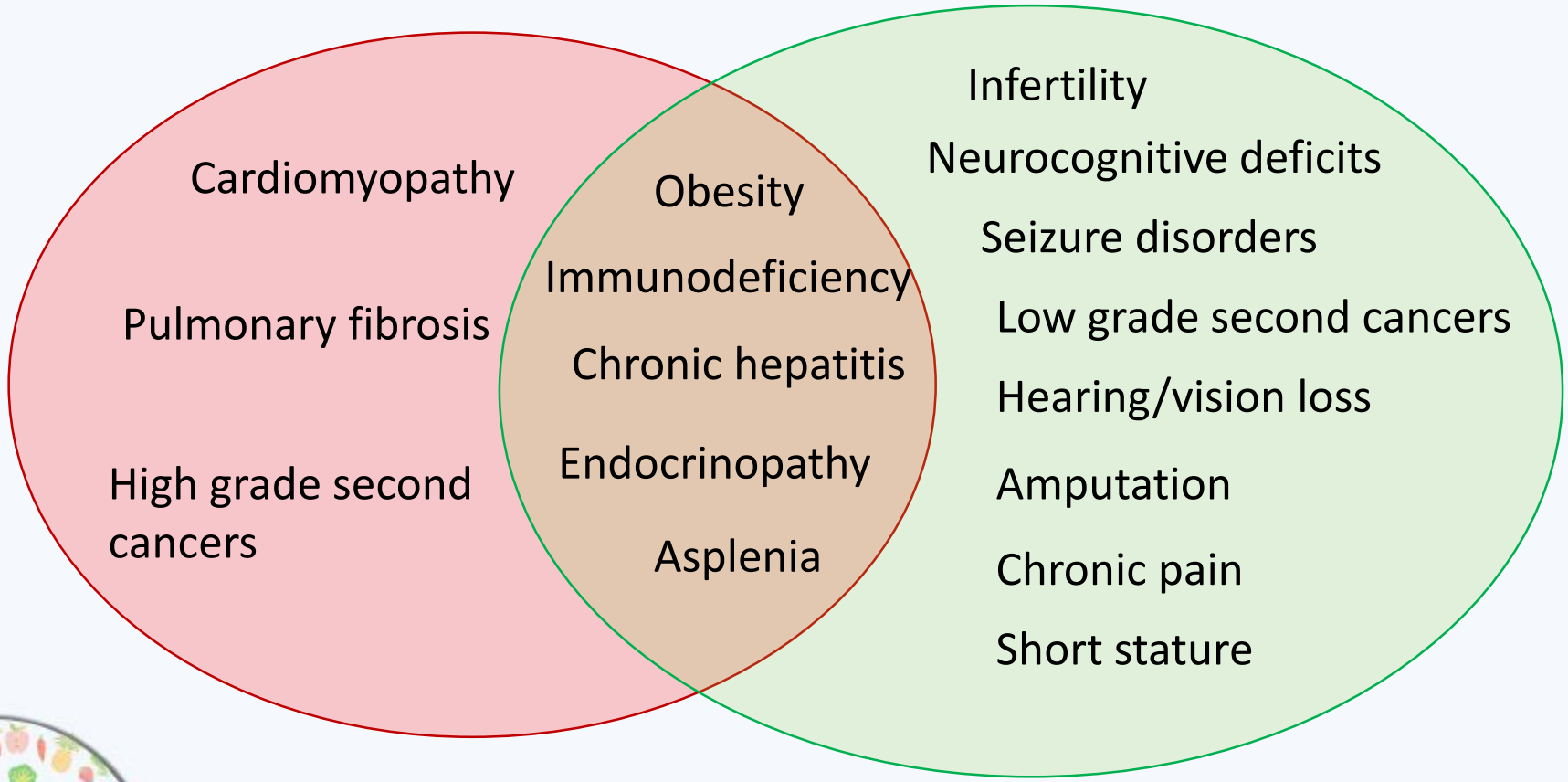


Col passare del tempo la **mortalità riferibile a progressione o recidiva del tumore** primitive **si reduce**, mentre **aumenta quella riferibile ai late effects** delle terapie antitumorali.

I *secondi tumori maligni* (SMR, 15.2; 95% CI, 13.9 to 16.6) e le **malattie cardiovascolari** (SMR, 7.0; 95% CI, 5.9 to 8.2) sono le cause principali di questo ecesso di mortalità.

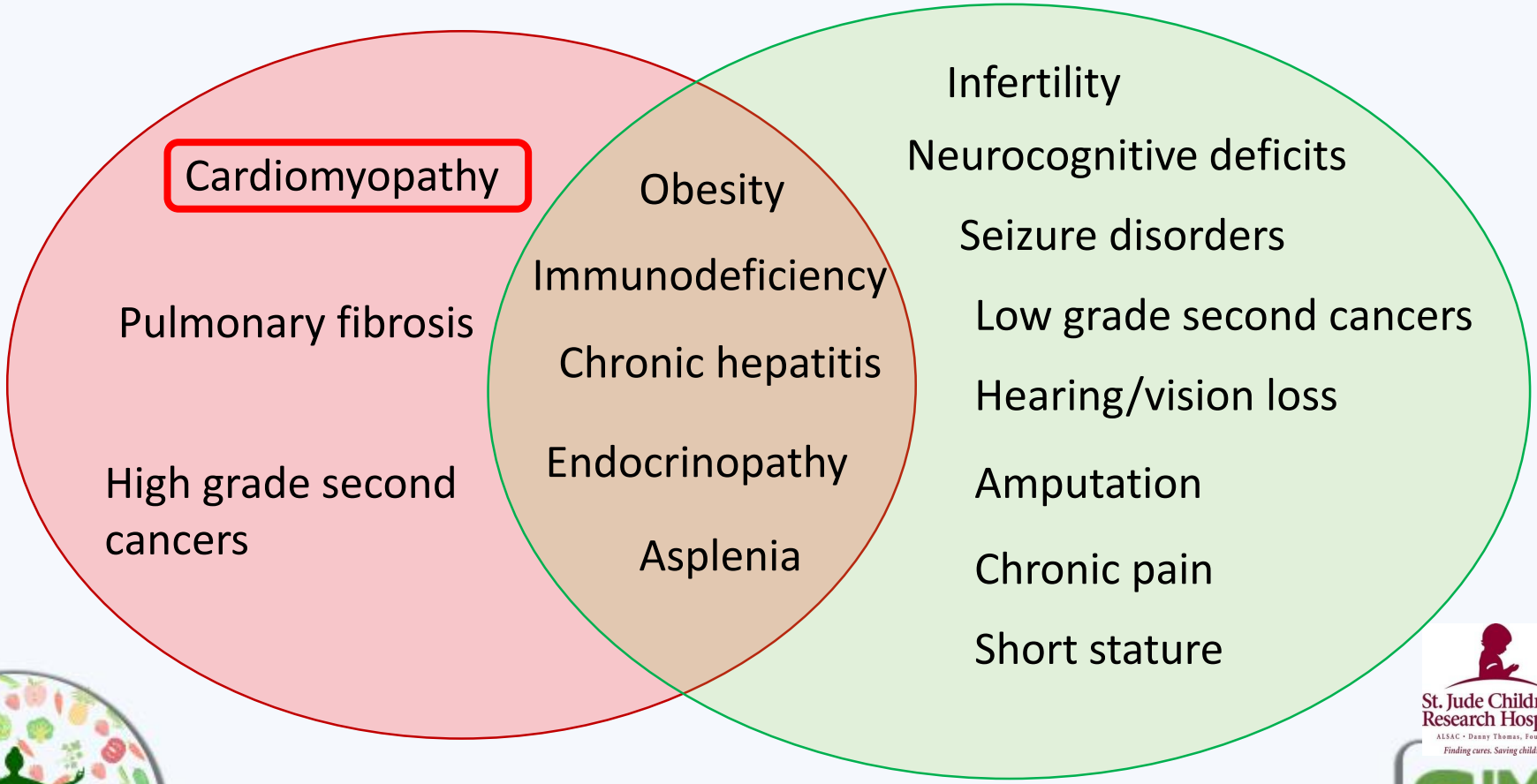
Late Effects

Life Threatening ← Life Altering



Spectrum of Physical Late Effects

Life Threatening → Life Altering



DIABETES RESEARCH AND CLINICAL PRACTICE 143 (2018) 432–442

Contents available at ScienceDirect

Diabetes Research and Clinical Practice

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International Diabetes Federation

Invited review

Cancer survivors: An expanding population with an increased cardiometabolic risk

Francesco Felicetti, Nicoletta Fortunati, Enrico Brignardello *

Transition Unit for Childhood Cancer Survivors, Città della Salute e della Scienza Hospital, Turin, Italy

Late cardiotoxicity is related both to the ***direct effects of cancer treatments*** on heart function and structure and to the worsening of CV risk factors, which can also be induced by anticancer therapies

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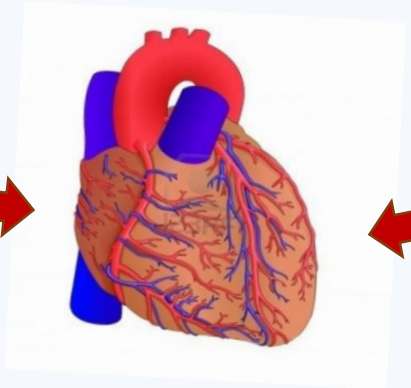
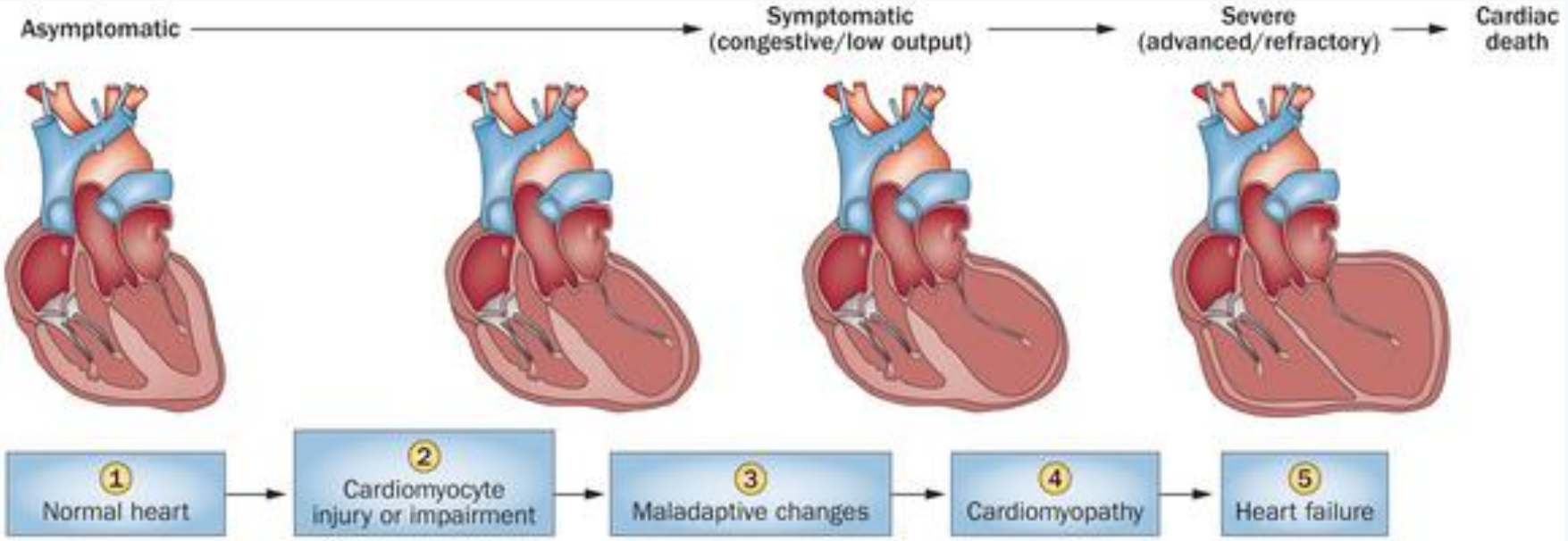
Direct effect of cancer treatments

Radiotherapy



Anthracyclines

Anthracycline: pathophysiology



Non-ischemic cellular degeneration → ***Diastolic dysfunction and later systolic dysfunction*** → ***Symptomatic cardiac dysfuncion***

