PEDIATRIC & ADOLESCENT CANCER SURVIVORSHIP

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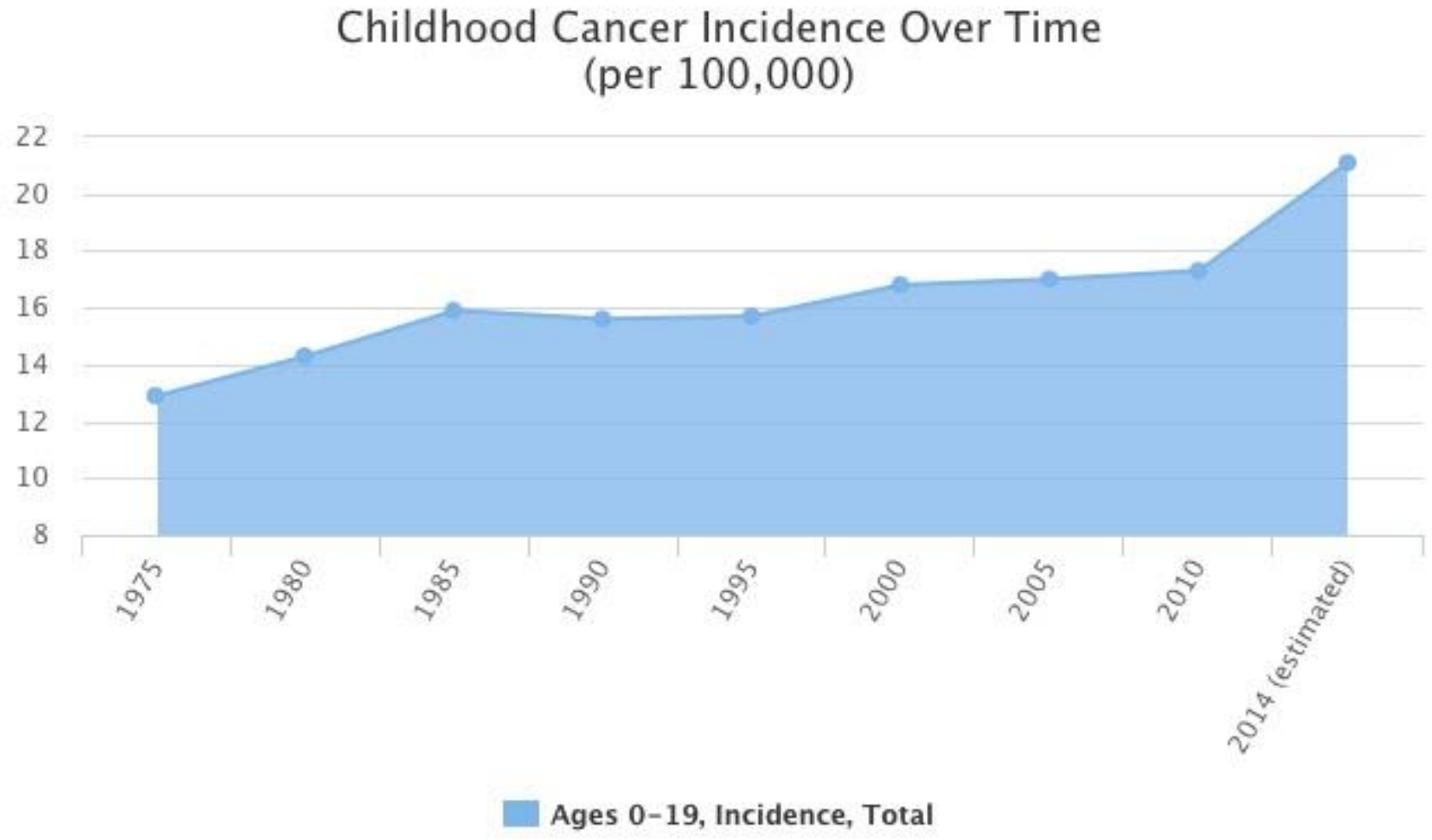
Objectives

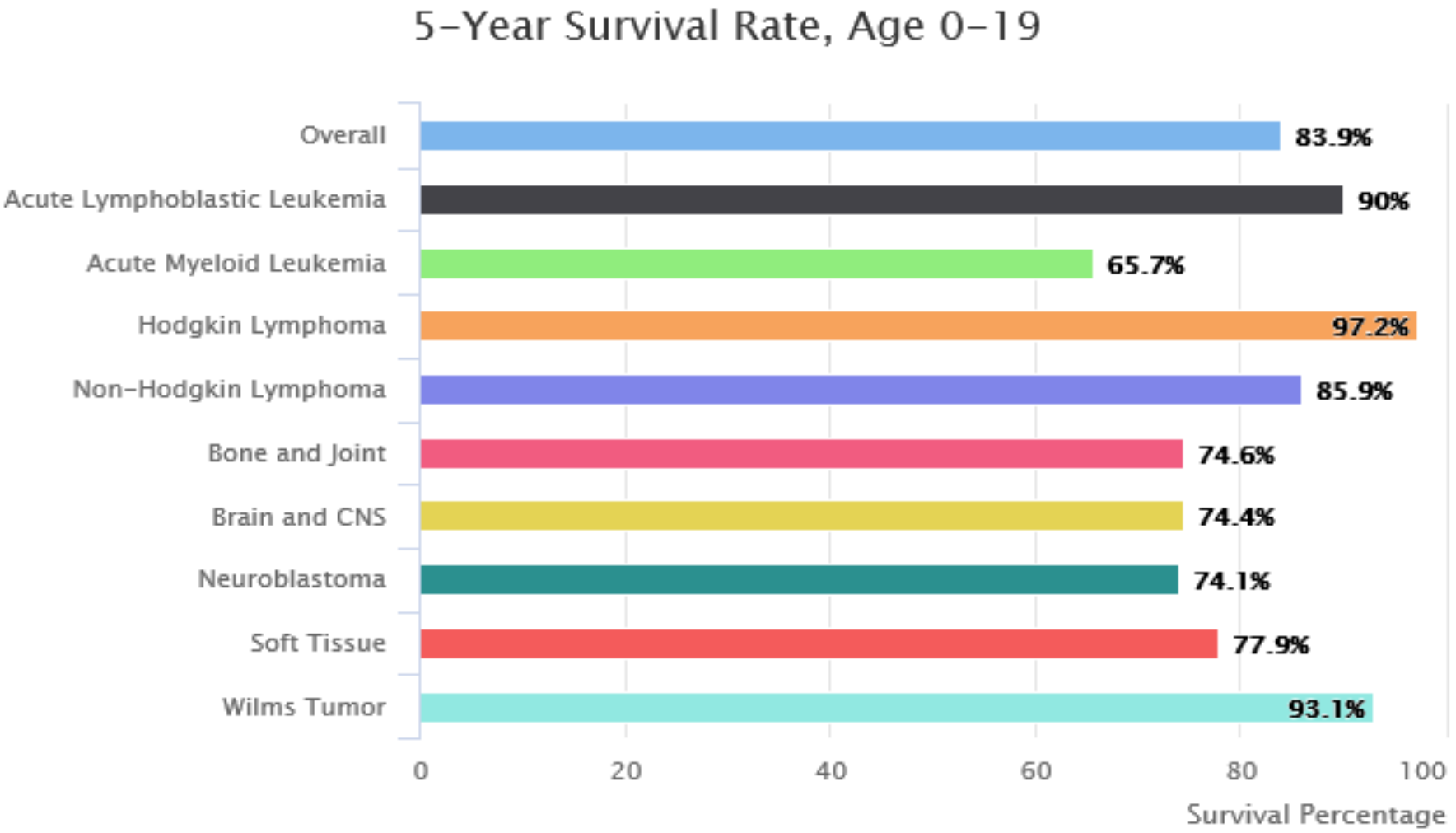
- Describe incidence of childhood cancer and survival rates and causes of early mortality.
- Understand the late effects of cancer treatment and the variables involved.
- Understand the benefits of screening and early detection as a means of prevention of late complications of cancer therapy.

