Follow Up Care for Children Who Have Had Cancer

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Care after Childhood Cancer

- Why do we need to talk about this?
- What are late effects and who is at risk for them?
- What resources are available to help when providing care for these patients?

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Why Do We Need to Talk About This?

Prevalence….

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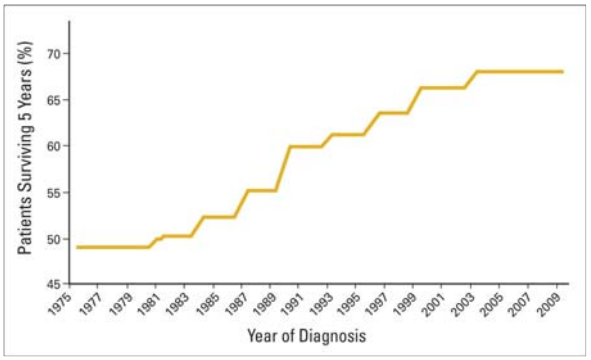
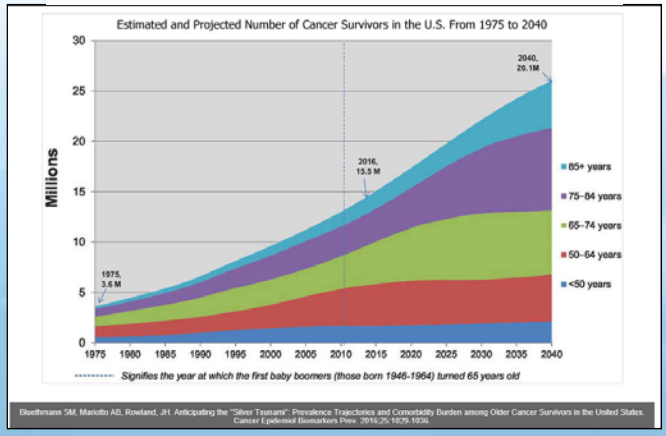
Growing Numbers of Cancer Survivors



The State of Cancer Care in America, 2014: A Report by American Society of Clinical Oncology.
JOP 2014;10:119-142 ©2014 by American Society of Clinical Oncology

> 15 million cancer survivors in US today



ASCO Post 2016. http://www.ascopost.com/issues/february-25-2016/ Bridging the Medical Gap in Long-Term Cancer Survivorship Care. ASCO JOP 2014;10:119-142

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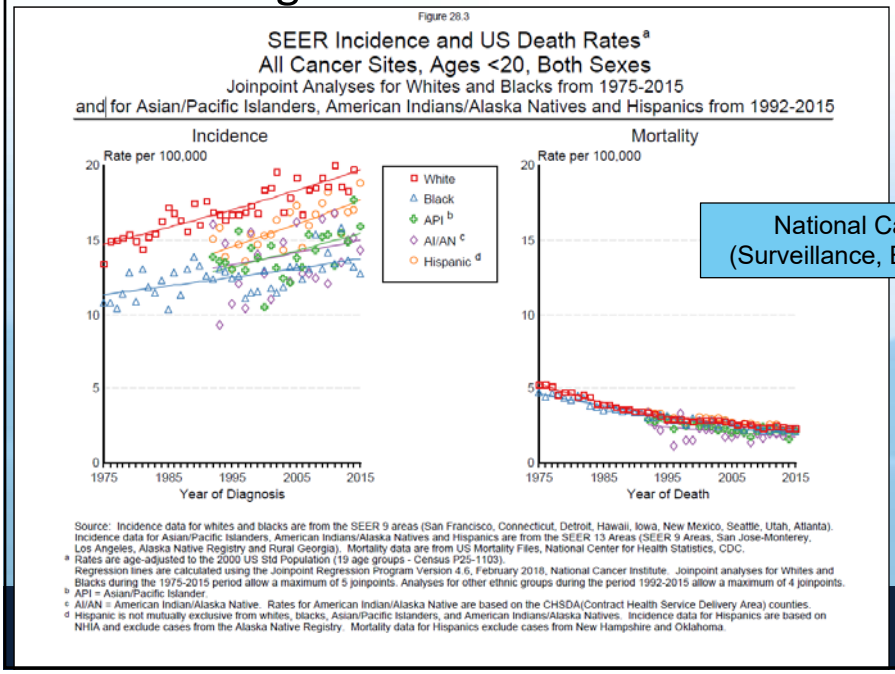
Growing Numbers of Childhood Cancer Survivors



National Cancer Institute - SEER Data
(Surveillance, Epidemiology, and End Results)

NCI SEER Data. https://seer.cancer.gov/csr/1975_2015. Accessed 3/2019.

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SEER Cancer Statistics Review 1975-2015

National Cancer Institute

Table 20.8

5-Year Relative Survival (Percent)

By Selected Primary Cancer Site and Year of Diagnosis

All Races, Males and Females

National Cancer Institute - SEER Data (Surveillance, Epidemiology, and End Results)

Ages 0-14

Site	1975-1977	1978-1980	1981-1983	1984-1986	1987-1989	1990-1992	1993-1995	1996-1998	1999-2001	2002-2007	2008-2014
All Sites											
All Races	58.0	62.4	67.1	68.1	71.7	75.8	77.4	79.3	80.8	82.8	83.8[c]
Whites	57.9	63.0	67.8	69.9	72.5	76.8	78.3	80.6	81.8	84.8	84.6[c]
Blacks	57.3	57.7	62.2	56.6	65.3	70.8	73.3	75.6	74.0	73.4	79.8[c]
Bone & Joint	49.9[d]	47.8	56.8[d]	57.3[d]	66.8[d]	67.4	74.2	70.3	69.3	77.6	80.7[c]
Brain & CNS	57.2	57.7	56.9	61.8	64.4	64.5	70.7	75.4	74.2	75.5	75.0[c]
Hodgkin lymphoma	80.9	86.8	88.1	89.9	87.1	96.8	94.6	96.1	94.4	97.5	97.9[c]
Leukemia	49.7	58.0	63.0	63.7	71.0	75.5	76.0	80.3	82.7	86.1	87.6[c]
Acute lymphocytic	57.2	65.7	71.3	72.3	77.7	83.1	83.9	87.0	88.5	91.9	90.6[c]
Acute myeloid	18.8	25.8	27.8[d]	30.6[d]	37.1[d]	42.2	40.6[d]	48.7	58.6	61.5	68.8[c]
Neuroblastoma[a]	52.5	56.6	54.8	52.3	63.2	76.0	66.5	66.5	72.2	73.7	74.8[c]
Non-Hodgkin lymphoma	43.2	52.7	67.0	69.8	70.8	76.9	80.7	83.2	89.8	84.6	88.5[c]
Soft tissue	61.3	74.2	69.2	73.0	66.4	79.8	76.7	70.6	76.9	84.7	80.9[c]
Wilms' tumor[b]	73.1	79.0	86.7	90.7	92.2	91.9	91.7	91.6	93.8	89.4	91.0[c]

Ages 0-19

Site	1975-1977	1978-1980	1981-1983	1984-1986	1987-1989	1990-1992	1993-1995	1996-1998	1999-2001	2002-2007	2008-2014
All Sites											
All Races	61.5	65.2	68.4	70.6	73.5	76.3	77.8	79.9	80.3	82.6	84.0[c]
Whites	61.3	65.9	69.3	72.5	75.0	77.6	78.5	81.1	81.4	84.1	84.8[c]
Blacks	59.4	60.3	62.5	58.3	64.3	68.7	74.2	73.9	74.8	73.1	78.8[c]
Bone & Joint	50.4	48.1	51.2	56.1	64.0	68.8	69.0	67.0	66.3	73.5	73.4[c]
Brain & CNS	59.1	58.1	58.5	63.9	66.0	66.5	71.5	76.2	74.7	75.5	75.5[c]
Hodgkin lymphoma	86.2	88.3	85.5	90.6	88.7	94.3	93.9	95.2	95.1	96.3	98.3[c]
Leukemia	44.9	53.2	58.1	60.4	67.6	71.3	71.9	76.6	77.6	81.9	85.4[c]
Acute lymphocytic	53.8	61.9	67.1	69.9	75.0	79.8	81.5	84.4	84.8	88.1	89.2[c]
Acute myeloid	18.7	26.2	27.2	31.4	37.6	41.9	38.6	46.3	51.9	59.8	67.1[c]
Neuroblastoma[a]	53.1	56.7	53.7	52.5	61.8	75.7	66.5	66.7	71.9	73.4	75.2[c]
Non-Hodgkin lymphoma	44.6	53.4	63.7	67.6	70.4	72.7	78.0	81.1	84.3	84.5	84.3[c]
Soft tissue	64.8	68.9	68.2	72.7	68.0	69.7	73.8	72.4	72.4	76.9	80.1[c]
Wilms' tumor[b]	72.6	78.4	86.8	91.0	92.2	91.3	91.8	91.6	93.8	89.5	90.4[c]

Source: SEER 9 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, and Atlanta).
Based on follow-up of patients into 2015. Expected survival rates are derived from the U.S. Annual Life Tables.

Note: Neuroblastoma and Wilms' tumor are not mutually exclusive from the other tumors presented in table.

[a] Neuroblastoma is defined as histologies 9490-9509.

[b] Wilms' tumor is defined as histologies 8959-8960.

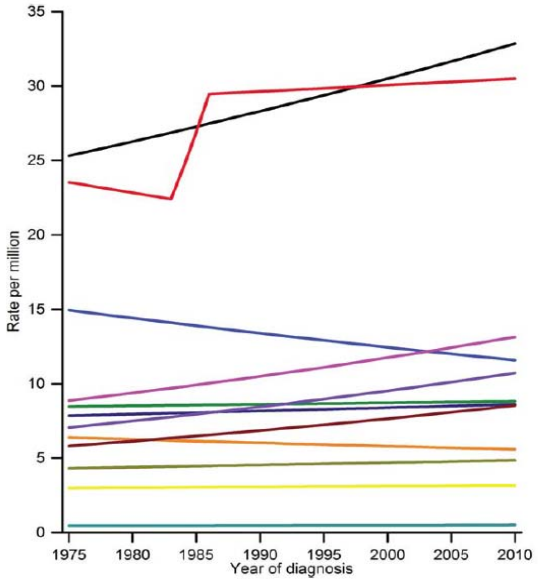
[c] The difference between 1975-1977 and 2008-2014 is statistically significant (p<.05).

[d] The standard error is between 5 and 10 percentage points.

[e] The standard error is greater than 10 percentage points.

[-] Statistic could not be calculated due to fewer than 25 cases during the time period.

NCI SEER Data. https://seer.cancer.gov/csr/1975_2015. Accessed 3/2019.



1 in 530 young adults 20-39 years old is a childhood cancer survivor

- Acute lymphocytic leukemia (ALL)
- Brain and CNS
- Hodgkin lymphoma (HL)
- Non-Hodgkin lymphoma (NHL)
- Bone tumors
- Neuroblastoma
- Testicular germ cell tumors
- Wilms tumor
- Acute myeloid leukemia (AML)
- Rhabdomyosarcoma
- Retinoblastoma
- Ovarian germ cell tumors

Ward et al. Childhood and Adolescent Cancer Statistics, 2014. CA Cancer J Clin 2014; 64:83-103.

FIGURE 2. Trends in Pediatric Cancer Incidence Rates by Site, Ages Birth to 19 Years, 1975 to 2010.

CNS indicates central nervous system. Note: Lines represent joinpoint fitted trends. Benign and borderline brain tumors are not included. Malignant bone tumors include osteosarcoma and Ewing sarcoma. Average annual percent change for cancers with significant trends during 1975 through 2010: acute lymphocytic leukemia (0.7*), acute myeloid leukemia (1.1*), non-Hodgkin lymphoma (1.1*), testicular germ cell tumors (1.2*), and Hodgkin lymphoma (−0.7*). Source: Surveillance, Epidemiology, and End Results (SEER) program, 9 SEER Registries, National Cancer Institute.

Why Do We Need to Talk About This?

Provider Gaps….