Lipshulz SE et al, Nature Reviews Clinical Oncology 2013

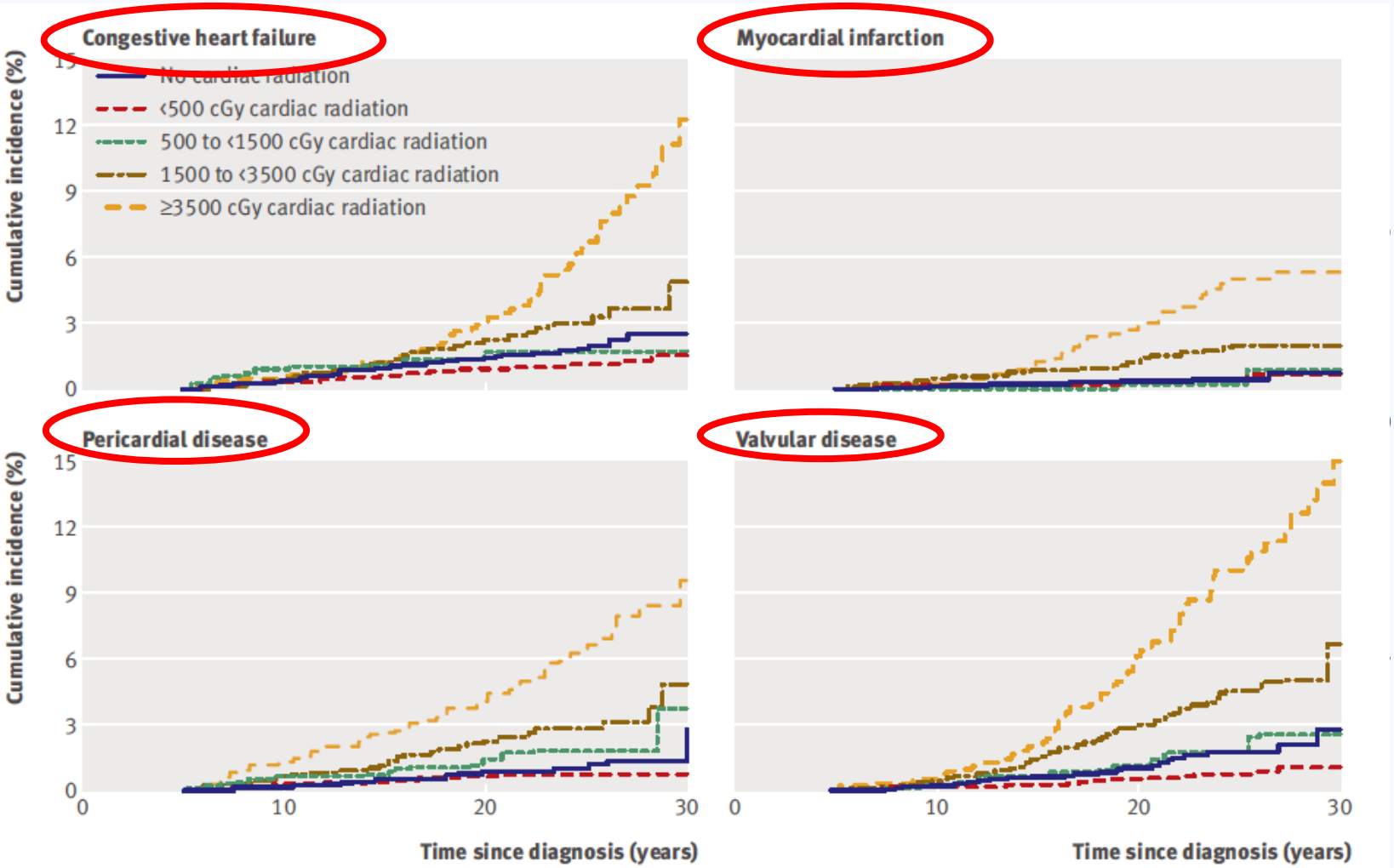


Fig 4 | Cumulative incidence of cardiac disorders among childhood cancer survivors by average cardiac radiation dose

Mulrooney et al, BMJ 2009

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Late cardiotoxicity is related both to the direct effect of cancer treatments on heart function and structure and to the ***worsening of CV risk factors***, which can also be induced by anticancer therapies.

RT and classical CV risk factors

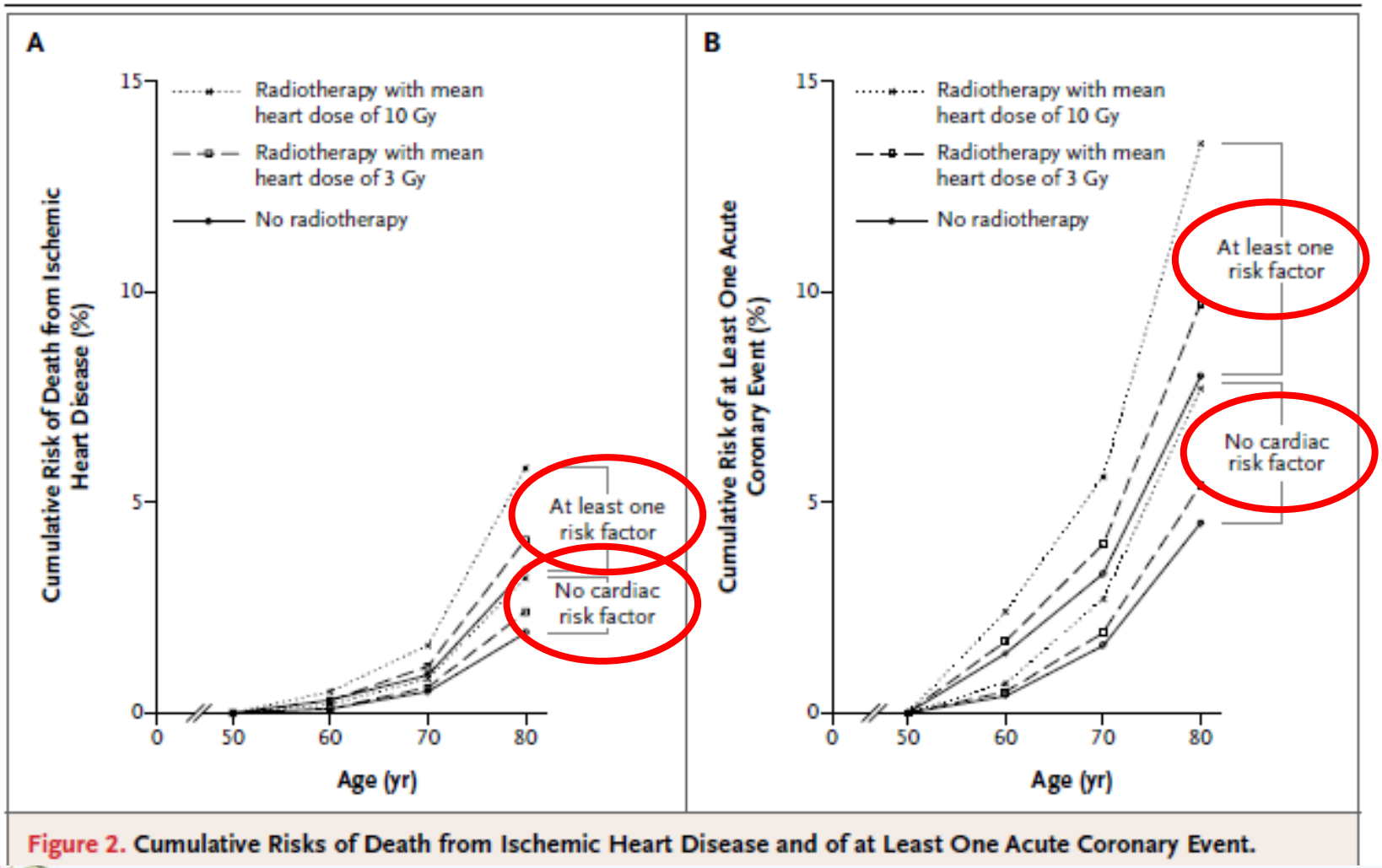


Figure 2. Cumulative Risks of Death from Ischemic Heart Disease and of at Least One Acute Coronary Event.

Darby et al, NEJM 2013

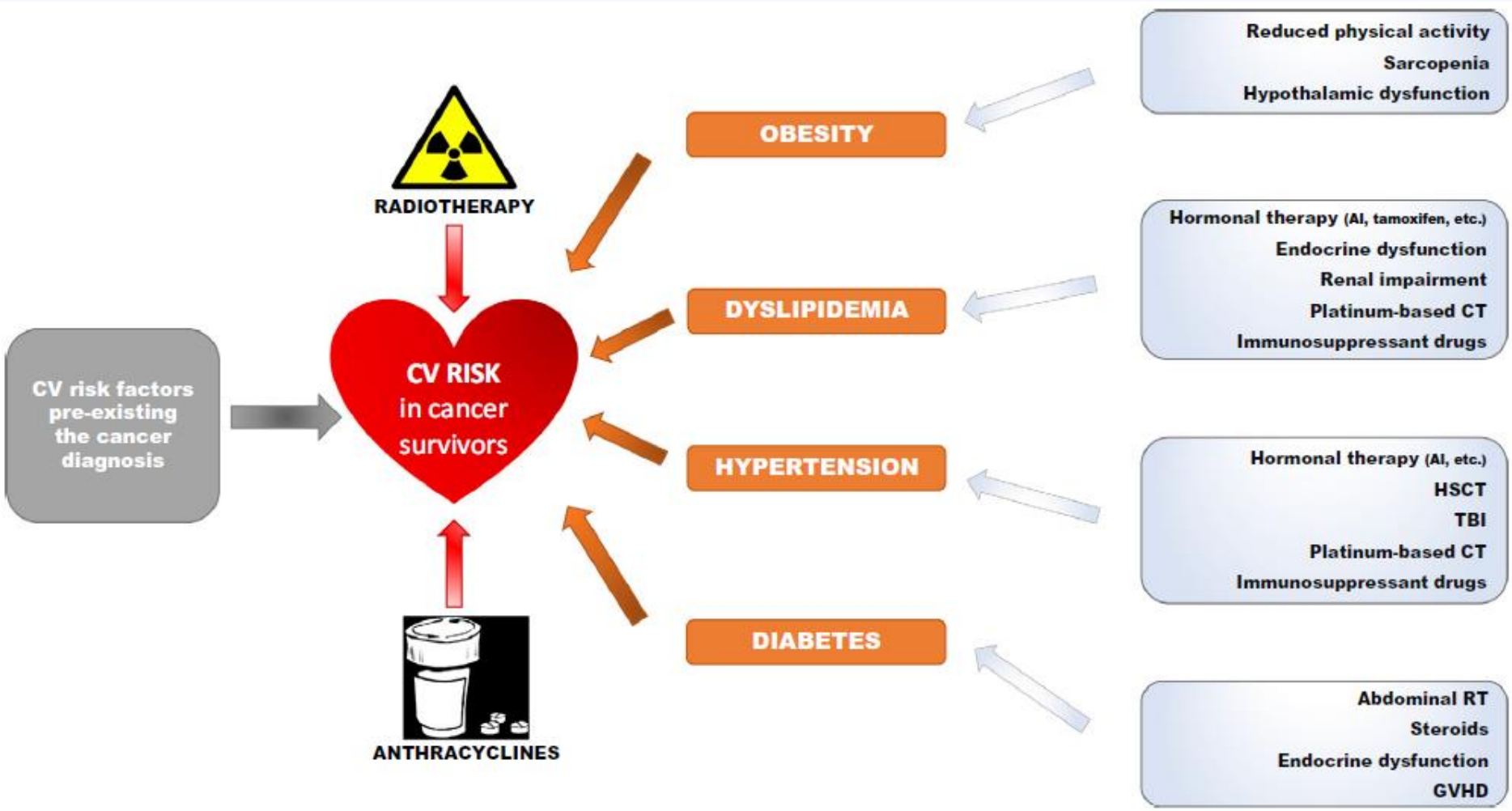
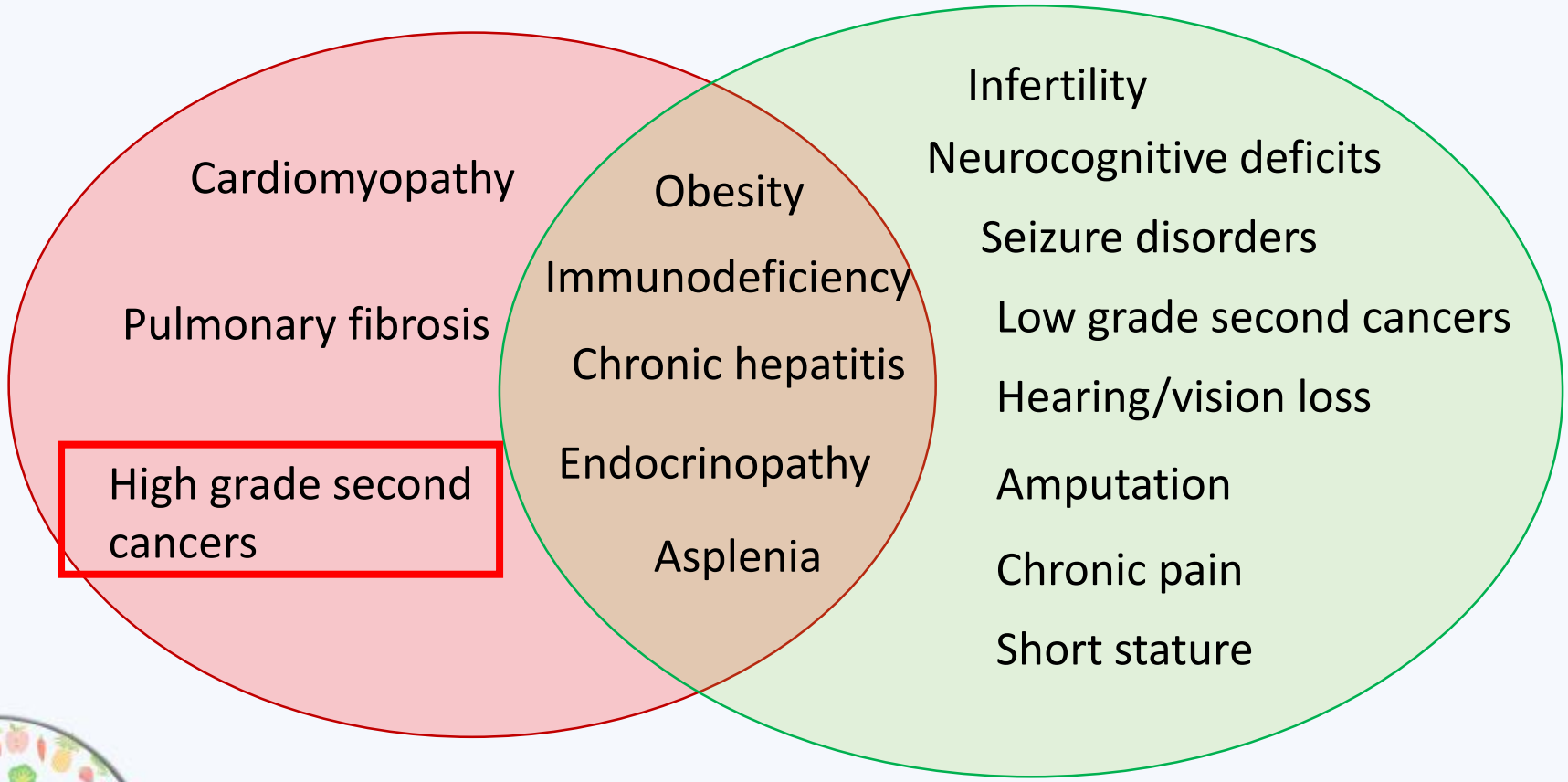