Childhood Cancer Incidence



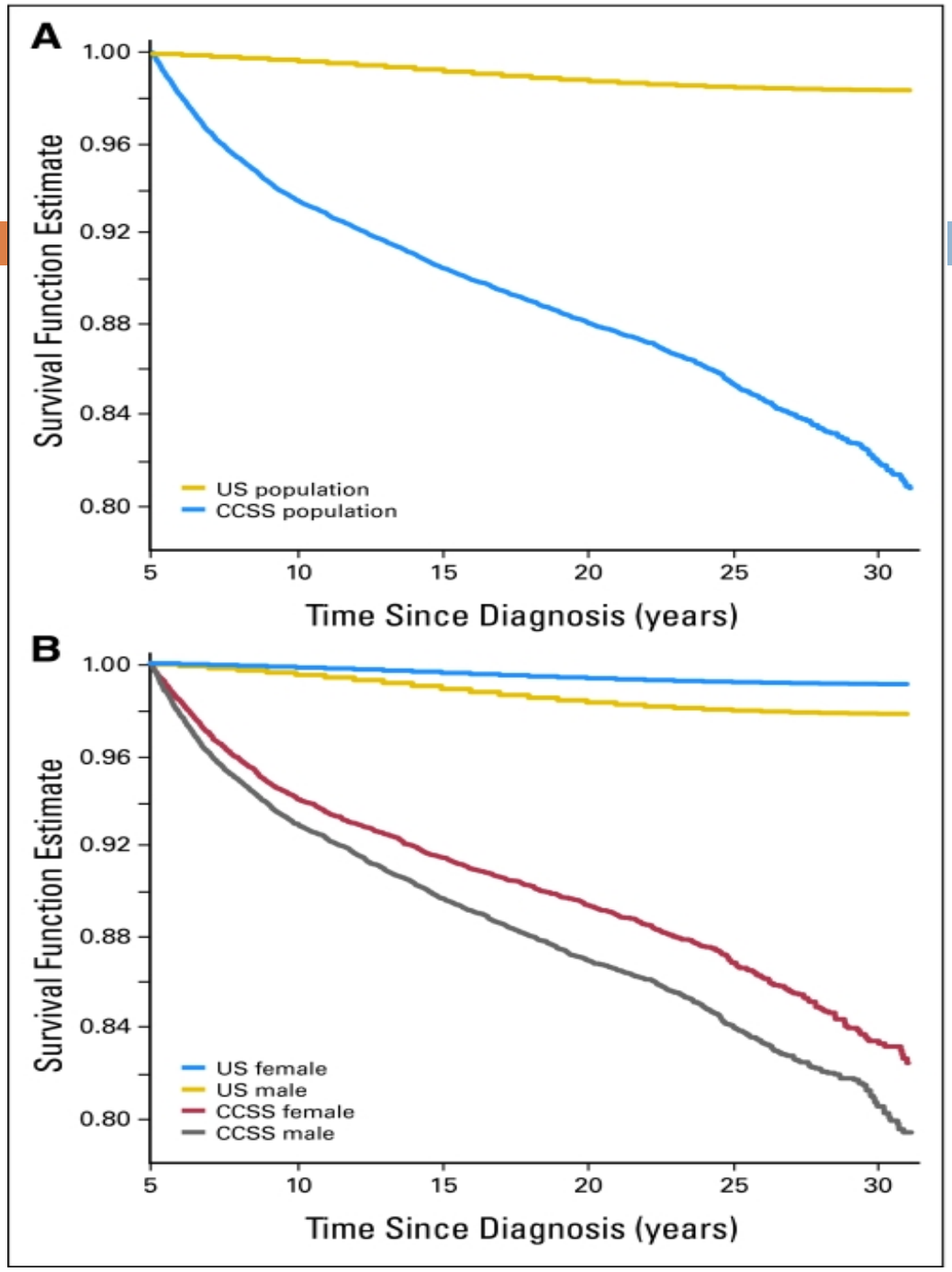
Source: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER 9 area. Age 0-19.

