Follow Up Care for Children Who Have Had Cancer

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THE UNIVERSITY OF KANSAS
CANCER CENTER

Disclosure

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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?

Why Do We Need to Talk About This?

Prevalence....
Growing Numbers of Cancer Survivors

> 15 million cancer survivors in US today

Growing Numbers of Childhood Cancer Survivors

National Cancer Institute - SEER Data (Surveillance, Epidemiology, and End Results)
### Table 24-8

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>5-Year Relative Survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All sites</td>
<td>58.5</td>
</tr>
<tr>
<td>Male</td>
<td>63.0</td>
</tr>
<tr>
<td>Female</td>
<td>54.5</td>
</tr>
<tr>
<td>All races</td>
<td>59.9</td>
</tr>
<tr>
<td>Male</td>
<td>64.0</td>
</tr>
<tr>
<td>Female</td>
<td>55.9</td>
</tr>
<tr>
<td>Brain &amp; CNS</td>
<td>62.0</td>
</tr>
<tr>
<td>Acute myeloid leukemia (AML)</td>
<td>25.0</td>
</tr>
<tr>
<td>Acute lymphoblastic leukemia (ALL)</td>
<td>85.0</td>
</tr>
<tr>
<td>Neuroblastoma</td>
<td>80.0</td>
</tr>
<tr>
<td>Ewing sarcoma</td>
<td>65.0</td>
</tr>
<tr>
<td>Rhabdomyosarcoma</td>
<td>80.0</td>
</tr>
</tbody>
</table>

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

**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 lymphoblastic 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.

Reference

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

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)
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
Why Do We Need to Talk About This?

Knowledge Gap....

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
When presented with female survivors 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

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.

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

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-Hogèse 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
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

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
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

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?

Location, Location, Location
Age
Gender
Genes
Surgery
Chemotherapy
Radiation
Lifestyle
Health Behaviors

Risk-based survivor care

Cancer-Related Morbidity
Host Factors
Premorbid conditions
Genetic
BRCA, ATM, p53 polymorphisms
Tumor Factors
Histology
Site
Biology
Response
Treatment Factors
Surgery
Chemotherapy
Radiation
Transplant
Tobacco
Diet
Alcohol
Exercise
Sun
Aging
Treatment Events
Health Behaviors
Age
Gender
Race

NCI at the NIH. http://www.cancer.gov/cancertopics/pdq/treatment/lateeffects/Patient/page1
Risk-based survivor care

Host Factors
- Age
- Gender
- Race

Premorbid conditions

Cancer-Related Morbidity

Genetic
- BRCA, ATM, p53 polymorphisms

Tumor Factors
- Histology
- Site
- Biology
- Response

Treatment Factors
- Surgery
- Chemotherapy
- Radiation
- Transplant

Treatment Events

Health Behaviors
- Tobacco
- Diet
- Alcohol
- Exercise
- Sun

Aging

Tumor type and site determines treatment

<table>
<thead>
<tr>
<th>Stage 1 Wilm’s tumor</th>
<th>Medulloblastoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Nephrectomy</td>
<td>• Surgical resection</td>
</tr>
<tr>
<td>• Brief course of chemotherapy, usually with less toxic agents</td>
<td>• Cranial-spinal radiation</td>
</tr>
<tr>
<td></td>
<td>• Intense chemotherapy with more toxic agents</td>
</tr>
</tbody>
</table>
Risk-based survivor care

Host Factors
- Age
- Gender
- Race

Premorbid conditions

Genetic
- BRCA, ATM, p53 polymorphisms

Tumor Factors
- Histology
- Site
- Biology
- Response

Treatment Factors
- Surgery
- Chemotherapy
- Radiation
- Transplant

Cancer-Related Morbidity

Treatment Events

Health Behaviors
- Tobacco
- Diet
- Alcohol
- Exercise
- Sun

Aging

Chemotherapy Agent Influences Risk

Glucocorticoids and Methotrexate:
- bone mineral density deficit

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

Bleomycin and Busulfan:
- pulmonary fibrosis
Chemotherapy Dose Influences Risk

![Graph showing odds ratio and cumulative anthracycline exposure](image)