Fig. 1 – Cardiovascular risk factors in cancer survivors.

Felicetti […] Brignardello, Diab Res Clin Pract 2018

Late Effects

Life Threatening ← Life Altering



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 24, 2015 VOL. 373 NO. 26

Second Cancer Risk Up to 40 Years after Treatment for Hodgkin's Lymphoma

Michael Schaapveld, Ph.D., Berthe M.P. Aleman, M.D., Ph.D., Anna M. van Eggermond, M.Sc., Cécile P.M. Janus, M.D., Augustinus D.G. Krol, M.D., Ph.D., Richard W.M. van der Maazen, M.D., Ph.D., Judith Roesink, M.D., Ph.D., John M.M. Raemaekers, M.D., Ph.D., Jan Paul de Boer, M.D., Ph.D., Josée M. Zijlstra, M.D., Ph.D., Gustaaf W. van Imhoff, M.D., Ph.D., Eefke J. Petersen, M.D., Ph.D., Philip M.P. Poortmans, M.D., Ph.D., Max Beijert, M.D., Marnix L. Lybeert, M.D., Ina Mulder, Ph.D., Otto Visser, Ph.D., Marieke W.J. Louwman, Ph.D., Inge M. Krul, M.Sc., Pieternella J. Lugtenburg, M.D., Ph.D., and Flora E. van Leeuwen, Ph.D.

CONCLUSIONS

The risk of second solid cancers did not appear to be lower among patients treated in the most recent calendar period studied (1989–2000) than among those treated in earlier periods. The awareness of an increased risk of second cancer remains crucial for survivors of Hodgkin's lymphoma. (Funded by the Dutch Cancer Society.)

Nanni Moretti e quel tumore: «Ne ho sconfitto un altro, dopo 20 anni»

Table 2. Standardized Incidence Ratios, Absolute Excess Risks, and 30-Year Cumulative Incidences of Selected Subsequent Malignant Neoplasms.*

Second Cancer or Cancer Site	ICD Code	No. of Patients	Standardized Incidence Ratio (95% CI)	Absolute Excess Risk	30-Yr Cumulative Incidence (95% CI)
				no./10,000 person-yr (95% CI)	
Any cancer, excluding MDS†	—	884	4.6 (4.3 to 4.9)	121.8 (111.8 to 132.4)	32.5 (30.4 to 34.6)
Any solid cancer	C00–C80	757	4.2 (3.9 to 4.5)	100.5 (91.3 to 110.2)	28.5 (26.4 to 30.5)
Lip, oral cavity, or pharynx	C00–C14	20	3.2 (2.0 to 4.9)	2.3 (1.0 to 4.1)	0.5 (0.3 to 0.9)
Gastrointestinal tract	C15–C26	184	4.6 (3.9 to 5.3)	24.0 (19.7 to 28.7)	7.0 (5.9 to 8.3)
Esophagus	C15	38	9.5 (6.7 to 13.1)	5.6 (3.8 to 8.0)	1.5 (1.0 to 2.1)
Stomach	C16	39	7.4 (5.3 to 10.1)	5.6 (3.7 to 8.0)	1.6 (1.1 to 2.3)
Colon	C18	42	2.9 (2.1 to 3.9)	4.6 (2.6 to 7.0)	1.5 (1.0 to 2.1)
Rectum or rectosigmoid junction	C19–C20	25	2.6 (1.7 to 3.9)	2.6 (1.1 to 4.5)	1.0 (0.6 to 1.5)
Pancreas	C25	23	5.7 (3.6 to 8.5)	3.1 (1.7 to 5.0)	1.0 (0.6 to 1.6)
Lower respiratory system	C33, C34, and C45	193	6.7 (5.8 to 7.8)	27.3 (22.9 to 32.1)	7.1 (6.0 to 8.3)
Lung or bronchus	C34	176	6.4 (5.5 to 7.4)	24.6 (20.5 to 29.3)	6.4 (5.4 to 7.6)
Mesothelioma	C45	17	15.1 (8.8 to 24.2)	2.6 (1.5 to 4.3)	0.6 (0.3 to 1.1)
Skin					
Melanoma	C43	34	2.8 (1.9 to 3.9)	3.6 (1.9 to 5.9)	1.1 (0.7 to 1.5)
Nonmelanoma	C44	26	3.4 (2.2 to 5.0)	3.1 (1.6 to 5.1)	0.7 (0.4 to 1.2)
Soft-tissue sarcoma	C47–C49	22	12.0 (7.5 to 18.2)	3.3 (2.0 to 5.2)	0.7 (0.4 to 1.1)
Female breast‡	C50	183	4.7 (4.0 to 5.4)	54.3 (44.7 to 65.0)	16.6 (14.1 to 19.2)
Female genital organ					
Any	C51–C58	34	2.8 (1.9 to 3.9)	3.6 (1.9 to 5.9)	2.9 (2.0 to 4.2)
Corpus uteri	C54	16	3.6 (2.1 to 5.8)	1.9 (0.8 to 3.6)	1.6 (0.9 to 2.6)
Male genital organ					
Any	C60–C63	22	1.1 (0.7 to 1.7)	0.3 (−1.0 to 2.2)	1.8 (1.1 to 2.8)
Prostate	C61	18	1.0 (0.6 to 1.7)	0.1 (−1.1 to 1.9)	1.4 (0.8 to 2.4)
Urinary tract	C64–C68	39	3.5 (2.5 to 4.7)	4.6 (2.7 to 7.0)	1.3 (0.9 to 2.0)
Kidney	C64	12	2.3 (1.2 to 4.1)	1.1 (0.2 to 2.6)	0.4 (0.2 to 0.8)
Urinary bladder	C67	22	4.1 (2.6 to 6.2)	2.8 (1.4 to 4.6)	0.6 (0.3 to 1.1)
Thyroid gland	C73	23	14.0 (8.9 to 21.0)	3.5 (2.1 to 5.5)	0.8 (0.5 to 1.2)
Primary site unknown or ill defined	C76–C80	29	4.9 (3.3 to 7.0)	3.8 (2.2 to 5.9)	1.3 (0.8 to 1.9)
Blood, bone marrow, or lymphatic system	C82–C96	147	10.4 (8.8 to 12.2)	22.2 (18.4 to 26.5)	5.0 (4.1 to 6.0)
Non-Hodgkin's lymphoma	C82–88	104	13.4 (10.9 to 16.2)	16.0 (12.9 to 19.7)	3.7 (3.0 to 4.6)
Leukemia	C91–96	41	9.5 (6.8 to 12.9)	6.1 (4.2 to 8.5)	1.3 (0.9 to 1.7)

Summary of risk factors for SMNs in pediatric cancer survivors (Choi et al., Int J Cancer 2014)

Risk factor	SMN type(s)	Genetic aberrations	Time course after treatment	Additional risk factors
Chemotherapy7, 19 Alkylating Agents	AML M1 AML M2 with preceding MDS	Monosomy or partial deletion in Chromosome 5/7	5–7 years	Dose dependent risk Concurrent use of epipodophyllotoxins
Anthracyclines	AML	AML1-ETO (aka RUNX1-RUNX1T1) *t*(8;16)(p11;p13.3)	Acute onset within 2–3 years	High cumulative dose Concurrent use of alkylating agents
Epipodophyllotoxins	AML M2/M4/M5	MLL rearrangements – common t(8;21)(q22;q22) AML1-ETO (aka RUNX1-RUNX1T1)	Acute onset within 2–3 years	Increased frequency of administration Cumulative dose Concurrent administration with asparaginase, antimetabolites, alkylating agents
Ionizing Radiation[28–31,32–34]	Breast, Lung, Thyroid, Bone sarcomas, CNS tumors, NMSC	CPS (see Table 2)	10–15 years Up to 30 years after	Age <10 at radiation exposure >30 Gy to the mediastinum for breast cancers; Any radiation exposure for increased risk of sarcoma
Hematopoietic Stem Cell Transplant (HSCT)[35–-37,38,39,40]	AML, NHL, SCC		Up to 5 years after for PTLD/SCC 10–15 years	CT in primary treatment and conditioning regimen; TBI; GVHD