Survival Rates



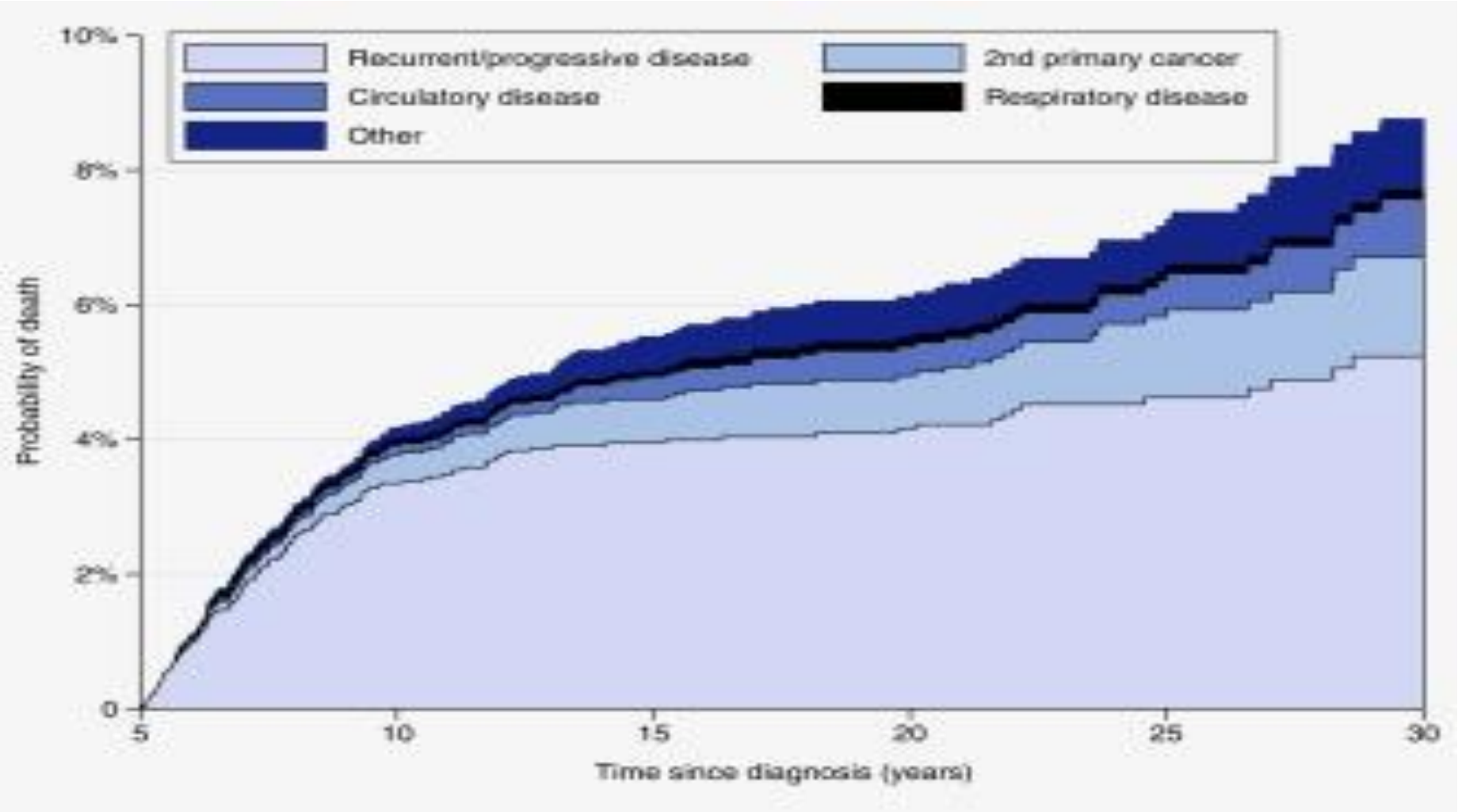
www.seer.cancer.gov

Mortality Data



J Clin Oncol. 2009 May 10;27(14):2328-38. doi: 10.1200/JCO.2008.21.1425. Epub 2009 Mar 30.

Causes of death



Int J Cancer. 2016 Jul 15;139(2):322-33. doi: 10.1002/ijc.30080. Epub 2016 Mar 30

About Survivors

- Survivors do not have complete knowledge of their diagnosis and treatment.
  - Approximately 30% of survivors can not accurately report their diagnosis.
  - Approximately 10% of patients do not recall receiving chemotherapy.
  - Only 30-50% recall receiving anthracyclines.
  - Approx. 30% are unaware of their risk for late effects.
  - Approximately 10% of patients do not recall receiving radiotherapy.

J Cancer Surviv (2016) 10: 363. doi:10.1007/s11764-015-0482-7

Late Effects

- Adverse long term health related outcomes that are dependent upon the therapeutic regimen a patient received as part of cancer therapy.
- Adverse events can occur months or years after cancer treatment.

Late Effects

- Causes
  - Location and extent of primary disease
  - Type and dose of cancer therapy
  - Genetic predisposition
- Host factors
  - Gender
  - Health habits
  - Age at time of treatment
  - Era of treatment