Radiation Fields Influence Risk

- Cranial radiation: neurocognitive, motor sensory deficits
- Endocrine gland radiation: growth, metabolism, and reproduction

<table>
<thead>
<tr>
<th>Anthracycline Dose*</th>
<th>Radiation Dose**</th>
<th>Recommended Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>&lt; 15 Gy or none</td>
<td>No screening</td>
</tr>
<tr>
<td>≥ 15 - &lt; 50 Gy</td>
<td>Every 5 years</td>
<td>Every 5 years</td>
</tr>
<tr>
<td>≥ 50 Gy</td>
<td>Every 2 years</td>
<td>Every 2 years</td>
</tr>
<tr>
<td>&lt; 250 mg/m²</td>
<td>Every 5 years</td>
<td>Every 5 years</td>
</tr>
<tr>
<td>≥ 15 mg/m²</td>
<td>Every 2 years</td>
<td>Every 2 years</td>
</tr>
</tbody>
</table>

*Based on doxorubicin-based equivalent dose. See dose conversion instructions in section 2.
**Based on radiation dose with potential impact to heart (radiation to chest, abdomen, upper thoracic, upper rib). See section 26.
### Radiation Dose Influences Risk

**Threshold Dose & Hypothalamic-Pituitary Dysfunction**

<table>
<thead>
<tr>
<th>HPA Disorder</th>
<th>Dose (Gy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GH deficiency</td>
<td>&gt; 18</td>
</tr>
<tr>
<td>Precocious Puberty</td>
<td>&gt; 18</td>
</tr>
<tr>
<td>LH/FSH deficiency</td>
<td>&gt; 30</td>
</tr>
<tr>
<td>TSH deficiency</td>
<td>&gt; 30</td>
</tr>
<tr>
<td>ACTH deficiency</td>
<td>&gt; 30</td>
</tr>
<tr>
<td>Hyperprolactinemia</td>
<td>&gt; 50</td>
</tr>
</tbody>
</table>

- 45-60 Gy for therapy for Primary CNS Tumors
- 18 Gy for CNS therapy for ALL (acute lymphoblastic leukemia)

**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.

Risk-based survivor care

Host Factors
- Age
- Gender
- Race

Premorbid conditions
- Age
- Gender
- Race

Health Behaviors
- Tobacco
- Diet
- Alcohol
- Exercise
- Sun

Genetic
- BRCA, ATM, p53 polymorphisms

Aging

Cancer-Related Morbidity

Tumor Factors
- Histology
- Site
- Biology
- Response

Treatment Factors
- Surgery
- Chemotherapy
- Radiation
- Transplant

Treatment Events

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


Risk-based survivor care

Host Factors
Premorbid conditions
Genetic
BRCA, ATM, p53 polymorphisms
Tumor Factors
Histology
Site
Biology
Response
Cancer-related morbidity

Health Behaviors
Aging
Treatment Factors
Surgery
Chemotherapy
Radiation
Transplant
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
Risk-based survivor care

- **Host Factors**
  - Age
  - Gender
  - Race
  - Premorbid conditions

- **Genetic**
  - BRCA, ATM, p53 polymorphisms

- **Tumor Factors**
  - Histology
  - Site
  - Biology
  - Response

**Cancer-Related Morbidity**

- **Health Behaviors**
  - Tobacco
  - Diet
  - Alcohol
  - Exercise
  - Sun

- **Aging**

- **Treatment Factors**
  - Surgery
  - Chemotherapy
  - Radiation
  - Transplant

- **Treatment Events**

Hudson et al, Cancer 2006

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Age at diagnosis influences risk

Younger patients are more vulnerable to neurocognitive dysfunction after cranial irradiation
Risk-based survivor care

- **Host Factors**
  - Age
  - Gender
  - Race

- **Premorbid conditions**

- **Health Behaviors**
  - Tobacco
  - Diet
  - Alcohol
  - Exercise
  - Sun

- **Genetic**
  - BRCA, ATM, p53 polymorphisms

- **Tumor Factors**
  - Histology
  - Site
  - Biology
  - Response

- **Treatment Events**
  - Surgery
  - Chemotherapy
  - Radiation
  - Transplant

- **Aging**

- **Treatment Factors**

- **Cancer-Related Late Effect Risk Profile**

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

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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)