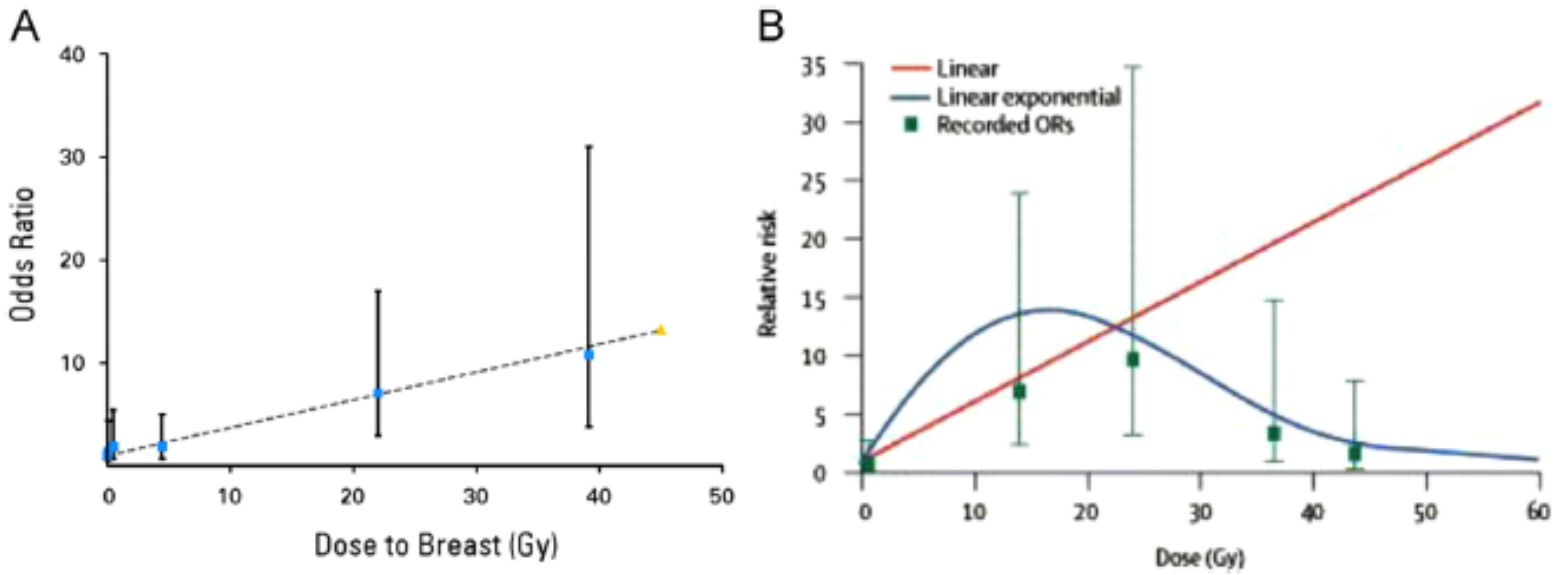
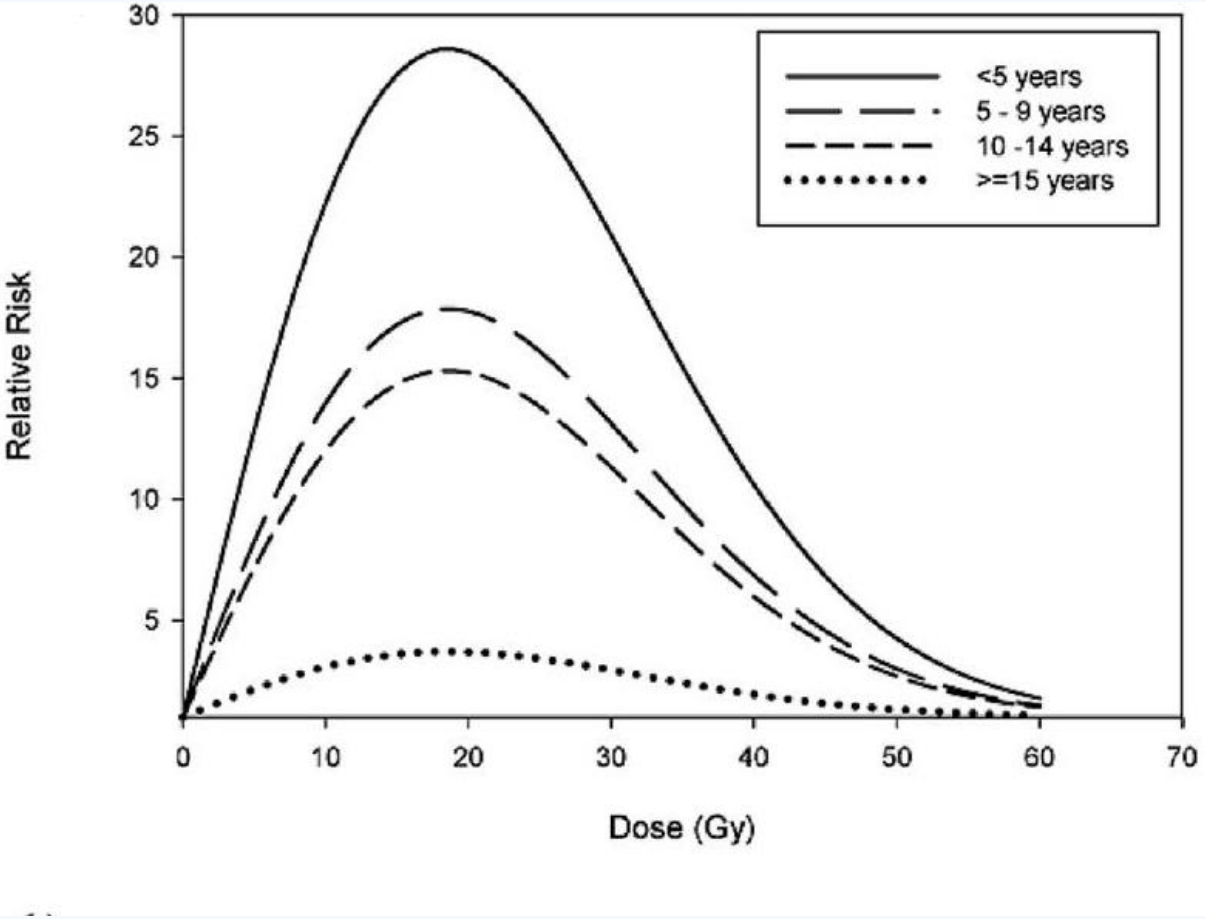


Figure 2. (A) The linear dose-response relationship between radiation dose to the breast and risk of breast cancer is shown. (B) In contrast to the linear relationship between radiation dose and breast, colorectal, and stomach cancer, the linear-exponential relationship between radiation dose and thyroid cancer is demonstrated. The peak risk occurs with thyroid radiation doses of 15 to 20 Gy, with diminishing excess risk with doses of >30 Gy. (A) Inskip PD, Robison LL, Stovall M, et al. Radiation dose and breast cancer risk in the Childhood Cancer Survivor Study. J Clin Oncol 2009;27:3901-7, and (B) From Sigurdson AJ, Ronckers CM, Mertens AC, et al. Primary thyroid cancer after a first tumour in childhood (the Childhood Cancer Survivor Study): a nested case-control study. Lancet 2005;365:2014-23, with permission.

Carcinoma tiroideo radioindotto



Carcinoma mammario in CCS

- La **radioterapia toracica rappresenta il principale fattore di rischio**, soprattutto se effettuata **in età compresa fra i 10 e 20 anni** (*Metayer et al. 2000, Inskip et al. 2009, Barcellos-Hoff 2013*).
- **Nelle pazienti trattate con RT toracica, dopo 25–30 anni l'incidenza cumulativa di carcinoma mammario varia fra il 12 e il 26%** (*Ng et al. 2002, Bhatia et al. 2003, Kenney et al. 2004, Taylor et al. 2007, Constine et al. 2008, De Bruin et al. 2009*). **Rischio che è paragonabile a** quello che presentato i soggetti portatori di mutazioni germinali a carico dei geni ***BRCA1* o *BRCA2*** (*Moskowitz et al. 2014*).
- **La latenza mediana** fra diagnosi oncologica pediatrica e il secondo tumore mammario varia **fra 6.7 e 39 anni** (*Gold et al. 2003, Taylor et al. 2007, 2008, Constine et al. 2008, Diallo et al. 2009, Friedman et al. 2010, O'Brien et al. 2010, Lange et al. 2014, Dorffel et al. 2015, Henderson et al. 2015*).
- Vi è una **relazione lineare fra dose** di radioterapia toracica ricevuta **e rischio di carcinoma** mammario, **"higher the dose, higher the risk"** (Travis *et al*. 2003, van Leeuwen *et al*. 2003, Guibout *et al*. 2005, Hill *et al*. 2005, Inskip *et al*. 2009, Berrington de Gonzalez *et al*. 2013), con **rischio più elevato per i pazienti che hanno ricevuto dosi > 20 Gy** (i.e. Hodgkin Lymphoma Survivors). Studi recenti hanno tuttavia evidenziato rischi elevati anche per pazienti trattati con dosi inferiori (Lange *et al*. 2014, Moskowitz *et al*. 2014).

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.

I *late effects* più frequenti e gravi, ai quali fanno riferimento le presenti raccomandazioni, riguardano:

- **Sistema Endocrino**
  - Gonadi
  - Tiroide
  - Metabolismo lipidico e glicidico
- **Apparato cardio-vascolare**
- **Apparato respiratorio**
- **"Secondi tumori" maligni:**
  - Leucemie secondarie
  - Tumori solidi
    - Mammella
    - Tiroide
    - Cute
    - Intestino
    - Polmone

Visita clinica

Età ≥ 25 anni 6-12 mesi Età < 25 anni annuale

Diagnostica senologica per immagini:

Età < 25 anni:

- nessuna evidenza circa la necessità di imaging nelle pazienti asintomatiche

Età ≥ 25 anni (se ≥ 8 anni dal completamento della RT):

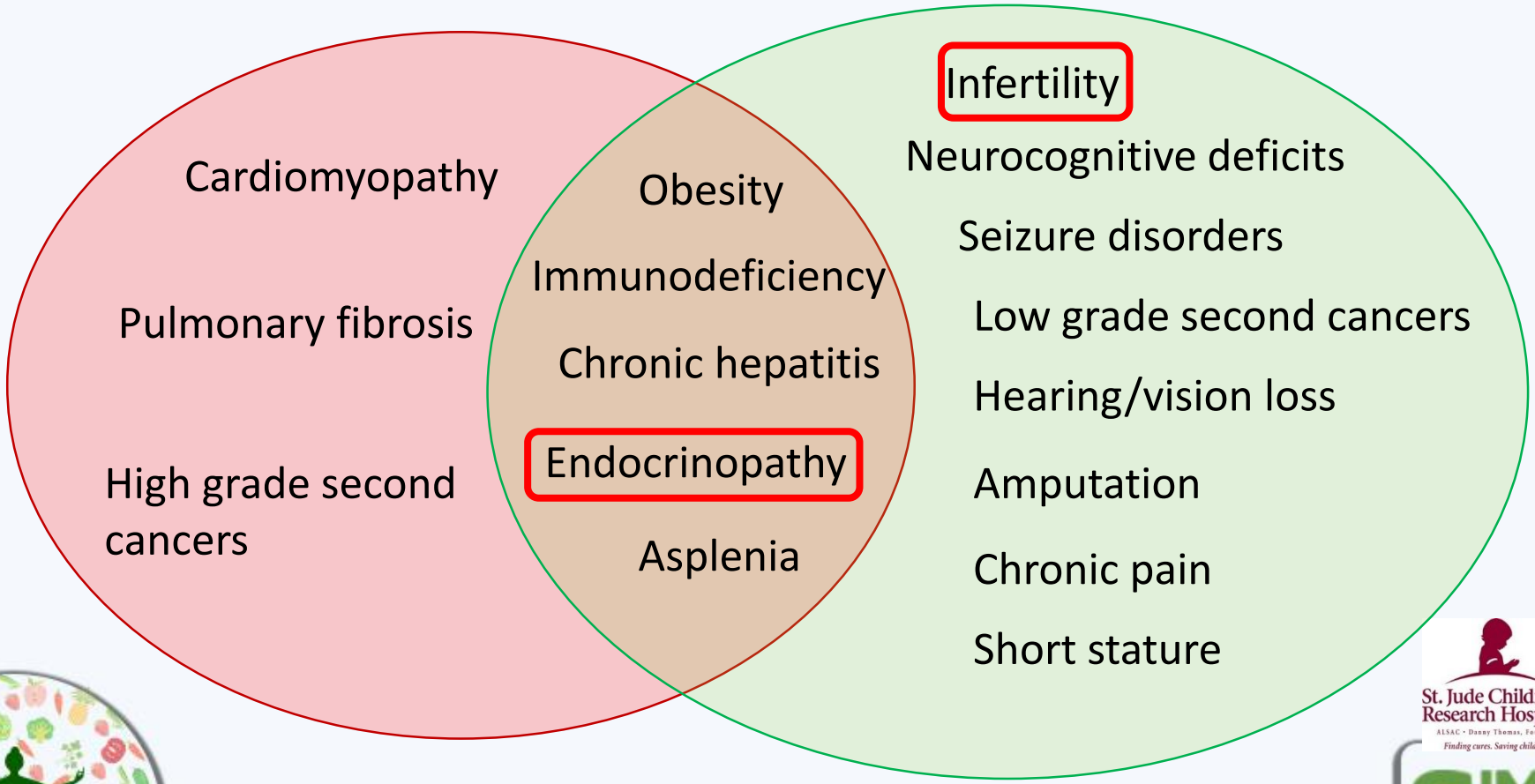
- **Mammografia annuale** (due proiezioni standard, eventualmente integrata con ecografia) **o risonanza magnetica mammaria, a cadenza annuale.**

Le raccomandazioni oggi disponibili in letteratura sono **concordi nel raccomandare fortemente un programma di screening senologico a cadenza annuale** in tutte le donne che abbiano effettuato un trattamento radioterapico che abbia coinvolto la regione mammaria. Il clinico che gestisce il follow-up - d'accordo con il radiologo - individuerà per ogni singolo soggetto la metodica più appropriata, tenuto conto delle evidenze scientifiche disponibili, della storia clinica della paziente e delle sue preferenze. Al fine di evitare ulteriore irradiazione della mammella, quando possibile ed almeno fino al compimento del trentacinquesimo anno di età, è preferibile l'utilizzo della risonanza magnetica.