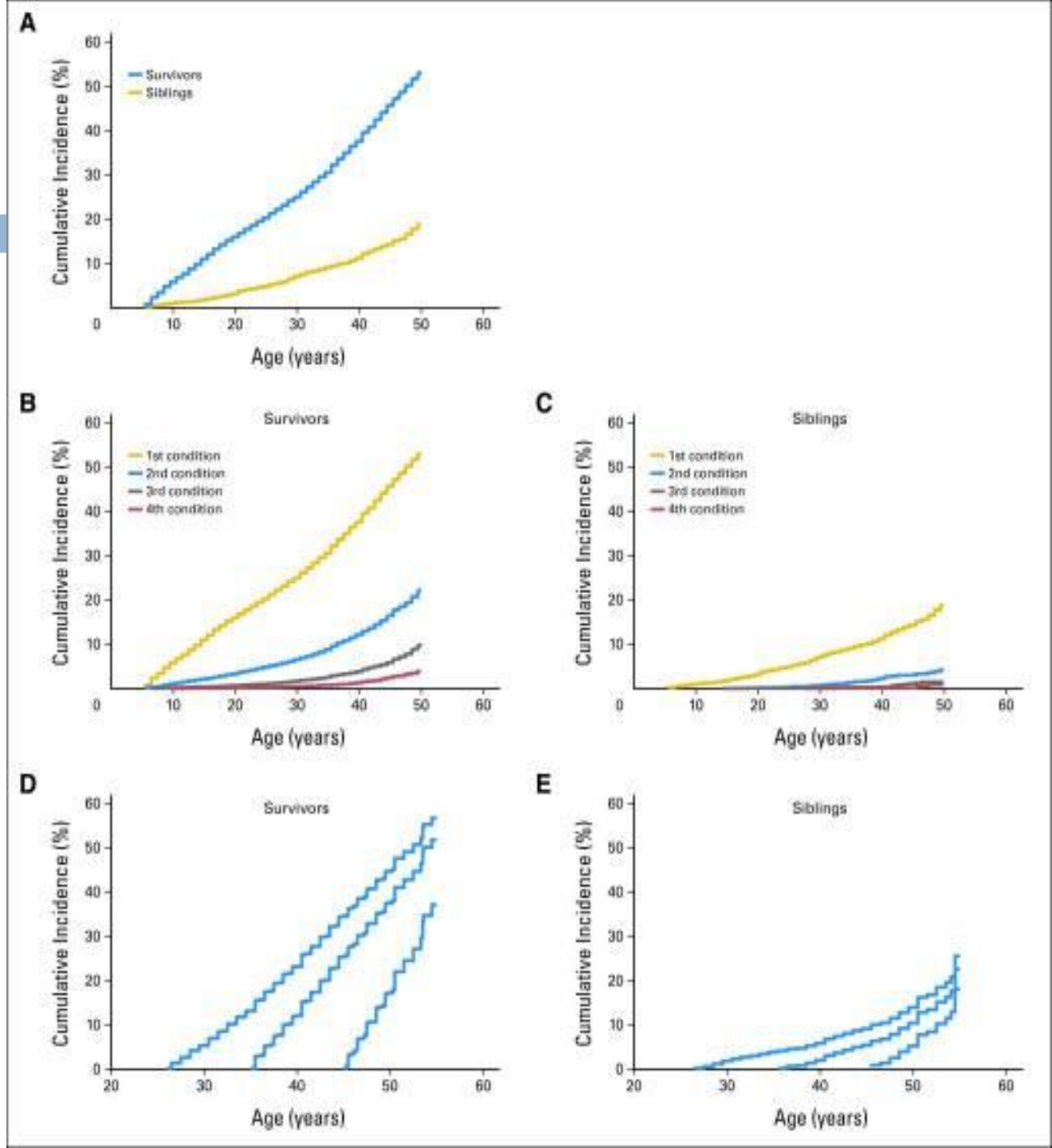
Late Effects- Genetics

Gene	Primary malignancy(s)	SMN type(s)
RB1[43,44]	Retinoblastoma (RB)	Soft tissues sarcomas, osteosarcoma, melanoma, CNS malignancies
BRCA1/2[45]	Primary Breast	Contralateral breast cancer, GI malignancies, ovarian tumors
NF1[46,47]	Optic pathway gliomas	Malignant peripheral nerve-sheath tumors, gliomas, t-AML
TP53[48,49]	Li-Fraumeni Syndrome: tumors of the breast, CNS, adrenocortical carcinomas, soft tissues sarcomas, leukemias (rare)	
MLH1[45], MSH2, MSH6	Hereditary Nonpolyposis Colorectal Cancer Syndrome (HNPCC or Lynch Syndrome): colon cancer, female reproductive cancers, other GI cancers	
VHL[47,50]	Von-Hippel Landau Syndrome: hemangioblastoma, renal cell carcinoma, pheochromocytoma	
DICER1[51,52]	DICER1 Syndrome: pleuropulmonary blastoma, cystic nephroma, ovarian tumors, soft tissue sarcomas	

Choi, D. K., Helenowski, I. and Hijiya, N. (2014), Secondary malignancies in pediatric cancer survivors: Perspectives and review of the literature. Int. J. Cancer, 135: 1764–1773. doi:10.1002/ijc.28991