ASCO Estimates National Oncologist Shortage

- ASCO analysis
  - number of practicing oncologists
  - number of training spots for new oncologists
  - oncology demand
- 2007, 2014
- Demand for oncologists predicted to grow 40%
- Supply of new oncologists predicted to grow 25%
- Shortage by 2025 (equivalent to 500,000 patient visits)

The State of Cancer Care in America, 2014: A Report by American Society of Clinical Oncology. JOP 2014;10:119-142 ©2014 by American Society of Clinical Oncology
ASCO Post 2016. http://www.ascopost.com/issues/february25,2016/ Bridging the Medical Gap in Long-Term Cancer Survivorship Care. ASCO. JOP 2014;10:119-142

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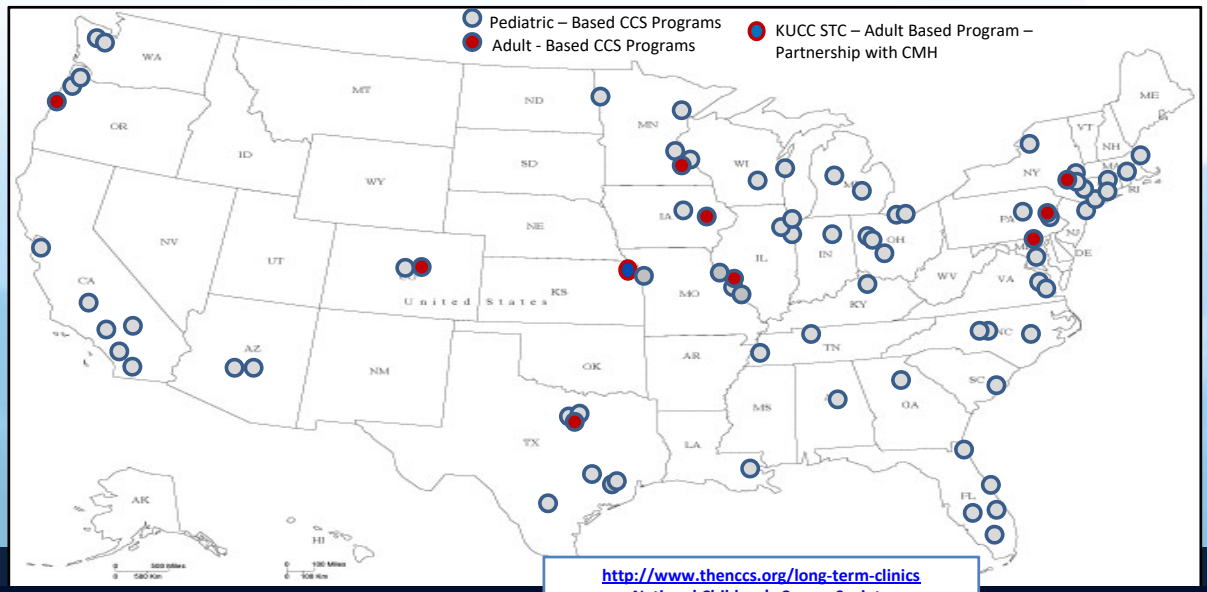
Survivorship Clinics for Childhood Cancer Survivors



http://www.thenccs.org/long-term-clinics
National Children's Cancer Society

Funding Source: MCA Partners Advisory Board, Tour de BBQ

Primary Care is Critical

- PCP's play critical role in survivorship
- Oncology visits decline 5 years after treatment
- "Patients expected both their oncologists and primary care providers to be involved" in management of their survivorship care

Blanch-Hartigan et al. Journal Clinical Oncology. 2014. Provision and Discussion of Survivorship Care Plans Among Cancer Survivors
Nekhlyudov. Journal Clinical Oncology. 2009. Doc, Should I See You or My Oncologist?
Salsberg E. Physician workforce shortages: implications and issues for academic health centers and policymakers. Acad Med. 2006; 81:782-87.
The State of Cancer Care in America, 2014: A Report by American Society of Clinical Oncology. JOP 2014;10:119-142 ©2014 by American Society of Clinical Oncology
ASCO Post 2016. http://www.ascopost.com/issues/february-25-2016/ Bridging the Medical Gap in Long-Term Cancer Survivorship Care. ASCO JOP 2014;10:119-142

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Why Do We Need to Talk About This?

Knowledge Gap….

VOLUME 28 · NUMBER 5 · FEBRUARY 10 2010
JOURNAL OF CLINICAL ONCOLOGY
ORIGINAL REPORT

Physician Preferences and Knowledge Gaps Regarding the Care of Childhood Cancer Survivors: A Mailed Survey of Pediatric Oncologists

Tara O. Henderson, Fay J. Hlubocky, Kristen E. Wroblewski, Lisa Diller, and Christopher K. Daugherty

R A C T

knowledge regarding the health care needs of
obtain pediatric cancer physicians' self-reported
on.

ologists in the United States.

Conclusion
Pediatric oncologists express a range of prefe
unfamiliar with LTFU surveillance guidelines.

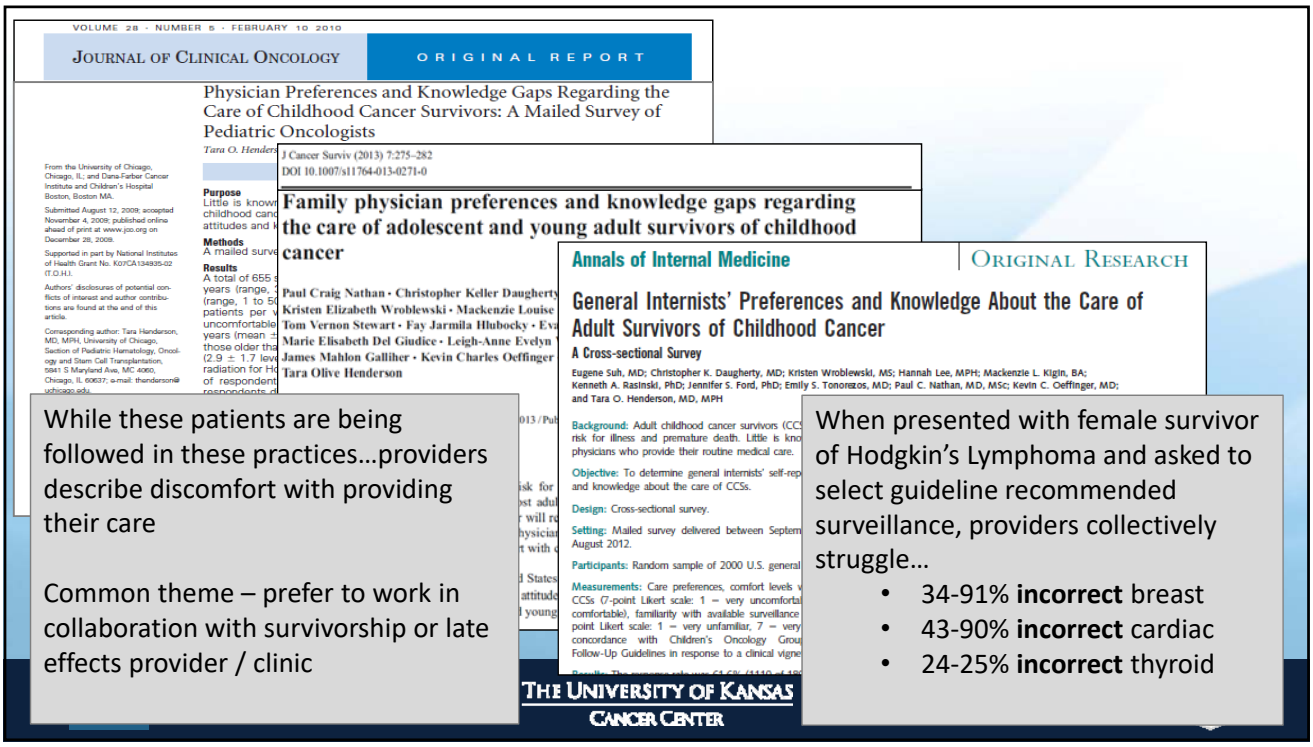
J Clin Oncol 28:878-883. © 2009 by American

When presented with clinical vignette of female survivor of Hodgkin's lymphoma…

- **34%** did not recommend appropriate surveillance for breast cancer
- **43%** did not recommend appropriate cardiac monitoring
- **24%** did not recommend yearly monitoring for thyroid function

Oncologists were…

- "…most comfortable" caring for survivors ≤ 21 years old
- "…less comfortable" with survivors between 21-30 years
- "…uncomfortable" with survivors ≥ 30 years



While these patients are being followed in these practices…providers describe discomfort with providing their care

Common theme – prefer to work in collaboration with survivorship or late effects provider / clinic

When presented with female survivor of Hodgkin's Lymphoma and asked to select guideline recommended surveillance, providers collectively struggle…

- 34-91% **incorrect** breast
- 43-90% **incorrect** cardiac
- 24-25% **incorrect** thyroid

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Survivorship Treatment Summary and Survivorship Care Plans

All patients should receive an individualized Treatment Summary

- Institute of Medicine
- American Cancer Society
- American College of Surgeons Commission on Cancer
- American Society of Clinical Oncology

Commission on Cancer Mandate - Survivorship Care Plans

- 25% all survivors by January 2016
- 100% all survivors by 2019

Blanch-Hartigan et al. Journal Clinical Oncology. 2014. Provision and Discussion of Survivorship Care Plans Among Cancer Survivors
Barton. Perspectives: Research in Context; A Cancer Journal for Clinicians. 2014.Oncologists and Primary Care Physicians Infrequently Provide Survivorship Care Plans
Commission on Cancer, 2011. Cancer Program Standards: Ensuring Patient-Centered Care.

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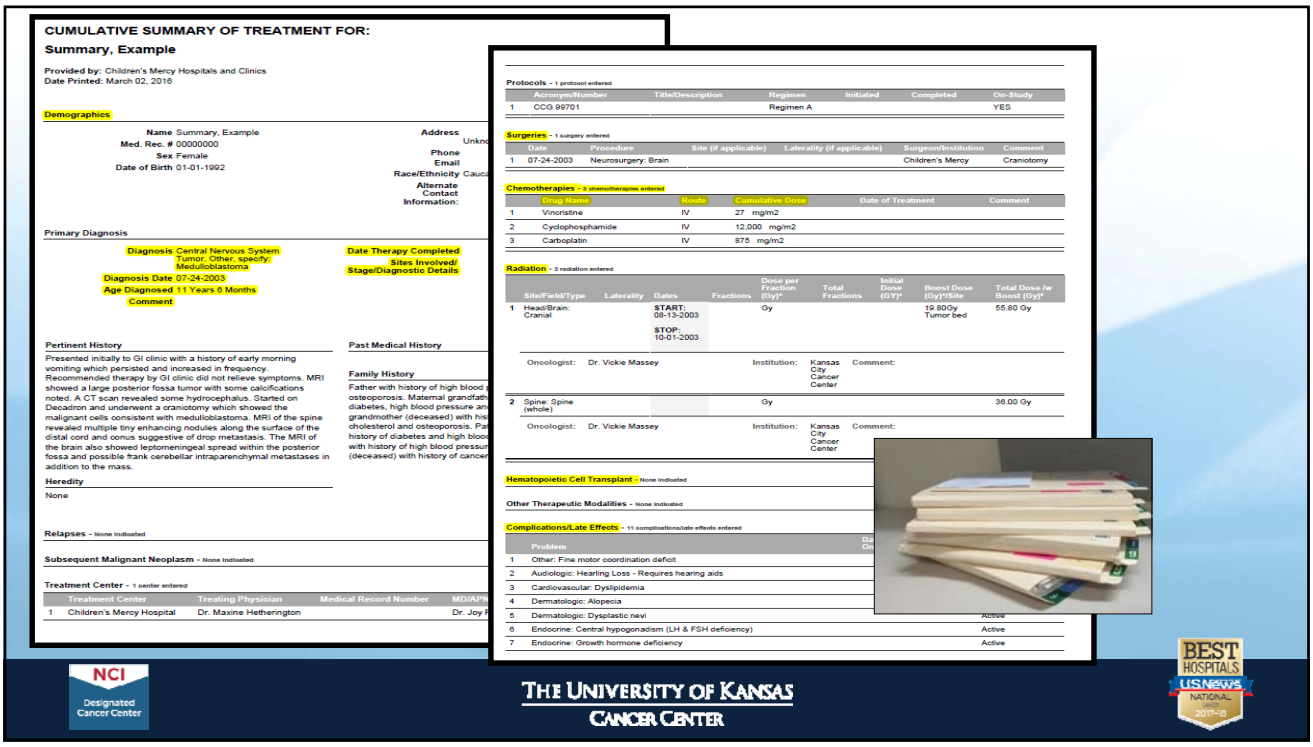

Treatment Summaries and Care Plans … How are we doing?

- <10% oncologists always / almost always provide Survivorship Care Plans
- <5% oncologists provide written Survivorship Care Plans and have full discussions with patients

PCPs who receive a treatment summary and Survivorship Care Plans were **over 9 times** more likely to discuss survivorship care with patients

Blanch-Hartigan et al. Journal Clinical Oncology. 2014. Provision and Discussion of Survivorship Care Plans Among Cancer Survivors
Barton. Perspectives: Research in Context; A Cancer Journal for Clinicians. 2014.Oncologists and Primary Care Physicians Infrequently Provide Survivorship Care Plans

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What is survivorship care? What are late effects?

- Health conditions related to prior cancer and cancer treatment
- May be physical or psychosocial
- May develop months to years after treatment
- May resolve or become chronic problems

3 out of every 4 childhood cancer survivors will develop
at least 1 survivorship-related health problem

NCI at the NIH. http://www.cancer.gov/cancertopics/pdq/treatment/lateeffects/Patient/page1
Oeffinger KC, et al; Chronic health conditions in adult survivors of childhood cancer. N Engl J Med. 2006;355:1572-82
Geenan Maud M, et al; *JAMA*. 2007;297(24):2705-2715. doi:10.1001/jama.297.24.2705

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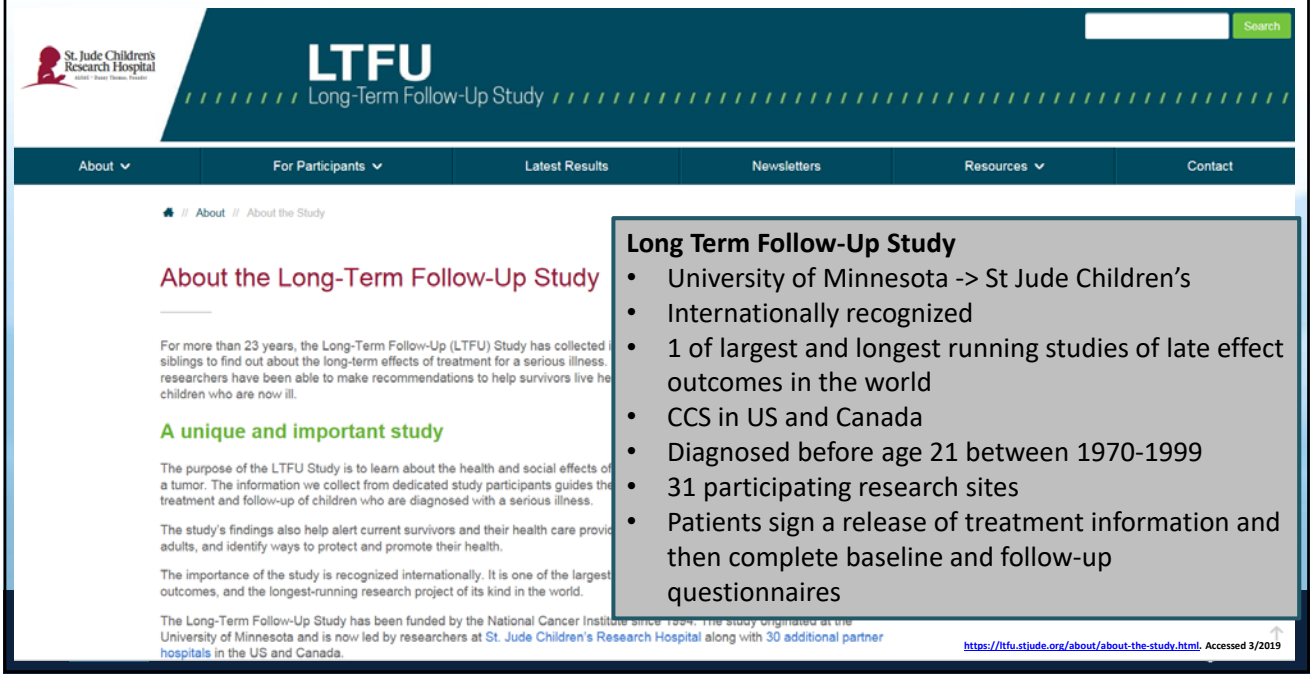
How do we know?