L'ETG mammaria potrà essere utilizzata, a discrezione dello specialista radiologo, come integrazione della mammografia e della risonanza magnetica. L'ETG potrà essere inoltre utilizzata come esame di screening in pazienti selezionate di età inferiore a 25 anni, se il rischio di carcinoma mammario risulta particolarmente elevato (familiarità, dose erogata, etc.)

Spectrum of Physical Late Effects

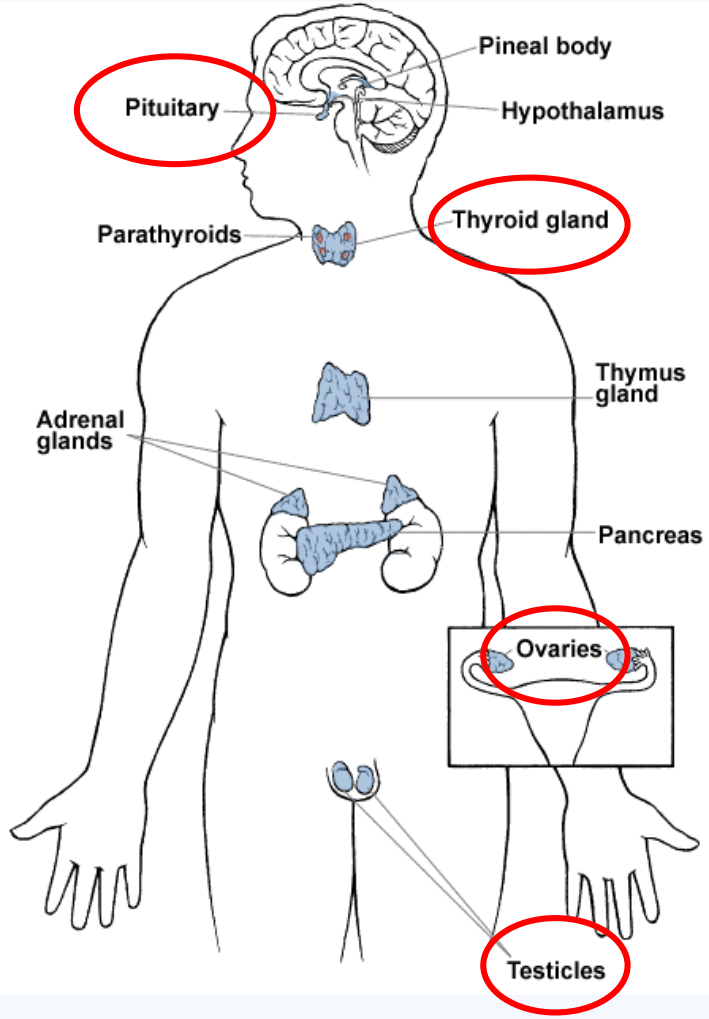
Life Threatening → Life Altering



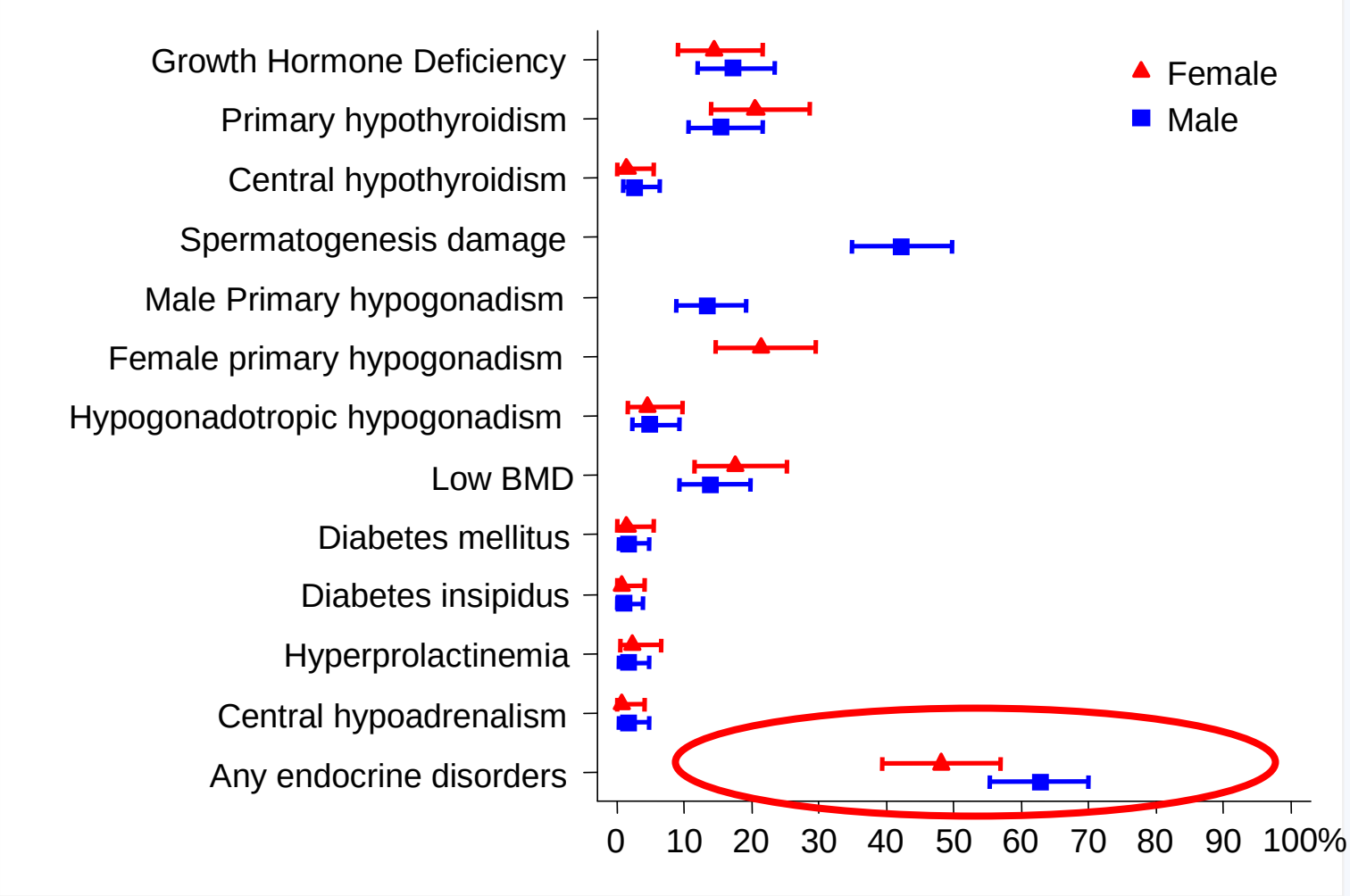
Complicanze endocrinologiche

- **Sono I late effects più frequenti**
  - Ipopituitarismo
  - Tireopatie
  - Ipogonadismo ed infertilità
  - Dislipidemia
  - Obesità
  - Osteoporosi

- **Causate da:**
  - (Chirurgia)
  - Chemioterapia (Alchilanti)
  - Radioterapia



ENDOCRINOPATIE IN CHILDHOOD CANCER SURVIVORS



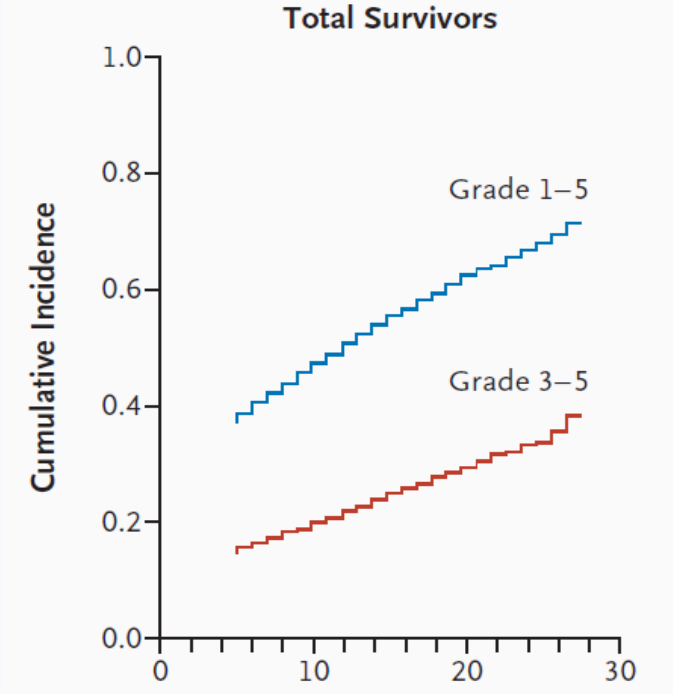
Brignardello et al., Eur J Endocrinol 2013

The price of success

The NEW ENGLAND JOURNAL of MEDICINE

Chronic Health Conditions in Adult Survivors of Childhood Cancer

Kevin C. Oeffinger, M.D., Ann C. Mertens, Ph.D., Charles A. Sklar, M.D.,



- 10,397 ***childhood cancer survivors*** con età media di **26.6 anni** (diagnosi 1970-1986)

- Popolazione di controllo di fratelli sani

- **62.3% dei CCS aveva almeno una malattia cronica e il 27.5% una malattia grave o potenzialmente mortale**

- Rispetto ai controlli**, il rischio di avere una malattia cronica è risultato 3.3 volte** (95% CI, 3.0 to 3.5); **8.2 volte quello di malattie gravi o potenzialmente mortali**

N Engl J Med 2006;355:1572-82.