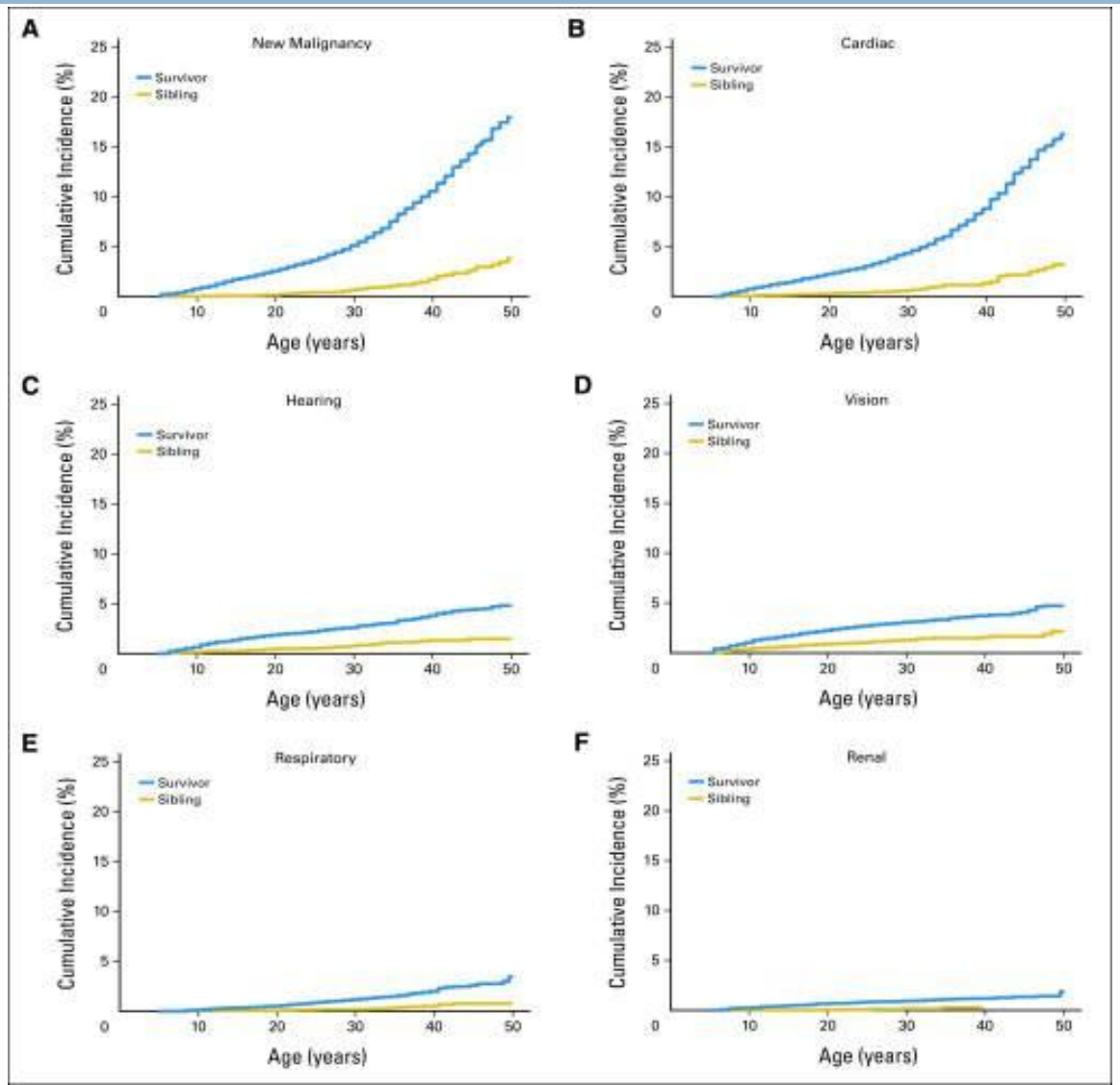
Late Effects

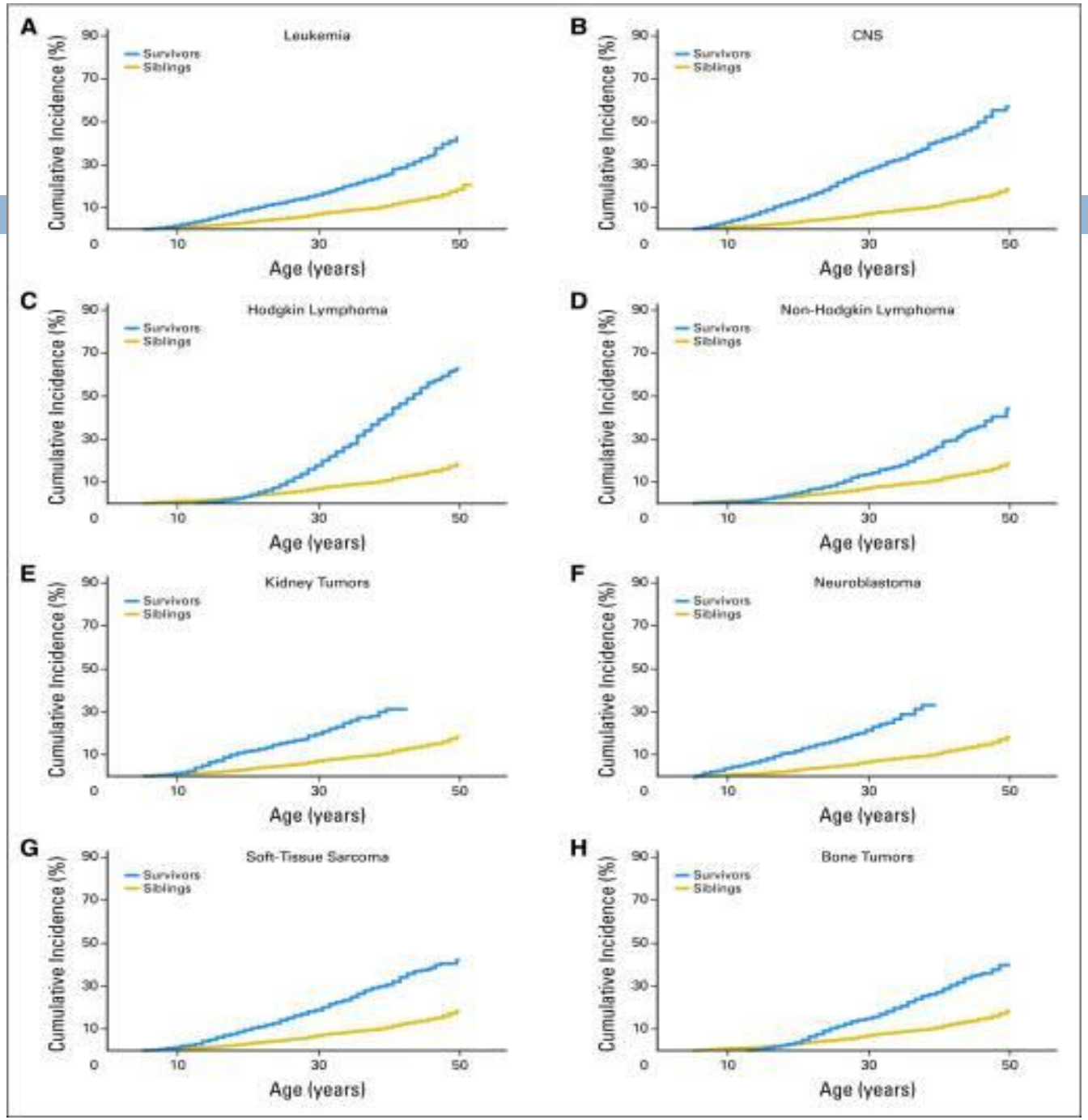
- 24 yo survivor has the same cumulative incidence of a grade 3-5 health condition as a 50 sibling.
- By age 50, 23% of survivors had 2 or more severe, disabling, life-threatening, or fatal health condition compared with only 4.3% of sibs.
- 25% of 'healthy' survivors had a new grade 3-5 health condition within 10 years.



J Clin Oncol. 2014 Apr 20;32(12):1218-27. doi: 10.1200/JCO.2013.51.1055. Epub 2014 Mar 17.

Late Effects




A
Leukemia
B
CNS
C
Hodgkin Lymphoma
D
Non-Hodgkin Lymphoma
E
Kidney Tumors
F
Neuroblastoma
G
Soft-Tissue Sarcoma
H
Bone Tumors
Survivors
Siblings
Cumulative Incidence (%)
Age (years)
0
10
30
50
10
30
50
70
90

Any Cancer Experience- Psychosocial Issues

- Increased risk for smoking, drinking, and other risky behaviors
- Increased risk for not completing school
- Poor body image and self-esteem
- Social Withdrawal
- Increased risk of mental health disorders
  - Depression and anxiety
  - Post-traumatic stress
  - Chronic Fatigue

Any Cancer Experience- Psychosocial Issues

- Risk Factors
  - Female gender
  - Adolescents and Young Adults
  - Prior Trauma
  - Previous mental health history
  - Poor support system
  - Family History of Mental Health disorders
  - CNS cancer or Bone Marrow Transplantation
  - Low Socioeconomic status

Chemotherapy

- Anthracyclines- Doxorubicin, Daunorubicin
- Epipodophyllotoxins- Etoposide
- Alkylating agents- Cytoxan
- Radiation- Cranial or Craniospinal
- Bone Marrow Transplant