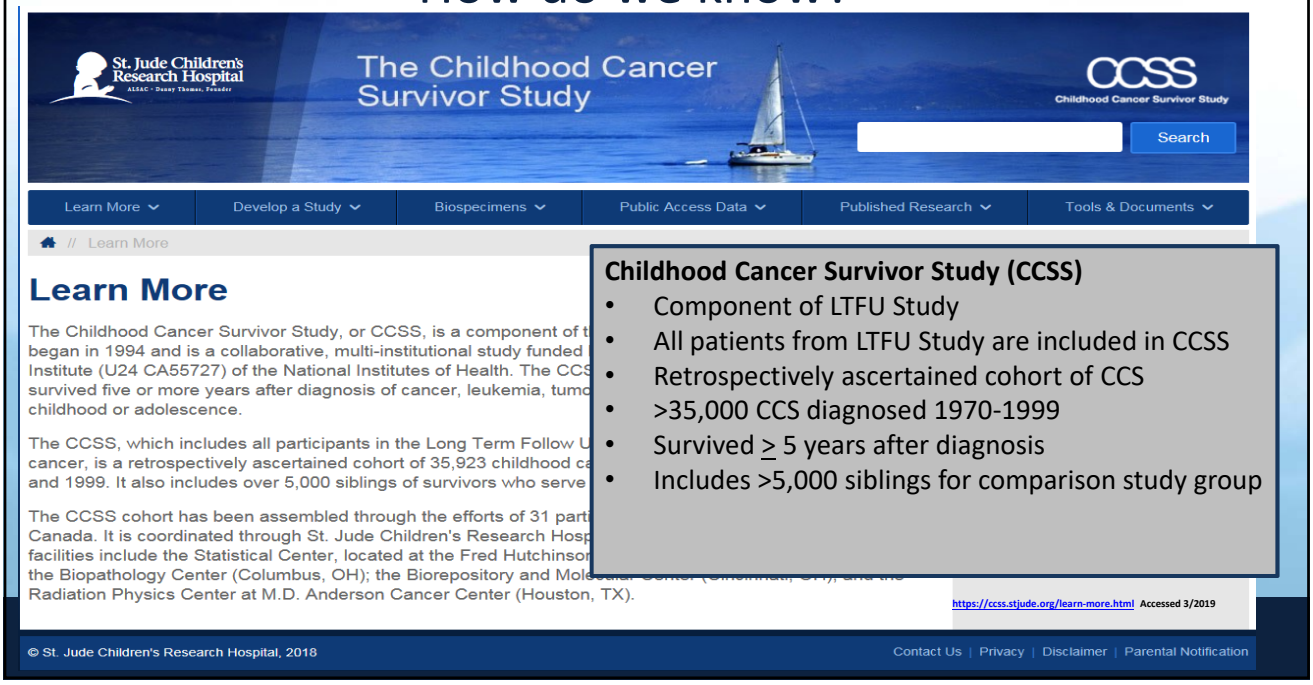


Long Term Follow-Up Study

- University of Minnesota -> St Jude Children's
- Internationally recognized
- 1 of largest and longest running studies of late effect outcomes in the world
- CCS in US and Canada
- Diagnosed before age 21 between 1970-1999
- 31 participating research sites
- Patients sign a release of treatment information and then complete baseline and follow-up questionnaires

https://ltfu.stjude.org/about/about-the-study.html. Accessed 3/2019

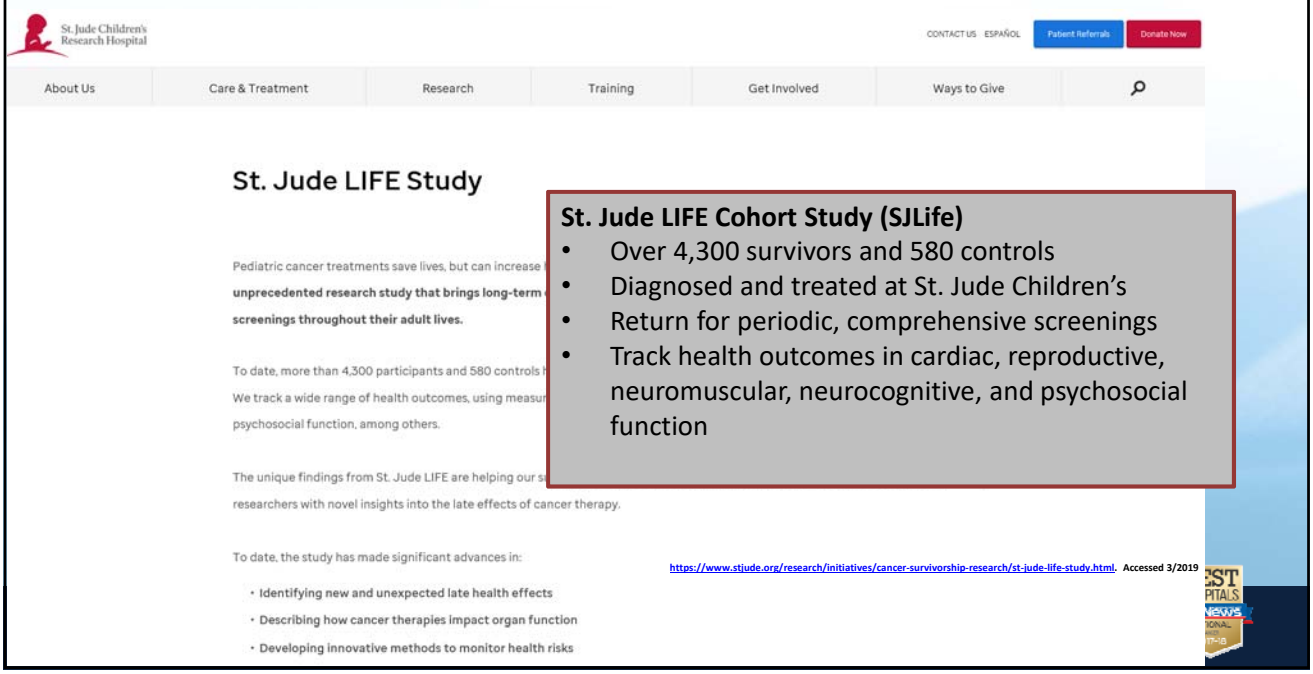
How do we know?



Childhood Cancer Survivor Study (CCSS)

- Component of LTFU Study
- All patients from LTFU Study are included in CCSS
- Retrospectively ascertained cohort of CCS
- >35,000 CCS diagnosed 1970-1999
- Survived ≥ 5 years after diagnosis
- Includes >5,000 siblings for comparison study group

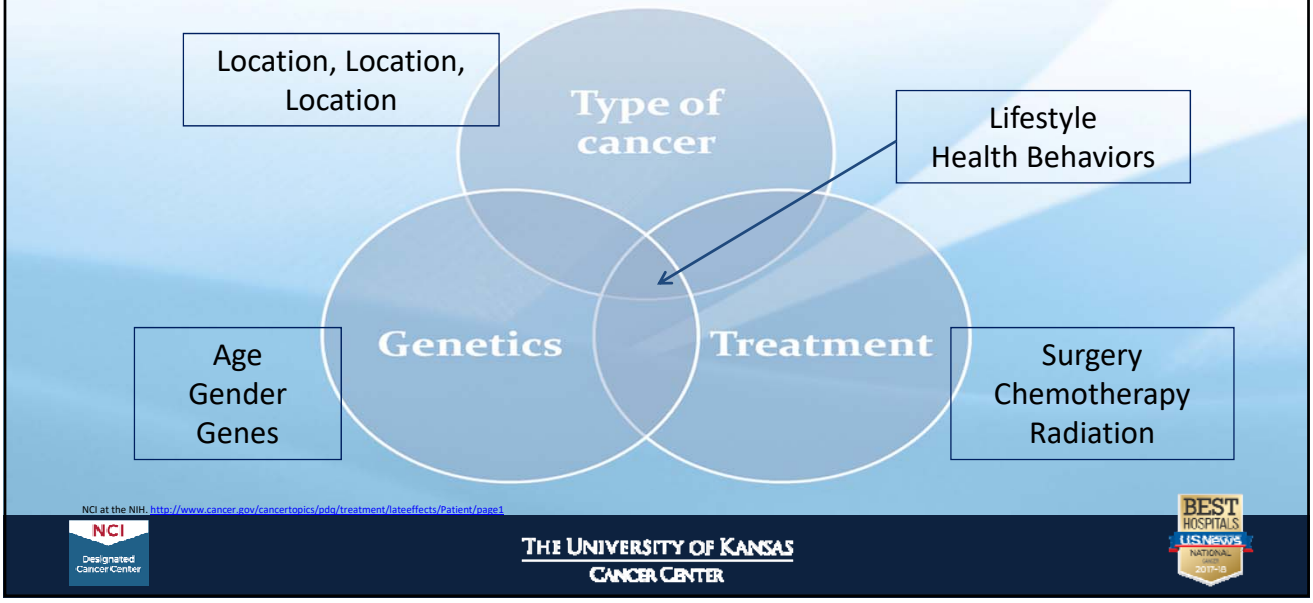
How do we know?



St. Jude LIFE Cohort Study (SJLife)

- Over 4,300 survivors and 580 controls
- Diagnosed and treated at St. Jude Children's
- Return for periodic, comprehensive screenings
- Track health outcomes in cardiac, reproductive, neuromuscular, neurocognitive, and psychosocial function

What causes late effects?



NCI at the NIH. http://www.cancer.gov/cancertopics/pdq/treatment/lateeffects/Patient/page1

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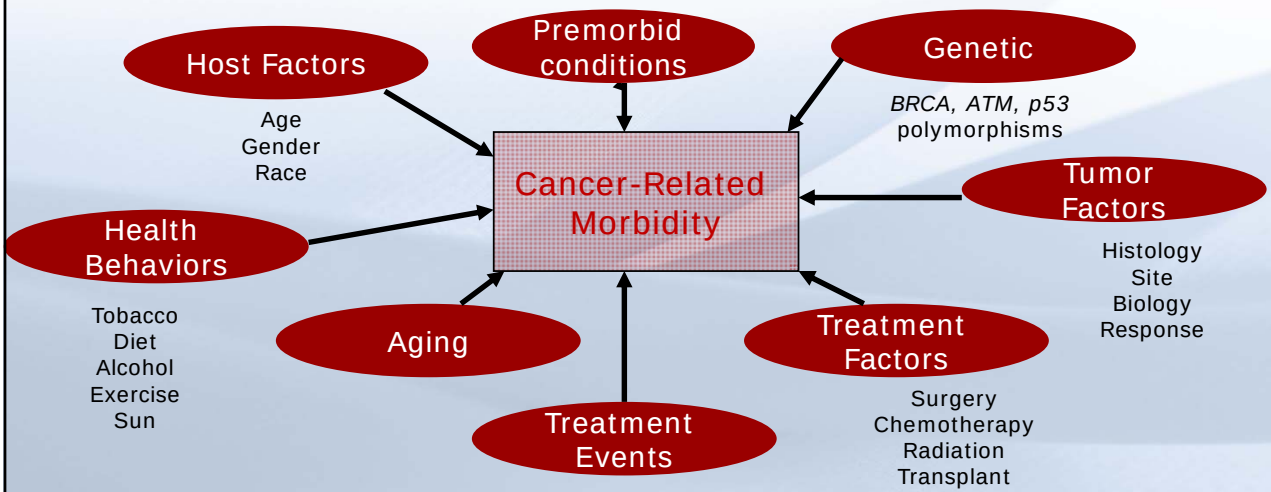
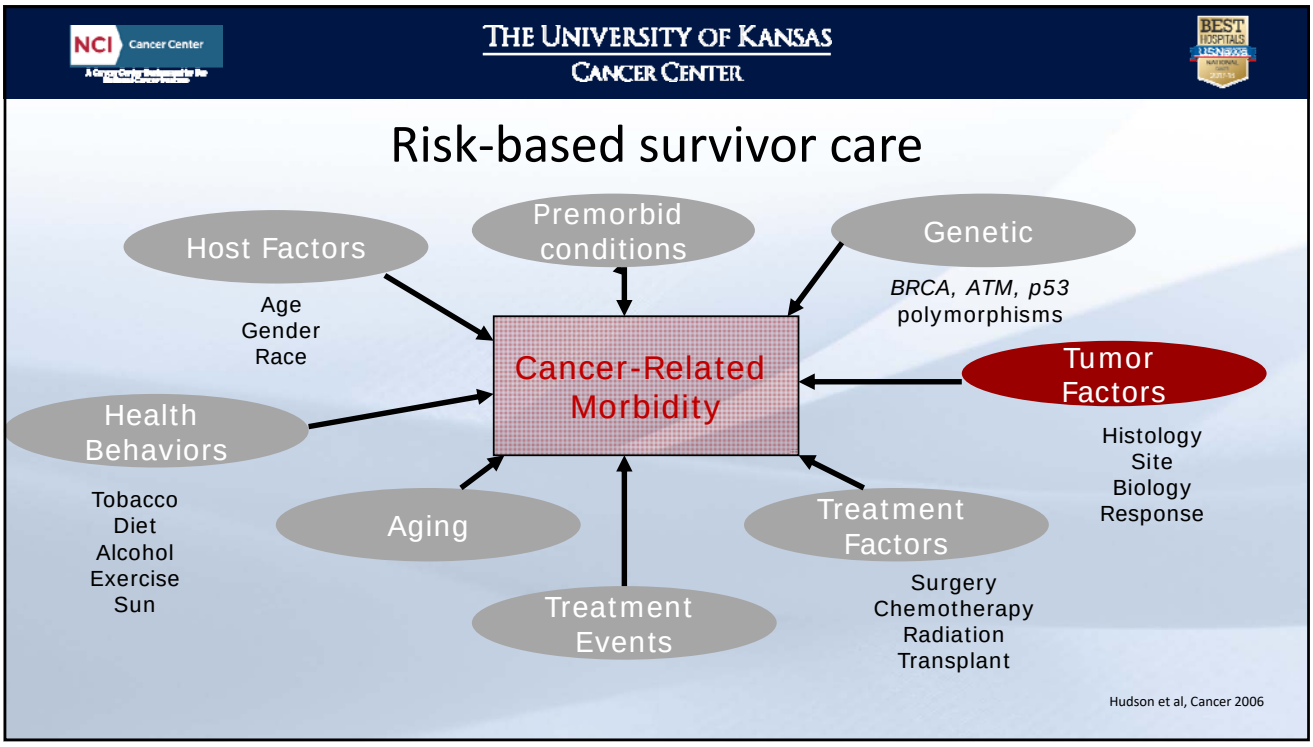
Risk-based survivor care