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

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

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)
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

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”
Table 3: Perceived Usefulness of Various Methods for Assisting General Internists’ Ability to Care for CCSs Independently

<table>
<thead>
<tr>
<th>Type</th>
<th>Mean Utility Rating/Percentage With rating of 4+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Access to long-term follow-up guidelines for CCSs</td>
<td>4.0/5.5</td>
</tr>
<tr>
<td>Medical education seminar and courses about cancer follow-up care</td>
<td>3.2/4.4</td>
</tr>
<tr>
<td>Website with information and opportunity for questions and answers</td>
<td>3.5/4.0</td>
</tr>
<tr>
<td>Patient-specific standardized letter from specialist with follow-up recommendations given to the patient</td>
<td>3.7/5.7</td>
</tr>
<tr>
<td>Ability to telephone or e-mail specialist for advice</td>
<td>3.4/5.5</td>
</tr>
<tr>
<td>Expected routes of re-referral to cancer specialists</td>
<td>3.4/5.4</td>
</tr>
<tr>
<td>Pamphlets on follow-up cancer care</td>
<td>2.9/3.6</td>
</tr>
<tr>
<td>Expected access to investigations (e.g., computed tomography scan, magnetic resonance imaging, and positron emission tomography scan) for suspected recurrence</td>
<td>3.1/4.4</td>
</tr>
<tr>
<td>Expected access to support services (e.g., social work, psychology)</td>
<td>3.0/3.6</td>
</tr>
<tr>
<td>More medical or support staff in primary care office</td>
<td>2.7/2.6</td>
</tr>
</tbody>
</table>

CCS = childhood cancer survivor

* On a scale of 1 (not at all useful) to 4 (very useful)

#1 - Guideline Awareness / Access

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

http://survivorshipguidelines.org/
#2 - Patient Specific Guidance

- Treatment Summary
- Survivorship Care Plan
Request Survivorship Care Plan

In addition to annual cardiopulmonary history and exam:
- Fasting lipids
- A1C / glucose
- EKG
- Echo every 2yr
#3 - Access to Survivorship Team

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

<table>
<thead>
<tr>
<th>Type</th>
<th>Mean Utility Rating/Percentage With Rating of 4*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Access to long-term follow-up guidelines for CCs</td>
<td>3.8/85.5</td>
</tr>
<tr>
<td>Medical education seminars and courses about cancer follow-up care</td>
<td>3.2/44.0</td>
</tr>
<tr>
<td>Web site with information and opportunity for questions and answers</td>
<td>3.4/59.0</td>
</tr>
<tr>
<td>Patient-specific standardized letter from specialist with follow-up recommendations for the primary care physician sent directly to you</td>
<td>3.7/79.9</td>
</tr>
<tr>
<td>Patient-specific standardized letter from specialist with follow-up recommendations given to the patient</td>
<td>3.4/54.2</td>
</tr>
<tr>
<td>Ability to telephone or e-mail specialist for advice</td>
<td>3.4/54.2</td>
</tr>
<tr>
<td>Expedited routes of referral to cancer specialists</td>
<td>3.5/64.1</td>
</tr>
<tr>
<td>Pamphlets on follow-up cancer care</td>
<td>2.9/50.6</td>
</tr>
<tr>
<td>Expedited access to investigations (e.g., computed tomography scan, magnetic resonance imaging, and positron emission tomography scan) for suspected recurrence</td>
<td>3.1/64.2</td>
</tr>
<tr>
<td>Expedited access to support services (e.g., social work, psychology)</td>
<td>3.0/56.6</td>
</tr>
<tr>
<td>More medical or support staff in primary care office</td>
<td>2.7/26.8</td>
</tr>
</tbody>
</table>

CCs = childhood cancer survivors.
* On a scale of 1 (not at all useful) to 4 (very useful).
KUCC Survivorship Transition Clinic

Patient Population

Location – 32 counties
- Kansas
- Missouri
- Iowa
- Oklahoma

Ages
- 18-62 y/o

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
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

Thank You