Gestione dei *late effects*

CONSAPEVOLEZZA
(del paziente e del medico)

CureSearch
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: _____ ☑ Sections 1 & 2 applicable to all patients	Date of Diagnosis: _____ Prior to 1972: ☐ Section 3 Prior to 1993: ☐ Section 4 1977 - 1985: ☐ Section 5	End Therapy Date: _____ 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

1977–1985: ❑ Section 9

CHEMOTHERAPY: ❑ Yes ❑ No If yes: ✓ Section 10 *and* applicable guidelines for specific chemotherapy agents below

Chemotherapy Agent (mark if patient received)		Applicable guideline sections	
Asparaginase		Section 40	
Bleomycin		Section 35	
Busulfan		Sections 11(M), 12(M), 13(F), 14, 15, 16	
Carboplatin – all doses		Sections 11(M), 12(M), 13(F), 14, 21, 22	
– myeloablative dose or age < 1 year at diagnosis		See also: Section 20	**Note**: Myeloablative dose = conditioning for HCT
Carmustine		Sections 11(M), 12(M), 13(F), 14, 15	
Chlorambucil		Sections 11(M), 12(M), 13(F), 14	
Cisplatin		Sections 11(M), 12(M), 13(F), 14, 20, 21, 22	
Cyclophosphamide		Sections 11(M), 12(M), 13(F), 14, 17, 18	
Cytarabine: SQ, IT, IO, low-dose IV		Section 25	**Note**: Low-dose IV = all single doses < 1000 mg/m^2
Cytarabine: High-dose IV		Sections 23, 24	**Note**: High-dose IV = any single dose ≥1000 mg/m^2
Dacarbazine		Sections 11(M), 12(M), 13(F), 14	
Dactinomycin		Section 36	
Daunorubicin*		Sections 32, 33(M), 34(F)	

Note: There is a paucity of literature to support isotoxic dose conversion; however, the above conversion factors may be used for convenience in order to gauge screening frequency. Clinical judgment should ultimately be used to determine indicated screening for individual patients.

[redacted] [redacted] Ependimoma 18/05/1985

ORGANO	TEST	anno						
TSA (RT)	Ecodoppler							
CUORE(RT)*	Ecocardiogramma	OK 2013						
RENE(cbdca)	funz. Renale	ok 2012	ok 2015	ok 2016				
APP. URINARIO(cpm,RT)	Es. urine	ok 2010	ok 2014	ok 2016				
OSSO(RT, mtx)	MOC	ok us 2004						
FEGATO (mtx)	transaminasi	ok 2012	ok 2015					
	ETG							
SMN(RT)								
CUTE/TESS. MOLLI(RT)	Vis. Dermatologica	ok 2015						
GASTRO-INTEST(RT)	ETG	ok 2008						
TIROIDE(RT)	funzionalità	ok 2012	ok 2015	ok 2016				
	ETG	nodo 2011	nodo 2015	nodo 2016				
	FNAB							
DISLIPIDEMIA(RT, cbdca)	assetto lipidico	ok 2012	ok 2014	P 2016				
	glicemia							
GONADI(cbdca,RT)	es. ormonali	ok 2009	ok 2014	ok 2016				
	Liquido seminale							
ASSE IPOTALAMO-IPOFISI(RT)	GH							
	ACTH/Cortisolo	ok 2009	ok 2014					
	PRL	ok 2009	ok 2014					
	Diabete insipido	NO 2013						
SNC(RT)	EO neurologico	P 2011	P 2012	P 2014	stabile 2016			
	RMN	meningioma2012	ok 2014	ok 2015				
	Funz. Neurocognitiva	P 2011	P 2015					
OCCHIO(RT)	Visita oculistica							
ORECCHIO(cddp)	Visita ORL							

* 30.6 Gy spinale

individual patients.

Il follow-up a lungo termine

- Il modello organizzativo presa in carico **“globale e continuativa”** del paziente (secondo il modello della Rete Oncologica Piemonte e Valle d’Aosta).

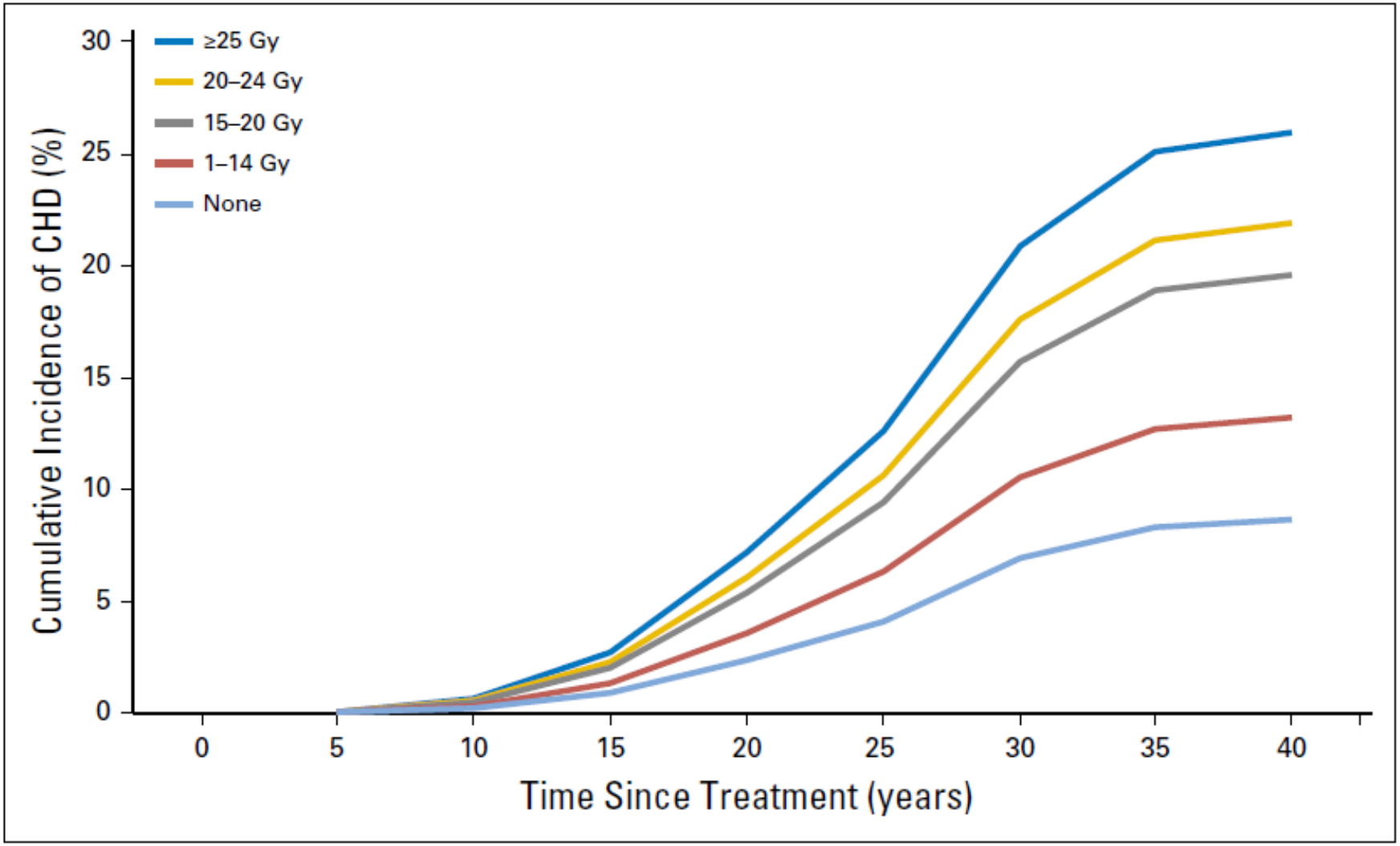
- **Personalizzazione del follow-up** (esami strumentali e di laboratorio, cadenza delle visite di controllo) **in funzione della stratificazione del rischio** (diagnosi oncologica e pregressi trattamenti antitumorali).

Gestione dei *late effects*

CONSAPEVOLEZZA
(del paziente e del medico)

CONTROLLI CLINICI PERIODICI
(anamnesi, esame obiettivo, …)

ESAMI STRUMENTALI E LABORATORISTICI



Van Nimwegen et al., JCO, 2016

Prospective Coronary Heart Disease Screening in Asymptomatic Hodgkin Lymphoma Patients Using Coronary Computed Tomography Angiography: Results and Risk Factor Analysis

- **179 pazienti asintomatici curati per linfoma di Hodgkin**
- **Follow-up mediano: 11.6 years**
- **Età mediana alla CCTA: 42.0 years**
- **Coronaropatia è stata documentata in 46 patients (26%)**
- **Stenosi gravi,** che hanno richiesto intervento di **rivascolarizzazione miocardica mediante angioplastica o BPAC,** sono state osservate **in 12 pazienti (6.7%)**

Girinsky et al., Int J Radiat Oncol Biol Phys 2014

Current expert opinion by the European Association of Cardiovascular Imaging and the American Society of Echocardiography recommend screening with a functional noninvasive stress test in asymptomatic individuals for CAD detection 5–10 years after exposure in high-risk patients, with reassessment every 5 years

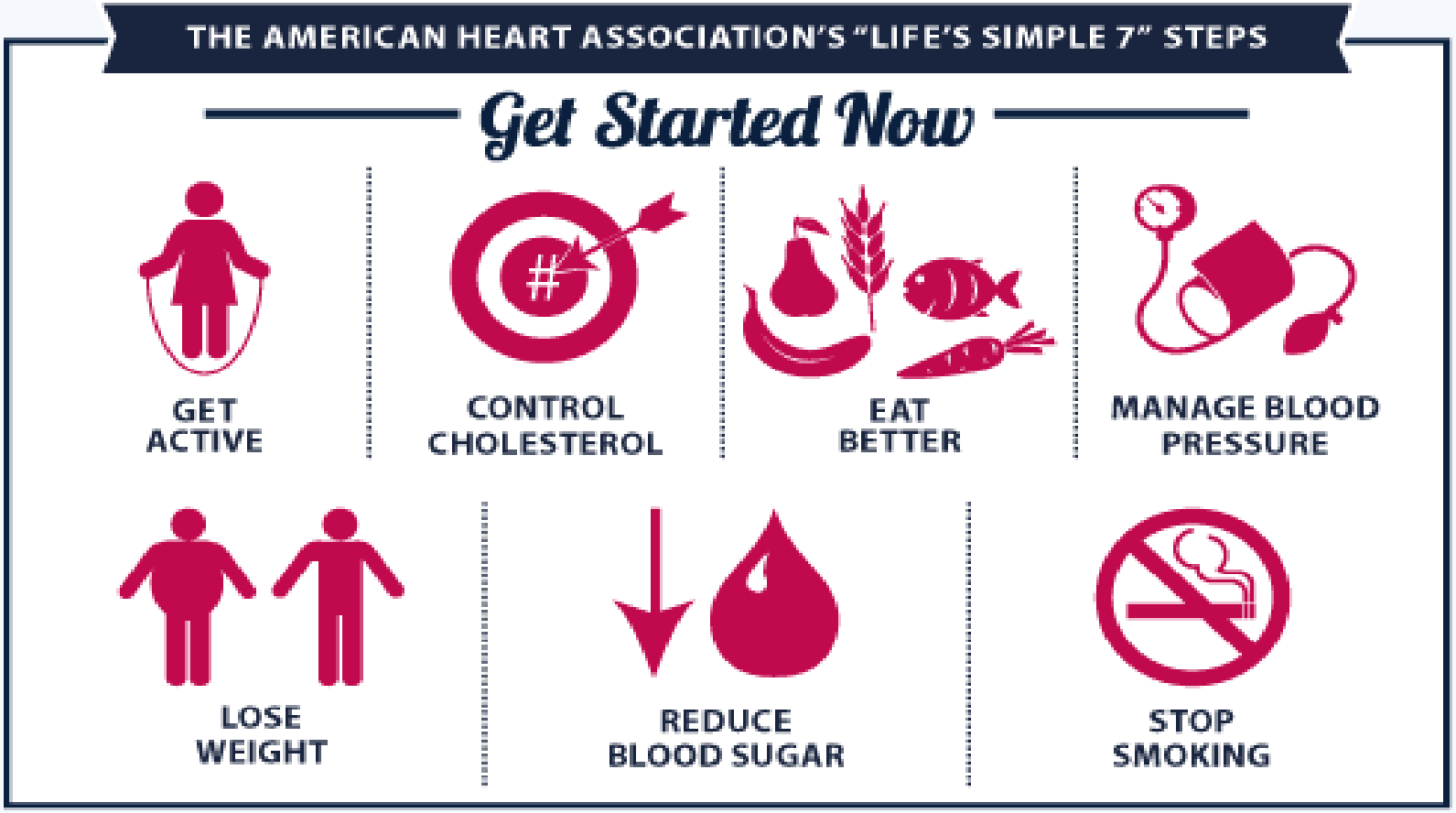
Canadian Journal of Cardiology 32 (2016) 831–841

Society Guidelines

Canadian Cardiovascular Society Guidelines for Evaluation and Management of Cardiovascular Complications of Cancer Therapy

Detection and Prevention of Cardiotoxicity

There are currently no consistent recommendations on the frequency and modality with which cardiac imaging should be performed in patients at risk of LV dysfunction related to cancer therapy. **Existing surveillance protocols are on the basis of methodology from clinical trials and expert opinion**.