Chemotherapy

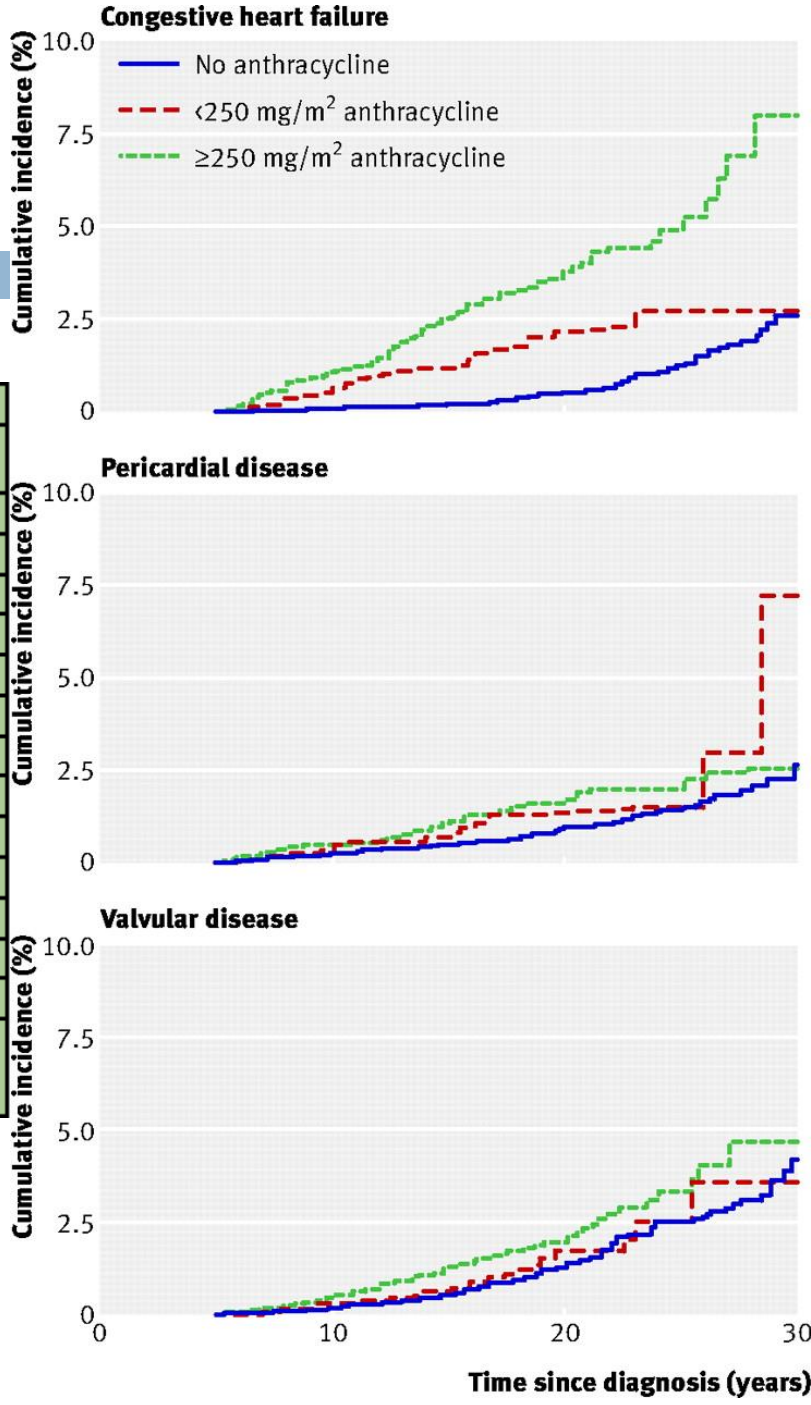
- Anthracyclines
  - Dilated cardiomyopathy and arrhythmias
    - Doxorubicin
    - Daunorubicin
    - Idarubicin
    - Mitoxantrone

Cardiac Toxicity

RECOMMENDED FREQUENCY OF ECHOCARDIOGRAM (or comparable cardiac imaging)			
Age at Treatment*	Radiation with Potential Impact to the Heart§	Anthracycline Dose†	Recommended Frequency
<1 year old	Yes	Any	Every year
	No	< 200 mg/m²	Every 2 years
		≥ 200 mg/m²	Every year
1-4 years old	Yes	Any	Every year
	No	<100 mg/m²	Every 5 years
		≥100 to <300 mg/m²	Every 2 years
		≥300 mg/m²	Every year
≥5 years old	Yes	<300 mg/m²	Every 2 years
		≥300 mg/m²	Every year
	No	<200 mg/m²	Every 5 years
		≥200 to <300 mg/m²	Every 2 years
		≥300 mg/m²	Every year
Any age with decrease in serial function			Every year

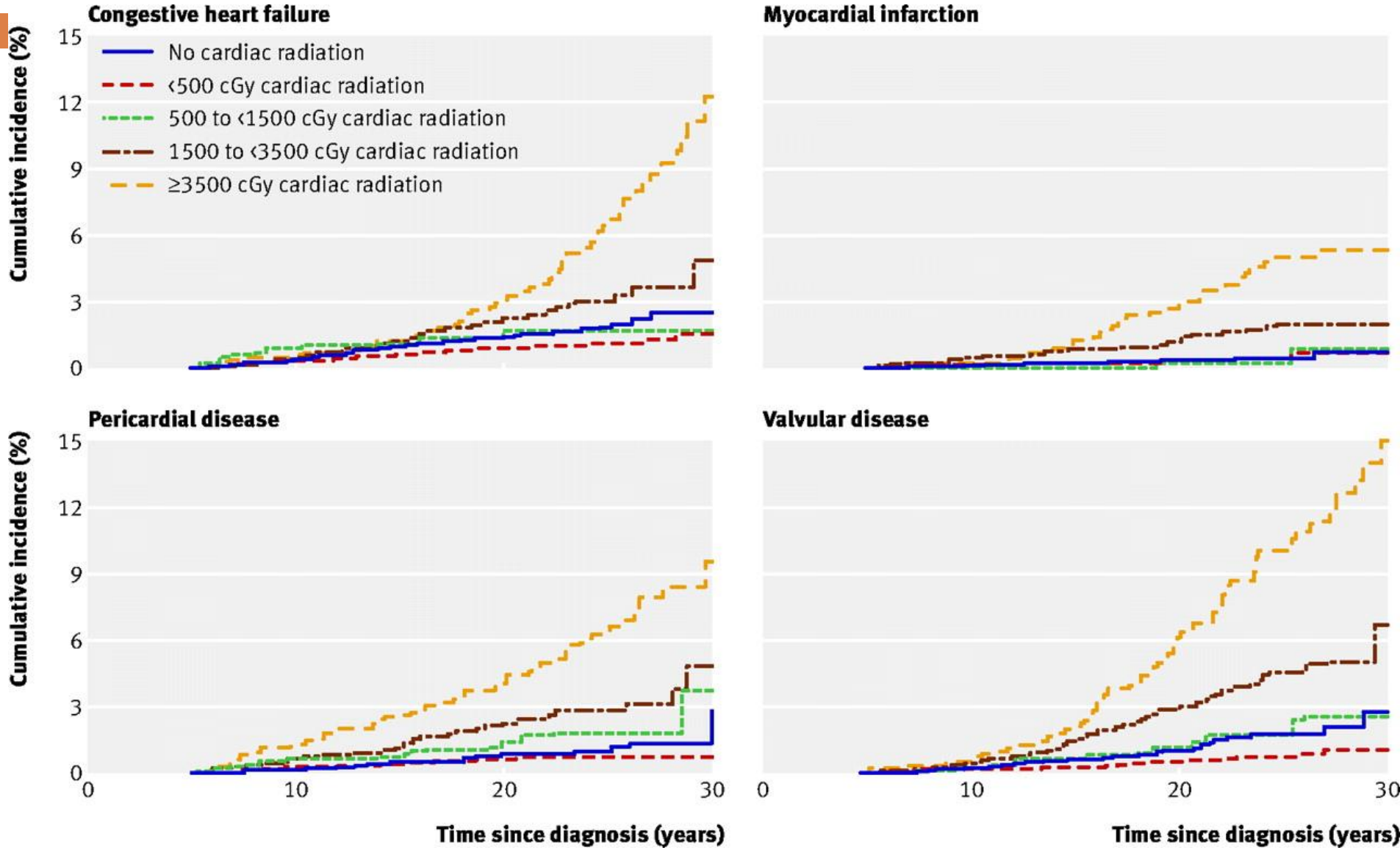
*Age at time of first cardiotoxic therapy (anthracycline or radiation [see Section 81], whichever was given first)
§See Section 81
†Based on doxorubicin isotoxic equivalent dose [see conversion factors on previous page, "Info Link (Dose Conversion)"]