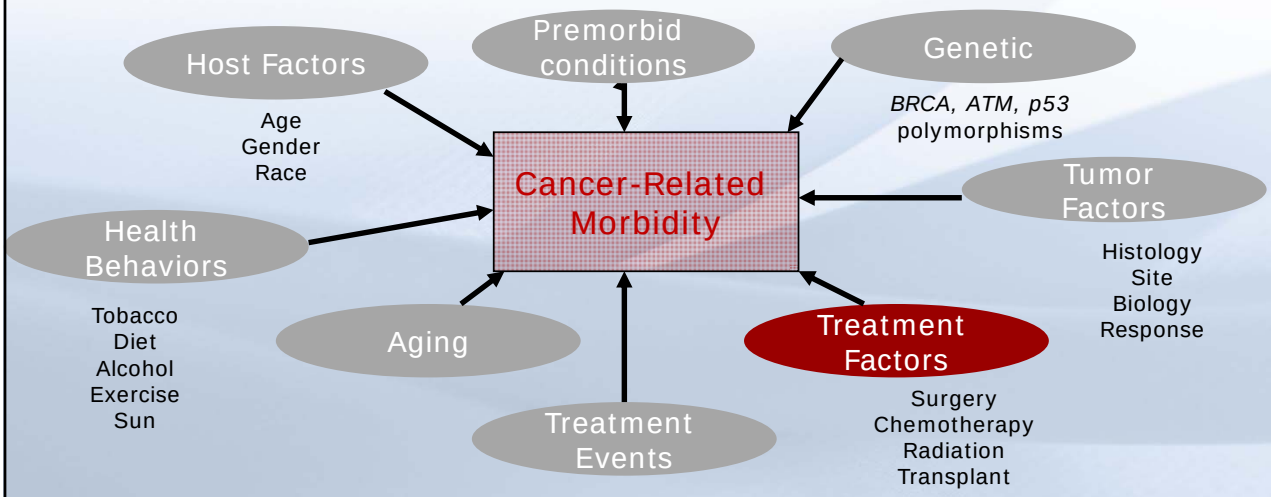
Hudson et al, Cancer 2006



Tumor type and site determines treatment

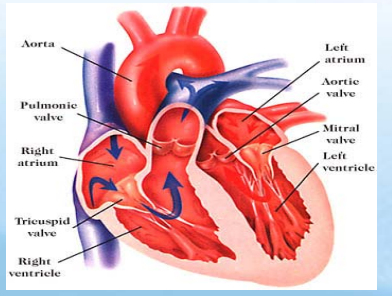
Stage 1 Wilm's tumor	Medulloblastoma
• Nephrectomy • Brief course of chemotherapy, usually with less toxic agents	• Surgical resection • Cranial-spinal radiation • Intense chemotherapy with more toxic agents

Risk-based survivor care



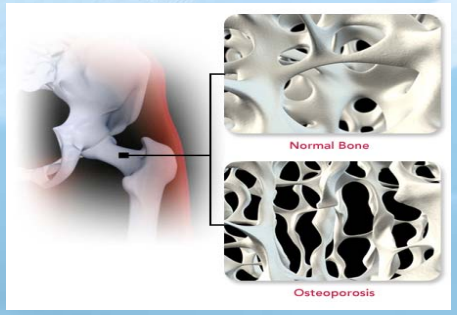
Hudson et al, Cancer 2006

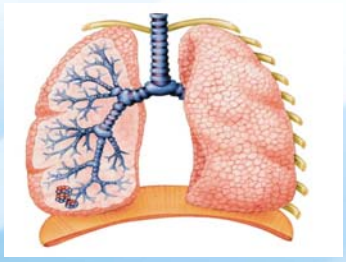
Chemotherapy Agent Influences Risk



Anthracyclines (doxorubicin,daunorubicin): cardiomyopathy / subclinical LV dysfunction

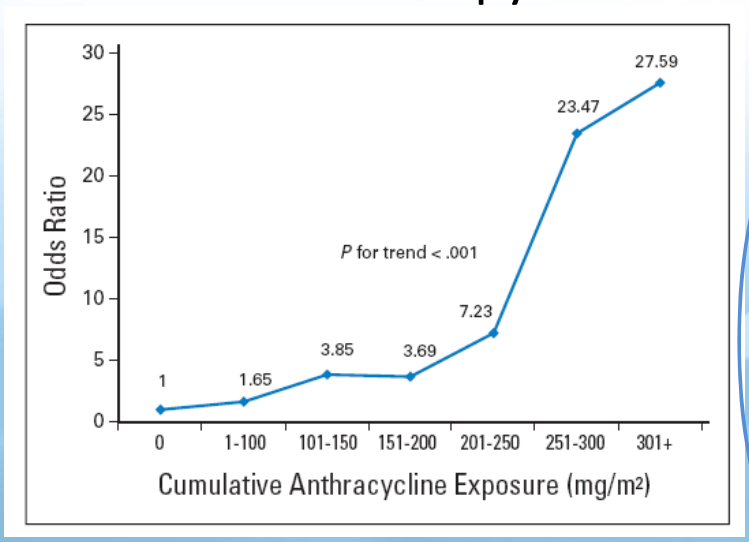
Glucocorticoids and Methotrexate: bone mineral density deficit





Bleomycin and Busulfan: pulmonary fibrosis

Chemotherapy Dose Influences Risk

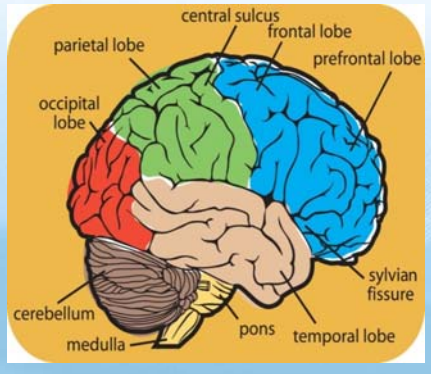


Blanco JG, et al. *J Clin Oncol*. 2012 May 1; 30 (13): 1415-1421

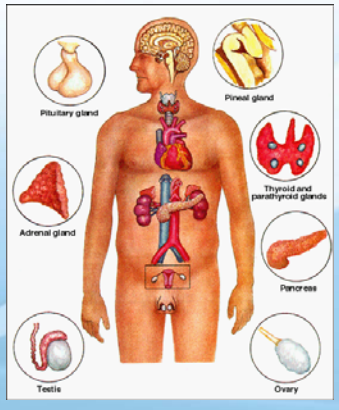
Recommended Frequency of Echocardiogram		
Anthracycline Dose*	**Radiation Dose****	**Recommended Frequency**
None	< 15 Gy or none	No screening
	≥ 15 - < 35 Gy	Every 5 years
	≥ 35 Gy	Every 2 years
< 250 mg/m²	< 15 Gy or none	Every 5 years
	≥ 15 Gy	Every 2 years
≥ 250 mg/m²	Any or none	Every 2 years

*Based on doxorubicin isotoxic equivalent dose. See dose conversion instructions in section 33.
**Based on radiation dose with potential impact to heart (radiation to chest, abdomen, spine [thoracic, whole], TBI). See section 76.

Radiation Fields Influence Risk



Cranial radiation:
neurocognitive, motor sensory deficits



Endocrine gland radiation:
growth, metabolism, and reproduction

Radiation Dose Influences Risk

Threshold Dose & Hypothalamic-Pituitary Dysfunction

HPA Disorder	Dose (Gy)
GH deficiency	≥ 18
Precocious Puberty	≥ 18
LH/FSH deficiency	> 30
TSH deficiency	> 30
ACTH deficiency	> 30
Hyperprolactinemia	> 50

Table 3. Risk Factors, Diagnostic Studies, and Treat

Disorder	Highest Risk		
GH deficiency	≥18 Gy CRT Pretransplant CRT TBI Young age Tumor near HPA Hydrocephalus		
Gonadotropin deficiency	≥30 Gy CRT Tumor near HPA		
Precocious puberty	18-24 Gy CRT Female Young age Tumor near HPA		
		+/− GnRH stimulation test +/− GH stimulation test	
TSH deficiency	≥30 Gy CRT TBI Tumor near HPA Hydrocephalus	Free T4, TSH (8 AM) Nocturnal TSH surge TRH stimulation test	L-thyroxine
ACTH deficiency	≥30 Gy CRT Tumor near HPA Hydrocephalus	Cortisol (8 AM) Adrenal stimulation test	Hydrocortisone
Hyperprolactinemia	≥50 Gy CRT Tumor near HPA	Prolactin	Dopamine agonis

45-60 Gy for therapy for Primary CNS Tumors

18 Gy for CNS therapy for ALL (acute lymphoblastic leukemia)

Shaw. 2009. Journal Pediatric Oncology Nursing. 26(5) 295–302

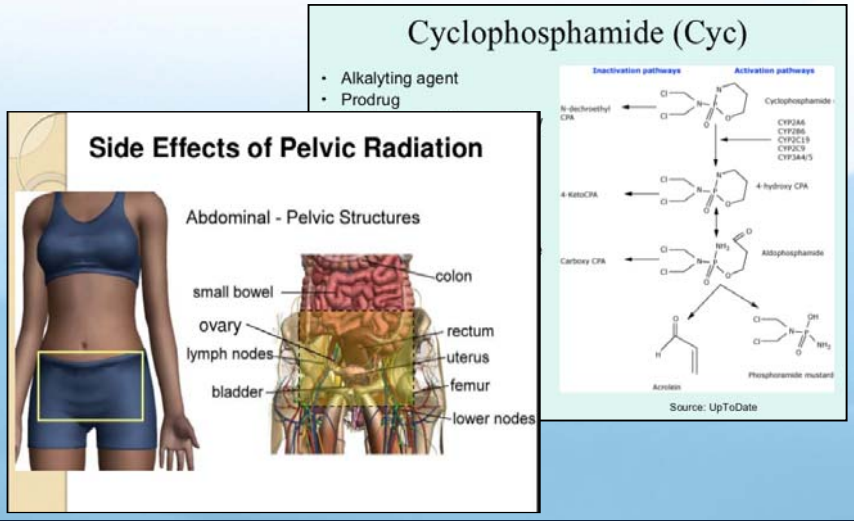
Combination therapy influences risk

Chest radiation:
Heart valve disorders
Coronary artery disease
Cardiomyopathy

Anthracyclines:
Cardiomyopathy
Subclinical LV systolic dysfunction

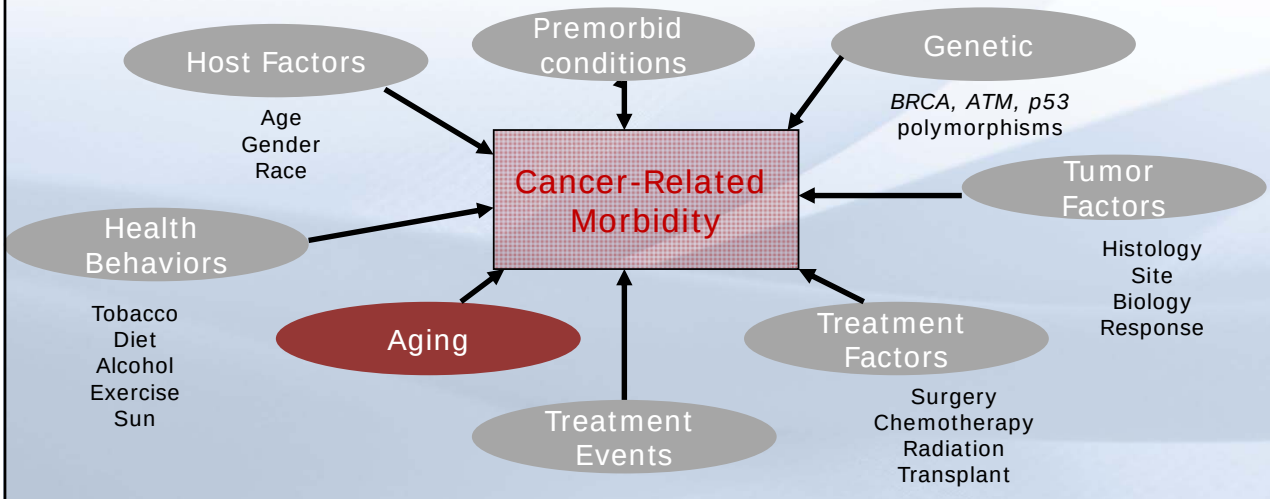
Combination therapy influences risk

Combined modality therapy including alkylating agents and gonadal radiation increases risk of gonadal dysfunction and infertility