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

Original Article

Lifestyle and Metabolic Syndrome in Adult Survivors of Childhood Cancer

A Report From the St. Jude Lifetime Cohort Study

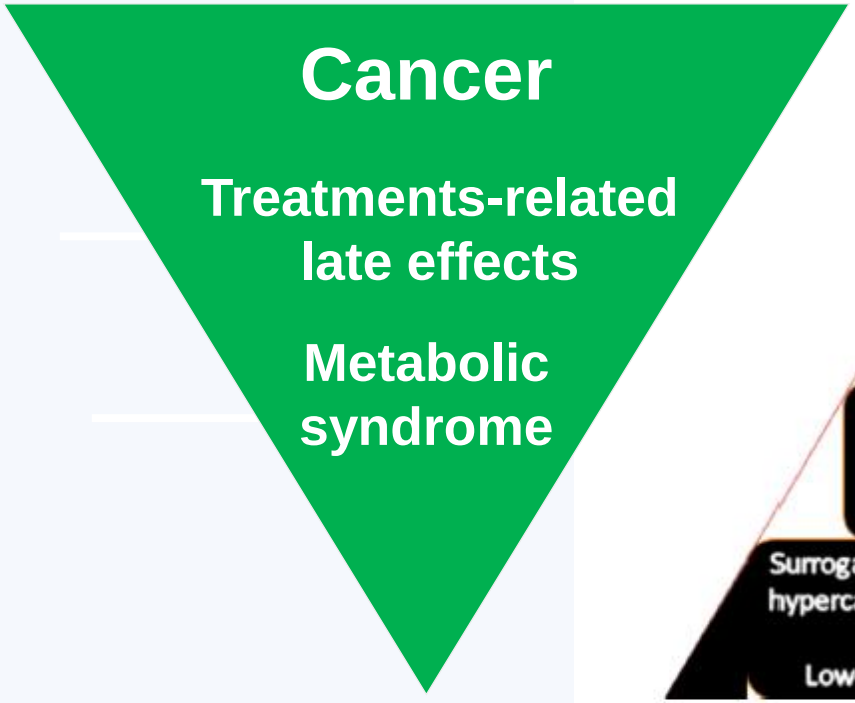
Webb A. Smith, MS[1]; Chenghong Li, MS[2]; Kerri A. Nottage, MD[3]; Daniel A. Mulrooney, MD[1,4]; Gregory T. Armstrong, MD[1]; Jennifer Q. Lanctot, PhD[1]; Wassim Chemaitilly, MD[5]; Joseph H. Laver, MD[4]; Deo Kumar Srivastava, PhD[2]; Leslie L. Robison, PhD[1]; Melissa M. Hudson, MD[1,4]; and Kirsten K. Ness, PhD[1]

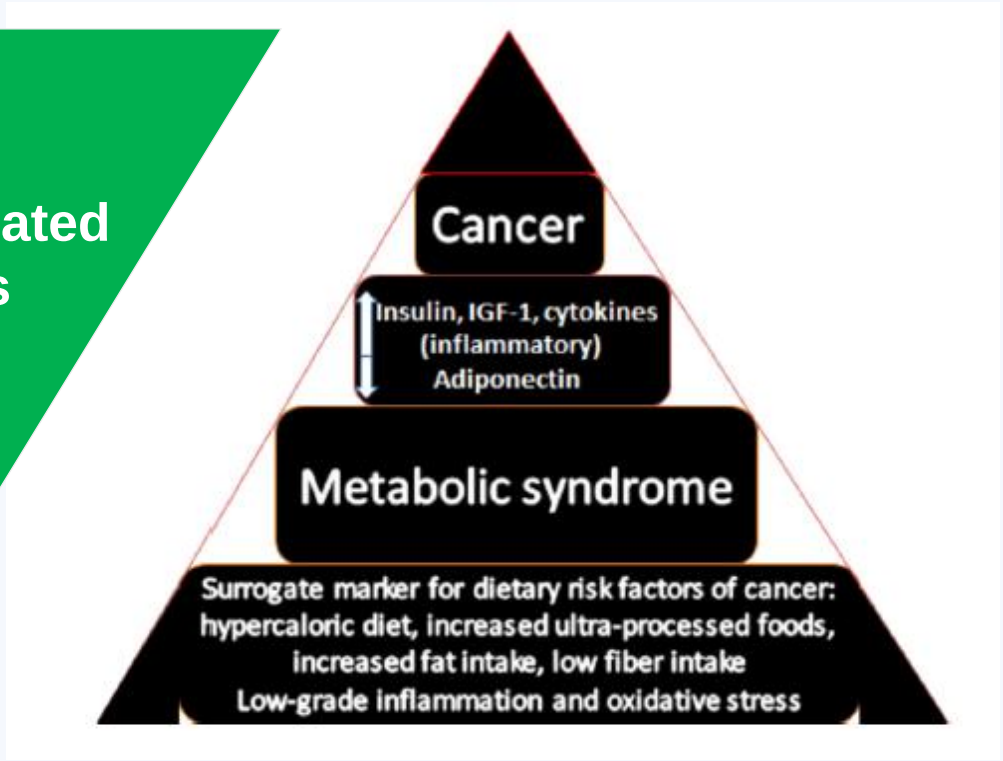
BACKGROUND: Childhood cancer survivors (CCS) are at an increased risk of developing metabolic syndrome (MetSyn), which may be reduced with lifestyle modifications. The purpose of this investigation was to characterize lifestyle habits and associations with MetSyn among CCS. **METHODS:** CCS who were ≥10 years from diagnosis, aged >18 years, and participating in the St. Jude Lifetime Cohort Study completed medical and laboratory tests and a food frequency questionnaire. The Third Report of the National Cholesterol Education Program Adult Treatment Panel criteria were used to classify participants with MetSyn. Anthropometric, food frequency questionnaire, and self-reported physical activity data were used to characterize lifestyle habits according to World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) recommendations. Those who met ≥4 of 7 recommendations were classified as having followed guidelines. Sex-stratified log-binomial regression models were used to evaluate associations between dietary/lifestyle habits and MetSyn, adjusted for age, age at cancer diagnosis, receipt of cranial radiotherapy, education, and household income. **RESULTS:** Among 1598 CCS (49.2% of whom were male, with a median age of 32.7 years [range, 18.9 years-60.0 years]), 31.8% met criteria for MetSyn and 27.0% followed WCRF/AICR guidelines. Females who did not follow WCRF/AICR guidelines were 2.4 times (95% confidence interval, 1.7-3.3) and males were 2.2 times (95% confidence interval, 1.6-3.0) more likely to have MetSyn than those who followed WCRF/AICR guidelines. **CONCLUSIONS:** Adherence to a heart-healthy lifestyle is associated with a lower risk of MetSyn among CCS. There is a need to determine whether lifestyle interventions prevent or remediate MetSyn in CCS. *Cancer* 2014;120:2742-50. © *2014 American Cancer Society.*

KEYWORDS: childhood cancer survivor, metabolic syndrome, dietary intake, healthy lifestyle.

"Common soil hypothesis"

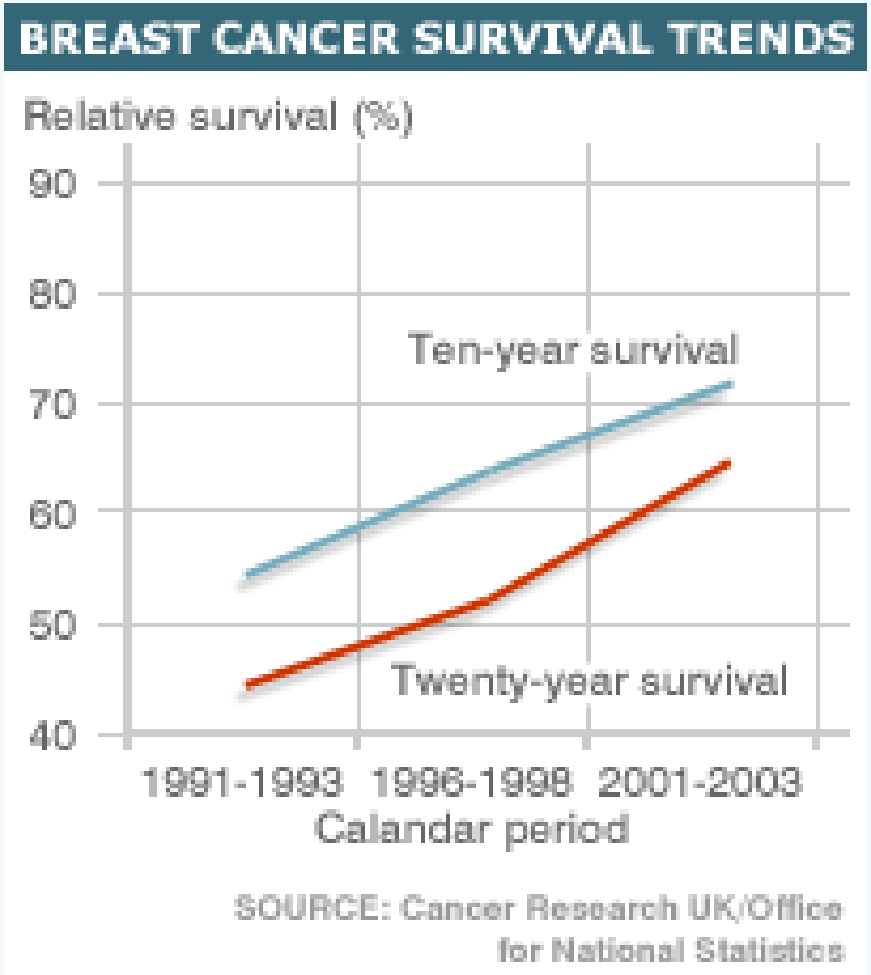
Metabolic syndrome and cancer: which direction?