http://www.survivorshipguidelines.org/pdf/LTFUGuidelines_40.pdf



https://doi.org/10.1136/bmj.b4606 (Published 09 December 2009)

Cardiac Toxicity



Chemotherapy

- Secondary Malignancies
  - Epipodophyllotoxins- Etoposide
  - Anthracyclines
  - Alkylating agents
    - Nitrogen Mustard
    - Cytoxan
  - Stem Cell Transplant
  - Radiation

Second Malignant Neoplasms

Primary Diagnosis	N	Breast	Thyroid Cancer	CNS Tumors	Sarcoma	Bone	Leukemia	Melanoma	Lymphoma	GI Carcinomas	NMSC
HL	247	**94**	**36**	7	19	6	14	11	14	14	**163**
Leukemia	152	16	**23**	**45**	4	4	9	11	10	2	**138**
Soft tissue sarcoma	80	10	7	3	**18**	**12**	3	6	2	2	**23**
Bone cancer	74	**21**	9	3	5	9	6	5	1	7	**20**
CNS tumor	68	3	12	**18**	6	5	3	4	4	2	**40**
NHL	43	**6**	**7**	4	2	5	2	2	4	2	**27**
Neuroblastoma	33	2	**8**	1	4	0	4	0	1	0	**6**
Wilms tumor	33	**5**	2	0	**7**	**5**	2	3	0	4	**13**
Total	1,160	157	104	81	65	46	43	42	36	33	**430**

Chemotherapy

- Infertility or Premature Ovarian Failure
  - Nitrogen Mustard
  - Dacarbazine
  - Procarbazine
  - Cytoxan
- Avascular Necrosis/ Osteopenia/ Osteoporosis- Steroids
- Pulmonary Fibrosis- Bleomycin