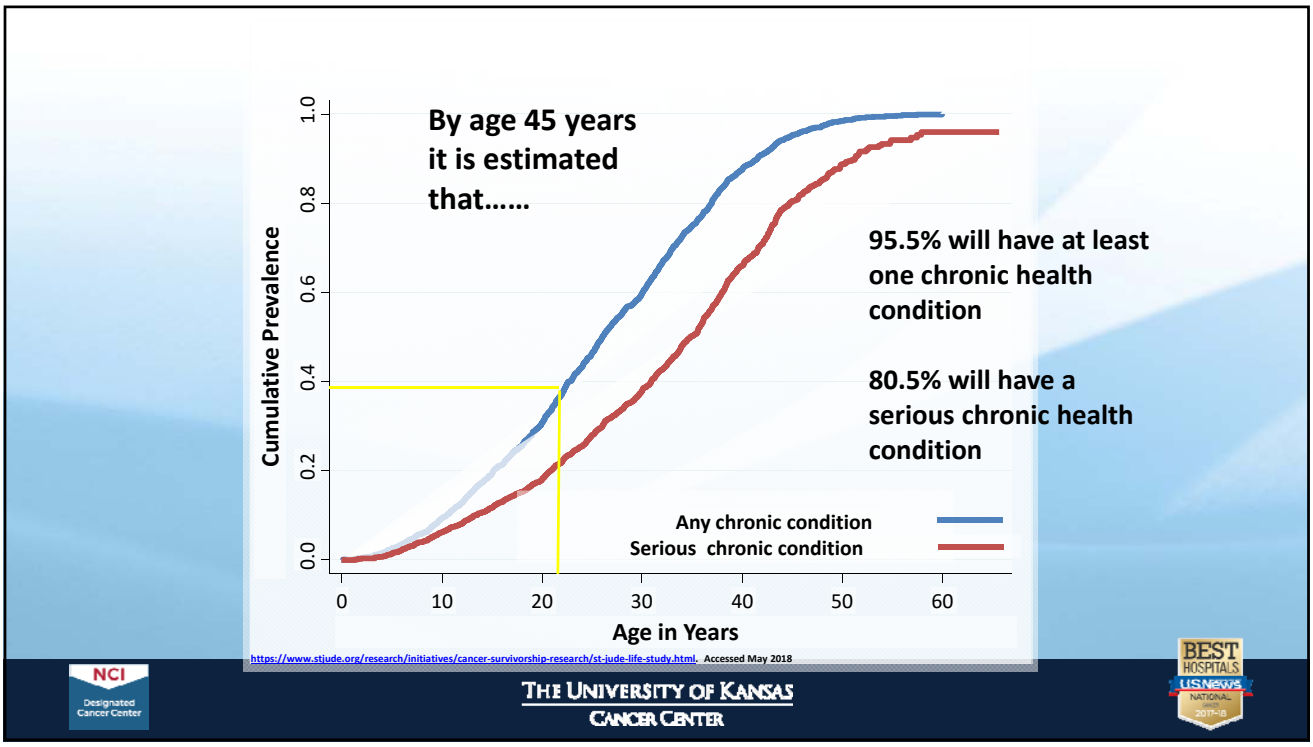


Reference

Risk-based survivor care



Hudson et al, Cancer 2006


By age 45 years it is estimated that……
95.5% will have at least one chronic health condition
80.5% will have a serious chronic health condition
Cumulative Prevalence
0.0
0.2
0.4
0.6
0.8
1.0
0
10
20
30
40
50
60
Age in Years
Any chronic condition
Serious chronic condition
https://www.stjude.org/research/initiatives/cancer-survivorship-research/st-jude-life-study.html. Accessed May 2018
NCI Designated Cancer Center
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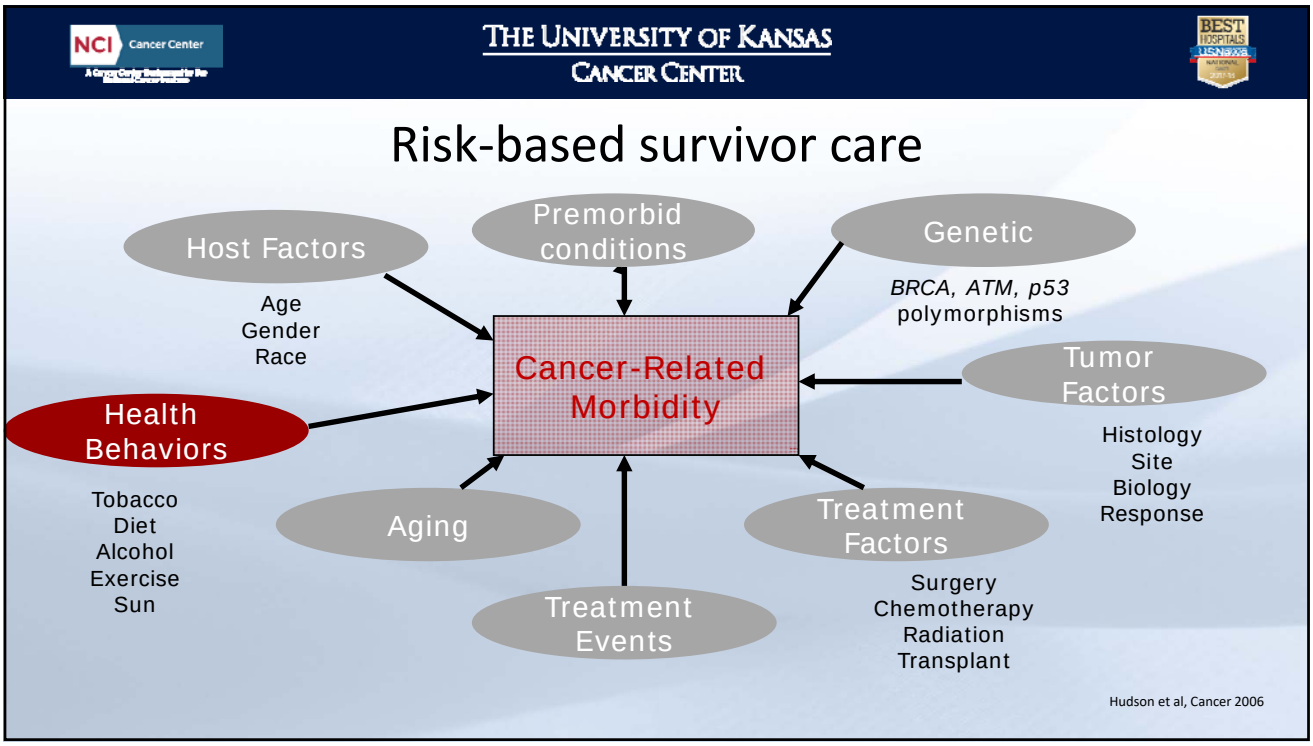
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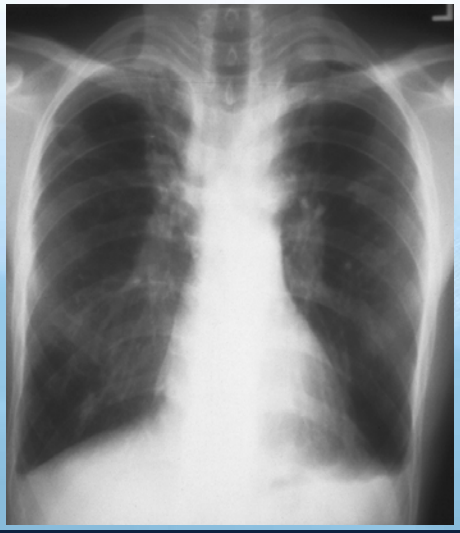
Risk-based survivor care
Host Factors
Age
Gender
Race
Premorbid conditions
Genetic
BRCA, ATM, p53 polymorphisms
Cancer-Related Morbidity
Health Behaviors
Tobacco
Diet
Alcohol
Exercise
Sun
Tumor Factors
Histology
Site
Biology
Response
Aging
Treatment Factors
Surgery
Chemotherapy
Radiation
Transplant
Treatment Events
Hudson et al, Cancer 2006

Health habits influence risk

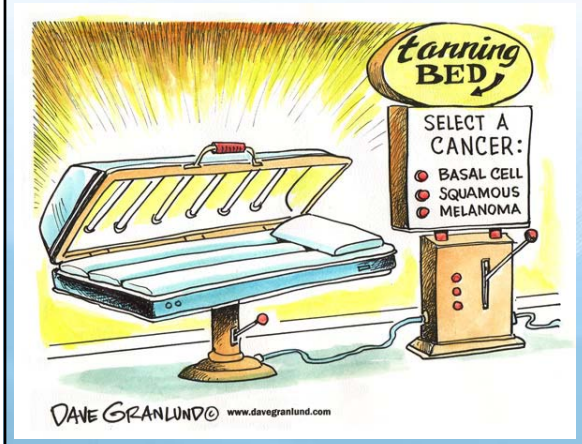


Pulmonary toxicity:

- Bleomycin
- Busulfan
- Chest radiation

Smoking increases the risk of lung injury.

Health habits influence risk



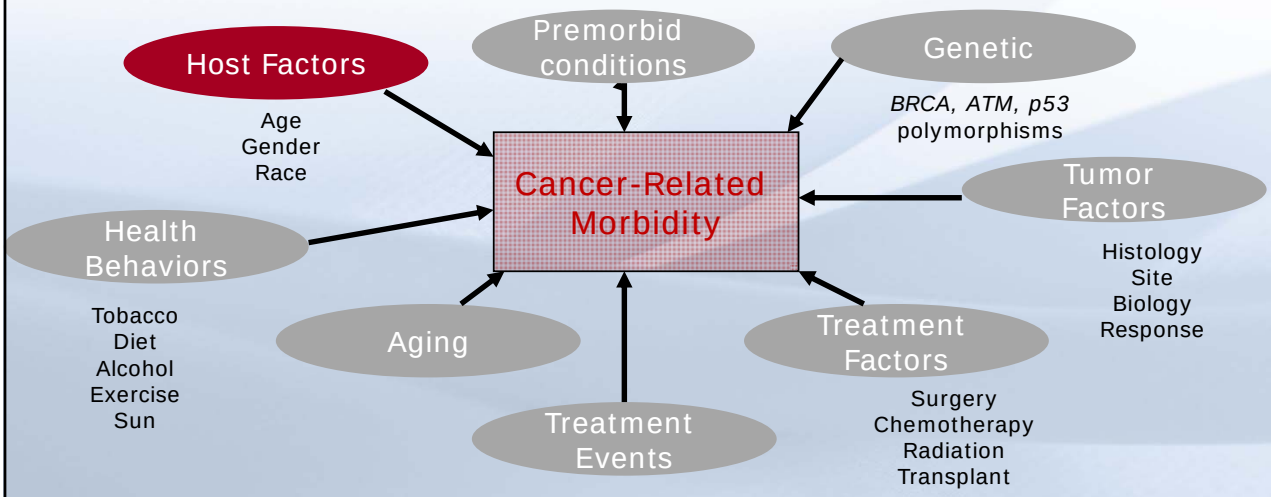
Skin cancer risk

- Radiation therapy
- Sun exposure

Risk for developing skin cancer is 6.3 times higher in patients who received radiation therapy than the general population

Perkins, J, et al. JCO 2005

Risk-based survivor care

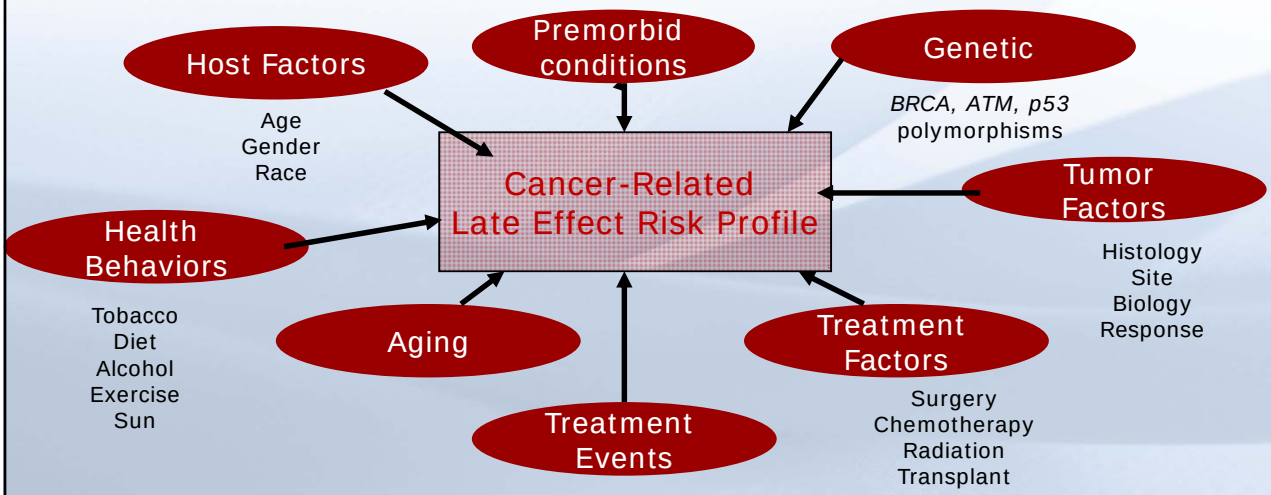


Hudson et al, Cancer 2006

Age at diagnosis influences risk

Younger patients are more vulnerable to neurocognitive dysfunction after cranial irradiation