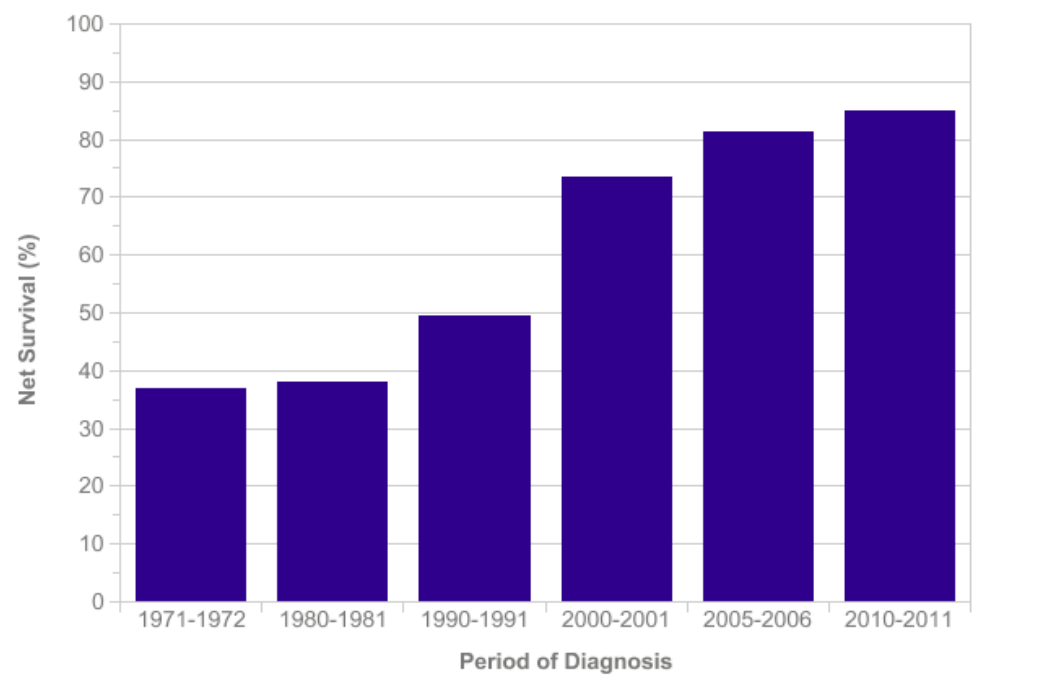
Esposito K et al, Endocrine 2013

ADULT CANCER SURVIVORS
CARCINOMA MAMMARIO



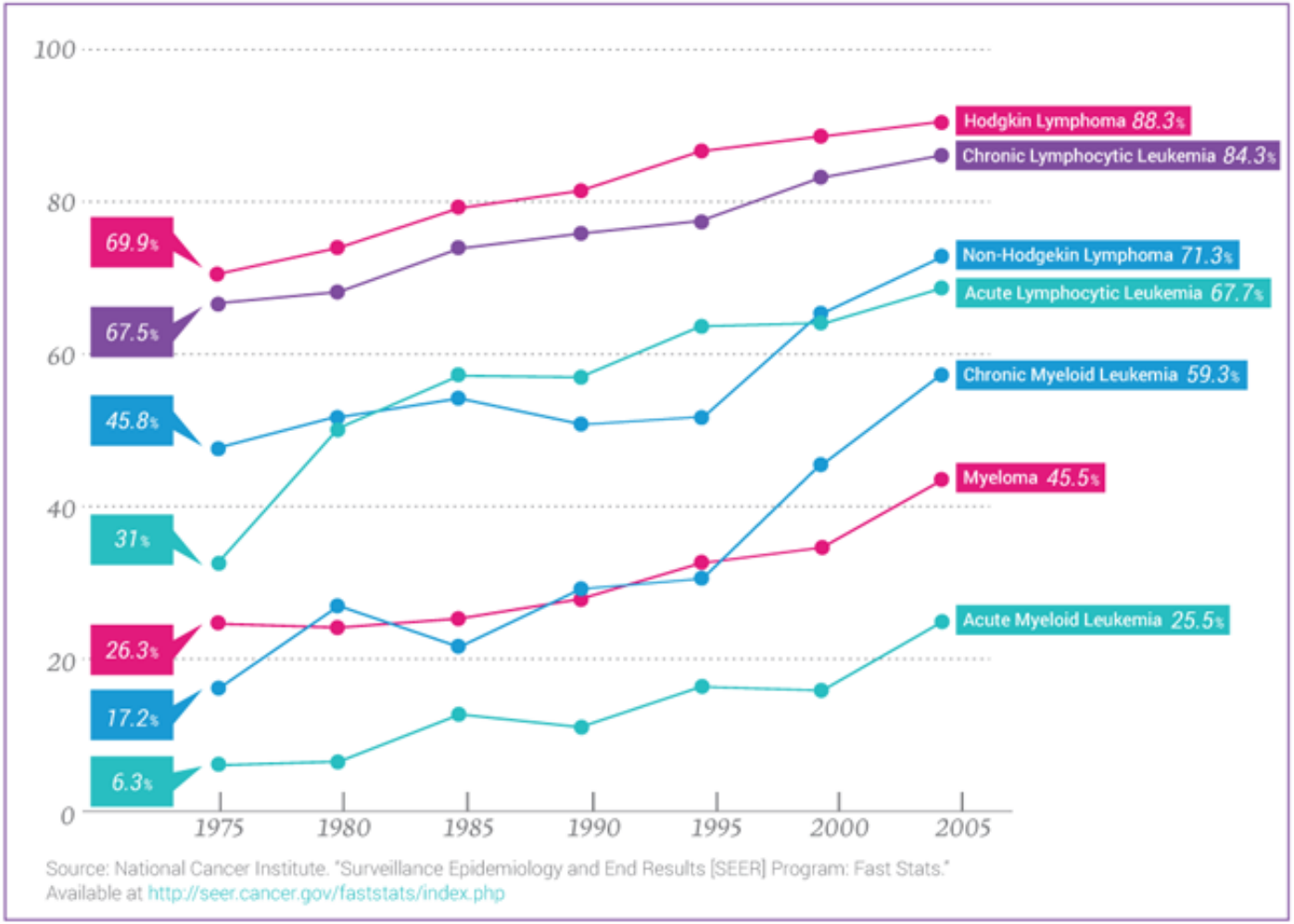
ADULT CANCER SURVIVORS
CARCINOMA PROSTATA

Prostate Cancer (C61): 1971-2011
Age-Standardised Five-Year Net Survival, England and Wales



Prepared by Cancer Research UK
Original data sources:
Survival estimates were provided on request by the Cancer Research UK Cancer Survival Group at the London School of Hygiene and Tropical Medicine.

ADULT CANCER SURVIVORS
NEOPLASIE EMATOLOGICHE



Source: National Cancer Institute. "Surveillance Epidemiology and End Results [SEER] Program: Fast Stats."
Available at http://seer.cancer.gov/faststats/index.php

20th Edition

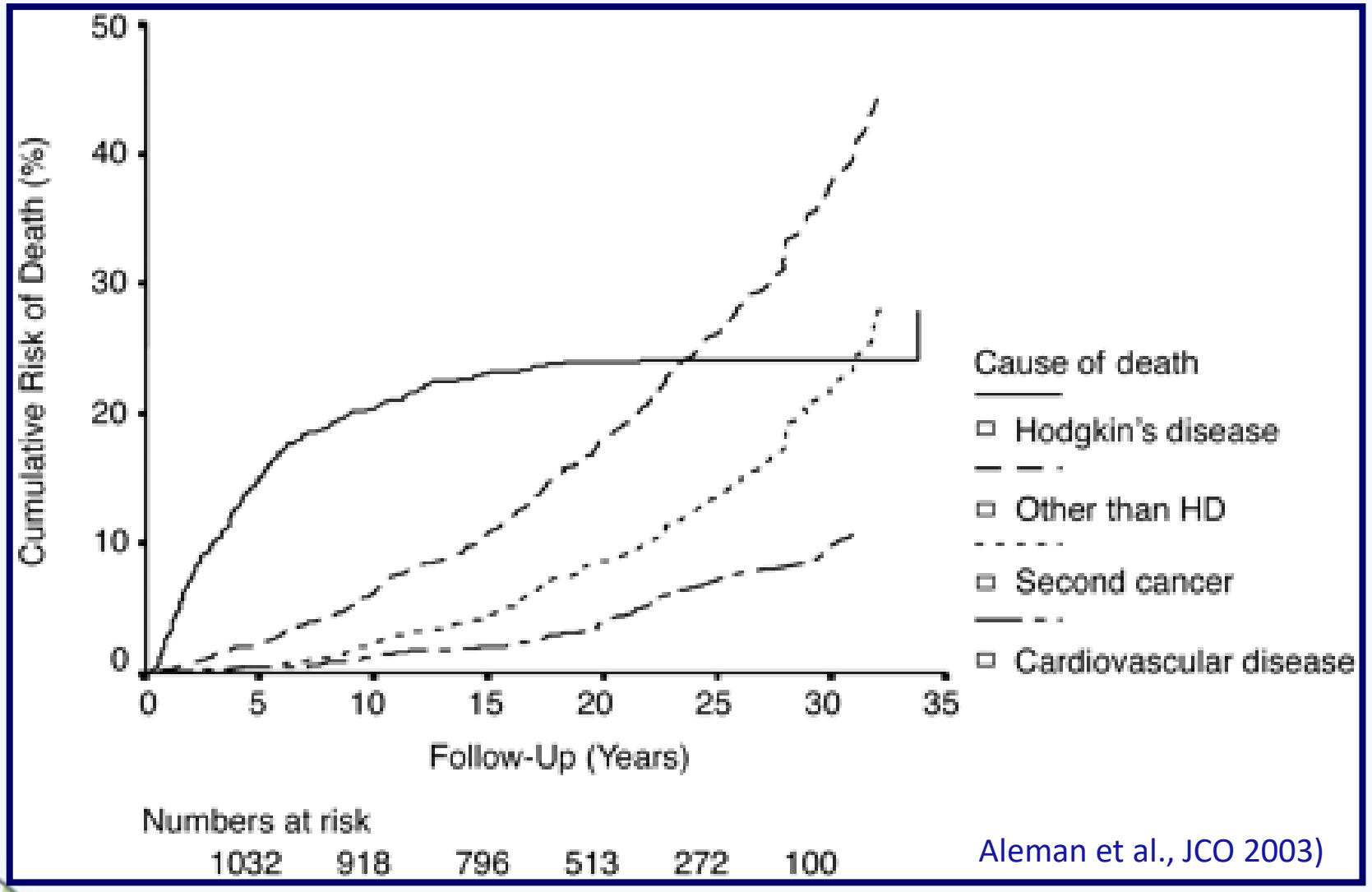
HARRISON'S

PRINCIPLES OF

INTERNAL MEDICINE

"Because of the very high cure rate in patients with Hodgkin's lymphoma, **long-term complications have become a major focus for clinical research**. In fact, in some series of patients with early-stage disease, **more patients died from late complications of therapy than from Hodgkin's lymphoma itself.** This is particularly true in patients with localized disease. The most serious late side effects include second malignancies and cardiac injury".

Mortalità in HL *survivors*



Aleman et al., JCO 2003)

GUARIRE
AD OGNI COSTO

GUARIRE
AL MINOR COSTO
POSSIBILE

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.

Dai *CCS* agli *Adult Cancer Survivors* …

Prevalenza: *CCS* = 0.15% → 40.000

ACS = 2.7% → 1.500.000

(Dati AIRTUM 2014)

✓Per **quali adult cancer survivors** può essere utile il LTFU?

✓**Chi** deve fare il LTFU?

FORMAZIONE

ASPETTATIVA DI VITA

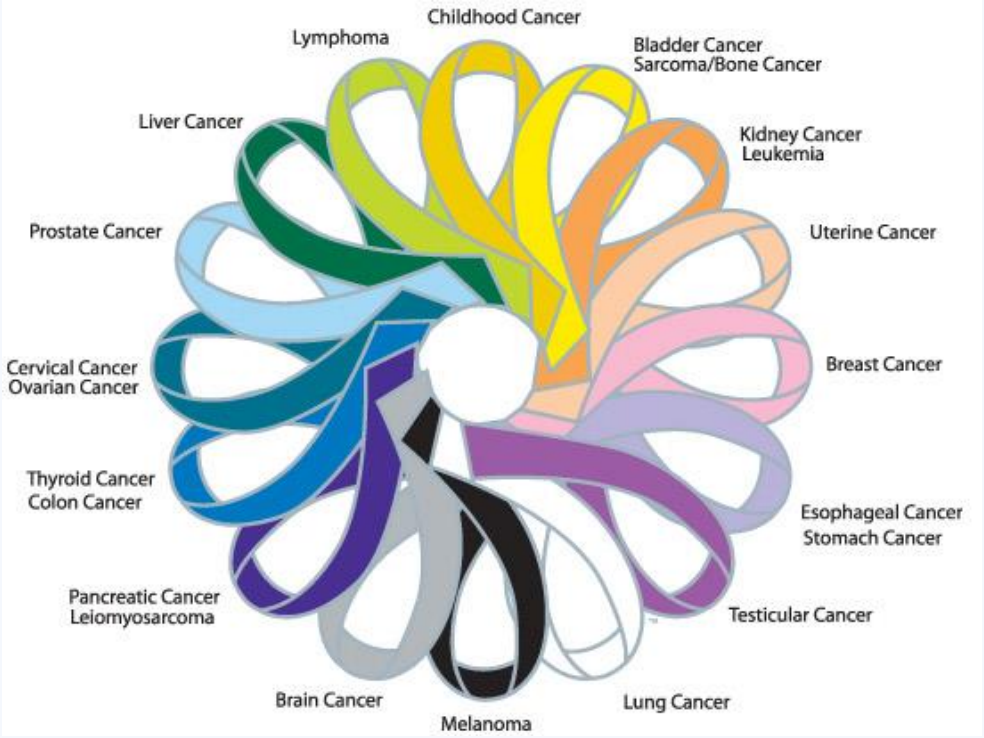
Work in progress …

- Formazione
- Ottimizzazione dei protocolli di follow-up
- Raccolta dati
- Coinvolgimento del medico di famiglia

www.thelancet.com/oncology Vol 14 July 2013

Treating the patient doesn't stop with their last cycle of therapy.

Care



SSD Unità di Transizione
per Neoplasie Curate in Età Pediatrica
Enrico Brignardello
Francesco Felicetti
Nicoletta Fortunati
Margherita Dionisi Vici