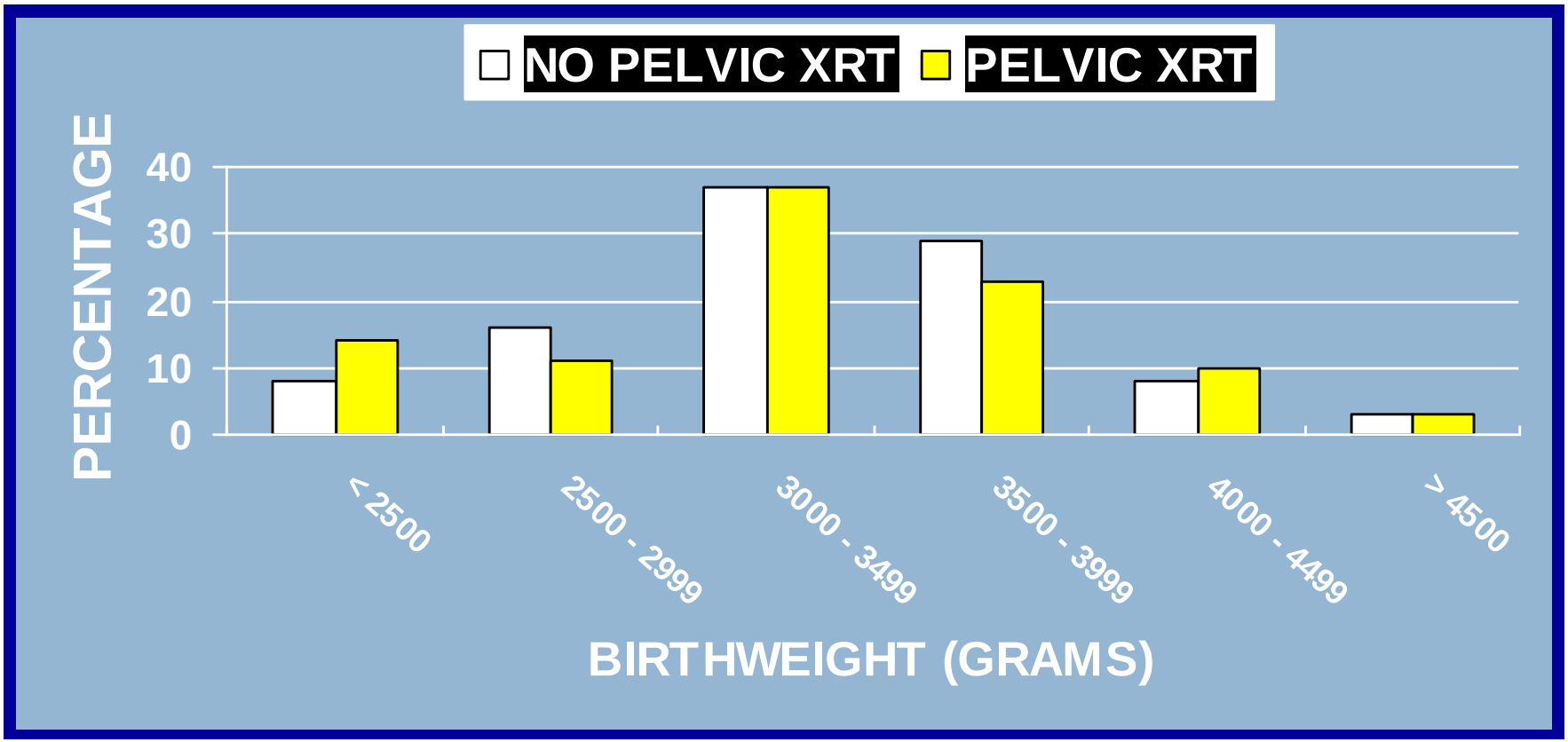
Radiation

- Cranial
  - Growth hormone deficiency
  - Metabolic Syndrome
  - Endocrine Dysfunction
  - Hearing loss
  - Visual disturbance/ Cataracts
  - Dental caries
  - Neurocognitive Deficits
    - Executive Functioning, Learning issues
- Secondary Malignancies
  - Thyroid dysfunction
  - Breast Cancer
  - Thyroid Cancer

Radiation

- Liver/Spleen dysfunction
- Premature births/ Low Birth weight/ Small for gestational age

Radiation-Abdominal Tumors

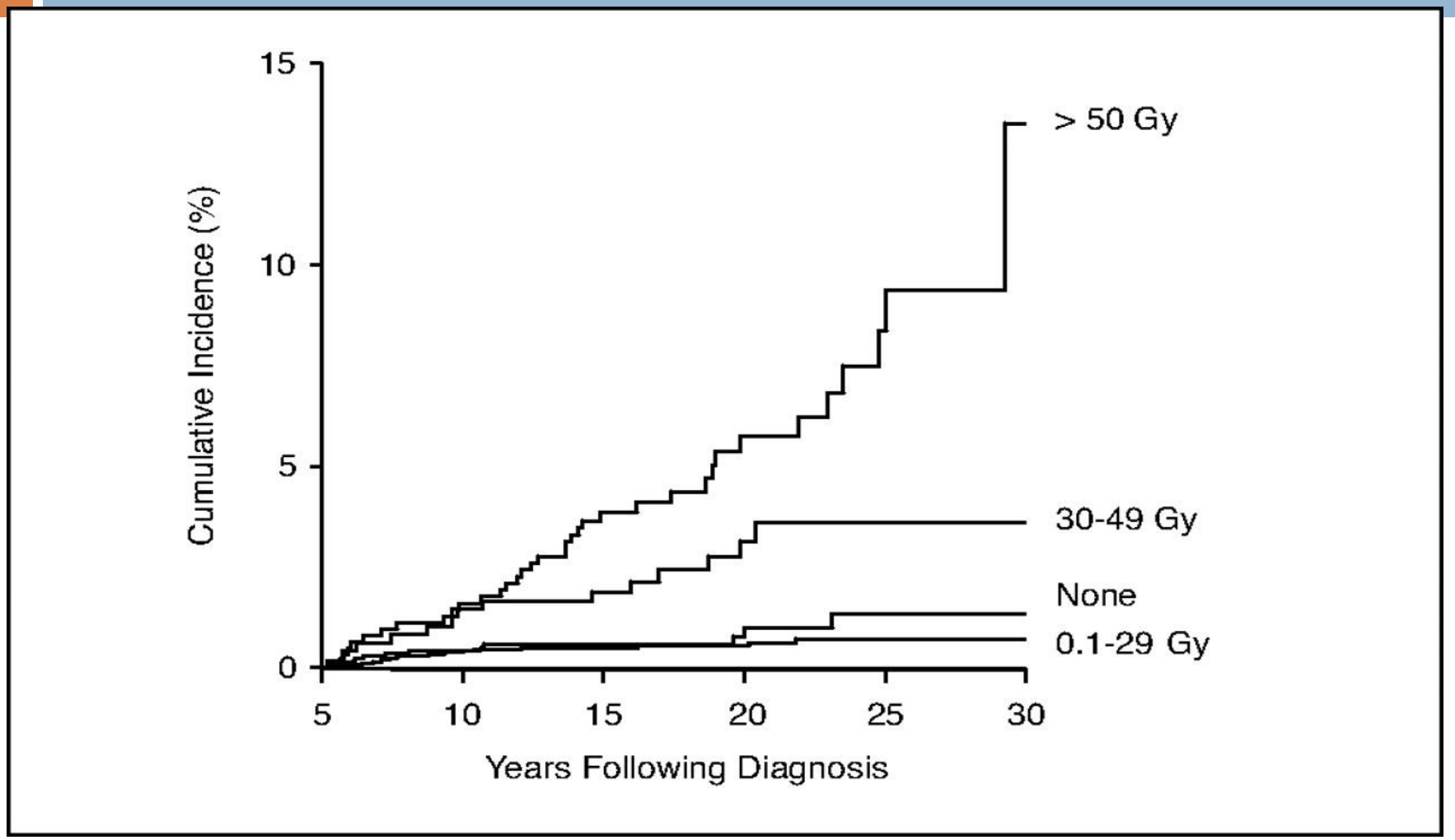


Am J Obstet Gynecol 2002;187:1070-1080

Skin Cancer

- Non-melanoma skin cancer is the most frequently diagnosed secondary malignant neoplasm.
  - Locations include head and neck (43%), back (24%), chest (22%), abdomen and pelvis (5%), extremity (3%) and unknown (4%).
  - Ninety percent of non-melanoma skin cancers occur in prior areas of radiation.

Brain Tumor- Stroke Risk



Surgery

- Abdominal Tumors
  - Bowel obstruction
  - Chronic abdominal pain
  - Poor GI motility
- Musculoskeletal problems
  - Leg length discrepancies
  - Pain
  - Disability from limb sparing surgery

Pregnancy Outcomes- Offspring

	Offspring of Survivors (N = 2198)	Offspring of Siblings (N = 4544)
Chromosomal Syndrome	0.2% (4)	0.1% (6)
Single Gene Disorder	0.6% (14)	0.2% (10)
Major Congenital Malformation	2.7% (59)	2.8% (127)

Am J Hum Genet 1998;62:45-52

Prevention

- Health maintenance – age appropriate monitoring, age appropriate general health screening including cancer screening, eye exams, dental exams
- Exposure related screening – cardiac, second malignant neoplasms, pulmonary disease, neuropsychological screening, psychosocial screening
- Patient education – risk reduction (alcohol, tobacco, exercise, sun exposure), anticipatory guidance (e.g. fertility and pregnancy)

https://childrensoncologygroup.org/index.php/survivorshipguidelines

The Good News!!!