Risk-based survivor care



Hudson et al, Cancer 2006

What are Some of the Most Common Things – Late Effects or Late Effect Concerns

Psychosocial
Fertility / Reproduction
Endocrine Dysfunction
Cardiac
Secondary Malignancies

Some of the Most Common – Late Effects or Late Effect Concerns

Psychosocial

Anxiety, Depression, Social Withdrawal, Education/Employment, Relationships

Risk Factors:

- Any Cancer Experience

Interventions:

- Awareness / Screening – GAD7, PHQ9
- Counseling / Social Services
- Medications

Some of the Most Common – Late Effects or Late Effect Concerns

Fertility / Reproduction

Risk Factors:

- Radiation - Cranial / Gonadal / TBI
- Chemo
  - Alkylating Agents (Cyclophosphamide, Ifosfamide)
  - Heavy Metals (Carboplatin, Cisplatin)

Interventions:

- Early fertility referral / counseling
- Cryopreservation

Some of the Most Common – Late Effects or Late Effect Concerns

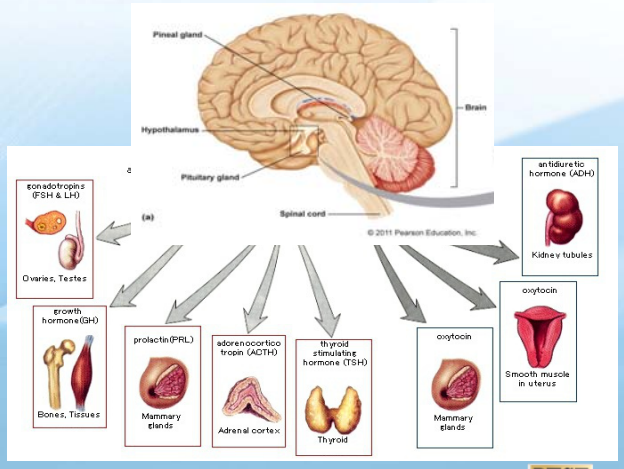
Endocrine Dysfunction

Risk Factors:

- Radiation - Cranial / End Organ

Interventions:

- Awareness / ROS / exam
- HPA labs, DEXA screening, TSH monitoring



Some of the Most Common – Late Effects or Late Effect Concerns

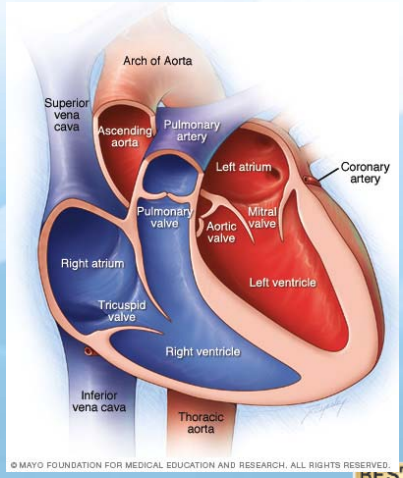
Cardiac

Risk Factors:

- Radiation – Chest / TBI
- Chemo
  - Anthracyclines (doxorubicin, daunorubicin, Idarubicin)

Interventions:

- EKGs, guideline-based echo screening
- Education on symptoms



Some of the Most Common – Late Effects or Late Effect Concerns

Secondary Malignancies (SMN)

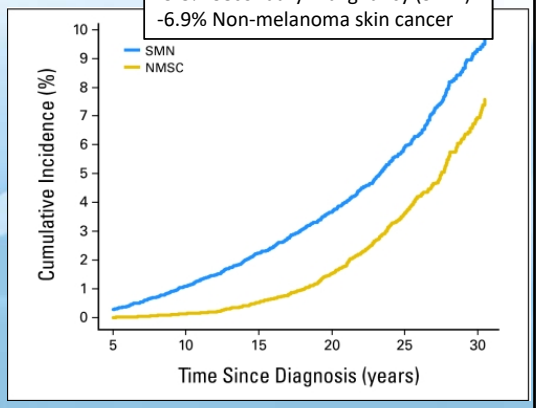
CCSS – 30 year data >14,000 CCS
-9.3% Secondary Malignancy (SMN)
-6.9% Non-melanoma skin cancer

Risk Factors:

- Younger age (at diagnosis), Female
- Radiation
- Chemo
  - Alkylating Agents (Cyclophosphamide, Ifosfamide)
  - Anthracyclines (doxorubicin, daunorubicin, Idarubicin)
  - Etoposide, teniposide

Interventions:

- Regular exams, Guideline based screenings



Meadows, et al. Journal Clinical Oncology. 2009.

Breast cancer	Radiation: TBI	72	**Physical**	
			Clinical breast exam	**Yearly**, beginning at puberty until age 25, then every 6 months
			Screening	
			Breast MRI	**Yearly**, as an adjunct to mammography beginning 8 years after radiation or at age 25, whichever occurs last
			Mammogram	**Yearly**, beginning 8 years after radiation or at age 25, whichever occurs last
Colorectal cancer	Radiation: TBI	85	**Screening**	
			Regular screening selected from the options below based on informed decision-making between patient and provider	Beginning 5 years after radiation or at age 30 years (whichever occurs last)

Radiation-Related Colorectal Cancer Screening Options

Test	Frequency
Multitarget stool DNA test	Every 3 years
Colonoscopy	Every 5 years

*Positive results should be followed up with timely colonoscopy.

Note: Colonoscopy is considered the gold standard for colorectal cancer screening in high-risk populations; however, recognizing that not all survivors are willing or able to undergo colonoscopy, multitarget stool DNA testing is deemed a reasonable alternative. Alternative stool-based testing (i.e., annual fecal immunochemical testing (FIT) or high-sensitivity guaiac-based fecal occult blood testing) or alternative structural examination (i.e., every 5 year CT colonography or flexible sigmoidoscopy) may also be considered if colonoscopy or multitarget stool DNA testing are not feasible or acceptable to the survivor. All positive results from these alternative testing methods should be followed up with timely colonoscopy.

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So… What now?
How to best help the patients in your practice

- Things we tell every survivorship patient
- Obtaining a treatment summary
- Obtaining a survivorship care plan
- Locating the guidelines
- Getting support from survivorship team

Things We Tell Every Patient

Things we tell every survivorship patient

- Exercise is medicine
- Healthy diet is critical
- Obesity increases cancer risk
- HPV vaccines help prevent GU and head / neck cancers
- Sunscreen
- Skin cancer exams (radiation therapy)

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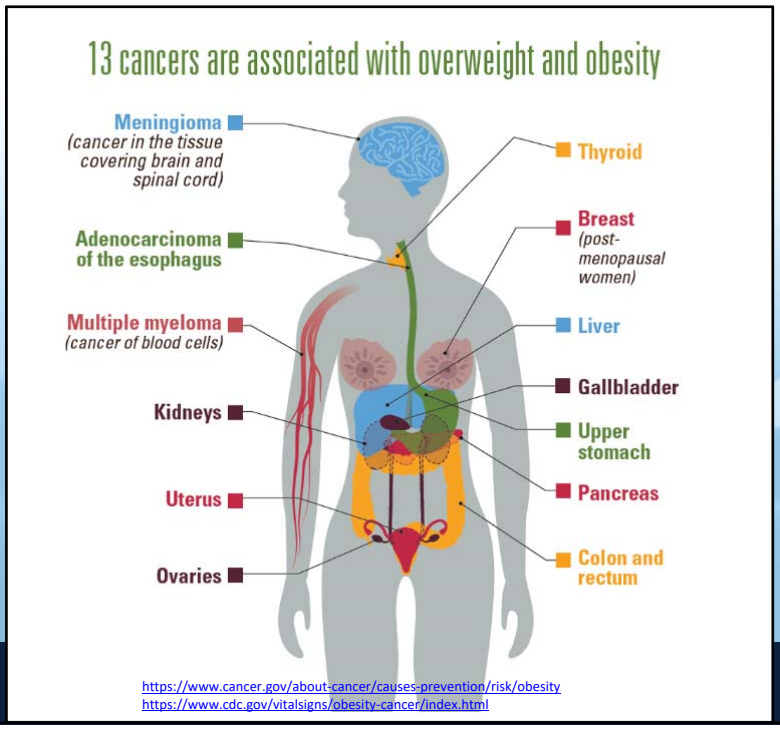

https://www.cancer.gov/about-cancer/causes-prevention/risk/obesity
https://www.cdc.gov/vitalsigns/obesity-cancer/index.html

Obesity is…

- Clearly linked to an overall increased cancer risk and an increased risk of many individual types of cancer
- Most types of cancer associated with overweight / obese states have increased from 2005-2014

Table 3. **Perceived Usefulness of Various Methods for Assisting General Internists' Ability to Care for CCSs Independently**

Type	Mean Utility Rating/Percentage With Rating of 4*
Access to long-term follow-up guidelines for CCSs	3.8/85.5
Medical education seminars and courses about cancer follow-up care	3.2/44.0
Web site with information and opportunity for questions and answers	3.4/59.0
Patient-specific standardized letter from specialist with follow-up recommendations for the primary care physician sent directly to you	3.7/79.9
Patient-specific standardized letter from specialist with follow-up recommendations given to the patient	3.4/54.2
Ability to telephone or e-mail specialist for advice	3.4/55.1
Expedited routes of re-referral to cancer specialists	3.4/54.7
Pamphlets on follow-up cancer care	2.9/30.6
Expedited access to investigations (e.g. computed tomography scan, magnetic resonance imaging, and positron emission tomography scan) for suspected recurrence	3.1/44.2
Expedited access to support services (e.g. social work, psychology)	3.0/36.6
More medical or support staff in primary care office	2.7/26.8

CCS = childhood cancer survivor.
* On a scale of 1 (not at all useful) to 4 (very useful).

What Would Help?

3 Most Highly Rates Themes

- #1 - Guideline Awareness / Access
- #2 - Patient-specific letter summary and recommendations
- #3 –Specialist access for collaboration / support

84% requested "collaboration with a cancer center-based physician or long term follow-up clinic"

Ann Intern Med. 2014;160:11-17. doi:10.7326/M13-1941

NCI Designated Cancer Center

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Table 3. **Perceived Usefulness of Various Methods for Assisting General Internists' Ability to Care for CCSs Independently**

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Access to long-term follow-up guidelines for CCSs	3.8/66.5
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Web site with information and opportunity for questions and answers	3.4/59.0
Patient-specific standardized letter from specialist with follow-up recommendations for the primary care physician sent directly to you	3.7/79.9
Patient-specific standardized letter from specialist with follow-up recommendations given to the patient	3.4/54.2
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* On a scale of 1 (not at all useful) to 4 (very useful).

Ann Intern Med. 2014;160:11-17. doi:10.7326/M13-1941

#1 - Guideline Awareness / Access

- http://survivorshipguidelines.org/
- https://www.nccn.org/professionals/physician

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http://survivorshipguidelines.org/

CHEMOTHERAPY

ANTHRACYCLINE ANTIBIOTICS (CONT)

Sec #	Therapeutic Exposure	Potential Late Effects	Periodic Evaluation	Health Counseling/ Further Considerations
33	**Anthracycline Antibiotics** Daunorubicin Doxorubicin Epirubicin Idarubicin Mitoxantrone **Dose Conversion** To gauge the frequency of screening, use the following formulas to convert to doxorubicin isotoxic equivalents prior to calculating total cumulative anthracycline dose. Clinical judgment should ultimately be used to determine indicated screening for individual patients. Doxorubicin: Multiply total dose x 1 Daunorubicin: Multiply total dose x 0.5 Epirubicin: Multiply total dose x 0.67 Idarubicin: Multiply total dose x 5 Mitoxantrone: Multiply total dose x 4	**Cardiac toxicity** Cardiomyopathy Subclinical left ventricular dysfunction Congestive heart failure Arrhythmia	**HISTORY** **Shortness of breath** **Dyspnea on exertion** **Orthopnea** **Chest pain** **Palpitations** **If under 25 yrs: abdominal symptoms (nausea, vomiting)** Yearly **PHYSICAL** **Blood pressure** **Cardiac exam** Yearly **SCREENING** **ECHO (or comparable imaging to evaluate**	**HEALTH LINKS** **Heart Health** **Cardiovascular Risk Factors** **Diet and Physical Activity** **COUNSELING** Maintain appropriate weight, blood pressure and heart-healthy diet. Regarding exercise: - Regular exercise is generally safe and should be encouraged for patients who have normal LV systolic function. - Survivors with asymptomatic cardiomyopathy should consult cardiology to define limits and precautions for physical activity. - Cardiology consultation may be reasonable to define limits and precautions for physical activity for high risk survivors (i.e., those requiring an ECHO every 2 years) who plan to participate in intensive exercise. If QTc interval is prolonged: Caution regarding use of medications that may further prolong the QTc interval (e.g., tricyclic anti-depressants, antifungals, macrolide antibiotics, metronidazole). **POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION** ac MRI as an adjunct imaging modality when echocardiographic images are suboptimal. ology consultation in patients with subclinical abnormalities on screening evaluations, left tricular dysfunction, dysrhythmia, or prolonged QTc interval. le patients only: For patients who are pregnant or planning to become pregnant, tional cardiology evaluation is indicated in patients who received: 50 mg/m² anthracyclines 5 Gy chest radiation, or thracycline (any dose) combined with chest radiation (≥15 Gy) luation should include a baseline echocardiogram (pre- or early-pregnancy). For e without prior abnormalities and with normal pre- or early-pregnancy baseline ocardiograms, follow-up echocardiograms may be obtained at the provider's discretion. se with a history of systolic dysfunction or with pre- or early-pregnancy systolic function are at highest risk for pregnancy-associated cardiomyopathy. Such individuals uld be monitored periodically during pregnancy and during labor and delivery due to eased risk for cardiac failure. **SYSTEM = Cardiovascular** **SCORE = 1**

Recommended Frequency of Echocardiogram

Anthracycline Dose*	Radiation Dose**	Recommended Frequency
None	< 15 Gy or none	No screening
	≥ 15 - < 35 Gy	Every 5 years
	≥ 35 Gy	Every 2 years
< 250 mg/m²	< 15 Gy or none	Every 5 years
	≥ 15 Gy	Every 2 years
≥ 250 mg/m²	Any or none	Every 2 years

*Based on doxorubicin isotoxic equivalent dose. See dose conversion instructions in section 33.
**Based on radiation dose with potential impact to heart (radiation to chest, abdomen, spine [thoracic, whole], TBI). See section 76.

Additional Informatic

Although Mitoxantrone technically belongs

ded in this section because of its cardiotoxic potential.

COG LTFU Guidelines – Page 40

Version 5.0 - October 2018

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Table 3. **Perceived Usefulness of Various Methods for Assisting General Internists' Ability to Care for CCSs Independently**

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Web site with information and opportunity for questions and answers	3.4/59.0
Patient-specific standardized letter from specialist with follow-up recommendations for the primary care physician sent directly to you	3.7/[illegible]9
Patient-specific standardized letter from specialist with follow-up recommendations given to the patient	3.4/5[illegible].2
Ability to telephone or e-mail specialist for advice	3.4/55.1
Expedited routes of re-referral to cancer specialists	3.4/54.7
Pamphlets on follow-up cancer care	2.9/30.6
Expedited access to investigations (e.g. computed tomography scan, magnetic resonance imaging, and positron emission tomography scan) for suspected recurrence	3.1/44.2
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More medical or support staff in primary care office	2.7/26.8

CCS = childhood cancer survivor.
* On a scale of 1 (not at all useful) to 4 (very useful).

Ann Intern Med. 2014;160:11-17. doi:10.7326/M13-1941

#2 - Patient Specific Guidance

- Treatment Summary
- Survivorship Care Plan

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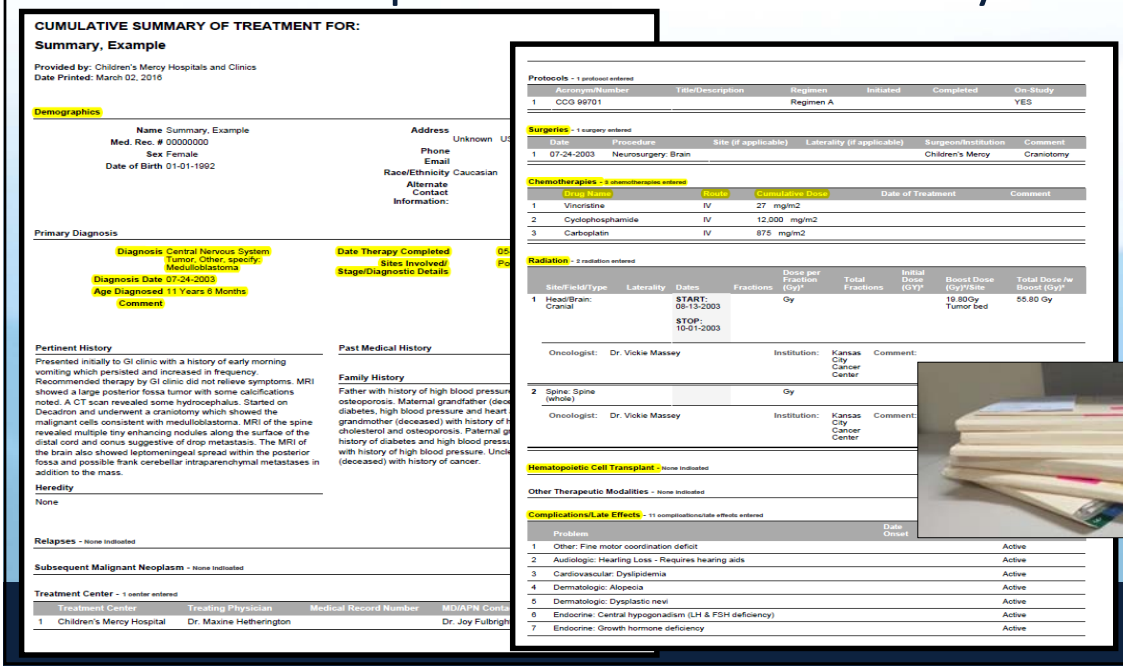
Request Treatment Summary



CUMULATIVE SUMMARY OF TREATMENT FOR:
Summary, Example

Provided by: Children's Mercy Hospitals and Clinics
Date Printed: March 02, 2016

Demographics

Name Summary, Example
Med. Rec. # 00000000
Sex Female
Date of Birth 01-01-1992

Address Unknown
Phone
Email
Race/Ethnicity Caucasian
Alternate Contact Information:

Primary Diagnosis

Diagnosis Central Nervous System Tumor, Other, specify: Medulloblastoma
Diagnosis Date 07-24-2003
Age Diagnosed 11 Years 6 Months
Comment

Date Therapy Completed
Sites Involved/ Stage/Diagnostic Details

Pertinent History

Presented initially to GI clinic with a history of early morning vomiting which persisted and increased in frequency. Recommended therapy by GI clinic did not relieve symptoms. MRI showed a large posterior fossa tumor with some calcifications noted. A CT scan revealed some hydrocephalus. Started on Decadron and underwent a craniotomy which showed the malignant cells consistent with medulloblastoma. MRI of the spine revealed multiple tiny enhancing nodules along the surface of the distal cord and conus suggestive of drop metastasis. The MRI of the brain also showed leptomeningeal spread within the posterior fossa and possible frank cerebellar intraparenchymal metastases in addition to the mass.

Heredity

None

Past Medical History

Family History

Father with history of high blood pressure, osteoporosis. Maternal grandfather (deceased) diabetes, high blood pressure and heart. grandmother (deceased) with history of h cholesterol and osteoporosis. Paternal g history of diabetes and high blood pressu with history of high blood pressure. Uncle (deceased) with history of cancer.

Relapses - None indicated

Subsequent Malignant Neoplasm - None indicated

Treatment Center - 1 center entered

	Treatment Center	Treating Physician	Medical Record Number	MD/APN Contact
1	Children's Mercy Hospital	Dr. Maxine Hetherington		Dr. Joy Fulbright

Protocols - 1 protocol entered

	Longitude Number	Title/Description	Regimen	Initiated	Completed	On-Study
1	CCG 99701		Regimen A			YES

Surgeries - 1 surgery entered

	Date	Procedure	Site (if applicable)	Laterality (if applicable)	Surgeon/Institution	Comment
1	07-24-2003	Neurosurgery: Brain			Children's Mercy	Craniotomy

Chemotherapies - 3 chemotherapies entered

	Drug Name	Route	Cumulative Dose	Date of Treatment	Comment
1	Vincristine	IV	27 mg/m2		
2	Cyclophosphamide	IV	12,000 mg/m2		
3	Carboplatin	IV	875 mg/m2		

Radiation - 2 radiation entered

	Site/Field/Type	Laterality	Dates	Fractions	Dose per Fraction (Gy)*	Total Fractions	Initial Dose (GY)*	Boost Dose (Gy)/Site	Total Dose /w Boost (Gy)*
1	Head/Brain: Cranial		START: 08-13-2003 STOP: 10-01-2003		Gy			19.80Gy Tumor bed	55.80 Gy
	Oncologist: Dr. Vickie Massey				Institution: Kansas City Cancer Center		Comment:		
2	Spine: Spine (whole)				Gy				
	Oncologist: Dr. Vickie Massey				Institution: Kansas City Cancer Center		Comment:		

Hematopoietic Cell Transplant - None indicated

Other Therapeutic Modalities - None indicated

Complications/Late Effects - 11 complications/late effects entered

	Problem	Date Onset	
1	Other: Fine motor coordination deficit		Active
2	Audiologic: Hearing Loss - Requires hearing aids		Active
3	Cardiovascular: Dyslipidemia		Active
4	Dermatologic: Alopecia		Active
5	Dermatologic: Dysplastic nevi		Active
6	Endocrine: Central hypogonadism (LH & FSH deficiency)		Active
7	Endocrine: Growth hormone deficiency		Active

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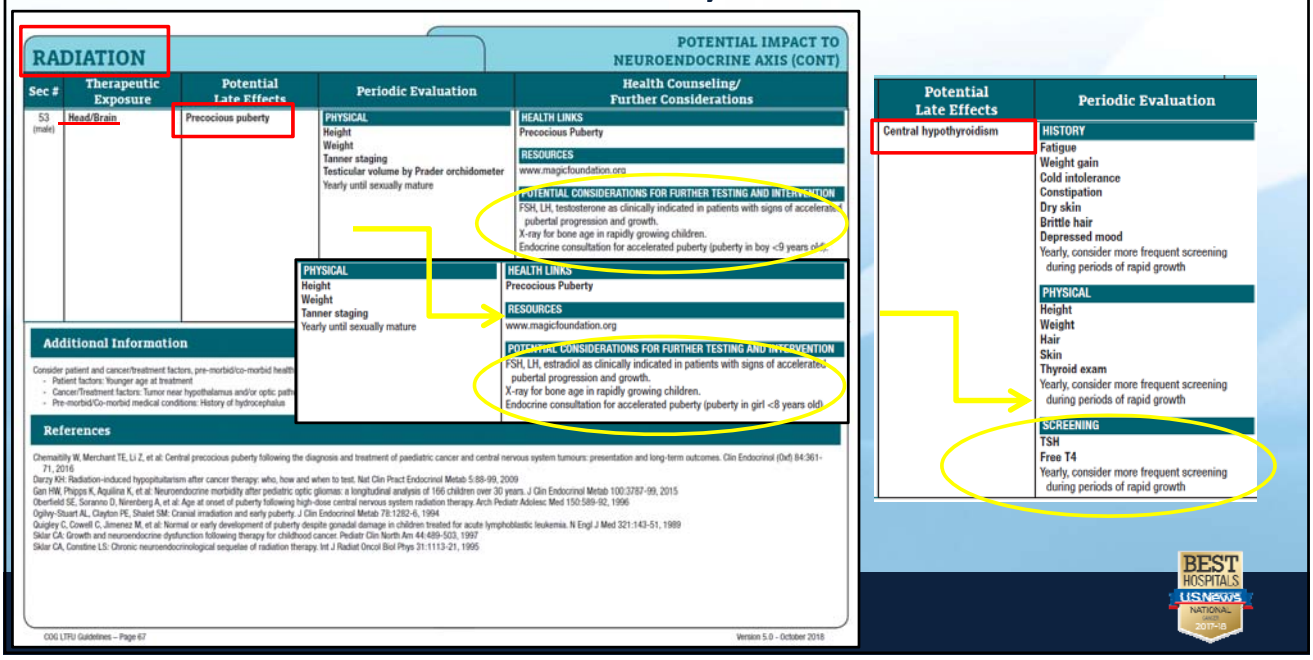
Treatment Summary -> Guidelines



RADIATION

POTENTIAL IMPACT TO NEUROENDOCRINE AXIS (CONT)

Sec #	Therapeutic Exposure	Potential Late Effects	Periodic Evaluation	Health Counseling/ Further Considerations
53 (male)	Head/Brain	Precocious puberty	PHYSICAL Height Weight Tanner staging Testicular volume by Prader orchidometer Yearly until sexually mature	HEALTH LINKS Precocious Puberty RESOURCES www.magicfoundation.org POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION FSH, LH, testosterone as clinically indicated in patients with signs of accelerated pubertal progression and growth. X-ray for bone age in rapidly growing children. Endocrine consultation for accelerated puberty (puberty in boy <9 years old)

Additional Information

Consider patient and cancer/treatment factors, pre-morbid/co-morbid health
- Patient factors: Younger age at treatment
- Cancer/Treatment factors: Tumor near hypothalamus and/or optic path
- Pre-morbid/Co-morbid medical conditions: History of hydrocephalus

PHYSICAL
Height
Weight
Tanner staging
Yearly until sexually mature

HEALTH LINKS
Precocious Puberty

RESOURCES
www.magicfoundation.org

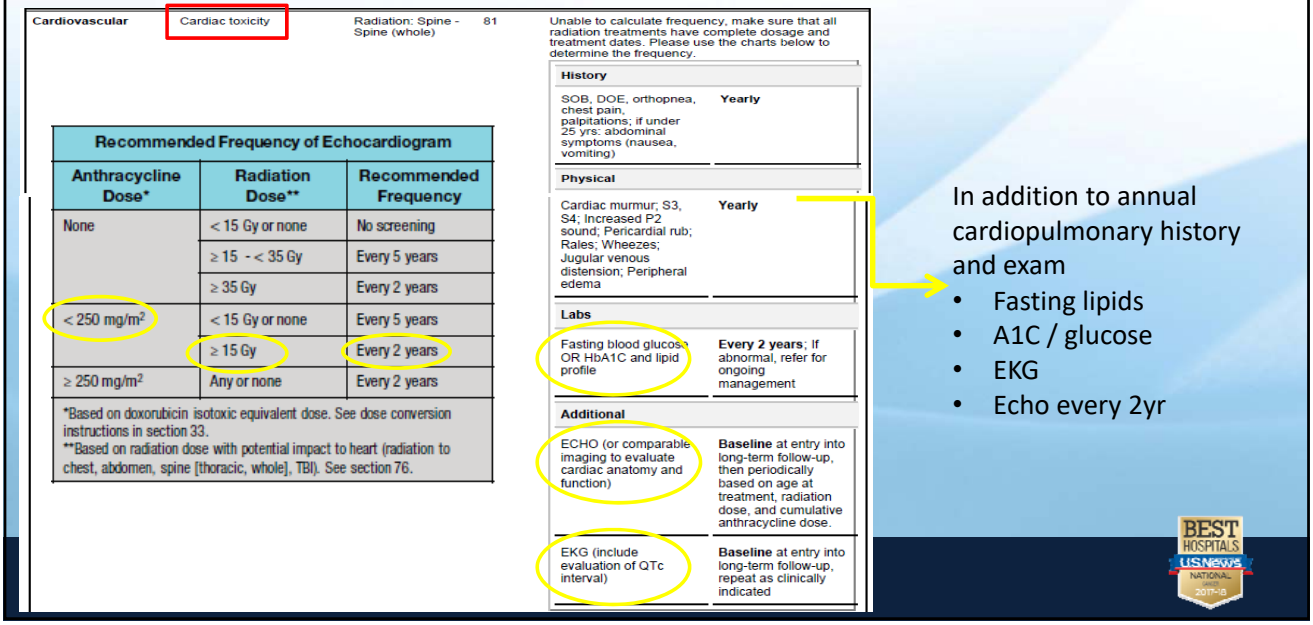
POTENTIAL CONSIDERATIONS FOR FURTHER TESTING AND INTERVENTION
FSH, LH, estradiol as clinically indicated in patients with signs of accelerated pubertal progression and growth.
X-ray for bone age in rapidly growing children.
Endocrine consultation for accelerated puberty (puberty in girl <8 years old)

References

Chemaitilly W, Merchant TE, Li Z, et al: Central precocious puberty following the diagnosis and treatment of paediatric cancer and central nervous system tumours: presentation and long-term outcomes. Clin Endocrinol (Oxf) 84:361-71, 2016
Darzy KH: Radiation-induced hypopituitarism after cancer therapy: who, how and when to test. Nat Clin Pract Endocrinol Metab 5:88-99, 2009
Gan HW, Phipps K, Aquilina K, et al: Neuroendocrine morbidity after pediatric optic glioma: a longitudinal analysis of 166 children over 30 years. J Clin Endocrinol Metab 100:3787-99, 2015
Oberfield SE, Soranno D, Nirenberg A, et al: Age at onset of puberty following high-dose central nervous system radiation therapy. Arch Pediatr Adolesc Med 150:589-92, 1996
Ogilvy-Stuart AL, Clayton PE, Shalet SM: Cranial irradiation and early puberty. J Clin Endocrinol Metab 78:1282-6, 1994
Quigley C, Cowell C, Jimenez M, et al: Normal or early development of puberty despite gonadal damage in children treated for acute lymphoblastic leukemia. N Engl J Med 321:143-51, 1989
Sklar CA: Growth and neuroendocrine dysfunction following therapy for childhood cancer. Pediatr Clin North Am 44:489-503, 1997
Sklar CA, Constine LS: Chronic neuroendocrinological sequelae of radiation therapy. Int J Radiat Oncol Biol Phys 31:1113-21, 1995

Potential Late Effects	Periodic Evaluation
Central hypothyroidism	HISTORY Fatigue Weight gain Cold intolerance Constipation Dry skin Brittle hair Depressed mood Yearly, consider more frequent screening during periods of rapid growth PHYSICAL Height Weight Hair Skin Thyroid exam Yearly, consider more frequent screening during periods of rapid growth SCREENING TSH Free T4 Yearly, consider more frequent screening during periods of rapid growth

Request Survivorship Care Plan



Cardiovascular | Cardiac toxicity | Radiation: Spine - Spine (whole) 81

Unable to calculate frequency, make sure that all radiation treatments have complete dosage and treatment dates. Please use the charts below to determine the frequency.

Recommended Frequency of Echocardiogram

Anthracycline Dose*	Radiation Dose**	Recommended Frequency
None	< 15 Gy or none	No screening
	≥ 15 - < 35 Gy	Every 5 years
	≥ 35 Gy	Every 2 years
< 250 mg/m²	< 15 Gy or none	Every 5 years
	≥ 15 Gy	Every 2 years
≥ 250 mg/m²	Any or none	Every 2 years

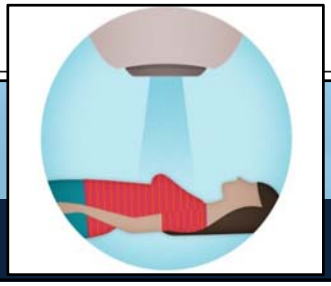
*Based on doxorubicin isotoxic equivalent dose. See dose conversion instructions in section 33.
**Based on radiation dose with potential impact to heart (radiation to chest, abdomen, spine [thoracic, whole], TBI). See section 76.

History	
SOB, DOE, orthopnea, chest pain, palpitations; if under 25 yrs: abdominal symptoms (nausea, vomiting)	**Yearly**
Physical	
Cardiac murmur; S3, S4; Increased P2 sound; Pericardial rub; Rales; Wheezes; Jugular venous distension; Peripheral edema	**Yearly**
Labs	
Fasting blood glucose OR HbA1C and lipid profile	**Every 2 years**; If abnormal, refer for ongoing management
Additional	
ECHO (or comparable imaging to evaluate cardiac anatomy and function)	**Baseline** at entry into long-term follow-up, then periodically based on age at treatment, radiation dose, and cumulative anthracycline dose.
EKG (include evaluation of QTc interval)	**Baseline** at entry into long-term follow-up, repeat as clinically indicated

In addition to annual cardiopulmonary history and exam

- Fasting lipids
- A1C / glucose
- EKG
- Echo every 2yr

Breast cancer	Radiation: TBI	72	**Physical**	
			Clinical breast exam	**Yearly**, beginning at puberty until age 25, then every 6 months
			Screening	
			Breast MRI	**Yearly**, as an adjunct to mammography beginning 8 years after radiation or at age 25, whichever occurs last
			Mammogram	**Yearly**, beginning 8 years after radiation or at age 25, whichever occurs last
Colorectal cancer	Radiation: TBI	85	**Screening**	
			Regular screening selected from the options below based on informed decision-making between patient and provider	Beginning 5 years after radiation or at age 30 years (whichever occurs last)



Radiation-Related Colorectal Cancer Screening Options

Test	Frequency
Multitarget stool DNA test	Every 3 years
Colonoscopy	Every 5 years

*Positive [illegible] be followed up with timely colonoscopy.

Note: Colonoscopy is considered the gold standard for colorectal cancer screening in high-risk populations; however, recognizing that not all survivors are willing or able to undergo colonoscopy, multitarget stool DNA testing is deemed a reasonable alternative. Alternative stool-based testing (i.e., annual fecal immunochemical testing (FIT) or high-sensitivity guaiac-based fecal occult blood testing) or alternative structural examination (i.e., every 5 year CT colonography or flexible sigmoidoscopy) may also be considered if colonoscopy or multitarget stool DNA testing are not feasible or acceptable to the survivor. All positive results from these alternative testing methods should be followed up with timely colonoscopy.

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Table 3. **Perceived Usefulness of Various Methods for Assisting General Internists' Ability to Care for CCSs Independently**

Ann Intern Med. 2014;160:11-17. doi:10.7326/M13-1941

Type	Mean Utility Rating/Percentage With Rating of 4*
Access to long-term follow-up guidelines for CCSs	3.8/85.5
Medical education seminars and courses about cancer follow-up care	3.2/44.0
Web site with information and opportunity for questions and answers	3.4/59.0
Patient-specific standardized letter from specialist with follow-up recommendations for the primary care physician sent directly to you	3.7/79.9
Patient-specific standardized letter from specialist with follow-up recommendations given to the patient	3.4/54.2
Ability to telephone or e-mail specialist for advice	3.4/55.1
Expedited routes of re-referral to cancer specialists	3.4/54.7
Pamphlets on follow-up cancer care	2.9/30.6
Expedited access to investigations (e.g. computed tomography scan, magnetic resonance imaging, and positron emission tomography scan) for suspected recurrence	3.1/44.2
Expedited access to support services (e.g. social work, psychology)	3.0/36.6
More medical or support staff in primary care office	2.7/26.8

CCS = childhood cancer survivor.
* On a scale of 1 (not at all useful) to 4 (very useful).

#3 - Access to Survivorship Team

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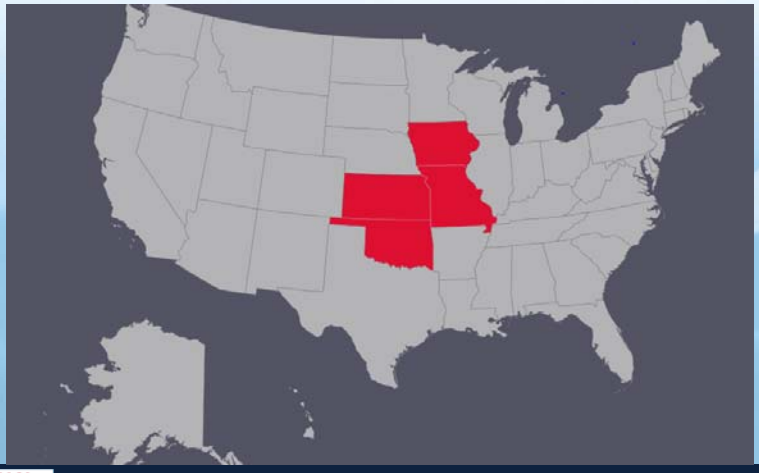
KUCC Survivorship Transition Clinic

Patient Population



Location – 32 counties

- Kansas
- Missouri
- Iowa
- Oklahoma

Ages

- 18-62 y/o

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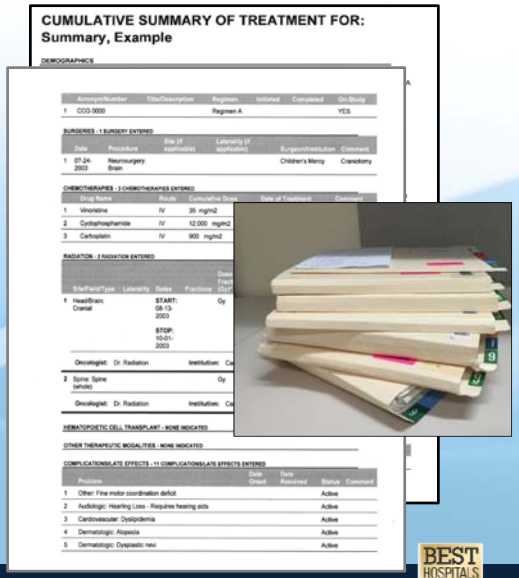
KUCC Survivorship Transition Clinic

What We Have Learned

- Most patients do not have treatment summaries or survivorship care plans
- Time intensive to create
- Critically important
- Supportive treatment summary software program linked to COG guidelines



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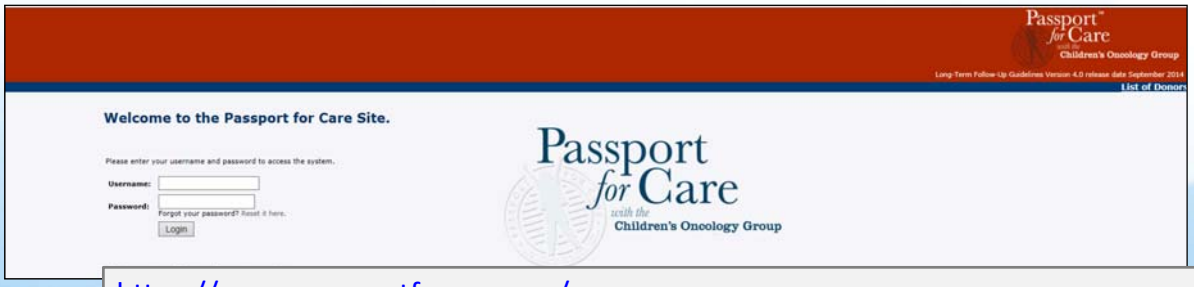
KUCC Survivorship Transition Clinic

- Collaborate with PCPs
- Annual survivorship visits
- Provide patient and PCP
  - Treatment Summary
  - Survivorship Care Plan
- Patient Education
- Guideline-based testing that is indicated
  - Order at KU
  - Provide list back to PCP to order locally

Educate and Empower Patients



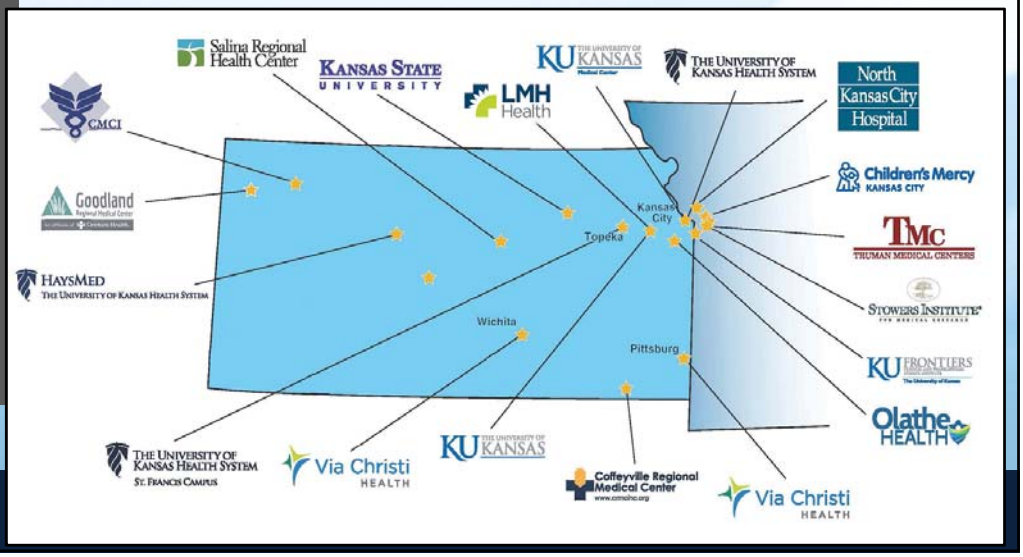
https://www.passportforcare.org/

- Provider inputs treatment information
- Program pulls recommended screening guidelines
- Mapped to COG Long-Term Follow-Up Guidelines
- Treatment Summary and Survivorship Care Plan
- Patient Portal - access anytime / anywhere

Midwest Cancer Alliance (MCA)

An outreach arm of KU Cancer Center

Network of hospitals, physician groups, cancer support and research organizations across Kansas and western Missouri



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Thank You